Clinical Aspects and Outcomes of Lateral Skull Base Surgery

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Clinical Aspects and Outcomes of Lateral Skull Base Surgery

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Chapter 1.1

General Introduction

"The feasibility of an operation is not the *best* indication for its performance."

Henry, Lord Cohen of Birkenhead *(1900-1977)*
Annals of the Royal College of Surgeons of England 6:3, 1950

General introduction

Aims and outline of this thesis

Neuro-otology and skull base surgery have emerged from a desire to excise lesions in the skull base and cerebello-pontine angle which have been hitherto unresectable because of their anatomical site, size and varying degrees of vascularity. The incredible advances in microsurgical techniques following the advent of the operating microscope, neuroimaging in diagnosis, neuro-anaesthesia, intraoperative cranial nerve monitoring, microsurgical instrumentation, ultrasonic cavitrons and lasers as well as endoscopy and

neuronavigation, as well as improved patient care has meant that the majority of lesions can be successfully excised. The development of numerous innovative approaches to the lateral and anterior skull base has enabled this. We have seen virtually every lesion, whether it be neoplastic, vascular or inflammatory involving the skull base primarily or by secondary invasion as well as intracranial pathology being surgically approached in ever increasing numbers.

Multidisciplinary team (MDT) working and the creation of the MDT clinic has optimised patient care and management and facilitated the development of clinical databases and the measurement of outcome and audit. Along with the more prevalent use of classifications this has been critical for the comparison of clinical outcomes between surgical departments. This enables not only the establishment of an evidence base for a particular procedure or therapy but it also provides us with an integral part of a revalidation process for individual doctors within our profession.

The challenge is to excise the lesion completely whilst maintaining neural integrity in order to preserve the best quality of life for the patient. This is thus the rationale for this thesis on clinical aspects and outcomes of lateral skull base surgery.

Chapter 1.2

Some historical aspects of skull base surgery

Sir Charles Ballance said:
"In ancient atlases some unexplained lands are marked "hic sunt leones" (meaning here there are lions!). Few dare to explore a terra incognita but the danger lies not in removing disease but in leaving it there". [1]

Skull base surgery has emerged from a search for adequate approaches to remove lesions situated in a bony no-mans land between otology and neurosurgery. The raison d'etre for the evolution of these techniques to excise inaccessible and often vascular pathological processes was the removal of bone in the skull base rather than by elevating or retracting dura. This evolution has been a natural corollary of the rapid and exciting development of surgery itself in the last five centuries.

The sixteenth century brought with it the introduction of original investigation and the beginning of the modern anatomical period as can be seen from these drawings by Leonardo da Vinci (1452-1519) from his anatomical codices of the skull base and cranial nerves.[2,3] He drew these nerves and the optic chiasm as well as a three-dimensional reconstruction of the brain. In order to understand the internal anatomy of the brain he used a wax casting technique of the ventricular system. He had to remove the brain from the calvarium and inject melted wax through the fourth ventricle. Tubes were inserted into the lateral ventricles through the brain tissue to allow the air to escape as the wax was injected. The wax hardened as it cooled and the brain was removed leaving the wax cast of the ventricular system. (Figure 1) The small and rather faint lowermost figure in the centre is probably the first known drawing of the skull base.

Unfortunately Leonardo's *Magnum Opus* on anatomy did not appear in print until the twentieth century because although the drawings were circulated around the artists in Italy in the sixteenth century, thanks to a close friend Francesco da Melzi,[4] they were lost in the latter half of that century. They were discovered in the eighteenth century by William Hunter (1728-1793) the elder brother of the renowned Scottish anatomist scientist and surgeon John Hunter.[5]

Physicians for the first time began to correlate disease with anatomical structure. Surgeons were unskilled "barber-surgeons". They were barbers who were not medically qualified but dared perform minor surgical procedures on their clients. Once it was necessary for aspiring surgeons to be medically qualified in order to go on and train in surgery and practice as surgeons they felt they were "one cut above" the physicians and sought to be recognised as such.

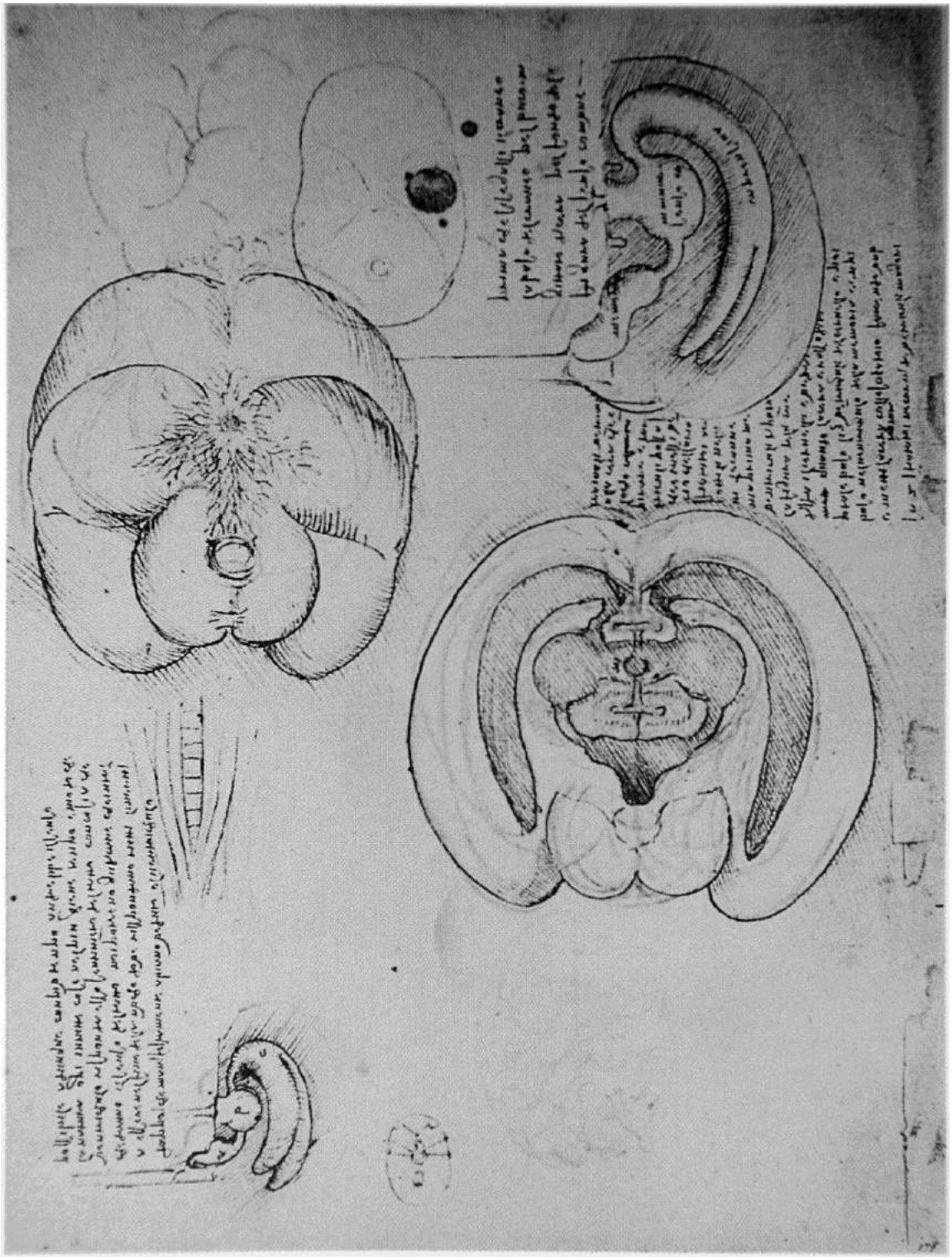

Figure 1: From Leonardo da Vinci. *Quaderni d'anatomia, 6 vols.* Christiana: Jacob Dybwad, 1911-1916; also see Hopstock H. Leonardo as an anatomist. In: Singer C., ed. *Studies in the History of Medicine,* Oxford: Clarendon Press, 1921; 153-191; and Leonardo da Vinci. Keele K.D., Pedretti C. *Corpus of the anatomical studies in the Collection of Her Majesty the Queen at Windsor Castle.* New York: Harcourt Brace Jovanovich, 1979.
Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

Hence in the United Kingdom on completion of their training they ceased to use the title "Dr" but reverted to "Mr" in order to differentiate themselves from the physicians and so that the general public would know that they were surgeons.

During this century the reintroduction of human anatomical dissection, lost for some 1400 years from the time of the Alexandrians, had a catalytic influence on the practice of a number of high profile innovative anatomists (Leonardo da Vinci, Berengario da Carpi, Niccolo Massa and Andreas Vesalius) and out of their anatomical studies the science and art of surgery grew. Pivotal in this regard was the great anatomist Vesalius (1514-1564) a visionary surgeon who used his cadaveric anatomical discoveries in the practice of surgery.[6] Interestingly only two eponyms bearing his name are in use, the foramen of Vesalius, a small opening between the foramen ovale and the foramen rotundum, and the vein of Vesalius, which acts as an emissary and runs within this foramen. The use of these eponyms has been abandoned since the structures to which they refer are only seen in 10% of cadaver dissections.
Modern neurosurgery has its roots in the book published by Berengario da Carpi (1470-1550) in 1518.[7] This work is devoted to the treatment of head injuries.

The barber-surgeon Ambroise Pare (1510-1590), one of the forefathers of modern surgery, rose from humble beginnings as a poorly educated Huguenot, to become a surgical dresser in a Paris Hospital on his way to a long military career. This enabled him to incorporate a great deal of practical knowledge into his surgery. He also designed some very practical surgical instruments. He looked after King Henry II of France after he sustained a significant head injury from which he died. The pre-morbid symptomatology led Pare to postulate that he died from from a tear in one of the cortical bridging veins which indeed proved to be the case at post-mortem examination.[8]

The top left portion of the title page of Ambroise Pare's collected work shows a trephination scene.[9] (Figure 2) His work represented the remarkable advances that were taking place at that time. He discussed the use of trepans, shavers and scrapers. His book describes how to remove osteomyelitic bone; how to incise dura and evacuate blood clots and pus -procedures that were only previously approached with fear and trepidation.

The seventeenth century often called "the insurgent century" was a period of rapid scientific development thanks to the contributions of Isaac Newton (1642-1727),

Francis Bacon (1561-1625), William Harvey (1578-1657) and Robert Boyle (1627-1691). It spawned the advent of the scientific society for example the Royal Society of London and the Academie Des Sciences in Paris facilitating public communication of new scientific discoveries including many endeavours in anatomy and physiology. Amongst these famous names was Thomas Willis (1621-1675) who made a substantial contribution to brain anatomy not just by describing the "Circle of Willis" which immortalised his name but also for re-classifying the nine cranial nerves which were recognised at that time.[10] It was not until Soemerling's work in 1778 that all 12 cranial nerves were identified.[11] Willis was an Oxford educated London practitioner and he published his *Cerebri Anatomie* in London in 1664.[10]

Figure 2: The enlarged trephination panel of the title page of Ambroise Pare's collected works on surgery showing a trephination scene.(From Pare A. *The Workes of That Famous Chirurgion Ambroise Parey Translated out of Latine and Compared with the French by Tho. Johnson...*London: Richard Coates, 1649)
Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

Humphrey Ridley (1653-1708), who wrote the first book in English on the anatomy of the brain in 1695,[12] was educated at Merton College Oxford and at the University of Leyden. He was largely responsible for the shift in medical opinion moving away

from the Greek theory that function was located in the ventricles to recognising that it was a property of brain parenchyma and that the brain was a distinct anatomical entity. A number of Ridley's observations are of interest to skull base surgeons. He wrote the first description of the intracavernous venous sinuses and his description of the "Circle of Willis" was even more accurate than Willis' and defined the posterior cerebral and superior cerebellar arteries as separate entities.

Johan Schultes (Scultetus) of Ulm (1595-1645) wrote the *Armamentarium Chirurgicum (The Arsenal of Surgery)* which was published by his nephew in 1655.[13] The significance of this work was the precise detail of the surgical instrument design at that time and he presented a catalogue of tools documenting instruments from antiquity to the current time.[13] The surgeons of the day recognised the significance of Schultes work and it was translated into many languages and was, therefore, able to reach and influence surgery throughout Europe. A number of these instruments are still in use today.
As well as the elucidation of neuroanatomy the seventeenth century also saw an increase in physiological experimentation the findings of which were then disseminated through the newly formed scientific societies.

The more accurate and detailed anatomical descriptions of the time along with the advances in physiology and the development of more refined customised surgical instrumentation enabled surgeons to consider operating on the brain and skull base.

The eighteenth century was the era of the adventurous surgeons such as John Hunter (1728-1793)[14] and Sir Percival Pott (1714-1788). John Hunter was a great Scottish surgeon, who was regarded as one of the most distinguished scientists and clinicians of his day, remarkable for his careful observation and scientific method in medicine and also for his discoveries in natural history, biology and surgery. In 1767 at the youthful age of 39 John Hunter was elected Fellow of the Royal Society based on his numerous significant contributions to medical science and it is interesting that although he was later to publish his work he had not done so formally at that time.[14] (Figure 3)

In 1776 he was appointed Surgeon-extraordinary to King George III and in 1786 received the Copley medal which was the highest award of the Royal Society. The famous Hunterian museum in The Royal College of Surgeons of England in London contains a precious, quite remarkable collection of Hunter's biological material,

human and animal skeletons, anatomical dissections and specimen pots reflecting this famous surgeon's scientific endeavour and original thought.

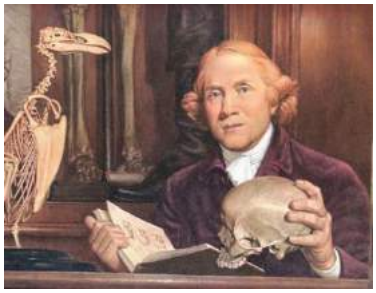

Figure 3: Young John Hunter in his study.

Percival Pott was a great believer in surgical intervention and was one of the most adventurous surgeons of this time of intense medical and surgical activity. Neuroanatomical scientists and surgeons were trying understand the patho-physiology as well as the anatomy in order to rationalise the surgical management of brain pathology. Pott described osteomyelitis of the skull resulting in pus collecting under the pericranium and causing "Potts puffy tumour".[15]

Lorenz Heister (1683-1758) published an influential surgical textbook in 1718 which subsequently became a classic.[16] He introduced a number of useful surgical techniques including a "zig-zag" suture to compress and control bleeding from the cut scalp edge. This technique was later adopted by Harvey Cushing for opening a scalp flap.

Francois Quesney (1694-1774) supported the view that brain tumours could be amenable to surgery based on his experience of draining brain abscesses and removing foreign bodies.[17] Although a few sporadic cases had been described earlier, it was around this time that the possibility of operating on a brain lesion was considered and carried out.

The first accurate description, illustration and classification of the 12 cranial nerves was submitted by Samuel Thomas von Sommering (1755-1830) in his doctoral thesis entitled *De Basi Encephali et Originibus Nervorum Cranio Egredientium in 1778.*[11] This was a magnificent work presenting accurate anatomy in an artistically beautiful manner. Not only did he describe the cranial nerves but also the topography of the brain hemispheres and the pineal gland and optic chiasm. It was unsurpassed in giving surgeons of this era an understanding of the anatomy of the brain.

Using a four-colour printing technique Jacques Fabian Gautier D'Agoty (1717-1785) comparative anatomist and neurologist produced some remarkable illustrations of views of the brain and in particular transnasal views of the skull base.[18] (Figure 4)

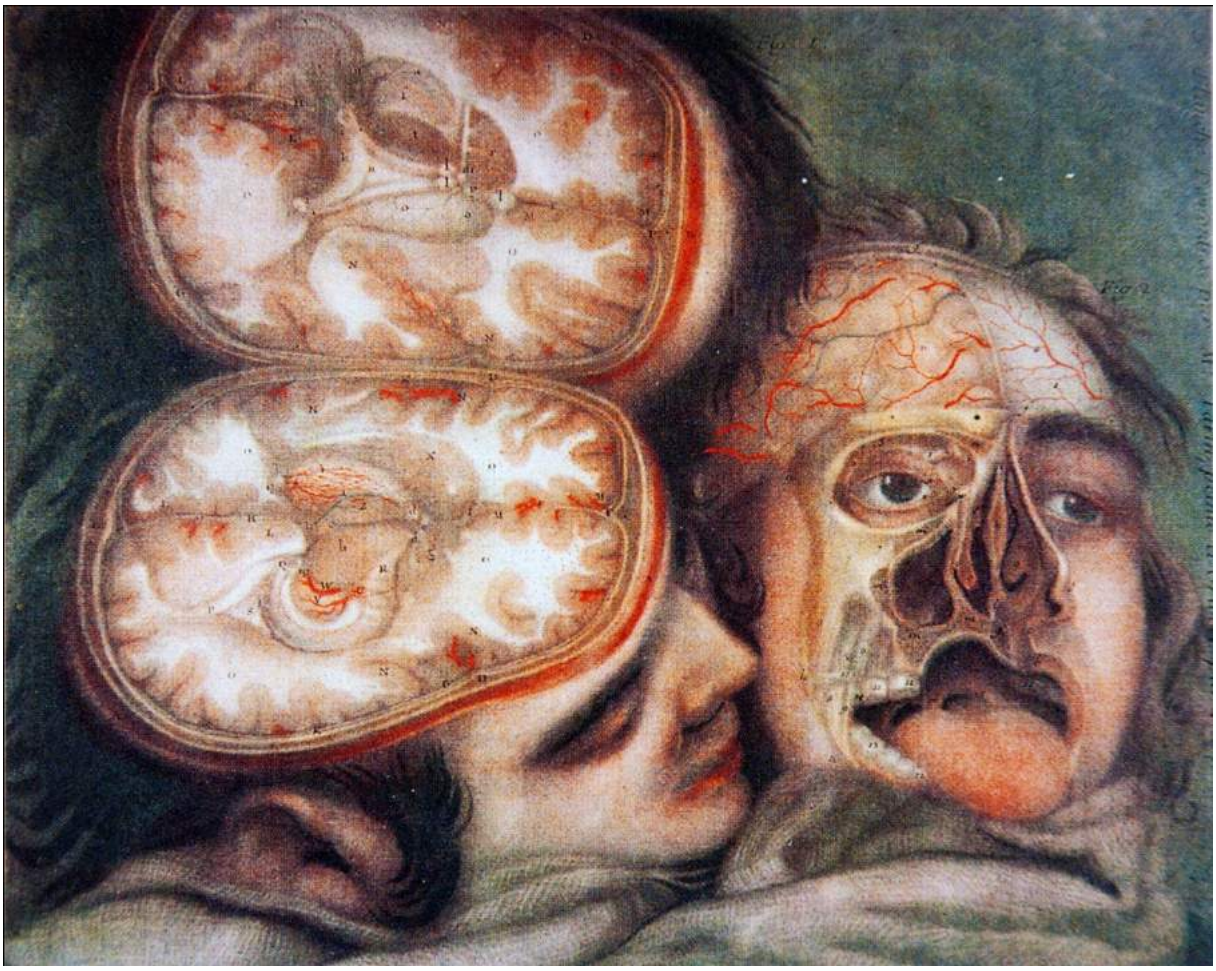

Figure 4: These colour plates of Gautier D'Agoty were not designed to illustrate surgical approaches but to help the surgeon by illustrating the anatomy of these regions. (from Gautier D'Agoty JF. *Anatomie de la tete.* Chez le sieur Gautier, M.Duverney. Paris: Quillau,1748). Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

In order to advance surgical approaches to and technique in brain and skull base surgery a better comprehension of ways of treating intracranial infection, cerebral localisation and a means of rendering the patient insensitive to pain during the procedure was needed and this was to come in the next century.

The nineteenth century was notable for the introduction of Anaesthesia, antisepsis and cerebral localization. The profound effect that these three medical advances have

had on medicine as a whole and neurosurgery in particular is encapsulated in this quote from Walter Dandy's book *Surgery of the brain:-*

"Surgery of the brain is the outgrowth of three discoveries of the nineteenth century, namely, anesthesia, asepsis and cerebral localisation. Without asepsis or antisepsis, surgery of the brain would never be possible. With asepsis and without cerebral localisation, it could be of but little value. With both asepsis and cerebral localisation and without anesthesia, it would be possible but greatly limited. Although anesthesia had been in use nearly a quarter of a century before Lister's great discovery, surgery of the brain made no great advance. And 17 additional years were required before the three combined discoveries were sufficiently secure and adequately correlated to permit this field of surgery to be fairly launched."[19]

Walter Dandy 1945

With the use of nitrous oxide as an anaesthetic agent in 1844, followed by ether in 1846 in the United States and subsequently the use of chloroform by JY Simpson (1811-1870)[20] in the United Kingdom the profound effect of anaesthesia on the future of surgery dawned on the surgeons of that era.

Control of infection was critical if the surgical mortality figures were to improve. Following the discovery that puerperal fever, with its high mortality, was spread by the contaminated hands of the obstetrician, Holmes and Semmelweis discovered that hand washing pre- and postoperatively, particularly following postmortem examination, dramatically reduced the mortality. This advice was not accepted by the surgeons at that time and even when the concept of bacterial contamination propounded by Louis Pasteur (1822-1895) and Robert Koch (1843-1910) was proposed it was only reluctantly accepted by surgeons. It was the revolutionary work of Lord Lister (1827-1912) which finally proved that with antiseptic techniques the incidence of infection due to contamination could be dramatically reduced and the natural corollary of antisepsis in the operating theatre was introduced.[21]

Sir Charles Bell (1774-1842), a Scottish surgeon and anatomist was a productive writer of this period. He made many significant contributions to the neurosciences including the differentiation of the motor and sensory components of the spinal root. His papers on surgery were beautifully illustrated by his own drawings, a feature that was to become common in the literature on skull base surgery.[22] Bell was the first to show an insitu view of an acoustic neuroma and its relationship to the CP angle and figure 5 shows his beautiful pencil drawing.[23]

Figure 5a:
Sir Charles Bell

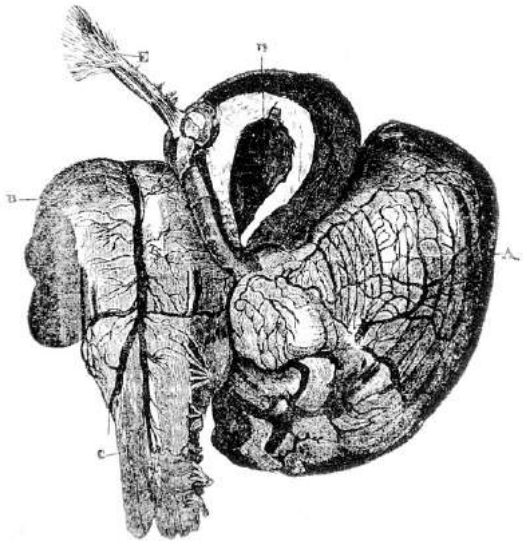

Figure 5b:
(b) Pencil drawing by Sir Charles Bell of an *in situ* acoustic neuroma showing the nerve and the relationship of the tumour to the CP angle. (from Bell C. *The Nervous System of the Human Body: Including the papers delivered to the Royal Society on the subject of nerves.* Washington DC: Duff Green 1833. Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

Paul Broca (1824-1880)[24] and others and later Carl Wernicke (1848-1904)[25] discovered that each part of the brain had a specific function. Studies by David Ferrier (1843-1928) on dogs in which brain function was localised by ablation confirmed the veracity of the earlier work and defined this cerebral localisation more specifically.[26]

The early part of the nineteenth century brought with it the emergence of neuro-pathology following the seminal works of Morgagni and others.

Jean Cruveilhier (1791-1874), the first Professor of pathology in Paris, was the first to illustrate neuropathology in colour.[27] He elegantly illustrated an early example of

a subfrontal tumour most probably an olfactory groove meningioma and in figure 6 can be seen the extension of the tumour through the cribriform plate.

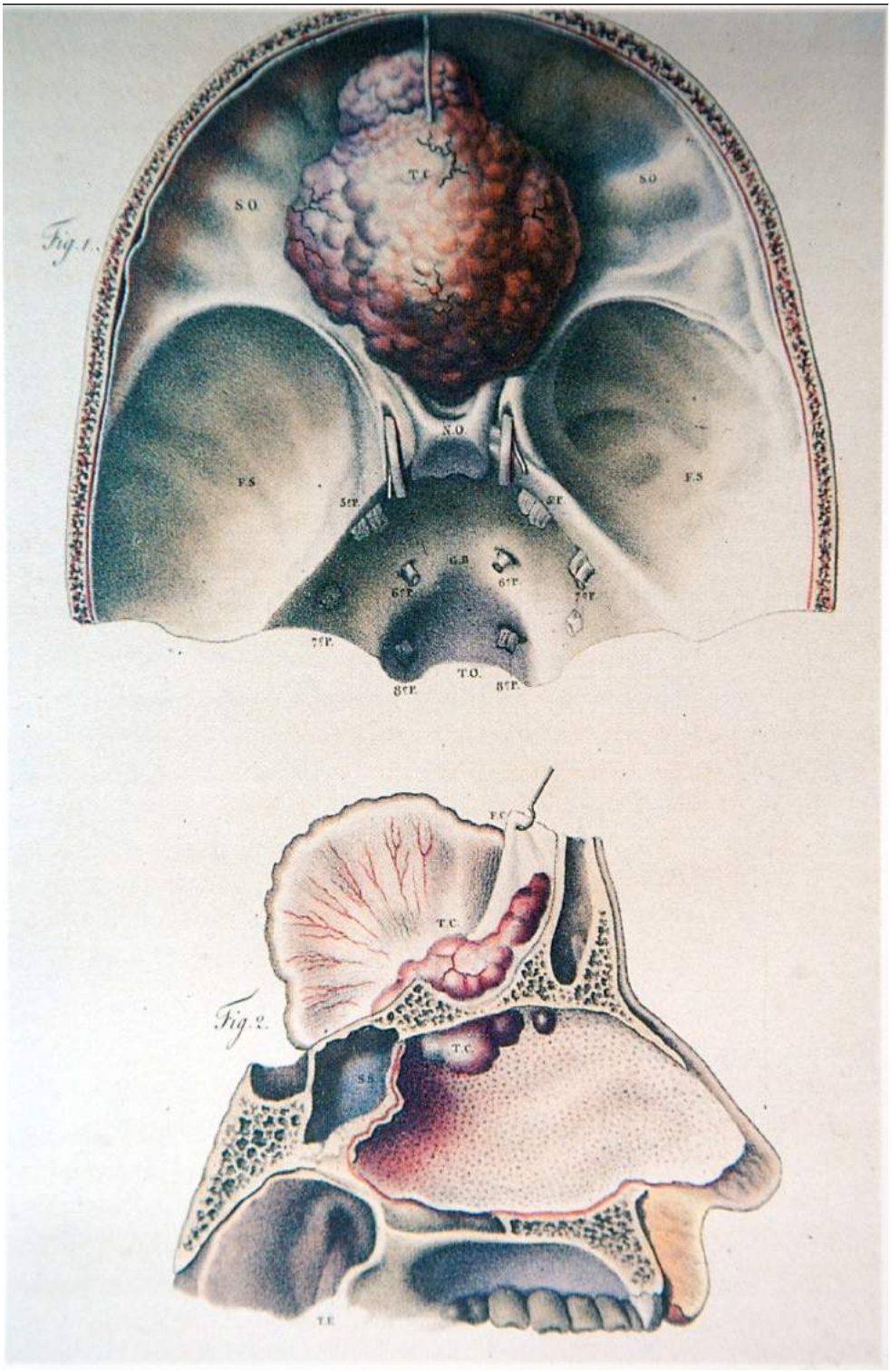

Figure 6: Cruveilhier beautifully illustrated a subfrontal tumour, probably a meningioma of the olfactory groove. In the lower drawing tumour extension through the cribriform plate can be seen. (From Cruveilhier J. *Anatomie pathologique du corps humain.* Paris: J-B. Bailliere, 1829-1842). Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

Harvey Cushing was later to recognise Cruveilher's work and in particular his accuracy in recording neuropathology and its clinical correlation and used some of the illustrations in his book on acoustic neuromas (1917)[28] and his classic writings on meningioma (1938).

The latter part of the nineteenth century saw the first successful attempts at surgery to the skull base. William W Keen (1837-1932) Professor of surgery at Jefferson Medical College in Philadelphia was an advocate for the use of Listerian techniques in surgery. He wrote a monographs on neurosurgery entitled *Linear Craniotomy*[29] and performed one of the earliest successful resections of a brain tumour in 1888 in the same year as he drained cerebrospinal fluid from the lateral ventricle. After visiting Victor Horsley in England and realising the serious morbidity and mortality resulting from blood loss during intracranial procedures at a time before blood transfusion he adopted Horsley's 2 stage approach.

Wilhelm Wagner (1848-1900) was concerned that in order to gain access to the intracranial contents surgeons had to use a hammer and chisel and left unsightly scars and boney defects leaving the brain unprotected. He worked on cadavers and devised the osteoplastic flap elevating the bone with the soft tissues still attached. He published his results in 1889.[30]

The talented Scottish surgeon William Mcewan (1848-1924) successfully removed a brain tumour from a child of 14 years.[31] He achieved recognition from the early age of 40 when he presented his results of only 3 deaths in 21 neurosurgical cases in his classic paper on cranial surgery to The British Medical Association.[32] In 1893 Mcewan published his brilliant monograph on *Pyogenic infective Diseases of the Brain and Spinal Cord*.[33] The first 50 pages was on the anatomy of the temporal bone and venous drainage of the head based on cadaveric dissection of 450 skulls! This outstanding work comprised 350 pages with 60 illustrations. Mcewan's morbidity and mortality statistics were remarkably low, reflecting his meticulous application of aseptic techniques and cerebral localisation, and were not inferior to those reported in the literature today.

Another pioneer of cerebral localisation was Sir Victor Horsley (1857-1916) who used faradic stimulation to localise motor functions in the cerebral cortex, internal capsule and spinal cord in primates[34] and with F Gotch used a galvanometer to show that electrical currents can be demonstrated in brain tissue.[35] He used beeswax to help arrest bleeding from bone,[36] proposed a decompressive craniectomy for patients with inoperable intracranial tumours and developed a technique to section the posterior root of the trigeminal nerve for trigeminal neuralgia. He worked with Robert Henry Clarke (1850-

1926) to invent a stereotactic apparatus the application of which allowed precisely localised areas of the brain to be stimulated or destroyed in order to refine cerebral localisation and intracranial surgical technique.[37] For 40 years this was restricted to animals before it was finally applied to humans by Spiegel *et al* in 1847, a landmark in neurosurgical technique.[38] Horsley's contributions to neurosurgery have been so significant that he is considered to be the father of neurosurgery.

Sir Charles Ballance (1856-1936) (Figure 7) should be considered amongst the first of the "modern" pioneers in skull base surgery.

Figure 7: Sir Charles Ballance

Ballance was one of the first surgeons to perform a radical mastoidectomy with ligation of the jugular vein and one of the first to graft the facial nerve. In 1907 Ballance published one of the first modern textbooks on neurosurgery.[39]
He was said to be the first surgeon to successfully remove an acoustic neuroma in 1894, which is described on page 283 of this book[39] but it is now believed that this was in fact a meningioma and that Thomas Anandale, Professor of Surgery in Edinburgh, was probably the first on the 3rd May 1895.[40](Figure 8)

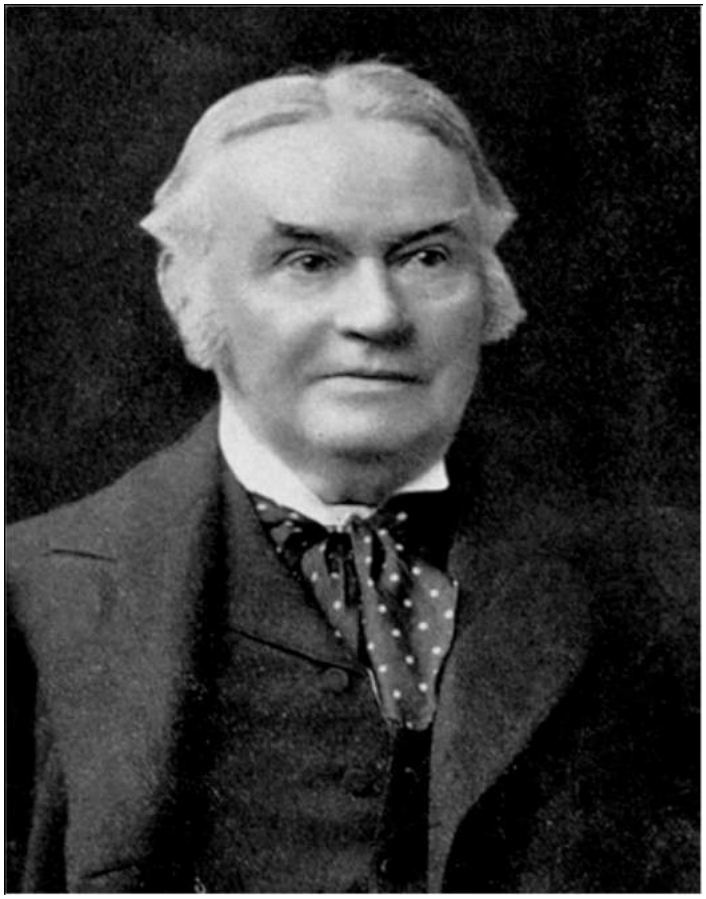

Figure 8: Professor Thomas Anandale of Edinburgh

Ballance also wrote *Essays on the Surgery of the Temporal Bone* in 1919 and this book has been very influential on the development of skull base surgery.[41]

Fedor Krause (1857-1937) was the father of German neurological surgery and a skull base surgeon. He wrote a three volume atlas on neurosurgery and was one of the first to describe the neurosurgical techniques and in particular he described in detail the approaches to the posterior cranial fossa and a number of other interesting skull base techniques.[42]Krause was one of the first surgeons to advocate surgical removal of cerebellopontine angle tumours. This is his technique for using a finger to digitally remove a posterior fossa tumour.(Figure 9)

Thierry de Martel (1875-1940), an engineer, was able to apply his knowledge to invent instruments for skull base surgery. Two of these have been very influential on the subsequent development of this subspecialty. An electric motor driven trephine that disengaged on penetrating the inner table of the skull , and a metal guide to be passed between two burr holes to facilitate the passage of a Gigli saw changed the face of craniotomy for ever.[43]

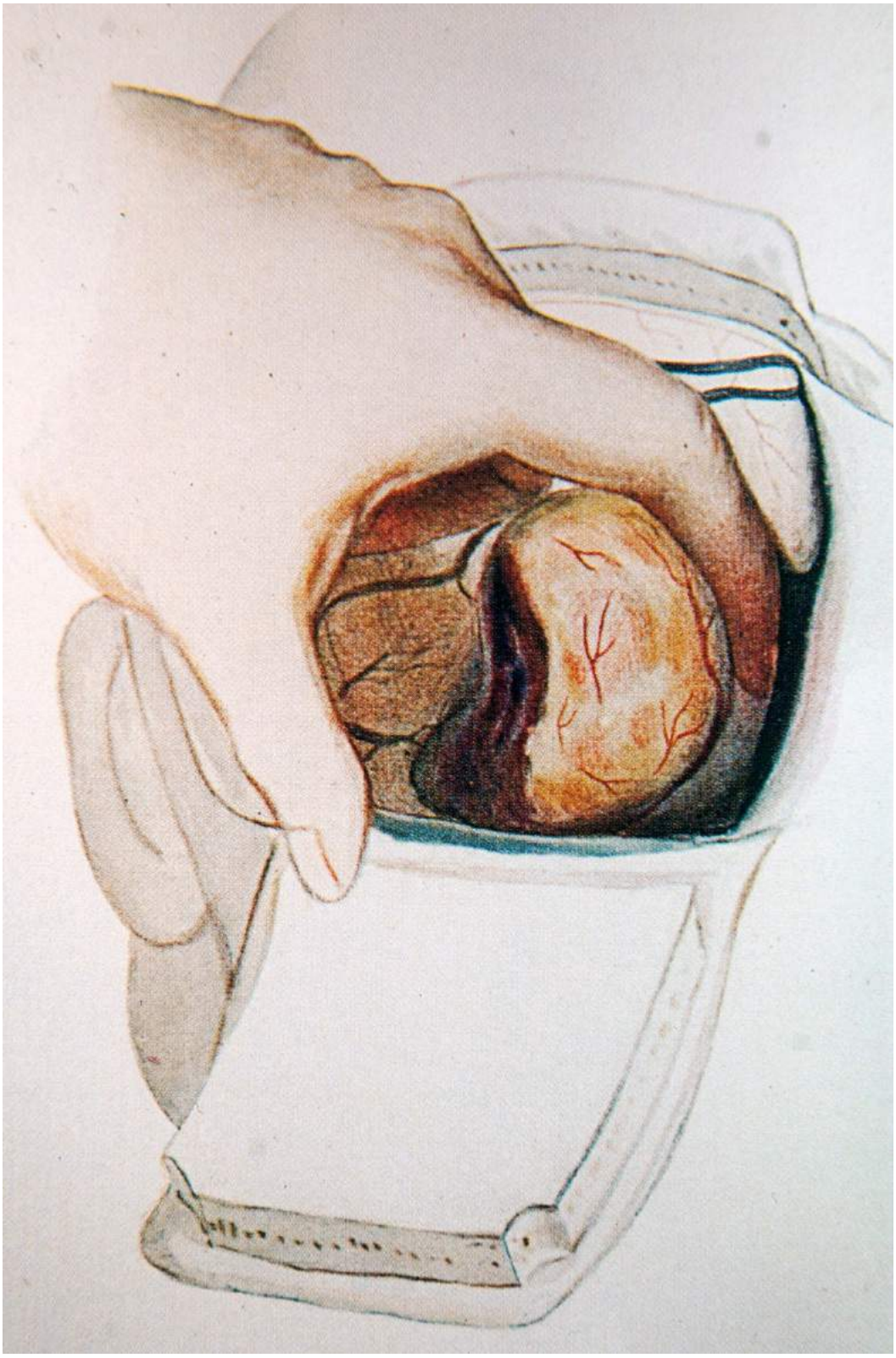

Figure 9: Krause's technique of using a finger to digitally dissect out a cerebellopontine angle tumour. (From Krause F. *Surgery of the Brain and Spinal Cord Basde on Personal Experiences,*3 vols. Translated by Haubold H and Thorek M. New York: Rebman, 1909-1912.) Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

De Martel, who was fascinated by operative photography as well as cerebellopontine angle tumours. He introduced the sitting position for posterior fossa surgery and designed a special chair to retain the patient in the correct position. Many surgeons did not adopt this technique because of the risk of air embolism.

Macewan's classic monograph on pyogenic diseases of the brain and spinal cord[33] was extremely influential on Harvey Cushing, a later pioneer in neurosurgery. He wrote this on the flysheet of a copy he was giving away to Alfred Pattison, "This was one of the first real glimmers of light for the prospective neurosurgeon. Handed on with warm regards by Harvey Cushing." (Figure 10)

Figure 10: Harvey Cushing MD with microscope in his office.

Harvey William Cushing (1869-1939) the father of American neurosurgery was a leading authority on the pituitary gland, a pioneer of endocrinology and a Pulitzer prize-winning biographer. He played a major role in the development of skull base surgery. Not only did he describe the disease which bears his name [44] but he brought the sphygmomanometer to North America and accomplished a great many things not the least of which was a dramatic reduction in mortality of vestibular schwannoma surgery. He was a true pioneer in approaches to the skull base and transsphenoidal surgery. (Figure 11) His meticulous surgical technique and the development of innovative operations like this low approach to the middle fossa for the treatment of trigeminal neuralgia was responsible for making surgery of the skull base and posterior fossa relatively safe.[45]

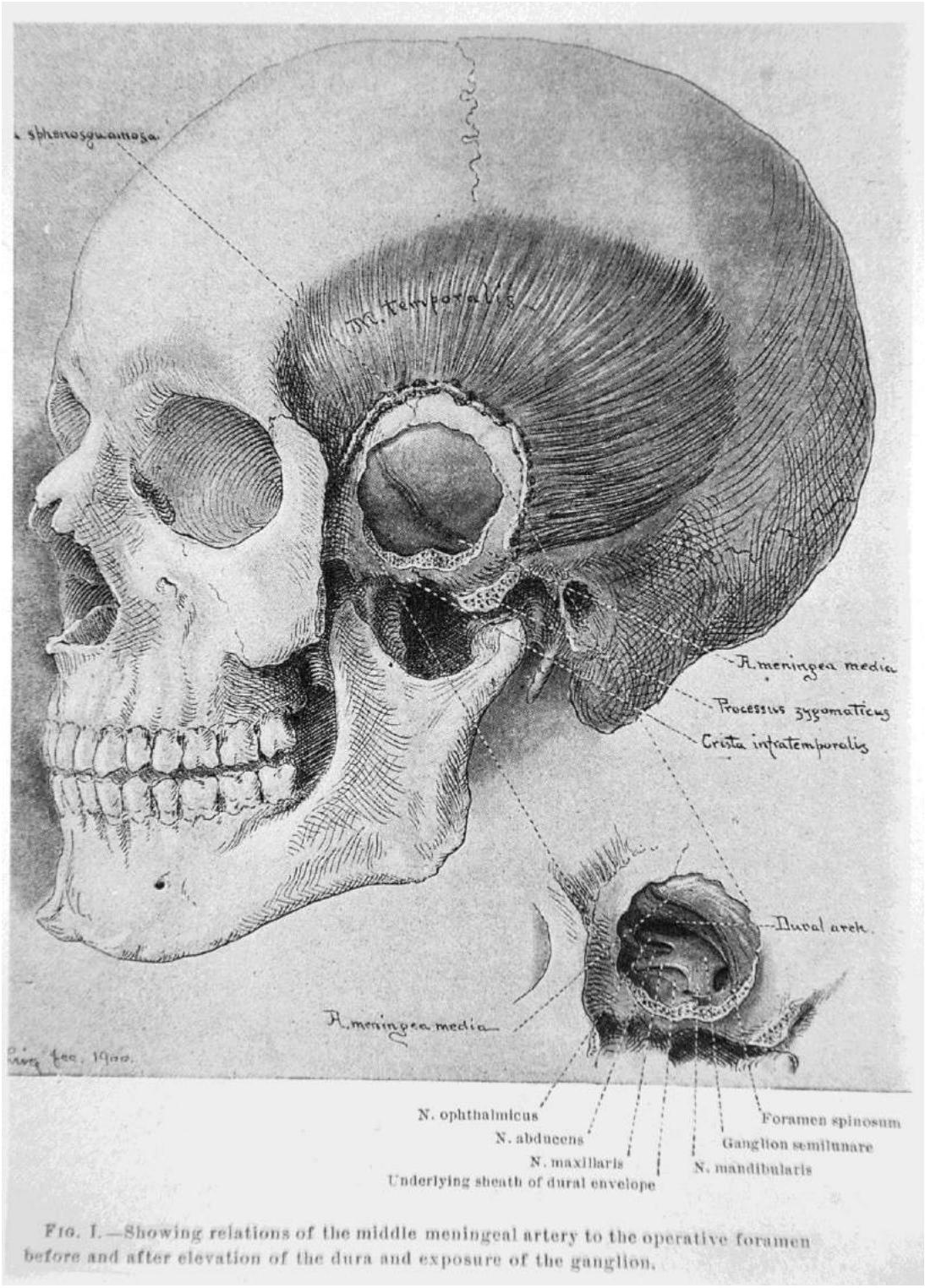

Figure 11: An illustration from a paper by Harvey Cushing showing how resection of the zygoma provides access for a low approach to the middle fossa for the treatment of trigeminal neuralgia. (From Cushing H. *A method of total extirpation of the Gasserian ganglion for trigeminal neuralgia by a route through the temporal fossa and beneath the middle meningeal artery*. JAMA 1900;34:1035-1041.) Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

In the beginning of the 20th century Cushing developed many of the basic surgical techniques in neurosurgery. He became established as a leader and expert in the field. Under his influence neurosurgery became a new and autonomous surgical discipline.
In 1917 Cushing published his work on acoustic neuroma which was based on 30 cases!! [46] He used a subcapsular resection and he sewed the edges of the tumour remnant together not attempting to extract it from the nerves and brainstem. The mortality from other series around that time was 70% and he attributed this high mortality to excessive surgical speed and finger enucleation of tumours in the posterior fossa. Cushing was able to reduce the mortality to 15% which was quite remarkable in those days.[46]

If Cushing was the Father of American skull base and neurosurgery Walter E. Dandy (1886-1946) was his prodigal son. (Figure 12)

Figure 12: Walter Dandy

Dandy was one of Cushing's trainees at the John Hopkins Hospital in Baltimore, but when Cushing was appointed to Harvard Medical School Dandy was not invited to follow him which subsequently led to an intense rivalry. Dandy developed the technique of ventriculography which led on to the understanding of the aetiology of hydrocephalus and its diagnosis. Gas contrast ventriculography afforded the neuro-surgeon for the first time the opportunity to localise a tumour by delineating the displacement of injected air in the ventricles. Dandy promulgated the utilisation of a recovery room in which the patient could be intensively nursed in the immediate postoperative period and this was introduced in 1923.
Dandy was a dextrous, aggressive, radical, and innovative surgeon who worked tirelessly. A day's schedule could include 5 or 6 operations 6 days a week. He had a great battle with Cushing over the treatment of acoustic neuromas. Dandy was the first to show that they could be removed in their totality rather than by intracapsular removal as proposed by Cushing. In 1922 Dandy published a paper on the surgical removal of acoustic neuromas and he failed to mention Cushing's classic monograph of 1917.
This oversight led to a missive being sent from Cushing to Dandy in which Cushing questioned the probity of Dandy's conduct. Cushing ended the note to Dandy thus:-
"but you must not forget your manners and this last note of yours is in extremely bad taste. Always your friend, Harvey Cushing."
Krause in 1898 and Frazier in 1913 performed suboccipital eighth nerve sections for intractable Meniere's disease but Dandy popularised this operation following publication of his paper in 1928.

Herbert Olivecrona (1891-1980) showed that the facial nerve could be preserved intact anatomically in 65% of surgical cases of acoustic neuroma which was remarkable in those days but it is salutary to remember that his surgical mortality was 29% in 1949.

Charles Frazier (1870-1936) Professor of surgery at the University of Pennsylvania, worked closely with a neurologist William G. Spiller on a treatment for trigeminal neuralgia. Frazier devised a subtemporal approach to the Gasserian ganglion and as suggested by Spiller he simply divided the sensory root between the brainstem and the ganglion which was significantly safer than total resection of the ganglion.

In 1953 John Conley described the use of vein graft to reconstruct the internal carotid artery and one year later Parsons and Lewis described subtotal resection of the temporal bone for cancer of the ear.

Bill House (Figure 13), the modern fore-father of otoneurological surgery, in his landmark paper of 1963 described the use of the middle fossa approach for a variety of conditions.

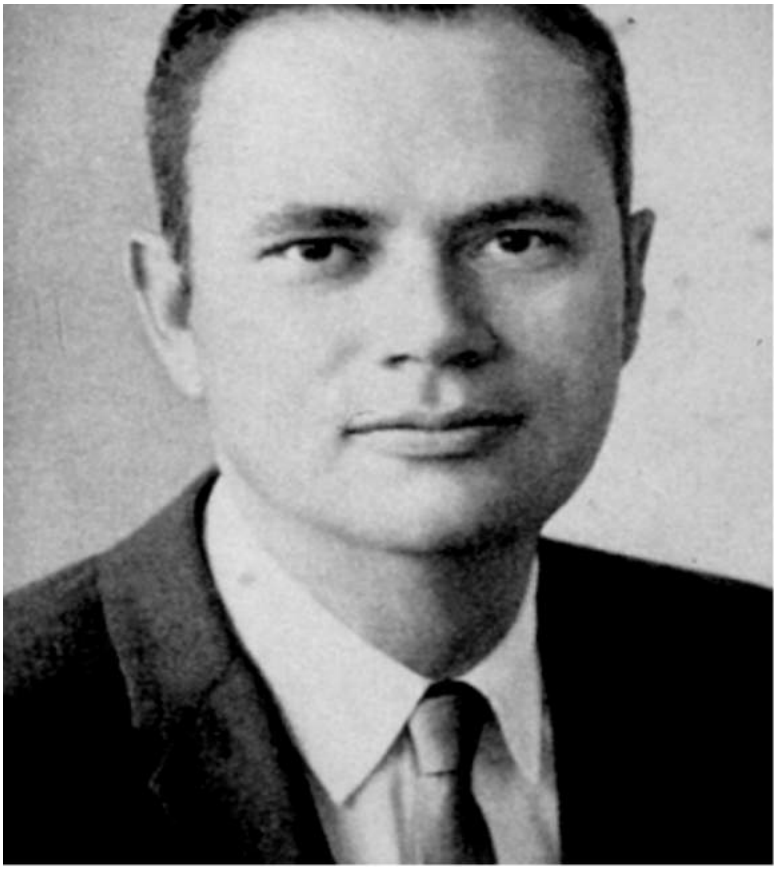

Figure 13: William House

In this illustration from House's paper of 1966, tumour in the internal auditory canal in a middle fossa approach can be seen. (Figure 14)

He also revitalised interest in the translabyrinthine approach to acoustic neuromas first described by Panje in the early 1920's. (Figure 15)

Also in 1966 Hitselberger and House described the combined suboccipital and translabyrinthine excision of CP angle tumours although interestingly this had been first described in 1904 by Fraenkel and Hunt.
These papers laid the foundations of modern skull base surgery and with Glasscock's description of controlling the intrapetrous carotid artery and Fisch's Type A, B and C approaches to the intratemporal structures, infratemporal fossa, cavernous sinus and nasopharyngeal regions respectively the modern era was born. (Figure 16)

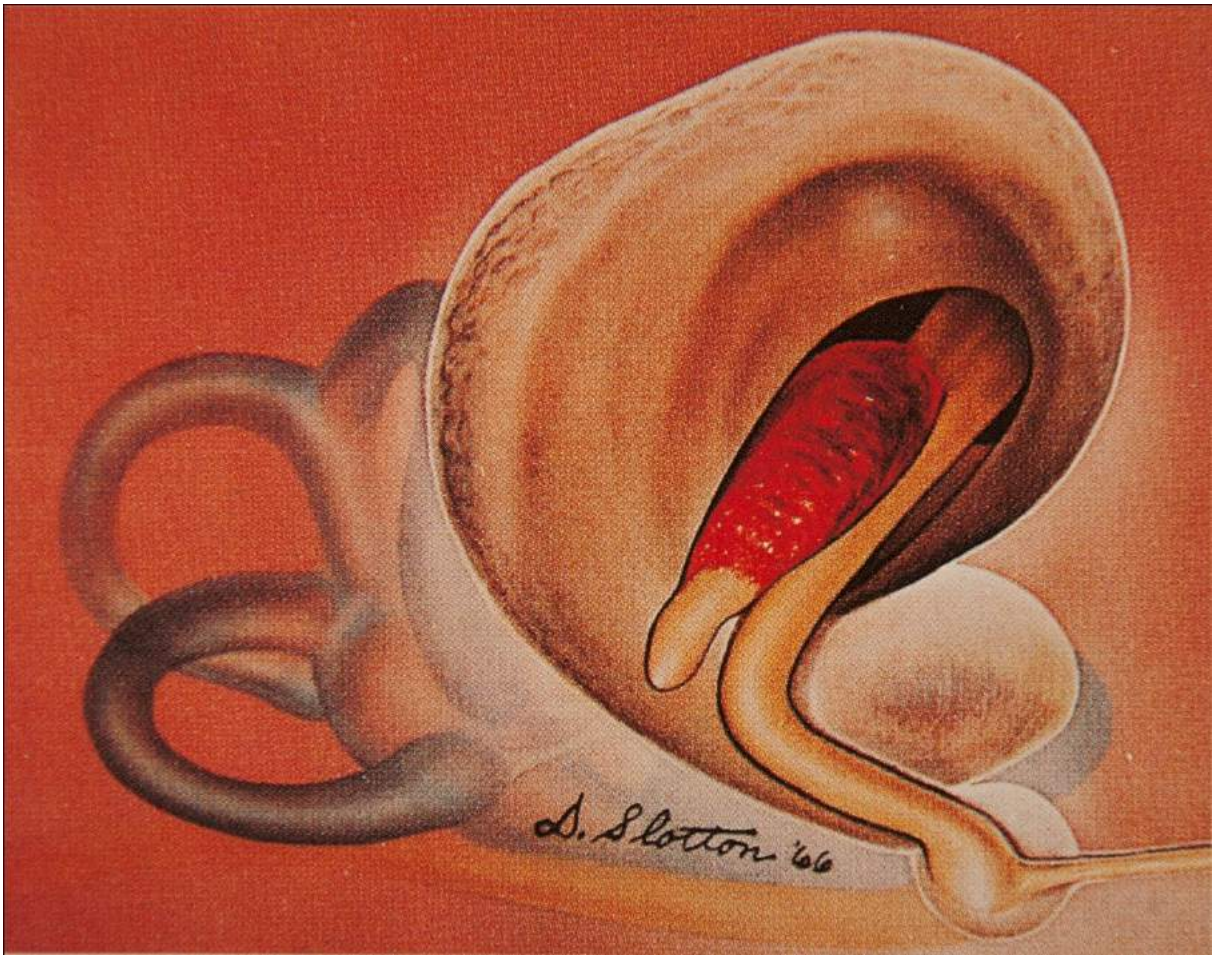

Figure 14: Middle fossa approach to tumour in the internal auditory canal (IAC) arising from the superior vestibular nerve. The facial nerve is to the right of the tumour in the IAC and the greater superficial petrosal nerve can be seen coming off the geniculate ganglion at the bottom right of the illustration.(From Hitselberger WE, House WF. Acoustic tumor surgery : the significance of vital sign changes. *Arch Otolaryngol* 1966; 84:37-42.) Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

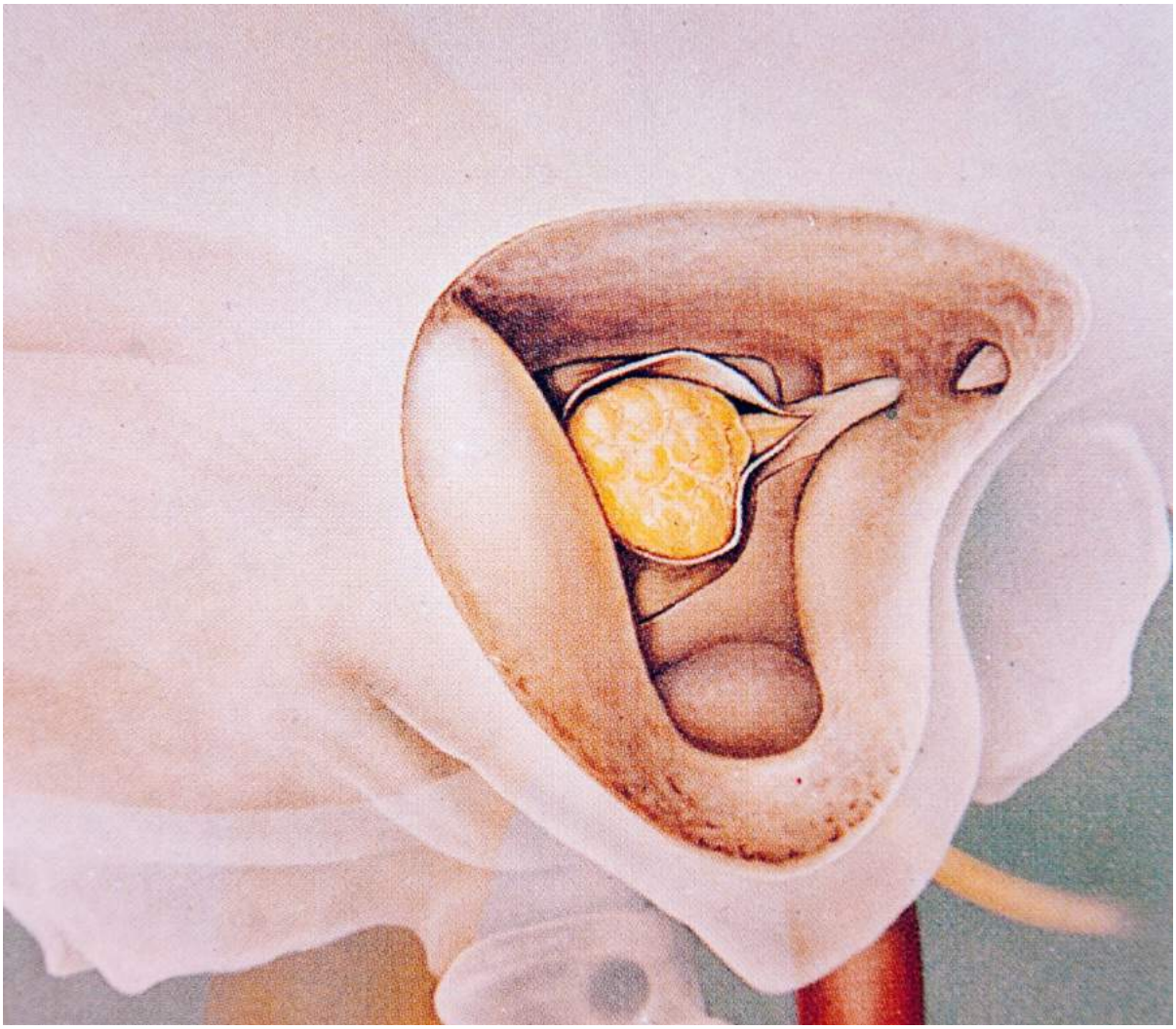

Figure 15: The translabyrinthine approach to the cerebellopontine angle (CPA). The vestibular schwannoma can be seen in the CPA and within the IAC. Hitselberger WE, House WF. A combined approach to the cerebellopontine angle. A suboccipital-petrosal approach. (*Arch Otolaryngol* 1966;84:267-285.) Illustration reproduced with kind permission of James Tait Goodrich author of Chapter 2 in Janecka I.P. and Tiedemann K., eds in Skull Base Surgery, Anatomy, Biology and Technology. Lippincott-Raven, Philadelphia- New York 1997.

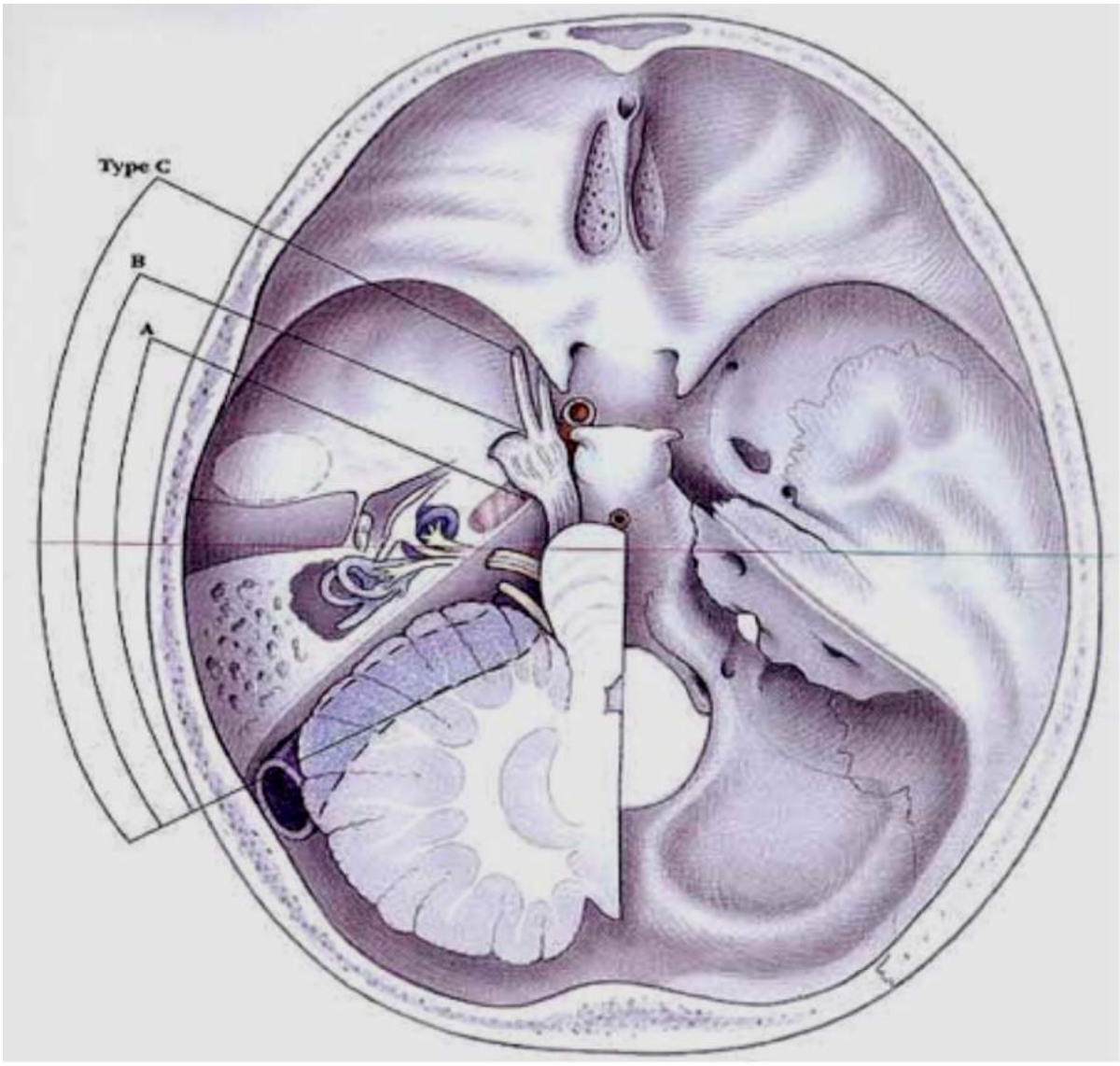

Figure 16: The extent of the bony excision in Fisch type A, B and C approaches are marked out on the base of the skull in this illustration. Reproduced with kind permission from Figure 9.1 Chapter 9, page 121 'Infratemporal fossa approaches' in *'Atlas of Neurotology and Skull Base Surgery'* Ed: Robert K Jackler Mosby-Year Book Inc. 1996.

This along with innovative anterior-cranio-facial resections for nasal tumours and olfactory neuroblastomas, clever transoral approaches to intradural lesions of the cranio-vertebral junction, as well as the far lateral approach for lesions around the foramen magnum and, of course, the development of neuronavigation techniques for anatomically difficult and inaccessible lesions sets the scene for the modern era of lateral skull base surgery.

References

1. Ballance CA. The Lister Memorial Lecture. Delivered in the Theatre of the Royal College of Surgeons of England on April 5th,1933. Dundee: D C Thomson, 1933;67-68.
2. Leonardo da Vinci. Quaderni d'Anatomia, 6 vols. Christiania: Jacob Dybwad, 1911-1916. See also Hopstock H. Leonardo as an anatomist. In: Singer C, ed. Studies in the history of Medicine Oxford: Clarendon Press, 1921;153-159.
3. Leonardo da Vinci. In: Keele KD, Pedretti C, eds Corpus of the Anatomical Studies in the Collection of Her Majesty The Queen at Windsor Castle. New York: Harcourt Brace Jovanovich, 1979.
4. Goodrich JT. Sixteenth Century Renaissance Artand Anatomy:Andreas Vesalius and His Great Book- A New View. Med Heritage 1985;1:280-288.
5. James Palmer. ed. The Works of John Hunter. Longman, London, Rees, Orme, Brown, Breen, 1835, 4 vols.
6. Vesalius A. De Humani Corporis Fabrica Libri Septum. Basel: Ex Officina Joannis Oporini, 1543.
7. Berengario da Carpi J. Tractatus de Fractura Calvae Sive Cranei. Bologna: Impressum per Hieronymum de benedictus, 1518.
8. Pare A. Le Methode Curative des Playes et Fractures de la Teste Humaine. Paris, 1561.
9. Pare A. The Workes of That Famous Chirurgion Ambroise Pare Translated Out of Latine and Compared with the French by Tho. Johnson, London, Richard Coates, 1649.
10. Willis T. Cerebri Anatomie: cui Accessit Nervorum Descriptio et Usus London: J Flesher, 1664.
11. Soemmering ST. Dissertatio Inauguralis Anatomica de Basi Encephali et Originibus Nervorum Cranio Egredientium Libri Quinque. Gottingae: Apud A Vanderboech vid, 1778.
12. Ridley H. The Anatomy of the Brain Containing Its Mechanisms and Physiology: Together with Some New Discoveries and Corrections of Ancient and Modern Authors upon That Subject. London: Sam Smith, 1695.
13. Scultetus J. χειροπλοθηκη. Armamentarium chirurgicum XLIII: Typis & Impensis Balthasari Kuhnen, 1655.
14. The Works of John Hunter. ed. James Palmer (London, Longman) Rees, Orme, Brown, Breen, 1835, 4 vols.
15. Pott P. Observations on the Nature and Consequences of Wounds and Contusions of the Head, Fractures of the Skull, Concussions of the Brain. London: C Hitch and L Hawes, 1760;X-XI.
16. Heister L. Chirurgie in welcher alles was zur Wund-Artzney gehoret, nach der neuesten und besten Art. Numberg: J Hoffmann, 1718.
17. Quesnay F. Remarques sur les Playes de Cerveau, etc. Mem Acad R Chir 1743;1:310-316.
18. Gautier D'Agoty JF. Anatomie de la tete. Chez le sieur Gautier, M Duvernay. Paris: Quillau,1748.
19. Dandy WE. Surgery of the brain. In: Lewis' Practice of Surgery. Hagerstown, MD: WF Prior, 1945;6-7.
20. Simpson JY. Discovery of a new anaesthetic agent, more efficient than sulphuric ether. Lond Med Gaz 1847;5 n.s.:934-937.
21. Lister J. Collected Papers. Oxford: Clarendon Press, 1909.
22. Bell C. Illustrations of the Great Operations of surgery. London: Longmanet al., 1821;6.
23. Bell C. The Nervous System of the Human Body; Embracing the Papers Delivered to the Royal Society on the subject of Nerves. Washington, DC. Duff Green,1833. Plate V.
24. Broca P. Remarques sur le Siege de la faculte du language articule suivie d'une observation d'aphemie (perte de la parole). Bull Soc Anat Paris 1861;36:330-357.
25. Wernicke C. Der aphasische Symptomenkomplex. Breslau: M Cohn & Weigert, 1874.

26. Ferrier D. The Functions of the Brain. London: Smith, Elder,1876.
27. Cruveilher J. Anatomie pathologique du corps humain. Paris: J-B Bailliere, 1829-1842.
28. Cushing H. Tumors of the Nervus Acusticus and the Syndrome of the Cerebellopontine angle. Philadelphia: WB Saunders, 1917.
29. Keen WW. Linear Craniotomy. Philadelphia: Lea Brothers, 1891.
30. Wagner W. Die temporare resektion schadeldacher an stell der trephanation. Centralbl Chir 1889;16:833-838.
31. Macewan W. Localisation of cerebral lesions and antiseptic trephining. Lancet 1881;2:581-582.
32. Macewan W. An address on the surgery of the brain and spinal cord. BMJ;2:302-309.
33. Macewan W. Pyogenic Infective Diseases of the Brain and Spinal Cord. Glasgow: J Maclehose, 1893.
34. Horsley VAH, Sharpey-Shafer EA. A record of experiments upon the functions of the cerebral cortex. Phil Trans R Soc (B)1889;179:1.
35. Gotch F, Horsley VAH. On the mammalian nervous system, its functions, and their localisation determined by an electrical method. Phil Trans R Soc (B)1891;182:267-326.
36. Horsley VAH. Antiseptic wax. BMJ 1892;1:1165.
37. Horsley VAH, Clarke. The structure and functions of the cerebellum examined by a new method. Brain 1908;31:45-124.
38. Spiegel EA, Wycis HT, Marks M, Lee AJ. Stereotaxic Apparatus for Operations on the Human Brain. Science 1947;10;106(2721):349-350.
39. Ballance CA. Some Points in the Surgery of the Brain and its Membranes. London: Macmillan, 1907.
40. Ramsden RT. "A brilliant surgical result, the first recorded": Annandale's case, 3rd May 1895. J Laryngol Otol. 1995;109(5):369-73.
41. Ballance CA. Essays on the Surgery of the Temporal Bone. London: Macmillan, 1919.
42. Krause F. Surgery of the Brain and Spinal Cord Based on Personal Experiences. Published in 3 bvols. Translated by Haubold Hand Thorek M. New York:Rebman, 1909—1912.
43. De Martel T. Un point de technique operatoire dans la craniectomie. Presse Med 1908; 16:641-643.
44. Cushing H. Papers relating to the pituitary Body, Hypothalamus, and Parasympathetic Nervous System. Springfield, IL: Charles C Thomas, 1932.
45. Cushing H. A method of total extirpation of the of the Gasserian ganglion for trigeminal neuralgia. By a route through the temporal fossa and beneath the middle meningeal artery. JAMA 1900;34:1035-1041.
46. Cushing HW. Tumors of the Nervus Acusticus and the Syndrome of the Cerebello-pontine Angle. WB Saunders Company, Philadelphia and London 1917.

Chapter 1.3

The multidisciplinary team: management, prognosis and outcome of lateral skull base pathology

The multidisciplinary skull base team and patient management

The development of a true multidisciplinary team is critical in modern skull base surgery.[1] It is vital that skull base surgeons work together with neurosurgeons as a close-knit team including plastic and reconstructive surgeons, neuro-ophthalmic surgeons, interventional neuro-radiologists, neuro-anaesthetists, oncologists, audiological scientists, electrophysiologists, speech and language therapists and clinical nurse specialists. The careful management options of all patients should be discussed in a regularly held multidisciplinary team meeting (MDT) having studied high quality multi-planar fine cut images of the pathology.

Establishing a multidisciplinary team is not always straightforward, however, as it may not be the natural inclination of the egocentric surgeon to work alongside colleagues in a specialty that he might regard as inferior to his own! Collaboration within the team is based on mutual respect for one another's clinical skills, flexibility and an open enquiring mind and a desire to optimize patient management as well as insight into the importance of the esprit de coeur and reputation of the unit. There should be no question of the pre-eminence of one subspecialist over another otherwise relationships may deteriorate into a co-existence of a precarious nature. It will be neither constructive nor stimulating for the team if, as Derome complained, one of them is "co-opted in this surgery in a purely ancillary role"[2]. On the contrary disciplines should be co-operative rather than competitive[3] and sharing subspecialist knowledge, concepts and ideas is essential in promulgating the progress of the team. The skull base surgeon must be receptive to the acquisition of neurosurgical skills and likewise the neurosurgeon should develop neuro-otological ones. It is also important that the contribution of the non-surgical members of the MDT to the discussion of patient management carries equal weight. A recent study raises the question of whether a re-evaluation of the leadership of MDTs is required with clinicians from a variety of specialties being given opportunities to develop skills necessary to lead MDTs and improve team performance and patient care.[4,5] Multidisciplinary simulation-based team training is feasible and well received by surgical teams. Non-technical skills can be assessed alongside technical skills, and differences in performance indicate where there is a need for further training.[6] Some concerns about MDT meetings have been voiced with non-attendance being

associated with not having protected time to attend the meetings and discussions being unequal amongst the participants, and patient-centred information being ignored.[5] Good leadership of MDT meetings is necessary to foster inclusive case discussion and protected time to attend as well as improved case selection and working in a more structured way will facilitate the necessary improvements. Clinicians recognize the value of MDT meetings in terms of effective co-ordination and communication with patients but there is a view that other aspects of relationship building are hindered in the multidisciplinary setting and that organizational and teamwork issues may need to be addressed to optimize the implementation of the multidisciplinary approach to these meetings.[7,8] Improved decision making between health-care team members and patients will produce more positive treatment outcomes.

This complex surgery based on a multidisciplinary team approach needs to be rationalized and regionalized to facilitate the investigation, to improve planning, reduce the number of complications, conserve financial resources and improve final outcome and quality of life for our patients.[9]

Prognosis and outcome

The determination of the prognosis of a pathology is dependent on the outcome of the treatment which is dictated by current best clinical practice.

Prognosis (from the Greek meaning fore-knowing) is a medical term to describe the likely outcome of an illness.

Outcome means the consequence or conclusion and surgical outcome is, therefore, the aftermath or end result of surgery.

An accurate and detailed analysis of surgical outcome is mandatory to establish an evidence base for a specific surgical procedure.

The first call for evidence-based medicine was by Pierre Charles Alexandre Louis in Paris in 1836.[10] Louis scrupulously charted the course of a disease and developed a systematic approach to collecting information.

His guiding motto was *"Ars medica tota in observationibus".*[11]

The vast amount of data gathered permitted him to make comparisons and systematically and statistically evaluate the efficacy of treatments.

In the past two decades "Evidence-based medicine" has come to represent a systematic approach to published research as a basis of clinical decisions.

Coined by Sackett at McMaster University Medical School in Canada, the term has spread globally and provoked an article by Rangachari in 1997 entitled "Evidence-based medicine: old French wine with a new Canadian label?"[12]

Sackett [913-17] has stated that "Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research." Evidence based medicine is not restricted to Levels Ia and Ib evidence (Table 1)[18] i.e. meta-analyses of randomised trials (RCT) and individual randomised trials but involves the identification of the best external evidence with which to answer the clinical questions.[14] The best available external clinical evidence is clinically relevant research, often from the basic sciences of medicine, but especially from patient centred clinical research into the accuracy and precision of prognostic markers and the efficacy and safety of therapeutic, rehabilitative and preventive regimes. "Without current best external evidence practice risks becoming rapidly out of date to the detriment of patients"[13]. Good doctors use both individual clinical expertise and the best external evidence and neither alone is enough.

Because Level Ia evidence, the systematic review of several randomised trials (Table 1), and level Ib evidence, the randomised trial, "is so much more likely to inform us, it has become the "Gold standard" for judging whether a treatment does more harm than good."[13,14]

Table 1: Grading of evidence[18]

Ia:	systematic review or meta-analysis of RCTs.
Ib:	at least one RCT.
IIa:	at least one well designed controlled study without randomisation.
IIb:	at least one well-designed quasi-experimental study, such as a cohort study.
III:	well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, case-control studies and case series.
IV:	expert committee reports, opinions and/or clinical experience of respected authorities.

"If no randomised trial has been carried out our patient's predicament, we follow the trail to the next best external evidence and work from there."[13]

In other words evidence-based medicine is not restricted to levels Ia and Ib evidence it involves tracking down the best external evidence with which to answer our clinical questions.[14]

It is clearly much more likely that level I evidence will be achieved in medicine and particularly therapeutics than in surgery. There are a number of reasons for this and let us take the treatment of Meniere's disease as an example and an illustration as to why level I evidence has been difficult to achieve in surgery.

Firstly, Meniere's disease is characterised by a triad of symptoms, attacks of vertigo, tinnitus and, at least initially, fluctuant hearing loss with a pathological basis of endolymphatic hydrops of the scala media. Many scientific papers fail to define what the authors mean by Meniere's disease and since electrocochleography is the only way of making an objective electrophysiological assessment of the degree of endolymphatic hydrops it would not be unreasonable to use this as an entry criterion to a study of this disease. Very few papers define their entry criteria and, therefore, comparisons of treatment outcomes in different patient series are compromised by this lack of definition.

Secondly, the disease pursues a very variable course and is of a remitting nature.

Thirdly, the number of patients needed to increase the power of the study and make it statistically valid.

Fourthly, the length of time necessary to validate the result.

Finally, centres which attract sufficiently large number of patients are usually tertiary referral centres where the patients have been sent because they have been refractory to medical treatment and are expecting a surgical solution. It is difficult to justify putting these patients into a randomised controlled trial. Ten years ago out of the 4376 papers on Meniere's disease published and on Medline only 75 or 1.7% were clinical trials or randomised controlled studies. There were only 9 (0.2%) on conservative surgery for Meniere's disease and 5 of these were the famous Danish "Sham study" initially reported by Thomsen *et. al.* in 1981.[19] All 5 references were of the same study, that is the same series of patients in different phases.[20] This study was the only randomised double blind controlled trial on conservative surgery in Meniere's disease and, therefore, the only one fulfilling the "gold standard" criterion

for level Ib evidence. It compared endolymphatic sac decompression with a sham procedure of cortical mastoidectomy. Sadly the study was flawed both statistically and in its design. From a statistical point of view the small sample sizes made the study of too low a power to be helpful but very importantly it brought to light major ethical concerns about sham surgery and although no further studies of this type have been performed since, it is worrying that otolaryngologists may have been led to perform sham operations based on these results.

It is perhaps the difficulties in the application of evidence-based medicine to surgical procedures that a number of caveats have been raised in recent articles. Anastasiu *et al* in 2007[21] pointed out that the problem arises when the patient's option is different from the medical decision. Who has to decide? Based on what logic or arguments? Another paper sets our arguments for the claim that even though explicit guidelines and codifications can play a practical role in informing clinical practice, they rest on a body of tacit or implicit skill that is in principle ineliminable.[22] It forms the basis of good judgement and unites the integration of research, expertise and values. Empiric data and theoretical arguments suggest an alternative RCT design for surgery. This is called an expertise-based RCT.[23] It may have enhanced validity, applicability, and ethical integrity compared with a conventional RCT. The expertise-based RCT allows a trial investigating the effectiveness of two well recognised surgical procedures for a given problem.

In a disease such as vestibular schwannoma, if the tumour is sufficiently small the patient can be offered the three current management options of, watch wait and rescan, surgical removal and stereotactic radiotherapy either by single dose gamma knife radiosurgery or by conventional multiple fraction radiotherapy.[24] It is vital that an evidence base is built up for each of the three management modalities by analysing in detail treatment outcomes in large series so that patients are able to make an informed choice about the management of their tumours. The difficulty in performing randomised trials of surgery versus radiotherapy is immediately apparent since patients with a vestibular schwannoma often fall into 2 groups. Firstly those who favour surgical excision because they have a tumour and wish to have it removed and after a satisfactory exit scan can close that chapter of their life and get on with the next one. Secondly those concerned about undergoing a major intracranial procedure and would rather have the less invasive radiotherapy

treatment and are happy to be followed up in the long term by interval scanning. Publication of detailed outcomes informs choice in this respect but in view of these necessarily limiting factors this has to be usually level III occasionally level IIb evidence.

Outcome of treatment determines the quality of life of our patients.

Outcome measures

The impact of a disease state on an individual patient has been categorised by the World Health Organisation (WHO) [25]as follows:-

1. *Mortality.*
2. *Functional morbidity; impairment of function.* This refers to limitation of function of a part of the body. In relation to this thesis, neurological deficit.
3. *Disability:* restriction in daily activity as a direct result of the neurological impairment.
4. *Handicap;* the impact on social activity as a result of the disability.
5. *Distress;* the psychological reaction to a disease state and its functional impact.

These definitions refer to lateral skull base pathology and post-operative outcome measures in this thesis. They comprise the main domains contributing to the overall quality of life of the patients in these surgical series. Surgical morbidity and impairment of function are the determinants of disability, handicap and distress.

Aims and outline of this thesis

The general aim of this thesis was to provide clinicians with a detailed analysis of relevant clinical aspects of rare lateral skull base pathology and surgical outcomes of benign and malignant disease in order to establish an evidence base and inform decision making in patient management.

The following objectives were set:

- To study clinical factors and determinants of early diagnosis and referral patterns of vestibular schwannoma.

- To develop modifications of surgical technique to facilitate transtemporal access to the cerebellopontine angle(CPA) and in order to obviate the need to alter or modify the selected approach.
- To devise an original new classification for staging primary CPA cholesteatoma and modifying existing classifications of petrous temporal bone cholesteatoma and facial nerve function based on anatomical and clinical factors respectively.
- To study the growth characteristics of vestibular schwannoma.
- To study and discuss former and current management strategies in neurofibromatosis type 2 (NF2) patients and to analyse the surgical outcome of the translabyrinthine approach for NF2 vestibular schwannoma.
- To elucidate the factors affecting facial nerve outcome following surgery in a large series of patients with vestibular schwannoma over three decades.
- To determine surgical outcomes and to establish an evidence base for surgery by detailed analyses of multiple point databases for vestibular schwannoma, trigeminal neuroma, microvascular decompression of the facial nerve for hemifacial spasm and the outcome of radical surgery and postoperative radiotherapy for squamous cell carcinoma of the temporal bone.

References

1. Sharp MC, MacfArlane R, Hardy DG, Jones SE, Baguley DM, Moffat DA. Team working to improve outcome in vestibular schwannoma surgery. Br J Neurosurg 2005;19:122-127.
2. Derome P. Les tumeurs spheno-ethmoidales. Possibilites d'exerese et de reparation chirurgicales. Neurochirurgie 1972;18(1):1-164.
3. Kozarek RA. The society for gastrointestinal intervention. Are we, as an organisation of disparate disciplines, cooperative or competitive? Gut Liver 2010;4:S1-8.
4. Lamb BPH, Vincent C, Sevdalis N, Green JS. The role of oncologists in mutidisciplinary cancer teams in the UK: an untapped resource for team leadership? J Eval Clin Pract 2011;17:1200-1206.
5. Lamb BW, Sevdalis N, Arora S, Pinto A, Vincent C, Green JS. Teamwork and Team Decision-making at Multidisciplinary Cancer Conferences: Barriers, Facilitators, and Opportunities for Improvement. World J Surg 2011;35:1970-1976.
6. Undre SKM, Sevdalis N, Gautama S, Selvapatt N Williams S, Sains P, McCulloch P, Darzi A, Vincent C. Multidisciplinary crisis simulations: the way forward for training surgical teams. World J Surg 2007;31:1843-1853.
7. Bellardita LDS, Spatuzzi AL, Valdagni R. Multidisciplinary Versus One-on One Setting: A Qualitative Study of Clinicians' Perceptions of Their Relationship With Patients With Prostate Cancer. J Oncol Pract 2011;7:1-5.
8. Fleissig AJV, Catt S, Fallowfield L. Multidiscplinary team in cancer care:are they effective in the UK? Lancet Oncol 2006;7:935-943.
9. David DJ. Craniofacial surgery: the team approach. Aust N Z J Surg 1977;47:193-198.

10. Louis PCA. Researches on the effects of blood-letting in some inflammatory disease, and on the influence of tartarised antimony and vesication in pneumonia. Am J Med Sci 1836;18:102-111.
11. Osler W. The Influence of Louis on American Medicine. In: An Alabama Student and Other Biographical Essays 1909; New York:189-210.
12. Rangachari PK. Evidence-based medicine: old French wine with a new Canadian label? J R Soc Med 1997;90:280-284.
13. Sackett D. Evidence-based medicine. Lancet 1995;346:1171.
14. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence-based medicine: what it is and what it isn't. BMJ 1996;312:71-72.
15. Sackett DL. Evidence-based medicine. Semin Perinatol 1997;21:3-5.
16. Sackett DL. Evidence-based medicine. Spine (Phila Pa 1976) 1998;23:1085-1086.
17. Sackett DL. A 1955 clinical trial report that changed my career. J R Soc Med 2010;103:254-255.
18. Straus SE SD. Using research findings in clinical practice. BMJ 1998;317:339-342.
19. Thomsen J, Bretlau P, Tos M, Johnsen NJ. Meniere's disease: endolymphatic sac decompression compared with sham (placebo) decompression. Ann NY Acad Sci 1981;374: 820-830.
20. Bretlau P, Thomsen J, Tos M, Johnsen NJ. Placebo effect in surgery for Meniere's disease: a three-year follow-up study of patients in a double blind placebo controlled study on endolymphatic sac shunt surgery. Am J Otol 1984;5:558-561.
21. Anastasiu MSV, Popa F. Evidence-based medicine, conceptual challenge or the future of daily practice? Chirurgia (Bucur) 2007;102:527-530.
22. Thornton T. Tacit knowledge as the unifying factor in evidence based medicine and clinical judgement. Philos Ethics Humanit Med 2006;1:E2.
23. Bednarska E, Bryant D, Devereaux PJ. Orthopaedic surgeons prefer to participate in expertise-based randomized trials. Clinical orthopaedics and related research 2008;466:1734-1744.
24. Lloyd SK, Kasbekar AV, Baguley DM, Moffat DA. Audiovestibular factors influencing quality of life in patients with conservatively managed sporadic vestibular schwannoma. Otol Neurotol 2010;31:968-976.
25. Watkinson JCGM, Wilson JA. Treatment outcomes. In: Stell and Maran's Head and Neck Surgery; Fourth Edition. Watkinson JC, Gaze MN, Wilson JA: Eds Butterworth-Heinemann Oxford, 2000:159-162.

Chapter 2

Vestibular schwannoma

Chapter 2.1

Referral patterns in vestibular schwannomas – 10 years on

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Clinical Otolaryngology 2004;29(5):515-517

Abstract

Diagnostic imaging techniques, symptom awareness and education of local sources of referral in vestibular schwannomas, including general practitioners, have all improved in the last 10 years. The referral patterns in vestibular schwannomas in Cambridgeshire in the period 1981–1993 has been reported.[1] A direct comparison was made with regard to referral patterns seen in the last 10 years paying particular emphasis to source of referral, diagnosis at referral and symptoms/size at presentation.
The incidence of vestibular schwannomas in the region is compared and discussed. Patients' managed by the 'watch and wait' policy were particularly scrutinized, as they were not discussed previously. Retrospective analysis of computerized database was used. We have demonstrated an increase in the proportion of referrals with known vestibular schwannoma to 90% of all referrals. No significant change in length of history prior to referral, source of referral or principal presenting symptom were found. An overall decrease in tumour size was found but an increase in the percentage with larger tumours (>4.5 cm). We attribute the significant findings to an increase in availability of magnetic resonance (MR) scanners in the country during the past 10 years. It appears that some tumours would still present with no symptoms until late and therefore will elude identification until large in spite of a low threshold for MR scanning.

Diagnostic imaging techniques, symptom awareness and education of local sources of referral in vestibular schwannomas, including general practitioners, have all improved in the last 10 years. The referral patterns in vestibular schwannomas in Cambridgeshire in the period 1981–1993 have previously been reported.[1] The objective of this study is to investigate potential changes in the referral patterns and status of patients being referred for investigation or management of vestibular schwannoma. A direct comparison is made with regard to referral patterns seen in the last 10 years paying particular emphasis to source of referral, diagnosis at referral and symptoms/size at resentation. The incidence of vestibular schwannoma is also calculated using the data.

Methods

The computerized database of patients who have undergone surgical removal of a vestibular schwannoma was reviewed as in the previous study. The database is

completed prospectively while patients are seen in the outpatients department. In addition, the database of 'watch and wait' patients who are being monitored rather than undergoing surgery is being scrutinized particularly. This database was initiated since the previous paper as the practice of continued monitoring of patients with vestibular schwannoma was less common 10 years ago.

Results

A total of 318 patients underwent surgery and three patients were referred to clinic who remained under observation during April 1981 to December 1993, of whom 152 were men with mean age of 52.1 and standard deviation 12.3. During the period, January 1994 to December 2002, 539 patients underwent surgery, 83 patients were referred to clinic and remained under observation until at present, and in four patients a decision was taken to treat by stereotactic radiotherapy. Of these, 308 patients were men with mean age of 54.8 and standard deviation of 13.7. Some data was incomplete particularly for the watch and wait group. Therefore, patients have been excluded from some aspects of analysis. Of a total of 947 patients, only 24 were excluded.

In the previous study,[1] a trend could be seen in the status of referrals being made to the team in Addenbrooke's Hospital. By including the newer data from the last 10 years, the percentage of referrals with known vestibular schwannoma was seen to continue to increase. This trend continues but can be seen to flatten out to ∞90% (Figure 1).

The number of cases having surgery has increased steadily to 1996 after which there is a very large increase in patients having surgery. This returns to a lower level again in 2001. The graph showing the number of referrals shows that although the number of patients seen by the department from the district has remained similar, the number of patients being sent to the department from regional and supra-regional sources is also much greater from 1994 to 1999 (Figure 2).

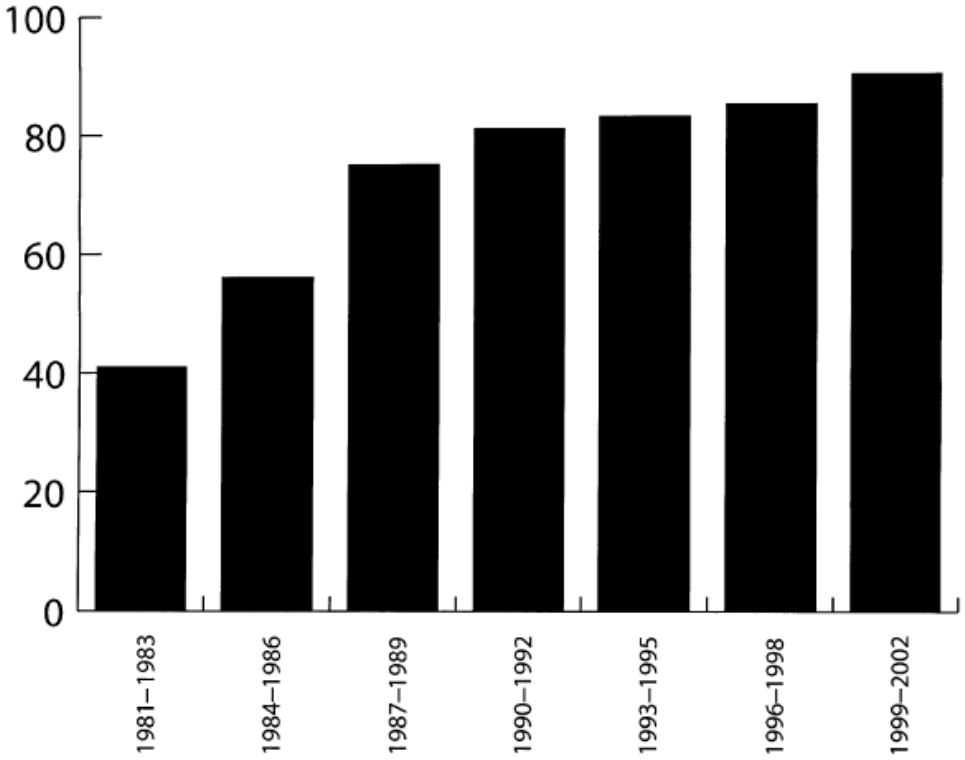

Figure 1: Proportion of referrals with known vestibular schwannoma.

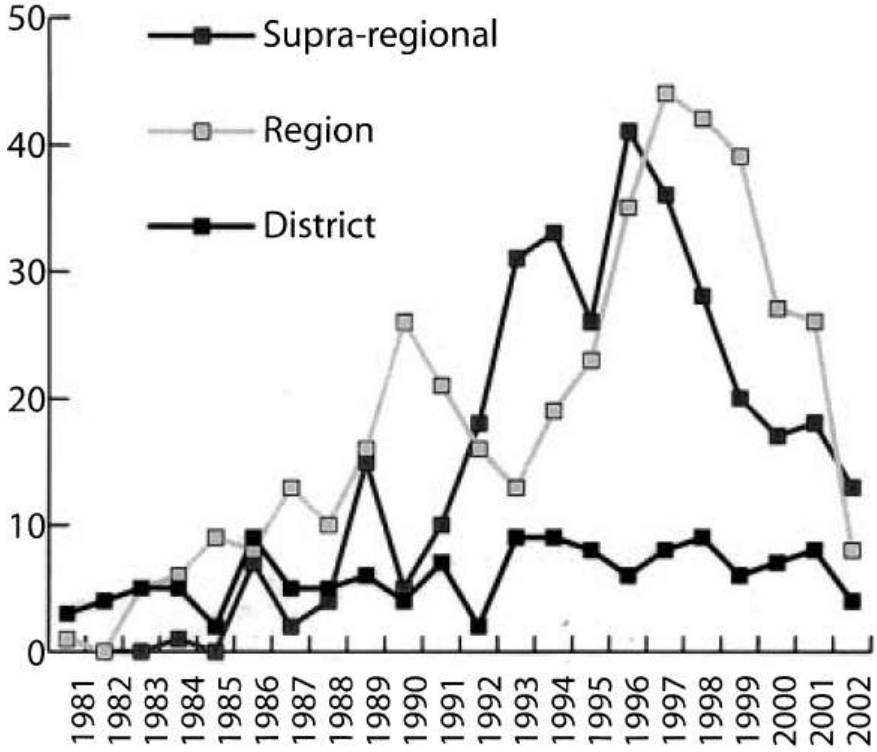

Figure 2: Number of referrals per year, divided by origin of referral.

This probably is the cause of the increase in the number of cases having surgery during this period.
The data for source of referral was examined using the chi-squared test for independence. Examination of the source of referral does not appear significantly different from the findings previously (P = 0.8208). The vast majority of cases are referred from ENT clinics and the proportions of each group of referrer has remained approximately the same with time.

Tumour size is recorded in the database by grouping the maximum diameter on magnetic resonance (MR) into bands. Median size was therefore analysed using the chi-squared test, analysis indicating a significant decrease in median tumour size (P = 0.0004), but also an increase in the number of tumours >4.5 cm in diameter in the later time period. The graph of average tumour size per year shows great variation but no overall downward trend (Figure 3).

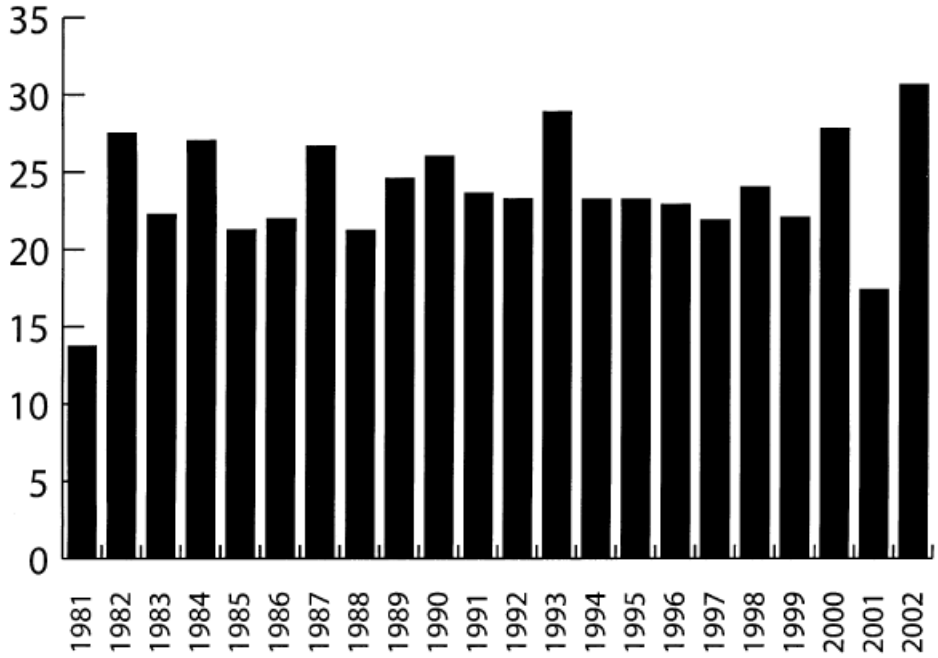

Figure 3. Median tumour size per year.

Length of history was examined comparing the two groups, before the end of 1993 and after the beginning of 1994. The mean length of history was 41.97 months (sd 51.613) and 44.65 months (sd 108.64) respectively. The Mann–Whitney U-test was used as the data was not normally distributed.

This did not show any significant reduction in length of history between the two groups (P = 0.4726). Analysis of the distribution of principal presenting symptom using the chi-squared test indicated that there was no significant difference between the two time periods (P = 0.271) (Table 1).

Examining the data for incidence of vestibular schwannoma gives a figure of 0.83 per 100 000 per year based on a catchment population of 480 000 for the year 2002. Previous years showed great variation and overall we estimate the incidence to be 1.36 per 100 000 per year taking into account the change in catchment population for Addenbrooke's Hospital. Analysis of data applicable to patients from further afield was not possible because of difficulties in accurate assessment of the population.

Table 1: Principal presenting symptoms for 1981–1993 and 1994– 2002

Principal presenting symptom	1981–1993 (%)	1994–2002 (%)
Progressive hearing loss	58	59
Tinnitus	12	13
Imbalance	10	10
Sudden hearing loss	10	8
Facial numbness	5	3
Visual disturbance	1	1
Headache	1	1
Otalgia	1	1
Facial weakness	0	1
Vertigo	0	1

Discussion

During the study period for the first examination of referral pattern, there were very few patients not proceeding immediately to surgery. The number being entered for observation has become a significant proportion of the total. Patients are generally put under observation on the grounds of tumour size, patient choice and co-morbidity.

The most common presenting symptom remains hearing loss as it has in previous studies.[2,3] The highest proportion of referrals remains from ENT surgeons. As one

would expect, little has changed to alter these factors in the 10 years since the previous study.

In the era of freely available MR scans, it is unsurprising that a greater proportion of referrals have a diagnosis of vestibular schwannoma at referral. This does appear to have reached a plateau at around 90% however. It appears that as the curve continues there will always be some small number of patients referred without prior diagnosis of vestibular schwannoma. As it has been stable at this point for around 10 years, we feel it is unlikely that this will change without some new diagnostic modality.

We believe that the substantial increase in the number of cases being referred from outside the local area in the years 1994–1999, and subsequent decrease in referrals represents the advent of widely available MR scans and the identification of patients at an earlier stage followed by clearance of the pool of small, symptomatic schwannomas previously not identified. A similar pattern was seen in otosclerosis with the advent of stapedectomy. Alternative explanations for the recent reduction in referrals are that patients are not being referred and are monitored in their local hospitals, that they are being referred directly for management by radiosurgery or that they are being referred elsewhere. The experience of one of the authors (SJ) in other centres in the East Anglian region is that this is not the case and that all cases of vestibular schwannoma are referred to Addenbrooke's no matter how small. The fact that both regional and supra-regional referrals follow the same pattern suggests that the same phenomenon is occurring in both groups of patients. We feel that this is not seen in the local group, as the population is so much smaller that any such trend may not be seen.

Our estimate of incidence compares similarly with other recently published rates of incidence of between 0.5 and 2 per 100 000 per year.[4,5]

The decrease in median tumour size is encouraging and supports the earlier observation of Selesnick et al.[6] The fact that a considerable number of huge tumours (>4.5 cm) are still being diagnosed indicates the need for continued vigilance in the diagnosis of these lesions.

Acknowledgements

This paper was previously presented at the 4th International Conference on Vestibular Schwannoma and other CPA Lesions. Some of its data are published in the conference proceedings.

References

1. Moffat DA, Hardy DG, Irving RM et al. Referral patterns in vestibular schwannomas. Clin Otolaryngol 1995;20:80–83.
2. Moffat DA, Hardy DG, Baguley DM. Strategy and benefits of acoustic neuroma searching. J Laryngol Otolaryngol 1989;103:51–59.
3. Awan MS, Qureshi HU, Sheikh AA et al. Vestibular schwannomas: clinical presentation, management and outcome. J Pak Med Assoc 2001;51:63–67.
4. Seedat RY, Claasen AJ, Mol DA. Incidence and management of acoustic neuromas in South Africa. Otol Neurotol 2002;23:996–998.
5. Howitz MF, Johansen C, Tos M et al. Incidence of vestibular schwannoma in Denmark 1977–1995. Otol Neurotol 2000;21;690–694.
6. Selesnick SH, Jackler RK, Pitts LW. The changing clinical presentation of acoustic tumours in the MRI era. Laryngoscope 1993;103;431–436.

Chapter 2.2

Growth characteristics of vestibular schwannoma

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Abstract

Objective: To assess the growth characteristics of small to medium sized vestibular schwannomas in patients undergoing watch, wait and rescan management.

Study Design: Cohort study using prospectively collected size and tumour morphology data.

Setting: Tertiary referral centre for skull base surgery.

Subjects and Methods: 381 patients with sporadic unilateral vestibular schwannomas and two or more magnetic resonance scans were included. Linear measurements were used to assess tumour size. The point of growth and pattern of growth progression were assessed. Data was analysed using appropriate statistical techniques.

Results: 33% of tumours demonstrated significant growth. Mean size at presentation was 9.9mm (SD 4.8). For growing tumours, mean size at final review was 13.7mm (SD 4.8). This was a statistically significant increase in size ($p<0.0001$). Mean annual change in size for growing tumours was 2.3mm (SD 2.3). 52.4% of growing tumours showed radiologically demonstrable first growth within eighteen months of presentation. 7.2% of tumours showed radiologically demonstrable first growth after five years of follow up. There were no demographic or morphological predictors of growth.

Conclusions: Tumour growth is usually slow and is most likely to occur within the first three years of observation. Growth may occur after five years of follow up. A protocol for the scanning of patients is suggested based on the findings of the study.

Introduction

Several authors have demonstrated that a significant proportion of vestibular schwannomas do not grow and those that do grow usually grow slowly.[1-15] An understanding of the natural history of vestibular schwannomas has altered the current available management options. Conservative management by watch, wait and rescan has become accepted as a viable alternative to surgery or stereotactic radiotherapy for these patients.[16] Figure 1 shows the increase in the number of patients being managed conservatively at Addenbrooke's Hospital, Cambridge.

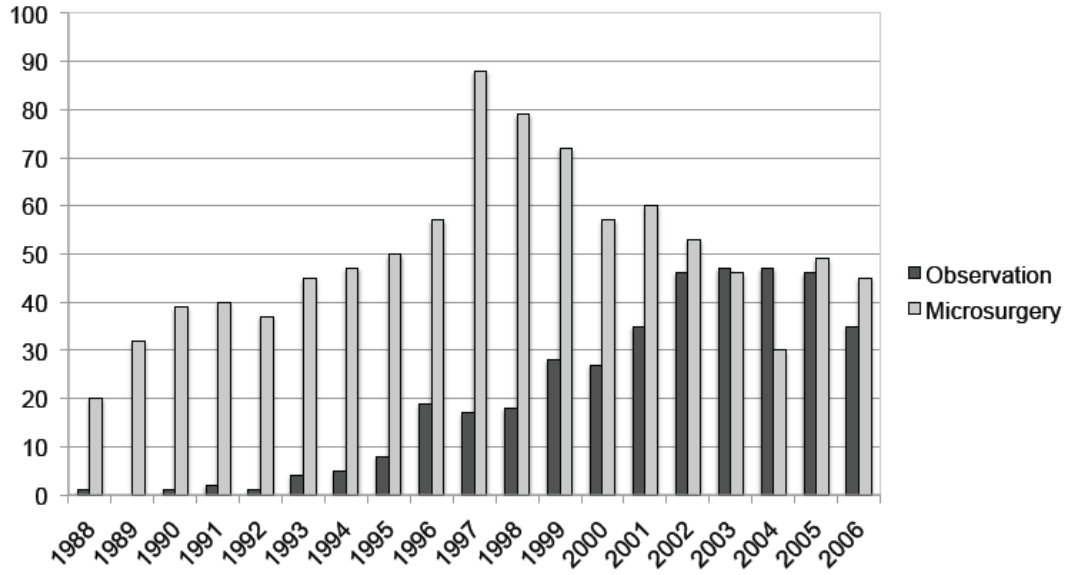

Figure 1: Histogram illustrating the increasing popularity of conservative management of sporadic vestibular schwannomas over time.

Whilst there are a number of papers on the subject, much of the literature regarding growth characteristics of vestibular schwannomas has been compromised by poor study design. Many consist of small cohorts of patients.[17,18] There is considerable inconsistency in the methods used to assess tumour size making comparison of studies difficult.[6,14,19] Furthermore, some papers include patients with tumours the size of which were measured using computed tomography (CT) or include patients with neurofibromatosis type 2.[19-21]

Several aspects of tumour growth characteristics of vestibular schwannoma still require clarification. They include characterization of progression of growth in growing tumours and also the likelihood of tumours beginning to grow after a period of no growth.

This paper describes the growth characteristics of a large cohort of sporadic unilateral vestibular schwannomas who underwent a period of conservative management and investigates the growth characteristics over time. It also provides an evidence based protocol by which to manage these patients based on the natural history of the tumour.

Methods

A prospectively updated database of patients with sporadic unilateral vestibular schwannomas who initially underwent a period of conservative management has been maintained at Addenbrooke's Hospital, Cambridge since February 1988 by the senior author(DAM) and by December 2007, 475 patients with unilateral sporadic vestibular schwannomas had been added to the database. The criterion for offering otherwise healthy patients an initial period of conservative management were that their tumours must not be *significantly* indenting the brainstem. This generally equated to tumours measuring less than 20mm *including the canalicular portion.* Occasionally, elderly patients or those with concurrent medical conditions where major surgery and prolonged general anaesthesia would pose a considerable risk and also those reluctant to have surgery or radiotherapy underwent initial conservative management in the presence of a larger tumour.
Some patients with small tumours opted for surgery because they wanted to have their tumour removed and, in addition, some patients with small tumours and disabling symptoms of vertigo were offered surgical excision as a primary treatment.
We do not advise stereotactic radiotherapy for small tumours unless they show significant growth.
All patients on the database who had undergone at least two MRI scans were included in the study. Those patients with neurofibromatosis type 2 and those whose imaging suggested pathology other than a vestibular schwannoma were excluded as were those patients who had been monitored using CT scanning.

The magnetic resonance imaging (MRI) scans of all patients were reviewed. All digitised scans were reviewed on the Picture Archiving and Communications System (PACS) that was introduced at Addenbrooke's Hospital in August of 2005. The software used for size assessment was General Electric Medical Systems Centricity Enterprise Web version 3.0. Access to scans performed prior to the introduction of PACS was very limited. However, data on tumour size had been prospectively

recorded from measurements taken by senior neuroradiologists on the original database and these measurements were used in the absence of earlier imaging.

Tumour size was assessed using linear measurements. Volumetric measurements were not performed. The slice providing the most representative part of the tumour was identified in the axial and coronal planes. Maximal size was measured in three axes, medio-lateral, antero-posterior and cranio-caudal.

For tumours with extracanalicular extension, maximal medio-lateral measurements were made along the long axis of the internal auditory canal and included the intracanalicular portion of the tumour. Antero-posterior measurements were made in an axis parallel to the posterior face of the temporal bone. Axial images were used for these measurements. Cranio-caudal size was assessed using coronal images.

For the intracanalicular portion of larger tumours and for those tumours confined to the canal, measurements were again recorded in all three planes. The medio-lateral dimension was measured along the long axis of the internal auditory canal with the medial limit of the internal auditory canal being defined by a line drawn along the posterior face of the temporal bone. The antero-posterior dimension of the intracanalicular portion was measured perpendicular to the long axis of the internal auditory canal. Cranio-caudal measurements were made in a direction perpendicular to the internal auditory canal.

The morphological features of the tumour were recorded and in particular a number of characteristics of the intracanalicular portion of the tumour were measured. This included the position of the lateral extent of the tumour, the proportion of the canal filled with tumour and the presence of canal expansion.
The image was magnified two fold and the integrated measurement tool included in the Centricity imaging software was used to make the measurements. Partial volume averaging usually made the margins of the tumour slightly blurred therefore a best estimate of the margins of the tumour was performed.

Volumetric analysis was not performed for a number of reasons. Firstly, the availability of older scans was limited and techniques for measuring volume in these cases are time consuming. Secondly, volumetric measures derived from linear measurements have an extremely large error.[23] Thirdly, there is some evidence that tumour growth is equally well identified using either linear measurements or

volumetric measurements.[24] Finally, accurate software for measuring volume directly in large numbers of tumours was not available.

Based on the literature investigating inter-observer error, tumour growth was defined as greater than 2mm increase in the maximal tumour diameter in a direction parallel to the internal auditory canal on subsequent scans.[23,25] Tumour growth rate was calculated by measuring tumour size on the most recent scan and subtracting the size of the tumour measured on the first scan. This figure for overall growth was then divided by the number of years under observation to produce an annual growth rate. The pattern of tumour growth was also recorded.

Data was stored in encrypted form on a Filemaker Pro v. 9 database (Apple Inc.). Data was analysed using the Statistical Package for Social Sciences v. 16 (SPSS Inc.). Parametric data was analysed using the Student t-test. Categorical data was analysed using the Chi-square test. Correlation data was analysed using the Pearson's correlation coefficient. Statistical significance was set at the 5% level.

Although there were no significant ethical issues resulting from this study, approval was obtained from the National Research and Ethics Committee.

Patients

There were 381 patients on the database with at least two MRI scan results. There were 175 males (46%) and 206 females (54%). The mean age at diagnosis was 60.9 years (SD12.1). The age range was 26 to 98 years. There were 187 right sided tumours (49%) and 194 left sided tumours (51%). The mean interval between first and last scans was 4.2 years (SD 3.2; range 0.5 to 17 years).

Results

For the whole cohort, the mean tumour size at presentation was 9.9mm (SD 4.8). The mean tumour size on the most recent scan was 11.1mm (SD 5.1), a statistically significant difference ($p<0.0001$; Student t-test). 238 patients had intracanalicular tumours at presentation (62.4%). 23.5% of intracanalicular tumours extended into the cerebellopontine angle during the follow up period. The proportion of tumours changing in size is shown in figure 2. 236 tumours did not change in size (59.3%).

123 tumours increased in size (32.5%) and 31 tumours underwent involution (8.1%). For growing tumours, the mean size at presentation was 9.7mm (SD 4.5) and the mean size at review was 13.7mm (SD 4.8), a statistically significant difference ($p<0.0001$: Student t-test).

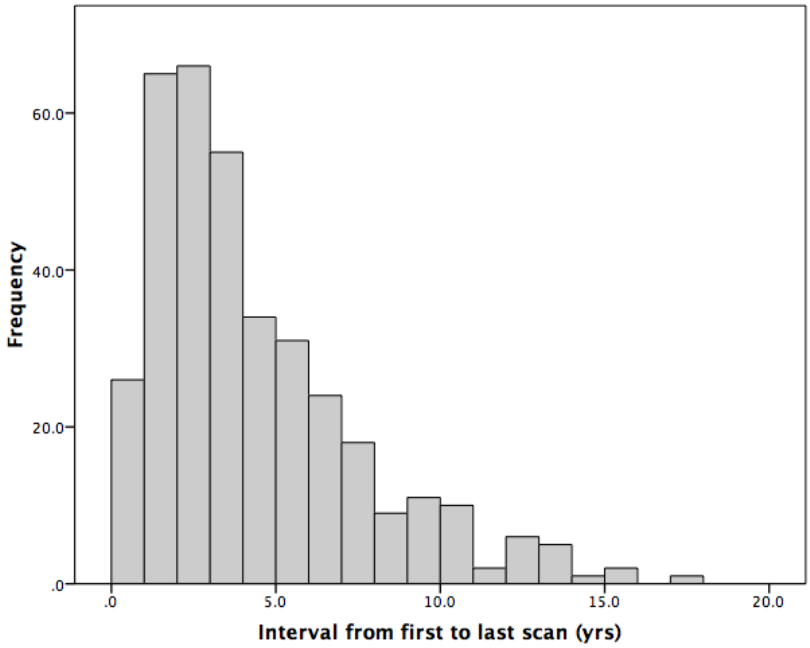

Figure 2: Histogram illustrating the range of follow up periods in the study cohort.

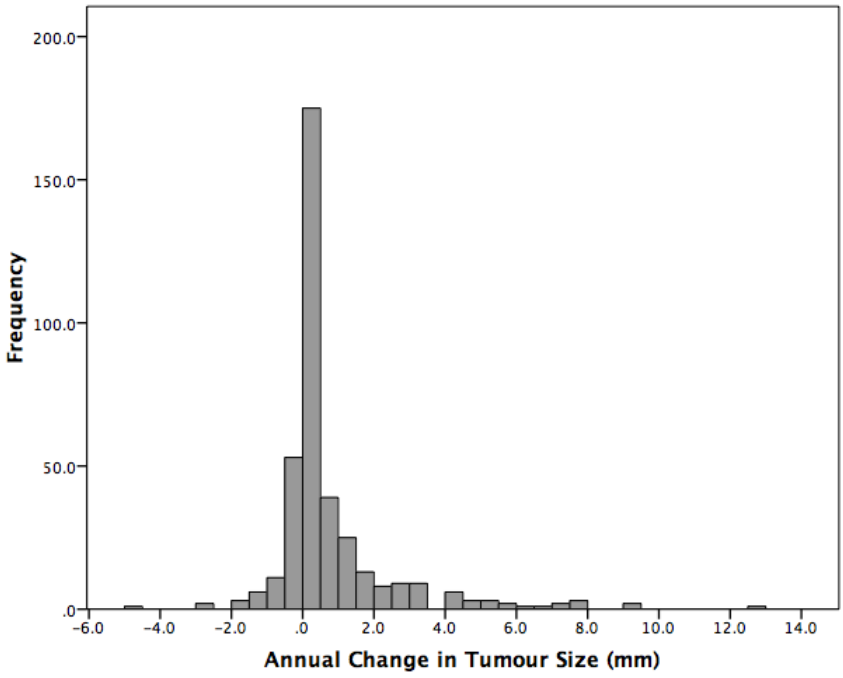

Figure 3: Pie chart illustrating the proportion of tumours demonstrating growth over the duration of the study.

For the whole cohort, the mean change in tumour size over the study period was 1.3mm (SD 3.2; range -12 to 15mm). The mean annual change in size for the whole cohort was 0.7mm (SD 1.8; range -5 to 12.5mm). The distribution of annual change in size for the whole cohort is shown in figure 3.

The mean change in tumour size over the study period for growing tumours was 4.7mm (SD 2.9; range 2 to 12.5mm). The mean annual change in tumour size for growing tumours was 2.3mm (SD 2.3; range 0.3 to 12.5). Those tumours that were intracanalicular at presentation had a faster annual growth rate than tumours that had already extended into the cerebellopontine angle by the time they presented (1.0mm/annum (SD 1.9) vs 0.3mm/annum (SD 1.5); $p<0.0001$).

Figure 4 shows a Kaplan-Meier survival plot illustrating the temporal point of growth in growing tumours. It shows that the vast majority of growing tumours show radiologically demonstrable growth within three years of presentation. Table 1 summarises this data and shows the proportion of tumours displaying first growth at any given time interval following diagnosis. It is clear that 52.4% of tumours start to grow in the first eighteen months following presentation. Subsequently, the number of tumours that start growing progressively reduces over time but growth was demonstrated after five years in 7.0% of tumours. Those that start to grow earlier tended to grow more quickly.

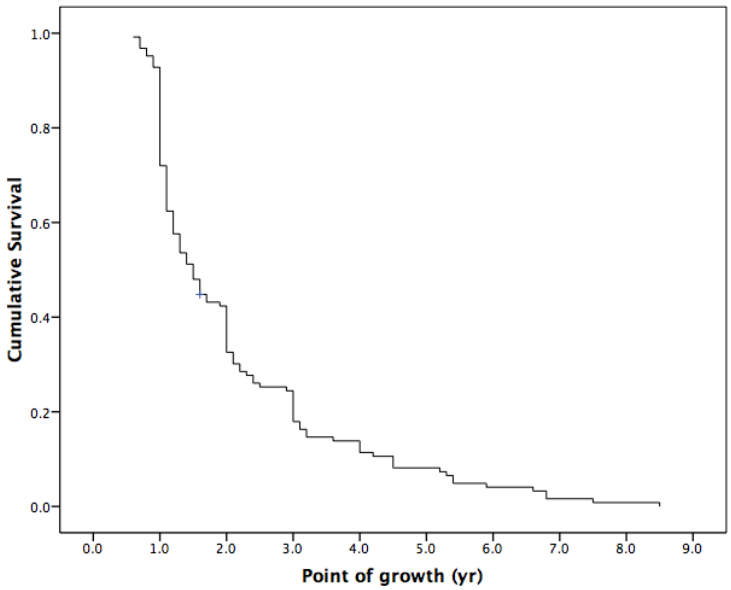

Figure 4: Histogram illustrating the distribution of annual change in size for the whole study cohort.

Table 1: Table showing the point at which growth is first documented on imaging following diagnosis. The mean growth rate per annum of tumours that start to grow at each time interval is also shown.

Interval (months)	Number growing (%) n=124	Mean Growth Rate (mm/annum)
0-18	65(52.4)	3.2
19-30	28 (22.6)	1.5
31-42	13 (10.5)	1.3
43-54	8 (6.5)	1.0
55-66	4 (3.2)	1.0
67-78	1 (0.8)	1.1
79-90	4 (3.0)	1.0

The progression of growth was very variable. Figure 5 shows the types of growth progression. The pattern of progressive growth and a period of no growth followed by growth was the most common.

39.6% and 40.5% of patients had expansion of the internal auditory canal at presentation and review respectively. Tables 2 and 3 show the proportion of the internal auditory meatus filled and the lateral extent of the tumour in the study cohort. There was no statistically significant difference in these parameters at presentation or final review either in the whole cohort or the growing tumour cohort.

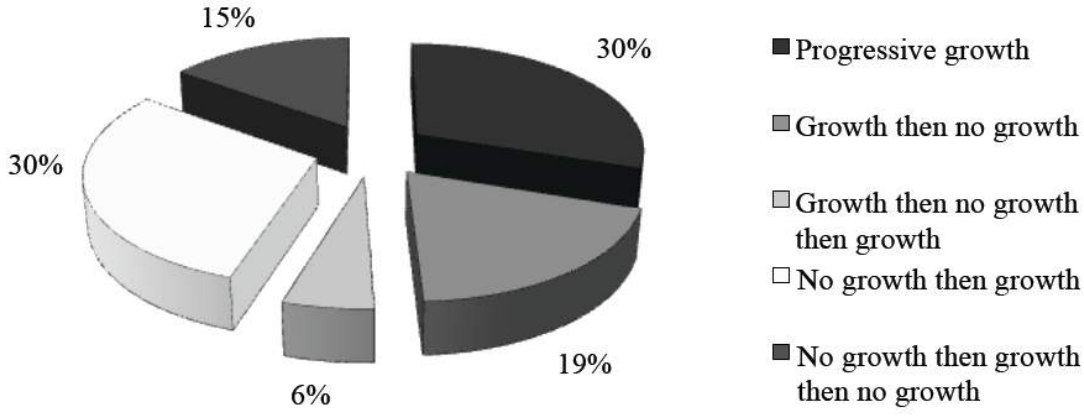

Figure 5: Histogram illustrating the distribution of annual change in size for growing tumours.

Table 2: Table showing the proportion of the internal auditory canal filled at presentation and review.

Proportion of canal filled (%)	Number of patients (%)	
	Presentation	Review
0-25	41 (10.8)	38 (9.9)
26-50	79 (20.7)	82 (21.6)
51-75	69 (18.0)	58 (15.3)
75-100	192 (50.5)	203 (53.2)

Table 3: Table showing the extent of the lateral margin of the tumour within the internal auditory meatus at presentation and at review.

Lateral margin of tumour	Number of patients (%)	
	Presentation	Review
Medial third	14 (3.6)	14 (3.6)
Middle third	45 (11.7)	48 (12.6)
Lateral third	69 (18.0)	65 (17.1)
Up to fundus	237 (62.2)	227 (59.5)
Into labyrinth	17 (4.5)	27 (7.2)

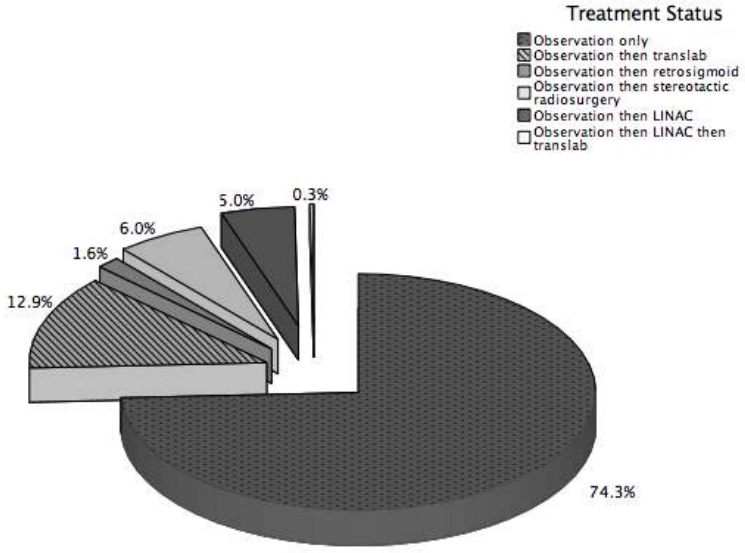

Figure 6: Kaplan Meier Survival plot of growing tumours showing the point at which tumours first demonstrated radiological evidence of growth following diagnosis.

The eventual outcomes of all patients is shown in figure 6. Eighty six percent of those demonstrating no growth or regression remained on a conservative management policy. In contrast 57.6% of those patients who demonstrated growth underwent active treatment either surgery or stereotactic radiotherapy.

With regard to factors that might predict growth, there was no correlation between growth and any demographic or any feature of tumour morphology. This is illustrated in table 4.

Table 4: Table showing the correlation between annual change in tumour size and various potential predictors of growth.

	Whole Cohort		Growing Tumours	
	Correlation coefficient	p value	Correlation coefficient	p value
Age	-0.058	0.265	-0.067	0.467
Sex		0.383		0.265
Side		0.217		0.224
Size at presentation	-0.102	0.052	0.089	0.33

Discussion

Summary of Findings

This paper confirms that 59% of sporadic unilateral vestibular schwannomas that undergo a period of conservative management do not grow over a five year period but those that do grow may grow up to 15mm although the mean growth is much slower at 2.3mm per annum. The point at which growth is first documented is within eighteen months of diagnosis in 52.4% of patients but importantly 7.2% of tumours demonstrated radiological evidence of growth for the first time after 5 years. The growth patterns were unpredictable but the majority either grew from the outset or had a period of no growth followed by demonstrable growth. There were no demographic or tumour morphological predictors of growth.

Comparison with the Literature

The literature on this subject is very heterogeneous and many papers have significant flaws. These include:

- Small study cohorts.[17,18]
- The retrospective nature of the majority of the literature.[21,26]

- Significant selection bias due to inclusion of only elderly patients or patients with concurrent illness.[11]
- The use of different imaging modalities. Early studies often included patients who had computed tomography imaging only.[1,2]
- Variations in the technique for measuring tumour size.[6,14,19]
- An inherent inter- and intra-observer error when measuring tumour size.[23]
- Differences in the definition of growth.
- Short follow up periods.[27,28]
- The inclusion of patients with neurofibromatosis type II in many papers.[19-21]

It is important to take these factors into account when interpreting the literature on vestibular schwannoma growth.

In the literature, the mean tumour size at presentation ranges from 7.8 to 12.8mm.[1-15] The proportion of tumours growing varies widely and ranges from 15 to 75% depending on the series.[1-15] The annual growth rate for growing tumours ranges from 1.6 to 4.7mm. Two very similar meta-analyses have been performed in the past 3 years. Smouha et al. included 19 studies in their analysis with a total of 1345 patients.[29] They found that 43% of tumours grew and that the mean growth rate was 1.9mm per annum. Yoshimoto included 26 studies with 1340 patients.[30] He found that 46% of tumours grew with a mean annual growth rate of 1.2mm per annum. The proportion of tumours growing in this cohort was smaller than these. A more recent review of the literature by Nikolopolous et al. showed similar findings.[31]

With regard to the point at which growth is first demonstrated following diagnosis, most authors concur with the view that tumour growth is much more likely during the first few years following diagnosis.[5] Some authors have suggested that patients can be discharged after five years as tumours do not grow beyond this time point.[3] In this series, it is clear that this is not the case and that follow up should continue certainly beyond five years. It is very unlikely, however, that a tumour will grow quickly if growth begins after several years of observation.

Strengths and Weaknesses of the Paper

This study includes one of the largest cohorts of patients with prospectively collected data regarding tumour size in the current literature. The prospective nature of data collection provided a reliable and complete dataset for the patient cohort which augments the current literature. The follow up period was longer than most other series. It used consistent and systematic techniques for measurement of tumour size

and excluded tumours that were not sporadic vestibular schwannomas. It also used robust statistical techniques to analyse the data.

The use of linear measurements in the assessment of tumour size is open to criticism. The reproducibility of measurements limits the definition of growth to 2mm or more when on occasions clear growth had occurred at smaller measurements. A single maximal diameter in the medio-lateral direction was used and this clearly excludes tumours from the growth cohort that demonstrated growth limited to any other axis, although this was rare. In addition, it is important to highlight that an increase in tumour size is harder to demonstrate using linear measurements in larger tumours than in smaller tumours because the same increase in volume in a large tumour will result in a relatively smaller increase in diameter than in a smaller tumour.

The authors were also unable to re-measure tumour size for earlier tumours because of the unavailability of scans. The authors also ensured that all patients with tumours that did not resemble vestibular schwannomas were excluded. However, in the absence of histological analysis it is possible that the study included some tumours that were not vestibular schwannomas. Large tumours were generally not included in the study as many were treated with microsurgery or radiotherapy as a primary treatment. This may have skewed the results. Similarly, some growing tumours included in the study were treated during the study period. This may also have skewed the results. In particular, it is important to point out that whilst 7.2% of the cohort with demonstrable growth started growing after five years of follow up, this figure may be higher as a significant number of tumours had not been observed for 5 years or more.

Recommendations for Follow Up of Sporadic Vestibular Schwannomas_Undergoing Observation

Based on the results of this study, the authors would suggest that an early scan six months following diagnosis should be performed. This will identify the few tumours that grow rapidly. Scanning should then take place annually for the next three years, the period during which growth is most likely to occur. Subsequently, tumours could be scanned every two years for six years and then every three years subsequently. This protocol balances the need to observe tumours regularly with the costs of overscanning tumours that are unlikely to grow.

Conclusions

This study suggests that observation is a safe method of managing the majority of small and medium sized vestibular schwannomas. Only 33% of small to medium sized sporadic unilateral vestibular schwannomas demonstrate growth. The majority do so within 3 years of diagnosis although growth is unpredictable and may occur well after five years following diagnosis. Scanning intervals can be increased over time but observation should continue beyond five years.

Acknowledgements

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References

1. Zollner C, Bockenheimer S. The growth rate of acoustic neuromas: a report of three cases. Arch Otorhinolaryngol 1985;241(3):259-64.
2. Silverstein H, McDaniel A, Norrell H, Wazen J. Conservative management of acoustic neuroma in the elderly patient. Laryngoscope 1985;95:766-70.
3. Stangerup SE, Caye-Thomasen P, Tos M, Thomsen J. The natural history of vestibular schwannoma. Otol Neurotol 2006;27(4):547-52.
4. Ferri GG, Modugno GC, Pirodda A, Fioravanti A, Calbucci F, Ceroni AR. Conservative management of vestibular schwannomas: an effective strategy. Laryngoscope 2008;118(6): 951-7.
5. Martin TP, Senthil L, Chavda SV, Walsh R, Irving RM. A protocol for the conservative management of vestibular schwannomas. Otol Neurotol 2009;30(3):381-5.
6. Caye-Thomasen P, Hansen S, Dethloff T, Stangerup SE, Thomsen J. Sublocalization and volumetric growth pattern of intracanalicular vestibular schwannomas. Laryngoscope 2006; 116(7):1131-5.
7. Meyer TA, Canty PA, Wilkinson EP, Hansen MR, Rubinstein JT, Gantz BJ. Small acoustic neuromas: surgical outcomes versus observation or radiation. Otol Neurotol 2006;27(3):380-92.
8. Flint D, Fagan P, Panarese A. Conservative management of sporadic unilateral acoustic neuromas. J Laryngol Otol 2005;119(6):424-8.
9. Nader R, Al-Abdulhadi K, Leblanc R, Zeitouni A. Acoustic neuroma: outcome study. J Otolaryngol 2002;31(4):207-10.
10. Sakamoto T, Fukuda S, Inuyama Y. Hearing loss and growth rate of acoustic neuromas in follow-up observation policy. Auris Nasus Larynx 2001;28:S23-7.
11. Perry BP, Gantz BJ, Rubinstein JT. Acoustic neuromas in the elderly. Otol Neurotol 2001; 22(3):389-91.
12. Nutik SL, Babb MJ. Determinants of tumor size and growth in vestibular schwannomas. J Neurosurg 2001;94(6):922-6.
13. Tschudi DC, Linder TE, Fisch U. Conservative management of unilateral acoustic neuromas. Am J Otol 2000;21(5):722-8.

14. Shin YJ, Fraysse B, Cognard C, Gafsi I, Charlet JP, Berges C, et al. Effectiveness of conservative management of acoustic neuromas. Am J Otol 2000;21(6):857-62.
15. Selesnick SH, Johnson G. Radiologic surveillance of acoustic neuromas. Am J Otol 1998; 19(6):846-9.
16. Backous DD, Pham HT. Guiding patients through the choices for treating vestibular schwannomas: balancing options and ensuring informed consent. Otolaryngol Clin North Am 2007;40(3):521-40.
17. Anand VT, Kerr AG, Byrnes DP, Smyth GD. Non-surgical management of acoustic neuromas. Clin Otolaryngol Allied Sci 1992;17(5):406-10.
18. Rosenberg SI, Silverstein H, Gordon MA, Flanzer JM, Willcox TO, Silverstein J. A comparison of growth rates of acoustic neuromas: nonsurgical patients vs. subtotal resection. Otolaryngol Head Neck Surg 1993;109:482-7.
19. Massick DD, Welling DB, Dodson EE, Scholfield M, Nagaraja HN, Schmalbrock P, et al. Tumor growth and audiometric change in vestibular schwannomas managed conservatively. Laryngoscope 2000;110(11):1843-9.
20. Mirz F, Jorgensen B, Fiirgaard B, Lundorf E, Pedersen CB. Investigations into the natural history of vestibular schwannomas. Clin Otolaryngol Allied Sci 1999;24(1):13-8.
21. Yamamoto M, Hagiwara S, Ide M, Jimbo M, Arai Y, Ono Y. Conservative management of acoustic neurinomas: prospective study of long-term changes in tumor volume and auditory function. Minim Invasive Neurosurg 1998;41(2):86-92.
22. Irving RM, Beynon GJ, Viani L, Hardy DG, Baguley DM, Moffat DA. The patient's perspective after vestibular schwannoma removal: quality of life and implications for management. Am J Otol 1995;16(3):331-7.
23. Cross JJ, Baguley DM, Antoun NM, Moffat DA, Prevost AT. Reproducibility of volume measurements of vestibular schwannomas - a preliminary study. Clin Otolaryngol 2006;31(2): 123-9.
24. Rosenberg SI. Natural history of acoustic neuromas. Laryngoscope 2000;110(4):497-508.
25. Marshall AH, Owen VM, Nikolopoulos TP, O'Donoghue GM. Acoustic schwannomas: awareness of radiologic error will reduce unnecessary treatment. Otol Neurotol 2005;26(3):512-5.
26. Charabi S, Thomsen J, Mantoni M, Charabi B, Jorgensen B, Borgesen SE, et al. Acoustic neuroma (vestibular schwannoma): growth and surgical and nonsurgical consequences of the wait-and-see policy. Otolaryngol Head Neck Surg 1995;113(1):5-14.
27. Levo H, Pyykko I, Blomstedt G. Non-surgical treatment of vestibular schwannoma patients. Acta Otolaryngol Suppl 1997;529:56-8.
28. Niemczyk K, Vaneecloo FM, Lemaitre L, Lejeune JP, Skarzynski H, Dubrulle F, et al. The growth of acoustic neuromas in volumetric radiologic assessment. Am J Otol 1999;20(2):244-8.
29. Smouha EE, Yoo M, Mohr K, Davis RP. Conservative management of acoustic neuroma: a meta-analysis and proposed treatment algorithm. Laryngoscope 2005;115(3):450-4.
30. Yoshimoto Y. Systematic review of the natural history of vestibular schwannoma. J Neurosurg 2005;103(1):59-63.
31. Nikolopoulos TP, Fortnum H, O'Donoghue GM, Baguley DM. Acoustic Neuroma Growth: A Systematic Review of the Evidence. Otol Neurotol 2010;31(3):478-485..

Chapter 2.3

Management of the high jugular bulb in translabyrinthine surgery

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N. Quaranta
P. Chang

Laryngoscope 2003;113(3):580-582

Introduction

The translabyrinthine approach for the removal of acoustic neuromas provides the widest and most direct access to the cerebellopontine angle.[1] This is achieved by virtue of the removal of bone over the cranial fossae and sigmoid sinus. The jugular bulb is one of the more chal-lenging areas to skeletonize. The wall of the bulb is thin-ner and less forgiving than that of the sigmoid sinus. Management of the high jugular bulb is an essential skill for the neurotologic surgeon performing the translabyrin-thine approach. Saleh et al.[2] noted that the jugular bulb compromises exposure of the internal auditory canal (IAC) in the translabyrinthine approach in 24% of cases. Failure to control the bulb not only compromises access to the IAC, but also may lead to the life-threatening complications of air embolism and primary hemorrhage.

In the retrosigmoid approach, a high jugular bulb represents a limitation to the lateral exposure of the tu-mor.[3] However, this does not represent a contraindication in the translabyrinthine approach.[4]

A safe technique to inferiorly displace a high jugular bulb in the translabyrinthine approach is detailed and illustrated.

Technique

Adequate Access to the Jugular Bulb

The key to management of a high jugular bulb in the trans-labyrinthine approach is adequate access and good visualisation. A wide-field mastoidectomy provides the basis for adequate lat-eral access in the translabyrinthine approach. This includes skel-etonization of the whole length of the sigmoid sinus with a large diamond paste burr. Failure to do so may lead to a traumatic laceration of the more fixed inferior end of the lateral sinus as the sigmoid wall is retracted posteriorly. Another prerequisite for adequate access to the bulb is complete skeletonization of the descending portion of the facial nerve. This optimizes the anterior exposure of the jugular bulb (Figure 1).

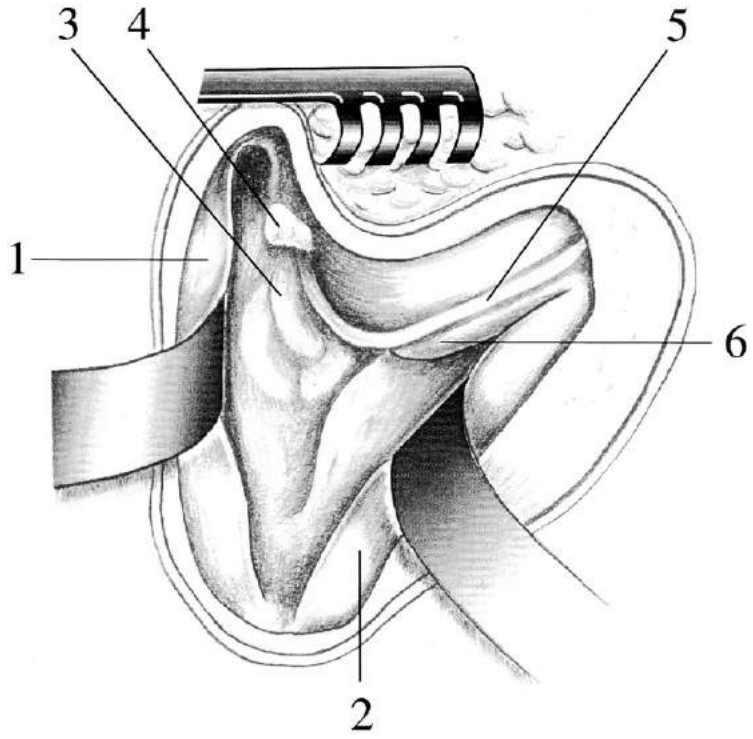

Figure 1: Adequate access to the jugular bulb is by virtue of a wide-field mastoidectomy and skeletonization of the descending portion of the facial nerve. All the figures are a right ear. 1) Middle cranial fossa dura, 2) sigmoid sinus, 3) lateral semicircular canal, 4) incus, 5) facial nerve, 6) jugular bulb.

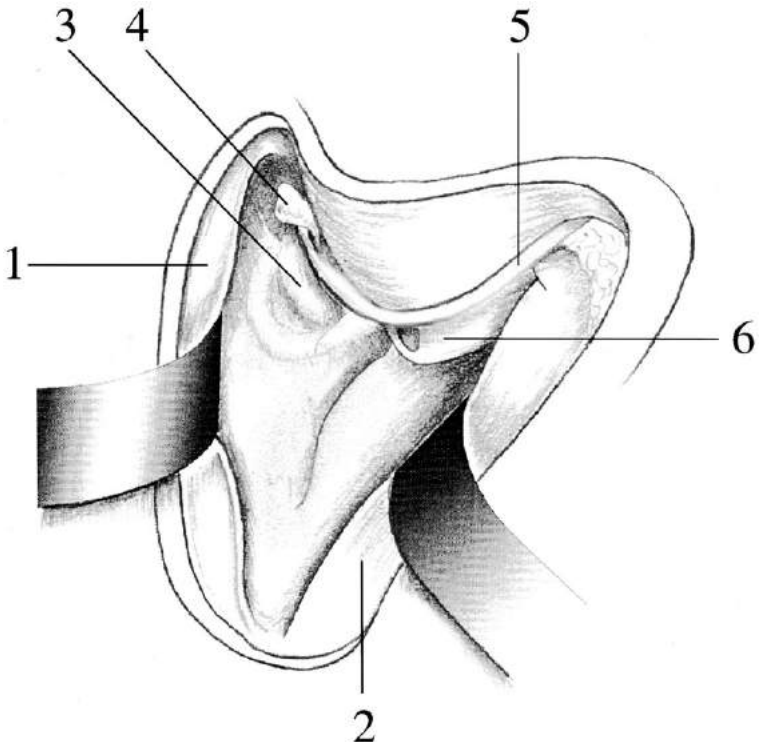

Figure 2: The lateral and superior aspects of the jugular bulb are skeletonized. (Legend as Figure 1).

Skeletonization of the Jugular Bulb

The jugular bulb is skeletonized only once it is adequately exposed. An eggshell of bone is left over its lateral and superior aspects (Figure 2).

Progressive Lowering of the Jugular Bulb

A small patch of Surgicel (Ethicon, Neuchâtel, Switzerland) is placed over the superior aspect of the dome of the exposed bulb, followed by a 5-to 10-mm disc of bone wax, slightly broader than the diameter of the exposed tissue. A neurosurgical lintine and a large, blunt, broad-based instrument (such as the curved end of a blunt dural elevator) are used to impact the bone wax gently through the bony defect onto the jugular bulb (Figure 3).

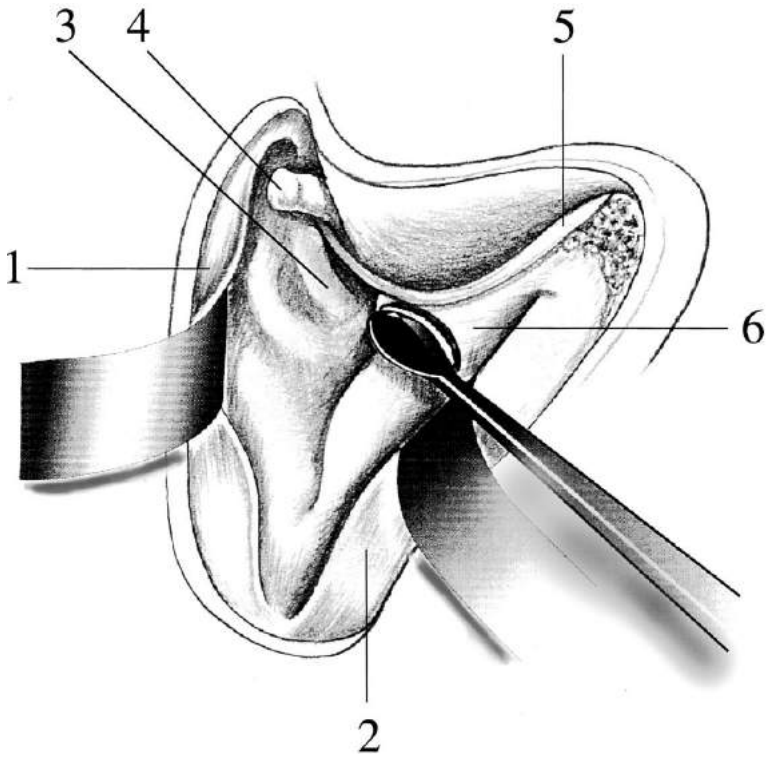

Figure 3: The jugular bulb is progressively lowered by the gentle impaction of bone wax over the exposed jugular bulb. Legend as Figure 1.

The bone wax is further impacted over the jugular bulb by gently drilling on the bone wax with a large diamond paste drill (Figure 4). The bone wax serves to protect the delicate bulb, lower its height, and immediately seal any breach of the wall of the bulb. The surgeon gently removes the bone over the rim of the bulb with a broad diamond drill by feel as much as by direct vision. These steps may need to be repeated a number of times to lower the bulb to an appropriate level. Further discs of

bone wax, impacted with lintine and the drill, serve to progressively displace the bulb inferiorly. At the same time, the added layers of bone wax further increase the protection of the bulb.

Utilizing this technique, the jugular bulb can be lowered as much as necessary to provide the necessary access to the IAC. The end point of lowering the jugular bulb is adequate access to drill a caudal trough to define the inferior border of the IAC (Figure 5). To preserve the lower cranial nerves, drilling inferior to the IAC should not be pushed beyond the cochlear aqueduct.

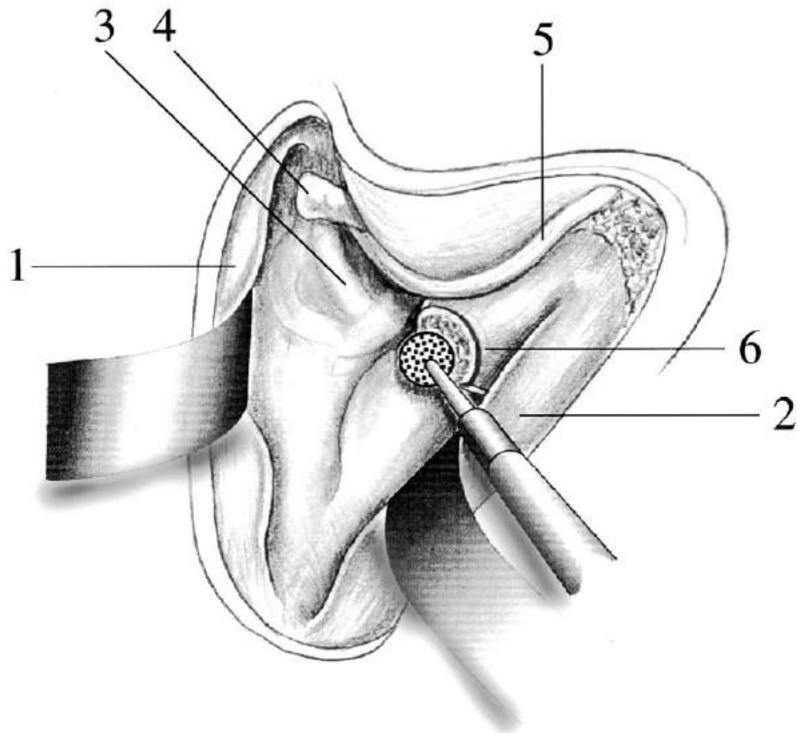

Figure 4: A diamond drill is used to further impact bone wax over the bulb and to continue to gently uncap its osseous covering. Legend as Figure 1.

Removal of the Spicule of Bone Between Sigmoid Sinus and Jugular Bulb

With the bulb under control, the thin spicule of bone lying between the jugular bulb and the distal end of the sigmoid sinus can be safely drilled to maximize exposure. The subsequent steps of the translabyrinthine approach are then performed.

Discussion

The series of the Otoneurosurgical and Skull Base Surgery Unit in Cambridge numbers more than 750 acoustic neuromas resections to date. The technique de-tailed has been employed successfully to manage all cases of high jugular bulb, regardless of height. The jugular bulb has never proven to be a contraindication to the translaby-rinthine approach.

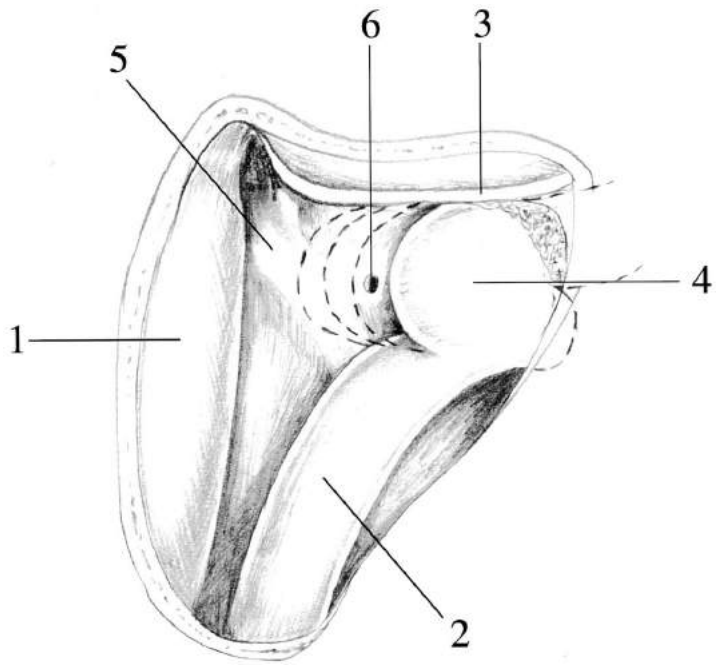

Figure 5: The jugular bulb can be lowered as much as necessary to provide the necessary access to the IAC. 1) Middle cranial fossa dura, 2) sigmoid sinus, 3) facial nerve, 4) jugular bulb, 5) internal auditory canal, 6) cochlear aqueduct.

There are still some opponents to the philosophy of displacing the jugular bulb inferiorly to obtain a wider exposure of the IAC.[4] It is argued that there is a high risk of bleeding from the bulb, central venous infarction, and damage to the contents of the pars nervosa of the jugular foramen.[4] None of these complications has been seen by the authors with the use of this technique.

Using this technique, the chances of bleeding from the jugular bulb is minimized for a number of reasons. First, the endothelium of the jugular bulb wall does not come into contact with any of the surgical instruments or the drill throughout the operation. The wall of the jugular bulb is always protected by Surgicel and bone wax before the bone over the bulb is further uncapped with a diamond burr (Figure 4). Second, the bulb is separated from the over-lying bone by the application of gentle pressure over

the bone wax and the neurosurgical lintine. As opposed to the sigmoid sinus, the dome of the jugular bulb is only mini-mally attached to the overlying bone, lending itself to easy blunt dissection.

The technique described does not occlude the lumen of the lateral sinus. Rather, it only lowers the apex of the dome of the bulb (Figure 5). Therefore, the complications associated with lateral sinus occlusion or damage to the pars nervosa do not arise.

In the event of any inadvertent injury to the jugular bulb, the same technique can also be used to control bleed-ing. This controls even torrential bleeding quickly and safely. Since the pieces of bone wax are significantly wider then the defect in the bulb, it is sealed rapidly and pre-vents the chance of air embolization.

Conclusion

The technique described is rapid and reliable in pro-viding the necessary access to the IAC in the translaby-rinthine approach, by safely overcoming the potential haz-ard of the high jugular bulb.

References

1. Fagan P, Sheey JP, Chang P, Doust BD, Coakley D, Atlas MD. The cerebellopontine angle: does the translabyrinthine approach give the adequate access? Laryngoscope 1998;108:679–682.
2. Saleh E, Aristegui M, Taibah AK, Mazzoni A, Sanna M. Management of high jugular bulb in translabyrinthine ap-proach. Otolaryngol Head Neck Surg 1994;110:397–399.
3. Rauch S, Xu WZ, Nadol JB. High jugular bulb: Implications for posterior fossa neurotologic and cranial base surgery. Ann Otol Rhinol Laryngol 1993;102:100–107.
4. Friedman R, Brackmann DE, van Loveren HR, Hitselberger WE. Management of the contracted mastoid in the translabyrinthine removal of acoustic neuroma. Arch Otolaryngol Head Neck Surg 1997;123:342–344.

Chapter 2.4

Moffat classification of facial nerve function

David A. Moffat

A Supplemental Issue for The 11th Keio University International Symposium for Life Sciences and Medicine.Consensus Meeting on Systems for Reporting Results in Acoustic Neuroma

Keio Journal of Medicine 2001;Vol 50,Suppl 4:38-39

Summary

A reliable and sensitive facial nerve grading system is necessary to accurately assess facial nerve function after injury and to enable a meaningful comparison of facial nerve outcome after vestibular schwannoma surgery between surgical units. A number of previously published facial nerve grading systems have been proposed. The House-Brackmann (HB) grading system for facial nerve function, which was adopted as a universal standard for grading facial nerve recovery by the Facial Nerve Disorders Committee of the American Academy of Otolaryngology-Head and Neck Surgery in 1985, has moderate test-retest reliability and interobserver agreement. The deficiencies of this grading system are that HB grade III is unsatisfactory and poorly discriminatory with regard to the eye and that na account has been taken of nervus intermedius function. Also, there is no means of recording the presence of synkinesis and hemifacial spasm. This chapter proposes a new facial nerve grading system that corrects these shortcomings.

Introduction

A reliable and sensitive facial nerve grading system is necessary to accurately assess facial nerve function after injury and to enable a meaningful comparison of facial nerve outcome after vestibular schwannoma surgery between surgical units. A nurnber of facial nerve grading systems have been published.[1-13] House[8] published a detailed and critical analysis of these systems in 1983 and proposed a grading system that incorporated their strengths and eradicated their weaknesses. He divided facial nerve grading systems into three categories: gross, regional, and specific.

Gross systems[1,3,5,8] give an overall grading of facial function. No effort is made to weight different areas of the face or to consider secondary effects such as synkinesis or mass movement. Regional systems[2,4,6] require that an observer assess different are as of the face independently. Facial movements in these areas are then summed and scores expressed either in nominal form or as a percentage of normal. Specific systems [7,9,10] address the presence or absence of various associated symptoms and signs, and utilize a scoring system for qualitative and quantitative defects. Secondary effects are scored separately.

Recently proposed facial grading systems have either been objective or subjective. The Burres-Fisch linear measurement index (BF-LMI), published in 1986[11], is an objective system that involves the measurement of five standard facial expressions.

In 1990, Croxon et al.[14] compared the HB facial grading system with the BF-LMI with the purpose of determining which of the two systems would be best for clinical application. The authors found a high degree of correlation between the two systems in spite of the fact that the HB scale was subjective and qualitative and the BF-LMI was objective and quantitative. It was stated that the BF-LMI was time consuming and cumbersome to use. Murty et al. in 1994[12] proposed a simplified version of the BF-LMI, and this method has also demonstrated a high degree of correlation with the HB facial grading system using a desktop digital imaging program.

As part of an excellent overview, Chee and Nedzelski[13] proposed a subjective system entitled the Sunnybrook (Toronto) facial grading system. This subjective method assesses the face at rest and during voluntary movements. It also assesses the presence or absence of secondary defects associated with each of five voluntary movements and also grades the severity of these if present. The authors suggest the use of the HB facial grading system for stabie facial nerve dysfunction but advocate the Sunnybrook system for monitoring changes in facial function because of its sensitivity and reliability.

The House- Brackmann (HB) grading system for facial nerve function was adopted as a universal standard for grading facial nerve recovery by the Facial Nerve Disorders Committee of the American Academy of Otolaryngology- Head and Neck Surgery in 1985.[10]. It has been used throughout the world since then and has enabled a meaningful comparison of facial nerve outcome after vestibular schwannoma surgery to be made between surgical units. House[8] proposed a six-point descriptive scale (Table 1) concluding that a gross system was the simplest and most practical to use clinically. In 1984, Brackmann and Barrs[9] provided an easy objective method of measuring facial function to assist in placing patients in the proper HB grade. The movements of the eyebrow and corner of the mouth are measured and the results are compared with measurements of the unaffected side. Movements are measured using a Scale with 0.25-cm divisions; there is a total possible score of 8 (4, or 1 cm for the mouth and 4, or 1 cm, for the eyebrow). These results are easily converted to the six-point sca1e. Various investigators have attempted to validate its reliability and sensitivity. Subjective assessments by Evans et al.[15] indicated an interobserver reliability of 93%, conduding that it was a robust system. Ross et al.[16] reported that clinical improvement could be detected in patients with facial paralysis over time even though the HB grade remained the same, casting doubt on its sensitivity as a grading tool. Rickenmann et al.[17] pointed out that when compared with a globa! reference the HB facial grading system did not meet the Carmines and Zeller[18] criteria required of a grading system of international standard. Correlations with objective methods have been applied since the availability of newer facial

imaging technology.[19] Ahrens et al.[20] used a computer-assisted rapid grading system and with computer-performed scoring found a moderate test-retest reliability and interobserver agreement.

Table 1: House-Brackmann facial nerve grading system

Grade	Description	Characteristics
I	Normal	Normal facial function in all areas
II	Mild dysfunction	Gross: slight weakness noticeable on close inspection; may have very slight synkinesis At rest: normal symmetry and tone Motion: Forehead: moderate to good function Eye: complete closure with minimum effort Mouth: slight asymmetry
III	Moderate dysfunction	Gross: obvious but not disfiguring difference between two sides; noticeable but not severe synkinesis, contracture and/or hemifacial spasm At rest: normal symmetry and tone Motion: Forehead: slight to moderate movement Eye: complete closure with effort Mouth: slightly weak with maximum effort
IV	Moderately severe dysfunction	Gross: obvious weakness and/or disfiguring asymmetry At rest: normal symmetry and tone Motion: Forehead: none Eye: incomplete closure Mouth: asymmetrical with maximum effort
V	Severe dysfunction	Gross: only barely perceptible motion At rest: asymmetry Motion: Forehead: none Eye: incomplete closure Mouth: slight movement
VI	Total paralysis	No movement

The well-recognized problem with this classification, however, has been House grade III. The attainment of this grade of function has generally been regarded by surgeons as a satisfactory outcome and indeed most series quote House grades I-lIl as satisfactory and House IV-VI as unsatisfactory. Many patients with this grade of facial nerve function are, however, incapacitated with a dry eye, or exposure keratitis, and many require a lateral or medial tarsorrhaphy or a gold weight in the upper eyelid.

The HB facial grading system does not take into account nervus intermedius function. The results of facial nerve outcome following vestibular schwannoma

surgery have ignored the sensory component of the nerve.[21]

In view of the effect of aberrant regeneration of the facial nerve on the patient's quality of life[22] with respect to nervus intermedius and the possible sequelae of crocodile tears, metallic taste in the mouth or dysgeusia, dry eye, and exposure keratitis, it is important to record the results with regard to the sensory component of the nerve as well as the motor component in any surgical outcome analysis.

This chapter suggests a new facial nerve grading system that corrects these deficiencies. Table 2 delineates the classification with regard to the motor component of the facial nerve. Grades I and II, IV, V, and VI equate to the HB grades, but synkinesis and hemifacial spasm are graded separately. Moffat grade III is subdivided into A and B to take into account eye discomfort and exposure keratitis, which can have such a profound effect on quality of life. The grading of nervus intermedius or the sensory branch of the facial nerve (Table 3) documents the patient's status with regard to crocodile tearing, metallic or aberrant taste, and dry eye, presented as a suffix. along with the presence or absence of hemifacial spasm and synkinesis.

Table 2: Moffat facial nerve grading system (motor component of the fadal nerve)

Moffat grade I equates to HB grade I
Moffat grade ll equates to HB grade ll
Moffat grade III is subdivided as follows:
Grade III A: competent eye closure, eye comfortable and in good condition with or without lubricants
Grade III B: competent eye closure, but eye dry and uncomfortable with evidence of exposure keratitis requiring lubricants and possibly medial or lateral tarsorrhaphy or a gold weight in the upper eyelid
Moffat grade VI equates to HB grade IV
Moffat grade V equates to HB grade V
Moffat grade VI equates to HB grade VI
HB, House-Brackmann

For example, a patient with a Moffat grade III B-C1 TO E1 HO S1 would have good eye closure but an uncomfortable eye with exposure keratitis, crocodile tears, no taste abnormality, a dry eye, no hemifacial spasm, but synkinesis present. A patient with a Moffat grade II CO TO EO H1 S1 would have almost normal facial movement with minimal asymmetry, no crocodile tears, no taste abnormality, no dry eye, but hemifacial spasm and synkinesis present.

This dassification allows a comprehensive, accurate, and reliable assessment of the patient's facial nerve status in all respects.

Table 3: Moffat facial nerve grading system (sensory: nervus intermedius function is classifted with a suffix)

Crocodile tears (C)
C0, no crocodile tears
C1, crocodile tears present
Metallic or aberrant taste (T)
T0, no aberrant taste
T1, metallic or aberrant taste present
Dryeye (E)
E0, no dry eye
E1, dry eye present
Hemifacial spasm (H)
H0, no bemifacial spasm present
H1, hemifacial spasm present
Synkinesis (S)
S0, no synkinesis present
S1, synkinesis present

References

1. Botman JWM, Jongkees LBW. The results of intratemporaI treatment of facial palsy. Pract Oto-Rhino-LaryngoI 1955;17:80-100.
2. Janssen FP. Ouvre de Postoperative Facialis-Verlamming. Thesis, University of Amsterdam, Amsterdam 1963.
3. May M. Facial paralysis. peripheral type: a proposed method of reporting (emphasis on diagnosis and prognosis, as well as e!ectrical and chorda tympani nerve testing). Laryngoscope 1970;80(3):331-390.
4. Adour KK, Swanson PJ Jr. Facial paralysis in 403 consecutive patients with Be!l's palsy. Trans Am Acad Ophthalmol OtolaryngoI 1971;75(6):1284-1301.
5. Peltersen E. Spontaneous course of Be!l's palsy. In: Fisch U (ed) Facial nerve surgery, Zurich, 1976. AesculapiuS, Birmingham, AL, 1977;337-343.
6. Yanagihara N. Grading of facial palsy. In: Fisch U (ed) Facial nerve surgery. Proceedings, third international symposium on facial nerve surgery, Zurich, 1976. Aesculapius, Birmingham, AL,1977;533-535.
7. Stennert E. Facial nerve paralysis scoring system. In: Fisch U (ed) Facial nerve surgery. Proceedings, third. international symposium on facial nerve surgery, Zurich, 1976. Aesculapius, Birmingham, AL,1977;543-547.
8. House JW. Facial nerve grading systems. Laryngoscope 1983;93:1056-1069.
9. Brackmann DE, Barrs DM. Assessing recovery of facial function following acoustic neuroma surgery. Otolaryngol Head Neck Surg 1984;92(1):88-93.
10. House TW, Brackmann DE. Facial nerve grading system. Otolaryngol Head Neck Surg 1985;93: 146-147.
11. Burres SA, Fisch U. The comparison of facial grading systems. Arch Otolaryngol Head Neck Surg 1986;112:755-758.
12. Murty GE, Diver JP, Kelly PJ, et al. The Nottingham system: objective assessment of facial nerve function in the clinic. Otolaryngol Head Neck Surg 1994;110(2):156-161.
13. Chee GH, Nedzelski JM. Facial nerve grading systems. Facial Plast Surg 2000;16:315-324.
14. Croxon G, May M, Mester SJ. Grading facial nerve function: House-Brackmann versus Burres-Fisch methods. Am J Otol 1990;11(4):240-246.
15. Evans RA, Haries ML, Baguley DM, et al. Reliability of the House and Brackmann grading system for facial palsy. J Laryngol Otol 1989;l03(11):1056.
16. Ross BG, Fradet G, Nedzelski JM. Development of a sensitive clinical facial grading system. Otolaryngol Head Neck Surg 1996;114(3):380-386.

17. Rickenmann J, Jaquenod C, Cerenko D, et al. Comparative value of facial nerve grading systems. Otolaryngol Head Neck Surg 1997;117(4):322-325.
18. Carmines EG, Zeller RA. Reliability and valid assessment. In: Sage University paper series on quantitative applications in social sciences. Sage, Beverly Hills, 1979;7-17.
19. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-174.
20. Ahrens A, Skarada D, Wallace M, et al. Rapid simultaneous comparison system for subjective grading scales for facial paralysis. Am J Otol 1999;20:667-671.
21. lrving RM, Viani L, Hardy DG, et al. Nervus intermedius function after vestibular schwannoma removal: clinical features and pathophysiological mechanisms. Laryngoscope 1995;105:809-813.
22. lrving RM, Beynon GJ, Viani L, et al. The patient's perspective after vestibular schwannoma removal: quality of life and implications for management. Am J Otol 1995;16(3):331-337.

Chapter 2.5

Factors affecting final facial nerve outcome in vestibular schwannoma surgery

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D.G. Hardy
R. Macfarlane

Skull Base, 2011 Submitted

Abstract

Objective: To determine factors affecting the long term facial nerve outcome of vestibular schwannoma surgery.

Study Design: Retrospective cohort study.

Setting: Tertiary referral centre for skull base surgery.

Methods and outcome measures: Facial nerve outcome was assessed using the House Brackmann (HB) classification at 2 years postoperatively. HBI/II was classified as normal facial function, a satisfactory result was HB I-III and an unsatisfactory result was categorised as HB IV-VI. Facial nerve outcome was analysed for the whole series and for the translabyrinthine and retrosigmoid approaches in tumour size increments and also exact tumour size. Satisfactory outcome was also determined for each sequential 3 year interval over the study period and outcome in the in the last 6 years was analysed separately. A univariate analysis was performed to determine the effect of sex, age, tumour size, operative approach and year of surgery on facial nerve outcome. A multivariate analysis was then performed. Nervus intermedius function and aberrant regeneration of the facial nerve in terms of hemifacial spasm, metallic taste and crocodile tears was determined at 3 and 24 months. A comparison was made of the incidence of these symptoms in the normal facial nerve function group and the partial recovery group at 24 months postoperative.

Patients: 652 patients with histologically proven sporadic unilateral vestibular schwannomas treated surgically either by the translabyrinthine or the retrosigmoid approach between the years 1981 and 2010 were included. There were 321 males and 331 females in the series. The age range was 13-86 years with a mean of 53.8 yrs (SD 12.6). Tumour size was measured as the maximum medio-lateral diameter in centimetres in the axial plane including both intracanalicular and extracanalicular portions.

Results: The mean tumour size was 2.6cm with a range of 0.7-5.5cm. There were 563 (86%) translabyrinthine operations and 89 (14%) retrosigmoid. The facial nerve was maintained intact in 97% of cases. Current facial nerve outcome from vestibular schwannoma surgery over the last 6 years is, for tumours less than 1.5cm, 95% were normal, 100% were satisfactory (HB I-III) and 0% unsatisfactory (HB IV-VI). For tumours 1.5-2.4cm in size, 83% were normal, 99% were satisfactory and 1% were

unsatisfactory. In tumours 2.5-3.4cm, 68% were normal, 96% were satisfactory and 4% unsatisfactory. Tumours 3.5-4.4cm produced a normal outcome in 52%, satisfactory in 80% and unsatisfactory in 20%. For tumours equal to and larger than 4.5cm, 50% were normal, 72% were satisfactory and 28% were unsatisfactory.
The results of a univariate and multivariate analysis showed that tumour size and year of operation were significant predictors of facial nerve outcome. There was insufficient evidence that sex, age and operation approach were associated with facial nerve outcome after adjusting for tumour size and year of operation.
The surgical learning curve was steepest in the first 50 patients and then flattened out until the last 6 years when there was a further incremental improvement.
Investigation of nervus intermedius function and aberrant regeneration of the facial nerve showed that there was a 13% chance of developing hemifacial spasm at some time post-operatively and of these patients there was a 42% chance of it resolving by 24 months.
There was a 36% chance of developing metallic taste at some time post-operatively and of these patients there was a 52% chance of it resolving by 24 months.
There was a 25% chance of developing crocodile tears at some time post-operatively and recovery is much less likely than with metallic taste and in only 15% did it resolve by 24 months.
There was a significantly greater likelihood of hemifacial facial spasm in the partial facial nerve recovery group compared with the normal facial function group. There was no significant difference, however, between these two groups when considering metallic taste and crocodile tears.

Conclusions: Facial nerve outcome of vestibular schwannoma surgery has improved dramatically over the past 40 years. Outcome depends not only on various clinical determinants but also intraoperative technical factors and facial nerve monitoring. It may also be influenced by the "team" learning curve and a change of personnel. The surgical learning curve may be reduced by proleptic appointments and by "surgical dovetailing" with inexperienced surgeons working alongside more experienced senior colleagues.

Introduction

The first successful preservation of the facial nerve during complete excision of a vestibular schwannoma is attributed to Sir Hugh Cairns in 1931.[1] Although McKissock reported a remarkable series of facial and cochlear nerve preservation in 1961[2], without the aid of magnification, the introduction of the operating microscope

in the same year by William House was an important milestone in vestibular schwannoma surgery.[3] These microsurgical advances paved the way to fulfilling the primary goal of vestibular schwannoma surgery which is complete tumour removal with minimal morbidity and mortality.[4]

Many centres throughout the world now achieve high rates of facial nerve preservation and good post-operative facial nerve function.[5-12] Unfortunately, anatomical continuity of the facial nerve does not always result in good long-term facial recovery and if rehabilitative procedures are to be performed, the most favourable results are likely if corrective surgery is undertaken relatively early.

It is important in counselling patients pre-operatively to inform them of the likely outcome with regards to facial nerve function including nervus intermedius[13] since this is an important pre-determinant of post-operative quality of life. It will also form part of an evidence base for the surgical modality of management in comparison with the other two modern modalities of observation with interval imaging and stereotactic radiotherapy. It is not only important for the surgeon to be able to quote his own facial nerve outcome figures but also to be cognisant of the predictive factors which influence facial nerve outcome in vestibular schwannoma surgery.

This detailed study of a large series of patients over three decades is an attempt to identify patient and surgical variables which influence facial nerve outcome and quality of life after vestibular schwannoma excision.

Methods and outcome measures

This study is a retrospective case note analysis of a series of patients with a unilateral sporadic vestibular schwannoma (VS) and preoperatively normal facial nerve function (House Brackmann Grade I) treated surgically either by the trans-labyrinthine or by the retrosigmoid approach by the senior authors (DAM with DGH or RMac) between the years 1981 and 2010 at Addenbrookes, Cambridge University Teaching Hospital. Clinical data was collected on a 250 point database using Filemaker Pro 6 initially and more recently on Filemaker Pro 10 software. Patients with neurofibromatosis type 2 (NF2) and those receiving preoperative stereotactic radiotherapy and those patients with recurrent tumour referred from other units were excluded from this analysis.

Facial nerve function was assessed at 3 months and one, two and 5 years postoperatively. The final facial nerve outcome was recorded at 2 years postoperatively for this data analysis.

Facial nerve function was assessed using the House and Brackmann (HB) grading system.[14] Totally normal function was classified as HB I but HB I/II was also recorded since some modern series quote this as normal. HBI-III was classified as a satisfactory outcome and HB IV-VI as unsatisfactory at 24 months after surgery. An analysis of the facial nerve outcome at 24 months post-operatively for the translabyrinthine approach and separately for the retrosigmoid approach was carried out for each tumour size increment <1.5cm, 1.5-2.4cm, 2.5-3.4cm, 3.5-4.4cm and equal to or greater than 4.5cm both in total numbers and percentages (tables 1 and 3). Facial nerve outcome for both approaches using the percentage of patients with HBI/II, HBI-III and HBIV-VI was tabulated (tables 2 and 4).
The rate of anatomical preservation of the facial nerve was recorded and the type of facial reconstruction and functional outcome was documented in those few cases where the facial nerve was lost (table 6). Nervus intermedius function and aberrant regeneration of the facial nerve in the form of altered taste and crocodile tears were recorded at 3 and 24 months postoperatively along with the percentage that developed and recovered over time.
Magnetic resonance imaging (MRI) was performed at 2 and 5 years postoperatively.

Chi-squared tests for trend were used to determine the individual effects of gender, tumour size (categorical) and operation approach on facial nerve outcome. (A Chi-squared test for trend is a version of the ordinary Pearson's Chi-squared test which takes into account the ordinal nature of the facial nerve outcome variable.) A Chi-squared test for trend was also used to compare HB grading in the first decade (1981-1990) with the second and third decades (1991-2010).

Data on exact tumour size was available for 652 out of 1018 patients on the database (64%), which was used to confirm the results using categories of tumour size. In order to investigate if there was a significant relationship between HB grading and tumour size, a linear regression model was applied to the exact tumour size data with facial nerve outcome entering the model as a predictor variable. Similarly, a linear regression method was used to evaluate the effect of age on facial nerve outcome.

Multivariate analysis was used in the form of a multiple logistic regression method to investigate predictors of satisfactory facial nerve outcome (HB I-III), and to determine if variables found to be significant univariately remain so after adjusting for other important variables.
A multiple logistic regression model was fitted to facial nerve outcome with sex, age, operative approach and year of operation after 1981 included as exploratory

variables in the model. Additionally, tumour size was included in the model as an exploratory factor variable, taking different levels corresponding to the pre-defined tumour size groups, with tumour size less than 1.5cm as the reference category. Results were also presented using exact tumour size as well. Male was used as the reference group for *gender*. Translabyrinthine approach was used as the reference group for *operative approach*.
Odds ratios (OR) were presented with 95% confidence intervals (95% CI) and p-values (see table 7 in results section).
It was important to determine if there was a trend in improvement over time particularly in relation to a surgical learning curve. Outcome was thus also analysed in the form of a bar chart of 3 year surgical segments over time and also by an assessment of facial nerve outcome in tumour size increments for the most recent 6 years of surgery in the series in tabloid form (table 9).

Patients

The surgical series was comprised of 652 patients with histologically proven sporadic unilateral vestibular schwannomas. There were 321 male patients and 331 females. The age range was 13 to 86 years with a mean of 53.8 years and a standard deviation (SD) of 12.6 yrs. The age distribution in decades can be seen in Figure 1.

Maximum mediolateral tumour diameter including the intracanalicular portion was used to assess tumour size since the series extends back to 1980 and this was the method used at that time. The authors are cognisant of the more recent measure of maximum intracranial tumour diameter (ICTD)[15] where solely intracanalicular (VS=0mm) tumours are stated as such. For the sake of consistency we have used the former measurement method throughout. Maximum tumour size was measured in centimetres for each individual tumour and also classified in increments as less than 1.5cm, 1.5-2.4cm, 2.5-3.4cm, 3.5-4.4cm, and 4.5cm or larger as in Figure 2.
There were 563 (86%) translabyrinthine operations and 89 (14%) retrosigmoid approaches performed.
The extent of the excision was classified as total, near total, subtotal and partial. Total removal was complete excision of the tumour. Near total was defined as complete excision apart from tiny remnants of capsule on a cranial nerve or brainstem. Subtotal excision meant greater than 95% of tumour removed and partial excision where less than 95% of the tumour was removed. The categorisation of the extent of tumour excision can be seen in Figure 3. The facial nerve outcome quantified as

normal, satisfactory and unsatisfactory, as previously defined, was determined in relation to the extent of the excision as seen in Table 5.

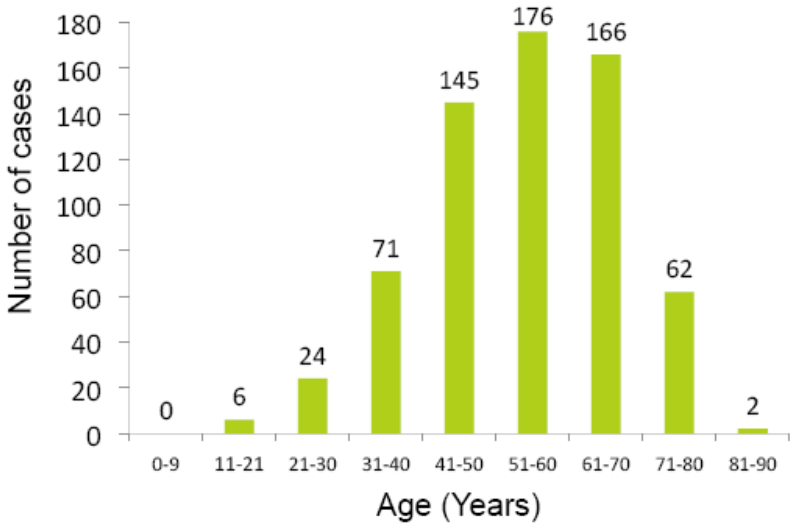

Figure 1: Distribution by age (n=652)

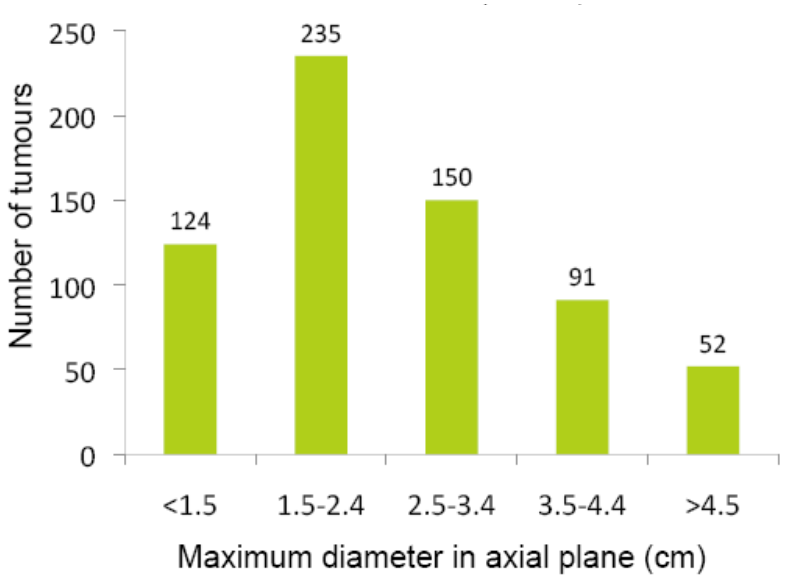

Figure 2: Tumour size (n=652)

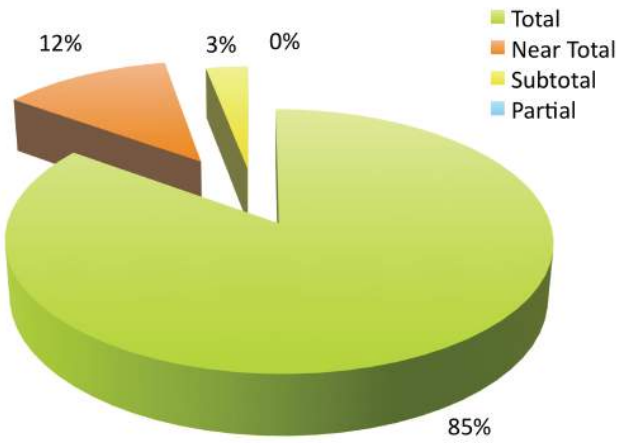

Figure 3: Extent of tumour excision (n=652)

Results and analysis

The 24 months postoperative functional facial nerve outcome for the whole series following translabyrinthine surgery for the various increments of tumour size can be seen in Table 1.
A summary in terms of HB I/II outcome classified as normal, HB I-III classified as satisfactory and HB IV-VI classified as unsatisfactory can be seen in Table 2.
For tumours less than 1.5cm, 79% had a normal functional outcome, 96% were satisfactory and only 4% unsatisfactory. The outcome for tumours 1.5-2.4cm was 68% normal, 94% satisfactory and 6% unsatisfactory. For tumours 2.5-3.4cm this dropped to 52% normal, 84% satisfactory and 16% unsatisfactory and for tumours 3.5-4.4cm, 45% normal, 76% satisfactory and 24% unsatisfactory and very large tumours equal to or greater than 4.5cm, 43% were normal, 74% satisfactory and 26% unsatisfactory.

A similar analysis for the smaller number of retrosigmoid cases is in table 3. It is important to note that we reserve this approach for patients with smaller tumours who have opted for hearing preservation surgery and the numbers , therefore of tumours 3.4-4.5 and equal to and larger than 4.4cm are too small to be meaningfully analysed.

Table 1: Facial nerve functional outcome at 24 months
Translabyrinthine surgery n=563

Tumour Size-cm	n	HBI n(%)	HBII n(%)	HBIII n(%)	HBIV n(%)	HBV n(%)	HBVI n(%)
< 1.5	97	64(66.0)	13(13.4)	16(16.5)	3(3.1)	0(0)	1(1)
1.5-2.4	195	93(47.7)	40(20.5)	51(26.2)	3(1.5)	1(0.5)	7(3.6)
2.5-3.4	126	44(34.9)	21(16.7)	41(32.5)	6(4.8)	2(1.6)	12(9.5)
3.5-4.4	98	23(23.5)	21(21.4)	30(30.6)	5(5.1)	2(2.0)	17(17.3)
> 4.4	47	11(23.4)	9(19.2)	15(31.9)	3(6.4)	1(2.1)	8(17.0)

Table 2: Facial nerve outcome at 24 months - HBI/II, satisfactory/unsatisfactory
Translabyrinthine surgery n=563

Tumor Size-cm	n	HBI/II normal	HBI-III satisfactory	HBIV-VI unsatisfactory
< 1.5	97	79%	96%	4%
1.5-2.4	195	68%	94%	6%
2.5-3.4	126	52%	84%	16%
3.5-4.4	98	45%	76%	24%
> 4.4	47	43%	74%	26%

Table 3: Facial nerve functional outcome at 24 months
Retrosigmoid surgery n=89

Tumour Size-cm	n	HBI n(%)	HBII n(%)	HBIII n(%)	HBIV n(%)	HBV n(%)	HBVI n(%)
< 1.5	31	19(61.3)	7(22.6)	4(12.9)	0(0)	0(0)	1(3.2)
1.5-2.4	38	26(68.4)	5(13.2)	6(15.8)	0(0)	0(0)	1(2.6)
2.5-3.4	12	4(36.4)	4(36.4)	2(18.2)	0(0)	0(0)	1(9.1)
3.5-4.4	4	0(0)	0(0)	3(75)	1(25)	0(0)	0(0)
> 4.4	5	1(20.0)	1(20.0)	2(40.0)	0(0)	0(0)	1(20.0)

Table 4: Facial nerve outcome at 24 months - HBI/II, satisfactory/unsatisfactory
Retrosigmoid surgery n=80

Tumour Size-cm	n	HBI/II normal	HBI-III satisfactory	HBIV-VI unsatisfactory
< 1.5	31	84%	97%	3%
1.5-2.4	38	82%	95%	5%
2.5-3.4	11	73%	91%	9%
Too few cases to analyse meaningfully for cases 3.5-4.4cm and >4.4cm.				

Table 5: Facial nerve outcome at 24 months related to extent of tumour excision

Tumour Excision	N=652	HBI/II normal	HBI-III satisfactory	HBIV-VI unsatisfactory
Total	636	61% (389)	88% (559)	12% (77)
Near total	26	46% (12)	73% (19)	27% (7)
Subtotal	1	(1)	(1)	(0)
Partial	0			

A summary in terms of HB I/II classified as normal, HB I-III classified as satisfactory and HB IV-VI classified as unsatisfactory can be seen in Table 4.

For tumours less than 1.5cm, 84% had a normal functional outcome, 94% were satisfactory and only 6% unsatisfactory. The outcome for tumours 1.5-2.4cm was 76% normal, 95% satisfactory and 5% unsatisfactory. For tumours 2.5-3.4cm this was 75% normal, 92% satisfactory and 8% unsatisfactory.

Total tumour excision was achieved in 85% of cases, near total in 12%, subtotal in 3% and there were no partial excisions. The facial nerve outcome categorised as normal (HB I/II), satisfactory (HBI-III) and unsatisfactory (HBIV-VI) for total, near total and partial excisions can be seen in Table 5.

Total tumour excision was achieved in 636 patients and 61% (389) had a normal facial nerve outcome (HBI/II), a satisfactory outcome was noted in 88% (559) and an unsatisfactory outcome in 12% (77). We usually attempt total tumour excision and where there is a less than total excision it is because we wish to preserve facial nerve function and optimise postoperative quality of life. Near total excision where remnants of tumour are left on the facial nerve, root entry zone or brainstem reflect adherence of matrix to one or more of these structures and reflect difficulty in dissection. This is reflected in the normal facial nerve outcome of 46% (12) satisfactory in 73% and unsatisfactory in 27% (7). There was only one subtotal and no partial excisions.

97% (632) of facial nerves were intact at the end of surgery and 20 (3%) of facial nerves were lost. The type of facial nerve repair and the post-operative functional facial nerve outcome and also static procedures can be seen in table 6. The most satisfactory results are obtained by direct anastomosis but it is often not possible to obtain enough length to be able to perform this procedure without placing the nerve repair under too much tension.

Table 6: Postoperative outcome of facial nerve reanimation procedures

Procedure	Patients (n=20)	Outcome – HB Grade
Direct anastomosis	1	3
	1	3
Cable graft	1	3
Facio-hypoglossal	1	3
	1	3
	1	3
	1	3
	1	3
	1	4
	1	4
	1	4
	1	4
Cross facial graft	1	3
	1	3
	1	4
	1	6
Static procedures:- Gold weight eyelid Fascial sling Face lift	4	n/a

Univariate analysis

Patient gender

There was no statistically significant difference in facial nerve outcome between males and females at the 5% level of significance. The resulting test statistic for the Chi-squared test by trend was 3.54 with a corresponding p-value of 0.06.

Patient age

There did appear to be a significant increase in age with increasing HB score after performing simple linear regression analysis (t-statistic = 1.99, p-value = 0.047). This was just significant univariately but not multivariately.

Tumour size

Tumour size in 1cm increments

As expected the facial nerve outcome was worse for larger tumours compared with smaller ones. The Chi – squared test statistic for testing the association between

tumour size and facial nerve outcome was 82.6 with a corresponding p-value of <0.0001. There was thus a strongly significant relationship between tumour size and facial nerve outcome.

Exact tumour size in mm

A linear regression model was applied to the exact tumour size data with facial nerve outcome entering the model as a predictor variable for the purposes of the test. Linear regression generated a t-statistic of 7.31 with a p-value of <0.0001 and there was a highly significant relationship between tumour size and facial nerve outcome.

Operative approach

A Chi-squared test by trend yielded a resulting test statistic of 9.13 with a corresponding p-value of 0.003. Thus the retrosigmoid approach appeared to result in a statistically better facial nerve result but this was not the case when adjusting for tumour size, age, sex and year of operation. This was probably because only patients with small tumours opting for hearing preservation surgery underwent a retrosigmoid procedure.

Surgery performed in the decade 1981-1990 compared with 1991-2010

Facial nerve outcome following surgery in the first decade (1981-1990) was significantly worse than in the succeeding two decades (1991-2010). A Chi-squared test by trend produced a statistic of 63.9 with a corresponding p-value of <0.0001 which was statistically significant at the 5% level. The operative learning curve is the most likely explanation for this and will be elucidated in the section on this.

Multivariate analysis

The multiple logistic regression method was used to investigate predictors of satisfactory facial nerve outcome (HB I/II). The model was fitted to the data and the results are shown in table 7.

Tumour size was found to be significantly associated with satisfactory facial nerve outcome. The larger the tumour size the lower the probability of observing a satisfactory facial nerve outcome. For those patients with tumours 2.5 to 3.4cm in size the odds of satisfactory facial nerve outcome were estimated to be over 4 times *lower* compared with those patients with tumours less than 1.5cm in size (OR 4.36, 95% CI 1.52 to 12.47). Similarly, for those patients with tumours 3.5cm to 4.4cm, the odds of satisfactory nerve outcome were estimated to be over 7 times *lower*

compared with those patients with tumours less than 1.5cm (OR 7.69, 95% CI 2.69 to 22.01). For those patients with tumours equal to or larger than 4.5cm, the odds of satisfactory nerve outcome were estimated to be over 16 times *lower* compared with those patients with tumours less than 1.5cm (OR 16.78, 95% CI 5.31 to 53.08). However, there was insufficient evidence of a difference in facial nerve outcome for those patients with tumours 1.5-2.4cm, compared with those patients with tumours less than 1.5cm (OR 1.44, 95% CI 0.48 to 4.31).

The year of operation was found to be a significant predictor of satisfactory facial nerve outcome. The more recent a patient was operated on, the more likely they were to experience a satisfactory outcome (OR 1.15, 95% CI 1.10 to 1.21). A patient operated on 10 years after another patient was estimated to have odds of satisfactory outcome about 4 times higher than the other patient (95% CI 2.55 to 6.53).

As can be seen by the p-values there is insufficient evidence that *sex, age or operative approach* were significant predictors of satisfactory facial nerve outcome after adjusting for the other variables.

The addition of a two-way interaction between the significant variables *tumour size* and *year of operation* was non-significant and was therefore not included in the final model.

Table 7: Results of a multiple logistic regression on satisfactory facial nerve outcome (HB I-III). n=652

	OR	95% CI	p-value
Female	0.782	0.463 to 1.319	0.36
Age at operation	0.983	0.963 to 1.003	0.09
Retrosigmoid app.	1.741	0.638 to 4.750	0.28
Number of years after 1981	1.151	1.098 to 1.206	<0.0001
Tumour size (cm)			
< 1.5 Reference			
1.5 – 2.4	0.694	0.232 to 2.077	0.51
2.5 – 3.4	0.229	0.080 to 0.657	0.006
3.5 – 4.4	0.130	0.045 to 0.372	0.0001
≥ 4.5	0.060	0.019 to 0.188	<0.0001

OR = Odds ratio. CI = Confidence interval

A Hosmer- Lemeshow goodness-of-fit test was used to evaluate the model fit. This test produced a Chi-squared test statistic of 12.83 on 8 degrees of freedom with a corresponding p-value of 0.12. Hence, there was no indication of a poor model fit.

As a sensitivity analysis, the same multiple logistic regression model was fitted to the data as before, except that the categorical tumour size variable was replaced with a continuous variable representing the exact tumour sizes. Please note that only n=345 patients were included in this multiple logistic regression analysis.
The results can be seen in table 8.

Table 8: Results of a multiple logistic regression on satisfactory facial nerve outcome (HB I-III). using exact tumour size in cm (n=345)

	OR	95% CI	p-value
Female	0.702	0.287 to 1.717	0.44
Age at operation	1.005	0.974 to 1.037	0.76
Retrosigmoid app.	3.843	0.408 to 36.152	0.24
Number of years after 1981	1.237	1.053 to 1.453	0.01
Tumour size (cm)	0.389	0.276 to 0.548	<0.0001

OR = Odds ratio. CI = Confidence interval

These results confirm the earlier findings that *tumour size* and *year of operation* were significantly related to a satisfactory facial nerve outcome. The probability of satisfactory outcome was significantly lower for larger tumour sizes. For a patient with a tumour 1cm larger than another patient the odds of satisfactory facial nerve outcome are estimated to be 2.57 times lower than for the other patient (95% CI 1.83 to 3.63). Again *sex, age* and *operation approach* were not significantly associated with satisfactory facial nerve outcome.
The Hosmer-Lemeshow goodness-of-fit test gave a Chi-squared test statistic of 10.49 on 8 degrees of freedom with a corresponding p-value of 0.23. Therefore, again this indicates no problem with model fit. The addition of two-way interaction term between the variables of *tumour size* and *year of operation* was non-significant and therefore not included in the final model.

Operative learning curve

The effect of the surgeon's learning curve reflecting a number of factors including evolution of technique and the surgical experience of the team can be seen in Figure 4. The steepest part of the learning curve occurs in the first 50 patients which was the number operated upon in the first 3 year time interval. The percentage of

patients with HB I-III or satisfactory facial nerve outcome compared with those with HB IV-VI or unsatisfactory outcome can be seen for succeeding 3 year time intervals. As can be seen from figure 5 and table 9 the facial nerve outcome from vestibular schwannoma surgery at present is based on an analysis of the past 6 years of surgery for these tumours. For tumours less than 1.5cm, 95% were normal (HB I/II), 100% were satisfactory (HB I-III) and 0% unsatisfactory (HB IV-VI). For tumours 1.5-2.4cm in size, 83% were normal, 99% were satisfactory and 1% were unsatisfactory. In tumours 2.5-3.4cm, 68% were normal, 96% were satisfactory and 4% unsatisfactory. Tumours 3.5-4.4cm produced a normal outcome in 52%, satisfactory in 80% and unsatisfactory in 20%. For tumours equal to and larger than 4.5cm, 50% were normal, 72% were satisfactory and 28% were unsatisfactory.

Table 9: Facial nerve outcome at 24 months - HBI/II, satisfactory/unsatisfactory
Last 6 years of vestibular schwannoma surgery n=173

Tumour Size-cm	n	HBI-II normal	HBI-III satisfactory	HBIV-VI unsatisfactory
< 1.5	22	95%	100%	0%
1.5 – 2.4	74	83%	99%	1%
2.5 – 3.4	27	68%	96%	4%
3.5 – 4.4	31	52%	80%	20%
> 4.4	20	50%	72%	28%

Nervus intermedius –aberrant regeneration of the facial nerve

Hemifacial spasm

At 3 months postoperative 61 (10%) of patients had some degree of hemifacial spasm (Table 10). By 24 months post-operative in 45 (74%) of these patients with hemifacial spasm it had resolved and in 16 (26%) it persisted but 17 patients developed hemifacial spasm between 3 months and 24 months. At 24 months therefore 33 (5%) of the cohort had persisting hemifacial spasm. There is thus overall a 13% chance of developing hemifacial spasm at some time postoperatively and a 42% chance that of these patients it will have resolved by 24 months.

Table 10: Hemifacial spasm at 3 months and 24 months

		Facial spasm at 24 months		
		No	Yes	Total
Facial spasm at 3 months	No	538	17	555
	Yes	45	16	61
Total		583	33	616

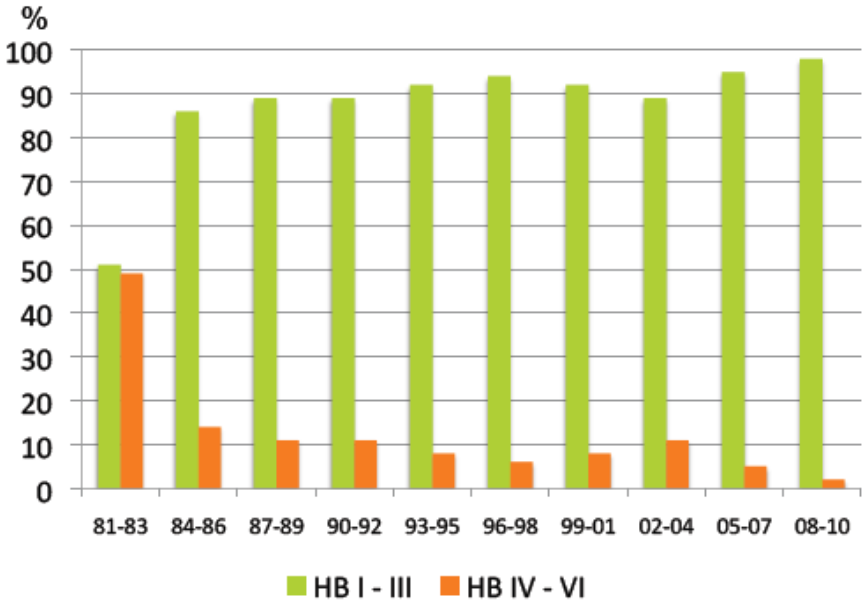

Figure 4: Operative learning curve, over 29 years

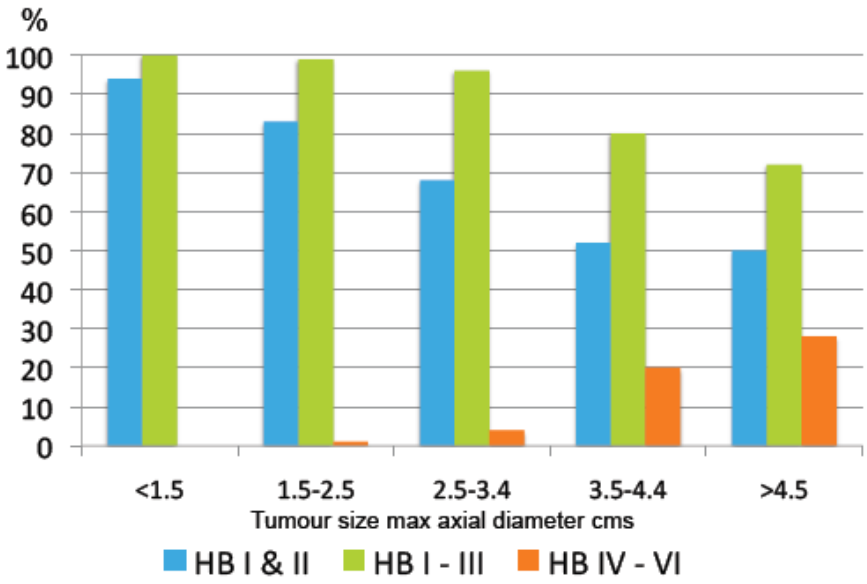

Figure 5: Facial nerve outcome of last 6 years.

The Fisher's Exact test p-value was 0.049. Therefore, there is a significant difference in the percentage of patients with hemifacial spasm at 24 months between the totally normal and partial recovery groups. Hemifacial spasm at 24 months appears to be associated with HB scores of II-IV.

Metallic taste

At 3 months postoperative 184 (30%) of patients had a metallic or salty taste in the mouth (Table 11). By 24 months post-operative in 116 (63%) of these patients with metallic taste it had resolved and in 68 (37%) it persisted but 37 patients developed metallic taste between 3 months and 24 months. At 24 months, therefore, 105 (17%) of the cohort had persisting metallic taste. There is thus overall a 36% chance of developing metallic taste at some time postoperatively and a 52% chance that of these patients it will have resolved by 24 months.

The incidence of metallic taste in the mouth at 24 months postoperative in patients with a HBI outcome was compared with those with partial recovery (HBII-IV). The Fisher's Exact test p-value was 0.11. Therefore, there was no significant difference in the percentage of patients with metallic taste at 24 months between the totally normal and partial recovery groups.

Table 11: Incidence of hemifacial spasm at 24 months – Normal function (HBI) compared with partial function (HBII-IV)

		Facial Nerve Outcome		
		HB I	HB II-IV	Total
Hemifacial spasm at 24 months	No	258	275	533
		96.3%	92.3%	94.2%
	Yes	10	23	33
		3.7%	7.7%	5.8%
Total		268	298	566

Table 12: Metallic taste at 3 months and 24 months

		Metallic taste at 24 months		
		No	Yes	Total
Metallic taste at 3 months	No	389	37	426
	Yes	116	68	184
Total		505	105	610

Crocodile tears

At 3 months postoperative 82 (14%) of patients suffered from crocodile tears (Table 12). By 24 months post-operative in 24 (29%) of these patients with crocodile tears the symptom had resolved and in 58 (71%) it persisted but 83 patients developed crocodile tears between 3 months and 24 months. At 24 months, therefore, 141 (24%) of the cohort had persisting crocodile tears. There is thus overall a 25%

chance of developing crocodile tears at some time postoperatively and only a 15% chance that of these patients it will have resolved by 24 months.

The incidence of crocodile tear at 24 months postoperative in patients with a HBI outcome was compared with those with partial recovery (HBII-IV). The Fisher's Exact test p-value was 0.50. Therefore, there was no significant difference in the percentage of patients with crocodile tears at 24 months between the totally normal and partial recovery groups.

Table 13: Crocodile tears at 3 months and 24 months

		Crocodile tears at 24 months		
		No	Yes	Total
Crocodile tears at 3 months	No	435	83	518
	Yes	24	58	82
Total		459	141	600

Discussion

The modern era of vestibular schwannoma excision was catalysed in 1964 when William House used the operating microscope and developed otomicrosurgical transtemporal and middle fossa approaches to the internal auditory canal and cerebello-pontine angle.[3] For the first time it was possible to remove the tumour and preserve the integrity of the facial nerve. Preservation of facial nerve function is a very important aspect of vestibular schwannoma surgery and a good post-operative outcome is critical for the patient's quality of life. It is an indicator of surgical excellence. Unfortunately, anatomical integrity of the nerve does not necessarily result in good functional outcome. The timing of facial nerve functional assessment is also important since in a significant number of patients facial function may deteriorate several days after surgery. Should this occur, subsequent recovery is not assured, and is rarely complete.[5,6,16,17] The speed of recovery is variable and depends upon whether the injury is neuropraxia in which case recovery may occur in 8-12 weeks or whether Wallerian degeneration occurs in which case tone will return in 5-6 months and the final facial nerve outcome will not be apparent until 12-18 months and occasionally up to 2 years.[5,6,18 19]

Electroneuronography is useful in the assessment of postoperative facial palsy, since patients with Wallerian degeneration have a worse prognosis than those with neuropraxia[20,21]. Absent electroneuronographic responses at one week postoperative or an action potential less than 1% of the amplitude of the contralateral response is a

predictor of poor facial nerve outcome. Incomplete degeneration with partial palsy is a good indicator of early recovery and a good prognosis. Neural regeneration provides good (HB I/II), but rarely perfect recovery (HB I).[22]
Based on our facial nerve outcome for the last 6 years of vestibular schwannoma surgery we have been able to achieve a satisfactory outcome (HB I-III) in 100% of tumours less than 1.5cm, 99% of tumours 1.5-2.4cm, 96% of tumours 2.5-3.4cm, 80% of tumours 3.4-4.4cm and 72% of tumours equal to or greater than 4.5cm.

It is known that tumour size is a predictor of facial nerve outcome.[5,6,9,12,23-25] Analysis of the factors affecting facial nerve outcome in our series revealed a highly statistically significant relationship between tumour size and outcome both univariately and multivariately including analysis of increments of tumour size and also exact individual tumour sizes within the cohort. Tumour size was found to be a significant predictor of facial nerve outcome, even after adjusting for year of operation, operation approach, sex and age.
Whilst there did appear to be a just significant correlation with age and operative approach and HB score univariately, after performing simple linear regression analysis, following multivariate analysis and adjusting for the other variables there was insufficient evidence that age or operative approach was a predictor of facial nerve outcome. There was no statistically significant correlation between sex and facial nerve outcome.

The year of operation was found to be a significant predictor of satisfactory facial nerve outcome. The more recently a patient was operated upon the more likely they were to have a satisfactory facial nerve outcome. These results confirmed our previous findings of an operative team learning curve for vestibular schwannoma surgery.[23,26] This study has demonstrated that, for a new surgical team, the steepest part of the surgical learning curve is in the first 50 patients. As has been clearly demonstrated by this study our percentage of good functional facial nerve results have increased with experience. It may be that in the future the effects of the learning curve can be minimised by subspecialty training fellowships and dovetailing surgical appointments so that an experienced surgeon can work alongside a less experienced one for some time until the requisite skills have been attained. Proleptic consultant appointments can be helpful in this regard as well as only replacing one subspecialist surgeon at a time within the team.
There are a number of other factors which can influence facial nerve outcome. Firstly and most importantly meticulous surgical technique with identification of the nerve with gentle atraumatic handling, sharp dissection and hydrodissection of the facial

nerve from the tumour capsule. The tumour may be most adherent to the facial nerve at the porus acousticus and developing the dissection of the nerve from the tumour in the internal auditory canal first followed by identification of the nerve at the root entry zone with debulking using the ultrasonic cavitron will facilitate the dissection at the porus. Facial nerve monitoring is important to help minimise trauma to the facial nerve during this dissection by alerting the surgeon to undue stretching or temperature change and also to delineate facial nerve fibres from tumour capsule. A number of scientific articles have been written on facial nerve monitoring in this surgery[8,10,23,26-28]. The morphology of the tumour may affect outcome particularly when bosselations of tumour are present or when the facial nerve is circumferentially encapsulated by tumour. The morphology and site of origin of the tumour may be affected by the position of the neurilemmal-glial junction. The position of the facial nerve in relation to the tumour may also affect outcome. Usually the facial nerve is medial in relation to the tumour and away from the surgeon but it can be rostral and rarely can be lateral and lying on the surface of the tumour and nearest to the surgeon and technically it is more difficult to achieve a good facial nerve outcome. In a previous study we could find no statistically significant difference in facial nerve outcome between solid and cystic tumours.[29]
The extent of the excision may affect facial nerve outcome. The degree of adherence to the brainstem can also influence facial nerve outcome and we have recently recorded that 10% of tumours were significantly adherent to the brainstem.[30]

Anatomical preservation of the facial nerve was achieved in 97% of our 652 patients. In our experience , primary facial nerve anastomosis or greater auricular or sural nerve cable grafting are the procedures of choice if the facial nerve is lost at surgery. Primary nerve anastomosis, although technically difficult can be achieved via the translabyrinthine approach[22]. One centimetre of length can be gained by taking the facial nerve out of the fallopian canal within the temporal bone and the efferent fibres from the geniculate ganglion are detached. This will usually provide sufficient length to allow direct anastomosis of the divided ends. The anastomosis is either suture or wrapped in a sheath of fascia lata and sealed with fibrin glue (Tisseel @, Immuno Ltd). Facial-hypoglossal anastomosis is the most satisfactory procedure for a poor functional recovery of an intact facial nerve. However timing is important and although spontaneous recovery of an anatomically intact facial nerve can occur up to 2 years following surgery[19] facial-hypoglossal anastomosis should be done within 12 months otherwise degeneration of the distal facial nerve and motor endplates in the facial muscles will compromise the success of the procedure. By utilising electro-neuronography to predict those patients unlikely to recover spontaneously, facial-

hypoglossal anastomosis can be undertaken early, and this may improve final facial nerve outcome. In skilled hands cross facial grafting can achieve satisfactory facial nerve outcome although it usually means 3 further surgical procedures.

Nervus intermedius function and aberrant regeneration following vestibular schwannoma surgery is important in outcome and quality of life[13].
This study has shown that overall there is a 13% chance of developing hemifacial spasm at some time postoperatively and a 42% chance that of these patients it will have resolved by 24 months.
There is a one in three chance of developing metallic taste postoperatively and in half of these patients it will have resolved by 24 months.
There is a one in four chance of developing crocodile tears at some time post-operatively and recovery is much less likely than with metallic taste, only in one of seven patients does it resolve by 24 months.
In terms of aberrant regeneration, a higher incidence of hemifacial spasm, metallic taste and crocodile tears in those patients with partial recovery (HBII-IV) of the facial nerve compared with those patients with a totally normal postoperative facial nerve function would seem likely. In this analysis, however, there was only a statistically significant difference (p=0.049, Fisher's Exact test) for hemifacial spasm but no statistical difference for metallic taste and crocodile tears.

References

1. Cairns H. Acoustic neurinoma of right cerebello-pontine angle.Complete removal. Spontaneous recovery from post-operative facial palsy. Proc Royal Soc Med 1931;25:35-40.
2. McKissock W.Acoustic tumours. Proc Royal Soc Med 1965;58:1078-1079.
3. House WF.Transtemporal bone microsurgical removal of acoustic neuromas:report of cases. Arch Otolaryngol 1964;80:731-742.
4. Hardy DG MR, Baguley DM, Moffat DA. Surgery for acoustic neurinoma. An analysis of 100 translabyrinthine operations. J Neurosurg 1989;71:799-804.
5. Moffat DA, Croxson GR, Baguley DM, Hardy DG. Facial nerve recovery after acoustic neuroma removal. J Laryngol Otol 1989;103:169-172.
6. Hardy DG MR, Baguley DM, Moffat DA. Facial nerve recovery following acoustic neuroma surgery. Br J Neurosurg 1989;3:675-680.
7. Kartush JM, Lundy LB. Facial nerve outcome in acoustic neuroma surgery. Otolaryngol Clin North Am 1992;25:623-647.
8. Lalwani AK, Butt FY, Jackler RK, Pitts LH, Yingling CD. Facial nerve outcome after acoustic neuroma surgery: a study from the era of cranial nerve monitoring. Otolaryngol Head Neck Surg 1994;111:561-570.
9. Fenton JE, Fagan PA. Facial nerve outcome after acoustic neuroma surgery. Surg Neurol 1995; 44:95-96.
10. Morikawa M, Tamaki N, Nagashima T, Motooka Y. Long-term results of facial nerve function after acoustic neuroma surgery--clinical benefit of intraoperative facial nerve monitoring. Kobe J Med Sci 2000;46:113-124.

11. Arts HA, Telian SA, El-Kashlan H, Thompson BG. Hearing preservation and facial nerve outcomes in vestibular schwannoma surgery: results using the middle cranial fossa approach. Otol Neurotol 2006;27:234-241.
12. Brackmann DE, Cullen RD, Fisher LM. Facial nerve function after translabyrinthine vestibular schwannoma surgery. Otolaryngol Head Neck Surg 2007;136:773-777.
13. Irving RM VL, Hardy DG, Baguley DM, Moffat DA. Nervus intermedius function after vestibular schwannoma removal: clinical features and pathophysiological mechanisms. Laryngoscope 1995;105:809-813.
14. House JW, Brackmann DE. Facial nerve grading system. Otolaryngol Head Neck Surg 1985; 93:146-147.
15. Tos M TJ. Proposal for Reporting Size of Vestibular Schwannoma. In: Acoustic Neuroma; Consensus on Systems for Reporting Results. Keio University International Symposia for Life Sciences and Medicine Kanzaki, Tos, Sanna, Moffat, Kunihiro, Inoue (Eds) Part 1 Tumor size 2003;10:3-7.
16. Gardner G RJ. Facial nerve function incerebellopontine angle tumour surgery. American Journal of Otology 1985;74-79.
17. King TT MA. translabyrinthine and transtentorial removal of acoustic nerve tumours. J Neurosurg 1980;52:210-216.
18. Morgan ADF, Fischer G, et al. Facial Nerve. New York: Masson Publishing USA Inc, 1985.
19. Bentivoglio PCA, Symon L. Surgical management of acoustic neuromas during the last five years. PartII: Results for facial and cochlear nerve function. Surg Neurol 1988;29:205-209.
20. Gantz BJ GA, Holliday M. Electroneurographic evaluation of the facial nerve. Method and technical problems. Ann otol Rhinol laryngol 1984;93:394-398.
21. Croxson GR, Moffat DA, Hardy DG, Baguley DM. Role of post-operative electroneuronography in predicting facial nerve recovery after acoustic neuroma removal: a pilot study. J Laryngol Otol 1989;103:60-62.
22. Whittaker CKLC. Translabyrinthine removal of large acoustic tumors. Am J Otol 1985;155-160.
23. Grey PL MD, Palmer CR, Hardy DH, Baguley DM. Factors which influence the facial nerve outcome in vestibulr schwannoma surgery. Clin Otolaryngol 1996;21:409-413.
24. Arriaga MA, Luxford WM, Atkins JS, Jr., Kwartler JA. Predicting long-term facial nerve outcome after acoustic neuroma surgery. Otolaryngol Head Neck Surg 1993;108:220-224.
25. Nutik SL. Facial nerve outcome after acoustic neuroma surgery. Surg Neurol 1994;41:28-33.
26. Moffat DA HD, Grey PL, Baguley DM. The operative learning curve and its effect on facial nerve outcome in vestibular schwannoma surgery. Am J Otol 1996;17:643-647.
27. Elsmore AJMN. The operative learning curve for vestibular schwannoma excision via the retrosigmoid approach. Br J Neurosurg 2002;16:448-455.
28. Nakao Y, Piccirillo E, Falcioni M, et al. Prediction of facial nerve outcome using electromyo-graphic responses in acoustic neuroma surgery. Otol Neurotol 2002;23:93-95.
29. Jones SE BD, Moffat DA. Are facial nerve outcomes worse following surgery for cystic vestibular schwannoma? Skull Base 2007;17:281-284.
30. Moffat DA. Percentage of vestibular schwannomas adherent to the brainstem. Personal communication 2011.

Chapter 3.0

Neurofibromatosis Type 2

Chapter 3.1

Management strategies in neurofibromatosis type 2

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Abstract

The objective of this study was to review the experience of the Neurotology and Skull Base Surgery Unit of Addenbrooke's Hospital in Cambridge, England, in the management of patients with neurofibromatosis type 2 (NF2). This was a retrospective review of the institution's series conducted at a neurotological tertiary referral centre. Over a 17-year period (1984–2001), 35 patients with NF2 were managed. These patients presented with multiple cranio-spinal neoplasms, including 62 cerebellopontine angle tumours of which 59 were vestibular schwannomas (nine patients with unilateral tumours and 25 patients with bilateral tumours). Clinical presentation, diagnosis and patient management were reviewed. The outcome parameters measured were tumour progression, the incidence of complications (hearing deterioration and facial nerve palsy) and the need for secondary intervention. Five vestibular schwannomas were treated with stereotactic radio-surgery (gamma-knife), all of which showed evidence of progression in size and/or deterioration in hearing. Thirty-one VS were conservatively treated with annual surveillance. In nine cases, the tumours had a follow-up shorter than 6 months and were therefore excluded from the results. In 13 cases the VS did not progress in size, and the hearing remained stable, while in the remaining nine cases, tumour progression was evident. In fifteen cases, surgery was performed at the authors' institution. In 11 cases a translabyrinthine approach was adopted, and in the remaining four cases a retrosigmoid approach was preferred. In all these cases, tumour removal was total and facial nerve function was House-Brackmann grade I–III in 55%. Successful hearing preservation was elusive in those patients in whom a hearing preservation approach was attempted. NF2 remains an extremely challenging disorder for the neurotologist and the patient alike. Early diagnosis offers distinct advantages to the patients, their families and the community at large. Of the treatment modalities, surgery unequivocally offers the most superior tumour control. Hearing preservation remains a challenge in these patients, but is optimised by the early detection of tumours in the NF2 patient.

Introduction

The hallmark of neurofibromatosis type 2 (NF2) is bilateral schwannomas arising from the vestibular nerves. The disease is inherited as an autosomal dominant gene with a high penetrance rate. NF2 has the highest spontaneous mutation rate of any

human genetic disorder (50%).[14] The incidence of NF2 is thought to be approximately 1:40,000 to 1:50,000.[4,6]

NF2 has the elements that make it one of the most devastating and formidable hereditary conditions. The gene deletion defect on the long arm of chromosome 22 means that tumour suppression is deficient, manifesting in neural tumours.[21,28,29] Central nervous system tumours (schwannomas, meningiomas, gliomas, neuromas) are multiple and occur in an unpredictable fashion. Any handicap from dysfunction of the facial, vestibulocochlear and the lower cranial nerves caused by cerebellopontine angle tumours has the added potential of being bilateral. Furthermore, in these patients, spinal tumours have the capacity to produce further handicap by spinal cord compression.

This condition tends to manifest itself in the second and third decade, often with insidious symptoms.[5]

In NF2, vestibular schwannomas may reach large dimensions before the onset of audiological, vestibular or facial symptoms. A delay in the diagnosis of this condition has significant ramifications both for the affected individuals and their planned families.

Early detection of NF2 allows those individuals with small vestibular schwannomas and useful hearing the advantage of being offered multiple treatment options and an optimal chance for hearing preservation. A surveillance programme with annual radiological and audiological reassessment provides the close vigilance for tumour progression that is necessary so that surgical intervention can be instituted in a timely fashion.

Materials and methods

The 17-years experience of the management of NF2 patients in the Neurotology and Skull Base Surgery Unit of Addenbrooke's Hospital was reviewed and analysed. Thirty-five consecutive patients with NF 2, presenting between 1984 and 2001, were managed by the unit. The 20 males and 15 females ranged in age from 8–55 years with a mean age of 29 years. In these patients, there were a total of 62 cerebello-pontine angle tumours, which included 59 vestibular schwannomas.

The modified National Institute of Health (NIH) Consensus Panel Criteria[1,5,10] were used as the diagnostic criteria for NF2 in the presented series.

Details of the clinical presentation, treatment and outcome of these NF2 patients were examined.

Table 1: Modified criteria of neurofibromatosis type 2

Modified criteria of neurofibromatosis type 2, n=35
1. Bilateral vestibular schwannoma 2. First degree relative with NFII and A, unilateral vestibular schwannoma B. meningioma, glioma, neurofibroma, schwannoma, cataracts, or cerebral calcification 3. Unilateral vestibular schwannoma plus meningioma, glioma neurofibroma, schwannoma, cataracts, or cerebral calcification 4. Multiple meningioma plus unilateral vestibular schwannoma 5. Multiple meningiomas plusglioma, neurofibroma, schwannoma, cataracts, or cerebral calcification

Results

Clinical presentation

Thirty-five patients fulfilled the modified NIH Consensus Panel Criteria of NF2, and the distribution can be seen in Table 1.

The diagnosis of NF2 in the study population was usually made at the referring institution. The average age of onset of symptoms was 29 years of age (range: 8–55 years of age). The average age at diagnosis of NF2 was 32.5 years of age (range: 8–58 years of age). The average delay in diagnosis of the condition was 3.5 years (range: 0–25 years), with a delay of more than 10 years in five patients (17%).

The clinical manifestations of the 35 patients with NF2 are shown in Table 2.

There were 62 cerebellopontine angle tumours, consisting of 59 vestibular schwannomas, two cerebellopontine angle meningiomas and one facial schwannoma. In nine cases, the vestibular schwannomas were unilateral, and in 25 patients, the vestibular schwannomas were bilateral. The diameter of the vestibular schwannomas was on average 22.1 mm (range: 3–60 mm, median 18.5 mm).

The neurotological manifestations of these vestibular schwannomas were most commonly progressive hearing loss, imbalance and tinnitus (Table 3).

Of the 59 cases of vestibular schwannomas, 51 were untreated on presentation. In eight cases, vestibular schwannomas had been operated on at the referring institution. In one patient with bilateral tumours, the full preoperative evaluation was not available, and therefore the presenting cranial neuropathies of 49 untreated vestibular schwannomas are described in Table 4.

Table 2: The clinical manifestations of NF2

The clinical manifestations of NF2, n=35 patients	
Unilateral vestibular schwannoma	9
Bilateral vestibular schwannoma	25
Intracranial meningioma	15
Spinal tumour	20
Presenile cataract	5
Peripheral nerve tumor	12
Cranial nerve schwannoma	8
Cranial calcification	2
Facial neuroma	1
IV ventricle ependymoma	1

Table 3: Neurotological features of vestibular schwannomas in NF2

Neurotological features of vestibular schwannomas in NF2, n=35		
	n	%
Hearing loss	27	77.1
Imbalance	24	68.6
Tinnitus	22	62.9
Headache	10	28.6
Mastoid ache	3	8.6
Facial twitching	3	8.6
Facial numbness	7	20
Raised intracranial pressure	4	11.4

Table 4: Cranial neuropathies in untreated vestibular schwannomas in NF2

Cranial neuropathies in 49 vestibular schwannomas		
	n	%
Cranial nerves III-IV-VI	1	2
Cranial nerve V	8	16.3
Cranial nerve VII	48 HB grade I	98
	1 HB grade II	2
Cranial nerves IX-XII	3	6
Cerebellar signs	6	12
Papilloedema	11	22.4

The audiological results were examined according to the guidelines of the American Academy of Otolaryngology – Head and Neck Surgery (AAO and HNS).[9] Eight had been previously surgically treated before referral, and their audiological results are not included. Five patients with vestibular schwannomas presented with dead ears. The remaining 46 vestibular schwannomas had a mean PTA of 33.87 dB HL (standard deviation: 20.02). The mean SDS was 79.94% (standard deviation: 28.13).

Treatment

The primary management strategy for the 51 untreated vestibular schwannomas was either conservative treatment with annual surveillance (31 tumours), stereotactic radiotherapy (5 tumours) or microsurgical removal (15 tumours).

A total of 31 tumours were assigned to the watch-andwait and rescan policy. Nine of these patients with vestibular schwannomas had a follow-up period shorter than 6 months at the time of publication, and for this reason, their outcome results were excluded. Therefore, there was a total of 22 tumours with a follow-up period that was considered long enough. In 13 of these 22 tumours, their size and the ipsilateral hearing remained stable for an average follow-up period of 4.27 years (range: 1–8 years). In nine cases, there was tumour progression and/or hearing deterioration, necessitating secondary intervention in six cases (stereotactic radiotherapy in five cases and surgery in one case). In two cases followed within the watchand-wait and rescan programme, facial nerve function deteriorated, one HB grade I to HB grade II and one patient with an HB grade II deteriorated to an HB grade III.

Stereotactic radiotherapy was employed as the primary treatment in the management of five vestibular schwannomas (bilateral tumours in one patient and unilateral tumours in three patients). In all cases in this subgroup, there was tumour progression and/or deterioration in hearing (Table 5).

In two patients there was a deterioration of facial nerve function from normal to House-Brackmann grade II in one and to House-Brackmann grade III in the other. Two patients required surgery following stereotactic radiotherapy as a secondary intervention. In one case the tumour was removed through a translabyrinthine approach, and an auditory brainstem implant (ABI) was inserted.

Of the 59 vestibular schwannomas in the 35 patients with NF2, 23 underwent surgery. Fifteen tumours were excised at the authors' hospital*, whilst eight were operated on previously at the referring institution.

Of the 15 vestibular schwannomas operated on in the authors' unit, there were 11 large tumours where a translabyrinthine removal was appropriate because there was no useful hearing, and the other four tumours were excised via a retrosigmoid approach. The average size of the vestibular schwannomas removed via a translabyrinthine approach was 43.9 mm (range: 24–60 mm). The postoperative House Brackmann facial nerve function was in three cases grade I, in three cases grade II, in four cases grade III, in one case grade IV and in four cases grade VI. All these patients showed no evidence of residual or recurrent disease on long-term follow-up.

In the other four surgical patients, hearing preservation was attempted. The average size of these vestibular schwannomas was 23.3 mm (range: 13–35 mm). The average pre-operative PTA was 28.12 dB HL (SD 11.43) with a mean SDS of 85.5% (SD 11.44), whilst complete tumour removal and acceptable facial nerve function (House Brackmann grade I in two cases, grade II in one case and grade III in one case) was achieved in all cases. No long-term hearing preservation was possible in any of these patients.

The parameters of outcome examined for each of the three therapeutic options for the vestibular schwannomas were tumour progression, hearing and facial nerve results and the need for secondary intervention. These results are reported in Table 5.

Discussion

In the last 10 years, there has been slow but steady progress in the management of this devastating condition. Microsurgical techniques, cranial nerve monitoring and advances in MR imaging have provided only a limited reduction in the morbidity and mortality of the NF2 patient. The most revolutionary advance in NF2 has been the painstaking research culminating in the determination of the molecular basis of NF2 with the identification of the protein Merlin.[29] This gene product is thought to signal cellular growth inhibition. It represents the potential for a diagnostic tool for the genetic screening of families.[13,15] Current molecular biological techniques enable detection of causative mutations in two-thirds of all classically affected individuals, with higher detection rates in severely affected patients and negligible detection in very mildly affected individuals.[11,16,20] Molecular genetics carries the greatest potential for a cure for this challenging condition in the future. Until such time, the greatest advantage for both the patient and the surgeon in managing this condition lies in early detection.

Table 5: Outcome of previously untreated vestibular schwannomas in neurofibromatosis type 2. (W and W watch and wait, HB House Brackmann)

Outcome parameters	(W&W)M Watch and wait, n=31		Gamma-knife, n=5		Microsurgical dissection n=15*	
	Pre-treatment	Post=treatment	Pre-treatment	Post=treatment	Pre-treatment	Post=treatment
Tumor progression	-	415		100%		0%
Hearing	32 dB HL	38.2 dB HL	22,5 dB HL	68.33 dB HL	41.64 dB HL	Dead ear
Facial nerve						
HB grade I	21 cases	20 cases	5 cases	3 cases	15 cases	3 cases
HJB grade II	1 case	1 case		1 case		3 cases
HB grade III		1 case		1 case		4 cases
HB grade IV						1 case
HB grade VI						4 cases
Secondary treatment						
	-	16% gamma-knife 81% continue W&W 3% surgery	-	- 60% W and W 40% surgery	-	0%

Delay in diagnosis

In the presented series, there was a discouraging and protracted delay in the diagnosis of NF2. In five of the 35 patients (14.3%), there were more than 10 years between the onset of symptoms and a definitive diagnosis of NF2. During this time, three of the NF2 patients proceeded to produce children without the benefit of genetic counselling. Each of these patients had two offspring with NF2. A similar delay between presentation with significant neurotological symptoms and an accurate diagnosis has been reported in both adult and paediatric NF2 patients in other series.[14,19]

Clinical presentation

The clinical presentation of vestibular schwannomas in the series was typical with progressive hearing loss, imbalance and tinnitus being the most common presenting symptoms. As in other studies, auditory symptoms prevail over vestibular symptoms.[5,18,19] However, there was a high proportion of patients (Table 3) who had symptoms of facial nerve twitching 3/35 (8.6%), facial numbness 7/35 (20%) and papilloedema 4/35 (11.4%). The incidence of the same clinical features with sporadic unilateral vestibular schwannoma within the same unit was lower, i.e. facial nerve twitching (3.5%), facial numbness (17.6%) and papilloedema (9.2%). Facial and trigeminal nerve dysfunction and raised intracranial pressure reflects the fact that the vestibular schwannomas in NF2 present later and larger than their unilateral sporadic counterpart. This is consistent with the fact that there was a marked delay in the diagnosis of NF2 in a proportion of the patients.

Spinal-cord tumours are common, occurring in 57% of the NF2 patients in this series, with the majority of these being asymptomatic. Only two patients required surgery for spinal-cord compression. Mautner et al.[18] also reported that spinal-cord tumours are asymptomatic and should therefore be managed conservatively. For this reason, the authors recommend imaging of the spinal cord on a biannual basis in the absence of spinal or nerve root compressive symptoms in their surveillance protocol MR (Table 6).

Treatment

There are three treatment options in the management of vestibular schwannomas in the NF2 patient: conservative treatment with annual surveillance, stereotactic radiotherapy and microsurgical removal. The choice of the appro priate treatment option for each individual patient is based on numerous patient, tumour and treatment factors (Table 7).

Table 6: NF2 annual surveillance protocol

NF2 annual surveillance protocol
♦ NF2 database update
♦ Annual audiology
♦ Pure-tone audiogram
♦ Speech audiogram
♦ Annual MRI of IAC and brain
♦ Biannual MRI of the spine
♦ Annual ophthalmology evaluation

Table 7: Factors determining treatment of vestibular schwannomas in NF2

Factors determining treatment of vestibular schwannomas in the NF2 patient
Tumour factors Size, bilaterality, brainstem compression, hydrocephalus, hearing, vestibular and facial function
Patient factors Patient's preference, age, tumour burden.
Treatment factors Previous treatment, primary and secondary rehabilitation of auditory, vestibular and facial function

Watch and wait and rescan

In the reported series, watch and wait and rescan proved to be the most efficacious of all the management options. Thirteen of the 22 vestibular schwannomas showed no radiological and audiological evidence of tumour progression at annual review. In nine cases, an increase in tumour size and deterioration in hearing was detected early by annual MRI and audiometry. Six of the nine tumours that progressed in size were suitable for a secondary intervention.

Stereotactic radiotherapy

Stereotactic radiotherapy in the series failed to control tumour growth or preserve hearing in the five patients referred for this primary treatment.

Surgery

Of the 15 patients to whom surgery was offered as the initial intervention, 11 were not appropriate for hearing preservation surgery on the grounds of tumour size and poor residual hearing. In four patients, hearing preservation surgery was attempted, but was not successful. In these patients, however, there was complete tumour

removal, no recurrence on follow-up and acceptable facial nerve function (House Brackmann grades I–III in 100% of the cases).

Hearing preservation is thought to be more elusive in NF2. It is acknowledged that the pathology of NF2-associated vestibular schwannomas is subtly different from that of sporadic vestibular schwannomas. In NF2, vestibular schwannomas have a greater prevalence of lobularity and entrapment of nerves.[13,26] Furthermore, temporal bone histological studies have shown that the vestibular schwannoma is more likely to infiltrate the cochlear nerve, and the plane between the cochlear and vestibular nerve is less distinct in the individual with NF2.[12] This often translates to poorer hearing preservation results in NF2 patients than in those with sporadic unilateral vestibular schwannomas,[22] however more recently surgeons report more comparable hearing results in NF2 and the sporadic form.[24]

In this series, the watch-and-wait and rescan programme demonstrated that more than 50% of the vestibular schwannomas were stable in size. Any tumour progression was detected without delay with the annual surveillance programme (Table 6). Sterotactic radiotherapy did not offer tumour control or hearing preservation. In all patients who underwent surgery, complete tumour removal was achieved, but long-term hearing preservation proved elusive.

Recommendations for early diagnosis

In this series, the delay in the diagnosis of NF2 and the subsequent poor outcome of these patients points to the critical need for the early detection of this condition. Clinical awareness of the genetic abnormality and its familial implications and timely screening makes early detection potentially self-perpetuating. In addition, there are the numerous benefits of better outcome, maximum opportunity for hearing preservation and prevention of neurological sequelae. The early implementation of auditory, vestibular, tinnitus and facial nerve rehabilitation is thus possible. The patient with NF2 diagnosed early can also benefit from timely genetic counselling, thereby decreasing the population of patients with NF2 and their contribution to the genetic pool. Genetic screening of first-degree relatives results in the early detection of other patients with this condition. MRI screening of families will also continue to contribute to the early identification of these patients. The authors recommend an aggressive screening protocol for the at-risk family members (Table 8).

Table 8: NF2 ycreening protocol for at-risk family members

NF2 screening protocol for at-risk family members
♦ Genetic evaluation with blood sampling for gene defect
♦ Audiology
♦ Pure-tone audiogram
♦ Speech audiogram
♦ MRI of brain and spine with Gadolin

The converse situation applies in the late diagnosis of NF2. The cascade of adverse events not only denies the NF2 patients optimal treatment, but also perpetuates the disease. Late detection carries a penalty borne both by the patient and the community. For the patient, there is the lost opportunity to prevent complications, implement rehabilitation and optimise the chance of hearing preservation. For the community, there is the missed chance of early detection of others with the condition, thereby increasing the prevalence of the disease and the subsequent financial burden of lifetime care.

The modified criteria for the diagnosis of NF2 includes the different phenotypes and takes into account those patients who may initially present with manifestations other than vestibular schwannomas. General acceptance of these modified criteria offers a wider net to detect NF2 patients. Twenty-three percent of the patients in the presented series would not have been included if the strict criteria of the NIH were employed.[5]

Recommendations for management

Surveillance programmes need to be established at only selected tertiary neuroto-logical referral centres so as to maximise the experience with this uncommon condition. This will help address the current dilemma of numerous institutions treating small numbers of patients and therefore diluting the experience of this disease.

Earlier detection of NF2 will inevitably increase the number of patients presenting with small vestibular schwannomas and useful hearing. All patients diagnosed should undergo a comprehensive initial assessment. The patient with a small vestibular schwannomas (<2 cm) and useful hearing should be offered the option of either a retrosigmoid or middle-cranial-fossa approach hearing preservation surgery at the time of diagnosis or at the point at which there is evidence of tumour progression detected on annual surveillance. Of all of the options, surgery is the only treatment modality offering the possibility of tumour eradication. Whilst hearing preservation was elusive in this series, the detection of smaller tumours may lead to

more favourable hearing preservation results in the future, particularly with the adoption of the middle cranial fossa approach. Patients in whom hearing preservation has not been successful can be offered auditory brainstem or cochlear implantation (where the cochlear nerve has been preserved).[17] All patients continue in the surveillance protocol for life.

Despite all the measures to maximise early detection, there will continue to be a significant proportion of NF2 patients who will have large vestibular schwannomas (>2 cm) at the time of presentation. In all patients with large life-threatening tumours, surgical intervention is indicated for the fit patient and stereotactic radiotherapy when there is a substantial risk from general anaesthesia and major intracranial surgery and if the tumour is less than 3 cm in diameter. In patients with bilateral large vestibular schwannomas and useful hearing on one side but no useful hearing in the contralateral ear, the contralateral tumour should be excised first to retain some hearing. There may be an argument in favour of placing an auditory brainstem implant at the time of excision to rehabilitate the patient in the presence of some hearing in the other ear. This may prove to be an advantage to the patient when it becomes necessary to excise the second tumour. Conservative management is advised in patients with bilateral medium-size tumours until one or both tumours become life threatening or the hearing deteriorates.

The role of stereotactic radiotherapy is yet to be clearly determined in the NF2 patient. From the reported experience in the paper and in the literature, tumour control is poor, the surgery may be more technically difficult with less satisfactory outcome and in those patients requiring surgery after stereotactic radiotherapy, the reported facial nerve results are very disappointing.[7,23,25] Recent studies report the risk of hearing loss to be about 65% following radiotherapy.[8] In the last few years, there have been six cases described of suspected malignant transformation of vestibular schwannomas following stereotactic radiotherapy.[2,3,7,27] Two of these cases were patients with NF2. All these patients showed some response to radiotherapy in the early stages. Subsequently, at intervals ranging from 0.5 to 5.6 years, all six patients developed rapid tumour progression and cranial nerve palsies. All cases were uniformly fatal within months. In the context of NF2, where there is already a low risk of malignant transformation of vestibular schwannomas, the role of stereotactic radiotherapy must be further evaluated.[5] Until then, stereotactic radiotherapy should be reserved for life-threatening tumours in the medically unfit.

Conclusion

Neurofibromatosis type 2 is one of the most challenging conditions in neurotology. Early diagnosis offers distinct advantages to the patients, their families and the community at large. Depending upon their clinical status, the patients can be offered watch and wait and rescan, stereotactic radiotherapy or surgery as management options. They should have the benefit of an experienced multidisciplinary tertiary referral unit, general counselling, early implementation of rehabilitation, screening of family members as well as access to a patient support group. The patient should have the best chance of hearing preservation and the lowest risk of neurological sequelae, with their concomitant effect on the quality of life.

The detection of small vestibular schwannomas with useful hearing is possible by minimising the delay in the diagnosis and adopting a tight surveillance programme established in selected specialised tertiary referral institutions. Early diagnosis of NF2 remains the single most important factor for the best outcome in this condition; until genetic therapy in the future yields a cure for this devastating condition, it will help to reduce the prevalence of the disease in the community. Of the treatment modalities, surgery is the only one to achieve eradication of the tumour. Hearing preservation remains a challenge in these patients, but is optimised by the early detection of tumours in the NF2 patient.

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References

1. Acoustic Neuroma. NIH Consensus Statement. 1991;9:1–24.
2. Bance M, Guha A. Radiation-induced malignant tumors after stereotactic radiosurgery. Otol Neurotol 2001;22:124–125.
3. Comey CH, McLaughlin MR, JHD, Martinez AJ, Lunsford LD. Death from a malignant cerebellopontine angle triton tumour despite sterotactic radiosurgery: Case report. J Neurosurg 1998;89:653–658.
4. Evans DG. Neurofibromatosis type 2: genetic and clinical features. Ear Nose Throat J 1999;78: 97–100.
5. Evans DG, Huson SM, Donnai D, Neary W, Blair V, Newton V, Harris R. A clinical study of type 2 neurofibromatosis. Q J Med 1992;84:603–618.
6. Evans DG, Huson SM, Donnai D, Neary W, Blair V, Teare D, Newton V, Strachan T, Ramsden R, Harris R. A genetic study of type 2 neurofibromatosis in the United Kingdom. I. Prevalence,

mutation rate, fitness, and confirmation of maternal transmission effect on severity. J Med Genet. 1992;29:841–846.
7. Fagan P, Chang, P, Turner .J Triton tumor. J Neurosurg 1999;90:987–988.
8. Flickinger JC, Lunsford LD, Linskey ME. Gamma knife radiosurgery for acoustic tumors: multivariate analysis of four year results. Radiother Oncol 1993;27:91–98.
9. Guidelines of the hearing preservation in acoustic neuroma (vestibular schwannoma). Otolaryngol Head Neck Surg 1995;113:179–180.
10. Gutmann DH, Aylsworth A, Carey JC, Korf B, Marks J, Pyeritz RE, Rubenstein A, Viskochil D. The diagnostic evaluation and multidisciplinary management of neurofibromatosis 1 and neurofibromatosis 2. JAMA 1997;278:51–57.
11. Kluwe L, Bayer S, Baser ME, Hazim W, Haase W, Funsterer C, Mautner VF. Identification of NF2 germ-line mutations and comparison with neurofibromatosis 2 phenotypes. Hum Genet 1996; 98:534–538.
12. Linthicum FH, Brackmann DE. Bilateral acoustic tumors. A diagnostic and surgical challenge. (1980) Arch Otolaryngol 1980;106:729–733.
13. Louis D, Ramesh V, Gusella JF. Neuropathology and molecular genetics of neurofibromatosis type 2 and related tumours. Brain Pathol 1995;5:163–172.
14. MacCollin M, Mautner VF. The diagnosis and management of neurofibromatosis type 2 in childhood. Semin Paediatr Neurol 1998;5:243–252.
15. MacCollin M, Mohney T, Trofatter J, Wertelecki W, Ramesh V, Gusella J. DNA diagnosis of neurofibromatosis 2. Altered coding sequence of the merlin tumor suppressor in an extended pedigree. JAMA 1993;270:2316–2320.
16. MacCollin M, Ramesh V, Jacoby LB, Louis DN, Rubio MP, Pulaski K, Trofatter JA, Short MP, Bove C, Eldridge R, et al. Mutational analysis of patients with neurofibromatosis 2. Am J Hum Genet 1994;55:314–320.
17. Marangos N, Stecker M, Laszig R. Topodiagnosis of deafness: strategy for treatment of neurofibromatosis type 2. J Laryngol Otol 2000;27:3–7.
18. Mautner VF, Lindenau M, Baser ME, Hazim W, Tatagiba M, Haase W, Samii M, Wais R, Pulst SM. The neuroimaging and clinical spectrum of neurofibromatosis 2. Neurosurgery 1996;38:880–885.
19. Parry DM, Eldridge R, Kaiser-Kupfer MI, Bouzas EA, Pikus A, Patronas N. Neurofibromatosis 2 (NF2): clinical characteristics of 63 affected individuals and clinical evidence for heterogeneity. Am J Med Genet 1994;52:450–461.
20. Parry DM, MacCollin MM, Kaiser-Kupfer MI, Pulaski K, Nicholson HS, Bolesta M, Eldridge R, Gusella JF. Germ-line mutations in the neurofibromatosis 2 gene: correlations with disease severity and retinal abnormalities. Am J Hum Genet 1996;59:529–539.
21. Rouleau GA, Merel P, Lutchman M, Sanson M, Zucman J, Marineau C, Hoang-Xuan K, Demczuk S, Desmaze C, Plougastel B, et al. Alteration in a new gene encoding a putative membrane-organizing protein causes neuro-fibromatosis type 2. Nature 1993;363:515–521.
22. Samii M. Hearing preservation in bilateral acoustic neurinomas. Br J Neurosurg 1995;9:413–424.
23. Schulder M, Gangadhar, SS, Kwartler, JA, Cho, ES. Microsurgical removal of a vestibular schwannoma after strereotactic radiosurgery: Surgical and pathologic findings. Am J Otol 1999; 20:364–368.
24. Slattery WF, Brackmann DE, Hitselberger W. Hearing preservation in neurofibromatosis type 2. Am J Otol 1998;19:638–643.
25. Slattery WH, Brackmann DE. Results of surgery following stereotactic irradiation for acoustic neuromas. Am J Otol 1995;16:315–319.
26. Sobel RA. Vestibular (acoustic) schwannomas: histologic features in neurofibromatosis type 2 and in the unilateral cases. J Neuropathol Exp Neurol 1993;2:106–113.
27. Thomsen J, Mirz F, Wetke R, Astrup J, Bojsen-Moller M, Nielsen E. Intracranial sarcoma in a patient with neurofibromatosis type 2 treated with gamma knife radiosurgery for vestibular schwannoma. Am J Otol 2000;21:364–370.
28. Trofatter JA, MacCollin MM, Rutter JL, Murrell JR, Duyao MP, Parry DM, Eldridge R, Kley N, Menon AG, Pulaski K, et al. A novel moesin-, ezrin-, radixin-like gene is a candidate for the neurofibromatosis 2 tumor suppressor. Cell 1993;72:791–800.
29. Tsukita S, Yonemura, S, Tsukita, S. ERM (ezrin/ radixin/moesin) family: From cytoskeleton to signal transduction. Curr Opin Cell Biol 1997;9:70–75.

Chapter 3.2

Surgical outcome of the translabyrinthine approach for NF2 vestibular schwannoma

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Skull Base 2011 Submitted

Abstract

Objectives: To analyse the long term outcome of translabyrinthine surgery for vestibular schwannoma (VS) in Neurofibromatosis type 2 (NF2) in two large skull base surgical units in the United Kingdom.

Research type: Retrospective cohort study.

Setting: Two tertiary referral NF2 units.

Patients: Between 1981 and 2010, 128 patients with NF2 underwent 148 translabyrinthine operations for vestibular schwannoma. Bilateral surgery was performed in 20 patients. Preoperative stereotactic radiotherapy had been performed in 12(9.4%) patients.

Main outcome measures: Maximum mediolateral tumour diameter was used to assess tumour size. The extent of the excision was classified as total, near total, subtotal and partial. Recurrence rate was determined by magnetic resonance imaging (MRI). The House Brackmann (HB) facial nerve grading system was used to assess postoperative facial nerve outcome. Facial nerve results for each tumour size increment were compared with a similar surgical group of unilateral sporadic vestibular schwannoma. Where maximum SDS in the better hearing ear fell below 50%, Bamford-Kowal-Bench (BKB) sentence tests were performed and assessment for auditory implantation considered. The rates of auditory brainstem and cochlear implantation were recorded.

Results: Mean tumour size was 3.1cm with a range of 1.5-5.5cm. Total tumour excision was achieved in 66% of cases, near total in 24%, subtotal in 5% and partial removal in 5%. The recurrence rate was 13.9%. The perioperative mortality was 1.6%. Facial nerve outcome for the whole series at 2 years postoperatively was HB1 in 53.4%, HB1/2 in 61.3%, a satisfactory outcome (HB1-3) in 83.2% and unsatisfactory (HB4-6) in 16.8%. Facial nerve outcome assessed by tumour size increments was not as good in NF2 as in comparable unilateral sporadic VS. There were 9 patients who underwent surgery following failed stereotactic radiotherapy and 4 had a HB 1 result and in 5 it was HB3. Aberrant regeneration of the facial nerve produced a metallic taste in 46% of patients and 42% of these recovered within a year. Crocodile tears developed in 48% but of these only 6% recovered. There was no tinnitus present preoperatively in 27% and 22% of these developed tinnitus

postoperatively. In those patients with mild tinnitus preoperatively in 62% it remained the same, in 15% it disappeared and only in 23% did it worsen and then it was of moderate severity. In those patients with moderate tinnitus preoperatively in 60% it remained moderate, in 20% it was better and either became mild or disappeared and in 20% it worsened and became severe. The preoperative hydrocephalus rate was 26% and there were 4 (12%) preoperative ventriculo-peritoneal (VP) shunts performed and 1 (3%) postoperatively. The cerebrospinal fluid leak rate was 2.5%. Auditory implants were inserted in 58 patients of whom 56 underwent auditory brainstem implantation (ABI); 40 after unilateral VS surgery and 16 patients who had bilateral surgery. 2 patients had cochlear implant sleepers inserted.

Conclusions: The management of patients with NF2, particularly the Wishart phenotype, present the clinician with a formidable challenge. Despite modern imaging, earlier detection, and a concomitant move to early hearing preservation surgery, some patients are still presenting late with neurological compromise and a large tumour load. There is still an argument for management by observation until neurological compromise dictates interventional treatment particularly with the option of hearing rehabilitation with ABI or CI. The translabyrinthine approach provides a very satisfactory means of reducing the overall tumour volume and this paper in analysing 30 years of translabyrinthine surgery from the 2 largest skull base centres in the United Kingdom provides the evidence base to support this.

Introduction

As clinicians we are all only too aware of the challenge the management of Neuro-fibromatosis (NF2) presents us with. This disease is characterised by multiple benign tumours of the central and peripheral nervous systems, ocular and skin lesions and is diagnosed using the Manchester criteria.[1] It is inherited as an autosomal dominant and results from mutation of the NF2 tumour suppressor gene on chromosome 22q12.[2] Although these tumours are benign, the multiplicity of different types of tumour that occur in each patient make this a difficult disease to manage, requiring a specialist multidisciplinary team comprising a skull base surgeon, neurosurgeon, neurologist, geneticist, audiologist, radiologist, ophthalmologist and nurse specialist.[3,4]

Impairment of hearing is the symptom that has the greatest effect on the quality of life of patients with NF2.[5] This results from the presence of bilateral vestibular schwannomas (VS) in 90-95% of patients. The rate of progression of the hearing loss does not correlate with tumour growth[6] and occurs due to a combination of cochlear nerve compression and cochlear dysfunction, which often leads to total deafness.[7] Rehabilitation of hearing is essential to maintaining the quality of life of these patients. This requires the expertise of audiologists with specialist auditory implant experience within the NF2 team in order to optimise hearing aids in patients with residual hearing and provide timely assessment for auditory brainstem implants (ABI) and sometimes cochlear implants (CI) when hearing is lost.

The optimal management of VS in NF2 should minimise long-term morbidity and its effect on quality of life and to maximise rehabilitation, in particular with respect to hearing, facial nerve function, balance and tinnitus. The natural history of the majority of VS tumours in NF2 patients is progressive growth particularly with the Wishart phenotype. Surgical excision is favoured over radiotherapy in most centres owing to the aggressive nature of these tumours in terms of growth rates when compared with unilateral sporadic VS and the increased tumour load due to the appearance of metachronous tumours as well as the relatively young age at presentation.[8] Up to 20% of NF2 patients who undergo radiosurgery to their VS require further treatment at 8 years follow-up, with good control of growth in only 50%.[9] compared with 90-95% in unilateral sporadic VS. However, opinions differ between teams as to the optimum timing for VS removal, the surgical approach used for tumour excision[10] and whether auditory implantation should be offered when the first tumour is removed in anticipation of eventual hearing loss on the contralateral side.

For decades now the predominant management of watch, wait and rescan has centred on the preservation of neurological function and maintenance of the best quality of life for the patient. Surgery was considered only when there was critical neurological compromise with significant brainstem compression but before the development of hydrocephalus, papilloedema and ensuing decompensation.

With the recent publication of very successful hearing preservation results from middle fossa surgery from Iowa[11] and Dallas, USA[12] there has been a paradigm shift in opinion in some centres and a move to early surgery particularly for intra-canalicular tumours.[13] The majority of surgical units, however, have not adopted early hearing preservation surgery perhaps because of the substantial proportion of patients presenting late with large tumours and little or no hearing and also because of doubt over the maintenance of socially useful hearing in the long term particularly

in very young patients and some emerging evidence of good results from auditory brainstem implantation.

Translabyrinthine surgery remains an excellent way of excising large tumour loads as the shortest and most direct route to the CPA with an approach that is achieved at the expense of bony removal rather than cerebellar retraction and with visualistion of the proximal and distal intratemporal portions of the facial nerve.

Surgery in the CPA in NF2 presents us with specific difficulties firstly because of the large volume of tumour which is often bosselated and of variable biological activity, vascularity and adhesion to surrounding neurological structures as well as the presence of metachronous tumours and often difficult intraoperative decisions have to be taken concerning the totality of the excision and risk of compromise of the postoperative quality of life.

Much has been written about the outcome of translabyrinthine surgery for unilateral sporadic vestibular schwannoma[14,15] but to our knowledge there are no papers reporting long term results in a large series of translabyrinthine operations for vestibular schwannoma in NF2 .

We present the long term outcome of translabyrinthine surgery for vestibular schwannoma in a series of patients with NF2 managed in two of the largest skull base surgical units in the United Kingdom over three decades.

Methods

This study is a retrospective case note analysis. All patients were treated surgically in two tertiary referral NF2 units at Cambridge and Manchester University Hospitals, two of the four current lead NF2 units in England. Clinical data was collected on Filemaker Pro 6 initially and more recently on Filemaker Pro 10 software.

Patients were reviewed annually, or more frequently as symptoms dictated, in a multidisciplinary NF2 clinic. All patients underwent annual MRI head and three yearly MRI spine for tumour surveillance, with family members screened for NF2 as appropriate. [3] Annual pure tone audiograms and speech discrimination scores (SDS) were recorded in all patients. Where maximum SDS fell below 50%, Bamford-Kowal-Bench (BKB) sentence tests were presented in best-aided conditions at the optimum sound intensity identified by the SDS. A BKB score of less than 50% triggered an assessment for hearing implantation.

Patients

There were 128 surgical patients with NF2 in this series, 62 male patients and 66 females. There were 80 right sided tumours and 68 on the left.
The age range was 10 to 65 years with a mean of 29.5 years and a standard deviation (SD) of 13.9. The age distribution in decades can be seen in Figure 1a and below it Figure 1b is the age distribution in unilateral sporadic VS (where the mean age is 54.3 years) to demonstrate the much younger distribution and mean age in the NF2 patients.
148 translabyrinthine operations were performed. Staged bilateral surgery was performed in 20 patients. The follow up period was 1 to 30 years. There was a family history of NF2 in 54 (40%). The Wishart phenotype was present in 9(7%) patients. Preoperative stereotactic radiotherapy had been performed in 12(9.4%) patients. One tumour was malignant and excluded from the series.

Main outcome measures
Maximum mediolateral tumour diameter including the intracanalicular portion was used to assess tumour size since the series extends back to 1980 and this was the method used at that time. The authors are cognisant of the more recent measure of maximum intracranial tumour diameter (ICTD)[16] where solely intracanalicular (VS=0mm) tumours are stated as such. For the sake of consistency we have used the former measurement method throughout. Tumour size was classified as less than 1.5cm, 1.5-2.4cm, 2.5-3.4cm, 3.5-4.4cm, and 4.5cm or larger.
The extent of the excision was classified as total, near total, subtotal and partial. Total removal was complete excision of the tumour. Near total was defined as complete excision apart from tiny remnants of capsule on a cranial nerve or brainstem. Subtotal excision meant greater than 95% of tumour removed and partial excision where less than 95% of the tumour was removed. Patients were scanned annually postoperatively in the NF2 multidisciplinary clinics and the recurrence rate was recorded.

Perioperative mortality figures were recorded
The House Brackmann (HB) facial nerve grading system was used to assess facial nerve outcome. Totally normal function was classified as HB 1 but HB 1/2 was also recorded since some modern series quote this as normal. HB1-3 was classified as a satisfactory outcome and HB 4-6 as unsatisfactory at 24 months after surgery. Aberrant regeneration of the facial nerve in the form of altered taste and crocodile tears were recorded along with the percentage that recovered.

Figure 1. **Age range at surgery**

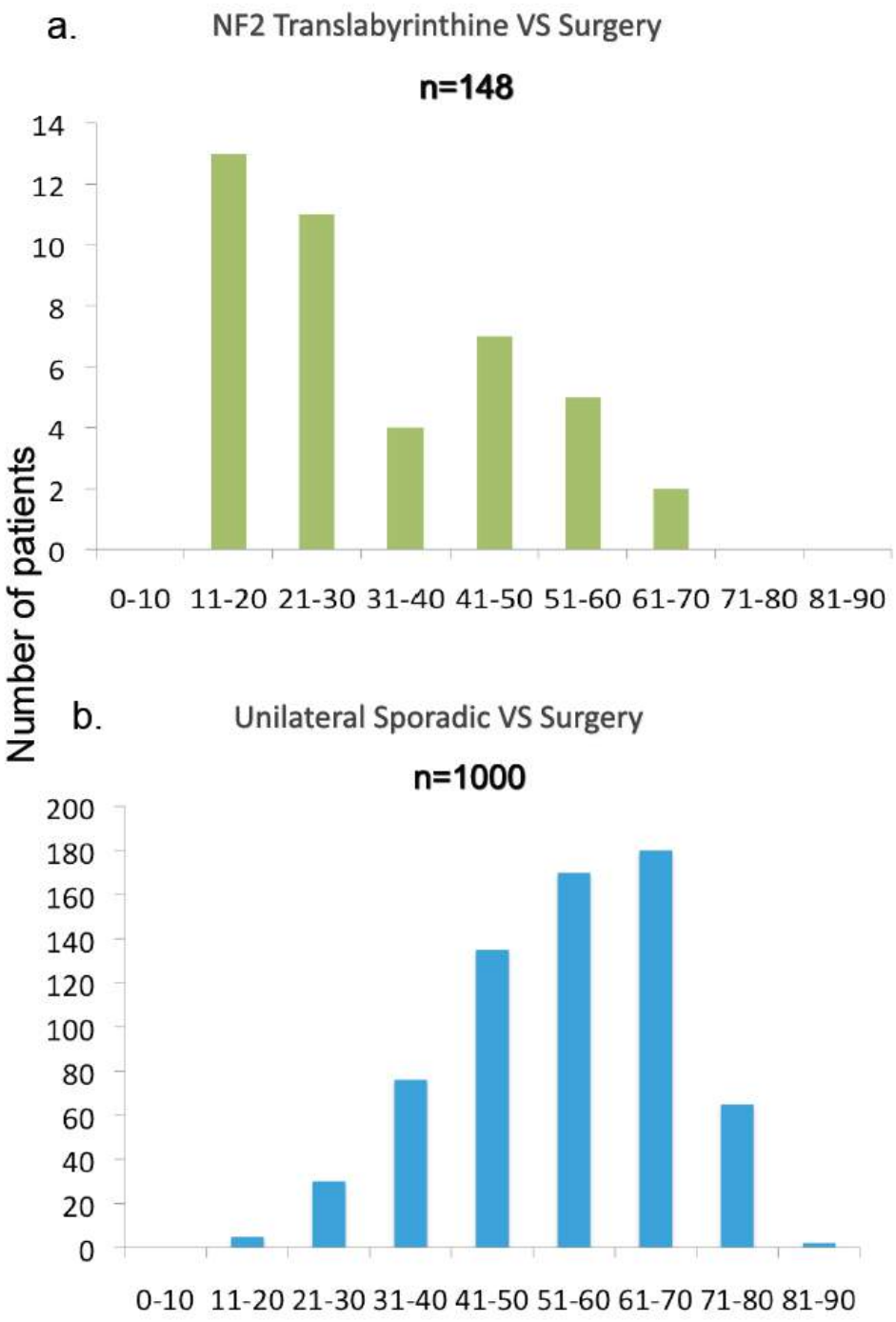

Figure 1a: A histogram of the age distribution in decades of this series of NF2 VS patients. The age range was 10 to 65 years with a mean of 29.5 years and a standard deviation of 13.9.

Figure 1b: Age distribution of a comparable series of unilateral sporadic VS patients showing a much older group than in NF2 with an age range of 13-86 years and a mean of 53.8 years and a standard deviation of 12.6.

The rate of anatomical preservation of the facial nerve was recorded and the type of facial reconstruction and functional outcome was documented.The incidence of preoperative hydrocephalus and pre- and postoperative ventriculo-peritoneal (VP) shunting was noted. The cerebrospinal fluid (CSF) leak rate was determined.

Outcome with regard to tinnitus was determined in detail. The type of tinnitus (continuous, intermittent or pulsatile), the frequency (high, medium or low pitched) and the severity (mild, moderate or severe). The classification of severity can be seen in Table1.

These parameters were recorded preoperatively and at 12 months postoperatively and changes were analysed to determine outcome.

Quality of life postoperatively was assessed simply as good, fair or bad and the definition of these can be seen in Table 2.

Table 1: Classification of tinnitus severity

Mild	=	Can only hear it when the ambient noise is very low
Moderate	=	Can hear it during the day above the ambient noise
Severe	=	Stops the patient from sleeping or wakens from sleep

Table 2: Quality of life outcome measure

Good	=	Complete recovery and capable of returning to previous occupation
Fair	=	Independent but unable to work
Poor	=	Dependent

The surgical outcome of the early patients in this series was at a time before more sophisticated quality of life (QoL) studies had been introduced and which scientific papers have been written subsequently starting with the modified SF36 questionnaire[17] progressing through to other more customised and well validated questionnaires such as the hearing, [18] tinnitus[19] and dizziness[20] handicap scores and more recently the Rankin scale of QoL[21].

It is difficult to relate surgical outcome to quality of life in these NF2 patients because they have multiple intracranial tumours which can affect hearing and balance through involvement of the eighth nerve complex, facial schwannomas may affect facial nerve function and sight may be affected by optic gliomas or meningiomas as well as spinal tumours producing sensory and motor deficits in the limbs. Again for the sake of consistency and completeness and realising the limitations of this basic measure we decided to include this general functional quality of life.

Patients were assessed for their suitability for auditory implantation. Hearing outcomes were reported according to our NF2 hearing assessment classification (Table 3).

Table 3: Assessment of hearing in NF2

Grade	Test	Deficit
1	>80% SDS in better hearing ear	Normal or near normal hearing with or without acoustic hearing aids
2	50-80% SDS in better hearing ear	Good benefit from acoustic hearing aids
3	<50% SDS in better hearing ear; >50% BKB	Adequate benefit from acoustic hearing aids, best aided condition
4	<50%SDS in better hearing ear; <50% BKB	Poor benefit from acoustic hearing aids, consider auditory implant
5	Auditory implant	

Speech discrimination score (SDS) is the percentage of phonemes within 10 monosyllabic words correctly identified at an optimal sound intensity.

Bamford-Kowal-Bench (BKB) Standard Sentence Lists comprise 21 lists, each having 16 sentences and 50 keywords (3 or 4 per sentence) presented at optimal sound intensity.

Maximum SDS and BKB scores were reported from the most recent measurements in all current patients. Hearing was defined as adequate in patients with a maximum SDS of at least 50% in the better hearing ear, a maximum SDS less than 50% with BKB scores over 50% in the better hearing ear or where the patient was a full time user of an auditory implant. Preoperatively patients with Grade 4 or 5 hearing were considered for an auditory implant or possibly as a sleeper for those with Grades 1-3 depending on the clinical situation.

The rates of auditory brainstem and cochlear implantation were recorded. Detailed audiological and electrophysiological and functional outcome of these patients are the subject of a further specific scientific publication.

Results

Tumour size

A histogram of preoperative tumour size in each 1cm increment in this series of NF2 patients can be seen in Figure 2a. The mean tumour size in the NF2 group was 3.1cm. The lower histogram (Figure 2b) is of a comparable surgical series of unilateral sporadic VS tumours where the mean size is 2.6cm. This shows clearly that the NF2

group had bigger tumours and this clearly relates to the watch, wait and rescan management policy already alluded to.

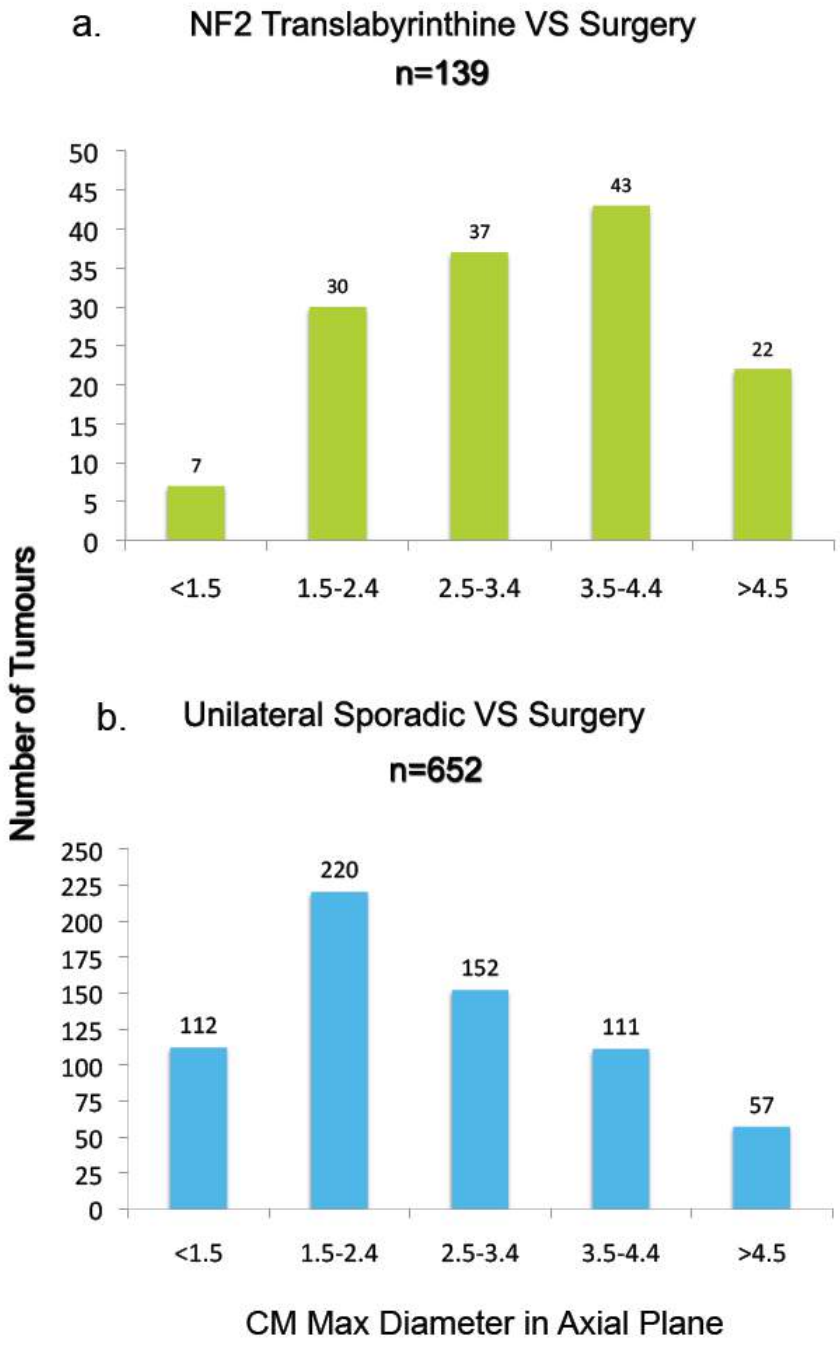

Figure 2a: Histogram of tumour size in 1 cm increments of this series of NF2 VS patients. The mean tumour size was 3.1cm.

Figure 2b: Histogram of tumour size in a comparable series of unilateral sporadic VS. The mean tumour size was 2.6cm which demonstrates that the NF2 group had larger tumours preoperatively.

Extent of tumour resection

The analysis of the extent of the excision can be seen in the exploded pye chart in Figure 3. It was possible to achieve a total excision in 66% of tumours. Near total excision represented 24% and subtotal excision in 5% and partial also in 5% of tumours .

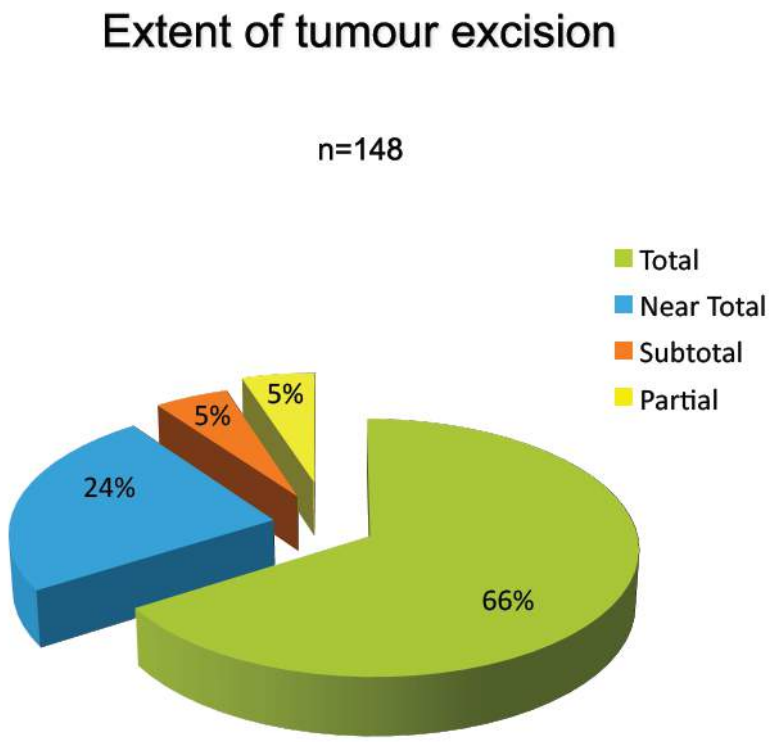

Figure 3: This exploded pye chart shows the extent of tumour excision in this surgical series. (Total = complete excision; near total = tiny remnants of capsule on a cranial nerve or brainstem; subtotal = greater than 95% of tumour excised; partial = less than 95% of tumour removed) Total excision was achieved in 66% of tumours. Near total resection represented 24% with subtotal excision in 5% and partial excision in 5%.

We are particularly challenged by a small cohort of patients of 7% who generally have the Wishart phenotype, are young, present late with huge tumours which are extremely vascular and are very adherent to the brainstem and some, less so recently in view of the emerging poorer results of stereotactic radiotherapy in NF2, have had gamma knife treatment and this can make the dissection much more difficult.

Patients were scanned annually postoperatively in the NF2 multidisciplinary clinics. Ipsilateral tumour recurrence has not been observed in any of the patients who had a total resection of tumour. Overall there was a recurrence rate of 13.9%.

Perioperative mortality

There were no peroperative deaths and the perioperative mortality was 1.6%, the 2 deaths were due to brainstem ischaemia and pulmonary embolism respectively.

Facial nerve outcome

For the series as a whole with a mean tumour size of 3.1cm 53.4% had an HB1 result with totally normal facial function. Many papers now quote HB 1/2 as normal and in this series HB 1/2 outcome was 61.3%. A satisfactory outcome (HB 1-3) was achieved in 83.2% of patients and an unsatisfactory outcome (HB 4-6) in 16.8%.

Studying a smaller subset of patients (Cambridge series; n=43), in tumours less than 2.5cm in size a satisfactory facial nerve outcome was achieved in 11/12 (92%) of patients and for tumours greater than 2.5cm it was 18/24 (80%) (See Table 4).

Table 4: Facial nerve outcomes after NF2 VS resection (n=43)

	HB 1-3	HB 4-6
VS Max diam <25mm	12	1
VS Max diam >25mm	24	6

As expected the larger the tumour the greater the likelihood of an unsatisfactory outcome but this is only a trend and because of the small numbers and weak power of the study the difference between the two groups did not reach statistical significance (p= 0.41 Fisher exact test).

If facial nerve outcome in NF2 is determined for tumour size increments as previously described, tumours less than 1.5cm had 100% HB 1, tumours 1.5-2.4cm had 58% HB 1 and 92% were satisfactory (Figure 4a.). In tumours 2.5-3.4cm the HB 1 outcome was 39% and 85% were satisfactory, in tumours 3.5-4.4cm HB1 was 44% and 89% were satisfactory and tumours greater than 4.5cm in size HB1 was 33% and 83% were satisfactory.

Comparing the facial nerve outcome in the NF2 cases with unilateral sporadic VS the results are not as good in NF2. The lower Figure 4b is a histogram of the facial nerve outcome following translabyrinthine surgery for unilateral sporadic VS in the last 200 patients of a series of 1000 cases dating back 30 years. For small tumours less than 1.5cm, 94% have a HB 1 result and 100% have a HB1 to 3 or satisfactory outcome.

For tumours of 1.5 to 2.4cm 83% have an HB 1 result and 99% a satisfactory result.

This drops to 68% HB 1 and 96% satisfactory for 2.5 to 3.4cm tumours and to 52% HB 1 and 80% satisfactory for tumours 3.5 to 4.4 cm and to 50% HB 1 and 72%

satisfactory for tumours larger than 4.5cm. The difference is thus more noticeable comparing the HB1 outcome than the satisfactory results.

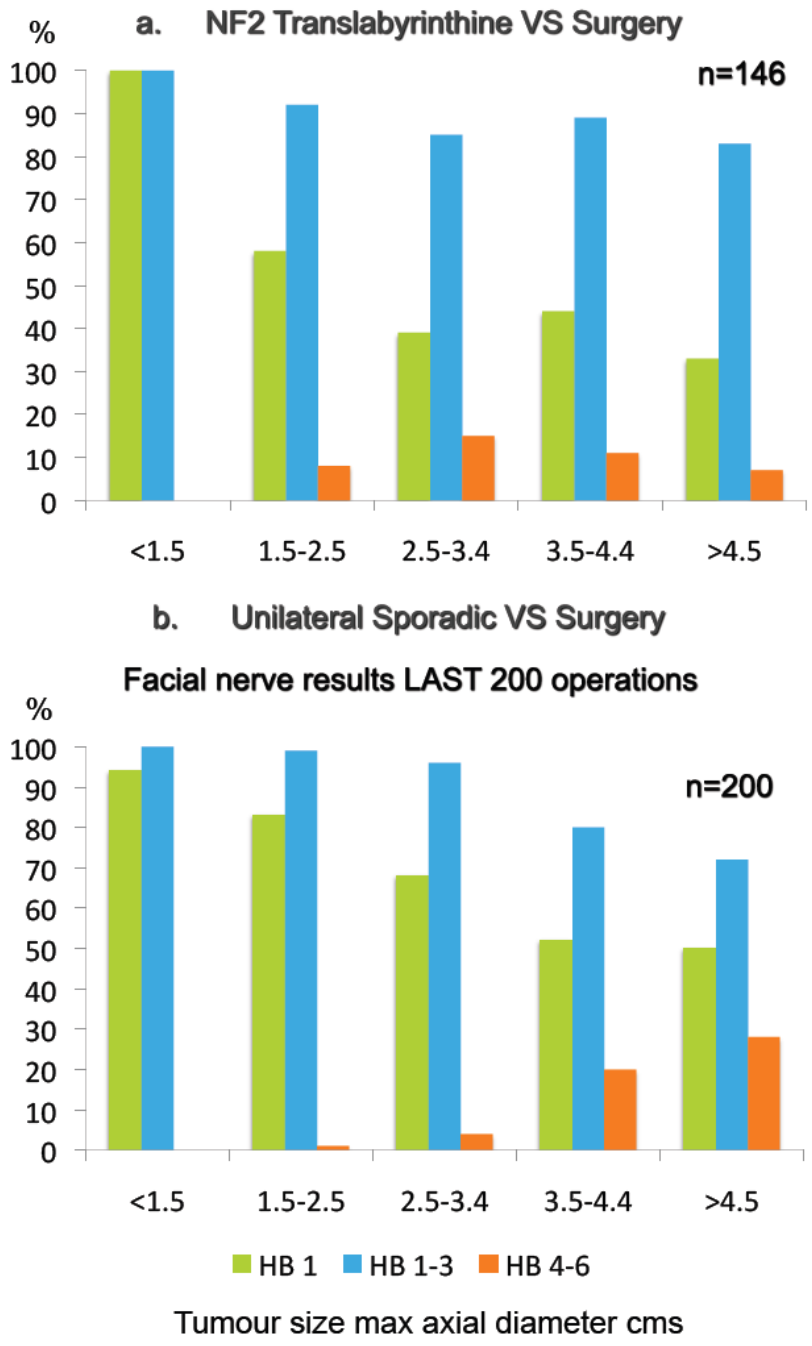

Figure 4a: Histogram of the facial nerve outcome at 2years postoperatively in this NF2 series of translabyrinthine VS excision in tumour increments of 1cm from <1.5cm to >4.5cm.

Figure 4b: Histogram of facial nerve outcome at 2 years postoperatively for a series of unilateral sporadic VS which is, in fact, the last 200 cases of a 1000 case series dating back 30 years. It can be clearly seen that the outcome is not as good in the NF2 cases as in the unilateral sporadic VS. The difference is not marked when considering satisfactory (HB1-3) versus unsatisfactory (HB 4-6) but can be clearly seen in the percentage of HB1 in the two groups.

There were 9 patients who underwent surgery for NF2 vestibular schwannoma following stereotactic radiosurgery (gamma knife) and 4 had a HB 1 result and 5 had HB 3 facial nerve outcomes. Although these outcomes are better than those reported in the literature this series is too small to draw any definite conclusion from at present.

Aberrant regeneration of the facial nerve occurs in some patients following surgery for VS. In this series 46% suffered a metallic or salty taste in the mouth and 42% of these recovered within 12 months. Gustatory epiphora or crocodile tears occurred in 48% of patients but only 6% of these recovered.

Fourteen (9.5%) of facial nerves were lost at surgery but clinical data was only available for seven. These were repaired by direct anastomosis (1), cable graft (3) and cross facial graft (3). The facial nerve outcome in this small group of patients can be seen in table 5.

Table 5: Postoperative outcome of facial nerve reanimation procedures

Procedure	Patients	Outcome – HB grade	n=7
Direct anastomosis	1	3	
Cable graft	1	3	
	1	3	
	1	5	
Cross facial graft	1	3	
	1	3	
	1	3	

Tinnitus

There was no tinnitus present preoperatively in 27% of the series. In the 73% where it was present the tinnitus was constant in 52%, intermittent in 21% and no patients had pulsatile tinnitus (Figure 5a).

High frequency tinnitus was present in 79% and 21% had medium frequency tinnitus and no patients described low frequency tinnitus (Figure 5b). The classification of severity can be seen in Table1. In 54% it was mild and in 46% it was moderate and there were no cases of severe tinnitus preoperatively (Figure 5c).

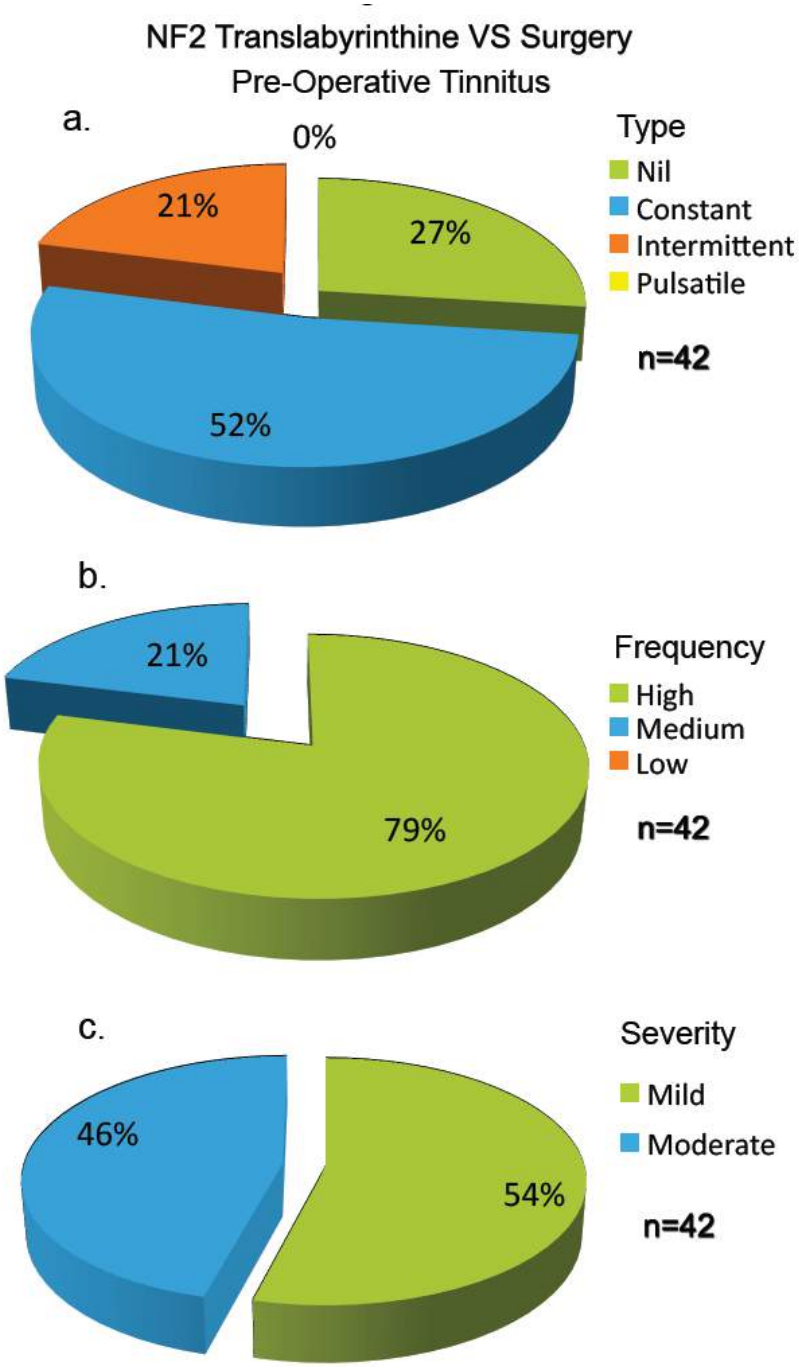

Figure 5a: Exploded pye diagram of the type of tinnitus present in the 73% of patients with preoperative tinnitus. In 52% it was constant and in 21% intermittent. There were no cases of pulsatile tinnitus.

Figure 5b:Exploded pye diagram of the frequency of the tinnitus. In 79% the tinnitus was high frequency and in 21% it was medium frequency. There were no cases of low frequency tinnitus.

Figure 5c:Exploded pye diagram of the severity of the tinnitus. The tinnitus was mild in 54% and moderate in intensity in 46% of cases. There were no patients with severe tinnitus preoperatively.

In the 27% of the series with no tinnitus preoperatively 22% developed tinnitus postoperatively and in half (11%) it was mild and the other half (11%) moderate in intensity (Figure 6a).
In those patients with mild tinnitus preoperatively in 62% it remained the same, in 15% it disappeared and only in 23% did it worsen and then it was of moderate severity. There were no cases of it becoming severe (Figure 6b).
In those patients with moderate tinnitus preoperatively in 60% it remained moderate, in 20% it was better and either became mild or disappeared and in 20% it worsened and became severe (Figure 6c).
Severe tinnitus only occurs in 2% of the unilateral sporadic VS following surgery.

Hydrocephalus and ventriculo-peritoneal (VP) shunts
The preoperative hydrocephalus rate was 26% and in 12% preoperative ventriculo-peritoneal (VP) shunts were performed and in 3% postoperatively. The incidence of hydrocephalus and the need for VP shunting was more frequent in the earlier part of this series which goes back 3 decades.

Cerebrospinal fluid leak
The cerebrospinal fluid leak rate was 2.5%. If this occurred within 14 days postoperatively a lumbar drain was inserted for 4 days. The re-exploration rate was 1%.

Quality of life
This was analysed as defined by the criteria set out in Table 2 with the limitation and caveats already discussed. A good postoperative quality of life with the patient capable of returning to their previous occupation was achieved in 73%. A fair outcome was seen in 17% and a poor outcome in 10%.

Auditory implants
Auditory brainstem implantation (ABI) has been a remarkable advance in the management of NF2 and there is also a place for cochlear implantation (CI) in some carefully selected cases. Auditory implants were inserted in 58 surgical patients of whom 56 underwent auditory brainstem implantation (ABI); 40 after unilateral VS surgery and 16 patients who had bilateral surgery. 2 patients had cochlear implant sleepers inserted.

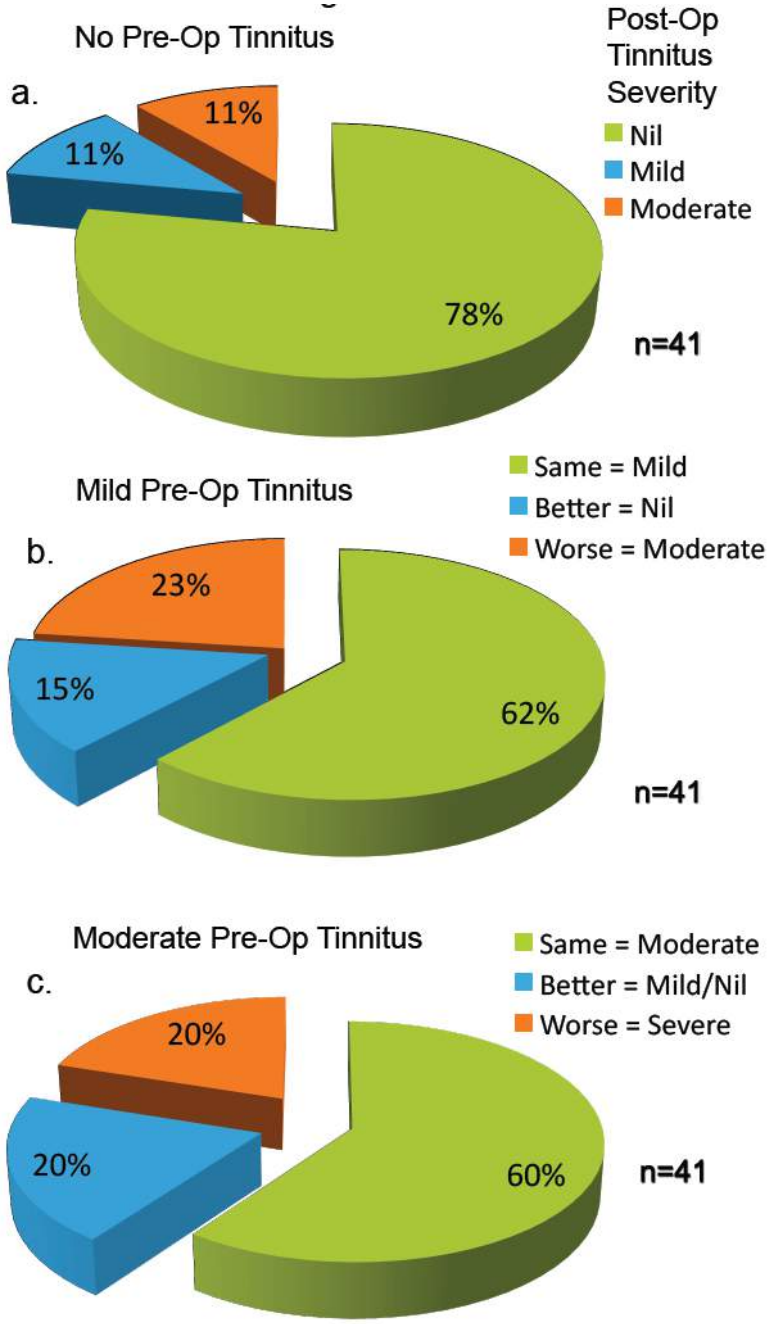

Figure 6a: Exploded pie diagram showing what happened postoperatively to the 27% of patients who had no tinnitus preoperatively. Seventy three percent remained with no tinnitus postoperatively but 22% developed tinnitus and in half (11%) it was mild and the other half (11%) moderate in intensity.

Figure 6b: Exploded pie diagram showing what happened postoperatively in those patients with mild tinnitus preoperatively. In 62% it remained the same, in 15% it disappeared and only in 23% did it worsen and then it was of moderate severity. There were no cases of it becoming severe.

Figure 6c: Exploded pie diagram of those patients with moderate tinnitus preoperatively. In 60% it remained moderate, in 20% it was better and either became mild or disappeared and in 20% it worsened and became severe.

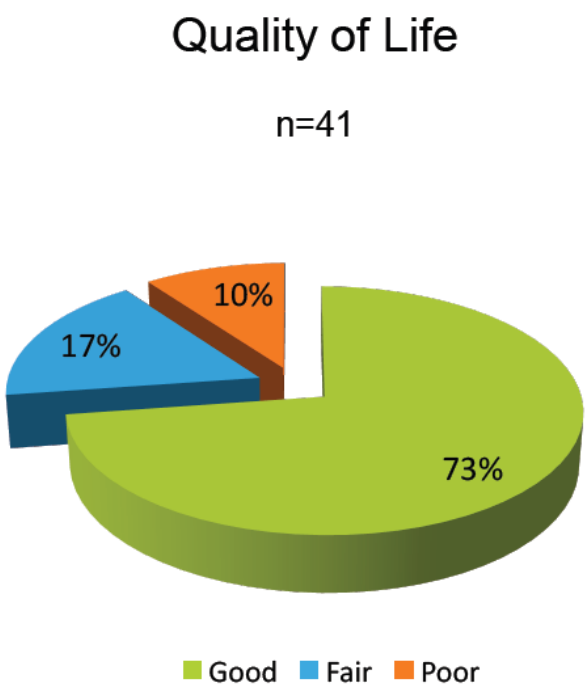

Figure 7: A simplistic quality of life outcome classification was analysed because it has been in use for 30 years. A good postoperative quality of life with the patient capable of returning to their previous occupation was achieved in 73%. A fair outcome was seen in 17% and a poor outcome in 10%.

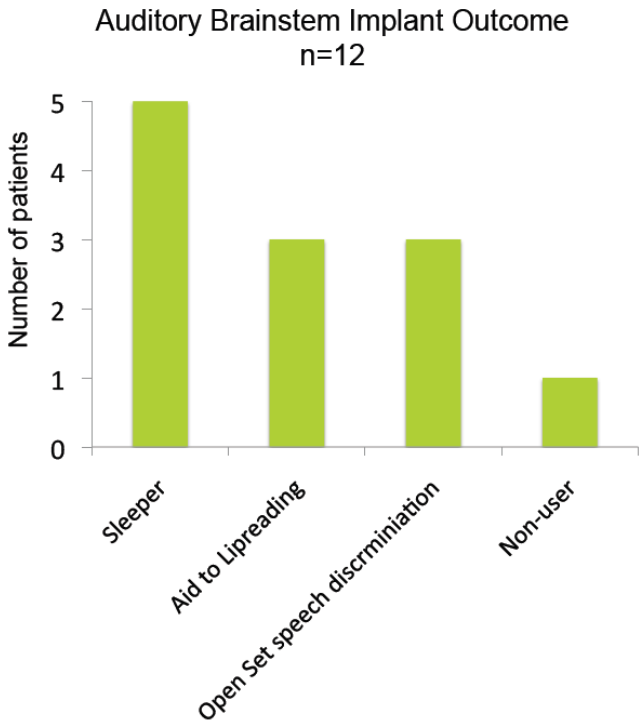

Figure 8: This histogram shows the ABI outcomes of the Cambridge subset of 12 patients. Five patients have had an ABI sleeper implanted. Three users have open set speech discrimination and in 3 the ABI is an aid to lip reading. One patient is a non-user.

Of the 56 patients with ABI the majority are full time users or have adequate hearing with a "sleeper" ABI. The non-users either have not been able to gain auditory perception from the implant or do not use their "sleeper" ABI. An analysis of the ABI outcome of a subset of patients (Cambridge) can be seen in the histogram (Figure 8).

Discussion

The appropriate timing of VS excision in NF2 patients is now decided by a meeting of the multidisciplinary team and depends on many factors including size of tumour, rate of growth, extent of brainstem compression, hearing loss, facial function, balance, other intracranial and metachronous tumours and informed patient choice.[10] When tumour growth is observed the timing of the decision to surgically excise the VS is important because the frequency of cochlear and facial nerve preservation is less and the risk of damage to the adjacent cranial nerves is greater in NF2 than in the unilateral sporadic VS tumours. The overall approach, however, also depends on the experience and outcomes of the NF2 department taking into consideration the phenotype and severity of the disease. Whilst several different strategies for managing these patients are valid and cogent arguments put forward for them it is essential that this is a patient-centred decision and that patients are well informed before taking it.

One management option, prevalent in years gone by, was watch, wait and rescan in order to preserve any useful residual hearing for as long as possible only offering surgical resection of the tumour when no useful hearing remained or significant brainstem compression was seen.[22] Certainly early in this 30 year series this was the predominant management of VS in NF2. Since tumours are likely to be of large volume by the time significant brainstem compression occurs, a tumour de-bulking strategy might have to be used as opposed to complete tumour excision in order to minimise surgical morbidity to the facial nerve, and latterly with adjuvant radio-therapy offered to treat the residual tumour.[23] On the basis that VS in NF2 are relatively aggressive particularly with the Wishart phenotype and that incomplete excision of VS often results in residual tumour and later recurrence,[24] this may result in even poorer facial nerve outcomes in the long term for those patients that require further surgery or radiotherapy following growth of residual and/or recurrent tumours.[25] More recently early surgery by the middle fossa approach has been proposed by some NF2 units in order to maximise the chances of hearing preservation and a good facial nerve outcome. Brackmann *et al*[13] have reported 70% hearing preservation rates and excellent facial nerve outcomes in their cohort

although 72% of tumours were under 1cm in size and 92% under 2cm. Middle fossa surgery represented 20% of all VS operations performed in their series of NF2 patients.

Offering surgery to all tumours, however small, may result in overtreatment and the excision of some tumours that, if observed, may never have grown or resulted in complete hearing loss. Although hearing preservation surgery should be offered to patients with growing tumours where socially useful hearing remains, even in the hands of the most experienced teams, rates of successful hearing preservation are often poor. Hearing was preserved in only one-third of patients where a retrosigmoid approach was used by Samii et al[22] and our experience reflects this with hearing preservation in one of five patients. As a result, we have favour the translabyrinthine approach.

Currently we believe in timely tumour resection and hearing rehabilitation and offer removal of the VS when there is evidence of growth on serial MRI or when significant brainstem compression is observed. We set out to achieve complete tumour resection in all patients while maintaining facial nerve function. A small remnant of tumour capsule may be left on the facial nerve or on the brainstem if very adherent in order to minimise the risk of neurological compromise and optimise post-operative quality of life.

William House[26] the forefather of modern skull base surgery revitalised interest in the translabyrinthine approach to CPA tumours which was first described by Panse in 1904.[27] Modern surgical and neuro-anaesthetic techniques enable any size of tumour to be excised by this approach. We favour the translabyrinthine approach in NF2 because the approach gives us the shortest route to the CPA, access is gained by bone removal rather than cerebellar retraction , the facial nerve is seen at both ends and complete removal of the vestibular nerves can be more easily achieved.

Surgery in the CPA in NF2 presents us with specific difficulties firstly because of the large volume of tumour which is often bosselated and of variable biological activity, vascularity and adhesion to surrounding neurological structures as well as the presence of metachronous tumours and often difficult intraoperative decisions have to be taken concerning the totality of the excision and risk of neurological compromise and its effect on postoperative quality of life.

Over 30 years and in this joint series we have been able to achieve total tumour excision in 66% of cases, capsular remnants (near total excision) were left in 24%, subtotal excision (>95% tumour volume excised) was achieved in 5% and partial removal in 5%. and the recurrence rate was 13.9% for the series as a whole. We have

had no episodes of tumour recurrence in those patients where total excision was achieved by a translabyrinthine approach.

A satisfactory facial nerve outcome (HB1-3) was achieved 83.2% postoperatively in this series as a whole and normal facial function (HB1) in 53.4%.

There were no intraoperative deaths and the perioperative mortality was 1.6% in this series of NF2 patients. Not surprisingly this was higher than a large series of unilateral sporadic VS cases where it was 0.3%.[28]

Generally the morbidity from surgery is relatively low for an intracranial procedure but tinnitus may become a significant symptom postoperatively. There was no tinnitus present preoperatively in one in four patients and of these one in five will develop it postoperatively. In those patients with mild tinnitus preoperatively in three out of four it will stay the same or improve and in only a quarter will it worsen and if it does it is very unlikely to be severe. In those patients with moderate tinnitus preoperatively in four out of five it remained the same or improved and in only one in five did it worsen and became severe. One unexplained factor in tinnitus following VS surgery is that loud noise exacerbates the tinnitus unlike idiopathic tinnitus where background noise masks and ameliorates the symptom.[29]

The preoperative hydrocephalus rate was 26% and of these 12% had preoperative ventriculo-peritoneal (VP) shunts performed and then postoperative VP shunt rate was 3%.

The cerebrospinal fluid leak rate was only one in forty operations and the risk of re-exploration for CSF leak was one in a hundred translabyrinthine operations.

Auditory implants were inserted in 58 patients of whom 56 underwent auditory brainstem implantation (ABI); 40 after unilateral VS surgery and 16 patients who had bilateral surgery. 2 patients had cochlear implant sleepers inserted.

Where both tumours are growing, excision of the VS in the worse hearing ear is offered with insertion of an ABI using a translabyrinthine approach to maximise access, facilitate facial nerve dissection and ensure complete vestibular nerve removal to minimise recurrence. In these patients, the insertion of a “sleeper” ABI is offered in anticipation of contralateral complete deafness in the future as hearing loss progresses in the contralateral ear or is lost due to surgery to excise the contralateral tumour. It is, as yet, unclear whether a “sleeper” ABI should be turned on prior to the loss of hearing on the contralateral side.[30] This would ensure continued stimulation of the auditory pathways, which may improve long term hearing rehabilitation.[31] Poor patient compliance, however, reflects the fact that it is unlikely that ABI will provide much in the way of rehabilitation where serviceable hearing remains on the contralateral side. Recent evidence has shown that CI provides superior hearing over BAHA and CROS-aids in patients with single-sided

deafness and that the CI does not interfere with speech understanding in the normal hearing ear.[32] Thus where serviceable hearing remains on the contralateral side ABI provides a much lower level of auditory rehabilitation than can be expected than from a CI. Our limited experience has shown that ABIs do not give the patients benefit until hearing is lost in the contralateral ear.

In this series two patients received CI in the operated ear where cochlear nerve preservation was attempted. The question remains over whether successful cochlear nerve preservation during VS surgery should be followed by insertion of CI rather than ABI.[33] Although hearing rehabilitation would be expected to be far better after CI than ABI, open set speech was only achieved by Lustig *et al* in two of four NF2 patients who received a CI where there was no hearing in the contralateral ear.[34] In common with reported series, we found that patients can expect the ABI to act at least as an aid to lip reading, although in some cases, open set speech discrimination is possible.[35,36] The problem remains that identifying patients who may benefit from a CI at VS resection is unreliable.

The recent development of implants with both cochlear and brainstem electrodes has been reported by Somers *et al* and may prove to be the best method of electrode stimulation of either the cochlea and/or brainstem in the future. Electrical stimulation of the cochlea nerve may encourage some recovery following surgery.[37]

Conclusions

Neurofibromatosis type 2 is a challenging disease and all management options should be considered by the multidisciplinary team. The earlier management protocol of watch, wait and rescan until tumour growth and neurological compromise has been more recently replaced by judicious timing of surgery in growing tumours in order to minimise neurological deficit and optimise hearing rehabilitation. In this joint 30 year series of NF2 patients from 2 of the largest UK skull base units the long-term outcome of the translabyrinthine surgery has been analysed in detail.

This was a younger population, often presenting late, with larger tumours than unilateral sporadic VS particularly in those with the more aggressive Wishart phenotype. Hydrocephalus was present to varying degrees in a quarter of the series one in ten necessitating preoperative VP shunting. A proportion of large vascular tumours were significantly adherent to the brainstem. The perioperative mortality, therefore, whilst low was five times greater than in unilateral sporadic VS, the percentage of total tumour excision was less and the facial nerve outcome was not as

good. The CSF leak rate was low. Quality of life postoperatively was good in 73% of patients.

Hearing rehabilitation is important and assessment for ABI should be considered to maintain quality of life and the possibility of CI or a combined ABI/CI implant considered in selected patients. The use of a "sleeper" ABI ensures that patients do not have a period of complete deafness if hearing is lost in the contralateral ear. Over a third of this series of patients received an ABI and two a cochlear implant.

Translabyrinthine surgery and auditory implantation has proved to be a satisfactory means of managing VS in NF2 patients.

References

1. Asthagiri AR, Parry DM, Butman JA, et al. Neurofibromatosis type 2. Lancet 2009;373(9679): 1974-1986.
2. Rouleau GA, Merel P, Lutchman M, et al. Alteration in a new gene encoding a putative membrane-organizing protein causes neuro-fibromatosis type 2. Nature 1993;10;363(6429): 515-521.
3. Evans DG, Baser ME, O'Reilly B, Rowe J,Gleeson M Saeed S, King A. Huson SM, Kerr R,Thomas N, Irving R, Macfarlane R, Ferner R, McLeod R,Moffat D, Ramsden R. Management of the patient and family with neurofibromatosis 2: a consensus conference statement. Br J Neurosurg 2005; 19(1):5-12.
4. Evans DG, Ramsden R, Huson SM, Harris R, Lye R, King TT. Type 2 neurofibromatosis: the need for supraregional care? J Laryngol Otol 1993;107(5):401-406.
5. Neary WJ, Hillier VF, Flute T, Stephens D, Ramsden RT, Evans DG. Use of a closed set questionnaire to measure primary and secondary effects of neurofibromatosis type 2. J Laryngol Otol 2010;124(7):720-728.
6. Fisher LM, Doherty JK, Lev MH, Slattery WH. Concordance of bilateral vestibular schwannoma growth and hearing changes in neurofibromatosis 2: neurofibromatosis 2 natural history consortium. Otol Neurotol 2009;30(6):835-841.
7. Evans DG, Huson SM, Donnai D, et al. A clinical study of type 2 neurofibromatosis. Q J Med 1992;84(304):603-618.
8. Samii M, Matthies C, Tatagiba M. Management of vestibular schwannomas (acoustic neuromas): auditory and facial nerve function after resection of 120 vestibular schwannomas in patients with neurofibromatosis 2. Neurosurgery 1997;40(4):696-705.
9. Rowe J, Radatz M, Kemeny A. Radiosurgery for type II neurofibromatosis. Prog Neurol Surg 2008;21:176-182.
10. Moffat DA, Quaranta N, Baguley DM, Hardy DG, Chang P. Management strategies in neurofibromatosis type 2. Eur Arch Otorhinolaryngol 2003;260(1):12-18.
11. Woodson EA, Dempewolf RD, Gubbels SP, Porter AT, Oleson JJ, Hansen MR, Gantz BJ. Long-term hearing preservation after microsurgical excision of vestibular schwannoma. Otol Neurotol 2010;31(7):1144-52.
12. Kutz JW Jr, Scoresby T, Isaacson B, Mickey BE, Madden CJ, Barnett SL,Coimbra C, Hynan LS, Roland PS. Hearing preservation using the middle fossa approach for the treatment of vestibular schwannoma. Neurosurgery 2012;70(2):334-40.
13. Brackmann DE, Fayad JN, Slattery WH, 3rd, et al. Early proactive management of vestibular schwannomas in neurofibromatosis type 2. Neurosurgery 2001;49(2):274-280
14. Brackmann DE, Green JD. Translabyrinthine approach for acoustic tumor removal. Otolaryngol Clin North Am 1992;25(2):311-29.
15. Hardy DG, Macfarlane R, Baguley D, Moffat DA. Surgery for acoustic neurinoma. An analysis of 100 translabyrinthine operations. J Neurosurg 1989;71(6):799-804.

16. Tos M, Thomsen J. Proposal for Reporting Size of Vestibular Schwannoma. In: Acoustic Neuroma; Consensus on Systems for Reporting Results. Keio University International Symposia for Life Sciences and Medicine Volume 10. Kanzaki, Tos, Sanna, Moffat, Kunihiro, Inoue (Eds) Part 1 Tumor size:3-7.
17. da Cruz MJ, Moffat DA, Hardy DG. Postoperative quality of life in vestibular schwannoma patients measured by the SF 36 Health Questionnaire. Laryngoscope 2000;110(1):151-5.
18. Humphriss RL, Baguley DM, Axon PR, Moffat DA. Change in hearing handicap after translabyrinthine vestibular schwannoma excision. Otol Neurotol 2004;25(3):371-8.
19. Baguley DM, Humphriss RL, Axon PR, Moffat DA. Change in tinnitus handicap after translabyrinthine vestibular schwannoma excision. Otol Neurotol 2005;26(5):1061-3.
20. Humphriss RL, Baguley DM, Moffat DA. Change in dizziness handicap after vestibular schwannoma excision. Otol Neurotol 2003;24(4):661-5.
21. Bruno A, Akinwuntan AE, Lin C, Close B, Davis K, Baute V, Aryal T, Brooks D, Hess DC, Switzer JA, Nichols FT. Simplified modified rankin scale questionnaire: reproducibility over the telephone and validation with quality of life. Stroke 2011;42(8):2276-9.
22. Samii M, Gerganov V, Samii A. Microsurgery management of vestibular schwannomas in neurofibromatosis type 2: indications and results. Prog Neurol Surg 2008;21:169-175.
23. Pollock BE, Link MJ. Vestibular schwannoma radiosurgery after previous surgical resection or stereotactic radiosurgery. Prog Neurol Surg 2008;21:163-168.
24. El-Kashlan HK, Zeitoun H, Arts HA, Hoff JT, Telian SA. Recurrence of acoustic neuroma after incomplete resection. Am J Otol 2000;21(3):389-392.
25. Roche PH, Khalil M, Thomassin JM. Microsurgical removal of vestibular schwannomas after failed previous microsurgery. Prog Neurol Surg 2008;21:158-162.
26. House WF. Translabyrinthine approach. In: House WF, Luetje CM (eds) Acoustic tumors. vol 2: Management. University Park Press, Baltimore, 1979;43-87.
27. House WF, Gardner G, Hughes RL. Middle cranial fossa approach to acoustic tumor surgery. Arch Otolaryngol 1968;88:631-641.
28. Moffat DA. Personal communication from the Hitselberger Lecture. Analysis of 1000 surgical cases of vestibular schwannoma over 30 years. Boston, 2010, USA.
29. Cope TE, Baguley DM, Moore BC. Tinnitus loudness in quiet and noise after resection of vestibular schwannoma. Otol Neurotol 2011;32(3):488-96.
30. Nevison B, Laszig R, Sollmann WP, et al. Results from a European clinical investigation of the Nucleus multichannel auditory brainstem implant. Ear Hear 2002;23(3):170-183.
31. Otto SR, Brackmann DE, Hitselberger WE, Shannon RV, Kuchta J. Multichannel auditory brainstem implant: update on performance in 61 patients. J Neurosurg 2002;96(6):1063-1071.
32. Arndt S, Aschendorff A, Laszig R, et al. Comparison of pseudobinaural hearing to real binaural hearing rehabilitation after cochlear implantation in patients with unilateral deafness and tinnitus. Otol Neurotol 2011;32(1):39-47.
33. Ahsan S, Telischi F, Hodges A, Balkany T. Cochlear implantation concurrent with translabyrinthine acoustic neuroma resection. Laryngoscope 2003;113(3):472-474.
34. Lustig LR, Yeagle J, Driscoll CL, Blevins N, Francis H, Niparko JK. Cochlear implantation in patients with neurofibromatosis type 2 and bilateral vestibular schwannoma. Otol Neurotol 2006;27(4):512-518.
35. Colletti V, Shannon RV. Open set speech perception with auditory brainstem implant? Laryngoscope 2005;115(11):1974-1978.
36. Grayeli AB, Kalamarides M, Bouccara D, Ambert-Dahan E, Sterkers O. Auditory brainstem implant in neurofibromatosis type 2 and non-neurofibromatosis type 2 patients. Otol Neurotol 2008;29(8):1140-1146.
37. Somers T. -Personal communication Aug 2011.

Chapter 4.0

Petrous temporal bone cholesteatoma and primary cerebellopontine angle cholesteatoma

Chapter 4.1

Petrous temporal bone cholesteatoma : a new classification and long-term surgical outcomes

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Skull Base 2008;18:107-115

Abstract

The goals of this retrospective case review were to analyze the long-term results of surgery for petrous temporal bone cholesteatomas and to propose a new classification system for these lesions. Patients with a surgically confirmed petrous temporal bone cholesteatoma were treated at Addenbrooke's Hospital, a tertiary referral center. Postoperative facial function, hearing, residual/recurrent cholesteatoma, and other complications were assessed in relation to preoperative signs, intraoperative findings, and surgical approach. Between 1983 and 2004, 43 patients were treated. There were no perioperative deaths. There was no long-term recurrence in 95.4% of the patients, possibly because of meticulous surgical technique, bipolar diathermy, and use of the laser to denature the cholesteatoma matrix that was adherent to the dura. At presentation, 95% of the patients had no socially useful hearing in the affected ear. Facial nerve function, however, was usually preserved. Both direct anastomosis and nerve grafting can improve facial nerve function from House-Brackmann grade VI to grade III if the palsy is not longstanding. Four patients had cerebrospinal fluid leakage; other complications were rare. The proposed classification facilitates surgical planning and predicts the postoperative outcome with regards to hearing.

Petrous temporal bone cholesteatomas are defined as cholesteatomas medial to the otic capsule and account for 4 to 9% of all petrous pyramid lesions.[1,2] Unfortunately, these lesions often invade the labyrinth and fallopian canal before they are diagnosed. They can be congenital or, more frequently, acquired. Histologically the two are indistinguishable. Congenital cholesteatomas are thought to arise from embryonic rests deposited in the temporal bone after the abnormal development of the first branchial groove. In contrast, acquired cholesteatomas originate in the tympanomastoid region and erode medially around or through the labyrinth. Cholesteatomas are locally destructive and erode bone. A number of mechanisms have been proposed to account for this behavior, including secretion of osteolytic enzymes, pressure necrosis, and osteitis and surrounding chronic granulation tissue.[3,4]

Preoperatively, the size, morphology, and anatomical site of the cholesteatomas are assessed by various imaging techniques, including high-resolution axial and coronal computed tomography (CT) and T2-weighted, T1-weighted, and B1000 diffusion-weighted magnetic resonance imaging (MRI). Obliteration of the cavity and blind sac closure techniques has increased the importance of postoperative imaging. The more traditional open cavity technique has become less popular because of the potential

for an otic discharge. Open techniques are also associated with a higher incidence of cerebrospinal fluid (CSF) leakage and intracranial infections. Furthermore, the medial aspect of the open cavity seals once the disease is medial to the labyrinth.
Classification of petrosal cholesteatomas has evolved from the two classes (supra-labyrinthine and infralabyrinthine-apical) proposed by Fisch,[5] to the additional translabyrinthine category proposed by Bartels,[6] to the five classes proposed by Sanna et al.[7] (supralabyrinthine, infralabyrinthine, massive labyrinthine, infra-labyrinthine-apical, and apical). Perhaps because our series is the largest yet, it became apparent that none of the existing classifications were adequate. We therefore propose a new Moffat-Smith classification. This classification system is more comprehensive than existing systems. Lesions involving the petrous apex and intracranial extension can be classified if necessary.

Materials and methods

Between 1983 and 2004, 43 patients (25 males, 18 females; median age, 34 years; age range,[7] to 75 years) with petrous temporal bone cholesteatomas referred to the Department of Otology and Skull Base Surgery at Addenbrooke's Hospital, Cambridge, were reviewed retrospectively. All the patients had surgical documentation of a cholesteatoma within the petrous bone medial to the otic capsule. Ten patients had undergone previous mastoid surgery elsewhere. The presenting signs and symptoms of all patients were documented, and CT scans were available to show the extent of disease.
Topographically, the petrous temporal bone cholesteatomas were grouped according to the proposed Moffat-Smith classification (Figure 1).

Postoperatively, patients were regularly followed both clinically and radiologically with high-definition CT, MRI, and B1000 diffusion-weighted scans. Scanning was indicated if clinical signs or symptoms suggested residual or recurrent disease. If the petrous cavity had been obliterated, patients underwent imaging annually. The median follow-up was 10 years (range, 9 months to 23 years); however, patients must be followed for life.
Pre- and postoperative morbidity, including hearing loss (air conduction measured by pure tone audiometry using the modified American Academy of Ophthalmology and Otolaryngology [AAOO] criteria of 4 rather than 3 KHz) and other cranial nerve deficits (as assessed at last consultation) were evaluated. Facial nerve function was graded according to the House-Brackmann (H-B) grading system.[8]

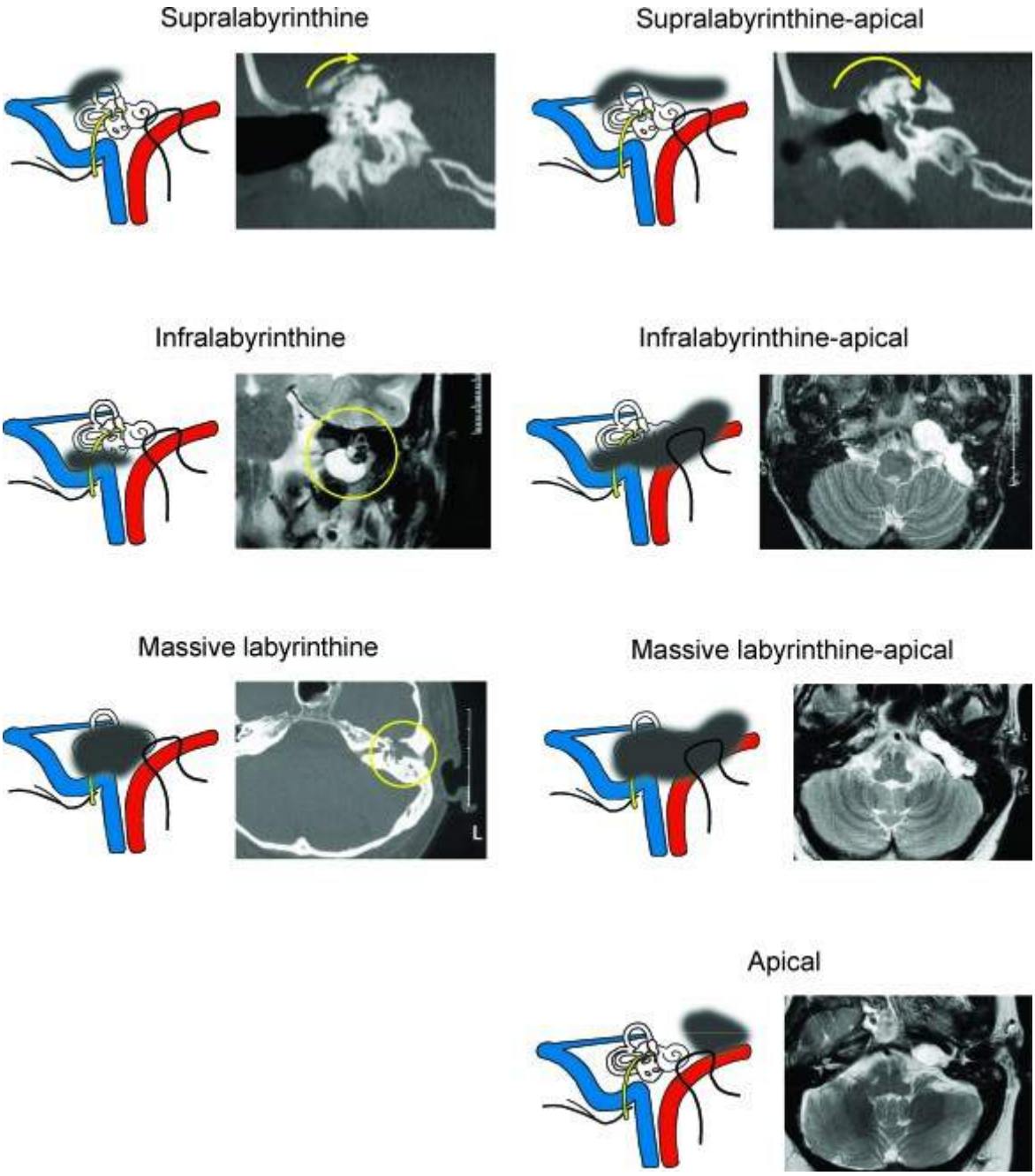

Figure 1: Moffat-Smith classification. Supralabyrinthine, above the labyrinth; supralabyrinthine-apical, above the labyrinth extending to the petrous apex; infralabyrinthine, below the labyrinth; infralabyrinthine-apical, below labyrinth extending to petrous apex; (more ...)

The site of cholesteatoma on the facial nerve was recorded as being proximal at or distal to the geniculate ganglion. The presence of CSF leakage and residual or recurrent cholesteatoma during follow-up were recorded.

The most common symptom was hearing loss (26 patients) (Table 1). However, significant hearing loss measured by pure tone audiometry was found in 95% of the

patients at presentation. The second most common symptom was facial nerve palsy with vertigo/imbalance and otorrhea occurring less frequently. Recurrent bacterial meningitis, sixth nerve palsy, and trigeminal neuralgia each occurred in one patient. The mean duration from the onset of symptoms to surgery was 18 months, but this period varied from 3 days to 20 years. Once referred, the mean latency to surgery was 6 months (range, 0 to 22 months). Twenty-four operations were performed on the left side and 19 were performed on the right side. Ten patients had had surgery elsewhere, and almost a third (13 patients) had a history of chronic otitis media. One patient had a history of trauma. Most patients had a massive labyrinthine lesion with or without apical extension (Table 2). Only 14% were suitable for surgery to preserve the otic capsule.

Table 1: Presenting Symptoms in 43 Patients with Petrosal Cholesteatomas

Symptom	No of patients (%)
Hearing loss	26 (60)
Facial palsy	22 (51)
Vertigo imbalance	14 (33)
Discharge	14 (33)
Tinnitus	5 (12)
Otalgia	3 (4)
Headaches	2 (5)

Table 2: Surgical Approaches Used to Treat 43 Petrous Temporal Bone Cholesteatomas Grouped According to Moffat-Smith Classification

Classification	No of Patients	Surgical Approach/No. of patients
Supralabyrinthine	6	TT-SL (+ 1 with MF)/4
Supralabyrinthine-apical	3	TT-SL/3
Infralabyrinthine	1	ST P/1
Infralabyrinthine-apical	3	ST P/3
Massive labyrinthine	10	ST P/2 Transotic/4 Transcochlear/1 IT type A/3
Massive labyrinthine-apical	17	ST P (=1 with MF)/16
Apical	3	ST P/3

TT-SL, transtemporal-supralabyrinthine; MF, middle fossa; ST P, subtotal petrosectomy; IT type A, infratemporal type A approach.

Results

There were no perioperative deaths, and 95.4% of the patients had no long-term recurrence. Two patients underwent re-exploration for a recurrence. One year after surgery in one patient the tegmen was eroded with a large pocket into the middle fossa. The other recurrence was found 6 years after surgery. Two years after surgery, two other patients underwent surgical re-exploration; one for a delayed CSF leakage and the other for a retraction pocket where no cholesteatoma was found.

Of the 21 patients with normal preoperative facial nerve function, only two deteriorated (Figure 2): one patient to grade II and the other to grade III. Preoperatively, two patients had H-B grade II; one patient this improved to grade I, and the other maintained at grade II. Most patients who were grade III before surgery remained at this level after surgery. However, one patient improved to grade I and one patient deteriorated to grade VI. The one patient who was H-B grade IV before surgery deteriorated to grade VI after surgery. Both patients who were H-B grade V before surgery improved: one to grade II and the other to grade IV. More than half of the patients who were H-B grade VI before surgery improved to grade III after surgery. One grade VI patient improved to grade II after primary anatomosis and nerve grafting. Other techniques used to treat patients with impaired facial nerve function included static slings, gold weights, and tarsorrhaphy (Table 3). In summary, if the preoperative facial nerve function was good; the likelihood of preserving facial nerve function after surgery was high.

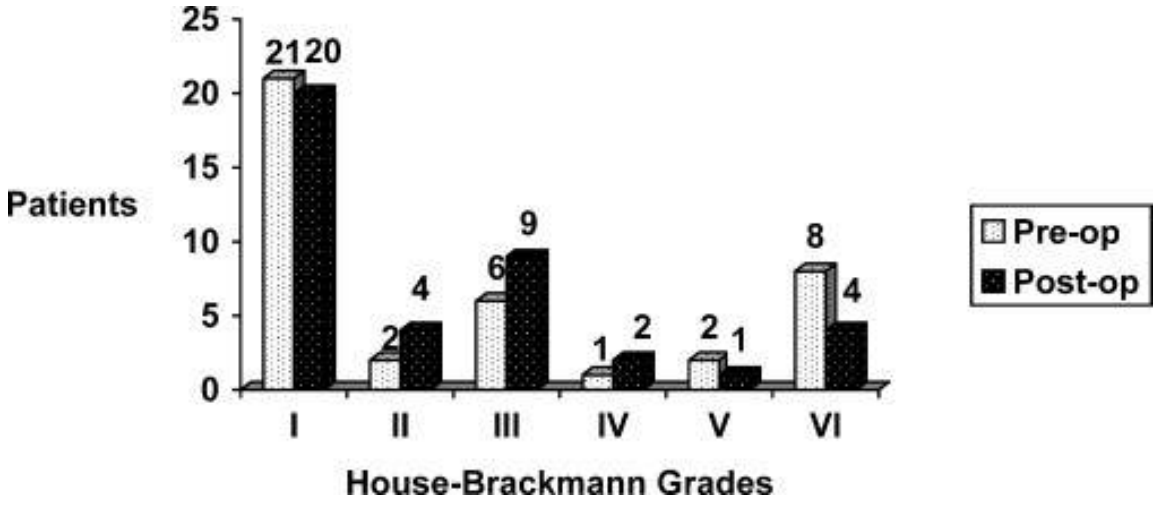

Figure 2: Comparison of the pre- and postoperative facial nerve function according to House-Brackmann grades.

Table 3: Facial Nerve Management.

Procedure	No. of patients
Dynamic	
Primary anastomosis	5
Great auricular nerve (initial surgery)	1
Sural nerve graft (13 months)	1
Static	
Fascia lata sling (18 months)	1
Temporalis hitch (42 months)	1
Gold weights	4*
Tarsorrhaphy	10†

*Two were revised once, one was revised twice, and two were removed.
†Five were later divided.

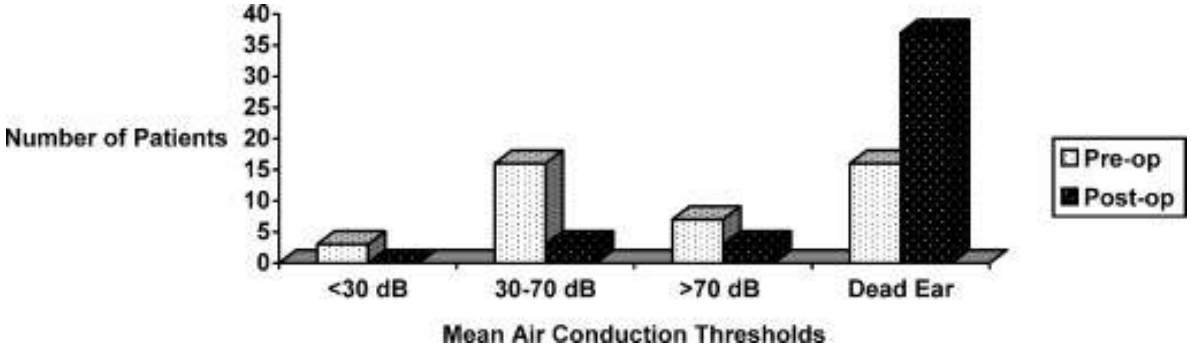

Figure 3: Comparison of the pre- and postoperative hearing levels as measured by mean air conduction thresholds.

The otic capsule was preserved in only 14% of the patients; therefore, only six patients had residual hearing (Figure 3).

Postoperatively, four patients developed CSF leaks. The CSF leaks were managed by surgical exploration in one patient. Lumbar drains were inserted for 5 days in two patients, and one patient required repeated lumbar punctures. One patient developed deep vein thrombosis (DVT). One patient experienced a septal cardiac infarction 6 days after surgery. One patient developed seizures and another a wound infection. Secondary procedures included resuturing a wound and the prophylactic insertion of lumbar drains at surgery in four patients.

Discussion

This is the largest series of petrous bone cholesteatomas reported in the world literature to date. The most common presenting symptom, hearing loss in the affected ear, occurred in 60% of our patients. However, as measured by pure tone audiometry at presentation, 95% had a significant hearing loss. These findings are consistent with reported rates of hearing loss of (64 to 100%) in other serie.[3,9,10,11] In this series, 51% had facial nerve weakness. Rates for facial nerve weakness preoperatively varies in series from 20 to 64%.[3,7,9,10,11,12] Vertigo/imbalance and discharge from the ear affected almost a third of our patients at presentation before surgery, but Burggraaff and coworkers reported that 61% of their patients suffered dizziness before surgery.[11] Tinnitus, otalgia, and headaches were less common manifestations.

A diagnosis of petrosal cholesteatoma must be considered in any patient presenting with recurrent bacterial meningitis, a sixth cranial nerve palsy, or trigeminal neuralgia.[3] It is apparent from our series and others that patients can have symptoms for as long as 20 years.[3] The diagnosis was delayed in a quarter of patients who had undergone surgery for assumed tympanomastoid disease. Others had their otorrhea treated medically. The mean wait for surgery in our department was 6 months, but immediate surgery was performed when clinically indicated.

Advances in CT and MRI have improved the detection and definition of the extent of the cholesteatomas, thereby improving the accuracy of preoperative assessment. High-resolution CT provides accurate details of the location of the disease, which appears as a “punched-out” or scalloped area of bone destruction. It has also been associated with elevation of the petrous ridge.[13] MRI differentiates cholesteatomas from other lesions such as cholesterol granulomas. Cholesteatomas are only hyper-intense on T2-weighted MRIs,[13] whereas cholesterol granulomas are hyperintense on both T1- and T2-weighted MRIs. The use of imaging before any mastoid surgery is performed would allow a petrosal cholesteatoma to be identified and hence result in earlier referral to a tertiary center. Earlier detection of cholesteatomas may reduce both preoperative and postoperative morbidity.

The routine use of CT scanning before any cholesteatoma surgery is important for determining the extent of bone erosion and the prognosis, which are critical for surgical planning and for obtaining informed consent for treatment. Preoperative CT is recommended for all patients with a history of facial nerve palsy, headaches, dizziness, or sensorineural hearing loss.11 B1000 diffusion-weighted MRI is a promising technique for detecting recurrences or residual disease without resorting to further surgery. The advent of non–echo-planar imaging (NON EPI) is exciting.

This modality can differentiate cholesteatomas from cholesterol cysts and mucosal thickening (Moffat D, unpublished observation).

As found by other authors, supralabyrinthine involvement was common and direct labyrinthine involvement was even more so.[14,15] In 1969, Glasscock and coworkers described the middle fossa approach, which can be used successfully to remove supralabyrinthine cholesteatomas that extend toward the petrous apex.[14] We used the transtemporal supralabyrinthine approach in patients with supralabyrinthine lesions with or without an apical extension. The transtemporal approach has two main advantages. It is the most direct route to the pathology, and bone removal avoids dural retraction. A variety of approaches can be used in patients with massive labyrinthine cholesteatomas. A subtotal petrosectomy is appropriate for infra-labyrinthine lesions with or without an apical extension. The transotic (trans-labyrinthine-transcochlear) and transcochlear approaches enable access to the petrous apex and clivus.[16,17] Fisch described several infratemporal fossa approaches to access more anterior structures, including the internal carotid artery.[18] We used this approach to resect massive labyrinthine lesions. Massive labyrinthine lesions with apical extensions and apical cholesteatomas were removed using a subtotal petrosectomy approach.

Our proposed classification allows logical surgical planning based on extent of disease and the involved anatomical areas. The goals of surgery for treatment of supralabyrinthine disease are preservation of preoperative hearing and removal of part of the middle fossa plate and squamosa. Superior retraction of the middle fossa dura using a Yasargil flexible arm retractor permits visualization and dissection of the cholesteatoma matrix from the otic capsule and middle fossa dura. An apical extension also can be excised through this approach. If, however, the cholesteatoma is extensive, it may be necessary to combine a supralabyrinthine approach with a classical middle fossa craniotomy. Only infralabyrinthine cholesteatomas can be excised via a subtotal temporal bone resection. The inferior portion of the temporal bone is removed, and this dissection can be extended to the petrous apex.

The approach to massive labyrinthine cholesteatomas depends on the extent of the anatomical site and on the difficulties of access and visualization. Various approaches such as the transotic, transcochlear, subtotal petrosectomy and a classical infratemporal Fisch type A approach can be considered. Massive labyrinthine apical cholesteatomas require a subtotal petrosectomy possibly combined with a middle fossa craniotomy. Again, only apical cholesteatomas require subtotal petrosectomy, although approaches via the middle cranial fossa and a retrosigmoid approach have been described. Thus, the grade of a cholesteatoma will determine the approach to use.

In this series, there were no perioperative deaths and 95.4% had no long-term recurrence. Two patients developed recurrence. One was detected at 1year after initial surgery; the other was found at 6 years after initial surgery. Consequently, these patients are never discharged even though a recurrence after petrous apex surgery is uncommon.[14] Macroscopically, it can be very difficult to remove a cholesteatoma matrix completely from dura, facial nerve, and carotid artery. Some surgeons have advocated wide excision of dura-bearing matrix and closure of the dural defect with connective tissue grafts. However, graft necrosis can lead to CSF leakage or infection, and this technique has now been abandoned.[15] At surgery, cholesteatomas adherent to dura were managed by the accepted technique of bipolar diathermy,[2,7] and since 1995 we have used a diode laser with a defocused beam to denature the matrix.

B1000 diffusion-weighted MRI is used to aid detection of recurrence and is performed on all patients annually for 3 years, every 2 years for the next 6 years, and every 3 years thereafter unless patients develop symptoms suggestive of a recurrence. Because only two patients had a recurrence, it is difficult to predict the level of postoperative morbidity associated with the surgical approach to any given grade of lesion. However, one could anticipate a recurrence when visualization is difficult during attempts to preserve the otic capsule and when it is difficult to clear cholesteatoma matrix from the dura.

In only 14% of the cholesteatomas could the otic capsule could be preserved. Only 3 of the 43 patients had normal preoperative hearing, but their supralabyrinthine cholesteatomas extended to the petrous apex and required a transtemporal supralabyrinthine approach. Few patients had useful hearing in the affected ear at presentation. Residual hearing was sacrificed to enable sufficient access to remove the cholesteatoma. This finding is consistent with the results of other studies, although Bartels preserved hearing in 34% of patients treated surgically.[6] When a cholesteatoma involves the only hearing ear, an open technique has been recommended. Exteriorizing the disease rather than excising it allows hearing to be preserved. Such patients must be monitored closely to avoid complications.[7,14,18]

Facial paresis is the most debilitating long-term complication associated with petrosal cholesteatomas. Preoperatively, only 21 (49%) of the patients had H-B grade I function. This level was maintained in all but two patients who deteriorated to H-B grades II and III after surgery. Of the two patients who were H-B grade II preoperatively, one improved to grade I and the other remained H-B grade II. Their outcomes suggest that if the facial nerve is functioning well before surgery, surgeons can be optimistic that facial nerve function can be preserved after surgery. Outcomes

of patients with poor preoperative facial nerve function (H-B grades III–VI) were less predictable, resulting in H-B grades II and IV after surgery.

Axon et al3 suggested that nerve ischemia occurs when the cholesteatoma involves the geniculate ganglion. Sanna et al[7] noted that the facial nerve was present as a fibrous band at the geniculate ganglion. We think that involvement of the intralabyrinthine segment of the facial nerve is significant in the development of ischemia because this segment of the nerve has the poorest blood supply. Postoperatively, more than half of the patients who were H-B grade VI who underwent primary anastomosis or nerve grafting achieved H-B grade III, and one patient achieved H-B grade II .

Because the motor end plate atrophies after 1 year, the duration of preoperative facial paralysis affects the likelihood of recovery of function postoperatively despite aggressive treatment. Various techniques involving gold weights and tarsorrhaphy have been used to reduce the morbidity associated with facial paresis (Table 3). In half the patients, these measures were temporary until facial nerve function recovered sufficiently.

Can any conclusions be drawn about which patients' facial nerve function will improve? The difficulty is that the series spans 23 years. In the early years, the decision of whether to decompress the nerve or whether to anastomose, or whether to interpose a cable graft depended on the surgeon's intraoperative assessment. If 50% or more of the cross-sectional area of the nerve was visibly damaged, excision and mobilization were pursued followed by direct anastomosis or placement of an interposition cable graft. If less than 50% of the cross-sectional area of the nerve was visibly damaged, decompression was performed. In recent years, it has become clear that patients with H-B grade IV or worse may do better with a graft. Only one of the four patients with a postoperative CSF leak required surgery. Other complications, including DVT, cardiac infarction, seizures, and wound infection, have been rare.

Traditionally, open cavities were fashioned to enable visualization of a potentially unsafe ear. However, these procedures may result in postoperative CSF leakage, otorrhea, otalgia, intracranial infections, and trauma to intrapetrous structures during aural toilet. CT and MRI, including B1000 diffusion-weighted MRI, enable detection of a cholesteatoma even if fat obliterates the mastoid cavity. Patients appear to remain asymptomatic with complete obliteration and blind sac closure, and this procedure is now preferred by several authors.[7,9,15,17,18,19,20,21] Others still use an open cavity technique, especially if the matrix cannot be removed completely.[12,14] However, an open cavity will not remain exteriorized if it is medial to the otic capsule; the pyramidal shape of the temporal bone will cause it to seal.

Conclusion

The best surgical approach to a cholesteatoma is based on several factors, including the extent and location of the disease, the presence of hearing and facial nerve function, and anatomical variation. Our proposed classification indicates the optimal surgical approach and therefore preoperatively predicts the level of surgical morbidity. The classification also enables results from different series to be compared. The recurrence rate in our series was low. Facial nerve function can usually be preserved. Preoperative facial nerve weakness may be improved by decompression or by using both primary anastomosis or nerve grafting techniques. However, remaining hearing in the affected ear may need to be sacrificed to enable complete removal of a cholesteatoma.

Commentary

Kim Louis J. (Division of Neurological Surgery, Barrow Neurological Institute, Phoenix, Arizona).
Moffat et al present 43 patients surgically treated for petrous bone cholesteatomas. Given that 10 patients had prior surgery and 13 suffered from chronic otitis media, their population was complex. Nonetheless, only four patients developed cerebrospinal fluid leakage, and the House-Brackmann grade of only four patients worsened across follow-up. Based on their rates of hearing preservation, the authors favor aggressive resection to preserve residual hearing. However, fewer than 5% of their patients had serviceable preoperative hearing. The follow-up was extremely long, with a median of more than 10 years. Overall, these impressive patient outcomes and anatomically based classification scheme showcase the senior author's tremendous clinical experience with this challenging entity.

Acknowledgment

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References

1. King TT, Benjamin JC, Morrison AW. Epidermoid and cholesterol cysts in the petrous apex of the petrous bone. Br J Neurosurg 1989;3:451–461
2. De Souza CE, Sperling NM, da Costa SS, et al. Congenital cholesteatomas of the cerebropontine angle. Am J Otol 1989;10:358–363.
3. Axon PR, Fergie N, Saeed SR, Temple RH, Ramsden RT. Petrosal cholesteatoma: management considerations for minimizing morbidity. Am J Otol 1999;20:505–510.
4. Profant M, Steno J. Petrous apex cholesteatoma. Acta Otolaryngol 2000;120:164–167.
5. Fisch U. In: Silverstein H, Norell N, editor. Neurological Surgery of the Ear. Birmingham, AL: Aesculapius Infratemporal fossa approach for extensive tumors of the temporal bone and base of skull 1977;33–53.
6. Bartels L J. Facial nerve and medially invasive petrous bone cholesteatomas. Ann Otol Rhinol Laryngol 1991;100:308–316.
7. Sanna M, Zini C, Gamoletti R, et al. Petrous bone cholesteatoma. Skull Base Surg 1993;3:201–213.
8. House JW, Brackmann DE. Facial nerve grading system. Otolaryngol Head Neck Surg 1985; 93:146–147.
9. Magliulo G, Terranova G, Sepe C, Cordeschi S, Cristofar P. Petrous bone cholesteatoma and facial paralysis. Clin Otolaryngol 1998;23:253–258.
10. Peron DL, Schuknecht HF. Congenital cholesteatoma with other anomalies. Arch Otolaryngol 1975;101:498–505.
11. Burggraaff B, Luxford WM, Doyle KJ. Neurotologic treatment of acquired cholesteatoma. Am J Otol 1995;16:480–485.
12. Gyo K, Sasaki Y, Yanagihara N. Dilemma in surgical treatment of petrous cholesteatoma [abstract] Nippon Jibiinkoka Gakkai Kaiho 1995;98:789–794.
13. Phelps PD, Lloyd GA. Magnetic resonance with gadolinium DPTA for the investigation of temporal bone tumours. Clin Otolaryngol 1989;14:251–262.
14. Glasscock ME, Woods CI, Poe DS, Patterson AK, Welling DB. Petrous apex cholesteatoma. Otolaryngol Clin North Am 1989;22:981–1002.
15. Atlas MD, Moffat DA, Hardy DG. Petrous apex cholesteatoma: diagnostic and treatment dilemmas. Laryngoscope 1992;102:1363–1368.
16. House WF, De La Cruz A, Hitselberger WE. Surgery of the skull base: transcochlear approach to the petrous apex and clivus. Otolaryngology 1978;86:770–779.
17. House WF, Hitselberger WE. The transcochlear approach to the skull base. Arch Otolaryngol 1976;102:334–342.
18. Fisch U. Tympanoplasty, Mastoidectomy, and Stapes Surgery. Stuttgart: Georg Thieme; 1994.
19. Coker NJ, Jenkins HA, Fisch U. Obliteration of the middle ear and mastoid cleft in subtotal petrosectomy: indications, technique and results. Ann Otol Rhinol Laryngol 1986;95:5–11.
20. Gantz BJ, Fisch U. Modified transotic approach to the cerebellopontine angle. Arch Otolaryngol 1983;109:252–256.
21. Yanagihara N, Matsumoto Y. Cholesteatoma in the petrous apex. Laryngoscope 1981;91:272–278.

Chapter 4.2

Staging and management of primary cerebellopontine cholesteatoma

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Abstract

Primary cerebellopontine angle (CPA) cholesteatoma grows slowly and silently in the subarachnoidal spaces. The diagnosis is often late, when the lesion has reached large dimensions. Surgical removal is the only available therapy. Fifteen consecutive cases of CPA cholesteatoma managed at a tertiary otoneurosurgical referral unit between September 1985 and April 1999 were reviewed. The study population, consisting of seven males and eight females, had a mean age of 44 years of age (range21–69) at the time of surgery. The clinical, audiological and radiological presentations were examined. The tumours were classified according to the Moffat classification of CPA cholesteatomas. In 67 percent of cases the presenting symptom was related to the vestibulocochlear nerve. The average duration of symptoms was 23 months (ranging from one month–10years). The hearing preservation approaches were utilized the most (11cases), while the translabyrinthine approach alone, or in association with a middle fossa craniotomy, was performed in four cases. Tumour removal was total in 12 cases and subtotal in three cases. In cases undergoing hearing preservation surgery the mean pre-operative pure tone average (PTA) for the frequencies 0.5,1,2, and 3kHz was 19.3 dBHL (SD13.84) and the mean pre-operative speech discrimination score(SDS) was 89.8 per cent (SD5.97). In 44.4 per cent of patients the hearing was preserved and the mean post-operative PTA was 20.29 dBHL (SD15.84). In five patients post-operative complications occurred. No perior post-operative death occurred in this series, one patiënt developed a recurrence 15years after the initial surgery.

Introduction

Cholesteatomas (epidermoids) of the cerebellopontine angle (CPA) comprise 0.2 to 1.5 per cent of all intracranial tumours, with the posterior cranial fossa being the most frequent site.[1] In a review article it was reported that 30 to 40 per cent of intracranial cholesteatomas are found in the cerebellopontine angle,where they account for six to seven percent of all CPA tumours.[1]

Cholesteatomas are cysts lined by squamous epithelium, supported by a layer of connective tissue. The accumulation of desquamating keratin into the cyst leads to its slow expansion.[2] It is commonly thought that they arise from rests of epithelial cells of the first branchial groove.[3] These cells may arise either from pluripotential embryonic cells located lateral to the site of neural tube closure or may be carried into the region of the CPA with the developmentof the otic or optic vesicles.[4,5]

CPA cholesteatomas are either primary (posterior fossa epidermoids) or secondary. Primary cholesteatomas are congenital cysts arising within the CPA. Secondary cholesteatomas represent extension of cholesteatomas that have arisen from the temporal bone, most commonly from the lateral tympanomastoid and petrous apex region.

The growth rate of cholesteatoma is slow and linear, unlike most neoplasms.[6] This slower growth rate along with its 'malleable' capsule means that with time it has the ability to engulf neurovascular structures in the CPA and the clefts within the cerebral cortex.[1] This slow growth is also reflected in the fact that erosion of the adjacent bone occurs with the characteristics of an expansile lesion, often with evidence of bone remodelling at the advancing margin of the lesion.

CPA cholesteatomas expand slowly in the relatively capacious area of the CPA cistern in the posterior cranial fossa. They can grow along pathways of least resistance anteriorly, reaching the prepontine cistern and eventually crossing the midline, superiorly invading the middle cranial fossa through the tentorium or inferiorly toward the foramen magnum.

The fact that they do not arise from cranial nerves, but tend to engulf neurovascular structures means that these lesions often reach large dimensions[1] before they before symptomatic and the diagnosis is made.[7,8]

These tumours are, therefore, diagnostically and surgically challenging.

Materials and method

Fifteen consecutive cases of CPA cholesteatoma were reviewed. These cases were managed at a tertiary otoneurosurgical referral unit between September 1985 and April 1999.

The study population, consisting of seven males and eight females, had amean age of 44 years of age (range 21–69) at the time of surgery. Three of the CPA cholesteatomas were on the right, and 12 on the left.

Details of the diagnosis and the pattern of referral were noted. The clinical, audiological and radiological presentations were examined. The tumours were classified according to the Moffat classification of CPA cholesteatomas (Table 1). The results of surgical management based on post-operative neurological deficits, degree of resection, complication rate and the recurrence rate on follow-up were also evaluated.

Tumour removal was considered either complete, subtotal or partial. Subtotal was defined as a removal of more than 95 percent of the lesion, and partial as when less

than 95 per cent of the lesion was exenterated.

The guidelines of the American Academy of Otolaryngology – Head and Neck Surgery (AAOHNS)[9] were followed when reporting the preoperative and post-operative hearing function. The follow-up of these patients was based on an annual clinical review and annual magnetic resonance imaging (MRI).

Table 1: Moffat classification of CPA cholesteatomas

Staging by origin	
A	Primary CPA cholesteatoma (epidermoids)
B	Secondary CPA cholesteatoma
Staging by extend	
1	Confined to Cerebellopontine angle
2	Extends anteriorly to: prepontine cistern contralateral side
3	Extends inferiorly to: foramen magnum
4	Extends superiorly to: (a) beyond tentorium (b) invade the middle cranial fossa
5	Extends medially: Via foramen of Luschka - Intracerebellar

Results

On review of the referral pattern of the CPA cholesteatomas, the patients were referred from otolaryngologists in six cases, neurologists in six cases, neurosurgeons in two cases and a general practitioner in one case. The patients were referred to the neurologist of the unit in five cases and to the neurosurgeons of the skull base team in10 cases.

The principal presenting symptoms of the 15 patients are outlined in Table 2. In 67 per cent of cases the presenting symptom was related to the vestibulo-cochlear nerve, with four patients complaining of imbalance, four of hearing loss and two of vertigo. The other 33 per cent comprised two patients with hemifacial spasm, two with seizures and one patient with trigeminal numbness.

The pre-operative clinical features and signs in this series of 15 patients can be seen in Tables 3 and 4. The average duration of symptoms was 23 months (ranging from one month to 10 years). Eight patients were diagnosed within one year of the onset of their symptoms, whilst seven were diagnosed beyond one year.

In Table 5 the CPA cholesteatoma location and surgical management is reported. Hearingpreservation approaches were utilized the most (11 cases), while the translabyrinthine approach alone, or in association with a middle fossa craniotomy,

was performed in four cases.

Table 2: Primary symptom of CPA cholesteatoma (N=15)

Imbalance	4
Hearing loss	4
Vertigo	2
Hemifacial spasm	2
Seizures	2
Trigeminal numbness	1

Table 3: Pre-operative and post-operative symptoms of CPA cholesteatoma (N=15)

	Pre-operative	Post-operative	
		Permanent	Temporary
Imbalance	11	6/13	2/13
Headache	8	3/13	
Hearing loss	8	*	*
Tinnitus	7	2/12	
Gait disturbance	3		2/13
Vertigo	3		1/13
Hemifacial spasm	2	0/13	
Seizures	2		1/13
Diplopia	1	2/13	5/13
Trigeminal neuralgia	1	1/13	

* See text for description. Two patients had a follow-up shorter than six months and were not included

Tumour removal was total in 12 cases and subtotal in three cases. The preservation of cranial nerves in the posterior and middle cranial fossa was usually possible, however, in five cases a cranial nerve was transected or lost during the operation, the VIth cranial nerve in two cases and in one case each the IVth, VIIth and IXth cranial nerve.

Post-operative temporary and permanent symptoms and signs presented by 13 patients are reported in Tables 3 and 4. Two patients had a follow-up shorter than six months at the time of series analysis and are not included. Post-operative unsteadiness was the most common symptom and on physical examination none of the patients could walk along a line, heel to toe, with their eyes closed reflective of mild vestibular disturbance. Only two patients could not do this with their eyes open indicating a more debilitating vestibular disturbance.

Complete pre-operative audiological assessment of the patients undergoing hearing preservation surgery was available in nine cases and has been reported in detail in another publication.[10] The mean pre-operative pure tone average (PTA) for

frequencies 0.5, 1, 2 and 3 kHz was 19.03 dBHL (SD 13.84) and the mean pre-operative speech discrimination score(SDS) was 89.8 per cent (SD5.97). In four of the nine patients the hearing was preserved and the mean post-operative PTA was 20.29dB HL (SD 15.84).Pre-operatively six patients were in AAOHNS[9] class A and three patients in class B. Postoperatively two patients were in class A and two in B. In all the patients in whom the hearing was preserved it was maintained at the pre-operative hearing level.

Table 4: Pre-operative and post-operative signs of CPA cholesteatoma (N=15)

	Pre-operative deficit	Post-operative deficit	
Cranial nerve		Permanent	Temporary
V	2/15	3/13	
IV	0/15	1/13	1/13
VI	2/15	2/13	1/13
VII			
HB grade I	12	7	
HB grade II	2	2	
HB grade III	0	2	
HB grade IV	0	0	
HB grade V	0	0	
HB grade VI	1*	2	
IX	1/15	3/13	1/13
X	0/15	3/13	1/13
XI	0/15	2/13	2/13
XII	0/15	0/13	1/13
Vestibular dysfunction			
Romberg	6/10	1/8	
Unterberger	6/10	1/7	
WALEO	6/10	2/8	
WALEC	7/10	8/8	
Cerebellar signs	1/13		1/13
Papilloedema	1/13		1/13

* Acquired from previous surgery at the referring institution;
WALEX, walk along a line heel to toe with eyes open;
WALEC, walk along a line heel to toe with eyes closed. Two patients had a follow-up shorter than six months and were not included.

Table 5: Location and surgical management of the 15 cholesteatomas

Moffat Classification	N	Surgical Approach
A1	4	3 RS
		1 transotic
A1,2	4	2 RS
		1 RS-RL
		1 TL
A1,2,3	1	1 RS
A1,2,4a	3	3 RS
A1,2,4b	2	1RL-MF
		1TL-MF
A1,2,3,4b	1	1TL-MF

RS, Retrosigmoid approach; RL, Retrolabyrinthine approach;
TL, Translabyrinthine approach; MF, Middle cranial fossa approach.

Table 6: Complications and secondary intervention

Complications	5	A septic meningitis
		Temporary CSF leak
		Pulmonary embolism
		A spiration
		Increased IC pressure
Secondary procedures	4	VP shunt
		Tracheostomy
		Jejunostomy
		Vocal cord Telfon injection

CSF, Cerebrospinal fluid; IC = Intracranial; VP shunt = Ventriculoperitoneal shunt.

The post-operative complications as well as the secondary procedures needed are reported in table 6. The patiënt with aseptic meningitis, the one with pulmonary embolism and the one with temporary cerebrospinal fluid leak were all managed conservatively. The patients who developed a post-operative aspiration related to dysfunction of the IXth, Xth and XIth cranial nerves required a tracheostomy and jejunostomy, while the patient who developed hydrocephalus required a ventriculo-peritonal shunt. A Teflon paste injection of the vocal fold was needed by a patient with poor Xth cranial nerve function. The peri-and post-operative mortality was zero. One patiënt developed a recurrence 15 years after the initial surgery. The mean follow-up was of 5.5 years.

Discussion

Pattern ofdiagnosis

Six cases were diagnosed by otolaryngologists. This reflects the fact that whilst

hearing loss is the presenting symptom in 40 per cent, the other 60 per cent presented with problems (vestibular dysfunction, hemifacial spasm, seizures, and trigeminal numbness) that were more likely to be dealt with by other physicians such as neurologists.

Delay in diagnosis

The duration of symptoms was on average 23 months. There was an unacceptable delay in the diagnosis of more than one year in 47 per cent of the patients in this series. This reflects the insidious nature of the symptoms, which is often perceived both by the patient and the primary clinician as nebulous. A delay in the diagnosis for decades was the rule before modern imaging techniques became available.[11] Even recent reported series measure the average duration of symptoms in years in these cases.[7,8] Delayed detection of these lesions results in large tumours on presentation. In this series the tumours were up to 8 cm in size.

Classification by staging

CPA cholesteatomas originate in the subarachnoid spaces and spread along paths of least physical resistance. Ulrich noted that cholesteatoma of the CPA 'adapt themselves to the available space between the skull and the brain'.[11]

If they originate in the CPA, they can therefore potentially spread in four different directions. Most commonly they extend anteriorly and invade the prepontine cistern. They can engulf or displace the basilar artery and encroach on the contralateral side. Inferior extension of the lesion is towards the foramen magnum, in which case the lower cranial nerves, the vertebral artery and the posterior inferior cerebellar artery (PICA) may be involved. The lesions may extend superiorly and reach the tentorium, potentially crossing the tentorial notch and invading the middle cranial fossa. The least common route of spread is medially from the CPA into the foramen of Lushka intothe fourth ventricle. Although no patients in the presenting study demonstrated this route of spread, interestingly it represents a much as 23 per cent in reported neurosurgical series.[7]

The Moffat classification of CPA cholesteatomas as seen in Table 1 takes into account both the origin and the extension of thepathology.

Since the spread of these lesions is multidirectional and not predictable the various routes of spread in this staging system are described by numbers indicating each direction. It is believed that this staging system could facilitate the reporting of results, as well as the discussion of appropriate surgical approaches.

Presentation

The commonest primary symptom of CPA cholesteatomas at presentation related to vestibulocochlear dysfunction and occurred in 67 per cent. These patients presented initially either with hearing loss, imbalance or vertigo. Less common presentations in the series were hemifacial spasm, seizures and trigeminal dysfunction. All these symptoms progressed slowly and may have fluctuated during the clinical course of the disease. The profile of these presenting symptoms is consistent with those in other series.[7,12,13]

Despite the large dimensions of the lesion, no untreated patients presented with a complete facial palsy. In two patients there was either hemifacial spasm or very mild facial weakness (House Brackmann grade II). In both cases the lesions were large and extensive(A1, 2, 4 and A1, 2, 3, 4). There were late signs in 20 per cent of the patients, two patients presenting with seizures and in one case increased intracranial pressure with papilloedema. The incidence of these late manifestations is significantly less than in earlier reported series.[11] The neuropathy seen in these patients such as facial spasm, trigeminal neuralgia, tinnitus, and seizures all reflect neural 'irritation' rather than total loss of function as these lesions expand.

Extent of disease

The Moffat staging system reflecting the origin and the extent of the disease is helpful clinically and anatomically in staging the disease and allows a comparisonof results between various surgical units.

All the cholesteatomas in this series were primary Moffat type A cholesteatomas. Those secondary to disease in the temporal bone (Moffat type B) have surgical and prognostic implications which may be different from primary CPA cholesteatomas.[14]

In this series only 27 per cent of the lesions were limited to the CPA (Table 5). The most common direction of spread was anterior and was seen in 73 per cent of the lesions. The next most common direction of spread was superiorly up to, or beyond, the tentorium. In two cases the lesion extended inferiorly. No lesion in the series spread posteromedially into the cerebellum. Spread in the anterior and superior directions is facilitated byt he capacious spaces where there is least resistance to spread.

Surgical approach

The posterior cranial fossa component of cholesteatoma may be removed either by the retrosigmoid approach or by one of the transpetrous approaches (retro-labyrinthine, translabyrinthine, transotic or transcochlear) or if necessary by a combined approach. Any superior extension significantly beyond the tentorium

across the incisura, requires the approach to be combined with a middle cranial fossa craniotomy (MCF). The division of the tentorium and the superior petrosal sinus dramatically increases access allowing the surgeon a wider operative field and obviates the need for retraction of the cerebellum and temporal lobe.

The possible choice of a transpetrous approach is determined by whether there is socially useful hearing present pre-operatively and also by the location and extent ofthe cholesteatoma in terms of the considerationof sacrificing the hearing in order to maximize visualization and facilitate complete excision of the cholesteatoma.

The retrolabyrinthine approach utilizes the space anterior to the sigmoid and posterior to the semicircular canals, but depends upon the anatomy and this may be very restricted. Surgical access can only be maximized by a thorough knowledge of the anatomy and the ability to skeletonize the semicircular canals. The trans-labyrinthine approach is ideal for a lesion limited to A1, 2, 3. The transotic approach grants further anterior access by removal of the cochlea. The transcochlear approach provides an unobstructed view of the prepontine region and contralateral CPA, but requires posterior transposition of thefacial nerve, that rarely results in a post-operative facial nerve function better than House Brackmann grade III.[15]

If the lesion extends superiorly beyond the tentorium (A4) these approaches may need to be combined with a wider MCF craniotomy and the division of the superior petrosal sinus and tentorium. When the cholesteatoma extends inferiorly and involves the foramen magnum (A3) wider retrosigmoid and suboccipital cranio-tomies are performed to facilitate access to the lower part of the lesion.

The retrosigmoid and the retrolabyrinthine only provide limited access to the prepontine region, but all the cranial nerves from the Vth to the XIth traverse the surgical field.

Cholesteatomas, however, tend to grow between the brainstem and the clivus and the anterior face of the brainstem is compressed and rotated so that it faces laterally towards the surgeon. This means that if the lesion does not totally engulf the basilar artery and does not encroach on the contralateral CPA the retrosigmoid approach alone or combined with the retrolabyrinthine approach, will allow total excision of the lesion.

Hearing preservation

The hearing preservation rate in this series was 44.4 per cent and, if preserved, the pre-operative hearing level was maintained post-operatively. The fact that cholesteatomas originate in the subarachnoid space and not from the cranial nerves themselves and that they tend to engulf the neurovascular structures may explain this finding.

Based on our findings a hearing preservation approach should always be executed when the preoperative hearing is in AAO-HNS class A or B.
The location and extent of the lesion, however, represents the main factor in the choice of the approach. Invasion of the middle cranial fossa requires a retrosigmoid or a retrosigmoid/retrolabyrinthine approach combined with a middle cranial fossa craniotomy and division of the superior petrosal sinus is often necessary. Extension of the lesion to the contralateral CPA or the total engulfment of the basilar artery requires a more anterior approach, such as transotic, if a total removal is warranted and hearing cannot be preserved.
When the pre-operative hearing is poor (AAO-HNS class C and D) the trans-labyrinthine and/or transotic approach are indicated. The transcochlear approach, although it provides the best view of the CPA and pre-pontine cistern carries with it a degree of post-operative facial nerve morbidity which the patient may not be prepared to pay since cholesteatomas are benign, indolent and slow growing.

Complications
In this series less than a quarter of the patients suffered permanent post-operative cranial nerve deficits. The incidence of these deficits has been reported in a number of other surgical series.[16,17] In most cases the anatomical integrity of the nerve can be preserved, but the tenacious adherence of the cholesteatoma matrix and the surgical manipulation required to excise it were responsible for the post-operative impairment. Only two patients, however, required secondary rehabilitative measures for lower cranial nerve deficits. The peri-operative mortality was nil.

Degree of resection
The high percentage (80 per cent) of total removal of thecholesteatoma in this series is due to the rational
combination of neuro-otological and neurosurgical approaches to the posterior and the middle cranial fossae. In addition when the tumour was not completely exenterated, no more than five per cent of the lesion was left behind. These micro-surgical techniques have increased the rate of total removal of these lesions,[7,13,16] however complete removal of thelesion is not always warranted and many factors have to be considered when planning the degree of excision. The age of the patient, the involvement of the lower cranial nerve and of vascular structures have to be carefully evaluated before and during surgery. Older patients are less likely to compensate for lower cranial nerves palsies and do not tolerate vascular compromise of neural structures as well as younger patients will. For these reasons a subtotal removal of the cholesteatoma may be advised when the risks to the patient

are high.[18]

Recurrences

Recurrence of the disease after a total removal of the lesion is unlikely to occur,[13] while a subtotal removal is associated with a 30 per cent incidence of recurrence at eight years.[16] Moreover, considering the slow growth rate of these lesions asymptomatic recurrence may be expected in a period of time equal to the patient's age.[6] In this series one recurrence occurred 15 years after the initial surgery. The follow-upperiod may not belong enough for a recurrent lesion to be manifest in magnetic resonance imaging (MRI) scans.

Primary CPA cholesteatomas grow slowly and silently in the subarachnoidal spaces. Their diagnosis is often late, when they have reached large dimensions. Surgical removal is the only available therapy. The surgical approach should optimize resection whilst minimizing morbidity. To achieve this the surgeon needs to consider the age of the patient, the location and extent of the tumour, the function of the cranial nerves and the extent of planned resection. The ability to optimize the approach for each individual patient is facilitated by the neurologist and the neurosurgeon working together in a skull base surgery team. This management philosophy resulted in complete removal of CPA cholesteatoma in 80 per cent of patients with minimal morbidity and no mortality.

References

1. Nager GT. Epidermoids involving the temporal bone: clinical, radiological, and pathological aspects. Laryngoscope 1975;2:1–22.
2. Love JG, Kernohan JW. Dermoidandepidermoidtumors (cholesteatoma) of the central nervous system. Am Med Assoc 1936;107:1876–83.
3. Kountakis SE, Chang CY, Gormley WB, Cabral FR. Migration of intradural epidermoid matrix: embryologic implications. Otolaryngol Head Neck Surg 2000;123:170–3.
4. Baumann CH, Busy PC. Paratrigeminal epidermoid tumors. J Neurosurg 1956;13:455–68.
5. Fleming JFR, Botterell EH. Cranial dermoid and epidermoid tumors. Surg Gynecol Obstet 1959;109:403–11.
6. Alvord E. Growth rates of epidermoid tumors. Ann Neurol 1977;2:367–70.
7. Yarsagil MG, Abernathey CD, SariogluA C. Microsurgical treatment of intracranial dermoid and epidermoid tumors. Neurosurgery 1989;24:561–7.
8. Brackmann D, Anderson RG. Cholesteatomas of the cerebellopontine angle. In: Silverstein H ed. Neurological Surgery of the Ear. Birmingham ALA: Aesculapius Publishing Co., 1979;340–4.
9. Guidelines for hearing preservation in acoustic neuroma (vestibular schwannoma). Otolaryngol Head Neck Surg 1995;113:179–80.
10. Mitchell T, Quaranta N, Chang P, Baguley DM, Moffat DA. Audiological presentation of cerebello-pontine angle cholesteatoma. Proceedings of the Sixth International Conference on Cholesteatoma & Ear Surgery Cannes, June 29th–July2nd2000.MagnanJ,ChaysA eds. Elsevier Science B.V.2000;1117–22.
11. Ulrich J. Intracranial epidermoids: a study of their distribution and spread. J Neurosurg 1964; 21:1051–8.
12. Yamakawa K, Shitara N, Genka S, Manaka S, Takakura K. Clinical course and surgical prognosis

of 33 cases of intracranial epidermoid tumours. Neurosurgery 1989;24:568–73.
13. Samii M, Tatagiba M, Piquer J, Carvalho GA. Surgical treatment of epidermoid cysts of the cerebellopontine angle. J Neurosurg 1996;84:14–9.
14. Burgraaf B, Luxford WM, Doyle KJ. Neurotologic treatment of acquired cholesteatoma. Am J Otol 1995;16:480–5.
15. Angeli SI, De La Cruz A, Hitselberger W. The transcochlear approach revisited. Otol Neurol 2001;22:690–5.
16. Talacchi A, Sala F, Alessandrini F, Turazzi S, Bricolo A. Assessment and surgical management of posterior fossa epidermoids tumors: report of 28 cases. Neurosurgery 1998;42:242–51.
17. Mohanty A, Venkatrama SK, Rao BR, Chandramouli BA, Jayakumar PN, Das BS. Experience with cerebellopontine angle epidermoids. Neurosurgery 1997;40:24–9.
18. De La Cruz A, Doyle KJ. Epidermoids of the cerebellopontine angle. In: Jackler RK, Brackmann DE, eds. Neurology. StLouis:Mosby-YearBook,1994:823–33.

Chapter 5.0

Trigeminal neuroma

Chapter 5.1

Surgical management of trigeminal neuromas: a report of eight cases

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Abstract

Objective: Trigeminal neuromas are rare tumours that may involve any part of the Vth nerve complex, including extracranial peripheral divisions of the nerve. A series of eight patients with intracranial trigeminal neuromas who underwent surgical management are presented.

Methods: The hospital records and radiological images were reviewed with regard to clinical presentation, surgical approach, operative findings, peri-operative morbidity and neurological outcome, and percentage of tumour recurrence.

Results: The principal presenting symptoms were those of involvement of the trigeminal nerve with sensory impairment in one or more of the three divisions. Tumour location was the prime determinant of surgical approach. Lateral skull base approaches were used as they are considered to be superior for identifying tumour origin, extension, and relationship to surrounding structures. Total excision of the tumour was carried out in three of the eight patients. In the remaining five patients some tumour was left purposely in order to minimize neurological deficit and optimize post-operative quality of life. There was no peri-operative mortality or major morbidity in our series. Five patients experienced symptomatic tumour recurrence and revision surgery was performed.

Conclusion: Management of trigeminal neuromas is complex and requires a multi-disciplinary approach. Pre-operative surgical planning allows tumour removal with preservation of important neural structures in the majority of cases. For large tumours occupying both the middle and posterior cranial fossae, the retrosigmoid/retrolabyrinthine/middle cranial fossa approach provides good exposure and results in minimal brain retraction. A Fisch type C approach is necessary for the largest tumours. Long-term follow up with interval imaging is mandatory to exclude long-term tumour recurrence.

Introduction

Trigeminal neuroma is a benign schwannoma of the Vth cranial nerve first described by Dixon in 1846.[1] Vestibular schwannoma is the most common tumour to present in the cerebellopontine angle (CPA) (81 per cent).[2] The remaining 19 per cent comprise a fascinating group of CPA tumours, of which meningioma (6.5 per cent), and CPA

cholesteatoma (4.6 per cent) are the most common.[2] Trigeminal neuromas are very rare intracranial tumours, accounting for 0.07 to 0.33 per cent of all intracranial tumours and 0.8 per cent to 8 per cent of intracranial schwannomas,[3,4] and comprise 1 per cent of CPA tumours.[2]

Because of the different neural root origins and direction of growth of these tumours along the trigeminal nerve, several classification systems have been suggested that have implications for the clinical findings, surgical approach, and outcomes of surgery in patients with these tumours. Jefferson[5] classified these tumours into three types: Type A, tumours located in the middle fossa that arise from the gasserian ganglion; Type B, tumours located predominantly in the posterior fossa that arise from the root of the trigeminal nerve; and Type C, tumours with significant components in both middle and posterior fossae (dumbbell shaped tumours).

Trigeminal neuromas often present incidentally and are challenging to manage. They have characteristic clinical and anatomical features.[6] They can originate from any section of the Vth cranial nerve and the corresponding symptoms and signs are largely determined by the tumour location. The majority of patients present with numbness involving one or all branches of the trigeminal cranial nerve, whereas motor involvement is an unusual feature.

Facial pain is not a consistent symptom in trigeminal neuromas and changes in the corneal reflex and decreased facial sensation are more common than pain.[5,7,9,10]

The diagnosis and management of trigeminal neuromas presents the skull base surgeon with a formidable challenge because of their rarity, and in particular their anatomical position. Presentation is often late and the surgeon may be faced with a large tumour in a young person. Early diagnosis depends on a high index of suspicion and good imaging.

We present the senior authors' (DAM and DGH) surgical experience of these difficult tumours. The modes of presentation, investigation, management strategies, surgical approaches, complications and outcome are analysed. A review of the literature and the controversies and dilemmas surrounding these tumours is discussed.

Patients and methods

Eight patients with trigeminal neuromas were treated at the Department of Neuro-otology and Skull Base Surgery, Addenbrookes Hospital, Cambridge, between 1991 and 2002. The hospital records and radiological images of these patients were reviewed. The imaging modalities employed consisted of computedtomography(CT) scanning including bone settings and magnetic resonance imaging (MRI) T1and T2-

weighted images with gadolinium DTPA enhancement. The site of the primary and recurrent tumour, the size, the surgical approach used, operative findings, rate of tumour recurrence, peri-operative morbidityand neurological outcome were all recorded.

In this series, there were five female and three male patients (See Table 1). The mean age of the patients was 28 years (range 22–41). Trigeminal neuromas tend to become manifest at a relatively young age. The duration of symptoms before referral ranged from two months to two years with a mean of 10 months.

Table 1: Demographics of patients with trigeminal neuroma

Demographics	No. of patients
Age	
20-30	6
31-40	1
41-50	1
Sex	
Male	3
Female	5

Results

Presenting clinical features

The principal presenting symptoms resulted from involvement of the trigeminal nerve, either as sensory impairment in one or more of the three divisions, or motor deficits of the muscles of mastication. All eight patients had facial numbness; four had facial pain and two patients had imbalance. Four patients complained of double vision and one patient, who had previous surgery elsewhere, already complained of facial weakness. On examination, six patients had involvement of V1, seven had V2 nerve involvement and five had V3 involvement. One patient had involvement of the motor branch of the trigeminal nerve. One patient who had previous surgery elsewhere had a facial nerve paralysis House-Brackman (HB) grade 3, one a III nerve paralysis, one a IV and two had a VI nerve involvement. Abnormal gait and cerebellar signs were present in four patients and one patient had weakness of the masseter muscle. Five patients had normal hearing at the time of presentation. Hearing loss was seen in three patients – one had a mild conductive hearing loss and two had a profound sensorineural hearing loss.

Tumor location

Pre-operative MRI scans were obtained routinely in all patients to identify the lesion,

its extent, morphology and anatomical site (Figures 1 and 2). Table 2 summarizes the sites of the tumours and classifies them according to Jefferson.

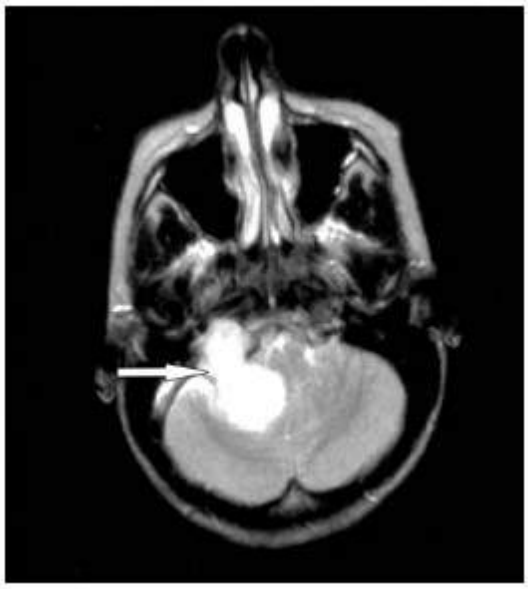

Figure 1: Axial T2-weighted MRI scan with gadolinium DTPA contrast demonstrating atypical enhancing dumbbell tumour occupying both middle and posterior fossae.There is significant brainstem compression.

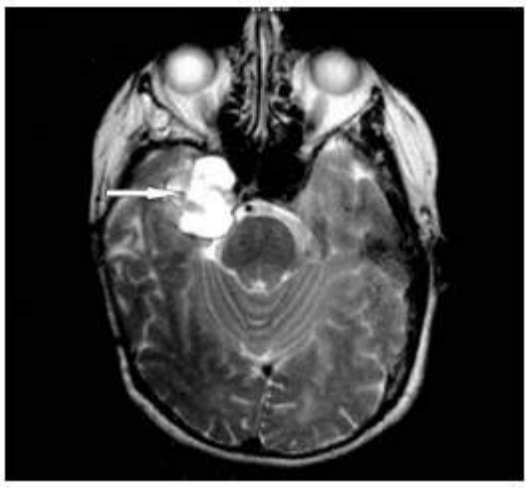

Figure 2: Axial T2- weighted MRI scan with gadolinium DTPA contrast showing atrigeminal neuroma located in the middle cranial fossa.

Table 2: Tumour location

Tumour location (Jefferson classification)	No. of patients
Type A – Middle fossa alone	4
Type B – Posterior fossa alone	1
Type C – Middle and posterior fossae	3

Surgical approach

The surgical approach in each case was determined by the anatomical location and extent of the tumour. A schematic presentation of the skin incision and lateral skull base approaches used are illustrated in Figures 3 and 4 respectively. In most instances lateral skull base approaches were adopted (see Table 3). The combined retrosigmoid/retrolabyrinthine/middle fossa approach was used in five patients. One patient had retrosigmoid/transtemporal/middle fossa approach and in another patient middle fossa approach was considered appropriate. One tumour was excised via Fisch type C approach.[11]

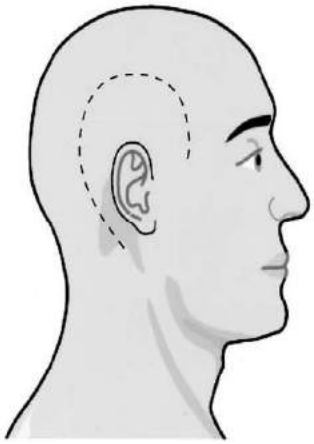

Figure 3: The skin incision used intrans temporal and middle fossa approaches to provide surgical access to the middle and posterior cranial fossae.

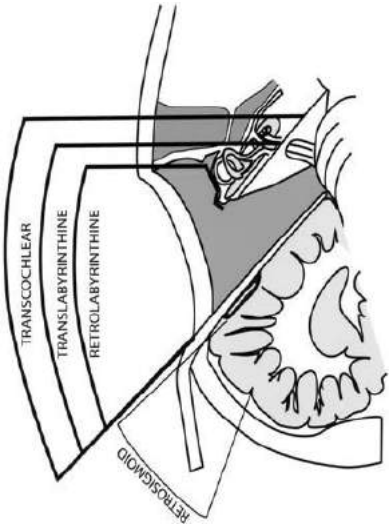

Figure 4: Schematic presentation of the lateral skull base approaches used for access to the middle and posterior cranial fossae.The retrolabyrinthine approach is a presigmoid posterior fossa cranio to my preserving the inner-ear structures.

Table 3: Surgical approaches in primary and revision surgery

Surgical approach	Number of patients	
	Primary procedure	Revision procedure
RS/RL/MF	5	0
RS/TT/MF	1	1
RS/MF	0	1
MF	1	0
Fisch B	0	1
Fisch C	1	0
Pterional	0	1

RS = Retrosigmoid, RL = Retrolabyrinthine, MF = Middle Fossa,
TT = Transtemporal (Translabyrinthine/Transcochlear)

These lateral skull base approaches allow good exposure of the tumour with minimal brain retraction. Total excision was possible in three of the eight patients and in five a balanced clinical judgement was used by the surgical team to determine the extent of the resection. In view of the indolent nature of these tumours, preservation of cranial nerve function was considered more important than total extirpation of every morsel of the tumour, particularly when the tumour capsule was inextricably involving cranial nerves or the cavernous sinus.

In those patients with recurrence of their tumour, the approaches were dictated by the site and extent of the tumour. One patient had retrosigmoid/transtemporal/middle fossa approach, whereas another patient had retrosigmoid/middle fossa approach. The Fisch type B[11] approach was considered appropriate in one case and a pterional approach was necessary in another case in order to provide better access to the tumour. The different approaches adopted for removal of these recurrences is also shown in Table 3.

Surgical outcome

The surgical outcome and a comparison of the neurological status pre-and post-operatively can be seen in Table 4. Facial numbness improved in two patients post-operatively, whereas symptoms like headache and facial pain settled completely. Diplopia remained a symptom in four patients. Of the five patients with pre-operative normal hearing, one developed mild sensorineural hearing loss, whereas in one patient with conductive deafness, the hearing returned to normal. Gait disturbance was present in three out of the four patients who presented with this sign pre-operatively. Improvement in the paralysis of the trigeminal nerve branches after the removal of the tumour was noticed in five patients. Post-operatively, one patient had paralysis of the trochlear and abducent nerves. There was one patient with oculomotor nerve, two with abducent nerve and three with grade 3 facial nerve

paralyses. Other complications included one patient with CSF meningitis which settled with antibiotics, one with post-operative seizures who needed long-term anti-epileptics and one developed mild hemiplegia which required rehabilitation. (see Table 4).

Table 4: Clinical features and cranial nerve involvement pre and post surgery.

Clinical features	No. of patients n = 8	
Presenting symptoms	Pre-operative	Post-operative
Facial numbness, paraesthesia	8	6
Facial pain	4	0
Headache	4	0
Diplopia	4	4
Seizures	0	1
Hearing - Normal	5	4
Conductive loss	1	0
Sensorineural loss	2	3
Gait disturbance	4	3
Cranial nerve involvement		
V1	6	5
V2	7	6
V3	5	3
Motor	1	0
VII	1	3
VIII	3	3
III	1	1
IV	1	1
VI	2	2
Cerebellar signs	4	3
CSF Leak	0	1
Mild hemiplegia	0	1

Recurrences

Five patients experienced symptomatic tumour recurrence (Figure 5). The interval between the primary surgery and revision surgery ranged from one to five years, with a mean of 2.9 years. In one patient a third operation was required for a further recurrence at an interval of 13 years from the first operation. Following revision surgery there was no mortality and the number of post-operative cranial neuropathies was largely unaltered except for one patient who had V3 deficit. The pure tone averages and speech discrimination scores remained at the pre-operative levels apart from one patient who had a mild hearing loss. Other post-operative complications from surgery for recurrent tumours included one patient with meningitis and two patients with seizures post-operatively where the middle fossa

(MF) route was used intra-operatively. One patient had deterioration in facial nerve function (from House–Brackmann grade 3 to grade 4). The outcomes of surgery for recurrent tumours are summarized in Table 5.

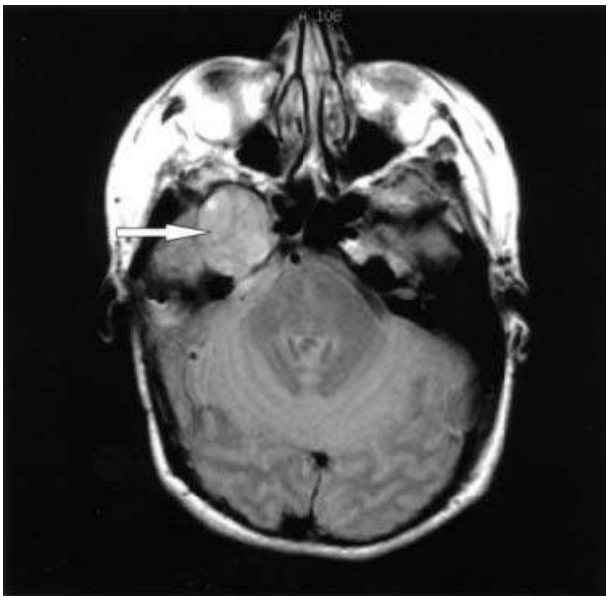

Figure 5: Axial T1-weighted un-enhanced MRI scan showing a recurrent tumour in middle cranial fossa. There is no evidence of mass defect, midline shift or hydrocephalus.

Table 5: Presentation and outcome following revision surgery for recurrent tumour

Clinical features	No. of patients n = 4	
Presenting symptoms	Pre-operative	Post-operative
Facial numbness, paraesthesia	4	4
Diplopia	2	2
Headache	1	0
Hearing loss deterioration	1	2
Gait disturbance	1	1
Cranial nerve involvement		
V1	4	3
V2	4	4
V3	3	4
Motor	-	-
VII	1	1
VIII	1	2
VI	1	1
IV	1	1
Lower cranial nerves (IX,X,XI)	1	1
Cerebellar signs	1	1
Meningitis	0	1
Seizures	0	2

Discussion

The presenting features in this series of patients were not significantly different from those observed in earlier reviews.[3,6,7] The majority of patients present with numbness involving one or all branches of the trigeminal cranial nerve, indicating involvement of the sensory branch, whereas motor involvement with weakness of the muscles of mastication is unusual and occurred in only one patient. The relationship between facial pain and tumours involving the trigeminal nerve has been a clinical curiosity. Several authors believed that facial pain is not a consistent feature in trigeminal neuromas and that changes in the corneal reflex and decreased facial sensation are more common than pain.[5,7,9,10] This observation is supported by this series where only 50 per cent of patients had facial pain. Bullitt et al.[12].suggested that pain in the form of trigeminal neuralgia is most commonly caused by tumours involving the trigeminal root. Interestingly, the quality of pain in the majority of patients with trigeminal neuroma differs from that in patients suffering from idiopathic trigeminal neuralgia.[7,13] Most patients with pain from neuromas have paroxysmal lancinating facial pain; however the episodes tend to last longer and do not always have specific triggering mechanisms. This pain does not respond to the medication commonly used to treat trigeminal neuralgia.[14]

McCormick et al.[7] found that 75 per cent of patients had other cranial nerve abnormalities at the time of diagnosis. The associated cranial neuropathies were largely determined by the location of the tumour and its relationship to adjacent neural and vascular structures. Tumours involving the posterior cranial fossa predominantly affected the VIIth and VIIIth cranial nerves whereas larger tumours involving the posterior cranial fossa were also associated with cerebellar and long-tract signs.[7,15] Motor deficit of the Vth or VIIth nerve was found to be significantly less frequent than generally reported, 12 per cent in this study, compared with 30 per cent reported by several authors.[8,10] Patients who presented with diplopia suffered mostly from deficits of the abducens nerve, supposedly secondary to compression by the tumour.[13] It is important to stress that diminished corneal reflex together with facial paraesthesia or facial pain, are not diagnostic of trigeminal neuroma, a similar symptom complex being shared by meningioma of Meckel's cave and cholesteatoma of the CPA. VIIIth nerve involvement was found in almost half of the patients in this series, concurring with previous studies.[8] Hearing may also be affected by impaired tensor tympani function due to loss of its trigeminal innervation. Also, hearing loss and facial nerve dysfunction have been reported in patients whose tumours have significantly eroded the petrous bone with damage to the inner and/or middle ear.[8]

The diagnosis of trigeminal neuroma is a difficult one to make on clinical grounds alone. Imaging is particularly important to establish the precise size, morphology and anatomical location of the tumour, and its relationship to neighbouring structures. This will determine the optimal surgical approach adopted for any one particular tumour. The primary radiological investigation for the diagnosis of these lesions should be high resolution CT scanning using bony windows, to determine the extend of bony erosion and MRI for soft tissue delineation. MRI has an added advantage in the pre-operative imaging of these tumours because of its multiplanar capability. Trigeminal neuromas appear slightly hyperintense on the T1-weighted images with significant enhancement after gadolinium DTPA injection. In view of this, a high resolution CT scan with bony windows and MR imaging with gadolinium DTPA enhancement are complementary in providing complete pre-operative information. Rarely, angiography is useful in pre-operative assessment as these tumours are not highly vascular and embolization is not necessary. In very large tumours, however, cerebral angiography may be valuable in order to identify the degree of displacement of intracranial vessels prior to undertaking surgery.[3] In anteriorly situated tumours, cerebral angiography shows the displacement of the intracavernous and petrosal segment of the intrapetrous carotid artery. When a significant posterior fossa component is present, dorsocranial displacement of the posterior cerebral and superior cerebellar arteries with downward displacement of the anterior inferior cerebellar artery has been reported.[17-19]

Trigeminal neuromas tend to displace surrounding neurovascular structures rather than engulf them.[20] Surgery for these lesions may be very challenging, particularly in large tumours. The potential of these tumours to extend into two intracranial compartments will influence the choice of surgical approach. The principles of microsurgery include careful dissection of the tumour capsule from the surrounding structures following adequate debulking of the tumour. The aim of total tumour removal[21,22] which offers the best chance of cure, and dramatically reduces the tumour recurrence rates,[6] must be balanced by the need to preserve the neural structures and, consequently, quality of life. Sindou and Pelissou[23] found that total removal of the tumour was achieved in only 50 per cent of cases because of the close relationship of the lesion to the CPA, petrous apex, cavernous sinus and multiple cranial nerves. Despite the emphasis on total removal in later series,[7] this has not always been possible,because of risks to vital structures.[6,7] In our opinion, it is important to be cognisant of postoperative quality of life and some compromise of the surgical ideal of total tumour removal may be of overriding importance to the patient since these indolent tumours are benign and slow growing. Our aim is preservation of cranial nerve function and to minimize post-operative complications.

If the tumour is found to be firmly adherent to the cavernous sinus, it may be left in order to reduce subsequent morbidity. Although this may result in a higher recurrence rate, recurrences can be observed with high resolution imaging and treated conservatively or with further surgery if necessary. Lateral skull base approaches allow good exposure of these tumours,[24] with minimal brain retraction obviating the need for two stage tumour resection.

Significant advances in neuroimaging, electrophysiological monitoring, microsurgical techniques, and newer skull base approaches have made a significant contribution towards achieving the surgical goal of complete tumour removal with minimal morbidity. There were no deaths or major morbidity in this series, which corresponds with other series reported in the literature.[7,13,21] Post-operative facial numbness improved in five cases, and facial pain was alleviated in all six cases where it was present pre-operatively. Hearing deteriorated in only one patient who had no previous hearing problems.

Reported recurrence rates are high. Taha et al.[4] reported a 60 per cent recurrence rate in his series and in this series it was similar. Injury or permanent damage to the trigeminal nerve branches has been inevitable in many cases.[7,9,22] Good quality of life with only trigeminal nerve symptoms is considered to be an excellent outcome.

Stereotactic radiotherapy in the form of either single dose radiosurgery (gamma knife) or fractionated from a linear accelerator source (LINAC) is reported as an effective treatment for small and medium size trigeminal schwannomas.[25] Some larger tumours, up to 3 cms in maximum diameter, may also be suitable for stereotactic radiotherapy if there is no significant brainstem compression. The upper limit of size for radiotherapy treatment is governed by the fact that tumours will swell in the immediate post treatment phase and this may increase brainstem compression and precipitate decompensation. Stereotactic radiotherapy has also been proposed as an alternative and minimally invasive primary treatment option for patients with newly diagnosed or residual trigeminal schwannoma, especially if the tumour size is small.[26,27] Tumour shrinkage was achieved in 565 of treated patients and tumour growth arrested in 44 per cent of a series reported by Huang et al. (1999).[27]

In this series, many cases were treated prior to the prevalent use of radiosurgery in this country and many of these tumours were very large and presented with varying degrees of brainstem compression and would not have been suitable for this form of treatment. For small tumours, expectant management with interval scanning was preferred, since the evidence base for treating these very rare tumours with radiosurgery had not yet been established. Recurrent tumours were treated by further surgical resection in concurrence with current opinion at that time.[21,22,24]

Stereotactic radiotherapy will certainly be considered as an alternative treatment option for any patient with a small tumour which has demonstrated significant growth on interval imaging and also for known residual or emergent recurrent tumour as this may obviate the need for revision surgery.

Conclusion

Trigeminal neuromas are rare benign slow-growing tumours most commonly occurring in young adults and their management is complex and requires a multidisciplinary approach. Total excision reduces the risk of recurrence but may be associated with significant morbidity and deterioration in quality of life. Pre-operative surgical planning based on high resolution imaging allows tumour removal with preservation of important neural structures in the majority of cases. Large tumours occupying both the middle and posterior cranial fossae, are best excised by a lateral skull base approach where good exposure is obtained at the expense of bone removal rather than brain retraction. Long-term follow up with interval imaging is mandatory to exclude tumour recurrence, which if it occurs may require stereotactic radiotherapy or further surgery.

- Trigeminal neuromas are rare benign slow-growing tumours most frequently seen in young adults. Their management is complex, and requires a multidisciplinary approach
- Total excision reduces the risk of recurrence but may be associated with significant morbidity
- A lateral skull base approach is needed for large tumours with both middle and posterior cranial fossa involvement
- Stereotactic radiotherapy may offer an alternative to surgery in some cases

References

1. Dixon J. Tumor of gassserian ganglion. Med Clin Trans London 1846;29:131.
2. Moffat DA, Saunders JE, McElveen JT, McFerran DJ, Hardy DG. Unusual cerebello-pontine angle tumours. J Laryngol Otol 1993;107:1087–98.
3. Samii N, Migliori MM, Tatagiba Babu R. Surgical treatment of trigeminal schwannomas. J Neurosurg 1995;82:711–18.
4. Taha JM, Tew JM, Van Loveren HR, Keller JT, El-Kalliny M. Comparison of conventional and skull base surgical approaches for the excision of trigeminal neurinomas. J Neurosurg 1995;82:719–25.
5. Jefferson G. The trigeminal neurinomas with some remarks on malignant invasion of the gasserian ganglion. Clin Neurosurg 1955;1:11–54.

6. Pollack IF, Sekhar LN, Jannetta PJ, Janecka IP. Neurilemonas of the trigeminal nerve. J Neurosurg 1995;70:737–45.
7. McCormick CP, Bello JA, Post KD. Trigeminal schwannoma. Surgical series of 14 cases with review of the literature. J Neurosurg 1988;69:850–60.
8. Bordi L, Compton J, Symon L. Trigeminal Neuroma. A report of eleven cases. Surg Neurol 1989;31:272–6.
9. Yasui T, Hakuba A, Kim SH, Nishimula S. Trigeminal neurinomas. Operative approach in eight cases. J Neurosurg 1989;71:506–511.
10. Arseni C, Dumitrescu L, Costantinescu A. Neurinomas of the trigeminal nerve. Surg Neurol 1975;4:497–503.
11. Fisch U. Infratemporal fossa approach for glomus tumors of the temporal bone. Ann Otol Rhinol Laryngol 1982;91:474–9.
12. Bullitt E, Tew JM, Boyd J. Intracranial tumors in patients with facial pain. J Neurosurg 1986; 64:865–71.
13. Day JD, Fukushima T. The surgical management of trigeminal neuromas. Neurosurgery 1998; 42:233–40.
14. Yonas H, Jannetta PJ. Neurinoma of the trigeminal root and atypical trigeminal neuralgia: their commonality. Neurosurgery 1980;6:273–7.
15. Friedman RA, Pensak ML, Osterhaus D, Tew JM, van Loveren H. Trigeminal schwannomas: the role of the neurotologist in multidisciplinary management. Otolaryngol Head Neck Surg 1999; 120:355–60.
16. Dany A, Pefferkorn JP, Vallat JN, Loubet R, Madoux M. Neurinome du ganglion de Gasser a development temporal. Neuro-Chirurgie 1970;16:349–56.
17. Bull JW, Schunk H. The significance of displacement of the cavernous portion of the internal carotid artery. Br J Radiol 1962;35:801–14.
18. Wullenweber R, Traupe H, Schwatz G. Angiographic demonstration of a trigeminal neurinoma. Neuroradiology 1976;10:225–9.
19. De benedittis G, Bernasconi V, Ettorre G. Tumors of the fifth cranial nerve. Acta Neurochir 1977; 38:37–64.
20. Beck DW, Menezes AH. Lesions in Meckel's cave: variable presentation and pathology. J Neurosurg 1987;67:684–9.
21. Dolenc VV. Frontotemporal epidural approach to trigeminal neurinomas. Acta Neurochir 1994; 130:55–65.
22. Al-Mefty O, Ayoubi S, Gaber E. Trigeminal schannomas: removal of dumbbell-shaped tumors through the expanded Meckel cave and outcomes of cranial nerve function. J Neurosurg 2002; 96:453–63.
23. Sindou M, Pelissou I. Trigeminal neurinomas. A special type of cavernous sinus tumors. In. Dolenc VV, ed. The cavernous sinus. A multidisciplinary Approach to Vascular and Tumorous Lesions. Wien: Springer-Verlag, 1987;355–376.
24. Goel A, Muzumdar D, Raman C. Trigeminal Neuroma: analysis of surgical experience with 73 cases. Neurosurgery 2003;52:783–90.
25. Pan L, Wang EM, Zhang N, Zhou LF, Wang BJ, Dong YF et al. Long-term results of Leksell gamma knife surgery for trigeminal schwannomas. J Neurosurg 2005;102:220–4.
26. Nettel B, Niranjan A, Martin JJ, Koebbe CJ, Kondziolka D, Flickinger JC et al. Gamma knife radiosurgery for trigeminal schwannomas. Surg Neurol 2004;625:435–44.
27. Huang CF, Kondziolka D, Flickinger JC, Lunsford LD. Stereotactic radiosurgery for trigeminal schwannomas. Neurosurgery 1999;45:11–16.

Chapter 6.0

Microvascular decompression of the facial nerve for hemifacial spasm

Chapter 6.1

Outcome following retrosigmoid microvascular decompression of the facial nerve for hemifacial spasm

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Abstract

This paper evaluates the outcome of retrosigmoid microvascular decompression of the facial nerve in a series of patients suffering from hemifacial spasm who had been referred to the skull-base team (comprising senior authors DAM and DGH). The paper is a retrospective review of 15 patients who underwent retrosigmoid microvascular decompression of the facial nerve at Addenbrooke's Hospital between 1985 and 1995. In this series it was possible to obtain complete resolution of hemifacial spasm in 93.3 per cent of cases in the short term and in 80 per cent in the long term.Twelve patients (80 per cent) were symptom-free post-operatively.Two patients had minor recurrence of symptoms occurring within six months of the procedure. One patient with no identifiable vascular impingement of the facial nerve had no improvement following surgery. Three patients suffered sensorineural hearing loss. Two patients complained of post-operative tinnitus, and transient facial palsy was noted in one patient. Retrosigmoid microvascular decompression of the facial nerve provides excellent long-term symptom control in a high percentage of patients with hemifacial spasm. Key words: Hemifacial Spasm; Nerve Compression Syndromes; Decompression; Surgical Procedures; Skull Base; Outcome Measures

Introduction

Hemifacial spasm is a disabling symptom associated with painful, involuntary paroxysmal contractions of the face beginning at the eye and spreading gradually over the rest of the face. The sustained contraction partly closes the eye and pulls the corner of the mouth towards the ear. The condition is thought to be secondary to irritation of the facial nerve as it exits the pons at the root entry zone. Several lesions (such as tumours, cysts, arteriovenous malformations and intrinsic brain stem lesions) can produce hemifacial spasm by direct infiltration or by extrinsic compression of the facial nerve and need to be excluded. Several medications have been reported to be effective in the treatment of hemifacial spasm, including carbamazepine,[1] baclofen,[2] gabapentin,[3] levetiracetam[4] and felbamate.[5] However most of these reports are case reports or pilot studies, and there are no large controlled studies with long-term follow up.The mechanism of action of these drugs in symptomatic relief is not known and their long-term use is further limited by side effects, particularly in the older age group, such as somnolence, dizziness, ataxia and weakness. The efficacy of medical treatment of patients with hemifacial spasm thus remains unclear. In view of the lack of evidence for the efficacy of drug therapy in

hemifacial spasm, with no reported placebo-controlled trials, some surgeons proceed directly to surgery without recommending prior drug therapy.[6] Botulinum toxin type A (BtA) has also been used successfully for symptomatic relief of hemifacial spasm. It causes flaccid paralysis of the muscles by blocking the release of acetylcholine at the neuromuscular junction. Although most studies report short-term results, those demonstrating longterm symptomatic relief have also been reported.[7] The side effects are mainly local and transient and include dry eye, ptosis, photophobia and diplopia. A recent Cochrane systematic review highlighted the paucity of available, placebo-controlled data but showed that BtA is effective and safe in the management of hemifacial spasm.[8] The main drawback of BtA is that relief lasts for only 12–18 weeks before symptoms reappear, and hence three to four injections per year are required to provide sustained relief of symptoms. Botulinum toxin type A by itself has little effect on the hemifacial spasm; the muscles continue to show electromyographically evident spasm despite clinical relief.[9] A repeat injection is thus needed once the effect of the previous one has worn off, and repeated injections require increasing dosage to achieve the same clinical effect.[10] Microvascular decompression of the facial nerve remains the treatment of choice and can provide sustained symptomatic relief in most patients with hemifacial spasm. Although Campbell and Keedy in 1947[11] were the first to report the effects of vascular compression of the VIIth cranial nerve, it was Gardner and Sava in 1962[12] who described microvascular decompression of the facial nerve for hemifacial spasm. Since the first publication of results from a series of patients undergoing this procedure in 1975,[13] microvascular decompression of the facial nerve has been reported to have a high success rate. Historically, the surgical procedure has been undertaken by neurosurgeons but otologists now usually manage disorders of the facial nerve, and with the advent of the multidisciplinary otological and neurosurgical team these patients may now be managed jointly. This paper represents the experience of the skullbase team at Addenbrooke's Hospital, Cambridge, with regard to microvascular decompression of the facial nerve for hemifacial spasm via the retrosigmoid approach. All patients were referred with a prolonged history of symptoms despite treatment with carbamazepine in some cases. Three patients had a history of botulinum toxin injections, which had not relieved their symptoms. Hemifacial spasm caused significant disability and distress, with marked reduction in quality of life, in all these patients. The technique, results, complications and overall outcome are presented.

Patients and methods

Fifteen patients who underwent surgery at Addenbrooke's Hospital between 1985 and 1995 were included in the study. Their clinical records were reviewed retrospectively with respect to symptoms, signs, investigations, indication for surgery, surgical findings, complications and ostoperative symptomatology.

Four patients were male and 11 were female, with ages ranging from 38 to 71 years and a mean of 55.2 years. Eight patients had symptoms on the right side and seven on the left side. Patients' duration of symptoms ranged from 18 months to 15 years, with a mean duration of 4.9 years. All the patients were referred with a prolonged history of symptoms causing disability and distress, with a significant reduction in quality of life.Thirteen patients had symptoms originating around the eye while two had symptoms originating primarily from the mouth area. Three patients had a history of botulinum toxin injections, which had not relieved their symptoms.

Pre-operative pure tone audiometry was performed in all cases.Thirteen patients had hearing within normal limits across the frequency spectrum. One patient had bilateral, symmetrical, highfrequency sensorineural hearing loss and one had conductive hearing loss due to tympanosclerosis. Pre-operative imaging with computed tomography (CT) or magnetic resonance imaging (MRI) was performed in all patients. There was no evidence of other intracranial pathology on imaging.

Table 1: Patient profile

Sex/age (years)	Side	Surgical findings	Revolution	Complications
F/61	L	AICA	Complete	None
F/51	R	AICA	Complete	None
F/68	L	None	None	None
F/48	L	Venous complex	Complete	HL, FP,T
F/40	R	AICA	Complete	H
F/71	L	AICA	Complete	H
F/68	L	Vertebral	Complete	None
M/50	L	AICA	Complete	None
M/43	R	PICA	Complete	None
M/69	L	Multiple vessels	Complete*	None
M/44	R	Multiple vessels	Complete	None
F/63	R	AICA	Complete	None
F/38	R	AICA	Complete	None
F/55	R	AICA	Complete*	T
F/59	R	AICA	Complete	None

Recurrence of mild symptoms within six months of surgery; F = female; M = Male; AICA = anterior inferior cerebellar artery; ICA = posterior inferior cerebellar artery; L = left; R = right; HL= hearing loss; FP = facial paresis; T = tinnitus

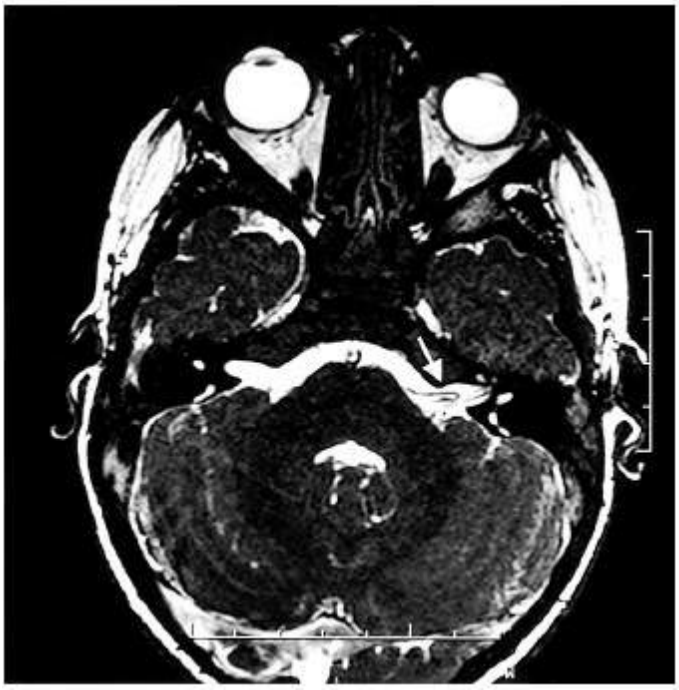

Figure 1: T2-weighted magnetic resonance imaging scan showing the loop of the anterior inferior cerebellar artery impinging on the VIIth nerve (arrow).

Operative procedure

All the procedures were performed using a retrosigmoid approach. The patient was placed supine on the operating table with the head turned to the opposite side and secured in a three-point headrest. After preparation of the skin, an inverted 'hockey stick' incision was made to raise the scalp flap and the pericranium. A posterior fossa craniotomy of approximately 5x4 cm was then completed, based anteriorly on the sigmoid sinus, bordered superiorly by the transverse sinus and extended inferiorly to the point where the occipital bone turns medially towards the foramen magnum. The posterior limit was set by the size of the bone flap. The craniotomy rectangle was cut using a high-speed drill with cutting and diamond paste burrs. Bone dust was harvested and used as bone paté to seal any opened mastoid air cells at the end of the procedure. The dura was then opened with a Y-shaped incision and the cerebellar hemisphere gently retracted posteriorly with a Yassergil flexi-arm retractor. The arachnoid was then opened over the VIIth and VIIIth nerve complex and the loop of the offending vessel identified at the root entry zone. The vessel was delicately mobilized from the neural bundle, a piece of muscle taken from the temporalis muscle was interposed between the vessel and the facial nerve root near the nerve entry zone, and a piece of Surgicel was placed over it. This was then secured with Tisseel fibrin glue (Biotek Pharma, Baxter Healthcare Ltd, Thetford, Norfolk, England).

The dura was then closed with a continuous suture and a patch of fascia lata glued over the dural closure with Tisseel. The wound was closed in layers and a classical neurosurgical head dressing applied. Patients were carefully monitored during the postoperative recovery period and discharged after five to seven days. They were followed up in the neurotology clinic, where assessment of surgical outcome, facial nerve function and post-operative audiometry was undertaken.

Results

Pre-operative imaging

Vascular loops were noted in the cerebellopontine angle (CPA) adjacent to the VIIth and VIIIth nerve complex at the root entry zone in three patients.

Surgical findings

Vascular loops were found touching or indenting the nerve complex at the root entry zone in 14 cases (93.3 per cent) (Table 1). These were identified as: the anterior inferior cerebellar artery (AICA) in nine patients (60 per cent); the posterior inferior cerebellar artery (PICA) in one patient; multiple vessels in two patients; a venous complex in one patient; and an ectatic left vertebral artery in one patient. In one patient there was no identifiable vascular loop impinging on the VIIth and VIIIth nerve complex.

Outcome of surgery

The results of surgery are shown in Table 1. Complete resolution of hemifacial spasm was seen in 14 patients (93.3 per cent) at three-month follow up. Twelve of these patients (80 per cent) showed complete resolution of symptoms after long-term follow up. It was possible to identify impingement on the nerve complex by a vascular loop in 12 of these 14 patients who improved completely following the procedure. In two patients (13.3 per cent) the hemifacial spasm resolved in the immediate postoperative period but mild recurrence of symptoms was noted six months post-operatively; one patient had impingement of multiple vessels on the nerve complex and in the other the PICA was implicated. However one patient, who had no identifiable vascular loop on surgery, showed no improvement following surgery.

Complications

Complications of surgery are shown in Table 1. Three patients (20 per cent) had a profound sensorineural hearing loss on the operated side. One patient (6.6 per cent) suffered immediate facial weakness and tarsorrhaphy was performed but the paralysis improved gradually to a House-Brackman grade III function. Post-operative tinnitus was noted in two patients (13.3 per cent).

Discussion

The anatomy of the CPA is very variable and it is well known that loops of arteries and veins are in close proximity to, and may impinge on, the VIIth and VIIIth nerve complex at the root entry zone.

Anatomical studies have shown a very close relationship between the AICA and the VIIth or VIIIth nerve.[14] In our series the AICA was the most common vessel causing compression of the facial nerve (60 per cent; Table 1). Samii et al.[15] reported that 59 per cent of cases in their series were also caused by the AICA. Zhang and Shun[16] reported that the AICA was the commonest artery involved in their series (57 per cent). Barker et al.,[6] however, reported that the commonest artery was the PICA (68.2 per cent); Magnan et al.[17] agreed, observing the PICA alone in 39 per cent of cases and the PICA in conjunction with the vertebral artery in 30 per cent of cases.

Vascular compression may not be the only cause of spasm in all cases. Aoki and Nagao[18] reported a case of hemifacial spasm in which no vascular abnormalities were observed during surgery and mere manipulation and surrounding dissection of the nerve resulted in resolution of symptoms.

The significance of the site of neural compression has been the source of much discussion. Many surgeons believe that compression of the nerve at the root entry zone is the most important aetiological factor.[16] Kondo,[19] however, stressed the importance of accurate identification of the offending vessel as multiple vessels may be in contact with the nerve and occasionally the main loop may be hidden behind a well developed flocculus and thus missed at surgery. Kondo believed that the significant point of compression is the neuroglial-neurolemmal junction. In our series recurrent symptoms were noted in one case in which multiple vessels were identified at the time of surgery. Magnan et al.[17] described endoscopic microvascular decompression and believed that the use of endoscopes in these cases aids in identification of the exact location of the neural compression and obviates the need to retract the flocculus and cerebellar hemisphere. These authors felt that this was important in reducing post-operative morbidity.

Imaging is important to exclude other pathologies causing hemifacial spasm, but its value in precise localization of the neural compression has been disappointing and the absence of an obvious vascular loop seldom excludes a vascular cause. Radiological findings on imaging with three-dimensional fast-spin echo MRI sequences have been reported to correlate well with surgical findings.[20] Although there remains controversy over the pathogenesis and management of hemifacial spasm[21,22] many series have shown that microvascular decompression can play an important role in relieving this very unpleasant and debilitating condition (Table 2).

Table 2: Succes rates after microvascular decompression.

Series	Patients (n)	Success rate (% symptom-free)
Iwakuma et al. (1982)[23]	74	97
Huang et al. (1992)[24]	310	88
Zhang & Shun (1995)[16]	300	92
Barker et al. (1995)[6]	612	79
Payner & Tew (1996)[25]	34	85
Illingworth et al. (1996)[26]	83	86
Magnan et al. (1997)[17]	50	80
Samii et al. (2002)[15]	145	92

Table 3: Complications.

Complications	Samii et al.[15] (n = 143)* (%)	Magnan et al.[17] (n = 60) (%)	Payner & Tew[25] (n = 34) (%)
Sensorineural hearing loss	15.9	5	15
Facial palsy: transient/ permanent	2.7/0	4.66/0	18/3
CSF leak	7	1.66	-

*One death due to intracranial infection. CSF = cerebrospinal fluid

In 2002 Samii et al.[15] reported a 59 per cent cure rate immediately post-operatively but this increased to 92 per cent after six months.

Magnan et al.[17] reported an overall success rate of 88 per cent in a series of 54 patients with hemifacial spasm, of whom 80 per cent were symptom-free post-operatively and the other 8 per cent had marked improvement of symptoms.

We report complete improvement in 93.3 per cent of our patients in the short term and in 80 per cent after long-term follow up.

The timing of symptom recurrence is not well documented in the literature. Payner and Tew[25] reviewed this and noted that only 1 per cent of cases that were initially cured recurred after two years.

They therefore concluded that patients who are symptom-free for two years after surgery can be considered cured. Although the cause of recurrence remains unclear Yamaki et al.[27] described atrophy of the muscle plug, resulting in recompression of the nerve. Variations in anatomy resulting in multiple vascular loops or shortened arteries stretching the nerve may account for partial recurrence.[19] Two patients in our series had a mild recurrence following surgery; both had identifiable vascular compression at surgery and the recurrences occurred by the sixmonth follow up. Whilst symptoms settled spontaneously in one patient, botulinum injections were required to cure the other.

Complication rates differ in the literature. Samii et al.[15] reported 15.9 per cent hearing loss in a series of 143 patients (Table 3); however only 8.3 per cent suffered a profound hearing loss – the remaining 7.6 per cent suffered decreased hearing acuity. McLaughlin et al.[28] reviewed a large series of 440 cases of microvascular decompression resulting from various pathologies and emphasized the need for intra-operative monitoring of the brain stem auditory response to minimize the risk of hearing loss. Use of the endoscope has been reported to be associated with a lower complication rate due to better visualization of the CPA.[17]

In our series there was no mortality and minimal morbidity, with hearing loss in three patients, no cerebrospinal fluid leakage and a transient facial palsy as the only neurological sequela.

Conclusion

Retrosigmoid microvascular decompression of the facial nerve for hemifacial spasm is a successful method of relieving patients of this very debilitating condition. It is associated with a high percentage of surgical cure and low recurrence rates.The morbidity is low and the procedure is well tolerated by patients. In our series it was possible to obtain complete resolution of hemifacial spasm in 93.3 per cent of cases in the short term and in 80 per cent in the long term. The findings at surgery correlated well with post-operative symptomatic control.

References

1. Alexander GE, Moses H 3rd. Carbamazepine for hemifacial spasm. Neurology 1982;32:286–7.
2. Sandyk R, Gillman MA. Baclofen for hemifacial spasm. Int J Neurosci 1987;33:261–4.
3. Daniele O, Caravaglios G, Marchini C, Mucchuit L, Capus P, Natale E. Gabapentin in the treatment of hemifacial spasm. Acta Neurol Scand 2001;104:110–12.
4. Deleu D. Levetiracetam in the treatment of idiopathic hemifacial spasm. Neurology 2004;62: 2134–5.
5. Mellick GA. Hemifacial spasm: successful treatment with felbamate. J Pain Symptom Manage 1995;10:392–5.
6. Barker FG, Jannetta PJ, Bissonette DJ, Shields PT, Larkins MV, Jho HD. Microvascular decompression for hemifacial spasm. J Neurosurg 1995;82:201–10.
7. Dutton JJ, Buckley EG. Long-term results and complications of botulinum A toxin in the treatment of blepharospasm. Ophthalmology 1988;95:1529–34.
8. Costa J, Espirito-Santo C, Borges A, Ferriera J, Coelho M, Moore P et al. Botulinum type A therapy for hemifacial spasm. Cochrane Database Syst Rev 2005;25:CD004899.
9. Geller BD, Hallet M, Ravits J. Botulinum toxin therapy in hemifacial spasm: clinical and electrophysiological studies. Muscle Nerve 1989;12:716–22.
10. Snir M,Weinberger D, Bourla D, Kristal-Shalit O, Doton G, Axer-Siegel R. Quantitative changes in botulinum toxin treatment over time in patients with essential blepharospasm and idiopathic hemifacial spasm. Am J Ophthalmol 2003;136:99–105.
11. Campbell E, Keedy C. Hemifacial spasm: a note on the etiology in two cases. J Neurosurg 1947; 4:342–7.
12. Gardner WJ, Sava GA. Hemifacial spasm - a reversible pathophysiologic state. J Neurosurg 1962; 19:240–7.
13. Jannetta PJ. The cause of hemifacial spasm: definitive microsurgical treatment at the brainstem in 31 patients. Trans Am Acad Ophthalmol Otolaryngol 1975;80:319–22.
14. Martin RG, Grant JL, Peace D, Theiss C, Rhoton AL Jr. Microsurgical relationships of the anterior inferior cerebellar artery and the facial-vestibulocochlear nerve complex. Neurosurgery 1980;6:483–507.
15. Samii M, Gunther T, Iaconetta G, Muehling M,Vorkapic P, Samii A. Microvascular decompression to treat hemifacial spasm: long-term results for a consecutive series of 143 patients. Neurosurgery 2002;50:712–18.
16. Zhang KW, Shun ZT. Microvascular decompression by the retrosigmoid approach for idiopathic hemifacial spasm: experience with 300 cases. Ann Otol Rhinol Laryngol 1995;104:610–12.
17. Magnan J, Caces F, Locatelli P, Chays A. Hemifacial spasm: endoscopic vascular decompression. Otolaryngol Head Neck Surg 1997;117:308–14.
18. Aoki N, Nagao T. Resolution of hemifacial spasm after posterior fossa exploration without vascular decompression. Neurosurgery 1986;18:478–9.
19. Kondo A. Follow-up results of microvascular decompression in trigeminal neuralgia and hemifacial spasm. Neurosurgery 1997;40:46–51.
20. Mitsuoka H, Tsunoda A, Okuda O, Sato K, Makita J. Delineation of small nerves and blood vessels with three dimensional fast-spin echo MR imaging: Comparison of presurgical and surgical findings in patients with hemifacial spasm. Am J Neuroradiol 1998;19:1823–9.
21. Adams CB. Microvascular compression: an alternative view and hypothesis. J Neurosurg 1989;70:1–12.
22. Ludman H, Choa DI. Hemifacial spasm: operative treatment. J Laryngol Otol 1985;99:239–45.
23. Iwakuma T, Matsumoto A, Nakamura N. Hemifacial spasm. Comparison of three different operative procedures in 110 patients. J Neurosurg 1982;57:753–6.
24. Huang CI, Chen IH, Lee LS. Microvascular decompression for hemifacial spasm: analyses of operative findings and results in 310 patients. Neurosurgery 1992;30:53–6.
25. Payner TD, Tew JM Jr. Recurrence of hemifacial spasm after microvascular decompression. Neurosurgery 1996;38:686–90.
26. Illingworth RD, Porter DG, Jakubowski J. Hemifacial spasm: a prospective long-term follow up of 83 cases treated by microvascular decompression at two neurosurgical centres in the United Kingdom. J Neurol Neurosurg Psychiatry 1996;60:72–7.
27. Yamaki T, Hashi K, Niwa J, Tanabe S, Nakagawa T, Nakamura T et al. Results of reoperation for failed microvascular decompression. Acta Neurochir (Wien) 1992;115:1–7.

28. McLaughlin MR, Jannetta PJ, Clyde BL, Subach BR, Comey CH, Resnick DK. Microvascular decompression of cranial nerves: lessons learned after 4400 operations. J Neurosurg 1999;90:1–8.

Chapter 7.0

Squamous cell carcinoma of the temporal bone

Chapter 7.1

The outcome of radical surgery and postoperative radiotherapy for squamous cell carcinoma of the temporal bone

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Objectives/Hypothesis: The objective was to analyze the clinical data and outcome of all the patients treated surgically for squamous carcinoma of the temporal bone in a tertiary referral department of skull base surgery over a 20-year period.

Study Design: Retrospective.

Methods: Thirty-nine patients with squamous carcinoma of the temporal bone were analyzed. The patients were staged according to the University of Pittsburgh system. The surgical technique, reconstruction of the surgical defect, postoperative radiotherapeutic treatment, follow-up regimen, and results were all described in detail.

Results: Disease-free survival for T2N0M0 tumors or stage II disease was 2/2 (100%). The survival for stage III disease was also 3/3 (100%). Overall, T3 tumors resulted in 3/6 (50%) survival. Overall, survival for stage IV tumors 11/32 (34.3%), and for T4 tumors, 11/29 (38%).

Conclusion: The overall disease-free survival for the entire series was 43.2%. Node-positive disease, poorly differentiated squamous cell histological findings, brain involvement, and salvage surgery were associated with a poorer outcome. The improved survival 15/23 (66%) of patients treated de novo in the study series compared with those treated with salvage surgery 8/23 (33%) suggested that early referral and aggressive primary surgical treatment with postoperative radiotherapy offer the greatest chance of cure.

Introduction

The first description of squamous cell carcinoma (SCC) of the temporal bone was credited to Schwartze and Wilde in 1775, but histopathological confirmation was not possible at that time.[1-3] The first relatively large review in the literature was published by Newhart[4] in 1917 and consisted of 34 well-documented cases of patients with middle ear carcinoma, most of them with advanced disease, who subsequently died.

In 1954, Parsons and Lewis[5] reported the first onestage subtotal resection of the temporal bone, proposing an alternative to the classic management of radical mastoidectomy with postoperative radiotherapy. Conley and Novack[6] described subtotal resection of the temporal bone for middle ear cancer in 1960. In their series, 66% of their cases were SCC and their 5-year survival rate was 18%. The authors concluded

that lesions which extended beyond the eustachian tube had a poor prognosis and that the aim of surgery was palliative. In 1975, Lewis[7] reported 100 cases of temporal bone resection for cancer, and 86 patients had SCC. The survival rate at 5 years was 25%, and the operative mortality compared with previous series improved from 10% to 5%. Recent studies have demonstrated that radical surgery in the form of en bloc extended temporal bone resection with conservation of the intrapetrous carotid artery but piecemeal removal at the petrous apex with postoperative radiotherapy can improve the 5-year survival in these aggressive tumors.[8]

We have recently analyzed in detail all the patients treated surgically for SCC of the temporal bone in a tertiary referral department of skull base surgery over a 20-year period. The management and outcomes are presented and compared with those in the literature. Based on the experience reported in the present study, our views on the current management of this difficult, aggressive tumor are presented.

Patients and Methods

Thirty-nine patients with SCC of the temporal bone who were treated at the Department of Otoneurological and Skull Base Surgery, Addenbrooke's Hospital (Cambridge, UK), over a 20-year period from 1982 to 2002 have been retrospectively reviewed. Patient data including age, sex, and referring unit, along with clinical presentation and disease stage, were analyzed in relation to the surgical management and patient outcome.

In an earlier study, Moffat et al.[8] analyzed 15 patients using the Clarke modification of the classification system proposed by Stell and McCormick,[3] as follows: *T1*, tumor limited to site of origin; *T2*, tumor extending beyond site of origin indicated by facial paralysis or radiological evidence of bone destruction; *T3*, involvement of parotid gland, temporomandibular joint, or skin (i.e., extracranial); and *T4*, involvement of dura/base of skull (i.e., cranial). In the current study, the patients were reclassified according to the University of Pittsburgh system reported by Arriaga et al.[9] in 1990, to allow outcome comparison with more recently presented series. Although it is appreciated that Hirsch[10] has recommended a modification of the University of Pittsburgh staging system according to facial nerve involvement, this has not altered the staging of the patients in the present series.

All patients underwent a preoperative cardiorespiratory assessment in view of the duration of the planned surgical procedure. No patient required cardiovascular intervention preoperatively. Audiometric analysis of the contralateral ear was performed and, if necessary, patients were fitted with a hearing aid to minimize the inevitable postoperative deficit caused by temporal bone resection.

Preoperative and postoperative contrast high-resolution computed tomography (CT) scans were performed. Bone and soft tissue windows in both axial and coronal planes were analyzed for bone erosion and soft tissue invasion. Following the advent of magnetic resonance imaging (MRI), patient assessment has included MRI scans with gadolinium DTPA enhancement in both axial and coronal planes to further improve assessment of soft tissue involvement.

After clinical and radiological investigations were complete, patients were staged according to the University of Pittsburgh staging system as follows: T1, tumor limited to the external auditory canal (EAC) without bony erosion or evidence of soft tissue extension; T2, tumor with limited EAC erosion (not full thickness) or radiological findings consistent with limited (>0.05 cm) soft tissue involvement; T3, tumor eroding the osseous EAC (full thickness) with limited (>0.05) soft tissue involvement of middle ear and/or mastoid, or causing facial paralysis at presentation; T4, tumor eroding the cochlea, petrous apex, medial wall of middle ear, carotid canal, jugular foramen, or dura, or with extensive (<0.05) soft tissue involvement (Table 1). Regarding node status, lymph node involvement is a poor prognostic sign and places the patient in an advanced disease stage (i.e., T1N1, stage III; T2N1, T3N1, or T4N1, stage IV). Metastasis status of M1 is stage IV disease and is considered a poor prognostic sign.

Table 1: Analysis of TNM staging of squamous cell carcinoma of temporal bone (n=39)

Staging	No. of patients
T2N0M0	2
T3N0M0	3
T3N1M0	3
T4N0M0	25
T4N1M0	6

In all cases, a decision had been made preoperatively by the unit *not* to sacrifice the intrapetrous carotid artery. This decision was based on previous work by Graham et al.,[11] who demonstrated that the morbidity and mortality following carotid sacrifice were so great that it was not justified. Thus, no preoperative angiography or balloon occlusion tests were performed.

The stage of the tumor at the time of presentation to the skull base surgery department predetermined the surgical approach adopted. Tumors that remained lateral to the tympanic membrane (T1N0, T2N0 [i.e., stages I and II) were treated with lateral temporal bone resection (LTBR). Patients with T3 and T4 tumors (stages III and IV) underwent an extended temporal bone resection as either a de novo procedure, if previously untreated, or as a salvage procedure, if they had prior

treatment with a canal wall down mastoidectomy and postoperative radiotherapy.
All patients were managed in the neurological critical care department and received mechanical ventilation for 24 to 48 hours. They were given minimal sedation and kept warm. Drains were removed at 24 to 48 hours, and nasogastric/gastrostomy feeding was commenced and maintained until the patients were discharged from the critical care department and awake enough to eat and drink.

Follow-Up Regimen
Patients were seen every 2 months for the first 12 months after surgery. This interval was increased to every 3 months for the second year and then to four visits monthly until 5 years after surgery. Following this regimen, they underwent annual review. No patient was lost to follow-up.
No routine scans were performed postoperatively unless the patient's clinical status dictated such examination. The rationale for this approach is that microscopic disease may not be visible and is difficult to detect in view of postsurgical artifact and scarring. The detection of recurrent disease deep to the flap reconstruction would not affect the patient's management because a radical excision and postoperative radiotherapy had been performed and there is no further management option available in the face of the poor outcome of chemotherapy in this SCC.

Surgical Techniques
Approach to primary disease is described in this section.

Lateral temporal bone resection
In LTBR, a 7 x 5-cm oval of skin that circumscribes the entire pinna is outlined. In view of the aggressive nature of this SCC, no aspect of the pinna is preserved to ensure a wide soft tissue margin. The edges of the skin and soft tissue are sutured together to isolate the fungating cancer of the ear canal during bony resection.
An extended cortical mastoidectomy is performed with a high-speed drill. The facial nerve is identified. A posterior tympanotomy is performed and elongated along the line of the vertical portion of the nerve, sacrificing the chorda tympani. The tegmen is traced medially and anteriorly toward the zygoma to provide a good bony margin along the anterosuperior canal wall. Inferiorly, the facial nerve is skeletonized down to the stylomastoid foramen, the landmark for this being the digastric ridge. The facial nerve is identified as it enters the parotid, and the resection carried anteriorly until the bony ear canal becomes mobile.
A superficial parotidectomy is performed preserving the extracranial portion of the facial nerve. The mandibular head is transected; the specimen is then removed en

bloc. The eustachian tube is obliterated by scarifying the mucosa of the mesotympanic end and then plugging it with bone wax, muscle, and fascia, and the middle ear is denuded of mucosa to create a receptive bed for the flap repair.

Extended temporal bone resection

Extended temporal bone resection involves a wider soft tissue resection than with LTBR. A 10 x 8-cm oval of skin inclusive of the entire pinna is included in the resection. The incision includes an inferior tail into the neck which is curvilinear and in a skin crease. This facilitates the inferior soft tissue dissection and allows slings to be placed around the great vessels and a supraomohyoid or Crile radical neck dissection to be performed.

A middle and posterior fossa craniotomy is performed. Bone is resected superiorly for 3 cm above the temporal line to expose the middle fossa dura and behind the sigmoid sinus by a similar amount to leave a residual margin of healthy bone. This allows compression of the sigmoid sinus and decreases the angulation of the drill and otological instruments, facilitating an en bloc resection and identification of the intrapetrous carotid artery.

Medial dissection extends through the labyrinth and ex-poses the intrapetrous carotid artery. Direct involvement of the arterial wall is rare, although histological involvement of the periarterial neural plexus has been described previously. If there is tumor attachment, it is necessary to macroscopically peel the tumor off the adventitia of the carotid artery wall.

Inferiorly, the sigmoid sinus and jugular bulb are mobilized from surrounding bone. If a previous radical neck dissection has been performed, the muscles remain attached to the specimen. If only a supraomohyoid dissection is necessary, the sternocleidomastoid and digastric muscles are freed from the mastoid tip.

At this stage in the procedure, the ascending ramus of the mandible is transected with a Gigli saw or a drill, and this and the head and coronoid process are dissected free and removed. This allows soft tissue assessment of pterygoids and infratemporal region, and adequate resections margins can be obtained if necessary with the help of multiple biopsies and frozen-section histopathological analysis. A total parotidectomy is completed, and the specimen is removed en bloc. The residual tip of the petrous bone is removed with a high-speed drill as a secondary procedure.

Management of parotid

The parotid gland and intraparotid nodes are not only the anterior resection margin of the tumor but also the first-echelon nodes draining the EAC. Therefore,

parotidectomy has become a routine component of surgical treatment of SCC of the temporal bone. For T1 and T2 tumors, a superficial parotidectomy is performed as the last step of the procedure; the parotid is removed en bloc with the lateral temporal bone. The specimen includes the mandibular head with the temporomandibular joint as part of the resection margin. For T3 and T4 tumors, a total parotidectomy is included with the primary specimen.

Dura and brain

Involved dura is resected with a wide margin. If a small volume of temporal lobe of the brain is involved by tumor, this is removed, leaving a healthy macroscopic margin. Without compromising the cancer resection margin, it helps to preserve as much dura as possible, particularly medially, so that fascia lata harvested from the thigh can be carefully sutured to it during closure to create a "watertight" seal. Currently, it is recommended that dural frozen-section biopsy specimens be taken from all margins to ensure that they are tumor free.

Facial nerve

Facial nerve preservation is possible in lateral temporal bone resections because the nerve is the medial limit of the resection. All facial nerves are sacrificed in T3 and T4 tumors to allow an en bloc resection to be performed. Facial nerve grafting was not performed.

Management of neck

Supraomohyoid neck dissections are routinely performed. First, this allows the great vessels of the neck to be harnessed with vascular slings and provides access to the skull base. In an extended resection the external carotid artery is ligated distal to its first few branches, being mindful that an arterial supply for free flap reconstruction is necessary. Second, it provides an opportunity for staging to determine whether postoperative radiotherapy to the neck is indicated. If suspect lymph nodes are located during the dissection, biopsy specimens are obtained for frozen-section analysis. Positive lymph node histological findings lead to a classic Crile radical neck dissection.

Reconstruction

Scalp rotation flaps were originally used with good results, particularly in elderly patients. Early free forearm flaps based on the distal radial artery (Chinese flaps) were successful, but the larger proximal forearm flap based on the antecubital artery was more utilitarian. The donor site must be skin grafted with these flaps; thus, more recently, lateral upper arm and thigh free flaps have been used allowing primary

closure of the donor site. They also have the advantage of providing more bulk to fill the large, triangular cross-sectional defect.

Pedicled myocutaneous flaps such as the trapezius flap have also been employed successfully. The pinna was routinely resected, so pectoralis major flaps were not used, because of the restriction in the length of the pedicle. Given the lack of bone available for osteointegration, prosthetic devices were restricted to glue-on devices. These were offered to all patients but routinely worn by few.

Radiotherapy

All patients received postoperative radiotherapy (50 –60 Gy) to both the primary site and the neck. Patients who had undergone previous radiotherapy received post-operative radiotherapy because the irradiated tissues were widely excised and the flap reconstruction provided sufficient new blood supply to tolerate a second dose.

Results

Thirty-nine patients with SCC of the temporal bone were treated during the 20-year period from 1982 to 2002. There were 19 male and 20 female patients. At the time of surgery, the mean patient age was 61.4 years (range, 37–79 y), with a median age of 64 years. All patients were tertiary referrals from consultant otologists. The mean follow-up time was 7.6 years (range, 6 mo–16 y).

Presenting Symptoms

The most common presenting symptoms were offensive otorrhea, which occurred in 27 of 39 patients (69%); pain in 25/39 (64%), and bleeding in 12/39 (31%). These three symptoms make up the classic triad in SCC of the temporal bone; rates of occurrence of other symptoms are shown in Figure 1.[12-16]

Predisposing Factors

Predisposing factors for the development of SCC of the temporal bone are uncertain, but chronic suppurative otitis media[3,8,17] and radiotherapy have been implicated. Ultraviolet light in the case of SCC of the EAC has also been described. Chronic suppurative otitis media causes chronic irritation, which is thought to lead to cell metaplasia and the formation of carcinoma. Nineteen (47.8%) of the 39 patients had a history of pre-existing chronic suppurative otitis media. Two patients 2/39 (5%) had had previous radiotherapy to the area 20 years before presentation, which is consistent with the latent period reported by Lustig et al.,[18], Lim et al.,[19] and Goh et al.[20]

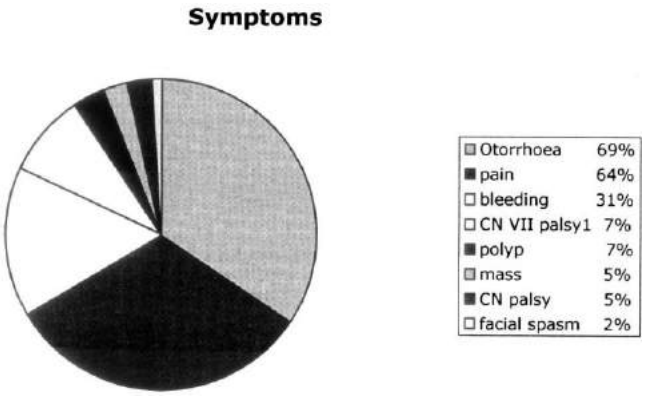

Figure 1: Presenting symptoms of squamous cell carcinoma of the temporal bone. CN = cranial nerve.

Table 2: Survival related to stage of TNM classification (n=37)

Stage	TNM	No.of patients	TNM survival (%)	Stage survival (%)	T Stage	T-stage survival (%)
II	T2N0M0	2	100	100	T2	100
III	T3N0M0	3	100	100	T3	
IV	T3N1M0	3	0			50 (3/6)
	T4N1M0	23	47.8 (11/23)	34.3 11/32	T4	
	T4N1Mo	6	0			38 (11/29)

Survival Related to Stage and TNM Classification

Survival related to stage and TNM classification is given in Table 2.

Tumor Stage

Thirty-nine patients presented to the unit. Two patients were excluded from the analysis because of the clinical decision to treat these patients palliatively from the outset and not attempt a curative resection. There were no patients with T1 disease in the present series (*stage I*), which reflects the tertiary referral nature of the department. Two patients (5%) had T2N0M0 disease (*stage II*). Both were female patients. Neither patient had had previous surgery for her disease. Both patients underwent lateral temporal bone resections, superficial parotidectomy, and supraomohyoid neck dissections. Scalp rotation flaps were used for wound closure, and each patient received postoperative radiotherapy. One patient died of breast cancer 23 months after surgery and was free of disease at time of death. The second patient has remained free of disease at 60 months. Disease-free survival was 100%

Three patients 3/37 (8%) presented with T3N0 disease (*stage III*). One of these patients underwent an extended temporal bone resection and two lateral temporal bone resections including resection of the temporomandibular joint. All patients

underwent a supraomohyoid neck dissection. The follow-up periods were 30, 114, and 120 months, and all three patients remained alive and free of disease at the time of writing. Disease-free survival was 3/3 (100%).

In *stage IV*, there were 32 patients (87%). Three patients presented with T3N1 disease. All underwent extended temporal bone resections. One patient underwent a supraomohyoid neck dissection, one had a Crile radical dissection, and one had had a previous radical neck dissection. All patients had a free flap closure of the defect, and all underwent postoperative radiotherapy to the primary and the neck. All three patients died of local disease recurrence at 6, 20, and 27 months postoperatively. All patients with T3 tumors and node-negative necks survived, and all patients with node-positive necks died. Thus, total T3 survival was 3/6 (50%).

Twenty-five patients presented with T4N0 disease. Two patients underwent the palliative procedure of extended modified radical mastoidectomy with local closure without curative intent. This was because coexisting medical conditions made the patients unfit for an extended resection. The remaining 23 patients underwent extended temporal bone resection as a curative procedure. One patient died of an acute myocardial infarction 1 week after surgery. The follow-up of the remaining patients ranged from 6 to 198 months. Survival in this group was 47.8% (11 of 23). Of the 14 patients who died of disease (including those who underwent the palliative procedures), 12 deaths occurred within 12 months of surgery, reflecting the aggressive nature of this malignancy.

Six patients presented with T4N1 disease. All underwent extended LTBR. All six patients died. Five patients were dead of disease at 10 months after surgery, and one patient whose SCC had developed in a basal cell carcinoma survived 22 months before also dying of disease recurrence.

Overall T4 tumor survival was 38%. Stage IV survival was 34.4%. The survival for the entire series was 11/29 (43.2%).

De Novo Versus Salvage Surgery

Of the 39 patients presenting for surgery, 19/39 (48%) had undergone some form of surgical procedure at the referring institution and thus were deemed salvage procedures. Twenty patients without previous intervention were defined as de novo patients. Of each subgroup, only patients with T4N0 disease had sufficient numbers, albeit small, to allow any comparison. In this group the survival of the de novo group was 7 of 11 (64%) as compared with 4 of 12 (33%) in the salvage group, suggesting that early referral and de novo treatment may offer a greater chance of survival, although this difference was not statistically significant (Table 3).

Table 3: Survival of De Novo versus Salvage surgery in T4N0 group (n=23)

Survival	De Novo	Salvage
T4N0	11	12
Alive	7	4
Dead	4	8
Total (%)	63	33

Lymph Node Involvement

Nine 9/39 (23%) patients were node-positive at surgery. All died of their disease at a mean time of 12.7 months (range, 4–27 mo) after surgery. Of the 30/39 (77%) patients who were node-negative at surgery, 28 had T3 or T4 disease. Fourteen of these 28 patients (50%) have remained alive and free of disease at a mean follow-up time of 86.8 months (range, 6–198 mo) after surgery.

Brain Involvement

Seven patients presented with brain involvement, only one of whom had nodal involvement. Two patients with brain involvement have remained alive and disease free at 10 and 11 years after surgery. All patients presenting with brain involvement were salvage patients with recurrent disease.

Carotid Involvement

Eight patients presented with carotid involvement, two of whom had nodal disease. Three patients were de novo treatment cases, and five were salvage cases. Only one patient has survived, but the follow-up time was only 9 months at the time of writing.

Overall Survival Against Time

As shown in Figure 2, most patients who died did so within the first year after surgery. There were only five patients who died 12 to 27 months postoperatively, and one patient thereafter. Therefore, it is likely that the patients are cured if they survive the first 12 to 24 months after treatment (Figure 2).

Histological Differentiation

Five patients had well-differentiated tumors, of which four were T4 and one was T2. Four of the five patients (80%) were alive at the time of writing, with a mean follow-up time of 73 months, and these were all de novo treatment cases (Figure 3). The only patients who were salvage cases patients in this group died.

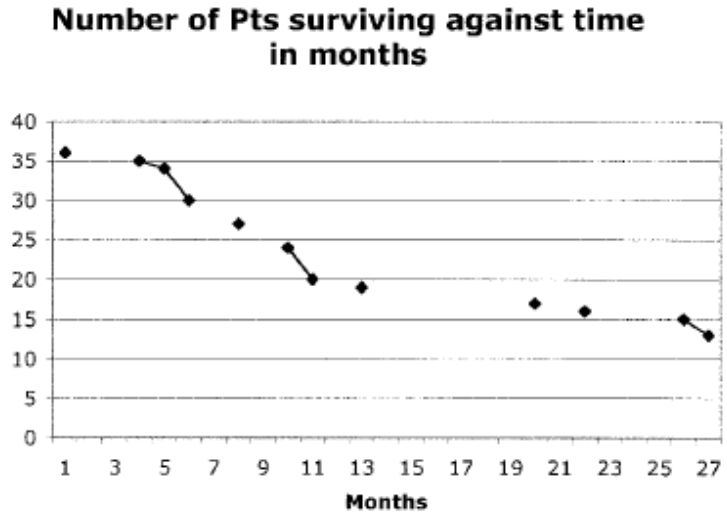

Figure 2: survival after surgery and radiotherapy.

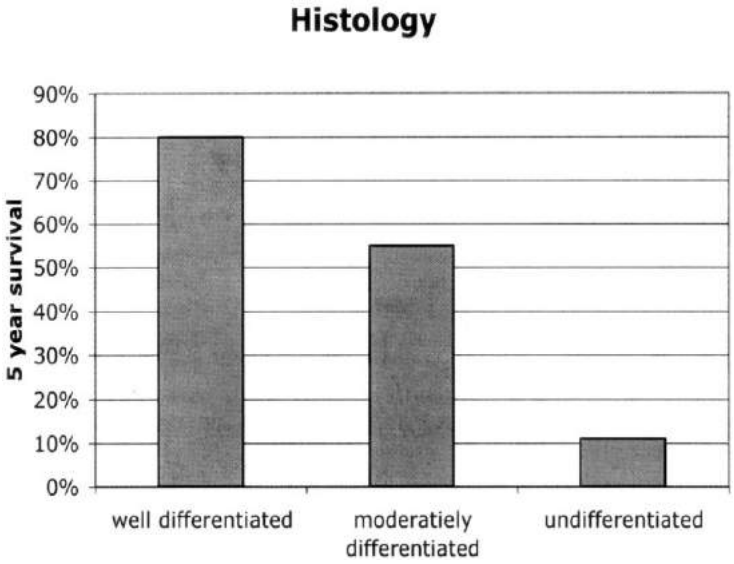

Figure 3: Survival versus histological differentiation.

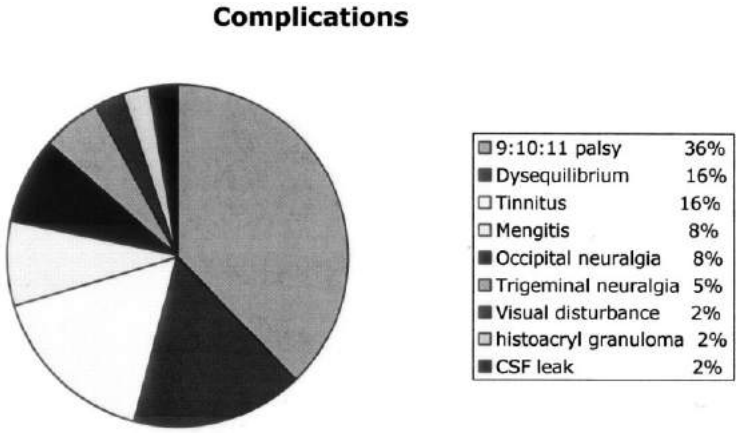

Figure 4: Complications after surgery and radiotherapy. CSF = cerebrospinal fluid.

Twenty-three patients had moderately differentiated disease, and 13 (55%) of these patients have remained disease free (Figure 3). Nine patients had poorly differentiated tumors. All patients had T4 (stage IV) disease. Only one patient 1/11 (11%) has remained alive and disease free at 80 months (Figure 4).

Complications

Six patients required a percutaneous gastrostomy feeding tube for enteral feeding. Four patients underwent medialization thyroplasty. Two patients had tracheostomies; one of these tracheostomies was successfully removed (Figure 4).

Discussion

The management of SCC of the temporal bone remains one of the current challenges for the skull base surgeon. Its late presentation, anatomical site, and aggressive nature are responsible for its insidious reputation. Not only is early diagnosis difficult, but satisfactory long-term curative results remain elusive.

Clearly, the management options are surgery, radiotherapy, or a combination of the two. The reported results from radiotherapy alone, salvage surgery after radiotherapy, and surgery followed by radiotherapy have been depressingly poor.

Early attempts to improve on the poor 5-year survival from canal wall down mastoidectomy with postoperative radiotherapy to the cavity included total en bloc temporal bone resection with carotid sacrifice.[11] The high level of morbidity and the scarcely improved survival rates following this extensive surgery made it difficult to justify and allowed “radiotherapy alone” and “noninterventionist” lobbies to make themselves heard.[17,21] However, the horrendous demise of patients with endstage disease with smelly discharge from an exophytic fungating tumor and associated bone pain polarized the debate concerning treatment risk/benefit and quality-of life issues. It is from this background that extended temporal bone resection with preservation of the intrapetrous carotid artery and postoperative radiotherapy has emerged as the treatment choice in our unit. The desire to scrutinize the results that can be achieved by this treatment modality was the raison d’etre of the present report.

Despite 20 years of experience in this population, the small number of patients still makes it difficult to draw statistical conclusions and provide evidence-based outcomes for such a rare disease. Although we arrive at conclusions as to the appropriate management based on our experience, there is no doubt that, to achieve sufficient numbers, a multicenter trial would be necessary.

The optimal surgical strategy for SCC of the temporal bone remains controversial. Sleeve resection with retention of the pinna is still supported as a treatment of T1 and T2 lesions of the EAC,[15] but it is difficult to believe that excision of the cancer field is not compromised. We think that LTBR with excision of the entire pinna, head, and ascending ramus of the mandible and with superficial parotidectomy is a necessity for this stage of tumor. The predominant morbidity associated with this approach is loss of pinna and, with current prosthetic advancements, is thought to be minimal. However, the authors recognize the lack of early-stage tumors in the present series.

For larger tumors (T3 and T4), extended temporal bone resection is necessary. Although, inevitably, there is some piecemeal resection around the periphery of the dissection to gain the correct angulation and access to the intrapetrous carotid artery to be skeletonized, the majority of the resection is en bloc. The removal of the petrous apex is inevitably piecemeal.

The en bloc versus piecemeal resection argument is an interesting one and is still active today. Those who support the latter have suggested that the mortality and morbidity associated with an extended temporal bone resection are too great to justify the minimal chance of cure.[21]

En bloc resection was first described by Campbell in 1951. In 1954, Parsons and Lewis[5] reported success with this technique. In 1961, Conley and Novak[6] reported a 27% operative mortality rate in their series that was substantially higher than the 5-year cure rate of 18%. In 1975, Lewis[7] improved on his earlier results in a series of 100 patients with a cure rate of 25%. Austin et al.,[12] Leonetti et al.,[14] Moody and Hirsch,[16] and Arena[22] and have reported a 2-to 3-year survival rate of 30% to 40%. The results reported in the current study support en bloc extended resection of the temporal bone with postoperative radiotherapy, and an overall survival rate of 16/37 (43.2%) in a series of 37 patients with a predominance of T3 and T4 lesions has been achieved.

Criticism of the reporting of results in the past has been directed toward the lack of a staging system and variation in treatments making comparisons between studies difficult. The present study has used the University of Pittsburgh staging system and suggests that its universal adoption would seem logical because it complies with the Union Internationale Contre le Cancer format and has been shown to have outcomes that correlate with clinical staging.[12,14,16,22]

Preoperative assessment and accurate staging of this disease are vital in ensuring that the procedure is adequate for each stage of disease. Arriaga et al.[23] have described 12 radiological areas that should be checked individually before staging is

complete to avoid understaging. Anterior and anteroinferior invasions into the temporomandibular joint and infratemporal fossa, respectively, are most often underdiagnosed radiologically. This was the case in the present series in a patient who was staged as having a T2 carcinoma but found to have more extensive infratemporal fossa spread at the time of surgery. The LTBR performed was not the treatment of choice, despite what appeared to be a macroscopic clearance of tumor. Given the proximity of the temporomandibular joint to the anterior margin of the resection, the authors advocate resection of the mandibular head in all lateral temporal bone resections for T1 and T2 lesions to ensure a wide clearance of disease.

Nodal disease has been previously reported in 10% to 13% of cases.[3,16] In the present series, 9/37 (23%) of patients presented with node-positive disease. It is important that no patient with node-positive disease at presentation survived. Death in these patients was a result of local recurrence, but nodal disease was an indicator of the aggressive nature of these tumors. This experience has led the authors to recommend a supraomohyoid neck dissection for all patients for staging and facilitation of the resection and flap reconstruction, as well as postoperative radiotherapy.

Histological differentiation of the tumor appears to be an important prognostic indicator, with four of five patients with well-differentiated tumors subsequently surviving; yet, in contrast, only one of nine patients with a poorly differentiated tumor remains alive and disease free, despite comparable tumor stage.

Many previously reported series have not analyzed outcome in relation to the histological subtypes of this tumor,[15,21,24,25] and this is a justifiable criticism.[22] No meaningful comparison between series can be made unless the histopathological degree of differentiation is considered.

Although brain involvement is usually associated with a poor outcome, the fact that two patients are alive and well at 10 and 11 years after resection does demonstrate that a cure is still achievable. All patients presenting with cerebral involvement had undergone primary resection at another institution and underwent salvage procedures.

In the present series of 39 patients, detailed staging inevitably meant relatively small numbers in each subgroup, and this precludes meaningful statistical analysis.

However, the accurate, detailed analysis of outcomes in the present retrospective surgical series does allow observation of the trends with regard to indications of poor prognosis. Node-positive neck disease, poorly differentiated SCC histological findings, brain involvement, and salvage surgery are associated with a poor outcome. The improved 15/23 (66%) survival of patients treated as de novo cases in the present series as compared with those treated as salvage cases 8/23 (33%) suggests

that early referral and aggressive primary surgical treatment with postoperative radiotherapy offer the greatest chance of cure.

References

1. Peele JC, Hauser CH. Primary carcinoma of the external auditory canal and middle ear. Arch Otolaryngol 1941;34:254–266.
2. Lewis JS. Cancer of the ear: a report of 150 cases. Laryngoscope 1960;70:551–579.
3. Stell PM, McCormick MS. Carcinoma of the external auditory meatus and middle ear: prognostic factors and a suggested staging system. J Laryngol Otol 1985;99:847–850.
4. Newhart H. Primary carcinoma of the middle ear: report of a case. Laryngoscope 1917;27:543–555.
5. Parsons H, Lewis JS. Subtotal resection of the temporal bone for cancer of the ear. Cancer 1954;7:995–1001.
6. Conley JJ, Novak AJ. The surgical treatment of tumour of the ear and temporal bone. Arch Otolaryngol 1960;71:635–623.
7. Lewis JS. Temporal bone resection: review of 100 cases. Arch Otolaryngol 1975;101:23–25.
8. Moffat DA, Grey P, Ballagh RH, Hardy DG. Extended temporal bone resection for squamous cell carcinoma. Otolaryngol Head Neck Surg 1997;116:617–623.
9. Arriaga M, Curtin H, Takahashi H, Hirsch BE, Kamerer DB. Staging proposal for external auditory meatus carcinoma based on preoperative clinical examination and computed tomography findings. Ann Otol Rhinol Laryngol 1990;99:714–721.
10. Hirsch BE. Staging system revision. Arch Otolaryngol Head Neck Surg 2002;128:93–94.
11. Graham MD, Sataloff RT, Kemink JL, Wolf GT, McGillicuddy JE. Total en bloc resection of the temporal bone and carotid artery for malignant tumors of the ear and temporal bone. Laryngoscope 1984;94:528–533.
12. Austin JR, Stewart KL, Fawzi N. Squamous cell carcinoma of the external auditory canal: therapeutic prognosis based on a proposed staging system. Arch Otolaryngol Head Neck Surg 1994;120:1228–1232.
13. Gillespie MB, Francis HW, Chee N, Eisele DW. Squamous cell carcinoma of the temporal bone: a radiographicpathologic correlation. Arch Otolaryngol Head Neck Surg 2001;127:803–807.
14. Leonetti JP, Smith PG, Kletzker GR, Izquierdo R. Invasion patterns of advanced temporal bone malignancies. Am J Otol 1996;17:438–442.
15. Nyrop M, Grontved A. Cancer of the external auditory canal. Arch Otolaryngol Head Neck Surg 2002;128:834–837.
16. Moody SA, Hirsch BE, Myers EN. Squamous cell carcinoma of the external auditory canal: an evaluation of a staging system. Am J Otol 2000;21:582–588.
17. Birzgalis AR, Keith AO, Farrington WT. Radiotherapy in the treatment of middle ear and mastoid carcinoma. Clin Otolaryngol Allied Sci 1992;17:113–116.
18. Lustig LR, Jackler RK, Lanser MJ. Radiation-induced tumors of the temporal bone. Am J Otol 1997;18:230–235.
19. Lim LHY, Goh YH, Chan YM, Chong VF, Low WK. Malignancy of the temporal bone and external auditory canal. Otolaryngol Head Neck Surg 2000;122:882–886.
20. Goh YH, Chong VF, Low WK. Temporal bone tumours in patients irradiated for nasopharyngeal neoplasm. J Laryngol Otol 1999;113:222–228.
21. Shih L, Crabtree JA. Carcinoma of the external auditory canal: an update. Laryngoscope 1990;100:1215–1218.
22. Arena S. Tumor surgery of the temporal bone. Laryngoscope 1974;84:645–670.
23. Arriaga M, Curtin HD, Takahashi H, Kamerer DB. The role of preoperative CT scans in staging external auditory meatus carcinoma: radiologic-pathologic correlation study. Otolaryngol Head Neck Surg 1991;105:6–11.
24. Manolidis S, Pappas D Jr, Von Doersten P, Jackson CG, Glasscock ME III. Temporal bone and lateral skull base malignancy: experience and results with 81 patients. Am J Otol 1998;19:S1–S15.
25. Pensak ML, Gleich LL, Gluckman JL, Shumrick KA. Temporal bone carcinoma: contemporary perspectives in the skull base surgical era. Laryngoscope 1996;106:1234–1237.

Chapter 8.0

Summary and conclusion
Summary in Dutch
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Summary and Conclusions

Neuro-otology and skull base surgery have emerged from a desire to excise lesions in the skull base and cerebello-pontine angle which have been hitherto unresectable because of their anatomical site, size and varying degrees of vascularity. The incredible advances in microsurgical techniques following the advent of the operating microscope, neuroimaging in diagnosis, neuro-anaesthesia, intraoperative cranial nerve monitoring, microsurgical instrumentation, ultrasonic cavitrons and lasers as well as endoscopy and neuronavigation, as well as improved patient care has meant that the majority of lesions can be successfully excised. The development of numerous innovative approaches to the lateral and anterior skull base has enabled this. We have seen virtually every lesion, whether it be neoplastic, vascular or inflammatory involving the skull base primarily or by secondary invasion as well as intracranial pathology being surgically approached in ever increasing numbers.
Multidisciplinary team (MDT) working and the creation of the MDT clinic has optimised patient care and management and facilitated the development of clinical databases and the measurement of outcome and audit. Along with the more prevalent use of classifications this has been critical for the comparison of clinical outcomes between surgical departments. This enables not only the establishment of an evidence base for a particular procedure or therapy but it also provides us with an integral part of a revalidation process for individual doctors within our profession.
The challenge is to excise the lesion completely whilst maintaining neural integrity in order to preserve the best quality of life for the patient. This is thus the rationale for this thesis on clinical aspects and outcomes of lateral skull base surgery.

Chapter 2.1

This chapter, which is a retrospective analysis of the clinical records of patients on a computerised database, compares the referral patterns of vestibular schwannomas (VS) over the period 1994 to 2004 with the previous referral patterns in Cambridgeshire over the period 1981 to 1993. Particular scrutiny was made of the source of referral, the diagnosis at referral and the neuro-otological symptoms as well as the size of the tumour at presentation. The paper demonstrated an increase in the proportion of patients being managed by watch, wait and rescan. There was also an increase in the proportion of referrals of patients with a known vestibular schwannoma to 90% of all referrals. There was no significant change in the length of clinical history prior to referral, the source of the referral or the principal presenting

symptom. In the more recent period a decrease in tumour size at presentation was found but an increase in the percentage with larger tumours greater than 4.5cm. We believed that this could be attributed to an increase in the availability of magnetic resonance imaging (MRI). Some tumours particularly those arising medially within the cerebello-pontine angle (CPA) would be initially asymptomatic and therefore present late eluding identification until they had become large despite a low threshold for MR scanning.

Future research
This should concentrate on early detection of VS by collecting evidence for investigating any unexplained unilateral audio-vestibular symptom or sign by the "gold standard" imaging technique of MRI. Two per cent of patients with VS have hearing within normal limits but recommendations on the precise degree of asymmetry of the pure tone audiogram which should trigger investigation by MRI should be ratified by the European Academy of Otology and Neuro-otology and published. The cost efficacy of screening for VS has already been published.
A further study of the number of patients who can be investigated and treated for VS for the cost of one missed diagnosis of a "bread- winner" where late presentation with a large tumour and a poor result leads to financial dependency on the State should be carried out as a justification for MRI screening and early diagnosis.

Chapter 2.2

This was an analysis of the pattern of growth of vestibular schwannoma in 381 patients undergoing watch, wait and rescan management. The pattern of growth was very variable between tumours and within the lifespan of an individual tumour. The study was important in showing that 33% of sporadic unilateral vestibular schwannomas demonstrated significant growth, 59% did not grow significantly and 8% showed a decrease in size. Overall 67% of the tumours in this series did not grow. The mean annual change in size of growing tumours was 2.3mm and 52.4% of growing tumours showed radiologically demonstrable first growth within eighteen months of presentation and 7.2% after 5 years of follow up. This is important because our findings are in contradistinction to a comparable study where the authors have suggested discontinuance of follow up after 5 years based on their findings of no growth after that period of time. This paper provides the evidence on tumour growth which is vital in counselling patients who may opt for a period of observation rather than active treatment of their vestibular schwannoma.

Future research
Rapid, accurate computerised methods need to be adopted to measure tumour volume which will provide accurate measurements of tumour growth and facilitate meaningful comparison of data between different units. Further studies are needed of long term growth of VS beyond 5 years and the relationship of fluctuant audio-vestibular symptoms and signs in relation to tumour growth and cystic change as well as other predictive factors most importantly genetic and tumour growth factors.

Chapter 2.3

This paper provides a detailed description of the surgical technique which has been devised to lower a high jugular bulb during translabyrinthine surgery. It is of great surgical relevance because some highly respected skull base units have been abandoning the translabyrinthine approach in favour of the retrosigmoid approach in cases of a high jugular bulb in the belief that to lower the bulb would be dangerous and too risky for the patient. The bulb can be safely lowered by a significant amount by careful bony dissection and skeletonisation, the retention of a ring of bone to stabilise the surgicel, and successive discs of soft bone wax applied to the dome of the bulb and lowered with gentle pressure over a wide area to minimise the risk of venous haemorrhage.

Future research
Techniques for stabilisation of the bone wax discs or tissue material used to protect and limit the risk of bleeding from the jugular bulb during lowering need to be developed so that a very high bulb often with a diverticulum present can be safely lowered and will be stabilised and retained in position. This will allow good access to the caudal end of the internal auditory canal and create the space between it and the lowered jugular bulb so that the ninth, tenth and eleventh cranial nerves can be safely dissecedt off large CPA tumours. We should study the incidence and natural history of benign intracranial hypertension produced by the stenosis at the level of a lowered jugular bulb. We also need to know which patients require stenting either from pressure studies or by clinical features and the outcome of stenting.

Chapter 2.4

This paper addresses the deficiencies of the commonly used House Brackmann (HB) facial nerve function classification by modifying it rather than proposing an entirely new classification. This is important since the HB grading system is used throughout the world. The author in proposing modifications has addressed the variable quality of life of the patients with HB 3 function. Some patients with HB 3 function have a reasonably comfortable eye with or without lubricants and do not suffer from exposure keratitis. A significant proportion, however, have a poor quality of life and are incapacitated by a dry eye, exposure keratitis, and many require a lateral or medial tarsorrhaphy or a gold or platinum weight in the upper eyelid. Also the HB grading system does not take into account nervus intermedius function and the possible sequelae of crocodile tears, metallic taste in the mouth or dysgeusia, as well as dry eye and exposure keratitist. The results of facial nerve outcome following vestibular schwannoma surgery have not reported the sensory component of the nerve.
The author's proposal is to divide HB 3 into A and B subgrades to take this into consideration on the basis of quality of life . The classification also provides a record of the presence or absence of crocodile tears, metallic or aberrant taste, dry eye, hemifacial spasm and synkinesis.

Future research
This should aim to reduce inter-observer error in the assessment of facial palsy and create a grading system that not only minimises this but at the same time should be accurate, easy to use and should include not only the eye but also aberrant regeneration of the facial nerve in all branches and include an assessment of metallic taste, crocodile tears, hemifacial spasm and synkinesis.

Chapter 2.5

This paper determines the factors affecting facial nerve outcome of vestibular schwannoma surgery in 652 patients over a thirty year period. The facial nerve was maintained intact in 97% of cases. Facial nerve outcome was assessed using the HB grading system. Over the last 6 years of the series a satisfactory outcome was achieved in 100% of patients with tumours less than 1.5cm in diameter dropping to 72% in the largest tumours over 4.5cm. The results of a univariate and multivariate

analysis showed that tumour size and year of operation were significant predictors of facial nerve outcome. There was insufficient evidence that sex, age and operation approach were associated with facial nerve outcome after adjusting for tumour size and year of operation. Investigation of nervus intermedius function and aberrant regeneration of the facial nerve showed that there was a 13% chance of developing hemifacial spasm at some time post-operatively and of these patients there was a 42% chance of it resolving by 24 months.
There was a 36% chance of developing metallic taste at some time post-operatively and of these patients there was a 52% chance of it resolving by 24 months.
There was a 25% chance of developing crocodile tears at some time post-operatively and recovery is much less likely than with metallic taste and in only 15% did it resolve by 24 months.

There was a significantly greater likelihood of hemifacial facial spasm in the partial facial nerve recovery group compared with the normal facial function group. There was no significant difference, however, between these two groups when considering metallic taste and crocodile tears.

The surgical learning curve was steepest in the first 50 cases and thereafter flattened out until the last 6 years of surgery when there was an incremental improvement. The use of the facial nerve monitor had already been shown to make a satisfactory facial nerve outcome 2.5 times more likely. The author describes the fine points of surgical technique which can optimise facial nerve outcome.

Future research
A determination of the degree of efficacy of hydro-dissection in facilitating atraumatic separation of the facial nerve from its capsule could be obtained from an outcome study.
It is known that the anatomical position of the facial nerve in relation to the tumour is variable and that the most favourable is where the nerve is medial to the tumour and the least favourable is where it is lateral and closest to the surgeon in the translabyrinthine approach. A comparison of facial nerve outcome in relation to the tumour and its anatomical position in the CPA is very important and would enable realistic counselling of patients with regard to expectations of a satisfactory outcome.

Chapter 3.1

This paper reviews the experience of the Cambridge Neuro-otology and Skull Base Surgery Tertiary Referral Unit in the management of patients with neurofibromatosis type 2 (NF 2) over a 17 year period. Thirty five patients with 62 cerebellopontine angle tumours of which 59 were vestibular schwannomas were studied. The outcome parameters measured were tumour progression, the incidence and degree of hearing deterioration, the development of facial palsy and the need for active intervention. All five of the patients treated by stereotactic radiosurgery (gamma knife) showed evidence of either progression in tumour size or deterioration in hearing threshold. 9/22 (41%) of NF2 tumours grew during the observation period compared with 33% of the unilateral sporadic vestibular schwannoma series. The majority of patients requiring surgery for their tumours underwent a translabyrinthine approach and only 4 had a retrosigmoid hearing preservation attempt. Early diagnosis is important in the management of NF 2 patient patients, their families and the community at large. Good results from hearing preservation surgery remain elusive in this challenging group of patients but the recent advent of auditory brainstem implantation (ABI) and in some cases cochlear implantation (CI) as well as encouraging results from hearing preservation attempts via a middle cranial fossa approach is altering NF 2 patient management and patients with smaller and growing tumours may be considered for surgery at a much earlier stage.

Future research

Long term hearing outcome with assessment using the hearing handicap index and other QOL studies will enable a realistic evaluation of the optimistic results emerging from some centres with regard to hearing preservation by the middle fossa approach and early surgery for tumours in NF 2. This is important since the majority of units are still observing tumours to preserve neurological function and reserving surgery for a time when the patients neurological status dictates it. The evolution of auditory implants has allowed surgery for growing tumours and the use of auditory brainstem implantation and in some cases when the cochlear nerve can be preserved, cochlear implantation either for second side surgery or as a sleeper for first side surgery. The clinical effectiveness of the drug Avastin and other similar growth factor inhibitors will need to be carefully assessed in future particularly in relation to their cost efficacy. Future outcome studies are needed to drive optimal patient management in NF 2.

Chapter 3.2

The management of patients with NF2 , particularly the Wishart phenotype, presents the clinician with a formidable challenge. Despite modern imaging, earlier detection and a concomitant move to early hearing preservation surgery, many patients are still presenting late with neurological compromise and a large tumour load.
In view of the rarity of NF 2 in the United Kingdom an analysis of the long term outcome of translabyrinthine surgery for VS in NF 2 in Cambridge and Manchester, two of the largest skull base units, has been carried out. The author believes that this is the first description of long term outcome of translabyrinthine surgery in NF 2.
Whilst not as good as in unilateral sporadic VS , total tumour excision was achieved in two thirds of the cases and near total in a quarter, Thus in 90% total or near total excision was possible. The recurrence rate was one in seven. The perioperative mortality was very low for this disease and there were no peroperative deaths. One in ten facial nerves were lost at surgery but these were large tumours with a mean size of over 3cm. Whilst facial nerve outcome for the series as a whole was not as good as in the unilateral sporadic VS a normal or near normal facial function was attained in almost two in three patients and an unsatisfactory outcome was only seen in one in six patients.

This paper provides the first publication of aberrant regeneration of the facial nerve following surgery for NF 2. Almost half of the patients developed a metallic taste in the mouth and almost half of these recovered. Crocodile tears were seen in just under half of the patients but the chance of recovery of this symptom was only one in seventeen. A very detailed analysis of outcome with regards to tinnitus is presented. There was no tinnitus present pre-operatively in one in four patients and of these one in five developed it post-operatively. In those patients with mild tinnitus pre-operatively in two of three patients it remained the same, in a quarter the tinnitus worsened and in one in six it disappeared.

In those patients with moderate tinnitus pre-operatively, in six out of ten it remained moderate, in one in five it was better and either became mild or disappeared and in only one in five did it worsen and become severe. Tinnitus is important in outcome measures and quality of life (QOL) because it may become the predominant symptom in patients post-operatively as the tumour has been removed, balance has improved and the hearing handicap improved when the distorted hearing is replaced by a “dead” ear. Unlike in idiopathic tinnitus where loud background noise masks the tinnitus the tinnitus following VS removal is exacerbated by noise.

One in eight patients had a pre-operative ventriculo-periotoneal (VP) shunt which reflects the proportion of large tumours in this series. Auditory implants were inserted in almost half of the patients, mostly auditory brainstem implantation, two thirds after unilateral surgery and one third after bilateral surgery. Two patients had cochlear implant sleepers inserted.
This paper provides the evidence base for translabyrinthine surgery for vestibular schwannoma in NF 2.

Future research
Electrophysiological studies of the cochlear and first order eighth nerve neurones as well as the auditory brainstem pathway should enable predictions of cochlear nerve integrity following surgery as well as predicting the candidacy and future success of cochlear implantation as an alternative or as well as ABI. It should also facilitate the further development of the combined cochlear and brainstem implant.

Chapter 4.1

The purpose of this paper was to perform a retrospective case note review and analysis of the surgical outcome of 43 patients with extensive petrous temporal bone cholesteatoma and to propose a more comprehensive classification system for these lesions. The new classification further subdivides anatomically the regions of the temporal bone described in existing anatomical classifications and facilitates surgical planning and helps to predict post-operative hearing outcome.
The long-term recurrence rate was less than five per cent, possibly because of meticulous surgical technique, bipolar diathermy of keratin deposits, and the use of the diode laser to denature the protein of the cholesteatoma matrix that was adherent to the dura. Facial nerve function was usually preserved but if necessary direct anastomosis of the nerve or cable nerve grafting can improve facial nerve function from HB 6 to 3 if the palsy is not long-standing, generally less than 12 months.

Future research
Two critical questions need to be answered. Firstly, long term studies are needed to confirm that in many instances where cholesteatoma matrix has been known to be left on a cranial nerve, the jugular bulb or intrapetrous carotid artery the disease either disappears or becomes inactive and re-exploration is only rarely required. We need to know why and what factors may affect recurrence.

Secondly, in order to reduce the risk of cholesteatoma recurrence a defocussed laser beam has been proposed to heat and therefore denature the protein of the cholesteatoma matrix on the dura. This would seem logical but we need the basic science to confirm this and the outcome comparison study to confirm it clinically.
Laboratory growth of cholesteatoma will facilitate this work.

Chapter 4.2

The first author has proposed a staging classification of primary cerebellopontine angle cholesteatoma based on neuro-anatomical considerations. The study of the long-term outcome of surgery for this rare and challenging pathology has been performed from a retrospective case note review of a fifteen years series. Fifteen consecutive surgical were included. In two thirds of the patients the principal presenting symptom was related to the cochlea-vestibular nerve. The average duration of symptoms was two years. Hearing preservation approaches were utilised in three quarters of the series. Tumour removal was total in four fifths of the patients and of these there was only one patient with a recurrence and this occurred fifteen years after the initial surgery. The per- and peri-operative mortality was zero. In nearly half of the patients who had undergone hearing preservation surgery the mean hearing threshold was preserved within 2dB of the mean pre-operative hearing threshold.

Future research
Cranial nerves in the CPA do not like having cholesteatoma dissected from them and although they may be intact post-operatively a significant proportion do not function in the long term. A knowledge of how much and what type of trauma causes permanent cranial nerve palsy is critical for outcome and post-operative QOL and will predetermine the extent of the surgical excision. Non echo-planar MRI scanning has a high sensitivity for recurrent disease and interval scanning is an important factor in the post-operative management of these patients.

Chapter 5.1

Trigeminal neuromas, which may involve any part of the fifth nerve bundle intra-cranially but may also include the extracranial peripheral divisions, are complex, very rare, and difficult to manage lesions. They require a multidisciplinary approach

The purpose of this paper was to analyse the surgical outcome of a series of eight patients with this pathology. Pre-operative surgical planning is critical and facilitates tumour removal with preservation of important neural structures in the majority of cases. Tumour location was the prime determinant of surgical approach. For large tumours presenting in the middle and posterior cranial fossae, the retrosigmoid/ retrolabyrinthine/middle cranial fossa approach provides good exposure and results in minimal brain retraction reducing post-operative morbidity. A Fisch type C approach is necessary for the largest tumours. Total tumour excision was possible in three of the eight cases. In the remaining five patients some tumour was left purposely in order to minimise neurological deficit and optimise post-operative quality of life. The five patients with incomplete tumour removal suffered symptomatic tumour recurrence and revision surgery was performed. There was no peri-operative mortality of major morbidity in this series. Long-term follow up with interval imaging is mandatory to exclude long-term recurrence.
This paper illustrates the importance of the risk/benefit analysis of total surgical excision of benign lesions compared with subtotal excision the latter reducing post-operative neurological deficit with its concomitant improved quality of life. This is particularly important with large lesions in both middle and posterior cranial fossae where small tumour remnants may be controlled with post-operative stereotactic radiotherapy or gamma knife.

Future research
Endoscopic anterior cranio-facial and pterional approaches provide very good access to the cavernous sinus and foramen lacerum and will have an increasingly important role to play in this anatomical area. Outcomes for these approaches for a variety of pathologies is required to develop an evidence base. The efficacy and control rate of stereotactic radiotherapy for rare lesions such as trigeminal neuroma and forpost-operative residual tumour control in the region of the cavernous sinus needs to be analysed and published.

Chapter 6.1

This paper evaluates the outcome of retrosigmoid microvascular decompression of the facial nerve in a series of patients suffering from hemi-facial spasm. This was a retrospective clinical case note review. Unlike unexplained audio-vestibular symptoms hemi-facial spasm can be assumed to be caused by a vascular loop usually at the root entry zone adjacent to the brainstem once a lesion of the whole length of

the facial nerve has been excluded by contrast enhanced MRI scanning. Complete resolution of the hemi-facial spasm was seen in ninety three per cent of this series in the short term and eighty per cent in the long term. Three patients suffered from a sensorineural hearing loss and two complained of postoperative tinnitus. A transient facial nerve palsy which recovered to a HB 1 or normal face occurred in one patient. Microvascular decompression surgery provides excellent long-term symptom control in a high percentage of patients with hemi-facial spasm.

Future research
Minimally invasive endoscopic retrosigmoid microvascular decompression of the facial nerve for hemi-facial spasm has been proposed. Haemorrhage in the CPA may be more difficult to control via this approach due to limited access and risk will be higher. A demonstrable advantage, therefore, needs to be proven by outcome and QOL studies to justify the added risk.
Relapse rate of hemifacial spasm may be determined by the type of material or tissue used to separate the verve from the vascular loop.. Long-term outcome studies for each of these individually will establish the optimal method of permanently removing the pressure of the loop from the nerve.

Chapter 7.1

All patients with squamous carcinoma (SCC) of the temporal bone treated by radical surgery and postoperative radiotherapy with curative intent in the Skull Base tertiary referral unit of Cambridge University Hospital over a 20 year period were studied. A detailed analysis of the clinical data and outcome in 39 patients was performed. In view of the late presentation to this unit of recurrence following treatment by radical mastoidectomy and radiotherapy to the temporal bone it was important to divide the series into those undergoing “salvage surgery” and those who had “de novo surgery”. The patients were staged according to the recent University of Pittsburgh system. Stage II disease was treated by lateral temporal bone excision and all patients with T2N0M0 tumours were cured. All patients with stage III disease were also occurred but overall only one half of the patients with T3 tumours survived reflecting the weighting for positive lymph node disease given by the Pittsburgh staging system. Overall survival for stage IV tumours was one in three patients and for T4 tumours was four in ten patients. The overall survival for the whole series was 16/37 (43%). Node-positive disease, poorly differentiated histo-pathology, brain involvement, and salvage surgery were were associated with a

poorer outcome. The improved outcome (66% -5yr survival) of patients treated de novo in this study series compared with those treated by salvage surgery (33% - 5yr survival) suggested that early referral to a multidisciplinary tertiary referral unit and aggressive primary surgical treatment with post-operative radical radiotherapy offer the greatest chance of cure. It is possible that in the case of salvage surgery for advanced lesions the overall improved outcome for this difficult and aggressive disease relates not only to radical surgery in the form of extended temporal bone resection but to the fact that the extent of tissue resection in the skull base excises the previous radiotherapeutic field and allows a second course of radical radiotherapy post-operatively facilitated by the presence of the
well perfused viable tissue of the free flap.

Future research

The author of this thesis is at present involved in DNA studies of post-operative SCC specimens in order to determine the aetiology of SCC of the temporal bone and its possible association with human papilloma virus (HPV) or the Epstein Barr virus. Discovery of the aetiology is critical for the management of this pathology. Prevention by vaccination may be an attainable goal.
In the interim early diagnosis, accurate staging and referral to a multidisciplinary tertiary centre is vital to outcome. Radical surgery with free flap repair and post-operative radiotherapy provides the best chance of cure. The recent proposal of pre-operative chemo-radiotherapy needs to be evaluated by outcome studies.

Samenvatting en conclusies

Neurotologie en schedelbasischirurgie zijn de verwezenlijking van een verlangen om aandoeningen aan de schedelbasis en in de brughoekregio chirurgisch te kunnen behandelen, welke aandoeningen, veelal tumoren, eerder niet chirurgisch verwijderd konden worden vanwege hun anatomische positie, de omvang van de tumor en verschillende mate van doorbloed zijn van die tumoren. Er zijn echter onvoorstelbaar grote vernieuwingen gerealiseerd op velerlei terrein, zodat de meerderheid van deze aandoeningen aan de schedelbasis en in de brughoekregio thans wel chirurgisch behandeld kunnen worden. Daarbij valt te denken aan de vooruitgang in de microchirurgische technieken na de invoering van de operatie-microscoop, de nieuwe mogelijkheden op het gebied van de neuroimaging en daarmee voor een betere diagnostiek, het ontstaan van het subspecialisme neuro-anesthesie, het intraoperatief kunnen registreren van de functie van hersenzenuwen zoals voor de nervus facialis en voor de gehoorzenuw, het nieuwe en zo verfijnde microchirurgische instrumentarium, de toepassing van de ultrasonore cavitron, de verschillende toepassingen van de laser, het kunnen toepassen van endoscopische technieken, de toepassing van de neuronavigatie alsook de verbeterde verzorging en bewaking van de patiënt postoperatief op een neurointensive care.

Dat alles maakt het mogelijk talrijke andere chirurgische toegangswegen te ontwikkelen zoals de laterale en voorste schedelbasisbenadering. Vrijwel iedere laesie, of het nu een neoplasma, een vaataandoening of een infectieus proces aan de schedelbasis betreft, ofwel primair daar gelegen of secundair daar gekomen, of vanuit de schedelholte zich uitbreidend in de schedelbasis, blijkt in een steeds grotere frequentie chirurgische benaderd te worden.

De patiëntenzorg en alle logistieke zorg daaromheen is verder verbeterd niet alleen door het operatief gaan samenwerken in multidisciplinaire teams maar ook door in poliklinisch werkzame multidisciplinair samengestelde behandelteams samen te gaan werken.

Deze organisatie in en rondom deze behandelteams leidde tot het opzetten van klinische databestanden en daarmee tot het aldus gaan evalueren van de behandelresultaten. Kwaliteitscontroles van buitenaf via audits werden daarmee gefaciliteerd.

Met de invoering van classificaties voor de afzonderlijke aandoeningen/tumoren werd het zo ook mogelijk om de uitkomsten van verschillende chirurgische behandelcentra goed te kunnen gaan vergelijken. Op die manier is het mogelijk geworden op grond van dergelijke vergelijkende studies klinische evidentie aan te tonen voor een bepaalde chirurgische procedure/toegangsweg of voor een bepaalde

behandeling. Het verschaft ook aan de chirurg de mogelijkheid op de hoogte te blijven van zijn eigen chirurgische resultaten.
De grote uitdaging in de neurotologie en de schedelbasischirurgie is om enerzijds een ruimteinnemend proces volledig uit te nemen en anderzijds tegelijk alle neurale en neurologische functies voluit te willen behouden om zo de allerhoogste kwaliteit van leven voor die geopereerde patiënt te helpen behouden.

Hoofdstuk 2.1

In dit hoofdstuk wordt een retrospectieve analyse gegeven vanwege vestibulaire schwannomen in de regio Cambridgeshire over de periode 1994-2004 en de periode 1981-1993 gebaseerd op een gecomputeriseerd databestand van de medische gegevens. Vergeleken worden de verschillen in de reden van verwijzing alsook verschillen in de grootte van de tumor en de klinische verschijnselen.
Deze studie toonde aan dat voor steeds meer patiënten een afwachtende "watch, wait and rescan" aanpak werd verkozen in plaats van een chirurgische excisie. Verder bleek de diagnose "vestibulair schwannoom" in toenemende mate al bij verwijzing en wel bij 90% gesteld te zijn. De duur van de ziektegeschiedenis totdat de verwijzing plaats had bleek over de tijd niet te zijn veranderd. Evenmin bleken de reden voor verwijzing, de locatie van de verwijzende instantie, of de hoofdklacht over beide perioden te zijn veranderd. In de meest recente van deze 2 perioden bleken bij een eerste verwijzing de tumoren gemiddeld kleiner in omvang te zijn, terwijl anderzijds het percentage tumoren met een doorsnede groter dan 4.5 cm ook was toegenomen. De toegenomen beschikbaarheid van de MRI (magnetic resonance imaging) wordt als verklaring voor het weten op te sporen van de kleinere tumoren aanvaard.
Vestibulaire schwannomen met name degene die meer mediaal in de brughoekregio nabij de hersenstam ontstaan kunnen langer zonder enige klinische symptomatologie groeien en zich daardoor in verhouding later met al een grotere diameter presenteren op het moment dat een eerste MRI onderzoek verricht wordt.

Toekomstig wetenschappelijk onderzoek
Het toekomstig onderzoek zou kunnen bestaan uit het met behulp van MRI-onderzoek analyseren van iedere onverklaarde eenzijdige gehoor-evenwichtsklacht of symptoom om te achterhalen in hoeverre een aldus zichtbaar te maken afwijking oorzaak zal zijn van die klacht.
Van de patiënten met een vestibulair schwannoom blijkt 2% een normale gehoordrempel te hebben. Er dienen aanbevelingen te komen over de precieze grootte van een

gehoorverlies in het toonaudiogram, waarna een verder onderzoek met MRI moet volgen. Een formele bevestiging van zo een richtlijn door de European Academy of Otology and Neurotology ondersteund met een publicatie in een wetenschappelijk tijdschrift moet dan volgen. Een kosten-baten analyse voor het zo systematisch speuren naar het voorkomen van vestibulaire schwannomen is al gekend en gepubliceerd. Om vroegdiagnostiek van vestibulaire schwannomen met behulp van MRI te kunnen rechtvaardigen is het nodig met elkaar te vergelijken enerzijds de totale kosten van een gemiste diagnose (bij b.v. een kostwinner) met een late klinische presentatie en een grote tumordiameter en de daarmee gepaard gaande slechtere uitkomst van therapie vaker leidend tot arbeidsongeschiktheid en daarmee een financiële afhankelijkheid van anderen, en anderzijds hoeveel personen voor diezelfde hoeveelheid kosten onderzocht en (zo nodig) behandeld kunnen worden met de diagnose vestibulair schwannoom.

Hoofdstuk 2.2

In dit hoofdstuk wordt voor 381 personen met een vestibulair schwannoom het groeipatroon geanalyseerd bij toepassen van “watch, wait and rescan” beleid. Het groeipatroon blijkt voor de tumoren onderling zeer te verschillen zowel wanneer dit voor de lange termijn geanalyseerd wordt als voor individuele gevallen. Deze studie toont dat er bij 33% van de sporadische eenzijdig voorkomende vestibulaire schwannomen een significante groei wordt vastgesteld, bij 59% geen significante groei werd gezien en bij 8% was er een afname in omvang.
De gemiddelde toename in doorsnede van een groeiende tumor bleek 2.3 mm. Na 18 maanden follow-up met imaging na de eerste diagnose bleek al bij 52.4% sprake van een groeiende tumor.
Na 5 jaar follow up was dat 72 %. Deze resultaten stemmen niet overeen met een andere eerdere vergelijkbare studie. De auteurs van die studie adviseren de follow-up van deze vestibulaire schwannomen al na 5 jaar te stoppen, omdat zij in hun studie na 5 jaar geen tumorgroei hebben waargenomen. Ons artikel toont echter wel aan dat er (ook na 5 jaar follow-up) nog tumorgroei voorkomt. Het is van belang om dergelijke informatie al te melden bij de eerste counseling van patiënten met een vestibulaire schwannoom ongeacht of zij al of niet neigen te zullen gaan kiezen voor een meer afwachtende “wait and scan” beleid in plaats van al direct te willen kiezen voor een vorm van actieve behandeling.

Toekomstig onderzoek
Er is behoefte aan snelle en precieze gecomputeriseerde methoden om volumemetingen van vestibulaire schwannomen beter en nauwkeuriger te kunnen gaan bestuderen in eenzelfde centrum alsook om dit tussen de verschillende centra te kunnen gaan vergelijken.

Chapter 2.3

In dit hoofdstuk wordt een gedetailleerde beschrijving gegeven van een chirurgische techniek om een hoog liggende bulbus jugularis tijdens translabyrinthaire chirurgie te kunnen verlagen. Kennis en vaardigheid hoe dat chirurgisch tot stand te brengen kan van groot nut zijn. Immers dit soms aanwezige anatomisch chirurgische probleem van een te hoge voorliggende bulbus jugularis was voor sommige hoog in aanzien staande schedelbasiscentra reden de translabyrinthaire toegangsweg in te ruilen voor de retrosigmoidale benadering in geval van een herkende hoge positie van de bulbus jugularis. Dit omdat men het chirurgisch "verlagen" van de anatomische positie van de bulbus jugularis als een te hoog chirurgisch risico beschouwt. Het is onze eigen ervaring dat de bulbus jugularis op een veilige manier aanzienlijk verlaagd kan worden door een zorgvuldige dissectie van de benige structuren rondom en door vervolgens via skeletiniseren een zeer dun ringvormig beweeglijk benig eiland als top op de bulbus jugularis behouden kan worden. Deze dunne benige koepel over de bulbus jugularis helpt om het daarop te plaatsen chirurgische materiaal "surgical" evenals de vervolgens daarover heen aan te brengen lagen van zachte beenwas te stabiliseren.
Door vervolgens dit alles gelijkelijk met een zachte druk aan te brengen zal de voorliggende bulbus jugularis verder uit de chirurgische toegangsweg gaan verdwijnen. Op deze wijze wordt het risico op ongewenste bloedingen geminimaliseerd.

Toekomstige research
Er bestaat een behoefte aan nieuwe en betere chirurgische technieken om de laagjes beenwas of weefseldelen te stabiliseren. Die laagjes worden gebruikt om de koepel van de bulbus jugularis af te dekken en zo veilig te helpen verlagen en om die koepel, die vaak een diverticulum kent, daarna in die verlaagde positie te houden. Aldus wordt zo dan een goede toegang verkregen tot het caudale deel van de inwendige gehoorgang. Daarbij ontstaat ruimte tussen enerzijds het caudale deel van de inwendige gehoorgang en de bulbus jugularis anderzijds, zodat dan de 9de, 10de en de 11de

hersenzenuw veilig van de grote brughoektumor afgeprepareerd kunnen worden. Wij zouden verder willen nagaan, wat de incidentie is en wat het natuurlijk beloop is van de benigne craniale hypertensie die het gevolg is van de vernauwing ter hoogte van de gecomprimeerde bulbus jugularis. Wij zouden ook willen achterhalen welke van deze patiënten een stent behoeven op basis van studies met drukmetingen of op grond van klinische verschijnselen. Verder zouden wij beter willen leren kennen wat het werkelijke effect is van een stent procedure.

Hoofdstuk 2.4

Dit hoofdstuk gaat in op de tekortkomingen van de algemeen gebruikte House Brackman (HB) classificatie om de mate van functiestoornis van de nervus facialis te benoemen. In dit hoofdstuk stellen wij een modificatie voor van deze House Brackman (HB) classificatie. Omdat de House Brackman (HB) classificatie al zo algemeen wereldwijd wordt toegepast is er voor gekozen om een modificatie van deze classificatie voor te stellen in plaats van met een geheel nieuwe classificatie op te komen. Kern van de door ons voorgestelde modificatie in deze classificatie regardeert de kwaliteit van leven bij patiënten met een House Brackman (III) (HB III) klasse. Sommige personen met een House Brackman III (HB III) klasse hebben een redelijke mate van ooglidsluiting al of niet met traanvocht vervangende oog-druppels/zalf en zonder verschijnselen van een keratitis. Echter een belangrijk deel van de personen met een House Brackman III (HB III) klasse hebben een slechte kwaliteit van leven en worden geïnvalideerd door een droog oog, een keratitis ten gevolge van een onvoldoende ooglidfunctie, en vele onder hen behoeven een laterale of mediale tarsorhaphie of de plaatsing van een plaatje goud of platinum in het bovenste ooglid.
De House Brackman classificatie houdt ook geen rekening met de dysfunctie van de nervus intermedius en de mogelijke daaruit voorkomende klachten zoals krokodillentranen, een metalen of een vieze smaak in de mond, een pijnlijk te droog oog of een keratitis als gevolg van een gestoorde ooglidfunctie. De rapportages over resultaten van de nervus facialisfunctie na chirurgie vanwege vestibulaire schwannomen maken geen melding van de sensorische component van de nervus facialis functie.
De auteur van dit proefschrift stelt daarom voor de House Brackman III (HBIII) klasse onder te verdelen in een klasse HBIIIA en HBIIIB om daarmee aandacht te geven aan dat aspect van kwaliteit van leven. Deze subclassificatie maakt het nu ook mogelijk in de beoordeling van de nervus facialisfunctie mee te nemen het al of niet

aanwezig zijn van krokodillentranen, een metalen of anderszins een vieze smaak, een droog oog, een hemifaciaal spasme en synkinesie.

Toekomstige research
Toekomstige research zou gericht moeten zijn enerzijds om via een nieuwe classificatie het effect van een verschillende beoordeling door verschillende beoordelaars (inter observer difference) van de nervus facialisfunctie te helpen verminderen en anderzijds te helpen bijdragen aan een grotere mate van nauwkeurigheid in de beschrijving. Tegelijk is er behoefte aan een grotere gebruiksvriendelijkheid van die nieuwe classificatie. In die nieuwe classificatie is niet alleen meer aandacht nodig voor de situatie van het oog maar ook voor de betekenis van een aberrante regeneratie van de verschillende motorische takken van de nervus facialis. Onderdeel van die nieuwe classificatie zal ook moeten zijn het registreren en meewegen van het voorkomen van een afwijkende smaak, krokodillentranen, een hemifaciaal spasme en synkinesiën.

Hoofdstuk 2.5

In dit hoofdstuk wordt voor 652 patiënten, die geopereerd werden vanwege een vestibular schwannoom, geanalyseerd welke factoren invloed hebben op de post-operatieve functie van de nervus facialis. Anatomisch gezien bleef in 97% van de gevallen de nervus facialis intact. De House Brackmann classificatie werd gebruikt om de functie van de nervus facialis vast te stellen. Gedurende de afgelopen 6 jaar werd in deze serie een voldoening gevend resultaat bereikt bij alle tumoren met een diameter van ≤ 15 mm en dit percentage zakte tot 72% voor de tumoren met een diameter ≥ 45 mm.
De uitkomsten van een univariabele en multivariabele analyse toonde dat de tumorgrootte en het jaar waarin de operatie verricht werd significant voorspellende factoren zijn om de uitkomst van de functie van de nervus facialis postoperatief te voorspellen. Er was onvoldoende evidentie in deze serie dat geslacht, leeftijd en operatieve toegangsweg geassocieerd waren met de postoperatieve nervus facialis-functie na gecorrigeerd te hebben voor de grootte van de tumor en het jaar van de operatie.
Onderzoek naar de functie van de nervus intermedius en een aberrante regeneratie van de nervus facialis toonde aan dat de kans om postoperatief een hemifaciaal spasme te ontwikkelen op enig moment 13% is en dat bij 42% van die 13% binnen 24 maanden spontaan een genezing intrad.

Wanneer er preoperatief al een partiële nervus facialis functieverlies aanwezig was bleek de kans op het hebben van een hemifaciaal spasme significant vergroot. Er was echter geen significant verschil in deze voor de aspecten een "metaalachtige" smaak en het hebben van krokodillentranen.

De chirurgische leercurve was het steilste voor de eerste 50 operaties en nadien vlakte deze curve af tot voor 6 jaar geleden. Immers sinds 6 jaar is er weer een forse verbetering ingetreden met het gaan gebruiken van facialismonitoring tijdens de operatie. Met een factor 2,5 verbeterde de kans op een goede uitkomst van de nervus facialisfunctie.
In deze rapportage worden de fijne chirurgische kneepjes beschreven welke de postoperatieve uitomsten voor de nervus facialis functie helpen te verbeteren.

Toekomstige research
In hoeverre "Hydro-dissectie" van de nervus facialis van de tumorkapsel bijdraagt aan een meer atraumatische dissectie kan nagegaan worden in een prospectief opgezette studie ter evaluatie van de uitkomsten van de dissectie van vestibulaire schwannomen.
Het is algemeen bekend, dat de anatomische positie van de nervus facilis ten opzichte van de tumor kan variëren. Een mediaal beloop ten opzichte van de tumor wordt als de meest gunstige positie beschouwd. Een lateraal beloop en een voorliggend beloop van de nervus facialis ten opzichte van de tumor – gezien vanuit de positie van de chirurg langs de translabyrinthaire toegangsweg – geldt als de meest ongunstige positie. De betekenis van sommige variabelen, zoals de grootte van de tumor en de precieze anatomische locatie van de tumor in de brughoek, op de uiteindelijke postoperatieve uitkomst van de nervus facialisfunctie verdienen nadere studie. Verwacht wordt dat de uitkomsten van dergelijke studies relevante kennis zullen gaan opleveren om preoperatief een betere inschatting van de te verwachten postoperatieve facialisfunctie te kunnen geven.

Hoofdstuk 3.1

In hoofdstuk 3.1 worden voor een periode van 17 jaar de resultaten bij patiënten met neurofibromatosis type 2 (NF2) vermeld vanuit het "Cambridge Neuro-otology and Skull Base Surgery tertiary referral Centre".
Deze studie omvat in totaal 35 patiënten met tezamen 62 brughoektumoren, waarvan 59 van deze 62 histologisch een vestibulair schwannoom waren. Als parameters werden beoordeeld de groeisnelheid van de tumor, het al of niet

voorkomen van een gehoorverlies en de ernst van een aanwezig gehoorverlies, het ontstaan van een gestoorde nervus facialisfunctie en het al of niet bestaan van een noodzaak om een behandeling te starten. In totaal kregen 5 van deze 35 patiënten een stereotactische radiotherapie (gamma knife) en bij al deze 5 werd nadien of een groeiende tumor of een toename van het gehoorverlies vastgesteld. Tijdens een follow-up met imaging technieken werd bij 9/22 (41%) van de NF2 patiënten tumorgroei vastgesteld, wat hoger is dan de 33% bij de hiervoor gekend eenzijdige sporadische voorkomende vestibulaire schwannomen.
Voor de meerderheid van de NF2 patiënten die een chirurgische behandeling ondergingen had dit plaats langs de translabyrinthaire route. Slechts voor 4 personen gebeurde dit langs de retrosigmoidale route met als argument een preservatie van het gehoor te willen bewerkstelligen. Het realiseren van vroeg-diagnostiek bij NF2 patiënten wordt als belangrijk ervaren voor het optimaal kunnen begeleiden van deze patiënten zelf, hun familie alsook de maatschappij als geheel. Het blijft moeilijk om frequent een gehoorsparende operatie te bereiken bij deze zo bijzondere groep van patiënten met NF2. Toch is er in deze vooral vooruitgang geboekt door de toepassing met auditory brainstem implantation (ABI) en in gevallen waarin de nervus cochlearis nog intact was met cochleaire implantatie. Bovendien worden opnieuw in verschillende centra succesvol gehoorsparende operaties langs de middelste schedelgroeve (middle fossa) benadering voor de groep kleine vestibulaire schwannomen verricht. Die ontwikkeling stimuleert op dit moment om vroegtijdig te kiezen voor een chirurgische behandeling langs de middelste schedelgroeve in geval van kleine vestibulaire schwannomen met nog een betekenisvol gehoor aan die zijde.

Toekomstige research
Vanuit sommige centra worden op dit moment opmerkelijk goede resultaten gemeld over gehoorsparende uitkomsten na operaties voor vestibulaire schwannomen langs de weg van middelste schedelgroeve. Evenzo wordt dit gemeld voor vroegtijdige chirurgie bij NF2 patiënten. Het wordt nodig gevonden om deze operatieresultaten opnieuw te evalueren tezamen met kwaliteit van leven studies. Evenzo om het behoud van het gehoor op de lange termijn te analyseren en daarbij ook de "hearing handicap index" te gebruiken. Omdat de meeste centra voor NF2 patiënten een afwachtend "wait and scan" beleid als de behandelingsstrategie hebben om de goede neurologische functies zo lang mogelijk te helpen behouden en om pas tot een chirurgische behandeling over te gaan wanneer de neurologische toestand van een NF2 patiënt dat echt vereist, is het nuttig preciezer de resultaten van een vroegtijdige behandeling te leren kennen. Het hedentendage ter beschikking hebben van deels implanteerbare hoortoestellen heeft

het zoal mogelijk gemaakt een cochleaire implantaat te plaatsen zolang de gehoorzenuw nog anatomisch intact is. Momenteel wordt er ook al een cochleair implantaat aan de dove geopereerde zijde als "sleeper" geplaatst wanneer er contralateraal toch nog een horend oor is om zo mettertijd de gehoorfunctie te kunnen gaan overnemen (door dat eerdere cochleaire implantaat te gaan activeren) wanneer het gehoor dat aan die genoemde contralaterale zijde gaat wegvallen. Wanneer het zinloos is in het binnenoor een cochleair implantaat te plaatsen omdat de gehoorzenuw anatomisch niet meer intact is, blijft er de mogelijkheid om de gehoorbanen rechtstreeks met een tegen de hersenstam geplaatst " auditory brainstam implant (ABI)" te stimuleren.
Groeiremmende medicijnen zoals Avastin dienen op hun therapeutisch effect nader onderzocht te gaan worden, inbegrepen een kosten-baten analyse van zo een behandeling.
Toekomstige lange termijn analyses van de verschillende behandelmodaliteiten bij NF2 zijn nodig om te komen tot de allerbeste behandelingen voor deze NF2 patiënten.

Hoofdstuk 3.2

De behandelend arts van NF2 patiënten heeft een moeilijke taak vanwege de vele dilemma's in het bijzonder bij de jonge patiënten met al grote tumoren (het Wishart phenotype). Ondanks de hedendaagse vernieuwingen in beeldvormende technieken om dergelijke tumoren beter te kunnen afbeelden, het feit dat deze tumoren eerder opgespoord blijken te worden en de hedendaagse mogelijkheden voor gehoorsparende chirurgie, is het toch nog zo dat de meeste NF2 patiënten laat met toch al grote tumoren en met neurologische verschijnselen gepresenteerd worden.
Omdat patiënten met een NF2 diagnose en tegelijk een brughoektumor in het Verenigd Koninkrijk zeldzaam zijn is er voor gekozen om vanuit 2 van de grotere schedelbasis centra, te weten Cambridge en Manchester, een lange termijn analyse uit te voeren van de resultaten van de verrichte translabyrinthaire brughoekchirurgie bij NF2 patiënten. Naar ons beste weten is dit de eerste lange termijn analyse van de resultaten van translabyrinthaire brughoekchirurgie bij NF2.
De resultaten van brughoekchirurgie bij NF2 zijn minder goed dan voor eenzijdige vestibulaire schwannomen gekend worden. Toch lukte het een volledige tumorverwijdering te bereiken in 2/3 van deze gevallen en nog eens bij ¼ van de gevallen een vrijwel volledige tumorverwijdering te realiseren. Kortom bij 90% van deze gevallen bleek een volledige of bijna volledige tumorverwijdering bereikt te zijn. Bij 1 op de 7 gevallen is een recidief tumor vastgesteld. De perioperatieve mortaliteit was mede gezien het ziektebeeld NF2 erg laag en er is geen peroperatief overlijden

voorgekomen. In een op de tien gevallen ging de anatomische continuïteit van de nervus facialis verloren. Het ging dan wel steeds om de grotere tumoren met een gemiddeld maximale diameter groter dan 3 cm. Ook voor de functie van de nervus facialis na translabyrinthaire chirurgie geldt dat deze minder goed is dan wat gebruikelijk is na dergelijke chirurgie voor geïsoleerd voorkomende vestibulaire schwannomen. Toch werd bij 2 van de 3 patiënten postoperatief een normale c.q. vrijwel normale nervus facialisfunctie verkregen. Een teleurstellende functie van de nervus facilis werd postoperatief bij 1 op de 6 patiënten vastgesteld.

In deze publicatie worden voor het eerst de uitkomsten beschreven voor een aberrante regeneratie van de nervus facialis na brughoekchirurgie bij NF2 patiënten. Bij ongeveer de helft van de geopereerde patiënten was er na de operatie een metaalsmaak in de mond en dit verdween nadien weer spontaan bij wederom de helft van die groep. Zo bleken krokodillentranen postoperatief voor te komen bij bijna de helft van deze NF2 patiënten, maar die klacht was meestal permanent en verdween op termijn bij alleen 1 op de 17 van hen.

In deze publicatie wordt zeer gedetailleerd gerapporteerd over de klacht oorsuizen.
Postoperatief had een van de vier NF2 patiënten geen oorsuizen en postoperatief ontstond er bij een vijfde van hen wel een oorsuizen.
Wanneer er preoperatief sprake was van een “mild oorsuizen”, bleef dat postoperatief zo bij tweederde van hen. Echter bij eenvierde van hen nam het oorsuizen postoperatief toe. Verder verdween het oorsuizen postoperatief bij 1/6 deel van die groep.
Wanneer er preoperatief sprake was van een “matig oorsuizen” bleef dit bij 6 van de 10 onveranderd, bij 1 op de 5 werd het milder of verdween het zelfs. Bij een op de 5 werd het erger en ging het zelfs over in een ernstig oorsuizen.
Oorsuizen is een belangrijk item als uitkomstmaat bij de kwaliteit van leven studies (QOL), omdat het na de tumorverwijdering postoperatief tot de belangrijkste klacht kan verworden. Immers de evenwichtklachten kunnen geleidelijk via een autonome compensatie verbeteren. Preoperatieve klachten over een onaangenaam horen in het aangedane oor kunnen verdwijnen als gevolg van een volledige uitval van het gehoor. Terwijl bij een klacht van oorsuizen in het algemeen die klacht overstemd kan worden door ander geluid vanuit de omgeving, wordt het oorsuizen na een operatie bij brughoekpatiënten juist erger bij aanwezigheid van rumoer in de omgeving.
Bij een op de acht van de patiënten was er preoperatief al een ventriculo-peritoneale (VP) shunt geplaatst, wat een indicatie is om aan te geven hoeveel grote brughoek-tumoren in deze serie voorkwamen. Bij de helft van de patiënten werd een deels

implanteerbaar hoortoestel in de vorm van een cochleair implantaat of een hersenstamimplantaat (ABI) geplaatst. Meestal ging het om een hersenstamimplantaat. Bij 2/3 deel was er sprake van een eenzijdige brughoek-chirurgie, bij het andere 1/3 deel had er beiderzijds brughoekchirurgie plaats gehad. Bij 2 patiënten was een cochleair implantaat als een "sleeper" geplaatst.

Toekomstige research
Studies naar de functionele intactheid van de nervus cochlearis zijn nodig om postoperatief met behulp van electrophysiologische stimulatie op het niveau van de cochleaire kernen en de eerste neuronen van de 8ste zenuw alsook van de hogere gehoorbanen op hersenstamniveau uitspraken te kunnen gaan doen over de functionele intactheid van de gehoorzenuw om zo het succes te helpen voorspellen van een eventuele cochleaire implantatie en van toepassing van een hersenstamimplantaat (ABI). Het zou zelfs kunnen gaan bijdragen aan de toepassing van een gecombineerde toepassing van een cochleair implantaat (CI) en een hersenstamimplantaat (ABI).

Hoofdstuk 4.1

Een retrospectieve analyse van de chirurgische resultaten van een uitgebreid rotsbeencholesteatoom bij in totaal 43 patiënten is het onderwerp van de in dit hoofdstuk beschreven studie. Het oogmerk was om tot een nieuwe meer omvattende en verfijndere classificatie met meer subklassen te komen. Deze nieuwe classificatie kent een onderverdeling op grond van anatomische regio's in het rotsbeen. Deze classificatie kan van nut zijn bij het opstellen van een preoperatieve planning en is tevens van nut bij het voorzien of per- en postoperatief het gehoor behouden kan worden. Het recidief percentage voor deze aandoening bleek op de lange termijn 2/43 (5%) te bedragen. Gemeend wordt dat dit goede resultaat te danken is aan een zeer zorgvuldige en precieze wijze van opereren, het toepassen van bipolair diathermie om keratineresten en cholesteatoommatrix te verwijderen alsook door de toepassing van een diode laser om de eiwitten in de cholesteatoom matrix adherent aan de dura te denatureren. De functie van de nervus facialis bleef doorgaans intact. In geval de nervus facialis onderbroken is of raakt tijdens de operatie is het relevant om peroperatief direct een end to end anastomose van de nervus facialis realiseren en wanneer het defect in de zenuw te groot is de continuïteit van de nervus facialis te helpen herstellen met behulp van een zenuw interpositie. Door zo te handelen kan in plaats van een HBVI nog een klasse HBIII bereikt worden in geval de facialisverlamming korter dan 12 maanden bestaat.

Toekomstige research
Op dit moment is er behoefte om het antwoord op 2 belangrijke vragen te krijgen. Lange termijn follow-up studies zijn nodig om te bevestigen dat veelal geen her-operaties meer nodig zijn vooral wanneer bekend is dat er resten van cholesteatoom-matrix zijn achtergebleven op een hersenzenuw, de bulbus jugularis of op de arteria carotis in zijn intratemporale beloop, omdat oftewel de ziekte verdwijnt of inactief wordt.
We dienen te achterhalen welke factoren zorgen voor een recidief van de aandoening.
Het tweede topic is of een gedefocuseerde laser straal door hittetoepassing succesvol het eiwit aanwezig in de cholesteatoommatrix aanwezig op de dura kan denatureren. Het ligt voor de hand dat dit zo zal zijn, maar laboratoriumresearch is nodig om dat te bevestigen. Klinische lange termijn follow-up studies zijn nodig om dit te bevestigen.

Hoofdstuk 4.2

In dit hoofdstuk wordt een door de eerste auteur voorgestelde classificatie besproken van primair in de brughoekregio voorkomende cholesteatomen. Die classificatie is gebaseerd op neuroanatomische overwegingen. Een retrospectieve analyse van de chirurgische resultaten van 15 opeenvolgende chirurgische gevallen over een periode van 15 jaar wordt beschreven. Bij 10/15 gevallen traden het eerst symptomen op op het gebied van het gehoor en/of duizeligheid. De gemiddelde duur van de klachten was 2 jaar. Een in opzet gehoorsparende operatieve benadering werd bij ¾ van deze gevallen toegepast. Bij 12/15 gevallen kon de tumor klinisch volledig verwijderd worden. Slechts bij een van deze 12 gevallen werd 15 jaar later een recidief tumor gevonden. Er was geen peroperatieve en geen perioperatieve mortaliteit. In geval een in opzet gehoorsparende chirurgische benadering was verkozen gelukte het bij een minderheid (4/9) om eenzelfde gehoor als preoperatief te behouden. Er was gemiddeld genomen slechts een gering verschil van 2 dB.

Toekomstige research
Het afprepareren van cholesteatoommatrix van een hersenzenuw is vaak nogal schadelijk voor een postoperatief nog aanwezige functie van die hersenzenuw. Chirurgische kennis over bij hoeveel trauma en van welk type trauma er wel of geen duurzame schade aan de functie van een bepaalde hersenzenuw ontstaat is bepalend bij het peroperatief bepalen van de uitgebreidheid van de excisie. Immers functieverlies van een of meerdere hersenzenuwen beïnvloedt in sterke mate postoperatief de kwaliteit van leven.

"Non echo-plenar MRI scanning" heeft een hoge sensitiviteit om een recidief van deze aandoening te kunnen opsporen en daarom is het nuttig met intervallen postoperatief met behulp van die methode de situatie van deze patiënten te volgen.

Hoofdstuk 5.1

Neurinomen van de nervus trigeminus zijn zeer zeldzame en complexe aandoeningen, die moeilijk te behandelen zijn.
De aandoening kan uitsluitend intracranieel gelegen zijn, maar extracranieel gelegen vertakkingen van deze zenuw kunnen evenzo betrokken zijn. Een multidisciplinair team is voor de diagnostiek en de behandeling nodig. De resultaten van een retrospectieve analyse van de behandelingsresultaten bij patiënten met een trigeminusneurinoom worden in dit hoofdstuk besproken. Een goede preoperatieve planning is essentieel en maakt het in de meeste gevallen mogelijk de tumor te verwijderen met behoud van belangrijke neurale structuren. De precieze locatie van de tumor bepaalde de te verkiezen chirurgische toegangsweg. De gecombineerde retrosigmoidale/ retrolabyrinthaire/middelste schedelgroeve benadering verschaft een goede toegang voor de grote in de middelste en achterste schedelgroeve gelegen tumoren. Slechts een geringe retractie van de hersenen is dan nodig wat de postoperatieve morbiditeit helpt te beperken. Een type Fisch C benadering is noodzakelijk voor de allergrootste tumoren. Een volledige verwijdering van de tumor werd voor 3 van de 8 gevallen bereikt. Bij de andere 5 patiënten werd met opzet een tumorrest achtergelaten om de neurologische schade postoperatief te beperken en zo te kiezen voor een meer optimale kwaliteit van leven situatie postoperatief. Bij alle 5 patiënten met een incomplete tumorverwijdering trad hernieuwde groei van de tumor op met daarmee gepaard gaande klinische verschijnselen. Hernieuwde chirurgie had bij elk van hen plaats. Er was geen peri-operatieve mortaliteit of ernstige invaliditeit in deze groep patiënten te betreuren. Een lange termijn follow-up van deze patiënten is met beeldvormige technieken noodzakelijk om een eventueel recidief van zo een tumor op de lange termijn te evalueren.
Dit hoofdstuk benadrukt heel duidelijk hoe belangrijk het is om de voordelen en de nadelen van een eventuele chirurgische behandeling van een qua weefseltype goedaardige tumor heel goed tegen elkaar af te wegen. Evenzo om goed af te wegen de voordelen van een subtotale tumorverwijdering en de daarmee verbonden geringe postoperatieve neurologische morbiditeit en zodoende een relatief betere kwaliteit van leven nadien ten opzichte van een mogelijke grotere postoperatieve morbiditeit bij een volledige verwijdering van de tumor.

Dit alles is in het bijzonder belangrijk bij de grote tumoren die zowel in de middelste als in de achterste schedelgroeve gelegen zijn, ook al omdat kleine resttumoren heel wel nabehandeld zouden kunnen worden met stereotactische radiotherapie ook wel gamma knife genoemd.

Toekomstige research
Een antero-faciale en pterionale endoscopie verschaft een goede toegang tot de sinus cavernous en het foramen lacerum. Het is de verwachting dat deze endoscopische methode nog in belang zal gaan toenemen voor de chirurgische benadering van dit operatiegebied. Het zal eerst nog nodig zijn om systematisch klinische resultaten van deze chirurgische methode voor verschillende ziektebeelden afzonderlijk te verzamelen om het nut van deze behandelingsmethode aan te tonen. Evenzo is het noodzakelijk dat de resultaten van stereotactische radiotherapie voor op zich zeldzame aandoeningen in dit gebied van de sinus cavernosus zoals een trigeminus neurinoom alsook voor postoperatieve resttumoren op hun effectiviteit en efficiëntie geanalyseerd worden en dat die gegevens vervolgens gepubliceerd zullen worden.

Chapter 6.1

Dit hoofdstuk beschrijft de resultaten die verkregen zijn bij een microvasculaire decompressie van de nervus facialis langs de retrosigmoidale benadering ter behandeling van een hemifaciaal spasme. Bij een hoog percentage van de personen met een hemifacial spasme als gevolg van een “vascular loop” wordt op de lange termijn een genezing bereikt. Voordat kan worden aangenomen dat een hemifacial spasme veroorzaakt wordt door een ‘vascular loop’ en wel doorgaans door druk ter plaatse van de ‘root entry zone’ van de nervus facialis nabij de hersenstam, dient eerst een (andere) ruimte-innemende aandoening met behulp van een MRI onderzoek van de brughoek met toepassing van contrast vloeistof te zijn uitgesloten. Bij 14/15 (93%) van de hiervoor aldus geopereerde personen werd op korte termijn en bij 12/15 (80%) van hen in deze serie (van n=15) werd op de lange termijn een volledige genezing van het hemifaciale spasme bereikt. Bij 3 personen trad postoperatief een sensorineural gehoorverlies op en bij 2 personen ontstond postoperatief de klacht tinnitus. Een voorbijgaande nervus facialisverlamming ontstond postoperatief bij een persoon en deze facialisfunctie herstelde spontaan tot bijna normaal (House Brackman klasse I).

Geconcludeerd wordt dat de operatietechniek van een retrosigmoidale micro-vasculaire decompressie vanwege een "vascular loop" een excellent resultaat oplevert, ook op de lange termijn.

Toekomstige research
Voorgesteld is om de decompressie van de nervus facialis in de brughoek vanwege een hemifaciaal spasme te gaan verrichten met behulp van een minimaal invasieve endoscopische benadering langs de retrosigmoidale toegangsweg. Een nadeel daarvan kan zijn dat een optredende bloeding in de brughoekregio langs deze beperkte toegangsweg moeilijker te beheersen is en dientengevolge kan er sprake zijn van een verhoogd operatierisico. Daarom is er een behoefte om met behulp van kwaliteit van leven studies na te gaan of er een voordeel is verbonden aan deze endoscopische operatietechniek en tegelijk of het veronderstelde voordeel zal opwegen tegen een verhoogd operatierisico.
Het percentage recidieven van een geopereerde hemifaciaal spasme zou wel eens afhankelijk kunnen zijn van het type materiaal of weefsel dat als interpositie gebruikt wordt om de nervus facialis te scheiden van de 'vascular loop'. Het is nodig om voor elk van deze als interpositie gebruikte materialen de lange termijn resultaten na te gaan en om zo te achterhalen welk materiaal - gebruikt voor een interpositie om de druk veroorzaakt door de vascular loop op de nervus facialis - het beste duurzaam is te verhelpen.

Hoofdstuk 7.1

In dit hoofdstuk worden de resultaten beschreven voor alle 39 patiënten die over een periode van 20 jaar in de Skull Base Unit van het Cambridge University Hospital behandeld werden voor een plaveiselcelcarcinoom in het rotsbeen met behulp van een in opzet radicale chirurgie gecombineerd met een postoperatieve radiotherapie. Een gedetailleerde analyse van de klinische gegevens en van de behandelings-resultaten bij deze 39 patiënten wordt gegeven. Deze serie werd opgesplitst in 2 groepen te weten een groep die "salvage surgery" kreeg en een groep met "de novo surgery" om aldus een betere kans op een recidief van het plaveiselcelcarcinoom na deze gecombineerde chirurgische en radiotherapeutische behandeling te kunnen beschrijven. De aandoening werd geklassificeerd volgens de recente stadiering van de Universiteit van Pittsburgh.
De stadium II klasse werd behandeld met behulp van een laterale excisie van het rotsbeen. Al deze personen werden genezen. Voor stadium klasse III geldt dit ook.

Voor stadium III en voor de patiënten met een T3 tumor en een positieve lymfklier bij toepassing van het Pittsburg classificatie systeem is de overleving effectief 50%.
Het overlevingspercentage voor stadium IV tumoren was een op de 3 patiënten en voor T4 tumoren was dit zo voor 4 van de 10 patiënten. Het overlevingspercentage voor de hele serie is 16/37 (43%). Een slechtere prognose wordt onder meer bepaald door positieve lymfklieren, een slechte histologische differentiatie van het plaveiselcelcarcinoom, ingroei in de hersenen en eerdere chirurgie toegepast voor deze aandoening.
In de groep patiënten die een eerste behandeling kregen in ons centrum is de 5 jaarsoverleving 66% en voor de groep personen waarbij in dit centrum voor een recidief tumor na een eerdere behandeling elders een hernieuwde behandeling werd verricht is de 5 jaarsoverleving 33%. Deze uitkomsten suggereren dat een vroegtijdige verwijzing naar een multidisciplinair 'tertiair referral unit' en het verkrijgen van een agressieve primair chirurgische behandeling gecombineerd met een radicale postoperatieve radiotherapeutische nabehandeling de grootste kans op een genezing bieden.
Het is mogelijk dat de over het geheel genomen verbeterde behandelingsresultaten voor de groepen met een hogere stadiering en met een recidief tumor van deze zo agressieve en moeilijk te behandelen aandoening niet alleen het resultaat zijn van een meer radicale chirurgie door een uitgebreide excisie van het rotsbeen te verrichten maar ook omdat de chirurgische excisie ruimer is dan het oorspronkelijk bestraalde gebied en zo ook een aanvullende radiotherapeutische nabehandeling van dat gebied mogelijk is mede omdat het weefsel van de vrije transplantaatlap een goede vasculaire doorstroming heeft.

Toekomstige research
De schrijver van dit proefschrift is momenteel betrokken bij studies om een DNA-analyse te verkrijgen van durante operation daartoe ter beschikking gesteld tumor weefsel om de etiologie van het plaveiselcelcarcinoom en de mogelijke relatie met het Humane Papilloma Virus (HPV) of het Epstein Barr virus na te gaan.
Het achterhalen van een oorzakelijke factor kan de te kiezen therapie beïnvloeden. Zo zou vaccinatie mogelijk een haalbare preventieve oplossing kunnen worden.

Voor de periode van nu is het allerbelangrijkste om een vroegdiagnose, een nauwkeurige stadiering en een verwijzing naar een multidisciplinair 'tertiary referral centre' te realiseren. Een radicale chirurgie met een gevascullariseerde vrije lap en aanvullend een radiotherapeutische nabehandeling geeft de beste kans op genezing.

De waarde van een preoperatief te geven chemoradiotherapie dient in de nabije toekomst door follow up studies nader bepaald te worden.

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Dr. David Baguley has been a loyal and supportive colleague and friend now for more than 25 years. We have worked closely together academically and clinically and he has matured into an audiological scientist with an international reputation which he richly deserves. I have found our professional association immensely rewarding in so many respects and I wish to thank him.

To Mr. David Hardy my neurosurgical colleague my sincere thanks. We set up the Department of Neuro-otology and Skull Base Surgery together in1981. Always a great enthusiast for transtemporal approaches, we discussed patients together, studied scans and planned our surgery. In the early days many of our approaches were not in the literature or in the textbooks but together we drew up what we believed to be the best possible management plan for the patient.

Mr Robert Macfarlane originally our Senior Registrar was groomed to take over as lead skull base neurosurgeon. What a wonderful colleague and such a precise skilful pair of hands, thank you so much Robert for being so pivotal in our excellent outcomes.

Professor Richard Ramsden my friend and colleague for many years. The second member of the "Royal London Hospital research triumvirate". Always enthusiastic about and encouraging of my academic and surgical ventures. Richard is a true kindred spirit and a loyal friend and I thank him.

Professor William "Bill" Gibson the third member of the triumvirate emigrated early to Australia but not before we had completed some very interesting research work together. Bill stimulated, fostered and encouraged my early efforts.

Andy Hibbs has been my "computer guru" for years now and I am immensely grateful to him for his patience and his meticulous and obsessional extraction of the data. His unrivalled understanding of Filemaker Pro software has ensured the accuracy of the data and facilitated its analysis.

Mr. Philip Ball, Head of the Photography and Illustration Service of Cambridge University, having been pivotal in fine tuning my Powerpoint presentations over the past two decades, has turned his computer and artistic skills to helping me to produce the illustrations for the papers in thesis and the design of the cover. I wish to thank him for his expertise and flair.

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Curriculum Vitae

The author of this thesis was born on the 27th June 1947 in Cardiff, South Wales. He was educated at St. Nicholas Grammar School in Northwood, London. In October 1965 he entered the Royal London Hospital Medical College, London University. He intercalated a BSc in biochemistry between his pre-clinical and clinical studies. He attained a first class honours degree and was awarded The Dame Edith Forbes Memorial Scholarship. After graduating from medical school in 1971 with an MBBS he pursued a career in surgery specializing in otolaryngology. He obtained his fellowship in Otolaryngology (FRCS) from the Royal College of Surgeons of England in October 1975. He was awarded a Thomas Wynne Jones Fellowship in Neuro-otology Skull Base Surgery at Stanford University, California, USA in 1979 to further his career in this sub-specialty.

He was appointed Consultant Surgeon at Addenbrooke's Hospital and Associate Lecturer of the University of Cambridge in1981.

In addition to running a general ENT service he established the Department of Neurotology and Skull Base Surgery in Cambridge which he has led with his neurosurgical colleagues over the last 30 years. This is now one of the leading units in the UK and attracts 60% of referrals from the district and region and 40% from the rest of the UK and abroad. He has a personal series of 1850 skull base procedures of which 1165 have been for excision of vestibular schwannoma including neuro-fibromatosis type 2 and auditory brainstem implantation. The clinical service has been underpinned by a very active research programme and has attracted 29 visiting fellows over 30 years.

As Chairman of the Intercollegiate Specialty Board and Panel of Examiners he helped to bring in the new FRCS examination in Otorhinolaryngology in a period of rapid and exciting change. Following this he was the British Association of Otorhino-laryngologist's representative on the Advisory Committee on Higher Surgical Training (SAC) and liason officer for Oxford and Trent. This role was critical for the maintenance of surgical excellence and the future development. of the specialty.

In the year 2000 He was awarded the TJ Harrison Prize by the Section of Otology of The Royal Society of Medicine for the best otological research (UK) over the previous 2 years and gave the Legard Lecture (Norwegian ENT Society) and the eponymous Brinkman Lecture and Medal (The Netherlands ENT Society) as well as The Gordon Smyth and Stirk-Adams Memorial Lectures and the Dr. SG Joshi Memorial Oration and various visiting professorships over the years.

In September 2009 he was awarded a Hunterian Professorship and Medal by the Royal College of Surgeons of England following his Hunterian Lecture.

He was invited to become a member of the American Otological Society in 2000 and is a founder and now committee member of the European Academy of Otology and Neurotology. He is a member of the Politzer Society and on the faculty of a large number of national and international courses. He was co-organizer of the 4th World Congress on Acoustic Neuroma which took place in Cambridge in July 2003. He is the Chairman of the Committee of Otology and Neurotology of the International Federation of ENT Societies (IFOS) and British representative on the general committee.

He is a Past President of The Section of Otology at The Royal Society of Medicine and was Master of The British Academic Conference in Otorhinolaryngology-Head and Neck Surgery which was held in Liverpool in 2009.

David Moffat has written 183 papers in peer reviewed scientific journals, 50 in non-peer reviewed publications, 28 chapters in books and been editor of two books.

List of peer reviewed publications

General otolaryngology

1. Moffat DA. Metastatic adenocarcinoma of the rectum presenting as an epulis: A case report . British Journal of Oral Surgery 1976;14:90-92. Also published in Oncology Abstracts 1976.

2. Moffat DA. Postural apnoea due to Large tonsils and adenoids. Journal of Paediatrics 1976; 89:3: 510.

3. Moffat DA, Ramsden RT, Shaw HJ. The styloid process syndrome: Aetiological factors and surgical management. Journal of Laryngology and Otology 1977;91:279-294.
This paper has been published in the 1978 Year Book of Otolaryngology.

4. Moffat DA, Ramsden RT. The deformity produced by a palsy of the marginal mandibular branch of the facial nerve. Journal of Laryngology and Otology 1977;91: 401-40.

5. Ramsden RT, Moffat DA, Gibson WPR, Jay, MM. S-Carboxmethylcysteine in the treatment of glue ear: A double blind trial. Journal of Laryngology and Otology 1977;91: 847-851.

6. Drake-Lee AB, Broughton SJ, Rampling A, Lancer JM, Moffat. DA. Necrotizing fasciitis. Journal of Laryngology and Otology 1983;97:193-196.

7. Harper JI, Duguid KP, Staughton RCD, Moffat DA. Oropharyngeal and laryngeal lesions in lipoid proteinosis. Journal of Laryngology and Otology 1983;97:877-880.
Presented at Section of Dermatology at Royal Society of Medicine by DA Moffat.

8. Grace ARH, Drake-Lee AB, Conn P, Kalinkiewicz, Moffat D. Metastatic Lingual carcinoma masquerading as Ludwig's angina. Journal of Laryngology and Otology 1984;98(5):535-7.

9. Harries MLL, Baguley DM, Moffat DA. Hearing aids a case for review. Journal of Laryngology and Otology 1989;103:850-852.

10. Wareing M, Irving RJ, Moffat DA. Parapharyngeal tumour presenting as recurrent uvular oedema. Journal of Laryngology and Otology 1993;107:640-641.

11. Fisher EW, Moffat DA, Quinn SJ, Wareing MJ, von Blumenthal H, Morris DP. Reduction in junior doctors' hours in an otolaryngology unit: Effects on the "out of hours" working pattern of all grades. Annals of the Royal College of Surgeons of England 1994;76(5):232-5.

Otology / otoneurological and skull base surgery

12. Moffat DA, Ramsden RT. Profound bilateral sensorineural hearing loss during Gentamicin therapy. Journal of Laryngology and Otology 1977;91:511-516.

13. Gibson WPR, Ramsden RT, Moffat DA. The immediate effects of Naftidrofuryl on the human electrocochleogram in Meniere's disorder (Preliminary Findings). Journal of Laryngology and Otology 1977;91:679-696.

14. Gibson WPR, Moffat DA, Ramsden RT. Clinical Electrocochleography in the diagnosis and management of Meniere's disorder. Audiology 1977;16:389-401.
Paper presented at the National Hearing Association,s "State of the Art Conference on the Fluctuant Hearing Loss of Meniere's Disease", June 2325,1978,Dundee, Illinois.

15. Moffat DA, Ramsden RT, Rosenberg G, Booth JB, Gibson WP. Otoadmittance measurements in patients with rheumatoid arhritis. Journal of Laryngology and Otology 1977;91:917-927. Paper presented to the Section of Otology at the Royal Society of Medicine by Moffat DA.

16. Ramsden RT, Moffat DA, Gibson WPR. Transtympanic electrocochleography in patients with syphilis and hearing loss. Annals of Otology, Rhinology and Laryngology 1977; 86:827-834. This paper has been published in the 1978 Year Book of Otolaryngology.

17. Ramsden RT, Gibson WPR,. Moffat DA. Anaesthesia of the tympanic membrane using iontophoresis. Journal of Laryngology and Otology 1977;91:79-785. This paper has been published in the 1978 ORL Digest.

18. Rosenberg G, Moffat DA, Gibson WPR, Booth JB. Middle ear functions in rheumatoid arthritis. Annals of Rheumatic Diseases 1978;37:522-524.

19. Moffat DA, Gibson WPR, Ramsden RT, Morrison AW, Booth JB. Transtympanic electrocochleography during Glycerol dehydration. Acta Otolaryngologica 1978;85 (3/4): 158-166.

20. Graham JM, Ramsden RT, Moffat DA, Gibson WPR. Sudden sensorineural hearing loss. Electrocochleographic findings in 70 patients. Journal of Laryngology and Otology 1978;92:581-589.

21. O'Connor AFF, Moffat DA. Otogenic intracranial hypertension (Otitic Hydrocephalus). Journal of Laryngology and Otology 1978;92:767-775.

22. Moffat DA, Booth JB, Morrison AW. Metabolic investigations in Meniere's disease: Preliminary findings. Journal of Laryngology and Otology 1979;93: 545-561.
Also published in "Interhaus" - Medilex Digest ORL August 1980;65-66.

23. Moffat DA. Transtympanic electrocochleography in Meniere's disease: Variation in the amplitude of the summating potential related to the clinical status. British Journal of Audiology 1979;13:149-152.

24. Moffat DA, O'Connor AFF. Bilateral internal carotid artery aneurysms in the petrous temporal bones. Archives of Otolaryngology 1980;106:172-175.

25. Kane, RJ, Moffat DA, O'Connor AFF. Outpatient myringoplasty. Journal of Laryngology and Otology 1980;94:1387-1393.

26. Morrison AW, Moffat DA, O'Connor AFF. Clinical usefullness of electrocochleography in Meniere's disease: An analysis of dehydrating agents. In "Symposium on Meniere's Disease". Otolaryngological Clinics of North America, 1980; 13/ 4:703-721.

27. Moffat DA, Booth JB, Morrison AW. Metabolic Investigations in Meniere's disease. Journal of Laryngology and Otology 1981;95:905-913.

28. Moffat DA, Campbell J, Reid A. Clinical and technical aspects of continous ERA recordings. British Journal of Audiology 1983;17:257-261.

29. Swanston AR, Grace ARH, Drake-Lee AB, Moffat DA. Anaerobic infection in acute mastoiditis. Journal of Laryngology and Otology 1983;97: 633-634.

30. Reid A, Birchall JP, Moffat DA. Auditory brainstem responses: Masking related changes in wave VI. British Journal of Audiology 1984;18:17-22.

31. Mitchell PL, Moffat DA, Fallside F (1984) Computer aided tinnitus characterisation. Clinical Otolaryngology 1985;9:35-4.

32. Shone GR, Moffat DA. Otoadmittance measurements in the diagnosis of otosclerosis. Journal of Laryngology and Otology 1986;100:149-154.

33. Croxson GR, Moffat DA, Baguley DM. Bruns bidirectional nystagmus in cerebello-pontine angle tumours. Clinical Otolaryngology & Allied Sciences 1988;13(2): 153-157.

34. Berrios GE, Ryley JP, Garvey TPN, Moffat DA. Psychiatric morbidity in subjects with inner ear disease. Clinical otolaryngology 1988;13:259-266.

35. Baguley DM, Moffat DA. Bruns bidirectional nystagmus in one hundred cases of acoustic neuroma. British Journal of Audiology 1988;22,3:227.

36. Baguley DM, Moffat DA. Disposable electrodes in auditory brainstem response audiometry. British Journal of Audiology 1988;22,3:219-221.

37. Moffat DA. The surgery of vertigo. Clinical Physics and Physiological Measurement 1988;9:282.

38. Pfleiderer A, Moffat DA.The Fascia Form Graft: A technique for the repair of large perforations of the tympanic membrane. Clinical Otolaryngology 1988;13:427-434.

39. Moffat D. The surgery of vertigo. Practitioner 1988;22;232(1459):1322-4.

40. Moffat DA, Hardy DG, Baguley DM. The Strategy and benefits of acoustic neuroma searching. Journal of Laryngology and Otology 1989;03:51-59.

41. Croxson GR, Moffat DA, Hardy DG, Baguley DM. The tole of post-operative electro-neuronography in predicting facial nerve recovery after acoustic neuroma removal: A pilot study. Journal of Laryngology and Otology 1989;103:60-62.

42. Moffat DA, Croxson GR, Baguley DM, Hardy DG. Facial nerve recovery after acoustic neuroma removal. Journal of Laryngology and Otology 1989;103:169-172.

43. Nigam A, Moffat DA, Varley EWB. Benign paroxysmal positional vertigo resulting from surgical trauma. Journal of Laryngology and Otology 1989;103:203-204.

44. McFerran DJ, Baguley DM, Moffat DA. Aberrant reinervation of the stapedius muscle following facial palsy. Journal of Laryngology and Otology 1989;103:205-206.

45. Moffat DA, Hardy DG. The early diagnosis and removal of acoustic neuroma: Is it cost effective? Journal of The Royal Society of Medicine 1989; 82(6):329-332.

46. Baguley DM, Moffat DA, Tsui YN. Audiological findings in medial and lateral acoustic neuromas. British Journal of Audiology 1989;23(2):158-159.

47. Moffat DA, Baguley DM, Hardy DG, Tsui YN. Contralateral ABR abnormalities in acoustic neuroma. Journal of Laryngology and Otology 1989;103:835-838.

48. Moffat DA, Harries MU, Baguley DM, Hardy DG. Unterberger's stepping test in the diagnosis of acoustic neuroma. Journal of Laryngology and Otology 1989;103:839-841.

49. Hardy DG, MacFarlane R, Baguley DM, Moffat DA. Facial nerve recovery following acoustic neuroma surgery. British Journal of Neurosurgery 1989;3:675-680.

50. Hardy DG, MacFarlane R, Baguley DM, Moffat DA. Surgery for acoustic neuroma: An analysis of one hundred translabyrinthine operations. Journal of Neurosurgery 1989;71:799-804.

51. Moffat DA, Hardy DG. Surgical management of large glomus jugulare tumours: The infra and transtemporal approach. Journal of Laryngology and Otology 1989;103: 1167-1180. Also presented as a Poster Paper at the 9th International Symposium of Neurological Surgery New Delhi, India Oct 9-13 1989.

52. Moffat DA, Baguley DM, Evans RA, Hardy DG. Mastoid ache in acoustic neuroma. Journal of Laryngology and Otology 1989;103:1043-1044.

53. Evans RA, Harries MLL, Baguley DM, Moffat DA. Reliability of the House and Backmann Brading System for Facial Palsy. Journal of Otology and Laryngology 1989;103:1045-1046.

54. Moffat DA, Cumberworth, VL, Baguley DM. Endolymphatic Hydrops Precipitated by haemodialysis:A case report.Journal of Laryngology and Otology 1990;104:641-642.

55. Chalstrey S, Pfleiderer AG, Moffat DA. The persisting Incidence and mortality of sinogenic cerebral abscess: A continuing reflection of late clinical diagnosis. Journal of Royal Society of Medicine 1991;84:193-195.

56. Jayaram M Baguley DM, Moffat DA. A speech in noise test for cochlear-retrocochlear differential diagnosis. Nimhans Journal 1991;9(1):19-22.

57. Farrell ML, Harries MLL, Baguley DM, Moffat DA. Bilateral acoustic neuroma: Post operative hearing in the contralateral ear. Journal of Laryngology and Otology 1991; 105:769-771.

58. Baguley DM, Jayaram M, Moffat DA. Prospective analysis of a screening procedure for acoustic neuroma. Nimhans Journal 1991;9 (1):13-1.

59. Moffa DA, Toner J, Baguley DM, Hardy DG. Posterior fossa vestibular neurectomy. Journal of Laryngology and Otology 1991;105 (12):1002-1003.

60. Baguley DM, Jayaram M, Moffat DA. Prospective analysis of a screening procedure for acoustic neuroma. Nimhans Journal 1991;9(1):13-18.

61. Jayaram M, Baguley DM, Moffat DA. Speech in noise: A practical test procedure. Journal of Laryngology and Otology 1992;106:105-110.

62. Blamires, TL, Friedman I, Moffat DA. Von Hippel Lindau disease with an invasive choroid plexus tumour Presenting as a middle ear mass. Journal of Laryngology and Otology 1992;106:329-331.

63. Cunliffe IA, Moffat DA, Hardy DG, Moore AT. Bilateral optic sheath meningioma in a patient with neurofibromatosis Type 2 . British Journal of Ophthalmology 1992;76(5): 310-312.

64. Baguley DM, Moffat DA, Hardy DG. What is the effect of translabyrinthine acoustic neuroma removal upon tinnitus? Journal of Laryngology and Otology 1992;106(4): 329-331.

65. Moffat DA, Baguley DM, Harries MLL, Atlas M, Lynch CA. Bilateral electrocochleographic findings in unilateral Meniere's disease. Otolaryngology - Head and Neck Surgery 1992;107:370-373.

66. Atlas MD, Moffat DA, Hardy DG. Petrous apex cholesteatoma; diagnostic and treatment dilemmas. Laryngoscope 1992;102:1363-1368.

67. Hardy DG, MacFarlane R, Moffat DA. Wound closure after acoustic neuroma surgery. British Journal of Neurosurgery 1993;7:171-4.

68. Moffat DA, Saunders JE, McElveen Jr JT, McFerran D, Hardy DG. Unusual cerebellopontine angle tumours. Journal of Laryngology and Otology 1993;107:1087-1098.

69. Moffat DA, Golledge J, Baguley DM, Hardy DG. Clinical correlates of acoustic neuroma morphology. Journal of Laryngology and Otology 1993;107(4):290-294.

70. Rudd MJ, Harries ML, Lynch CA, Moffat DA. Hearing loss fluctuating with blood glucose levels in Meniere's disease. Journal of Laryngology and Otology 1993;107: 620-622.

71. Wareing M, Irving RJ, Moffat DA. Parapharyngeal tumour presenting as recurrent uvular oedema. Journal of Laryngology and Otology 1993;107:640-641

72. Irving RM, Moffat DA, Hardy DG, Barton DE, Xuereb JH, Maher ER. Molecular genetic analysis of the mechanism of tumourigenesis in acoustic neuroma. Archives of Otolaryngology & Head Neck Surgery 1993;119:1222-8.
Winner of Oto-rhino-laryngological Research Society Prize 1994.

73. Moffat DA. Acoustic neuroma: triumphs outnumber the disasters. Br J Hosp Med 1993;50(1):69-70.

74. Moffat DA, Irving RM, Hardy DG. Sudden deafness in acoustic neuroma. Journal of Laryngology and Otology 1994;108(2):116-9.

75. Moffat DA**,** Ramsden RT. Intracanalicular acoustic neuromas: The case for early surgery. Clinical Otolaryngology Editorial 1994;19(1):1-2.

76. Irving RM, Moffat DA, Hardy, DG, Barton DE, Xuereb JH, Maher ER. Somatic NF2 gene mutations in familial and non-familial vestibular schwannoma. Human Molecular Genetics 1994;3(2):47-50.

77. Moffat DA**,** Gray RF, Irving RM. Mastoid obliteration using bone pate. Clinical Otolaryngology 1994;19(2):149-57.

78. Irving RM, Gray RF, Moffat DA. The troublesome mastoid cavity: Bone pate obliteration and **r**evision mastoidectomy compared. Clinical Otolaryngology 1994; 19(2):158-60.

79. Moffat DA. Endolymphatic sac surgery: analysis of 100 operations. Clinical Otolaryngology 1994;19(3):261-6

80. Von Blumenthal H, Fisher EW, Adlam DM, Moffat DA. Surgical emphysema : a novel complication of aural exostosis surgery. Journal of Laryngology and Otology 1994; 08(6): 490-1

81. Baguley DM, Irving, RM, Hardy DG, Harada T, Moffat DA. Audiological findings in glomus tumours. British Journal of Audiology 1994;28(6):291-7.

82. Irving RM, Moffat DA, Maher ER. Genetics of familial and non-familial skull base tumours. Clinical Otolaryngology 1995;20(1):5-11.

83. Irving RM, Beynon GJ, Viani L, Hardy DG, Baguley DM, Moffat DA**.** The patient's perspective after vestibular schwannoma removal: quality of life and implications for management. American Journal of Otology 1995;16 (3);331-7

84. Irving RM, Viani L, Hardy DG, Baguley DM, Moffat DA. Nervus intermedius function after vestibular schwannoma removal: clinical and pathophysiological mechanism. Laryngoscope 1995;105:809-13.

85. Moffat DA, Ballagh R. Rare tumours of the cerebellopontine angle. Clinical Oncology of Royal College of Radiologists 1995;7(1):28-41.

86. Morris DP, Ballagh RH, Hong A, Baguley DM, Moffat DA, Hardy DG. Thrombosed posterior-inferior cerebellar artery aneurysm: a rare cerebello-pontine angle tumour. Journal of Laryngology and Otology 1995;109 (5):429-30.

87. Moffat DA, Hardy DG, Irving RM, Viani L, Beynon GJ, Baguley DM. Referral patterns in vestibular schwannomas. Clinical Otolaryngology 1995;20 (1):80-3.

88. Moffat DA**,** Irving RM. The molecular genetics of vestibular schwannoma. Journal of Laryngology and Otology 1995;109(5):381-4.

89. Grey PL, Moffat DA**,** Hardy DG, Baguley DM, Beynon GJ. Audio-vestibular results after surgery for cerebello-pontine angle meningiomas. American Journal of Otology 1996; 17(4):634-8.

90. Harada T, Irving RM, Xuereb JH, Barton DE, Hardy DG, Moffat DA, Maher ER. Molecular genetic investigation of the neurofibromatosis type 2 (NF2) tumor suppessor gene in sporadic meningioma. Journal of Neurosurgery 1996;84(5):847-51.

91. Moffat DA, Hardy DG, Grey PL, Baguley DM. The operative learning curve and its effect on facial nerve outcome in vestibular schwannoma surgery. American Journal of Otology 1996;17(4):643-7.

92. Grey PL, Moffat DA, Hardy DG. Surgical results in unusual cerebellopontine angle tumours. Clinical Otolaryngology 1996;21(3):237-43.

93. Grey PL, Moffat DA, Palmer CR, Hardy DG, Baguley DM. Factors which influence the facial nerve functional outcome in vestibular schwannoma surgery. Clinical Oto-laryngology 1996;21(5):409-13.

94. Whitfield PC, Grey PL, Hardy DG, Moffat DA. The surgical management of patients with glomus tumours of the skull base. British Journal of Neurosurgery 1996;10(4):343-50

95. Lau DPC, Goddard MJ, Bottrill ID, Moffat DA. Epithelial-myoepithelial carcinoma of the parotid gland. An unusual cause of ear canal stenosis. Journal of Laryngology and Otology 1996;110(5):493-95.

96. Moffat DA, Grey PL, Ballagh RH, Hardy DG. Extended temporal bone resection for squamous carcinoma. Otolaryngology-Head and Neck Surgery 1997;116:617-23.

97. Baguley DM, Beynon GJ, Grey PL, Hardy DG, Moffat DA. Audio-vestibular findings in cerebello-pontine angle meningioma. Journal of Laryngology and Otology 1997;111 (11)**:**1022-6.

98. Lau DP, Wharton SB, Antoun NM, Bottrill ID, Moffat DA. Chondrosarcoma of the petrous apex. Dilemmas in diagnosis and treatment. Journal of Laryngology and Otology 1997;111 (4):368-71

99. Irving RM, Moffat DA, Hardy DG, Barton DE, Xuereb JH, Holland FJ, Maher ER. A molecular, clinical, and immunohistochemical study of vestibular schwannoma. Otolaryngology-Head and Neck Surgery 1997;116(4):426-30.

100. Moffat DA. Endolymphatic mastoid shunt surgery in unilateral Meniere's disease. Ear Nose and Throat Journal 1997;76(9):642-3,647-8,650-1.

101. Irving RM, Harada T, Moffat DA, Hardy DG, Whittaker JL, Xuereb JH, Maher ER. Somatic neurofibromatosis type 2 gene mutations and growth characteristics in vestibular schwannoma. American Journal of Otology 1997;18(6):754-60

102. Bath AP, Beynon GJ, Moffat DA, Baguley DM. Effective anaesthesia for transtympanic electrocochleography. Auris Nasus Larynx 1998;25(2):137-41.

103. Hollingworth W, Bell MI, Dixon AK, Antoun NM, Moffat DA, Todd CJ. Measuring the effects of imaging in patients with possible cerebellopontine angle lesions: A Four-Center study. Academic Radiology 1998;5(2):s306-9.

104. da Cruz M, Ahmed SM, Moffat DA. An alternative method for dealing with CSF fistulae in inner ear deformities. American Journal of Otology 1998;19(3):288-91.

105. Moffat DA, Baguley DM, Beynon GJ, da Cruz M. Clinical acumen and vestibular schwannoma. American Journal of Otologyn 1998;19(1):82-7.

106. Moffat DA, da Cruz M, Batten T, Hardy DG. Use of autologous osteocyte containing bone pate for closure of tegmental defects. American Journal of Otology 1998;19(6): 819-23.

107. Arullendren P, Jani P, Moffat DA, Baglin T. Internal jugular vein thrombosis in a patient with factor V Leiden mutation. Journal of Laryngology and Otology 1998; 112(4):383-6.

108. Baguley DM, Beynon G,J Moffat DA. An Investigation of the effect of structured teaching on a group of tinnitus patients after vestibular schwannoma removal. American Journal of Otology 1998;19(6):828-833.

109. Moffat DA**,** da Cruz MJ, Baguley DM, Beynon G,J Hardy DG. Hearing preservation in solitary vestibular schwannoma surgery using the retrosigmoid approach. Otolaryngology Head and Neck Surgery 1999;121(6):781-8.

110. da Cruz MJ, Moffat DA**,** Baguley DM, Beynon GJ, Hardy DG. Does choice of hearing selection criteria and reporting criteria affect the hearing preservation rate in vestibular schwannoma surgery? Otolaryngology Head and Neck Surgery 1999; 121(3):313-7.

111. Reece PH, Higgins N, Hardy DG, Moffat DA. An aneurysm of the petrous internal carotid artery. Journal of Larygology and Otology 1999;13(1):55-7.

112. Monem SA, Moffat DA, Frampton MC. Carcinoma of the ear: a case report of a possible association with chlorinated disinfectants. Journal of Laryngology and Otology 1999; 113(11):100.

113. Laing RJ, Smielewski P, Czosnyka M, Quaranta N, Moffat DA**.** A study of perioperative lumbar CSF pressure in patients undergoing acoustic neuroma (vestibular schwannoma) surgery. Skull Base Surgery 2000;10**:**179-185.

114. Shaida AM, McFerran DJ, da Cruz M, Moffat DA, Hardy DG. Cavernous haemangioma of the internal auditory canal. Journal of laryngology and Otology 2000; 114(6):453-455.

115. da Cruz MJ, Hardy DG, Moffat DA. Post-operative quality of life in vestibular schwannoma patients measured by the SF36 Health Questionnaire. Laryngoscope 2000;110(1):151-5.

116. da Cruz MJ, Hardy DG, Moffat DA. Clinical presentation of a group of NF2 patients to a tertiary referral skull base unit. British Journal of Neurosurgery 2000;14(2):101-4.

117. Beynon G, Baguley DM, Moffat DA, Irving RM. Positional vertigo as a first symptom of a cerebellopontine angle cholesteatoma: a case report. Ear Nose and Throat Journal 2000;79(7):508-10.

118. Forshaw MA, Hardy DG, Higgins Rescan, Moffat DA. Rupture of an internal carotid artery aneurysm in the petrous temporal bone. British Journal of Neurosurgery 2000;14 (5):479-482.

119. Stoddart RL, Baguley DM, Beynon GJ, Chang P, Moffat DA. Magnetic resonance imaging results in patients with central electronystagmography findings. Clinical Otolaryngology 2000;25(4):293-297.

120. Brewis C, Bottrill ID, Wharton SB, Moffat DA. Glomus jugulare tumour with metastases to cervical lymph nodes. Journal of Laryngology and Otology 2000;114(1):67-9.

121. Brewis C, Bottrill ID, Wharton SB, Moffat DA. Metastases from glomus jugulare tumours. Journal of Laryngology and Otology 2000;114(1):17-23.

122. Chiossone-Kerdel JA, Baguley DM, Stoddart RL, Moffat DA. An investigation of the audiological handicap associated with unilateral sudden sensorineural hearing loss. The American Journal of Otology 2000;21**:**645-651.

123. Chang P, Moffat DA, Baguley DM. Universal neonatal screening: a current view. Australian Journal of Otolaryngology 3 (5):543-550.

124. Chang P, Moffat DA. Neurofibromatosis type 2: a 15 year experience - a current review. Australian Journal of Otolaryngology 2000 3 (5): 528-42.

125. McFerran DJ, Mitchell TE, Baguley DM, Moffat DA. An experimental investigation of the resolution of tympanometry for microperforations of the tympanic membrane. Journal of Laryngology and Otology 2001;115(9):694-8.

126. Humphriss RL, Baguley DM, Peerman S, Mitchell TE, Moffat DA. Vestibular rehabilitation: an outcome study. Physiotherapy 2001;87(7):368-373.

127. Moffat DA. Moffat classification of facial nerve function. A supplemental issue for the 11th Keio University International Symposium for Life Sciences and Medicine. Consensus Meeting on Systems for Reporting Results in Acoustic Neuroma Keio Journal of Medicine; 50(4):38-39.

128. Martinez Devesa PM, Wareing MJ, Moffat DA. Meningioma of the internal auditory canal. Journal of Laryngology and Otology 2001;115(1):48-9.

129. Humphriss RI, Baguley DM, Peerman S, Mitchell TE, Moffat DA. Vestibular Rehabilitation:An Outcome Study. Physiotherapy 2001;87,7, 368-73.

130. Moffat DA, Quaranta N, Baguley DM, Hardy DG, Chang P. Staging and management of primary cerebellopontine cholesteatoma. Journal of Laryngology and Otology 2002; 116:340-345.

131. Chiossone-Kerdel JA, Quaranta N, Baguley DM, Moffat DA. Eustachian tube function after translabyrinthine vestibular schwannoma surgery. Clinical Otolaryngology 2002; 27(4):263-6.

132. Shaida AM, Moffat DA. Schwannomatosis in a child: or early neurofibromatosis type 2. Journal of Laryngology and Otology 2002; 116:551-55.

133. Quaranta N, Chang P, Moffat DA. Unusual MRI appearance of an intracranial cholesteatoma extension: The "Billiard Pocket Sign". Ear, Nose and Throat Journal 2002;81(9): 645-647.

134. Baguley DM, Axon P, Winter IM, Moffat DA. The effect of vestibular nerve section upon tinnitus: a review. Clinical Otolaryngology 2002;27(4):219-26.

135. Humphriss RL, Baguley DM, Moffat DA. Change in Dizziness Handicap following vestibular schwannoma excision. Journal of Vestibular Research 2002;111:280-281.

136. Moffat DA, Quaranta N, Baguley DM, Hardy DG, Chang P. Management strategies in neurofibromatosis type 2. European Archives of Otorhinolaryngology 2003;260(1):12-8.

137. Humphriss RL, Baguley DM, Sparkes V, Peerman SE, Moffat DA. Contraindications to the Dix-Hallpike manoevre: a multidisciplinary review. International Journal of Audiology 2003;42 (3):166-17.

138. Moffat DA, Quaranta N, Chang P. Management of the high jugular bulb in trans-labyrinthine surgery. Laryngoscope 2003;113(3)**:**580-2.

139. Humphriss RL, Baguley DM, Moffat DA. Change in dizziness handicap following vestibular schwannoma excision. Otology & Neurotology 2003;24(4): 661-5.

140. Quaranta N, Chang P, Baguley DM, Moffat DA**.** Audiological presentation of cerebello-pontine angle cholesteatoma. Journal of Otolaryngology 2003;32(4):217-21.

141. Kanzaki J,Tos M, Sanna M, Moffat DA. New and modified reporting systems from the consensus meeting on systems for reporting results in vestibular schwannoma. Otology & Neurotology 2003;24**:**642-649.

142. Humphrissm RL, Baguley DM, Moffat DA**.** Head-shaking nystagmus in patients with a vestibular schwannoma. Clinical Otolaryngology Allied Sciences 2003;28(6)**:**514-9.

143. Baguley DM, Jones SEM, Moffat DA. A small vestibular schwannoma arising from the inferior vestibular nerve. Journal of Laryngology and Otology 2003;117(6)**:**498-500.

144. Kanzaki J, Tos M, Sanna M, Moffat DA, Monsell EM, Berliner KI. New and modified reporting systems from the consensus meeting on systems for reporting results in vestibular schwannoma. Otology & Neurotology 2003;24(4):642-8; discussion 648-9.

145. Moffat DA, Chang P, Quaranta N, Baguley DM, Hardy DG. Management strategies in neurofibromatosis type 2. European Archives of Otorhinolaryngology 2003;260(1):12-8.

146. Moffat DA, Wagstaff SA. Squamous cell carcinoma of the temporal bone. Curr Opin Otolaryngology and Head Neck Surgery 2003;11(2):107-11.

147. Raghu M, Moumoulidis I, De R, Moffat DA. Chondrosarcomas of the temporal bone : presentation and management. Journal of Laryngology and Otology 2004;118(7):551-5.

148. Humphriss RL, Baguley DM, Axon PR, Moffat DA. Change in Hearing Handicap after Translabyrinthine Vestibular Schwannoma excision. Otology & Neurotology 2004; 25(3):371-8.

149. Moffat DA, Jones SEM, Mahendran S, Humphriss R, Baguley DM. Referral patterns in vestibular schwannomas – 10 years on. Clinical Otolaryngology Allied Sciences 2004; 29(5)**:** 515-7.

150. Phillips JS, Baguley DM, Patel H, Moffat DA. Tinnitus evoked by cutaneous stimulation. Neurology 2004;9;63(9):1756.

151. De R, Moffat DA. The GP's role in acoustic neuroma. Practitioner 2004;248(1660):501, 503-4,506.

152. Moffat DA**,** Wagstaff SA, Hardy DG.The outcome of radical surgery and postoperative radiotherapy for squamous carcinoma of the temporal bone. Laryngoscope 2005; 115(2):341-7.

153. Baguley DM, Jones S, Wilkins I, Axon PR, Moffat DA. The inhibitory effect of intravenous lidocaine infusion upon tinnitus after translabyrinthine removal of vestibular schwannoma: a double blind, placebo-controlled crossover study. Otology & Neurotology 2005;26(2):169-76.

154. Durvasula VS, De Baguley DM, Moffat DA. Laser excision of glomus tympanicum tumours: long-term results. European Archives of Otorhinolaryngology 2005;262(4): 325-7.

155. Sharp M, Macfarlane R, Hardy D, Jones S, Baguley D, Moffat D. Team working to improve outcome in vestibular schwannoma surgery. British Journal of Neurosurgery 2005;19(2):122-127.

156. Baguley DM, Humphriss R, Axon PR, Moffat DA. Change in tinnitus handicap after translabyrinthine vestibular schwannoma excision. Otology & Neurotology 2005; 26(5):1061-3.

157. Evans DGR, Baser ME, O'Reilly B, Rowe J, Gleeson M, Saeed S, King A, Huson SM, Kerr R, Thomas N, Irving R, Macfarlane R, Ferner R, McLeod R, Moffat D, Ramsden R. Management of the patient and family with neurofibromatosis 2: a consensus Statement. British Journal of Neurosurgery 2005;19(1):5-12.

158. Moffat DA, Durvasula, VSP, Stevens-King A, De R, Hardy DG. Outcome following retrosigmoid microvascular decompression of the facial nerve for hemi-facial spasm. Journal of Laryngology and Otology 2005;119(10):779-83.

159. Moumoulidis I, Brewis C, Moffat DA. Simultaneous contralateral vestibular schwannoma and glomus jugulare tumor: a case report**.** Ear Nose and Throat Journal 2005;84(5):290-2.

160. Cross JJ, Baguley DM, Antoun NM, Moffat DA, Prevos AT. Reproducibility of volume measurements of vestibular schwannomas – a preliminary study. Clinical Oto-laryngology 2006;31(2):123-9.

161. Baguley DM, Humphriss RL, Axon PR, Moffat DA. The Clinical Characteristics of Tinnitus in Patients with Vestibular Schwannoma. Skull Base 2006;16 (2):49-58.

162. Baguley DM, Moffat DA, Ramsden RT. Otology and audiology in the UK: isolated or integrated practice. Clinical Otolaryngology 2006;31(1):4-5.

163. Baguley DM, Phillips J, Humphriss Rl, Jones S, Axon PR, Moffat DA. The prevalence and onset of gaze evoked modulation of tinnitus and increased sensitivity to noise after translabyrinthine vestibular schwannoma excision. Otology & Neurotology 2006; 27(2):220-4.

164. Martinez D, Mitchell TE, Scott IS, Moffat DA. Malignant peripheral nerve sheath tumours of the head and neck: Two cases and a review of the literature. Ear Nose and Throat Journal 2006;(6):85 (6):392-6.

165. Malata CM, Tehrani H, Kumiponjera D, Hardy DG, Moffat DA. Use of anterolateral thigh and lateral arm fasciocutaneous free flaps in lateral skull base reconstruction. Annals of Plastic Surgery 2006;57(2):169-175.

166. Moffat D, De R, Hardy D, Moumoulidis I. Surgical management of trigeminal neuromas: a report of eight cases. Journal of Laryngology and Otology 2006;120(8):631-7.

167. Moumoulidis I, De R, Ramsden R, Moffat D. Unusual otological manifestations in Camurati Engelmann's Disease. Journal of Laryngology and Otology 2006;120(10): 1892-5.

168. Humphriss R, Baguley DM, Axon PR, Moffat DA**.** Preoperative audiovestibular handicap in patients with vestibular schwannoma. Skull Base 2006;16(4):193-9.

169. Moncrieff MD, Hamilton SA, Lamberty GH, Malata CM, Hardy DG, Macfarlane R, Moffat DA. Reconstructive options after temporal bone resection for squamous cell carcinoma. Journal of Plastic Reconstructive Aesthetic Surgery 2007;60(6):607-14.

170. Quaranta N, Baguley DM, Moffat DA. Change in hearing and tinnitus in conservatively managed vestibular schwannomas. Skull Base 2007;17(4):223-8.

171. Jones SEM, Bagule, DM, Moffat DA. Are facial nerve outcomes worse following surgery for cystic vestibular schwannoma? Skull Base 2007;17(5):281-4.

172. Mani N, Sudhoff H, Rajagopal S, Moffat D, Axon P. Cranial nerve involvement in malignant external otitis: implications for clinical outcome. Laryngoscope 2007; 117(5):907-10.

173. Sudhof H, Rajagopal S, Baguley DM, Ebmeyer J, Schmelzer A, Schreiber S, Moffat DA. A critical evaluation of the evidence on a causal relationship between Helicobacter pylori and otitis media with effusion. Journal of Laryngology and Otology 2008;122(9):905-11.

174. Moffat DA, Jones SEM, Smith W. Petrous temporal bone cholesteatoma: A new classification and long-term surgical outcomes. Skull Base 2008;18(2);107-15.

175. Sudhoff H, Rajagopal S, Mani N, Moumoulidis I, Axon PR, Moffat D. Usefulness of CT scans in malignant external otitis: effective tool for the diagnosis, but of limited value in predicting outcome. European Archives of Otorhinolaryngology 2008;265(1):53-56.

176. Del Pero MM, Moffat D, Sudhoff H. Unusual presentation of temporal bone involvement in Churg-Strauss Syndrome. Journal of Otology and Laryngology 2008;122(4):425-7.

177. Prasai A, Jones SE, Cross J, Moffat DA. A facial nerve schwannoma masquerading as a vestibular schwannoma. Ear Nose Throat Journal 2008;87(9):E4-6.

178. Del Pero M, Lloyd SKW, Moffat DA. Hearing improvement in a growing vestibular schwannoma. Skull Base 2009;19(2):159-62.

179. Lloyd SKW, Baguley DM, Butler K, Donnelly N, Moffat DA**.** Bruns' nystagmus in patients with vestibular schwannoma. Otology & Neurotology 2009;30(5):625-8.

180. Masterson L, Del Pero MM, Donnelly N, Moffat DA, Rytina E. Immunoglobulin G4 related systemic sclerosing disease involving the temporal bone. Journal of Laryngology and Otology 2010;124(10):1106-10.

181. Lloyd SK, Kasbekar AV, Baguley DM, Moffat DA. Audiovestibular factors influencing quality of life in patients with conservatively managed sporadic vestibular schwannoma. Otology & Neurotology 2010;31(6):968-76.

182. Kasbekar AV, Scoffings DJ, Kenway B, Cross J, Donnelly N, Lloyd SW, Moffat D, Axon P. Non echo planar, diffusion –weighted magnetic resonance imaging (periodically rotated overlapping parallel lines with enhanced reconstruction sequence) compared with echo planar imaging for the detection of middle-ear cholesteatoma. Journal of Laryngology and Otology 2010;29:1-5.

183. Joshi A, Jiang D, Singh P, Moffat D. Skull base presentation of multiple myeloma. Ear Nose Throat Journal 2011;90(1):E6-9.

List of abbreviations

AAO-HNS	American academy of otolaryngology - head and neck surgery
AAOO	American academy of ophthalmology and otolaryngology
ABI	Auditory Brainstem Implant
AICA	Anterior Inferior Cerebellar Artery
BKB	Bamford-Kowal-Bench
CI	Confidence Interval
CI	Cochlear Implant (in context)
Cm	centimetre
CN	Cranial Nerve
CPA	Cerebello-Pontine Angle
CSF	Cerebrospinal Fluid
CT	Computed Tomography
dB	Decibels
dBHL	Hearing level in decibels
DVT	Deep Venous Thrombosis
EAC	External Auditory Canal
ETBR	Extended Temporal Bone Resection
FP	Facial Paresis
Gadolin	Gadolinium DTPA
Gy	Gray – measure of radiotherapy dosage
HB	House – Brackmann classification or grading of facial nerve function
HL	Hearing Level
IAC	Internal Auditory Canal
IC	Intracranial
ICTD	Maximum intracranial tumour diameter
L	Left
LINAC	Linear accelerator
LTBR	Lateral Temporal Bone Resection
Mo	Month
M0-1	Presence of metastatic spread
MCF	Middle Cranial Fossa
MDT	Multidisciplinary team
MF	Middle Fossa
MRI	Magnetic Resonance Imaging
Mm	millimetre
n=	number in the series
N0-2	Lymph node involvement by tumour
NF2	Neurofibromatosis type 2
NIH	National Institute of Health
OR	Odds Ratio
p-value	a measure of statistical significance.
PACS	Picture Archiving and Communications System
PICA	Posterior Inferior Cerebellar Artery
PTA	Pure Tone Audiogram
Q	locus on chromosome (DNA sequence)
QoL	Quality of Life
R	Right

RL	Retrolabyrinthine
RS	Retrosigmoid
SCC	Squamous Cell Carcinoma
SD	Standard Deviation from the mean
SDS	Speech Discrimination Score
SF36	Social Function quality of life questionnaire
Stage I-IV	Stage of squamous cell carcinoma
T	Tinnitus
T1-4	Extent of tumour spread at primary site
TNM	Tumour staging at primary site, lymph node involvement, metastatic spread
T-statistic	Test statistic
TT	Transtemporal
V 1-3	Branches of the fifth cranial nerve or trigeminal
VP	Ventriculo-Peritoneal
VS	Vestibular Schwannoma
W&W	Watch Wait and rescan
Y	year
Yr	year
<n	less than a number (n=a number)
>n	more than a number (n=a number)

CI Confidence interval is a particular kind of interval estimate of a population parameter used to indicate the reliability of an estimate.

p-value is the probability of obtaining a test statistic at least as extreme as the one actually observed, assuming that the null hypothesis is true.