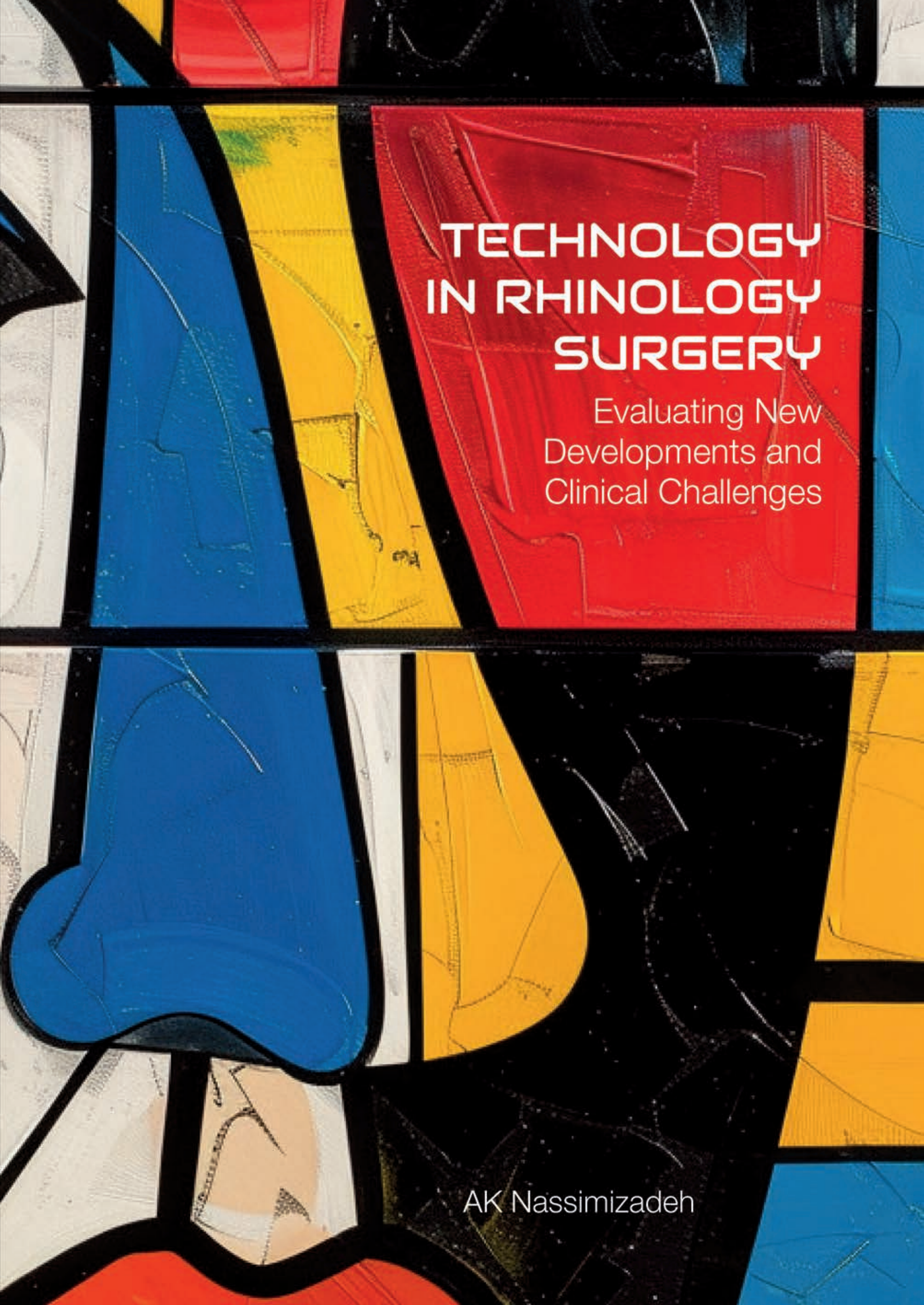

TECHNOLOGY IN RHINOLOGY SURGERY

Evaluating New Developments and Clinical Challenges

AK Nassimizadeh

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Printed by Proefschriftspecialist | proefschriftspecialist.nl

Layout and design: Ninke van Wiggen, persoonlijkproefschrift.nl

university of
groningen

Technology in Rhinology Surgery - Evaluating New Developments and Clinical Challenges

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
Rector Magnificus Prof. J.M.A. Scherpen
and in accordance with
the decision by the College of Deans.

This thesis will be defended in public on

Wednesday 25 September 2024 at 12.45 hours

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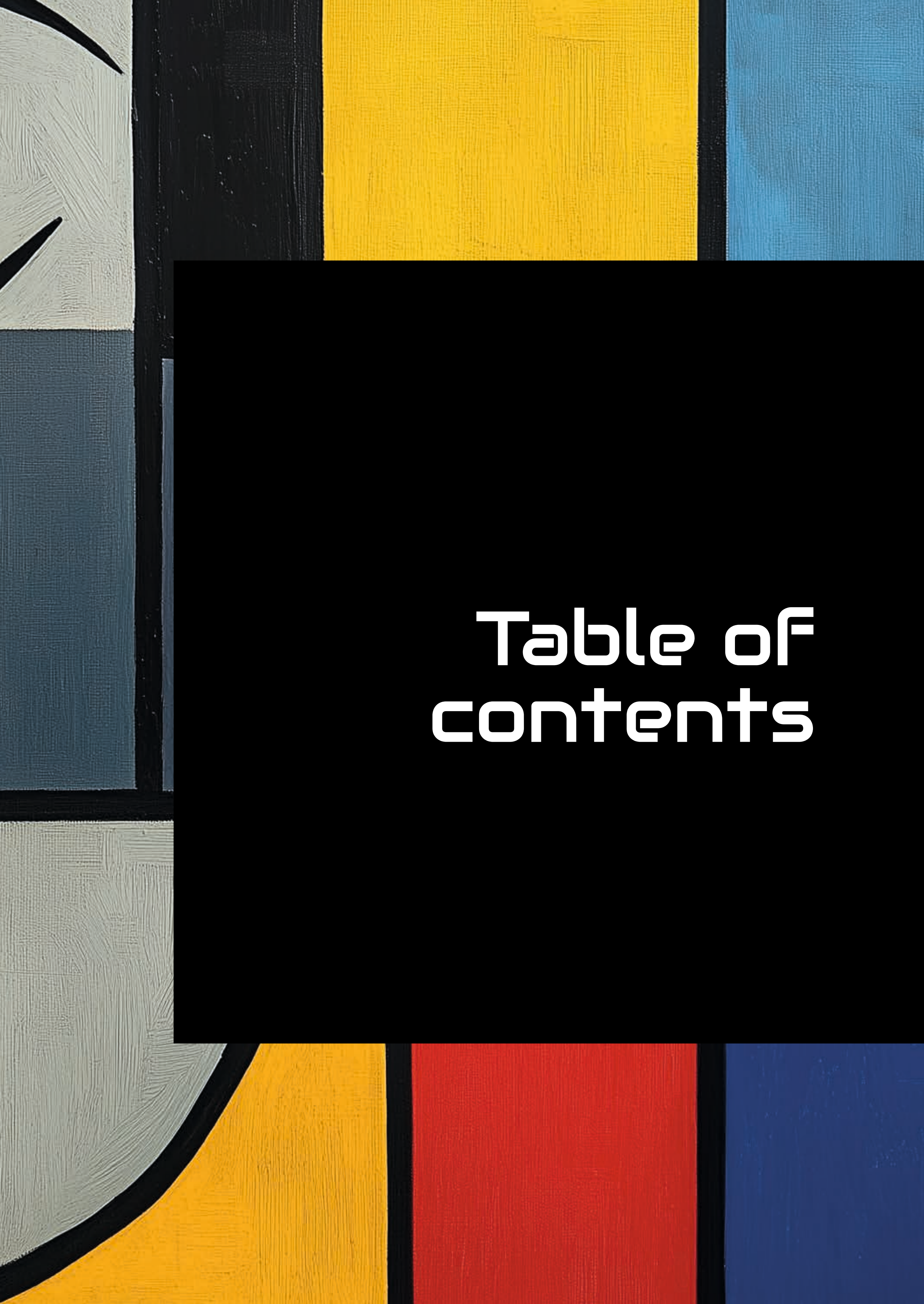

Table of contents

Table of Contents

1

Introduction

Introduction

In recent years, the field of endoscopic endonasal surgery has been propelled by rapid technological progress. The evolution of applied sciences has impacted both the diagnosis and treatment of nasal and sinus pathology. The first transformative shift came with the advent of minimally invasive endoscopic techniques, now aided by a groundswell of assistant technology.

Historically, endoscopy was first described by Hippocrates in Greece between 460 and 375 BC.[1] This work continued in the late 19th and early 20th centuries.[2-4] However, it was not until 1945 that Karl Storz began producing instruments for otorhinolaryngologists. Though modest in nature, the instruments used miniature lamps to visualise inside the human body through an endoscope. Despite its use in over 400 operations, the visual quality ascertained through Storz's work alone would not allow appropriate visualisation and access to the intricate anatomy of the nasal cavity and sinuses. Harold Hopkins pursued this limitation initially through fibre-optics, but fibre breaks, poor light transmittance and image resolution issues plagued these early designs. Hopkins found a solution in the late 1960s, with the placement of self-aligning glass rods in the air spaces between the lenses. This became commonly known as the Hopkins rod. A combination of both Storz and Hopkins work, alongside further modifications, created the concept of the modern endoscope.

Endoscopic surgery allowed direct access to anatomical locations, a reduction in retraction injury and minimised damage to neurovascular structures. Aesthetically, endoscopic surgery reduced the necessity for external access, as well as decreased patient morbidity and shorter postoperative recovery periods.[5]

Despite revolutionising the field, current endoscopic endonasal techniques involve the surgeon working within a two-dimensional (2D) environment. With intraoperative safety largely dependent on precise anatomical visualisation and recognition, the lack of stereopsis impairs depth perception. Experienced surgeons compensate for this with visual and tactile feedback, dynamic movements of the scope, light and shadows, and detailed anatomical knowledge. However, these compensatory mechanisms have been found, at times, to be misleading.[6-8]

This thesis evaluates the introduction of assistant technology and investigates new developments within this field. In order to interpret the outcomes of the present thesis, it is important to have a foundational knowledge of sinonasal anatomy.

Sinonasal Anatomy and Physiology

Sinonasal anatomy comprises of a complex combination of structures that interact to provide appropriate nasal function. The bony-cartilaginous septum divides the nasal cavity into two halves. In conjunction with the superior, middle and inferior turbinates, this framework facilitates airflow dynamics. Nasal airflow is regulated through alternating contraction and relaxation of the smooth muscles, which modulates resistance and direction of nasal inspiration. In addition to this, the highly vascularised nature of the turbinates contributes towards air conditioning through heat and moisture exchange.[9,10]

The nasal cavity is lined with pseudostratified columnar ciliated epithelium, alongside goblet cells, and a vascular lamina propria which contains serous and mucous producing glands. These work synergistically to filter, humidify and warm inspired air.[11] The mucosa is bound to underlying periosteum to form the Schneiderian membrane.

Homeostatic and immune system elements are consistent between the upper and lower respiratory tract, and form the basis of the unified airway.[12,13] Mucociliary clearance provides protection against pollutant, allergen and particle inhalation, and is aided by the cilia. Inspired particles are trapped in a thick mucous layer, and then propelled towards the nasopharynx through co-ordinated movements of the cilia. The rate is approximately 6mm per minute.[11]

Four pairs of paranasal sinuses, including the maxillary, ethmoid, sphenoid and frontal sinuses, are air filled spaces within the maxillofacial region. These sinuses theoretically provide structural support and reduce bone mass, while simultaneously improving voice resonance and protection in midface traumatic injuries.

The maxillary sinuses were first described by Leonardo da Vinci in the late 15th century, and are the largest of the paranasal sinuses.[11,14] These pyramid-shaped sinuses sit within the body of the maxilla infraorbitally, and superiorly to the first and second premolars. The sinuses communicate with the nasal cavity through the osteomeatal complex, that also drains the anterior ethmoid and frontal sinuses, and opens into the hiatus semilunaris. The uncinate process alongside the adjacent ethmoid bulla defines the hiatus semulunaris.[15] Arterial supply consists of the facial, infraorbital and palatine arteries, while lymphatic drainage reaches the submandibular nodes.[16]

The ethmoid sinuses exist within the labyrinth of ethmoid bone. The number, nature and size of these air cells are highly variable between the nasal septum and lamina papyracea.[16] The collection of sinus spaces are further divided into groups by the bony basal lamellae, the most critical being the basal lamellae of the middle turbinate. The anterior ethmoid is the key sinus which affects the common drainage pathway.[17] There are variable cells such as the Haller cells, first described in the mid-18th century, which further complicates the anatomy.[18] Blood supply for the ethmoid sinuses arises from both the internal and external carotid arteries, and includes both the ophthalmic and sphenopalatine arteries. Lymphatic drainage for the anterior ethmoidal cells is to the submandibular node, while the posterior cells drain to the retropharyngeal nodes.[16,18]

The frontal sinuses are triangular in nature, and are the only paranasal sinus to be absent on birth. Although the sinuses grossly form above the medial portion of the supraorbital crest, the right and left side develop independently, which results in significant asymmetry. Drainage occurs via the common pathway described earlier. Arterial supply includes the supraorbital and ethmoidal arteries, and lymphatic drainage is to the submandibular nodes.[15,16]

The sphenoidal sinuses are the most posterior cells, and contribute towards the skull base. Unlike previous sinuses, the sphenoid sinuses drain into the sphenoethmoidal recess above the superior concha.[20] Arterial supply corresponds to the posterior ethmoidal artery and drainage is via the retropharyngeal nodes.[16]

The nose and paranasal sinuses form together a functional unit.[11]

Olfaction

Olfaction is an understated, yet critical physiological function. It is through nasal sensory abilities that individuals can perceive thousands of odours, as well as the ability to detect the flavour of foods and hazards including natural gas, fire, and spoiled food. Olfactory function is closely linked to longevity and quality of life. Individuals with anosmia have been found to increase long-term sugar and salt intake, resulting in higher rates of chronic medical conditions such as renal disease, diabetes mellitus and hypertensive disorders.[21,22] Smell sensation also plays a critical role in please, kin recognition and pheromone detection.

As mentioned previously, the septum and nasal turbinates play a crucial role in the physiology of nasal airflow. Alteration to laminar airflow, directs air superiorly towards the olfactory epithelium, a specialised covering lining the upper regions of the septum, cribiform plate, and superior turbinate, and several areas of the middle turbinate. Velocity, air volume and direction can alter smell perception.

The cells found superiorly are derived embryologically from both the olfactory placode and the neural crest. Innervation, and therefore chemosensation, involves the olfactory nerve, trigeminal nerve, and autonomic fibres of the superior cervical ganglion. Trigeminal chemosensory nerve endings play a role in the identification of noxious stimuli including air pollutants, ammonia, and ethanol.[21]

Odorants are absorbed into the mucous covering the olfactory epithelium. The mucous in the olfactory cleft is derived from specialised Bowman's glands and differs in composition from the remainder of the nasal cavity. Secretions from these glands include odorant-binding proteins, growth factors, immune factors and biotransformation enzymes. The odorants bind to olfactory receptors found in the cilia. The process of transforming chemical energy into signal transduction requires a complex cascade dependant on G proteins inside cells activated the lyase enzyme and eventual opening of the ion channels to create action potentials. Olfaction changes throughout an individual's lifetime, with the process of receptor gene switching affecting the functional receptors found on neurons.[21]

The axons of the olfactory receptor cells project across the cribiform plate and number approximately 10 to 20 million. Each can respond to multiple stimuli and result in billions of combinations.[23] Axons from these olfactory neurons from nerve bundles (filia olfactoria) which synapse beyond the cribiform plate with other neurons in the olfactory bulb.

There is a second method for smell perception via retronasal olfaction.[24] Odorants in this scenario rise through the nasopharynx, through the posterior choanae and ascend superiorly to the olfactory epithelium. This form of olfaction plays a vital role in flavour perception. 80% of taste sensation is from olfaction.

Variations in Sinonasal Anatomy

Despite a basic similarity, sinonasal anatomy is one of, if not the most varied systems in individuals. The septum itself is rarely straight, with differences attributed to genetic, such as C or S shaped septums, and environmental factors, such as traumatic injury causing irregularities and dislocations.[25] It can be osseous and/or cartilaginous in nature. These deviations found in 26-96% of the population can cause obstruction of mucous outflow leading to pathological disease, as well as restricting surgical access during management.[26,27] Concha bullosa is pneumatisation of the turbinates, and the presence of dominant or unilateral concha preclude to higher rates of septal deviation.[15,27] These penuamtisations continue to develop even following adolescence precluding to consistently changing baseline anatomy.[28]

The maxillary sinus continues to develop until the third decade of life.[29] 29% of patients have variable septations which divides the maxillary antrum non-uniformly, and while developmental asymmetry is common, 1-11% of individuals have maxillary hypoplasia.[15,30] Mean volumes of the sinus remain inconsistent, influenced by both gender and ethnic differences.[31-33] Similarly, the maxillary sinus ostia can be in irregular locations or with accessory ostia which result in drainage complications.[14] Craniofacial syndromes which cause midface hypoplasia, chronic inflammation of mucosa during childhood and genetic disorders such as cystic fibrosis which affect mucociliary clearance can affect growth and bony thickness of the sinuses, with the maxillary sinus most commonly involved.[34-36] In conjunction with this, there are uncinate process variations that can contribute to impaired sinus ventilation and increased surgical difficulty.[11,15] Lateralisation narrows the infundibulum, and can preclude to hypoplasia of the sinus, as well as concha bullosa formation.[11,37]

While the bulla ethmoidalis is the largest and most nonvariant cell of the ethmoidal complex, other cells are highly inconsistent.[15] Ethmoid sinuses include agger nasi cells, located most anteriorly in the superior portion of the middle turbinate, with prevalence between 10-98%.[38-40] If these agger nasi cells pneumatise posteriorly, the frontal recess can be narrowed. Similarly, Haller or infraorbital cells are highly variable, present in 8-57% of the population.[15] Onodi cells originate from the posterior ethmoid and can pneumatise both laterally and superiorly above the sphenoid sinus. The presence and enlargement of these cells can interfere with exposure of the sellar floor and are difficult to examine in coronal planes of computed tomography (CT).[41,42] Supraorbital ethmoidal cells represent pneumatisation of the orbital plate of the frontal bone and drain into the lateral aspect of the frontal recess. Approximately 15% of individuals have one supraorbital ethmoidal cell, while 5% have multiple.[15]

Superior to the agger nasi are Kuhn or frontoethmoidal cells. Bent and Kuhn described four distinct types of frontal sinus cells, with Type 1 the most common.[39,43,44] Differences in ethnicity affect distribution, in addition to environmental factors.[45] These create highly variable frontal recess cells and each individual patient requires appropriate investigations prior to operative intervention. Moreover, there are newer variations of frontal sinus anatomy such as a fronto-septal rostrum in approximately 30% of patients.[46] Some patients also suffer from the absence of frontal bone pneumatisation, resulting in frontal sinus aplasia. Bilateral aplasia has been reported in 2-33% of individuals, and is more common in females.[47,48]

The sphenoid sinus is intimately related to variations in the surrounding structures, such as the cavernous sinus, internal carotid artery, optic and vidian canals. There are reports of dehiscence, as well as insertion of septations to the carotid canal. Inconsistency of such critical structures becomes important during endonasal approaches to the sella turcica, optic nerve and lateral sellar junctions.[15,49,50]

The height of the olfactory fossa is critical when discerning the upper limits of dissection, and has been classified by Keros into three groups. This classification system is related to the depth of the cribiform plate from the ethmoid roof, with the higher configurations being intimately related to a greater risk of injury.[51,52] The most common is Keros type 2, where the skull base is 4-7mm deep.[53] The crista galli is placed above the cribiform plate in the midline, and can be pneumatised from either the ethmoid sinuses or adjacent frontal sinuses.[15]

Given the highly surgical management nature of the rhinology field, these variations in anatomy can have dramatic consequences and affect patient outcomes.

Surgical Effects of Anatomical Variations

Variations in anatomy can preclude to pathology which includes altered nasal airway, increased risk of rhinosinusitis and development of polyposis as mentioned previously. In addition to pathology, inconsistency of anatomy influences surgical outcomes.

Maxillary sinus septa interfere with endoscopic sinus procedures, as well as irrigation and drainage of the sinus intraoperatively.[54] Moreover, maxillary hypoplasia predisposes to lamina papyracea injuries and orbital fat extroversion or orbital harm. It also may lead to dental problems and canine fossa elevation, in addition to hypoglobus and enophthalmos, which in turn can contribute to orbital asymmetry and diplopia.[15,54] The lamina papyracea itself can also have dehiscence which leads to orbital content prolapse and increases the risk of intraoperatively haemorrhage.[55] There is also the possibility of infraorbital nerve protrusion, a branch of the trigeminal nerve, into the sinus that can be injured during either endoscopic or open approaches to the sinus.[49]

Ethmoid sinuses can have alterations in the drainage pathway, known as an ethmomaxillary sinus. This frequently is accompanied by a hypoplastic maxillary sinus, which causes the aforementioned disturbances.[54] In addition to this, the presence of Haller cells increases the risk of orbital injuries.[55] Onodi cells retain an intimate association with the optic nerve, and heighten the threat of both nerve and internal carotid artery trauma.[15] Infection in this cell can also lead to neuropraxia of the optic nerve.[56] Supraorbital ethmoidal cells can be mistaken for the frontal ostium intraoperatively and mimic a septated frontal sinus. Failure of recognition increases the chance of orbital damage, skull base injury leading to cerebrospinal fluid (CSF) leak, and anterior ethmoidal artery injury.[57]

The variations of septation, shape and dimensions of the sphenoid sinus affect endonasal skull base approaches. Injury to the lateral, posterior or superior walls can lead to CSF leak, while protrusion of the optic nerve or internal carotid artery into the sinus can be catastrophic.[49,50,55,58,59] Dehiscence of the artery can also predispose postoperative infections to have a higher chance of reaching the cavernous sinuses. Other variable structures that cause concern include the vidian, maxillary, oculomotor, trochlear and abducens nerves.[60-62]

Complications from endoscopic endonasal approaches will be discussed at further length in **Chapter 3**. Given the high morbidity, and potentially fatal, complications of highly variable anatomy, the field of rhinology has attempted to mitigate the risk with improved surgical techniques and technology. While this thesis does not focus on surgical techniques, it will discuss technological improvements.

Mitigation of Anatomical Variations

Operations require accurate recognition of anatomical structures, which can prove difficult due to millimeter size of some critical elements. Occasionally, a clear view of these structures requires resolution beyond the naked eye. As a result, rhinologists have employed and implemented various modalities to assist them.

Imaging

Given the complexity of sinonasal anatomy, the field of rhinology has attempted to soften the risk through a combination of modalities. Principle amongst these is the use of imaging. CT and magnetic resonance imaging (MRI) provide a roadmap to surgical intervention through increased clarity and accuracy.[60,64] In recent years, a combination of endoscopic examination alongside CT imagining is considered the gold standard for preoperative workup. Coronal and sagittal reformatted scans are ideal for identification of the agger nasi cells.[15] Onodi cells continue to be difficult to evaluate in the coronal plane.[61] Also, identification of penumatisation of the anterior clinoid process or pterygoid process are heavily linked to optic nerve or internal carotid artery protrusion intraoperatively, even if not apparent on imaging.[39,52,65]

Visualisation

There is the option intraoperatively of utilising a microscope or an endoscope. While a microscope was initially introduced in the late 19th century, it was not under 1922 for it to become binocular in nature and allow stereopsis which increases safety in surgery.[66,67] The limitations of use, however, include the cumbersome nature of the instrument, the heavy weight which limits transportation, skin burns when used on high-power illumination, especially in otolaryngology surgery, the high costs and the restricted visualisation corridor.[63,68-70] Limited fields of vision rarely allows appropriate views of the optic and carotid protuberances, or the opticocarotid recess.[71] This is important when assessing beyond the sella, which includes the suprasellar and cavernous sinus.

This limited vision, fuelled the use of endoscopes in skull base surgical interventions which provides a panoramic wide-angle view. The combined use of angled lenses allows closer inspection of tumours, especially in the cavernous sinus and optic chiasm regions.[71] This superior visualisation revolutionised the field, despite the lack of stereopsis and the problems related to this drawback.

Neuronavigation

Navigation systems have gained popularity over the previous two decades and are now considered essential for certain high-risk cases. The use of navigation systems was first introduced in the early 1990s.[72-75] Although fluoroscopy was formerly used as the primary image-guidance technique, nowadays CT or MRI are used because of higher anatomical resolution.[72] These allow isotropic, multiplanar, high-resolution, thin-section images of the head, with optical enhancement. Although MRI provides increased soft tissue resolution, it has far less information regarding bony structures. As a result, CT is the preferred imaging technique.[76,77]

Navigation systems typically utilise either electromagnetic (radiofrequency) or optical (infrared) signals for localising instruments within surgical fields.[78] Optical systems rely upon the identification of light-emitting diodes on instruments picked up by camera arrays, while for electromagnetic systems, copper coils attached to instruments change the field generated by an emitter. The use of neuronavigation, irrespective of the system increases the efficacy of endonasal endoscopic approaches. There is increased safety, especially with major intracranial or intraorbital complications, as well as hospital stay.[73,79-81] There is also an improvement in identification of anatomical landmarks, especially in difficult, diseased or surgically revised environments.[78,81]

Despite the obvious benefits of navigation systems, they do become unreliable following a CSF leak that causes a cerebral shift. The equipment is also costly, as is the preoperative scans which increase radiation exposure. The navigation equipment also requires significant space in the operating theatre.[82]

Augmented Reality

Although augmented reality (AR) was first developed in the 1960s, the term only gained traction during the last decade of the 20th century.[83] The idea of AR-based surgery is to utilise pre-acquired radiological images and merge these with virtual generated reference points. The combination of these factors aims to improve visual perception intra-operatively, in addition to surgical precision.[84]

AR systems utilise a single screen where the endoscopic images and three-dimensional reconstructed background are fused together. At present, there are three forms of display technologies in augmented reality, which include see-through displays using optical transmissive technology, projection-based displays to see deeper internal structures, and video-based displays to directly superimpose preoperative information.[85]

4K Endoscopy

Introduced in 2015, the Ultra-HD 4K endoscope aimed to improve 2D visualisation.[86] Four thousand pixels on the longer axis improved the image resolution, and with it information per frame, four-fold when compared to HD.[87,88] The visualisation with this technology provided a more detailed view of both critical anatomical structures and pathology, which hoped to translate into improved safety, with operative times similar to the 2D HD endoscope.[86] In addition, the physical strain, ergonomics and weight are comparable with the traditional endoscope. Additional combinations of technology, such as with narrow band imaging (NBI) can further enhance visualisation.[86,89]

There are, however, disadvantages encountered still despite the breakthrough. There is a large variation in the red colour discrimination using the 4K endoscope, with delicate colour combination settings required. This can prove, at times, to be a hindrance if set up incorrectly especially within the sellar space.[86] Additionally, given the high quality of the images there are corresponding increases in image storage space, which requires significant registration, and the use of a 55-inch monitor can take space in an already congested operating theatre, especially with regards to appropriate distance for surgical visualisation.

When comparing this technology with 3D endoscopy there are advantages such as removal of a learning curve, but also the reduction of vision-related side effects. These side effects are more commonly found in other surgical disciplines, where there have also been reports that approximately 10% of surgeons cannot perceive stereoscopic depth, which negates a large proportion of benefits for 3D use.[90,91,92,93] However, despite the greatly improved resolution, basic data still indicates that 3D endoscope shows statistically significant reduction in errors and improved precision, while being comparable in surgical time overall.[94,95] Some authors, have delineated these differences further to highlight improved nasal phase operations using the 3D endoscope, but increased advantages with 4K 2D endoscopy with entering the intradural phase of anterior skull base operations.[95] These still need further research to highlight an appropriate system for different surgical situations. Additionally, there is the scope for visual improvement of the 3D endoscope to reach the same level as 4K 2D endoscopy, while maintaining stereopsis.

Scope and Outline of This Thesis

Despite dramatic advances, endonasal endoscopic operations continue to encounter complications including severe bleeding, blindness and damage to the central nervous system.[96] Factors which affect surgical results include operative experience, anatomical identification, and disorientation during surgery.[72,97,98] These disadvantages can be somewhat overcome through professional development, but not entirely.

The main drawback of conventional two-dimensional (2D) endoscopy is the lack of stereopsis. To mitigate this drawback, there has been the introduction of the three-dimensional (3D) endoscope. Unfortunately, little data is available with regards to its use and application.

The first part of this thesis is designed to close the knowledge gap and stress the importance of improving surgical outcomes given the highly variable nature of sinonasal anatomy, and the potential catastrophic consequences if injuries should occur intraoperatively.

In **Chapter 2**, there is an assessment of current literature surrounding endoscopic endonasal surgery with regards to the skull base. **Chapter 3** examines further the potential complications experienced with rhinological skull base procedures.

Chapter 4, 5, 6 and 7 establish the use of the 3D endoscope from an overall perspective, a visual analysis compared to traditional 2D endoscopes, and comparative randomised controlled trials using both models. These trials are designed to assess both novice and experienced users.

In view of the literature, **Chapter 8** provides a complete systematic review, which includes the studies highlighted in this thesis, of 3D endoscopy use in endonasal endoscopic approaches.

Chapter 9 (general discussion), reflects on the main findings described in **chapters 2-8** and discusses the relevance and implications of these findings. In addition, considerations for further improvements and research within this field are given.

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PART 1

Foundational Principles – Preliminary Work

2

Complications of Skull Base Surgery

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Excerpt In: Scott-Brown's Otorhinolaryngology and Head and Neck Surgery. 8th Ed. 2018

Search Strategy

The data in this chapter are supported by a Medline search using the key words randomized controlled trials, meta-analysis, evidence-based medicine, review literature, skull base (focusing on surgery and complications), skull base neoplasms (focusing on surgery and complications), postoperative complications, vestibular schwannoma (focusing on surgery and complications), cerebrospinal fluid rhinorrhoea (focusing on surgery, complications, prevention and control), cerebrospinal fluid otorrhoea (focusing on surgery, complications, prevention and control), CSF lumbar drainage, antibiotic prophylaxis, meningitis (focusing on surgery, complications, prevention and control), electromyography, intraoperative monitoring, facial nerve and facial nerve injuries (focusing on prevention and control), acetazolamide (focusing on adverse effects and therapy), papaverine (focusing on therapy), intracranial hypertension (focusing on therapy), hydrocephalus (focusing on therapy and drug therapy), CSF pressure, therapeutic embolization, meningioma, angiofibroma. In addition, the Cochrane database has also been searched.

Introduction

The evolution of skull base surgery has provided an intersection between various surgical specialities including neurosurgery, otolaryngology surgery, ophthalmology, oncology, radiology, head and neck surgery, as well as craniofacial and reconstructive surgery. In addition to this, the last decade has seen dramatic advances in surgical technique, neuronavigation and optics; including the triple chip cameras, endoscopic 3D systems and high definition screens, providing both precise surgical resection, as well as preservation of surrounding neurovascular structures. Intra-operatively, nerve monitoring has further aided the modern-day surgeon when managing varying pathologies within a delicate anatomical region. An improvement in surgical interventions, have been coupled with accurate radiological imaging, allowing both appropriate visualisation and management of anatomically remote and complex lesions to be safely resected. A collaborative multidisciplinary team, in conjunction with the dramatic advances in surgical technique and technology have resulted in improved patient care and reduced post-operative complications.

Despite a constant evolution, skull base surgery remains a challenging field of surgery, with important risks. As with any surgical procedure, identification and minimisation of complications is essential. Skull base tumours are intimately related to vital neurological structures, cranial nerves (CN), major arteries and venous sinuses, making surgical resection challenging. These problems may be compounded when large tumours directly invade important structures. Dural breaches predispose to cerebrospinal fluid (CSF) leakage and the close proximity to contaminated aero-digestive structures may expose the patient to an increased risk of infection.

In this chapter we will detail both intra-operative and post operative complications of skull base surgery.

Intra-operative Complications

Vascular

Arterial Haemorrhage

Transection of a major artery is a disastrous but fortunately rare event. Inadvertent excessive manipulation or direct forceful suction of an intracranial artery may lead to vasospasm and cerebral infarction. Gentle handling of vessels using neurosurgical patties for protection with medium/low suction and frequent irrigation with isothermic saline are mandatory operative techniques. Infiltration of vasoconstrictive agents prior to surgery, as well as local application of patties soaked in vasoconstrictive agents produce lower rates of morbidity intra-operatively.

The primary vessels at risk during lateral skull base surgery are the basilar artery and the anterior inferior cerebellar artery (AICA). The basilar artery may be injured during translabyrinthine or suboccipital approaches to very large vestibular schwannomas (VS). The anterior inferior cerebellar artery (AICA) is frequently in the surgical field during VS surgery. Injury to the AICA may result in Atkinson's syndrome – lateral tegmental pons infarction, which is often fatal.

Major vascular complications in anterior skull base surgery primarily effect the carotid within the sphenoid sinus, particularly in transsphenoidal surgery for patients with acromegaly. The specific difficulties within this cohort include the sinus being deeper, characterised by more septa and a reduced intercarotid distance, resulting in potential intra-operative surgical difficulties.[1] The intrasphenoid carotid artery can further complicate matters both pre and intra-operatively. Its presence can mimic a sinonasal mass with variations occurring in approximately 40% of patients, as well as aneurysms of the cavernous portion accounts for 2-9% of all intracranial aneurysms.[2,3] In conjunction with this, there are high rates of dehiscence shown in literature, with multiple other papers finding only a mucoperiosteal covering the intrasphenoid carotid artery coursing through the sphenoid sinus.[3] Sethi et al. described rates of dehiscence as high as 93%, although this paper did not define their criteria.[4] As a result, if the surgeon is not aware of such common variations, a damaged intrasphenoid carotid artery can result in both vascular and neurological complications and potentially death.

Embolization of selected vascular tumours such as meningiomas, paragangliomas and nasopharyngeal angiofibromas may reduce the risk of intraoperative and postoperative bleeding and even the operative time. Unfortunately, studies have yielded contradictory results, and, at present, there is no consensus on its use. The majority of studies have been retrospective, and the two prospective studies to date on the preoperative embolization of meningiomas have produced conflicting conclusions.[5,6] Major complications of such neuroradiological procedures include CVA, subarachnoid haemorrhage, intratumoral haemorrhage, raised intracranial pressure and CN palsies due to tumour swelling or embolization of the vaso vasorum and even death.

Venous Haemorrhage

Venous haemorrhage may be controlled using a variety of methods depending on location and quantity of bleeding. These include bone wax if the bleeding point has a bony perimeter, bipolar diathermy or repair using 6-0 or 7-0 monofilament suture if the vessel wall is easily visible, or placement of haemostatic agents such as oxidized cellulose (Surgicel), microfibrillary collagen (Avitene) or biological tissue glue, typically for more diffuse bleeding. Occasionally, large sinus perforations may require extraluminal packing to achieve haemostasis or even formal ligation. Anatomical studies have shown a unilateral non-functioning sigmoid sinus/jugular bulb is present in only 4 percent of normal subjects, so adverse postoperative sequelae, such as cerebral oedema or long-term benign intracranial hypertension following ligation, is infrequent.[7]

Air embolus

Air embolus is a rare complication that usually only happens when the patient is in the sitting position. This position leads to a reduction in intracranial venous pressure, if a defect in a venous sinus is created, a pressure gradient favouring the passage of air into the circulation is created.[8] The first sign is a sucking sound or venous crepitation at the site of entry. Later, hypotension, tachycardia, dysrhythmias and diminishing end-expiratory pCO_2 develop. When this complication is detected, inhalation anaesthesia is discontinued and 100 percent oxygen administered, while the bleeding site is controlled by direct pressure and the jugular veins are compressed in the neck. The patient is placed in the left lateral Trendelenburg position with the head lowered in order to trap the air embolus in the right side of the heart, preventing it entering the pulmonary circulation. The air can then be aspirated through a central venous catheter, or in its absence, needle aspiration of the right ventricle via a subxiphoid approach should be attempted.

Cranial nerve injury

Cranial nerve injuries are among the most debilitating complications encountered in skull base surgery. Most preoperative CN deficits persist postoperatively if due to tumour invasion rather than compression. Unlike sensory CN deficits, there is a good prospect of some recovery of motor CN function if a primary reanastomosis or cable graft is performed. Microdissection techniques and electrophysiological nerve monitoring enhance the preservation of CN during tumour resection.

Olfactory Nerve

The olfactory nerve is at risk and often unavoidable in anterior skull base procedures, specifically ethmoidal tumours or meningiomas of the sphenoid ridge and those involving stripping of the dura from the cribiform plate treated through an open approach. This is due to the position of nerve within the subarachnoid space, with only a meningeal sheath covering.

The olfactory epithelium is present at the apex of the nostrils bilaterally, covering an area of approximately 2-3cm^2. The epithelium consists of both trigeminal and olfactory nerve fibres, with trigeminal fibres sensitive to irritation and temperature rather than olfaction. Tumours involving the anterior fossa floor often lead to unilateral anosmia, which is usually not perceived, however occasionally can cause permanent bilateral anosmia.[9]

Management of patients with anosmia include safety advice and dietary advice. Smoke and gas detectors should be installed in their homes and patients require advice on healthy eating, with many foods unappetising without the sense of smell leading to an unbalanced diet.

Optic Nerve

The optic nerve is at risk in anterior skull base surgery, specifically pituitary tumours close to the optic chiasm. Blindness within tumour management may also be secondary to radiotherapy, leading to radiation keratitis, or direct radiation injury to the optic nerve. Visual-evoked potentials should be monitored during surgery. Sharp dissection around the nerve using the appropriate microscopic or endoscopic techniques will lower the risk of injury.

It is interesting to note there is a high level of protrusion and dehiscence of the optic nerve, with over 30% of the population having both protrusion and dehiscence, and various papers reporting rates of protrusion as high as 70%.[3] These difference in variations are attributed to ethnic background.[3] Without careful anatomical dissection will lead to post-operative visual difficulties, with increased risk of blindness from optic nerve damage within the sphenoid sinus.[3]

Cranial Nerves III, IV and VI

The cranial nerves III, IV and VI are at risk during operations of the petrous apex adjacent to the cavernous sinus and the anterior skull base. The trochlear nerve exits the posterior brainstem, has a relatively long intracranial course, but is well protected in the tentorium and is infrequently injured. Abducens nerve palsy has been reported after lumbar drain placement – it is not known whether this is through an ischaemic or traction injury. Abducens nerve palsy management tends to be symptomatic, with recovery tending to be slow and progressive. In paediatric patients occlusive patch therapy for eyes will help avoid amblyopia, until residual palsy improves. Monitoring of extra-ocular movements is important in recovery.

Trigeminal Nerve

The trigeminal nerve is at risk during lateral skull base surgery, such as large VSs, temporal bone resection and approaches to the clivus, nasopharynx and parasellar–parasphenoid compartments, when intentional neural section may be necessary for anatomical access. Trigeminal nerve branches are also at risk during anterior skull base procedures. With sensory innervation of the head mainly covered by the trigeminal nerve, except the occipital and maxillary joint area, disorders may lead to severe discomfort for the patient. Various forms of rehabilitation have been hypothesized and researched. With regards to conservative therapy, Vitamin B6 is traditionally used as a neurotrophic substance, however there is little clinical evidence to support its use. Nerve growth factor is a similar neurotrophin, with local use following damage increasing expression of tyrosine receptor kinase A. However, it is currently not available for clinical use and is still within research phases for possible neural repair and reconstruction. Surgically, there has been positive outcomes following reconstructions of the inferior alveolar and lingual branches of the trigeminal nerve, with suggestions that the same theories can be utilised for sensory nerve reconstruction. Possible interposition grafts include the great auricular nerve or the sural nerve for longer graft requirements. Both of these have drawbacks, with permanent sensory deficits over the ear lobe and calf respectively. If reconstruction and rehabilitation not a realistic option, typically carbamazepine or gabapentin are used as required to treat possible facial pain from trigeminal nerve dysfunction.[10]

Facial Nerve

Facial nerve damage frequently leads to decrease in a patients quality of life, despite successful lesion removal.[11] Pre-operative dysfunction is independently linked to post-operative paralysis, with informed consent essential.[11] Important anatomical variations lead to higher intra-operative complications, with appropriate knowledge of the superficial location of the stylomastoid foramen in infants integral. Other anatomical variations include absence of chorda tympani, lateralization of the vertical portion, duplication in the tympanic segment of the nerve and common bony defects of the fallopian canal. It is, however, important to be aware that the majority of facial nerve injuries in mastoid surgery occur in the presence of an anatomically normal facial nerve.[12] 70% of iatrogenic injury is located in the pyramidal segment (between tympanic and mastoidal segment) at the second genu.[11]

Orbicularis oculi and orbicularis oris muscles are typically routinely monitored intra-operatively via electromyographic (EMG) monitoring during mastoid procedures. The introduction of intraoperative facial nerve monitoring has facilitated early identification and localization of the facial nerve and is of prognostic value in predicting functional outcome.[13] Feedback from monitoring probably shortens the learning curve, as the surgeon adapts his technique to avoid manoeuvres that produce excessive EMG discharges, however this does not replace anatomical knowledge and surgical ability.

If the nerve is transected, a primary reanastomosis avoiding tension is the optimum management. If necessary, the nerve may be mobilized from the Fallopian canal to gain 0.8 cm of length. Removing a portion of the tympanic bone and retracting the parotid gland with a suture can add another 0.9 cm. In total, 1.7 cm of additional length is possible following complete mobilization of the facial nerve for a primary anastomosis.[14] Failing this, the next best option is cable grafting using the greater auricular nerve or the sural nerve. If there is poor or absent facial function one year postoperatively other facial reanimation techniques, such as gold weight upper lid implants, temporalis muscle transfer, cross-facial anastomosis or faciohypoglossal anastomosis techniques may be required. Despite advances, reconstruction techniques are not capable of restoring facial nerve function grade I or II, using House Brackmann grading system.[15]

Vestibulocochlear Nerve

Surgical ablation or resection causes a complete loss audiovestibular function, with symptoms differing depending on pre-operative function. Patients with preoperative good or near normal auditory and vestibular function, will have severe vertigo and noticeable hearing loss. Patients usually achieve satisfactory central vestibular compensation over several weeks, but for some vestibular exercises are invaluable. In addition, customized rehabilitation regimes in the preoperative phase may facilitate earlier vestibular compensation. Those patients with poor auditory and vestibular function, which is typical in those undergoing nerve resection in vestibular schwannoma surgery, or vestibular nerve section for Meniere's, often have a minimal change in symptoms post operatively.

The auditory nerve has no perineurium, and is therefore prone damage from mechanical trauma, as well as from vascular injury within the internal auditory canal during tumour resection. Hearing conservation in vestibular schwannoma surgery is an option in those with small acoustic tumours and good preoperative hearing (minimum mean pure tone audiometry 30 dB/70 percent speech discrimination). It can be performed by a middle fossa or retro mastoid approach depending on tumour location and may preserve useful hearing in 40–79 percent of cases.[16] The chance of hearing preservation is inversely related to tumour size, with 90% of tumours > 3cm involving the auditory nerve preoperatively.[11] Most techniques of intraoperative auditory monitoring only provide delayed feedback to the surgeon and have not improved hearing conservation results in the last decade. Unilateral hearing loss may be rehabilitated by a contralateral rerouting of the signal (CROS) hearing aid or a bone-anchored hearing aid.

Lower Cranial Nerves

The glossopharyngeal and vagus nerves travel closely together throughout most of their course in the skull base and any injuries often happen simultaneously. This may result in a potentially life-threatening complication due to chronic aspiration and recurrent pneumonia. Satisfactory functional recovery often takes place with peripheral lower CN dysfunction, so a temporary tracheostomy and gastrostomy are frequently advisable. However, brainstem dysfunction, especially involving the lower CN nuclei, often results in long-term bulbar problems necessitating laryngeal airway protection. A gastrostomy and tracheostomy will not prevent contamination of the lower respiratory tract. Epiglottopexy and epiglottic plication techniques, offer an alternative management option.[17,18]

Cardiac dysrhythmia

Vagal stimulation can cause a sinus bradycardia and hypotension. Brainstem stimulation may cause tachycardia and hypertension. Fortunately, any adverse cardiac event is invariably transient, although it is usually advisable for the surgeon to switch attention to work on another part of the tumour to allow consolidation of the recovered cardiac status in the patient.

Ophthalmological Complications

Due to the inherent close relationship of the eyes, as well as their neurovascular supply, to skull base surgery, there are clear risks to vision. Neurovascular injury is especially important in elderly patients with fragile periorbital capillaries. In certain scenarios, surgical necessity can lead to visual symptoms, with orbital floor removal producing vertical dystonia, excision of the medical canthal area causing canthal drift, as well as diplopia if two or more extraocular muscles are removed. Rehabilitation for these defects is difficult, with some surgeons opting occasionally for exenteriation of the orbit subsequently or reconstruction following radiation therapy. If reconstruction is sought, the temporalis muscle is most commonly used.[11,19]

Nasolacrimal duct blockage and the ensuing epiphora can usually be treated effectively with dacrocystorhinostomy. Ectropion and entropions can result from open surgery, with appropriate reconstructive methods extensively used for both cosmesis and corneal surface disorders. Corneal abrasion is the most common cause of post-operative blindness secondary to surgical drape position, foreign body injury or reduced tear production from intra-operative anticholinergic agents.

Lateral Skull Base Approach Complications

Lateral skull base approaches require intimate anatomical knowledge, in conjunction with precise surgical exposure of the lesion. To obtain this, an approach through the middle and inner ear may be required, resulting in careful dissection of structures.

Hearing loss can be due to drill-generated acoustic trauma, caused either by direct contact of the burr with the ossicles or endosteal membrane of the cochlea. Avoiding contacting the ossicles and systemic and local application of corticosteroids are the mainstay of protecting the inner ear against trauma.[11] If the inner ear is advertently opened, recognition, repair and avoiding suction of perilymph/endolymph can preserve underlying function.

Whilst the ideal approach to CPA lesions is still debated and will be discussed elsewhere within this book, the differing approaches confer different potential complications. 10-15% of CPA surgery procedures are complicated by a post operative CSF leakage, with the largest risk found in the translabyrinthine approach.[20] Tumour excision through the translabyrinthine approach can either be attempted to be total – with a 57% HB I – II facial nerve preservation rate, or surgeons can perform a functional resection, accepting they are leaving a thin rim of tumour on the nerve, achieving a 77% HB I - VI facial nerve outcome.[21] In relation to the retrosigmoid approach, the CSF leak and facial nerve palsy rates are lower (approximately 9% and 6% respectively), however there is a requirement of cerebellum retraction, which is related to its own complications, and furthermore there is compromised access to the internal auditory canal fundus due to the nature of this technique.[21,23] Further, the retrosigmoid approach, when compared to the translabyrinthine approach, is typically used for smaller tumours which is an independent risk factor for facial nerve outcomes. In comparison the middle fossa approach has greater risks of facial nerve damage (16%), as the anatomical course of the facial nerve may compromise tumour exposure, however has higher hearing preservation rates.[23,24] As a result, although the retrosigmoid approach would seem to provide the most versatile corridor for facial nerve preservation, the middle cranial fossa approach seems safest for hearing preservation for smaller tumours. The translabyrinthine approach would be reserved for larger tumours. Detailed knowledge of potential pitfalls of surgical technique is vital when assessing skull base lesion management, based on position and outcomes desired.

Anterior skull base endoscopic surgery risks

Within endoscopic surgery, unfavourable results are typically related to learning curve and time taken to adapt to a two-dimensional (2D) environment. With vision of vital importance in surgery, the 2D nature of surgery creates drawbacks, specifically with regard to a lack of stereopsis impairing depth perception. This may impair the surgeon's ability to recognise and manage anatomical structures. With the safety of skull base procedures largely dependent on precise anatomical knowledge, this remains a key concern. Experienced surgeons compensate for this difficulty through the use of visual and tactile feedback, dynamic movements of the scope, light and shadows and detailed anatomical knowledge. Image guidance is another recent advance, with recent studies highlighting higher number of cases of incomplete resection when image guidance unavailable.[19,25,26]

A further concern with endoscopic surgery is in relation to temperature during surgery. Bone drilling and cauterization within a narrow field delivers significant levels of thermal energy, which can continue despite suctioning and flushing. Incessant increase of the temperature in the intra-operative field can potentially harm neural structures, with temperatures over 42 degrees causing cerebral harm. Regular breaks are important during these procedures.

Post-operative Complications

Haematoma

This potentially fatal complication is usually due to inadequate haemostasis. With intradural haematomas, the source of bleeding is invariably vessels adjacent to the tumour. Careful bipolar diathermy effectively controls most bleeding but cannot be used immediately adjacent to important CNs as dysfunction inevitably follows. Surgicel may be helpful in many situations, but many surgeons are reluctant to allow this material to come into direct contact with CNs as increased postoperative neural oedema is possible. On occasions, application of a biological glue, such as Tisseal® provides very satisfactory haemostasis in these circumstances. Very occasionally one will encounter a patient with a previously unknown bleeding diathesis. If the administration of drugs and appropriate blood coagulation products fail, a combination of Surgicel with FloSeal® is effective.

Extradural haematomas may result from failed middle meningeal artery cautery or ligation and more superficially from branches of the superficial temporal artery. They may also arise from haemorrhage at the craniotomy site and require the judicious application of bone wax.

The rate at which neurological deficits develop varies with the location and source of bleeding. Arterial haemorrhage produces a rapid collection of blood. In contrast, venous haemorrhage results in a gradual neurological deterioration, often due to subdural haematoma formation, and may result in secondary hydrocephalus. Depending on the severity and rapidity of the patient's neurological deterioration, management varies from immediate decompression by wound opening at the bedside to surgical exploration in the theatre or computed tomography (CT) imaging. Most haematomas are rapid and precious time should not therefore be wasted on imaging studies.

Cerebrospinal fluid leak

This is the most common complication after VS surgery. CSF leak rates of approximately 10 percent are reported in the immediate postoperative period. However, late leaks may develop many months or years after surgery and up to 35 percent of leaks develop two weeks after VS surgery.[27] It is likely that neither the surgical approach nor the tumour size affect the postoperative CSF leakage rate and transient postoperative rises in CSF pressure may be responsible.[11,24,25,27] Cerebrospinal fluid leaks are also the most common anterior skull base complication with reported rates of occurrence between 3 and 19 percent.[28]

To prevent the development of CSF leaks a perioperative lumbar drain to lower CSF pressure may be left in place for up to five days, during which time the patient is kept on strict bed rest, with the head of the bed elevated at 15–30°. Unfortunately, patients often experience low-pressure headaches.[29] There is no evidence regarding the effectiveness of prophylactic lumbar drainage, but for established leaks it eliminates 50–90 percent.[29,30] Known complications of continuous lumbar drainage include brainstem herniation (may present with vagal nerve paresis and vocal cord paresis), Chiari type 1 malformation, infection, pneumocephalus and subdural haematoma.[27,28] A compression dressing is maintained over the wound to promote watertight healing.

Symptoms of CSF leak include pain or headache (especially positional), unexplained pyrexia and, more seriously, meningitis. Rhinorrhoea may present as a salty taste in the patient's mouth. High-flow CSF leaks lead to clear rhinorrhoea and, less frequently, otorrhoea or wound discharge. A sample should be sent for immunoelectrophoretic assay for beta transferrin, which is both highly specific and sensitive for CSF.

High-flow CSF leaks require surgical exploration and repair. Low-flow CSF leaks may be managed with bed rest and elevation of the head by 20–50°. In addition, a lumbar spinal drain may be used for up to five days. Wound leaks are managed by the insertion of further sutures and the application of a compressive head bandage. Acetazolamide is known to lower CSF pressure by inhibiting the enzyme carbonic anhydrase and by decreasing CSF production. Some units use this therapy but there is no evidence for its efficacy in the treatment of CSF leaks.[31] The use of prophylactic antibiotics remains uncertain. There is some evidence favouring the role of prolonged prophylactic antibiotics in patients with ventricular drains but no studies exist for lumbar drains.[32] Two large metanalyses have produced conflicting conclusions over the role of antibiotic prophylaxis in the prevention of meningitis in patients with basilar skull fractures and CSF fistulae.[33,35] The larger metanalysis found no reduction in meningitis.[34] It is known that prolonged antibiotic use encourages the development of resistant organisms and prophylactic antibiotics in patients with CSF fistulae are probably best avoided, due to poor penetration of the meninges.[35,36]

Infection

The incidence of wound infections is usually low. Recognized risk factors include tumour size, operative time and haematoma. Anterior skull base procedures performed in a cleaned but previously contaminated environment, where the wound is in close contact with the aerodigestive tract, have a rate of infectious complications of between 0 and 30 percent.[28,37] Frontal bone flap osteomyelitis may complicate craniofacial resection for anterior skull base tumours in certain cases.[38] Wound infection may lead to meningitis or a brain abscess. Meningitis is usually associated with a CSF fistula.

The risk of infection is minimized by the liberal use of perioperative irrigation and prophylactic antibiotics (for clean non-implant procedures and for clean contaminated procedures). Prophylactic antibiotics should be given on induction of anaesthesia to ensure high tissue levels at the time of surgery. Antibiotics given more than four hours after the end of surgery are not effective, either experimentally or in clinical trials.[39] The Infection in Neurosurgery Working Party of the British Society for Antimicrobial Chemotherapy recommends that surgery for clean and clean-contaminated surgery should be administered as a single intravenous dose on induction of anaesthesia, with additional doses every three hours for long procedures.[39] [Grade A/D] In support of these recommendations, a systematic review in the Cochrane database of prospective randomized controlled trials of patients undergoing major pulmonary, gynaecological, obstetric, urological, pelvic or abdominal surgery, who had been given either single or multiple dose prophylaxis, found no difference in surgical site infection rates.[40] This confirms the findings from an earlier review of similar patient groups.[41] In addition, prolonged antibiotic prophylaxis increases the risk of hospital acquired infection.[40]

Pneumocephalus

Intracranial air is often present after craniotomy and may be seen on CT, but usually resorbs after seven to ten days. The presence of pneumocephalus is pathognomonic for the presence of a CSF leak, with risks of meningitis as high as 30%.[42] It is rarely seen after posterior fossa surgery and is usually associated with surgery at sites that include the aerodigestive tract, as in anterior skull base procedures. Clinically significant pneumocephalus presents in 2–12 percent of postoperative craniofacial patients.[28] Air accumulating under pressure may create a tension pneumocephalus, which if unrecognized is a potentially fatal condition. The use of positive pressure ventilation and a lumbar catheter drain are risk factors. The lumbar drain creates a vacuum effect by lowering intracranial pressure and drawing air in through the wound. Treatment with needle aspiration via a craniotomy burr hole may be adequate. Surgical exploration to decompress the brain and seal air leaks may sometimes be necessary. About one-third are associated with CSF leaks and a thorough search for a fistula is, therefore, also advisable.

Hydrocephalus

This presents in the early postoperative period with headache, impaired consciousness, gait disturbance and incontinence. It is secondary to cerebral oedema or intracranial haemorrhage. Normal pressure hydrocephalus is due to chronic obstruction of arachnoid villi function. It has been reported following jugular bulb resection in association with unrecognized contralateral cerebral venous drainage insufficiency. The presence of post-operative hydrocephalus is approximately 6% within anterior skull base tumour resection.[43]

Epilepsy

Postoperative seizures may herald the development of haematoma, oedema, infarction or any complication causing mass effect and cerebral irritation. Temporal lobe manipulation carries a special risk of the development of this complication, which is not encountered with posterior fossa surgery. Manipulation or resection of brain parenchyma can result in an irritable epileptic focus. For high-risk procedures, consideration should be given to the use of carbamazepine, phenobarbitone or phenytoin for antiseizure prophylaxis. For postoperative seizures these drugs and diazepam are indicated. One medication is initiated at a time and the dosage increased until the seizure is controlled or the maximum serum level of the drug is reached. Another drug may then be added if necessary.

Headaches

There is a higher incidence of headache with the retrosigmoid approach for VS surgery, which may be debilitating and intractable.[22,23] This is a feature of VS surgery, with headache not as common using this approach in other posterior fossa tumours. It has been suggested that adherence of the dura to nuchal soft tissue, neck muscle spasm and aseptic meningitis from bone dust or fibrin glue is responsible.[44,45] It is more common following VS surgery for small tumours, although this may reflect individual psychological factors, causing patients of a 'sensitive disposition' with mild tumour symptoms to present early and also to be more likely to report local discomfort postoperatively. Intradural drilling of the internal auditory meatus deposits bone dust into the posterior fossa, and alternatively, it is postulated that larger VSs prevent wide distribution of bony debris. The use of cranioplasty techniques with bone or titanium mesh and acrylic reduces the incidence.[44,45]

Best Clinical Practice

General Practice

- ✓ Performing procedures in a multidisciplinary team, utilising the strengths of each member
- ✓ Regular frequency of surgeries; minimum once every two weeks

Pre-operative Management

- ✓ Otological and audiological examination – pure tone and speech audiometry
- ✓ Vestibular examination – 1/3 of patients with profound sensorineural hearing loss report subjective hearing loss, while twice as many shows pathological vestibular signs in caloric testing and/or vestibular evoked myogenic potentials
- ✓ Imaging – temporal bone imaging revealed high riding bulb in 32% (which can lead to the presence of bony defects of the hypotympanum), anterior sigmoid sinus in 34%, a low riding dura in 26% and an aberrant carotid artery in 0.02%

Vascular

- ✓ Discontinue aspirin and clopidogrel 7-10 days prior to surgery
- ✓ Warfarin discontinued 5 days pre-operatively, which is adequate time to reconstitute the coagulation factors. If at risk of thromboembolic event, use low molecular weight heparin 2 days after stopping warfarin or 3 days prior to operation, stopping 24 hours before surgery

- ✓ Pre-operative corticosteroid administration – to reduce inflammatory mediators which cause vasodilation, transduction and oedema
- ✓ Patient positioning should be reverse Trendelenburg, as head elevation reduces mean arterial pressure in the elevated area. Patient must be tilted in and out of position slowly to avoid sudden shift in blood.
- ✓ Ventilation technique maintaining normocapnia or mild hypocapnia to minimize bleeding, with some centres using high frequency jet ventilation.
- ✓ Highly vascular tumours may require preoperative embolization and ligation of feeding vessels. Should be performed 24 to 72 hours pre-operatively to provide adequate thrombosis and prior to re-formation of collateral blood supply.
- ✓ Bleeding is controlled using bone wax, bipolar diathermy, placement of haemostaic agents such as oxidised cellulose (Surgicel), microfibrillary collagen (Avitene) or a biological glue and repair using 6-0 or 7-0 monofilament suture.
- ✓ Occasionally, large venous sinus perforations require extraluminal or intraluminal packing or even ligation to achieve haemostasis.
- ✓ Decrease bleeding with controlled hypotensive anaesthesia.

Air embolus

- ✓ The first sign of this complication is a sucking sound or venous crepitation at the site of entry.
- ✓ Later hypotension, tachycardia, dysrhythmias and diminishing end-expiratory pCO_2 develop.

Cranial nerve injury

- ✓ Microdissection techniques and electrophysiological nerve monitoring enhance the preservation of CN during tumour resection.
- ✓ If the facial nerve is cut, primary reanastomosis avoiding tension is best. Failing this, cable grafting using the greater auricular nerve, or the sural nerve is the next best option, followed by facial-hypoglossal anastomosis.

Cardiac dysrhythmia

- ✓ Vagal nerve stimulation can cause a sinus bradycardia and hypotension.
- ✓ Brainstem stimulation may cause tachycardia and hypertension.

Temperature

- ✓ Regular flushing of endoscope.
- ✓ Site of bone drilling to be short and varied to avoid high temperature.

Haematomas

- ✓ Arterial haemorrhage produces a rapid collection of blood in the extradural space.
- ✓ Venous haemorrhage results in a gradual neurological deterioration, owing to subdural haematoma formation.
- ✓ Depending on the severity and rapidity of the patient's neurological deterioration, management varies from bedside wound opening to surgical exploration in the theatre or CT imaging.

Cerebrospinal fluid leak

- ✓ Immunoelectrophoretic assay for beta transferrin is both highly specific and sensitive for CSF.
- ✓ Cerebrospinal fluid lumbar drainage is effective in eliminating 50–90 percent of cases of CSF leaks after skull base surgery.

Infections

- ✓ There is a good evidence base to recommend a single intravenous dose antibiotic prophylaxis, given at induction of anaesthesia for skull base procedures.
- ✓ Meningitis is usually associated with a CSF fistula.

Pneumocephalus

- ✓ Air accumulating under pressure to create an acute elevation of intracranial pressure is potentially fatal.

Hydrocephalus

- ✓ This presents in the early postoperative period with headache, impaired consciousness, gait disturbance and incontinence.

Epilepsy

- ✓ Postoperative seizures may herald the development of haematoma, oedema, infarction or any complication causing mass effect and cerebral irritation.
- ✓ Temporal lobe manipulation carries a special risk.

Headaches

- ✓ There is a higher incidence of headache with the retrosigmoid approach for VS surgery, which may be debilitating and intractable.

Future Research

Despite the wealth of data on the pathophysiology of disease and our theoretical foundations for treatment, randomized trials have produced somewhat surprising results in the past. Prospective randomized controlled trials, which may need to be multicentred, are required to improve the evidence-base on the following issues.

- ✓ The efficacy of neuronavigation technology in reducing complications.
- ✓ Evaluation of newer tumour ablation techniques.
- ✓ The value of preoperative embolization of highly vascular tumours, addressing selection criteria, different materials and the timing in relation to surgery.
- ✓ The efficacy of CSF lumbar drainage for prophylactic prevention of postoperative CSF leaks. How long should the drain remain *in situ*? Should it drain at a certain rate, or would a lowered stable CSF pressure setting be more efficacious?
- ✓ The role of antibiotic prophylaxis in clean contaminated skull base procedures, with lumbar drains and in patients with a postoperative CSF leak.
- ✓ Use of novel monitoring techniques, such as four contact adherent systems for glossopharyngeal and vagus nerve monitoring during surgery. Utilise compound muscle action potentials from posterior pharyngeal wall.

Key Points

- ✓ The sound of crepitation at the site of a large perforation of a venous sinus and later cardiorespiratory distress should alert the surgeon to the possibility of an air embolus.
- ✓ Manipulation of the vagus nerve or brainstem may result in cardiac dysrhythmia and surgery should be halted until sinus rhythm returns.
- ✓ Cranial nerve injuries are among the most debilitating complications encountered in skull base surgery.
- ✓ Microdissection techniques and electrophysiological nerve monitoring enhance the preservation of CN during tumour resection.
- ✓ Cerebrospinal fluid leaks are among the most common postoperative skull base surgery complications.
- ✓ There is a good evidence base to recommend a single intravenous dose antibiotic prophylaxis, given at induction of anaesthesia for skull base procedures.
- ✓ Postoperative seizures may herald the development of haematoma, oedema, infarction or any complication causing mass effect and cerebral irritation.
- ✓ Most postoperative intracranial haematomas are rapid and require prompt surgical exploration, avoiding the delay of imaging studies.

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Reporting of Randomised Controlled Trials: A Fourteen-Year Review

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British Journal of Medicine & Medical Research. Aug 2015; 10(9): 1-18

Abstract

Purpose

Skull base surgery has experienced dramatic advances in the last decade. Recently, various surgical disciplines have conducted reviews of the quality of randomised controlled trials (RCTs). This is the first review of our knowledge regarding RCT quality within skull base surgery.

Methods

Systematic review of skull base surgery RCTs published between 2000 and 2014 was conducted. Literature search provided 96 papers. Duplicates and trials which did not meet our inclusion criteria were excluded. This left 28 papers for analysis. A total of 1785 patients participated in the trials. Consolidated Standards of Reporting Trials statement (CONSORT) and Jadad scale were used assess to the quality of reporting. These were our main outcome measures.

Results

The mean CONSORT score prior to 2011 was 16.9 (n = 17, range; 13 – 22), and post 2011 was 17.5 (n = 11, range; 12 – 22). The mean Jadad score was 3.1 (n = 28, range 2 – 5). CONSORT was found to increase significantly with both increasing sample size (rho=0.467, p=0.012) and Jadad scores (rho=0.540, p=0.003). Linear regression showed CONSORT increase by 0.36 (95% CI: 0.02 – 0.70, p=0.041) for each additional 10 patients included, and by 1.50 (95% CI: 0.58 – 0.24, p=0.002) for each increase of one in the Jadad score.

Conclusion

There are common omissions related to randomization, sample size calculations and availability of protocols. RCTs in skull base surgery are comparable to other surgical disciplines. We recommend utilisation of the CONSORT statement during protocol formation of RCTs to improve reporting of trials.

Introduction

Properly conducted trials, following scientific platforms are widely accepted as the foundations of treatment efficacy and safety.[1] The importance of such trials is that evaluation of a smaller population, where outcome of treatment variability is analysed, can effectively influence the management of the general population in the future. Retrospective trials contain serious potential bias, which could potentially influence outcomes. As a result it is globally adhered to that the gold standard for clinical investigations is the randomised controlled trial (RCT), however these are not without controversy.

RCT reporting should transparently convey the design, conduct, analysis and learning points.[2] Despite this, RCTs are still not being reported adequately.[3-5] Deficiencies within the aforementioned areas can create difficult interpretation and application.[3] On account of this, an international group of clinical trialists, statisticians, epidemiologists and biomedical editors created the original CONSORT (Consolidated Standards of Reporting Trials) statement.[4] This was a checklist and flow diagram published in 1995, with a revision produced in 2001.[4,5] The 22 item revised checklist and 4 stage flow diagram (enrolment, intervention, allocation, follow-up and analysis) served to reduce ambiguity regarding design and reporting of RCTs, enabling readers to understand the trial's conduct and assess results.[5,6] Data highlighted its use in improvement of quality of RCT reports, with usefulness dictated by continuous biomedical literature.[6-8] The CONSORT statement was further revised in 2010, extending the checklist to 25 items (Table 1).[9] The Jadad scale is a similar tool used to assess effectiveness of randomised controlled trials using a three item system, resulting in a score from 0 (low-quality study) to 5 (high-quality study) (Table 2). It has been found to contain many of the important elements that have empirically been shown to correlate with bias and it has known reliability and external validity.[10]

Reviews of RCT reporting within various surgical specialities, including paediatric, general and trauma surgery highlighting weaknesses.[11-13] Having first been described in the late nineteenth and early twentieth centuries, skull base surgery has experienced dramatic advances over the last decade.[14] This includes advances in surgical technique, neuronavigation and optics, as well as involvement of specialities outside of neurosurgery.[15] As a result, there is an understandable groundswell of interest within appropriate research within this domain. To our knowledge there is no such paper analysing the strength of skull base surgery reporting. We aim to utilise the CONSORT guidelines and Jadad scale to assess the quality of reporting, whilst simultaneously highlighting areas of research, and revealing future aspects of skull base surgery yet to be subjected to RCT.

Table 1. Changes to original CONSORT statement[9]

Item 1b (title and abstract)	We added a sub-item on providing a structured summary of trial design, methods, results and conclusions and referenced the CONSORT for abstracts article
Item 2b (introduction)	We added a new sub-item (formerly item 5 in CONSORT 2001) on "specific objectives or hypotheses"
Item 3a (trial design)	We added a new item including this sub-item to clarify the basic trial design (such as parallel group, crossover, cluster) and the allocation ratio
Item 3b (trial design)	We added a new sub-item that addresses any important changes to methods after trial commencement, with a discussion of reasons
Item 4 (participants)	Formerly item 3 in CONSORT 2001
Item 5 (interventions)	Formerly item 4 in CONSORT 2001. We encouraged greater specificity by stating that descriptions of interventions should include "sufficient details to allow replication"
Item 6 (outcomes)	We added a sub-item on identifying any changes to the primary and secondary outcome (endpoint) measures after the trial started. This followed from empirical evidence that authors frequently provide analyses of outcomes in their published papers that were not the pre-specified primary or secondary outcomes in their protocols, while ignoring their pre-specified outcomes (that is, selective outcome reporting). We eliminated text on any methods used to enhance the quality of measurements.
Item 9 (allocation concealment mechanism)	We reworded this to include mechanism in both the report topic and the descriptor to reinforce that authors should report the actual steps taken to ensure allocation concealment rather than simply report imprecise, perhaps banal, assurances of concealment
Item 11 (blinding)	We added the specification of how blinding was done and, if relevant, a description of the similarity of interventions and procedures. We also eliminated text on "how the success of blinding (masking) was assessed" because of a lack of empirical evidence supporting the practice as well as theoretical concerns about the validity of any such assessment.
Item 12a (statistical methods)	We added that statistical methods should also be provided for analysis of secondary outcomes
Sub-item 14b (recruitment)	Based on empirical research, we added a sub-item on "why the trial ended or was stopped"
Item 15 (baseline data)	We specified "a table" to clarify that baseline and clinical characteristics of each group are most clearly expressed in a table

Item 16 (number analysis)	We replaced mention of "intention to treat" analysis, a widely misused term, by a more explicit request for information about retaining participants in their original assigned groups
Sub-item 17b (outcomes and estimation)	For appropriate clinical interpretability, prevailing experience suggested the addition of "for binary outcomes, presentation of both relative and absolute effect sizes is recommended"
Item 19 (harms)	We included a reference to the CONSORT paper on harms
Item 20 (limitations)	We changed the topic from "interpretation" and supplanted the prior text with sentence focusing on the reporting of sources of potential bias and imprecision
Item 22 (interpretation)	We changed the topic from "overall evidence". Indeed, we understand that authors should be allowed leeway for interpretation under this nebulous heading. However, the CONSORT Group expressed concerns that conclusions in papers frequently misrepresented the actual analytical results and that harms were ignored or marginalised. Therefore, we changed the checklist item to include the concepts of results marching interpretations and of benefits of being balanced with harms.
Item 23 (registration)	We added a new item on trial registration. Empirical evidence supports the need for trial registration, and recent requirements by journal editors have fostered compliance.
Item 24 (protocol)	We added a new item on availability of the trial protocol. Empirical evidence suggests that authors often ignore, in the conduct and reporting of their trial what they stated in the protocol. Hence, availability of the protocol can instigate adherence to the protocol before publication and facilitate assessment of adherence after publication.
Item 25 (funding)	We added a new item on funding. Empirical evidence points toward funding source sometimes being associated with estimated treatment effects.

Table 2. Jadad Scale

Item	Maximum points	Description
Randomisation	2	1 point if randomisation mentioned. 1 additional point if the method of randomisation is appropriate. Deduct 1 point if the method of randomisation is inappropriate. (minimum 0)
Blinding	2	1 point if blinding is mentioned. 1 additional point if the method of blinding is appropriate. Deduct 1 point if the method of blinding is inappropriate. (minimum 0)
An account of all patients	1	The fate of all patients in the trial is known. If there are no data, the reason is stated.

Methodology

Search Strategy

The data within this paper is supported by a systematic literature review using MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials. The search included the key words (skull base) OR (pituitary) OR (acromegaly) OR (cushing) OR (transphenoidal) OR (endoscopic endonasal) OR (meningioma). We limited the search to including only human trials, published in English between 01/01/2000 to 31/11/2014.

Inclusion/Exclusion Criteria

The full inclusion and exclusion criteria are summarised in Table 3. Articles were included if they assessed a living human population with any skull base disease, using a prospective Randomised Controlled Trial between 01/01/2000 to 31/11/2014, with access to the full article in English. All other articles were excluded.

A subsequent level of screening excluded duplicate articles, and publications not related to skull base surgery, such as endocrinology of the HPA axis, pregnancy and in-vitro fertilisation (IVF) treatment.

Table 3. Inclusion/exclusion criteria

Inclusion Criteria	Exclusion Criteria
Patients with any skull base condition	Non-skull base related conditions
Human participants	Non-human participants, cadavers
Prospective randomised controlled trial	Retrospective non-randomised trial
Full journal article available	Abstracts
Trial related directly to management of skull base condition	Related to conditions outside of skull base
Published between 01/01/2000 to 31/11/2014	Published outside of date range
Produced in English	Foreign language
Published within MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials	Published outside of MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials

Method and Data Analysis

All papers which adhered to our inclusion and exclusion criteria were obtained either through use of the Athens account or from utilisation of the University Hospital Birmingham BaseDoc system. Articles were subsequently appraised using the CONSORT statement and the Jadad scale by two independent observers. Further data from each paper were extracted including number of authors, location of study, methodology, number of patients, year of publication and synopsis of study. These factors were divided into two classes, those that were ordinal or continuous, and those that were categorical. Comparisons between ordinal or continuous variables were made using Spearman's correlation coefficients, with linear regression models produced where significant associations were found.

Ordinal and continuous variables were then compared across categorical variables using Mann-Whitney or Kruskal-Wallis tests, as appropriate, with medians and ranges used as summary statistics. Where Kruskal-Wallis tests returned significant results, post hoc comparisons between all groups were made using Mann-Whitney tests, with the p-values Bonferroni corrected for the number of comparisons being made.

Finally, comparisons between categorical variables were made using Fisher's exact test. All analyses were performed using IBM SPSS Statistics 22 (IBM Corp. Armonk, NY), with $p<0.05$ deemed to be indicative of statistical significance.

Results

Study Selection

A combination of the key words aforementioned provided 96 papers using all databases. Duplicates were subsequently excluded leaving 75. Papers which were non-human, written in a foreign language, cadaver based and did not meet our inclusion criteria were also excluded. This left a total of 28 (Figure 1).[16-43]

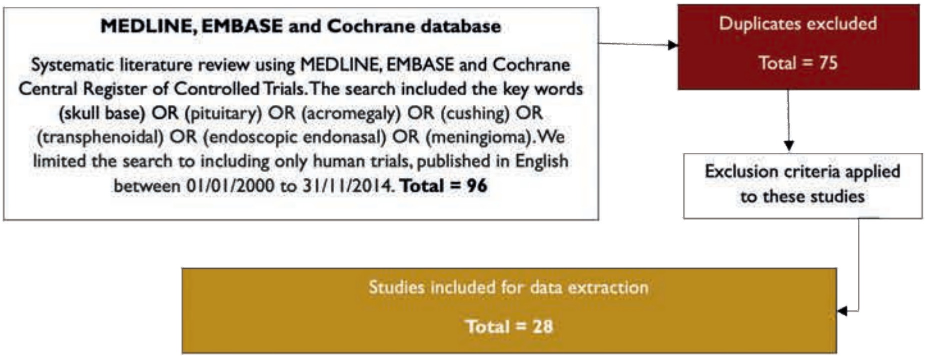

Figure 1. Search Results

A total of 1785 patients participated across all RCTs matching our inclusion and exclusion criteria between 2001 and 2014. The mean number of authors was 6.7 (range; 2[41] – 13[17]), when considering only named authors in collaborative studies. Approximately half of the studies were performed in Europe[16,17,21,24,25,26,30,32,34,36,38,39,42], with Italy and China producing the highest quantities of studies nationally; 5/28 each respectively (Figure 2). There were no RCTs produced outside of Europe, Asia and North America. The impact factor of journals ranged from 0.947[33] to 6.310[18] in 26 journals, whilst Surgical Neurology was discontinued and therefore did not receive at 2013 impact factor. The median impact factor was 2.347. Over half the studies were published in the last five years, ranging between 1 and 6 yearly.

All studies were prospective in nature. Blinding of participants, observers or surgeons occurred in 11 studies, whilst 4 used a placebo. There were a total of 3 double blinded, randomised controlled trials designed during the study period. These related to pre-operative medical treatment, peri-operative haemostasis control and post-operative analgesia. 13 of the studies investigated acromegaly, whilst other areas including meningioma, prolactinoma, craniopharyngioma and pituitary adenoma. 8 studies did not address a specific condition, investigating any lesion within the skull base (Figure 2).

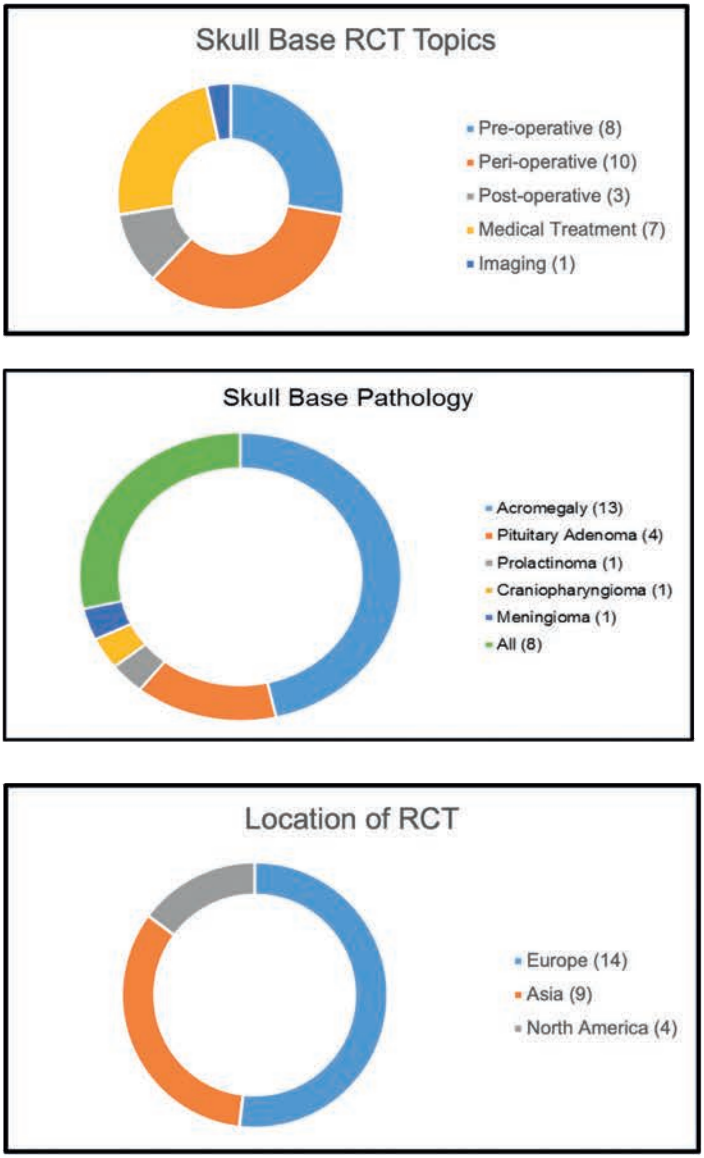

Figure 2. Overview of included studies

Data Analysis

The mean CONSORT score of papers published between 2001and 2014 was 16.9 (n = 17, range; 13 – 22), and from 2011 onwards was 17.5 (n = 11, range; 12 – 22). The mean Jadad score was 3.1 (n = 28, range 2 – 5). With regards to topics of investigation a majority (36%) related to peri-operative management, with less than half addressing surgical technique (Figure 2).

Data were available for a total of 28 studies. The data were complete for all factors considered, with the exception of the impact factor, where two values were missing due to the journals being discontinued. Since the CONSORT guidelines changed in 2010, the analysis was performed separately using both versions. However, since the two guidelines were so similar (rho=0.967), both sets of analyses returned comparable results, so only the more recent version of CONSORT was subsequently reported throughout.

Table 4 reports the correlations between the continuous factors being considered. CONSORT scores were found to increase significantly with both increasing sample size (rho=0.467, p=0.012) and JADAD scores (rho=0.540, p=0.003). In addition to this, higher impact factors were observed in papers with a greater number of authors (rho=0.622, p=0.001), and in the more recently published papers (rho=0.529, p=0.005).

Linear regression analysis was then performed to further quantify these relationships, the results of which are shown graphically in Figure 3. The CONSORT score was found to increase by 0.36 (95% CI: 0.02 – 0.70, p=0.041, Figure 3A) for each additional 10 patients included, and by 1.50 (95% CI: 0.58 – 0.24, p=0.002, Figure 3B) for each increase of one in the JADAD score. The impact factor was found to increase by 0.34 (95% CI: 0.18 – 0.50, p<0.001, Figure 3C) for each additional author, and by 0.17 (95% CI: 0.04 – 0.30, p=0.014, Figure 3D) in each subsequent year of the investigation.

Table 4. Correlations

	Number Of Authors	Year	Impact Factor (2013)	Patients (N)	CONSORT (Post-2010)	JADAD
Number Of Authors		0.362 (p=0.058)	**0.622 (p=0.001)**	0.085 (p=0.667)	0.039 (p=0.842)	-0.200 (p=0.308)
Year	0.362 (p=0.058)		**0.529 (p=0.005)**	0.219 (p=0.264)	0.114 (p=0.563)	-0.005 (p=0.980)
Impact Factor (2013)	**0.622 (p=0.001)**	**0.529 (p=0.005)**		0.176 (p=0.390)	0.185 (p=0.365)	0.084 (p=0.682)
Patients (N)	0.085 (p=0.667)	0.219 (p=0.264)	0.176 (p=0.390)		**0.467 (p=0.012)**	0.283 (p=0.144)
CONSORT (Post-2010)	0.039 (p=0.842)	0.114 (p=0.563)	0.185 (p=0.365)	**0.467 (p=0.012)**		**0.540 (p=0.003)**
JADAD	-0.200 (p=0.308)	-0.005 (p=0.980)	0.084 (p=0.682)	0.283 (p=0.144)	**0.540 (p=0.003)**	

Quoted coefficients are from Spearman's rho. Highlighted values are significant at p<0.05

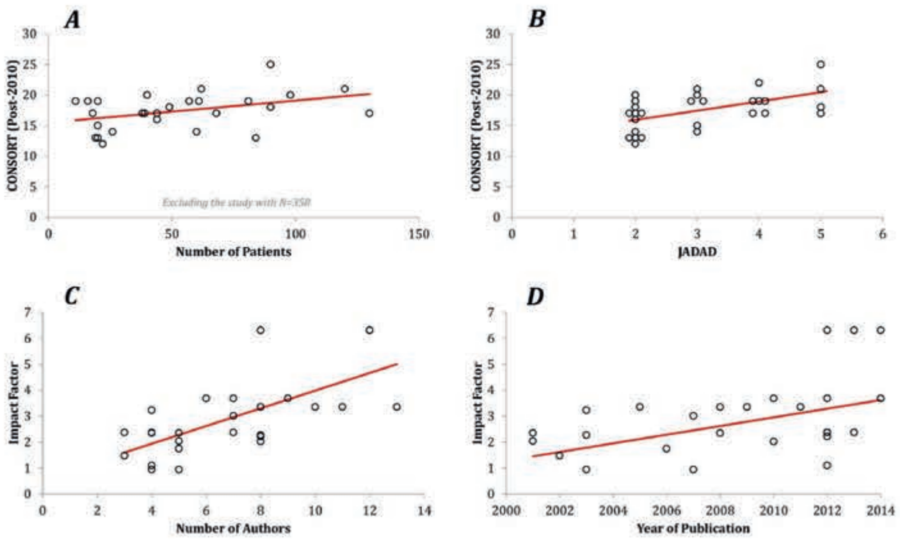

Figure 3. Regression Models

Table 5 reports the analysis of the categorical factors. As would be expected, studies with a placebo arm had significantly higher CONSORT (median 21 vs. 17, p=0.021) and JADAD (median 5 vs. 3, p=0.012) scores, with blinded studies also having significantly higher JADAD scores (median 4 vs. 2, p<0.001). In addition to this, both the number of authors (p=0.002) and the impact factor (p=0.003) were found to differ significantly by continent. Post-hoc analysis found that this was due to significant differences between Europe and Asia, with European papers found to have a significantly greater number of authors (median 8 vs. 5, post hoc p=0.018) and to be in significantly higher impact factor journals (median 3.35 vs. 1.75, post hoc p=0.021).

No significant differences in any of the outcomes by the type of study were detected. However, it must be noted that, due to the number of groups being compared and the small sample size, these tests had very low statistical power; hence the false negative error rate would be high in these analyses.

Table 6 reports the rates of placebo and blinding usage by continent and study type. The only significant finding was that none of the eight pre-operative studies employed blinding, compared to between 33% and 67% of the studies of other types (p=0.019).

Table 5. Categorical vs. continuous variables

	N	Number of Authors	CONSORT (Post-2010)	JADAD	Impact Factor (2013)	Year	Patients (N)
Continent		***p=0.002****	***p=0.314***	***p=0.061***	***p=0.003****	***p=0.128***	***p=0.706***
Asia	10	5 (2, 9)	18 (13, 20)	2 (2, 5)	1.75 (0.95, 3.69)	2008 (2001, 2012)	47 (16, 98)
Europe	14	8 (4, 13)	17 (12, 25)	3 (2, 5)	3.35 (2.04, 6.31)	2010 (2001, 2014)	52 (11, 358)
North America	4	5 (3, 7)	20 (17, 21)	5 (3, 5)	2.37 (1.75, 2.37)	2012 (2006, 2013)	80 (20, 130)
Type		***p=0.078***	***p=0.274***	***p=0.149***	***p=0.240***	***p=0.364***	***p=0.154***
Imaging	1	-	-	-	-	-	-
Medical Treatment	7	8 (3, 12)	17 (12, 22)	2 (2, 4)	3.35 (1.48, 6.31)	2011 (2001, 2014)	20 (11, 358)
Peri-Operative	9	4 (2, 8)	17 (14, 25)	4 (2, 5)	2.36 (0.95, 3.23)	2007 (2001, 2013)	57 (20, 130)
Post-Operative	3	7 (5, 8)	20 (17, 21)	3 (2, 5)	2.22 (1.75, 2.37)	2012 (2006, 2012)	68 (40, 120)
Pre-Operative	8	8 (4, 13)	19 (14, 21)	3 (2, 3)	3.35 (0.95, 6.31)	2010 (2003, 2014)	55 (16, 98)
Placebo		***p=0.686***	***p=0.021****	***p=0.012****	***p=0.964***	***p=0.135***	***p=0.632***
No	25	7 (2, 13)	17 (12, 22)	3 (2, 5)	2.37 (0.95, 6.31)	2010 (2001, 2014)	44 (16, 358)
Yes	3	5 (4, 8)	21 (19, 25)	5 (4, 5)	3.23 (1.75, 3.35)	2005 (2003, 2006)	90 (11, 120)
Blinding		***p=0.090***	***p=0.127***	***p<0.001****	***p=0.848***	***p=0.601***	***p=0.384***
No	17	8 (2, 13)	17 (12, 21)	2 (2, 3)	2.37 (0.95, 6.31)	2010 (2001, 2014)	44 (16, 98)
Yes	11	5 (3, 12)	19 (13, 25)	4 (2, 5)	2.37 (1.48, 6.31)	2007 (2001, 2014)	57 (11, 358)

*Data reported as median and range, with p-values from Mann-Whitney or Kruskal-Wallis tests, as applicable. *Significant at p<0.05*

Table 6. Categorical factors

	N	Placebo	Blinding
Continent		***p=0.359***	***p=0.416***
Asia	10	0 (0%)	3 (30%)
Europe	14	2 (14%)	5 (36%)
North America	4	1 (25%)	3 (75%)
Type		***p=0.416***	***p=0.019****
Imaging	1	-	-
Medical Treatment	7	1 (14%)	4 (57%)
Peri-Operative	9	1 (11%)	6 (67%)
Post-Operative	3	1 (33%)	1 (33%)
Pre-Operative	8	0 (0%)	0 (0%)

*p-Values from Fisher's exact test. *Significant at p<0.05*

Discussion

A majority of RCTs presented in this paper score below 18 using the CONSORT statement, producing possible questions regarding validity. There are common omissions related to randomization and blinding technique, sample size calculations and availability of protocols. Similar deficiencies in reporting randomization and blinding were highlighted in the Jadad score. A combination of these omissions leads to questioning of reliability. However, when compared to other subject areas, RCTs in skull base surgery score higher than other specialities.[11-13] In addition to this, blinding is difficult to achieve in surgical specialities, especially in relation to surgical technique. As a result, all cases of blinding found were in relation to medical treatment or post-operative pain control.

Results highlighted greater number of authors lead to publication within higher impact factor journals, which correlates to a modern initiative of collaborative research. Higher numbers of authors were present in papers from Europe, which significantly differed from other continents worldwide. It was also found that higher CONSORT score were found in papers with larger sample sizes. This was the only variable, in addition to Jadad score, which significantly influenced CONSORT score.

It is interesting to note that the deficiencies of surgical trials to adhere to the CONSORT statement was noted, with revisions made in 2008, creating a CONSORT statement for non-pharmacological treatment.[44] However, it was found that adherence to this revision was even poorer than the original CONSORT statement.[45] In addition to this, the difficulty of utilizing this revision, comparing it to the standard pre-2008 CONSORT statement would make for difficult result analysis. Ultimately it was decided to use the standard CONSORT statements for analysis of RCTs within this study period.

Limitations

The limitations in this study relate to the fact that analyses are performed are low on power due to the small sample size. However, the use of a fourteen year period was used due to the modern nature and explosion in differential skull base management. Papers prior to this would not be applicable to modern day management. Unfortunately, within this scenario of assessing a new field we cannot conclude that there is no difference within the non-significant tests, only that the sample size produced did not allow us to encounter one. A large genuine effect could be present within these areas, but would require a larger sample size.

Conclusion

The CONSORT statement was produced to reduce ambiguity regarding design and reporting of RCTs, with empirical results highlighting correlation with bias. It also has known reliability and external validity. In relation to skull base surgery, a relatively new field within medicine, there are deficiencies in reporting of randomization and blinding technique, sample size calculations and protocol availability. Despite this, there was appropriate reporting of multiple aspects of results and discussion. Our recommendation would be during the conception of RCT protocols, to consider the CONSORT statement, addressing all points with a view of providing easily reproducible results and improvement in readers understanding. This will produced less ambiguous study reporting. We would also respond favourably to a reproduction of our work in future years when greater numbers of studies are available.

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PART 2

Three-Dimensional Endoscopy – A Step Forward in Endoscopic Endonasal Management

4

Three-Dimensional Hand to Gland Combat: The future of endoscopic pituitary surgery?

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Journal of Neurology Surgery Reports. 2015 Nov; 76(2): e200-4.

Abstract

Objective

Describe our initial operative experience with a novel three dimensional high definition (3D HD) endoscopic endonasal approach, provide a case series and summarize current research present. This is the first case series in Europe using the new 3D HD endoscope.

Methods

Most current endoscopic endonasal techniques involve the surgeon working within a two-dimensional (2D) environment which creates drawbacks, specifically with regard to a lack of stereopsis impairing depth perception. In order to mitigate this, there has been the introduction of new three-dimensional (3D) endoscopes. These 3D endoscopes had worse image clarity compared to 2D HD, and as a result there has been the addition of HD to the 3D system.

Results

Though research evidence remains limited, there is no significant negative peri-operative or post-operative outcomes when compared to 2D endoscopic techniques. Although non-HD 3D endoscopic surgery produced a poorer image quality, resulting in subjectively increased difficulty navigating anatomical structures, the new 3D HD endoscope creates imaging quality similar to conventional 2D HD systems in addition to providing stereopsis.

Conclusion

Three-dimensional endoscopic endonasal techniques provide an exciting new avenue, effectively addressing potential depth perception difficulties with current two-dimensional systems.

Introduction

Endoscopic pituitary and skull base surgery was first described in the late 19th and early 20th centuries.[1-3] However, it was not until 1945 that Karl Storz began producing instruments for otorhinolaryngologists. Although modest, the instruments used miniature electric lamps to visualize the interior of the human body through an endoscope. Despite the complexity of design and > 400 operations, the visual quality achieved through Storz's work alone would not allow the modern accurate delineation of anatomical structures. Harold Hopkins pursued the limitations of visual quality initially through fiberoptics, but fiber breaks and image resolution limitations forced bundles to be replaced at rapid rates. This in conjunction with poor light transmittance resulted in the final solution from Hopkins in the late 1960s: the Hopkins rod. Hopkins utilized rods of glass in air spaces between the lenses. Due to the size, the rod-lenses would self-align, requiring no further support. Storz subsequently used Hopkins's design, with further modifications to produce what is now considered the modern endoscope.

The last decade has seen dramatic advances in surgical techniques, neuronavigation, and optics including the endoscopic camera and screens.[4] Despite the endoscope, historically intracranial tumors have been managed by neurosurgeons with various surgical approaches including postauricular, transpetrous, presigmoid, and frontotemporal craniotomy.[5–8] Endoscopic approaches have the potential to provide more direct access to the tumor site, a reduction in retraction injury to the surrounding normal brain, and a minimization of damage to neurovascular structures. Aesthetically, endoscopic approaches also provide a lack of external scars, as well as decreased patient morbidity and a potentially shorter postoperative recovery period.[9–12] In addition, vascularized nasal mucosal flaps for dural reconstruction have allowed successful primary and secondary repair of skull base defects, helping to further decrease the incidence of post procedure cerebrospinal fluid (CSF) leaks and further solidify the benefits of an endoscopic endonasal approach.[12]

Most current endoscopic endonasal techniques involve the surgeon working within a two-dimensional (2D) environment. With vision of vital importance in surgery, the 2D nature of surgery creates drawbacks, specifically with regard to a lack of stereopsis impairing depth perception.[13] This may limit the surgeon's ability to recognize and manage anatomical structures. With the safety of transsphenoidal procedures largely dependent on precise anatomical knowledge, this remains a key concern.[14] Experienced surgeons compensate for this difficulty through the use of visual and tactile feedback, dynamic movements of the scope, light and shadows, and detailed anatomical knowledge.[13] However, despite significant experience, these compensatory mechanisms may be misleading, with this effect well described in laparoscopic surgery with visual perceptual illusion the primary cause of error.[15,16]

To mitigate this lack of stereopsis, in 2012 a new three- dimensional (3D) endoscope was introduced, designed to overcome these visual difficulties. The first 3D endoscope utilized non-HD technology, producing a balance between stereopsis and visual clarity. As a result, in 2013, high definition (HD) was added to the 3D endoscope. Three-dimensional systems have already been shown to register, validate, and accurately navigate anatomical structures including soft tissue. There is an understandable groundswell of interest for the potential of such systems.[14,17] We present a case series of endoscopic sinonasal and skull base procedures performed using 3D non-HD scope technology (Visionsense Ltd, Petach Tilka, Israel), as well as the first reported case in Europe using the 3D HD endoscope, comparing these new methods with conventional 2D HD endoscopy.

Three-Dimensional High-Definition Case Report

A 71-year-old woman presented with a long-standing history of excessive sweating, increase in foot size, and arthralgia. However, there were no significant headaches upon presentation. On examination features of acromegaly were quite subtle. Despite minimal physical alterations, there were a significant number of complications of acromegaly in her medical history including colonic polyp, carpal tunnel syndrome, osteoarthritis, and hypertension.

Biochemical tests confirmed the diagnosis of acromegaly; growth hormone values during a glucose tolerance test were 5.1 µg/L. Insulin like growth factor-1 was elevated at 84 ng/L. A short Synacthen test with peak cortisol was 861 nmol/L; prolactin was normal. Magnetic resonance imaging of the skull base revealed an 11 x 8 x 10 mm eccentrically placed hypovascular lesion on the right side of the pituitary that was clearly demarcated. There was no compression of the optic chiasm, and the tumor was not invading the cavernous sinus. Subsequent 3D HD endoscopic transsphenoidal surgery under image guidance was performed.

Surgical Technique

The surgical technique adopted was similar to that used for other transsphenoidal pituitary surgery. The patient was positioned supine. Cocaine and adrenaline were applied topically within the nasal cavity. Following a posterior septectomy, a wide sphenoidotomy was performed preserving the blood supply for a potential rescue nasoseptal flap. Three- dimensional HD endoscopic equipment (Visionsense) with intraoperative image guidance (Stryker Nav 3, Fremont, California, United States) was utilized throughout, the former giving increased depth perception not seen with the 2D scope. The bony front wall of the sella turcica was removed exposing the “four blues” (left and right cavernous sinuses, superior and inferior intercavernous sinuses). A clinically apparent adenoma was located to the right of the pituitary, adjacent to the carotid. It was removed with an extracapsular technique. Floseal (Baxter, Hayward, California, United States) was applied for hemostasis followed by Surgicel (Ethicon) and two NasoPore (Stryker) dissolvable nasal packs.

Case Series Using 3D Non-HD Endoscope

We used the 3D scope on four sequential patients at University Hospitals Birmingham NHS Trust (Table 1). The surgical technique adopted was similar to that used for conventional 2D endoscopic surgery but with the 3D giving increased depth perception not seen with the 2D scope.

Table 1. Case series of patients who had three-dimensional non-high-definition endoscopy.

Patient demographic	Procedure	Indication	Intraoperative and postoperative complications	Need to convert to conventional 2D endoscopy?
46-year-old female	Trans-sphenoidal hypophysectomy	Pituitary-dependant Cushing's syndrome	Nil	No
44-year-old female	Middle antrostomy and left sided biopsy of lesion of maxillary antrum	Maxillary sinus lesion on imaging	Nil	No
78-year-old female	Endoscopic drainage of right maxillary mucocele, expanding into right nasal cavity	Right sided epiphora and nasal obstruction.	Nil	No
38-year-old female	"Re-do" transphenoidal hypophysectomy	Pituitary dependant acromegaly	Nil	No

Surgical Setup for 3D Endoscopy

The operating room setup for the use of the 3D endoscope and screen, whether HD or not, is slightly different than conventional 2D. The screen is placed further away, to provide an improvement in visual quality, and all members of the surgical staff must wear 3D glasses to visualize the screen appropriately. Rigid head fixation is needed. In our experience, these small changes provided no hindrance to the operating surgeon, and there was no requirement to convert to conventional 2D endoscopy throughout the procedure.

Table 2. Comparison of endoscopic systems[a]

	2D HD system	3D non-HD system	3D HD system
Maneuverability	þþþ	þþþ	þþþ
Visual corridors	þþþ	þþ	þþ
Blood soiling	þþþ	þþ	þþþ
Depth perception	þ	þþþ	þþþ
Image quality	þþþ	þþ	þþþ
Ease of surgical Setup	þþþ	þþþ	þþþ

Abbreviations: 2D, two dimensional; 3D, three dimensional; HD, high definition.
[a]Based on the authors' experience.
þþþ ¼ Good.
þþ ¼ Room for improvement.
þ ¼ Poor.

Discussion

Endoscopic, endonasal approaches to the anterior skull base have grown in importance over recent decades, with the skull base having traditionally been solely a neurosurgical preserve. With endoscopic endonasal approaches gaining popularity due to reduced morbidity and superior aesthetic results, anterior cranial fossa malignancies can be safely managed surgically. This is well illustrated by lower levels of CSF leaks; shorter post-operative hospital stays and reduced risk of damage to neurovascular structures[5-8].

Previous well documented disadvantages of endoscopic surgery, specifically in visual quality, manoeuvrability and narrow visual corridors have however remained a barrier[14,17]. Visual quality is of paramount importance as safe surgical techniques require a competent surgeon to appropriately judge depth and recognise critical anatomical structures. Traditional endoscopic techniques function within a 2D environment, resulting in potential drawbacks in depth perception. An experienced surgeon develops compensatory mechanisms, relying on tactile premise, scope movements and anatomical knowledge. However, in the presence of distorted anatomy difficulties with depth perception are heightened. Visual perceptual illusions can be a major cause of error and resultant morbidity. Recently, 3D endoscopic techniques opportunities have become a commercial and clinical reality, with the aim of mitigating the drawbacks of 2D endoscopic surgery[13,-15,18-20].

Despite these technological advances research evidence remains limited, though subjective reports from both Otorhinolaryngologists, and neurosurgeons suggest that 3D technology improves task speed and efficiency[10,11].

3D Non-HD Endoscopy

In face of potential improvements in depth perception some limitations of endoscopic endonasal surgery remain, including decreased manoeuvrability within narrow spaces. These issues cannot be addressed with 3D endoscopic techniques and remain solely the responsibility of the operating surgeon. In fact, the reduced field of view obtained with new 3D endoscopes result in narrow corridors appearing even narrower. This is due to the three dimensional optic lens being less divergent providing a slightly narrower view. The drawback is principally addressed by experience and optimum scope placement, and within our experience did not cause any surgical problems. The non-HD three dimensional endoscope also has slightly worse blood soiling, due to the presence of two chips, two lenses, with each representing a single eye. As a result, blood soiling to a single lens will cause unilateral visual difficulties. Screen irrigation systems maintained from conventional 2D endoscopes reduce the significance of this blood soiling. The largest drawback of the non-HD 3D endoscope related to image quality with high definition 2D imaging more defined and displayed better contrast, although this has not been found to significantly alter surgical technique or outcomes[,13&19].

3D HD Endoscopy

Although reduced lens divergence, and resultant narrow corridors, continue to be present in the new HD endoscope, each single lens comprised of numerous planes, similar to the eye of a fly. This improvement of the lens leads to better results in relation to blood soiling, and subsequent image clarity.

As mentioned previously, the greatest drawback of the non-HD 3D endoscope was image quality and contrast. 3D HD endoscopy overcomes this drawback with image quality similar to that of the conventional high definition 2D imaging. The system also has an inherent focus system, which allows image quality to remain consistent throughout the working depths of endoscopic surgery, with the option of manual focusing if required. In our experience rare occasions required the use of manual focusing.

Conclusion

Though research evidence remains limited, small studies have highlighted no significant negative peri-operative or post-operative outcomes when compared to 2D endoscopic techniques in novel users with regard to operative times, blood loss, CSF leaks, length of stay or readmission rates[17]. With acclimatisation to the equipment it has been shown to be time effective, cost efficient, safe and technically beneficial[15,21]. These advantages, coupled with the scope for improvement and new evolution of three-dimensional image technology provides an exciting prospect for the future of anterior skull base surgery.

The evolution in endoscopy is comparable to the conception and advancement of the modern day television; from low pixelated, black and white images, to colour, followed by increased resolution prior to the introduction of HD televisions, and the current surge of three-dimensional functional systems. As a result, we believe three-dimensional endoscopy not to be a revolution, but instead the next logical evolution in endoscopic surgery. The biggest advantage is for neurosurgeons who currently use the microscope for stereoscopic surgery, as there is retention of stereopsis, resulting in a far easier transition than to conventional 2D endoscopy. ENT surgeons on the other hand have used 2D images throughout training so the advantages in additional information are far less apparent.

Three-dimensional (3D) endoscopic endonasal techniques provide an exciting new avenue for anterior skull base surgery, effectively addressing potential depth perception difficulties with current two-dimensional (2D) systems. The new 3D HD system negates the main drawback from previous 3D endoscopes; image quality, with resolution and contrast comparable to conventional 2D endoscopy.

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5

Endoscopic training – Is the future three-dimensional?

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Laryngoscope Investigative Otolaryngology. 2018 Oct; 3(5): 345-348.

Abstract

Background

Endoscopic surgery has a distinct disadvantage compared to direct vision; loss of binocular vision. Three-dimensional endoscopy has been welcomed due to the promise of improving stereopsis.

Methodology

Prospective randomised study of junior doctors with minimal endoscopic experience, using both two-dimensional and three-dimensional zero degree 4mm Storz endoscopes. Data was collected using validated, standardised training models, both objectively and subjectively.

Statistical Methodology

Paired comparisons between variables relating to the endoscopes were performed using Wilcoxon's tests. Operators were then split into groups based on their endoscope preference, with comparisons made using Mann-Whitney tests for Likert scale responses, Kendall's tau for ordinal variables, and Fisher's exact tests for nominal variables.

Results

Reduction of field of vision of three-dimensional endoscopy by 2%. Significant findings included decreased past-pointing, improved depth and perception and image quality.

Conclusions

The use of an endoscopic endonasal approach with three-dimensional technology has measurable advantages for novice users and highlights potential tailoring of future surgical training.

Introduction

Having initially been introduced in the late nineteenth and early twentieth centuries, it was not until the amalgamation of Karl Storz and Harold Hopkins' work on endoscopy where the field of otolaryngology flourished.[1] The introduction of the two-dimensional endoscope set a mile- stone in visualization of the surgical field, in addition to providing more direct access, a reduction in retraction injury, and a minimization of damage to neurovascular structures.[1,2] Similarly, patients also encountered decreased postoperative morbidity and shorter recovery periods.[3–5]

Despite multiple advances in surgical technology, surgeons using 4-mm endoscopes are required to operate within a two-dimensional (2D) environment, with lack of stereopsis creating its own drawbacks. Experienced surgeons mitigate this difficulty through the use of visual and tactile feedback, dynamic movements of the scope, light, and shadows, and detailed anatomical knowledge.[1,6,7] In essence, surgeons are capable of creating three-dimensionality through experience, commonly through years of training in otolaryngology. Other specialties, however, including neurosurgery and ophthalmology, as well as junior doctors with little to no endoscopic experience, are required to acquire a new skill set using an unfamiliar tool while operating in delicate surgical fields.[8,9]

In 2012, a new 4-mm three-dimensional (3D) endo- scope was introduced primarily to overcome the lack of stereopsis. 3D endoscopes have encountered an evolution of their own through improvements in image clarity and endoscopic quality. Recently, multiple studies have shown subjective improvements in precision of anatomy identification, stereoscopic depth perception, and surgical comfort.[2,10–12] Despite this, there has been minimal objective data collection with small studies highlighting post- operative outcomes, length of hospital stay, quantity of blood loss, and complication rates comparable to standard 2D techniques.[10,13] Additionally, Van Gompell et al.[14] documented a 52% field of view restriction with a different 3D endoscope in 2014.

There is understandable interest in the potential of 3D endoscopy. However, the limitations of some previous publications on this subject have been in the selection of experienced surgeons with small numbers. We conducted a study aimed at junior doctors and medical students with little to no endoscopic experience using both objective and subjective measures.[2,6,7,9,11–14]

Materials and Methods

Study Design

Prospective randomized trial incorporating both quantitative measures of endoscopic handling using a box-trainer and a validated qualitative questionnaire, in addition to calculating field of vision restrictions between the two different endoscopes. The study was conducted at the University Hospital Birmingham (UHB) NHS Foundation Trust in November 2016.

The study used Karl Storz 4-mm, 0-degree, 2D and 3D endoscopes. Participants were randomized into one of the following two groups: completing task with 2D endoscope followed by 3D endoscope or completing task with 3D endoscope followed by 2D endoscope.

Participants

Our sample population consisted of medical students and junior doctors with little to no experience of endoscopic surgery— measured as fewer than 10 endoscopic operative exposures (either 10 witnessed and/or less than four performed/assisted), working at the UHB NHS Foundation Trust.

Participants were excluded if they had observed greater than 10 endoscopic operations or performed/assisted in more than four.

A unique study identification number was assigned to each participant and baseline demographic data was collected.

Modified Box-Trainer Task

Participants performed one fundamental task—peg trans- fer (and transfer back to original peg).[15,16] Modifications were made to adapt box trainer task:

1. Use of singular port for both endoscope and instrument (straight Blakesley forceps) to simulate endoscopic surgery through the nose.
2. Task confined to distance between 30 mm and 50 mm (numerous anatomical studies have found the distance between nasal vestibule to anterior attachment of middle turbinate and superior turbinate within this range).[17–20]

At the beginning of the study, prior to beginning peg trans- fer, all participants were shown the box trainer opened and given a detailed explanation of the expected task.

Methods

All study participants were consented and randomized to begin the study using either the standard high definition two- dimensional (2DHD) endoscope or high definition three- dimensional (3DHD) endoscope. Participants were randomized using simple randomization—(flipping of a coin).

An explanation of the task was provided verbally and in written format. Participants were then required to perform the “modified box trainer task” with each endoscope according to their randomization. Quantitative measures including task completion time (in seconds), adjustment time (time taken to touch first bead), past pointing and number of drops were recorded by two independent assessors. The task was repeated for the second endoscope, with identical measures recorded.

Following completion of second cycle, participants were asked to fill out a qualitative questionnaire using a validated visual analogue scale, including demographic data and subjective measures of depth perception, field of vision, image clarity and manoeuvrability (Appendix 1).

Finally, we objectively calculated field of vision using standard measurements of 6 cm and 2 cm working distance. This was performed by two independent assessors using standardized 2-mm squared paper and calculating the percentage difference between the 2DHD and 3DHD endoscopes.

Statistical Methods

Paired comparisons between variables relating to the 2D and 3D endoscopes were undertaken using Wilcoxon's tests, with data summarized as medians and interquartile ranges (IQRs). Operators were then split into groups based on their stated preference, with comparisons made using Mann-Whitney tests for the Likert scale responses, Kendall's tau for ordinal variables, and Fisher's exact tests for nominal variables.

All analyses were performed using IBM SPSS 22 (IBM Corp., Armonk, NY), with $P < .05$ deemed to be indicative of statistical significance throughout.

Results

Table 1. Comparisons between 2DHD and 3DHD endoscopes

Variable	2DHD	3DHD	p-Value
Time to complete task (seconds)	107 (75 - 141)	86 (56 - 126)	0.153
Adjustment Time (seconds)	9 (5 - 13)	10 (5 - 19)	0.067
Past Pointing (VAS)	2 (0 - 5)	0 (0 - 2)	0.025
Number of drops (VAS)	2 (1 - 2)	1 (0 - 2)	0.501
Subjective depth perception (VAS)	4 (3 - 5)	8 (7 - 8)	<0.001
Field of view (VAS)	6 (5 - 7)	7 (5 - 8)	0.072
Image quality (VAS)	6 (5 - 8)	8 (7 - 9)	0.002
Manoeuvrability (VAS)	7 (6 - 8)	7 (6 - 8)	0.247

Data reported as median (IQR), with p-values from Wilcoxon's tests. Significant at $p < .05$. 2DHD = two-dimensional high definition; 3DHD = three-dimensional high definition; VAS = Visual Analogue Score.

A total of 35 operators took part in the study, with a median age of 28 years (IQR: 27–32). Most operators had previously observed at least one endoscopy (N = 27, 77%), and only 42% (N = 15) had previous operative experience. Comparisons between the two endoscopes (Table I) found no evidence of significant differences between the time ($P = .153$) or the adjustment time ($P = .067$), although the trend was for the latter to be longer in the 3D endoscopes irrespective of whether using this endo- scope first or second. However, past pointing was found to be significantly lower when using 3D endoscopes (median 0 vs. 2, $P = .025$), and depth perception (8 vs. 4, $P < .001$) and image quality (8 vs. 6, $P = .002$) were also found to be significantly improved with the 3D endoscopes.

Table 2. Comparisons between operators with different endoscope preferences

	Operator Preference		
	2D *(N=8)*	**3D *(N=27)***	**p-Value**
Strength of Preference (0-10 Visual analogue scale)	5 (3 - 7)	8 (7 - 8)	<0.001

Data reported as median (IQR), with p-values from Mann-Whitney tests. Significant at p<0.05

The majority of operators said that they preferred the 3D endoscope over the 2D endoscope (77%, N = 27). The magnitude of this preference was found to be stronger in those that were randomized to use the 3D endo- scope first, with a median score of 8 out of 10, compared to 5 out of 10 for those that preferred the 2D endoscope (P < .001, Table II). Comparisons were then made between the ages of those operators that preferred the 2D versus 3D endoscopes, but were not found to be statistically significant.

Table 3. Measuring Field of Vision

Distance between Endoscope tip and Target (cm)	Percentage Difference from 3DHD to 2DHD endoscope (%)
2	-2.38
6	-10.51

Comparisons were made between field of vision (Table III) and found a reduction of 2.38% and 10.51%, respectively, at 2 cm and 6 cm working distance.

Discussion

With the continuing expansion of endoscopic surgery including the endonasal approach to the skull base and brain, as well as transorbital neuro-endoscopic surgery, there are numerous specialities having to adapt to an unfamiliar tool through necessity. The main concern is the loss of stereoscopic vision.[9] With appropriate visualization vital for tissue and anatomical identification, previous research has highlighted the subjective preference for 3D endoscopy, as can be confirmed by our study, with the strength of preference statistically significant (P = < .001).[2,7,10,18] 3D endoscopy has shown comfort when opening the dura, improved visualization of complex airway anatomy with higher rates of precision when removing tissue, and increased sinus anatomy understanding in cadaveric dissection. [2,10–12]

Issues relating to previous publications on 3D endoscopy have included difficult tissue maneuverability due to increased scope size, especially in narrow nasal spaces, increased susceptibility to losing focus secondary to blood spoiling, and an adjustment period of surgeons adaptability.[9] Other potential limits have been a reduction in field of vision and the lack of angled scopes.[9,14] While we have demonstrated that the newer versions of the 3DHD endo- scope have a reduction in field of view, this is only modest (2% reduction with endoscope at 2 cm from target and 10.5% with endoscope held at

6 cm from target) (Table III). This compares very favorably to the previous study by Van Gompel et al.,[14] which showed a 52% reduction in field of view with a different 3DHD endoscope.

Conclusion

We believe further research using the Storz 0-degree, 4-mm, 3D endoscope would introduce further information into an exciting new field.

Our study design using novice users of endoscope technology is the first study to give objective data confirming the subjective preference for this technology by end users. We have shown a significant objective reduction in past pointing in novice users, while subjective improvements in depth and image clarity when comparing 2DHD endoscopy and 3DHD endoscopy. We believe through the current evolution of endoscopy we will see this technology become commonplace in simulation training and in our surgical theaters replacing existing 2DHD endoscopes.

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6

Three-dimensional endoscopy: The future of nasoendoscopic training

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Laryngoscope. 2019 Jun; 129(6): 1280-1285.

Abstract

Background
Three-dimensional (3D) endoscopy is an emerging tool in surgery which provides real-time depth perception. Its benefits have been investigated in surgical training, but the current literature lacks significant objective outcome data. We aimed to objectively compare the efficacy of 2D vs 3D high definition endoscopes in novice users.

Methods
Randomised crossover study of 92 novice medical students, who used both 2D and 3D endoscopes to complete two validated tasks in a box trainer. Time taken and error rates were measured, and subjective data collected.

Results
Wilcoxon's tests showed 3D technology was significantly faster than 2D (78 vs 95 seconds; $p=0.004$), and errors per task were significantly lower (3 vs 5; $p=<0.001$). 69% of participants preferred the 3D endoscope.

Conclusions
3D high definition endoscopy could be instrumental in training the next generation of endoscopic surgeons. Further research is required in a clinical setting.

Introduction

The introduction of endoscopy transformed visualisation of the surgical field, allowing minimally invasive surgery (MIS) for previously major open procedures.[1] Decreased post-operative morbidity and shorter recovery periods were seen thereafter.[1] A major disadvantage of endoscopy is the loss of binocular vision, limiting depth perception and consequently the accurate recognition and management of relevant structures.[2-5] Experienced surgeons combat the lack of depth perception using visual feedback, haptic feedback and detailed knowledge of anatomy, though these methods have been shown to be misleading.[6-9] Three-dimensional (3D) endoscopy has been introduced to endonasal sinus surgery (ESS) to provide real-time depth perception that could, in theory, improve surgical efficacy and thus patient outcomes. This paper will evaluate 3D endoscopy in a controlled pre-clinical setting, objectively and subjectively comparing it to two-dimensional (2D) endoscopy. A recent paper concluded that complication rates in endonasal sinus surgery have not changed since the late 1990s.[10] We believe that 3D endoscopy has the potential to demonstrate a long-overdue improvement.

Phillip Bozzini invented the endoscope in 1806. It consisted of an eyepiece and container using a candle for light, and was used as a cystoscope.[11,12] The endoscope was technically limited until Karl Storz compounded the Hopkins rod and Hirschowitz's fibre-optics to produce the modern rigid endoscope in the 1960s.[13] The landmark 1997 paper from Jho and Carrau introduced endoscopic transsphenoidal pituitary surgery.[14] More recent meta-analyses have found higher rates of total gross removal and remission for functioning pituitary tumours when using an endoscopic approach.[15,16] The endoscopic approach to the pituitary is less invasive, reduces postoperative pain and often negates the need for nasal packing.[5] However, a difficult transition from microscopic to endoscopic approaches is widely reported in the literature, largely due to ergonomic shortcomings, training issues and the loss of 3D visualisation.[2,5,16,17,18]

Depth perception is allowed by the interpretation of intuitive clues, and by stereopsis. Stereopsis describes the perception of depth produced by the reception of visual stimuli from both eyes in combination.[19] 3D endoscopy has been introduced into ENT surgery with the purpose of allowing stereopsis where traditional 2D endoscopes do not. Stereoscopic vision permits better visualisation of curvature and texture of surfaces, which is especially important for skull base surgeons who depend on the subtleties of the ventral skull base for safe entry into the cranial vault.[20] Images produced by the 3D system closely mimic the real world, resulting in an improved visuospacial orientation and theoretically improving surgical outcomes.

The endoscope used in this study incorporates dual 'chip-on-the-tip' technology in which two video chips create two digital images which are projected onto a screen.[19] Polarising glasses are worn to project a different image to each eye. Current polarising displays are relatively cheap, but the use of polarising screens and glasses can be challenging for some surgeons, contributing to vertigo.[20-22] Some displays have filtered almost 75% of light output by the time it reaches the eye, and so a dark background environment is required.[19,23] These are the major ergonomic shortcomings of 3D endoscopic technology. It is likely that technological improvements will circumvent these issues in future designs.[20]

Numerous studies evaluating the use of 3D technology in an ENT setting have suggested that it shortens the learning curve for novice surgeons,[20,22,23] and others advocate its use in surgical training.[24-26] In their landmark paper, the 'Southern Surgeons Club' group found that 90% of endoscopic surgical complications occurred in the first 30 patients of the learning curve, with the initial risk being tenfold of that after 50 operations.[27] If 3D endoscopy can shorten the learning curve, it will follow that patient outcomes will be improved.

A recent systematic review failed to find evidence of clinical superiority of 3D endoscopy over 2D in terms of resection rates, pituitary gland preservation and complications, although all included studies reported a subjectively improved depth perception with 3D endoscopy.[20] Four articles found that 3D endoscopy is useful for novices, reducing their learning curve for endoscopy skills. Shah et al. found that a group of experienced surgeons disliked the initial learning curve when using 3D technology, which could explain why clinical trials with experienced surgeons are yet to demonstrate objective superiority of the 3D endoscope.[28]

This study will evaluate the growing body of evidence advocating a reduced learning curve and increased performance in novices using 3D endoscopy. It will utilise the Karl Storz 3D HD endoscope that has not been used in previous studies. The current body of evidence on novices using 3D HD endoscopy in simulated surgical environments consists of an aggregate of just 39 subjects.[29-31] This study has the statistical power to demonstrate the hypothesised superiority of 3D HD endoscopy over 2D HD in novices.

Materials and Methods

This is a prospective randomised crossover study.

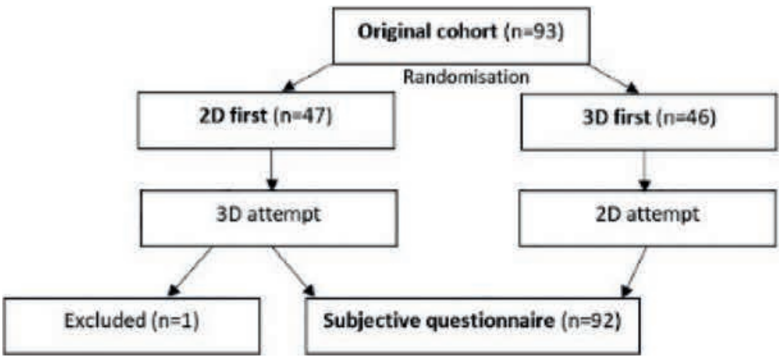

Figure 1. Experimental design. 2D = two dimensional; 3D = three dimensional.

Participants were consented and randomised to two groups, '2D first' and '3D first' which determined the mode of visualisation (2D or 3D) they used first. Each participant was required to carry out two standardised tasks in a laparoscopic box trainer. They then used the other endoscope setting to carry out the same tasks. Randomisation was used to minimise carryover bias or order bias. Participants were then asked to fill out a subjective questionnaire on baseline characteristics, endoscope preference and depth perception.

Sample

Participants were medical students from the University of Birmingham with little or no prior experience of endoscopy. Participants were excluded from the study if they had seen more than 10 endoscopy procedures, or if they had carried out more than three. We used the results of a small unpublished pilot study to carry out a power calculation, finding that to detect a significant reduction in time to completion of task, a sample size of 91 was required with a 2-sided 5% significance level and a power of 80%.

Endoscope

We used a Karl Storz 2nd generation rigid 0° 3D endoscope (Karl Storz GmbH & Co., Tuttlingen, Germany) on both 2D and 3D settings for visualisation.

Tasks

The practical aspect of the study was comprised of two tasks which involved moving pins placed in black plastic foam inside an endoscopic box trainer (figure 2). Written instructions were provided, and participants were shown an open view of the box trainer and the tasks prior to their first attempt. Participants were not allowed to see others completing the tasks. Tasks were designed upon the following principles: to replicate the spatial awareness and some of the dexterity that endoscopic sinonasal surgery requires; to assume no background knowledge or skill associated with nasoendoscopy; and to be completed relatively quickly (between 1 and 5 minutes) to ensure adequate throughput of participants. A singular port for endoscope and forceps was used to replicate sinonasal endoscopy. Tasks were confined to a distance between 30 and 50mm as numerous studies have found the distance between the nasal vestibule and the anterior attachment of middle and superior turbinates to be within this range.[32-34]

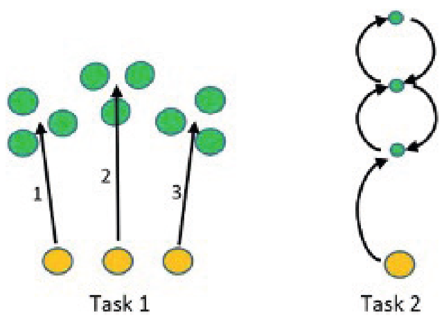

Figure 2. Task design

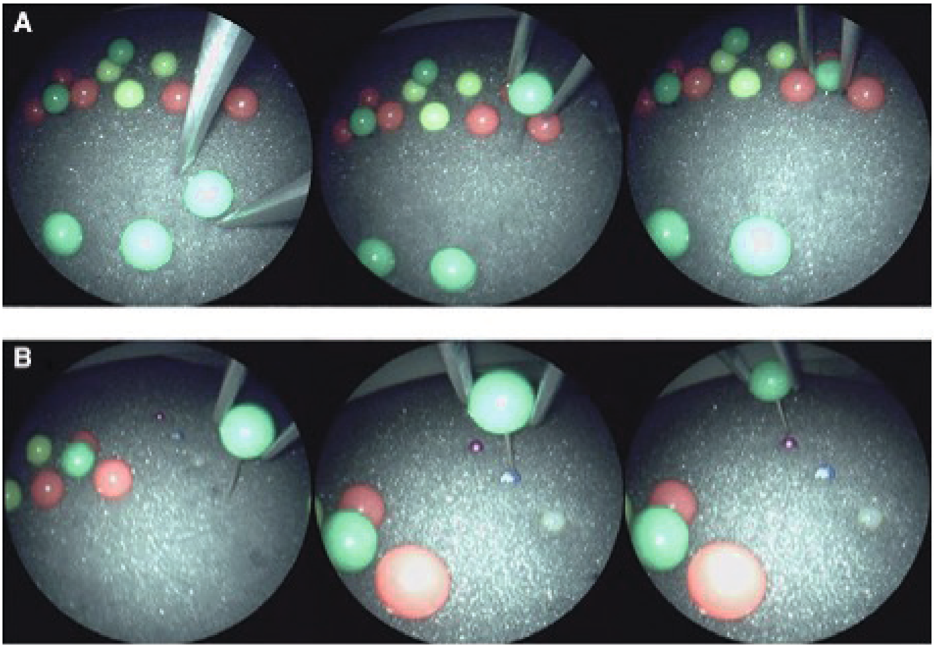

Figure 3. Photos taken of the tasks. (A) Task 1, where the green pins nearest to the endoscope were to be placed in the centre of the pins arranged in triangles. (B) Task 2, where the tip of the green pin was used to touch each of the smaller pins.

The first task was to grasp and transfer three pins into the middle of three separate targets. The target was made of three pins arranged in a triangular pattern. Targets were set at a standard distance of 30mm from the pins to replicate relevant sinonasal anatomy.[32-34] Task 1 was a modified version of the peg transfer, a validated task for endoscopic training, the modification being the placement of pin in foam rather than peg on a hook (figure 3(a)).[35] Participants then completed the second task, where they picked up another pin and used the tip to touch three small pinheads arranged in line. The pinheads were arranged over 50mm to replicate the length of the floor of the nasal cavity.[36] This task was described as a 'targeting landmarks' task, which has been described by many studies to measure endoscopic skills (figure 3(b)).[20,31,37,38]

Outcomes

Time taken to complete tasks was recorded, including adjustment time (the time taken to pick up the first bead). Errors made during completion of the tasks were also recorded. Errors were classified into those of accuracy (placing a pin outside the target) and those of dexterity (dropping a pin).

Analysis

Statistical analysis was carried out using SPSS from IBM Corp (Armonk, New York). $P<0.05$ was taken to be the level of significance throughout analysis.

Wilcoxon's tests were used for paired comparison of time taken to complete the tasks and errors with 2D vs 3D endoscopy. Data were summarised as medians and interquartile ranges (IQRs). Mann-Whitney tests were used to show the differences in performance between the 2D-first and 3D-first subgroups, showing the effect of carryover of skills. These were also used to show the relative improvement with 2D and 3D endoscopes to demonstrate the impact of technology on learning. Mann-Whitney tests were also used for Likert scale responses, and Fisher's exact test was used for nominal variables to measure subjects' preference of endoscope.

Results

A total of 93 participants took part in the study. Median age was 20, and the median year of medical study was the 2nd. Previous experience of endoscopy was minimal; 6 participants had assisted in one endoscopic procedure (all described their role as holding the endoscope in position for the surgeon) and none had assisted in more than one. Only one participant was excluded because they shut one eye when using the 3D endoscope as they 'found it easier'; unfortunately, doing this made the mode of visualisation 2D rather than 3D.

Table 1. Direct comparison 2D versus 3D using Wilcoxon tests.

Variable	2D	3D	Difference	*P* Value
Adjustment time, sec	7 (4 to 11)	5 (3 to 8)	–1 (–6 to 2)	.121
Task 1 time, sec	43.5 (29 to 57.75)	36.5 (25.25 to 46)	–6 (–24.75 to 9.25)	.020
Task 2 time, sec	39 (25.25 to 56.75)	32 (25.25 to 45)	–4.5 (–20 to 8.75)	.038
Total time, sec	94.5 (68.25 to 122)	78 (62 to 102.75)	–13.5 (–41 to 14)	.004
No. of drops	3 (1.25 to 4)	2 (1 to 3)	–1 (–2 to 1)	<.001
No. of inaccuracy errors	2 (2 to 3)	1 (1 to 2)	–1 (–2 to 0)	<.001
Total no. of errors	5 (3.25 to 6)	3 (2 to 4)	–2 (–3 to 0)	<.001

Data are presented as median (interquartile range). 2D = to dimensional; 3D = three dimensional.

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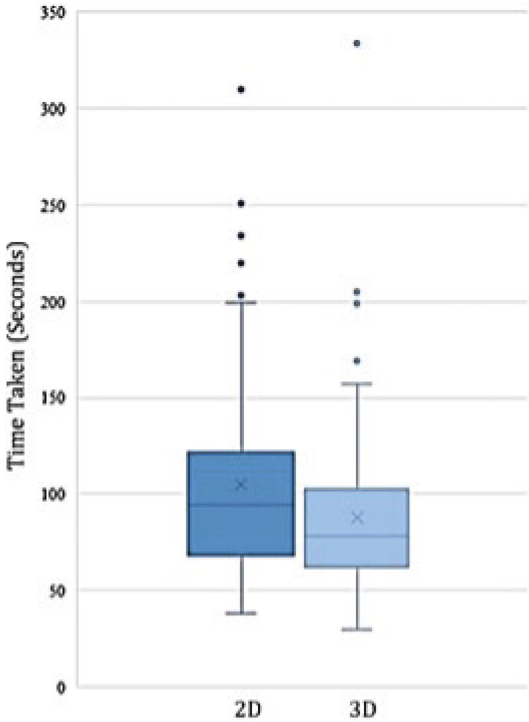

Figure 4. Box and whisker plots comparing overall time taken to complete tasks 2D versus 3D (P = .004). 2D = two dimensional; 3D = three dimensional.

Equal randomisation between groups A and B allowed carryover bias to be neutralised, thus permitting direct comparison of 2D and 3D. Wilcoxon's tests showed that attempts with 3D were significantly faster overall than 2D (median 78 vs 94.5 seconds; p=0.004). Large individual variation was observed with both settings (figure 4). No significant difference was observed between 2D and 3D in adjustment time (p=0.121). Total errors made during task completion were significantly reduced when using 3D (3 vs 5; p<0.001); these included errors of accuracy (1 vs 2; p<0.001) and dexterity (2 vs 3; p<0.001). Further comparisons between the objective outcome measurements for the two endoscopes can be seen in table 1. Subjectively, 68.5% (N=63) of participants preferred the 3D endoscope. Depth perception was found to be better with the 3D setting, with participants rating it median 7/10 compared to 4/10 for 2D (p<0.001).

Sub-group analysis was then carried out, comparing scores for those who used 2D first with those who used 3D first. Using a repeated task paradigm allowed us to assess the factor of learning in relation to the method of visualisation.

Our results demonstrated a significant carryover of skills from the first task to the second; Mann-Whitney tests showed that participants were significantly faster using either 2D visualisation (p=0.001) or 3D visualisation second (p=0.006), so participants were faster on their second attempt regardless of the endoscope they used. This demonstrates a learning effect, confirming a carryover bias in our study. Interestingly, the median number of errors made was not affected by the order of sequence, and participants using 3D endoscopy made significantly fewer errors than 2D regardless of whether they had already completed the task.

The magnitude of difference between 2D and 3D attempts was much greater in the 2D-first subgroup (34 vs 11, p<0.001), and these participants showed the lowest scores of any group on their second attempt using 3D. In other words, participants improved to a greater extent when using 3D visualisation on their second attempt. Once familiar with the task, participants were more competent using 3D than 2D (70 vs 74.5), although this difference was not statistically significant. In light of these results, we can conclude that 3D visualisation aids in shortening the learning curve of novices.

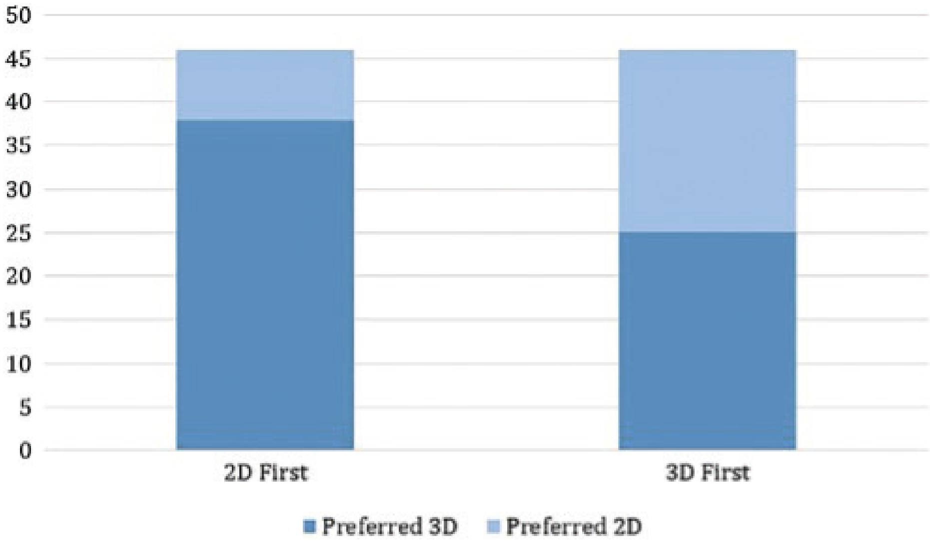

Figure 5. Fisher exact test showing endoscope preference stratified by order of endoscope (p = .007).

Fisher's exact test demonstrated that endoscope preference was significantly affected by the order of endoscope used (figure 5). 82.6% of those who used 2D first preferred 3D, and 54.3% of those who used 3D first preferred 3D (p=0.007).

Discussion

We evaluated the novice use of a 3D HD endoscope in a controlled pre-clinical environment, comparing it to 2D HD visualisation. We found that participants mostly preferred the 3D HD endoscope, performing tasks significantly faster and making significantly fewer errors than when using 2D HD. This confirmed the hypothesised superiority of 3D technology in our novice sample.

Similar results of a reduced time taken have been shown in previous pre-clinical studies using 3D endoscopy, but none to this level of significance.[21,29,30,38] Our finding of a reduced error rate is also in agreement with preceding studies.[21,28,30] The clinical benefits of a reduced error rate are clear. Furthermore, our results reinforce those found in many laparoscopic studies on 3D endoscopy.[39] It is important to consider that lower error rates during 3D attempts may have played a large part in the reduction in time taken with 3D. If a participant made an error, they generally had to go back and correct it, so it is unsurprising they both showed the same trend.

The evidence of improvement with 3D technology can be attributed solely to the form of visualisation; differences between endoscope manoeuvrability, field of view and image resolution were all negated by using the same endoscope with 2D or 3D settings.

On the Likert scale responses, we found that depth perception was significantly higher with 3D than with 2D. This provides a simple explanation for our results; with better depth perception, participants are likely to be more accurate and confident completing tasks, resulting in faster completion times alongside lower error rates. Depth perception in turn improves spatial awareness, which is an important cognitive factor for coordinating movements in a given environment. Egi et al. found that those with a low space perception ability performed endoscopic tasks better with 3D visualisation than with 2D ($p = 0.0085$).[37] Studies have identified other relevant cognitive factors that may be important in 3D endoscopy; one ENT paper and several laparoscopic papers have found that 3D endoscopy reduced task workload, a measure of cognitive processing required.[37,40-42]

Medical students are similar in terms of experience to those who will be training in endoscopy for the first time; both groups are novices. On this basis, we recommend the use of 3D technology for surgical training. The use of a single port and limitation of task distances to between 30 and 50mm ensured this study is relevant to working distances in endoscopic sinus surgery (ESS). The tasks themselves are based on validated endoscopic training tasks.[35,38] The outcomes of time taken, and error rates are highly relevant. When applied to surgery, the incremental effects of decreased time taken to complete tasks would result in quicker and more efficient operating times. There is evidence for 3D allowing a 30-minute reduction in pituitary adenoma resection operating time.[43] A shorter operative time leads to a lower risk of postoperative complications in both general and endoscopic surgery.[44,45] Furthermore, in our current rationalised healthcare systems where theatre time is at such a premium, any reduction in operative time improves theatre productivity and may offset some of the initial higher purchase costs of 3D technology, which is around £20,000 ($25,000) more expensive than 2D.

A number of ergonomic shortcomings, particularly reports of vertigo, have been cited as disadvantages of the 3D technology.[20,22] With newer technology, reports of vertigo have dwindled.[8] In our study, some participants reported feeling uncomfortable while adjusting to the 3D effect, but none reported a continuation of these feelings once they had adjusted. It is possible that our tasks were too short for participants to develop the feelings of vertigo that have previously been reported in clinical studies.

Our results suggest that 3D technology is more intuitive, and that it reduces the learning curve associated with endoscopic skills. This is in concordance with other papers.[20,22,23,46] Although our tasks were simple and quickly mastered, and thus not ideal for measuring a learning curve, our study certainly provides grounds for further clinical research.[47]

Limitations

Analysis demonstrated the presence of carryover bias which arose from one technology being used before the other. These biases were partly accounted for by randomising subjects into the two groups, allowing direct comparison of 2D vs 3D. Randomisation eliminated the possibility of allocation bias. Using only one analyst represents another important limitation in our study. Our low exclusion rate would normally be considered a weakness, but the collective lack of endoscopic experience among medical students meant that we acquired a relatively homogenous sample.

Further research

Larger prospective randomised studies are required to determine whether the efficacy of 3D endoscopy extends to real-world objective outcomes in endonasal surgery. Given the current evidence, these should be multicentre studies to provide the number of patients and experienced surgeons required to demonstrate significance. More rigorous research should be done assessing the performance of experienced surgeons using 3D vs 2D endoscopy. It would also be worthwhile comparing the learning curve among trainee surgeons using 3D endoscopy with those using 2D.

Conclusions

As the breadth of endoscopic procedures in endoscopic sinus and skull base surgery grows more expansive, so does the need for more advanced technology. We have demonstrated the efficacy of a new 3D HD endoscope when used by novices to complete simulated surgical tasks. In our sample, it was superior to 2D HD endoscopy in terms of time taken, errors made and the learning curve. This study provides the grounds for further evaluation in a clinical setting. We have shown that 3D endoscopy could be instrumental in training the next generation of surgeons.

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7

Breadth and depth: three-dimensional endoscopic field of view

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World Neurosurgery. 2019 July; 127: e717 – e721.

Abstract

Background

Three-dimensional (3D) endoscopy is an emerging tool in ENT and skull base surgery with the benefit of providing real-time depth perception. Several authors have claimed that field of view (FOV) is reduced in 3D endoscopes compared to regular two-dimensional (2D) endoscopes. We aimed to objectively compare the FOV of 2D and 3D endoscopes.

Methods

Using a standard 2D and two different 3D ENT endoscopes, images were captured of 1mm graph paper from a set distance of 6cm. Field of view was calculated from these images and compared between endoscopes.

Results

The VisionSense 3D endoscope had a slightly smaller field of view (9.1cm vs 10.1cm, -9.9%), and the Karl Storz 3D endoscope showed a slightly larger field of view (10.4cm vs 10.1cm, +3.0%). Results were complicated by different-shaped images produced by the 3D endoscopes.

Conclusion

Differences in field of view between 2D and 3D endoscopes used in ENT are not clinically significant. In consideration of these results, field of view should not be considered a limitation of all 3D technology.

Introduction

The transsphenoidal surgical approach to the pituitary was transformed upon introduction of the endoscope and the subsequent establishment of skull base surgery.[1,2] The superiority of the endoscopic over microscopic technique was reported in the landmark paper from Jho and Carrau, which advocated its use based on an improved field of view and larger perceived operating space.[3] Initial criticism of endoscopy focused on poor image quality and a loss of stereopsis.[2,4-6] Stereopsis is the subconscious evaluation of differences between the two separate images from each eye which gives a perception of depth. Image quality has been vastly improved by the introduction of HD technology into endoscopes.[7,8] Three-dimensional (3D) endoscopes have been developed to address the loss of stereopsis, aiding depth perception. Several simulated ENT studies have shown 3D endoscopy to objectively improve task efficiency and error rates.[9,10] Its application to skull base surgery has been mostly popular due to the restoration of stereopsis, allowing greater spatial orientation and consequently improving visualisation of the subtle skull base anatomy.[11]

Numerous studies have identified problems with the current 3D technology, particularly a subjectively reduced field of view.[11-13] Van Gompel *et al.* set out to objectively compare the field of view of two-dimensional (2D) and 3D endoscopes and found a 52% reduction in field of view when using 3D compared to 2D.[12] This finding, if validated, would identify a significant flaw in 3D endoscopy for visualisation of the surgical field. In our experience working with 3D, we have found a significantly smaller reduction in field of view than that claimed, so we set out to reproduce these results. In this study, we present our findings which show a significantly smaller reduction in field of view when using 3D endoscopes.

Materials and Methods

Endoscopes

For 2D visualisation, we used a Karl Storz 0° high definition (HD) 4mm rigid endoscope (Karl Storz GmbH & Co., Tuttlingen, Germany). For 3D visualisation, we used a VisionSense 0° VSIII second generation 3D HD 4mm endoscope (VisionSense Ltd., Petach Tilka, Israel), and a Karl Storz 2nd generation 3D HD 4mm endoscope (Karl Storz GmbH & Co., Tuttlingen, Germany).

Measurement

We used standard 1mm graph paper to assist our measurement and to negate the need for a standard metric ruler to be placed over the image for measurement (as done by van Gompel *et al.*). Both endoscopes were fixed at a distance of 6cm from the graph paper, which was held perpendicular to the endoscopes to avoid distortion. The images were captured and edited for clarity using Adobe Photoshop (Adobe Systems Inc., San Jose, CA).

Field of View Calculation

We measured the field of view by counting the number of small squares (each representing 1mm) across the image. It is important to note that the endoscopes produce different shaped images; the Storz 2D and 3D HD scopes produce a circular image, whereas the VisionSense 3D HD endoscope produces a rectangular image. Thus, to keep the method constant, we measured the FOV as the distance from one side of the image to the other through the centre (Figure 1). This reproduces van Gompel *et al.*'s methodology.

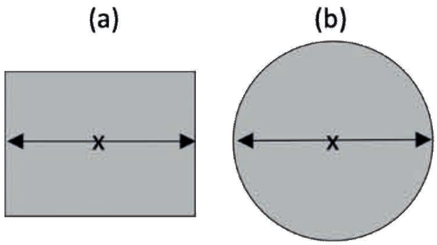

Figure 1. Measurement taken as field of view. 1(a) shows the measurement for the VisionSense endoscope, which produces a rectangular image; 1(b) shows the measurement for Storz endoscopes, which produce a circular image.

Analysis

The angular field of view (FOV_A) was calculated from the FOV measurements. FOV_A is a reliable measurement which, once calculated, is theoretically independent of the distance from a target (14). This can be obtained using the following trigonometrical equation:

$$\mathrm{FOV_A} = 2\tan^{-1}\frac{r}{d}$$

where *r=radius* and *d=distance from target* (Figure 2).

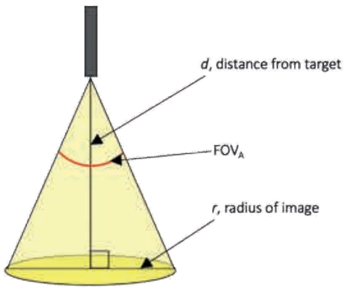

Figure 2. Simplified diagram showing the measurements used to calculate FOV_A.

The measurement *r* was taken as half of our field of view measurement, and the measurement *d* was thus taken as 6 cm.

Results

At a standard distance of 6cm, the field of view was 10.1cm for the 2D HD Karl Storz endoscope. For the 3D endoscopes, FOV was 9.1cm for the 3D HD VisionSense third generation endoscope, and 10.4cm for the 3D HD Karl Storz endoscope (Table 1). In comparison with 2D, these differences translated to a 9.9% decrease and a 3.0% increase in FOV respectively.

Table 1. Field of view measurements for each endoscope at distances of 6cm and 2cm from the graph paper.

	Field of view (% difference compared to 2D)		
Measurement	2D HD (Storz)	3D HD (VisionSense)	3D HD (Storz)
FOV (cm)	10.1	9.1 (-9.9%)	10.4 (+3.0%)
FOV_A (°)	80.2°	74.3° (-7.4%)	81.8° (+2.0%)

FOV_A was calculated to be 80.2° for the Storz 2D endoscope, 74.4° for the VisionSense 3D HD endoscope and 81.8° for the Storz 3D HD endoscope (Table 1). These results equated to a 7.4% reduction in FOV_A for the VisionSense 3D HD endoscope and a 2.0% increase in FOV_A for the Storz 3D HD endoscope.

The images taken by the endoscopes can be seen in Figure 3.

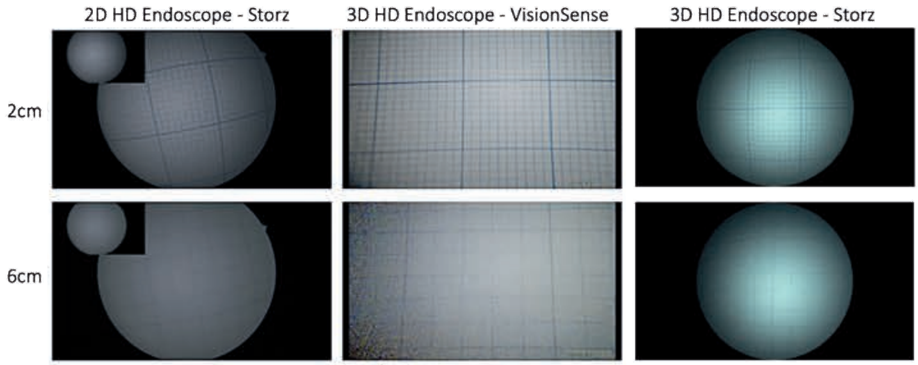

Figure 3. Side-by-side comparison of 2D HD, 3D HD VisionSense and 3D HD Storz endoscope fields of view at distances of 6cm and 2cm from the graph paper.

Discussion

Using a simple methodology, we found that the field of view in two different models of 3D HD endoscopes is within ±10% of that of 2D. We do not believe this change is clinically significant. These results are contradictory to those found by van Gompel *et al.*, and the subjective views of various authors.

Van Gompel *et al.* found that the 2D endoscope FOV was 8.3cm and the 3D VisionSense endoscope 4.0cm at a distance of 6cm, equating to a 52% reduction.[12] These findings were obtained using the VisionSense 3D SD (VSII) endoscope, an older version of the VisionSense endoscope we used. Van Gompel *et al.* did not calculate the field of view in a conventional way; as previously stated, endoscope field of view is typically measured as the so-called angular field of view (FOV_A). In our study, the VisionSense 3D HD endoscope demonstrated a 5.8° reduction in FOV_A, which is equivalent to a 7.4% reduction. Compare this to the 52% reduction in the older VisionSense endoscope, and it is clear that technological progress has been made.

The VisionSense 3D endoscope utilises ‘insect-eye’ technology to produce a 3D image.[15,16] This technology employs a collection of microscopic lenses on a single video chip at the distal end of the scope.[7] These lenses provide multiple images of the target, which are divided into ‘right’ or ‘left’ images and displayed into each eye of the surgeon, who wears polarised glasses.[7] Other designs include a dual-channel or dual chip-on-the-tip technologies which record two slightly different images for projection into each eye. The interpupillary distance and a reduced aperture diameter have been cited as reasons for a reduced field of view in VisionSense endoscopes, but these are relevant in dual-channel and dual chip-on-the-tip designs and not the VisionSense insect-eye design.[12] Furthermore, our 3D HD Storz endoscope, with the widest FOV of all those we measured, utilises dual chip-on-the-tip technology. There is currently very little evidence comparing the optical variables of chip-on-the-tip with those of dual-channel designs.

A reduced field of view may be an issue during the endonasal approach to the pituitary, where a wide field of view can improve surgical efficiency and where the range of movement of the endoscope is limited.[17] It is less of an issue for more intricate work in the sella turcica; it has been stated that the reduced field of view is advantageous in reducing interference and providing space to work with instruments, as the image is magnified relative to 2D.[2,12,18] It should be emphasised that a reduced FOV is not the only factor to be considered with visualisation of the surgical field. The resolution of the image is important, and often the edge of the image suffers from distortion or vignetting (a reduction of the image brightness towards the edge of the screen). It is more important to consider the proportion of the FOV that exhibits good optical performance.[14] Future studies comparing 2D vs 3D field of view should address this consideration.

This research is not intended to discredit the work done by van Gompel *et al.*, nor to void the opinions of various authors in the literature. It has been done to provide balance to the existing literature evaluating the field of view of 3D endoscopes in ENT surgery. Importantly, our FOV measurements suggest that optical measures from one type of endoscope cannot be generalised to 3D endoscopy as a whole. With a wide range of manufacturers and technologies used in different 3D endoscopes, it is unsurprising that there is variation between different manufacturers.

Limitations

Our image quality is substandard due to difficulties in achieving ideal lighting. Consequently, we may have marginally miscalculated our field of view, although this would have only resulted in a very small difference. Unfortunately, we did not have access to the VisionSense 3D SD endoscope used by van Gompel *et al.* However, with more recent versions available, this endoscope is less frequently being used in practice.

Conclusion

We demonstrated a small, clinically insignificant difference in field of view of two 3D endoscopes compared to 2D. Our results are not in keeping with the subjective and objective findings of previous authors. Numerous papers have cited the reduced field of view as a major drawback of 3D technology. Our results should change this outlook.

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PART 3

Amalgamation of Data Surrounding Three-Dimensional Endoscopy

8

Three-dimensional endoscopic endonasal surgery: a systematic review

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Laryngoscope. 2022 Oct; 132(10): 1895 – 1903.

Abstract

Objective

To systematically review the literature to identify studies comparing three-dimensional (3D) vs. two-dimensional (2D) endoscopy. The primary outcome was participant performance, and the secondary outcome was participant preference.

Methods

PubMed (US National Library of Medicine), Embase, Medline, Clinical Key, BMJ Case Reports and Cochrane library were systematically searched for articles published between 2005-2020, and references pertaining to these articles were screened. English-language studies reporting the use of the 3D endoscope for use in endonasal surgery, and those comparing outcomes with traditional 2D endoscopy, as well as studies containing either quantitative or qualitative data sets were included. Study characteristics, details of tasks, time taken to complete tasks, other performance-related outcomes, and participants preference were extracted.

Results

Ten studies were included in qualitative synthesis, totaling 512 participants. All studies used a Karl Storz endoscope for the 2D section of the study, with a mixture of Karl Storz, Visionsense and Shinko Optical endoscopes were used in the 3D phases. For time specific tasks, 6 studies were included in the analysis of the primary outcome. (3 studies were full procedures and were excluded due to impossibility of controlling confounding factors, 1 study did not report on measures of variability). PEG transfer (n=4) showed participants to be significantly faster when using 3D endoscopes ($p=0.003$). Touch tasks (n=4) showed no significance ($p=0.20$) between endoscope use, although considerable heterogeneity was observed ($I^2=63\%$). Two studies reported on data for additional time related tasks, but these showed no statistical significance between endoscopes ($p=0.72$). Six studies observed other performance-related outcomes (n=10), which showed a range of varying statistical significance ($p<0.001$ to no significance). The secondary outcome of participant preference was observed in 5 studies, with a preference for the 3D endoscope after pooling of 72% (95% CI:59% to 83%), which was significantly higher than 50% ($p=0.010$).

Conclusions

There is a growing body of evidence seemingly in support of three-dimensional visualisation, and we have managed to amalgamate this into our study. We have demonstrated a significantly shorter time of performing simulated, reproducible and controlled tasks and a strong preference of participants towards the use of 3D endoscopy. This study provides the grounds for further evaluation of the technology, and the potential for greater widespread use.

Introduction

Although the first description of endoscopic surgery came in the late 19th and early 20th centuries, it was not until Karl Storz produced instruments using miniature lamps in the 1940s that the field became truly remarkable.[1,2,3] The combination of this work with Hopkins' pursuit of visual limitations, as well as modifications including Hirschowitz's fibre-optics, lead to the construction of what we consider the modern endoscope.[2,3] Its introduction transformed visualisation within surgical procedures, as well as converting previous major open operations to a more minimally invasive manner. As a result, there was decreased post-operative morbidity, including pain, and shorter recovery periods.[4,5]

Despite its obvious success, the major disadvantage of endoscopy still exists, namely a loss of binocular vision. This lack of stereopsis has been found to reduce accurate recognition and management of key structures in multiple studies.[6,7,8] While surgeons with experience manage the limited depth perception with visual and haptic feedback, in addition to detailed anatomical knowledge, there is some evidence that this can still be misleading.[9,10]

In the last decade, the three-dimensional (3D) endoscope was introduced to otolaryngology, with the intention that depth perception may effectively improve surgical efficiency and patient outcomes. The idea that stereopsis permits better visualisation of curvature and texture of surfaces is well founded, and this is especially important for endonasal skull base surgeons who depend on such subtle information for successful outcomes.[11] Despite the link between improved visual acuity and surgical outcomes being well documented, there is still suboptimal information surrounding the use of 3D endoscopy. Studies have examined the learning curve for novice surgeons, the ergonomics of changing technologies, resection rates and complications, although these have typically been performed with small numbers of participants and in dramatically varying scenarios.[5,6,12,13,14] As a result, 3D endoscopy has still not found widespread acceptance or use in the field of otolaryngology.

Our study aims to collate and combine data from trials comparing 3D endoscopes to traditional two-dimensional (2D) endoscopes. The primary outcomes are those relating to participant performance in controlled pre-clinical trials with reproducible outcomes, as these minimise the effect of confounding factors. The secondary outcomes are those relating to participant preference and subjective impressions of the two types of endoscope, analysis of which will include all studies, regardless of design.

Aims

To systematically review the literature to identify studies comparing 3D vs. 2D endoscopy, and compare outcomes between these endoscopes.

PICO (Population of Interest, Intervention, Control, Outcome of Interest)

- Population of interest: Medical professionals who utilize endoscopic interventions.
- Intervention: Use of 3D endoscope.
- Control: Traditional 2D endoscope.
- Outcomes of interest:
    - Primary: Performance (e.g., time taken to complete tasks, numbers of errors, task failure).
    - Secondary: Preference (overall preferred endoscope, and subjective views on aspects of the endoscope).

Materials and Methods

For the purpose of this study, the inclusion criteria were:

1. Studies reporting the use of the three-dimensional endoscope for use in endonasal surgery, and comparing outcomes with traditional two-dimensional endoscopy
2. Studies containing either quantitative or qualitative data sets
3. English language literature

The exclusion criteria were:

1. No identifiable data reported
2. Non-English language articles

Two authors performed a comprehensive search of the literature independently. Literature search was performed with PubMed (US National Library of Medicine), Embase, Medline, Clinical Key, BMJ Case Reports and Cochrane library. Search terms included ‘three-dimensional endoscopy’, ‘3D endoscopy’, ‘3-D endoscopy’ and ‘nose’, ‘nasal’, ‘sinus’, ‘skull base’. The date range used was 2005-2020. The PRISMA (preferred reporting items for systematic reviews and meta-analyses) was used. There was no restriction of design of publications, although conference abstracts and review articles were excluded, and the final search date was 22nd July 2020.

The first two authors reviewed titles and abstracts independently. Discrepancies were resolved with open discussion. The literature was assessed per levels of evidence published by the Oxford Centre of Evidence Based Medicine. Once articles were identified, references were reviewed to identify any additional articles that had not been identified by the original search, which were then considered for inclusion in the review.

Statistical methods

For outcomes where sufficient data were available, the differences between 2D and 3D endoscopes were pooled using meta-analysis models. For ordinal or continuous outcomes, the analysis was based on means and standard deviations (SDs). As such, where studies summarised variables using medians and interquartile ranges (IQRs), the median was assumed to be an approximation of the mean, and the SD was assumed to be approximately equivalent to the IQR/1.35. Random-effects inverse-variance models were then used to pool the mean differences between 3D and 2D endoscopes across the studies. Where studies reported data within subgroups of participants, these were treated as separate cohorts for analysis. Where studies reported data for multiple tasks completed by the same set of participants, data were initially pooled across all tasks within a study using a random-effects inverse-variance model, with the resulting statistics then pooled across studies.

For analysis of the participants preference (i.e. 2D or 3D endoscope), the log-odds of the proportion that preferred the 3D endoscope was calculated for each study, and pooled using an intercept-only random-effects meta-regression model. The resulting pooled rate was then compared to a 50%, to test whether a significant majority of participants reported a preference for one of the endoscopes. The experience of trainees (novice vs. experienced) in each study was then added to the model as a covariate, to assess whether preference varied by experience. A sensitivity analysis was also performed which excluded the participants that reported no difference between the endoscopes from the denominator, on the rationale that these did not give a clear preference.

Analyses were performed using Review Manager 5.3 and Stata 14, with $p<0.05$ deemed to be indicative of statistical significance throughout.

Results

Systematic review

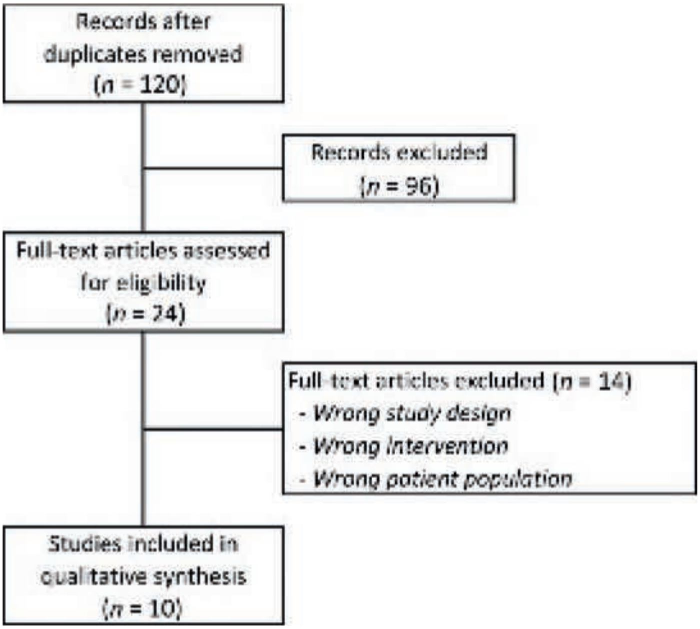

Figure 1. PRISMA flowchart.

The initial literature search yielded N=120 distinct articles, of which N=96 were excluded after title and abstract screening. The remaining N=24 studies underwent full-text screening, of which N=10 were found to meet the inclusion criteria, and were included in the meta-analysis (*Figure 1*).[15-24]

Table 1. Study characteristics

Study	Study Type	Country	N	Experience of Participants	Endoscope		Outcomes
					2D	*3D*	
Nassimizadeh[15] (2018)	Prospective Trial	UK	35	Novice	Karl Storz HD	Karl Storz 3D HD	Preference, Task Time, Adjustment Time, Past Pointing, No. Drops, Depth Perception, Field of View, Image Quality, Maneuverability
Bickerton[16] (2019)	Prospective Trial	UK	92	Novice	Karl Storz HD	Karl Storz 3D	Preference, Task Time, Adjustment Time, No. Drops, No. Errors, Depth Perception
Rampinelli[17] (2017)	Prospective Trial	Italy	68	Novice and Experienced	Karl Storz	Visionsense	Preference, Task Time
Ogino-Nishimura[18] (2015)	Prospective Case Series	Japan	73	Experienced	Karl Storz	Shinko Optical	Preference
Fraser[19] (2009)	Prospective Trial	USA	33	Experienced	*Not Reported*	Visionsense	Preference, Task Time
Ten Dam[20] (2019)	Prospective Trial	Netherlands	30	Novice and Experienced	Karl Storz HD	Visionsense Vsiii	Task Time, No. Errors, Depth Perception, Field of View, Image Quality, Maneuverability, Comfort
Albrecht[21] (2016)	Prospective Trial	Germany	46/4*	Experienced (2-10 Years)	Karl Storz HD	Visionsense SD and HD	Task Time, Depth Perception, Image Quality, Comfort

Table 1. Study characteristics (continued)

Study	Study Type	Country	N	Experience of Participants	Endoscope		Outcomes
					2D	*3D*	
Shah[22] (2011)	Prospective Trial	USA	15	Novice vs. Experienced	Karl Storz	Visionsense	Task Time, No. Errors
Barkhoudarian[23] (2013)	Retrospective Case Series	USA	160/NR**	Experienced	Karl Storz	Visionsense Vsii	Procedure Time
Tabaee[24] (2008)	Prospective Case Series	USA	26/2*	Experienced	Karl Storz	Visionsense	Procedure Time

n represents the number of participants (i.e., endoscopists) that were included in each study, unless stated otherwise.
**Number of procedures/number of participants.*
***n = 160 procedures were included, but the number of participants was not reported (NR).*

Characteristics of included studies

Details of the ten included studies are summarised in *Table 1*. These were based in Europe (N=5), the USA (N=4) and Japan (N=1), and included a total of N=512 participants (range 4-160). Participants were classified as novices in N=2 studies, experienced in N=5 studies, with the remainder (N=3) including a mixture of experience. All studies used a Karl Storz endoscope for the 2D section of the study, with a mixture of Karl Storz, Visionsense and Shinko Optical endoscopes used in the 3D phases.

The tasks performed by participants in each study are summarised in *Table 2*, with the outcomes being measured reported in *Table 1.*

Some studies included data for multiple tasks, for example Ten Dam et al. assessed five different tasks with both endoscopes. The majority of studies were prospective pre-clinical trials, which used specific tasks to test performance. However, three studies reported outcomes for full endoscopic procedures, with live patients used by Barkhoudarian et al. and Tabaee et al., whilst Ogino-Nisho utilized cadavers. Due to the impossibility of controlling for confounding factors in studies of full procedures, these studies were not included in the analyses of the primary outcomes of participant performance, but were included in the analysis of secondary outcomes related to participant preference.

Table 2. Details of tasks

Study	Task	Details
Nassimizadeh (2018)	1) PEG Transfer	PEG transfer (and transfer back to original PEG).
Bickerton (2019)	1) PEG Transfer	Grasp and transfer three pins into the middle of three separate targets.
	2) Touch Task	Pick up a pin, and use the tip to touch three small pinheads arranged in line.
Rampinelli (2017)	1) PEG Transfer (Grasping Movement)	Grab and remove three spherical targets from the nasal fossa with Weil-Blakesley forceps. Targets were positioned in different sites of the nasal cavity: 1) the upper border of nasal choana; 2) the posterior wall of the nasopharynx (midline); 3) the posterior part of the inferior meatus.
	2) Touch Task	Position the tip of an angled Seeker dissector through a metal circle 5 mm in diameter, located on the posterior wall of the nasopharynx and sagittally oriented.
Ogino-Nishimura (2015)	1) Full Procedure	Endoscopic endonasal surgical procedures on five cadavers.
Fraser (2009)	1+3) Cutting Task	Use Kerrison rongeurs (1, 1.5, 2, and 4 mm available) to remove the a portion of the transparent “sellar floor ” without removing any aspect of the red ring coloured around its border.
	2+4) Biopsy Task	Use down-angled pituitary to take four small ‘ biopsies ’ of a cotton swab.
Ten Dam (2019)	1) Identification Task	Identify six anatomical landmarks by placing the navigation system probe under direct endoscopic view on the appropriate landmark
	2) Touch Task	Place the navigation system probe exactly in the centre of five screw heads.
	3) Grasping and Retrieving	Retrieve coloured sponge discs from the maxillary and sphenoid sinus, using straight, grasping forceps.
	4) Grasping and Retrieving	Retrieve translucent tubes from the maxillary and sphenoid sinus, using a straight, grasping forceps
	5) Grasping and Retrieving	Retrieve ring shaped objects from the maxillary and sphenoid sinus

Table 2. Details of tasks (continued)

Study	Task	Details
Albrecht (2016)	1) Full Procedure	Functional endoscopic surgery for nasal polyposis
Shah (2011)	1) Ring Transfer / 2) Nerve Hook	An endoscopic dexterity training module was created to compare specific task performance between the 2D and 3D visualization systems
Barkhoudarian (2013)	1) Full Procedure	Surgical resection of pituitary disease – macroadenomas, microadenomas, nonadenomatous lesions, and recurrent tumours
Tabaee (2008)	1) Full Procedure	Endonasal endoscopic pituitary surgery

Table 3. Time taken to complete tasks

Study	N	Average Task Time (Seconds)			
		Task	*2D Endoscope*	*3D Endoscope*	*p- Value*
Nassimizadeh (2018)	35	1) PEG Transfer	107 (75-141)*	86 (56-126)*	0.153
Bickerton (2019)	92				
		1) PEG Transfer	43.5 (29.0-57.8)*	36.5 (25.3-46.0)*	0.02
		2) Touch Task	39.0 (25.3-56.8)*	32.0 (25.3-45.0)*	0.038
Rampinelli (2017) - Experienced	18				
		1) PEG Transfer	42.9 ± 17.7	38.9 ± 21.0	0.07
		2) Touch Task	41.2 ± 15.7	31.0 ± 14.6	0.002
Rampinelli (2017) - Novice	50				
		1) PEG Transfer	64.0 ± 36.0	59.8 ± 29.9	ns
		2) Touch Task	50.9 ± 21.5	50.2 ± 29.6	ns
Fraser (2009)	33				
		1) Cutting Task (2D First)	132 ± 70	151 ± 92	ns
		2) Biopsy Task (2D First)	125 ± 111	87 ± 39	ns
		3) Cutting Task (3D First)	45 ± 24	53 ± 20	ns
		4) Biopsy Task (3D First)	48 ± 22	45 ± 25	ns

Table 3. Time taken to complete tasks (continued)

Study	**N**	**Average Task Time (Seconds)**			
		Task	*2D Endoscope*	*3D Endoscope*	*p- Value*
Ten Dam (2019)	30				
		1) Identification Task	11.8 ± 5.4	12.8 ± 6.8	0.13
		2) Touch Task	12.4 ± 5.0	13.4 ± 9.2	0.32
		3) Grasping and Retrieving	17.9 ± 7.2	17.1 ± 7.9	0.26
		4) Grasping and Retrieving	18.3 ± 5.7	18.8 ± 8.4	0.39
		5) Grasping and Retrieving	29.6 ± 10.2	29.0 ± 15.5	0.3
Albrecht (2016)	4	1) Full Procedure	NR	NR	ns
Shah (2011)	15				
		1) Ring Transfer	37**	33**	0.52
		2) Nerve Hook	10.7**	10.2**	0.59
Barkhoudarian (2013)	160	1) Full Procedure	9456 ± 4278	8964 ± 2748	0.47
Tabaee (2008)	2	1) Full Procedure	8610 ± 1734	8556 ± 2658	ns

Averages for the 2D and 3D endoscopes are reported as means _ standard deviations, unless stated otherwise. Mean differences were then calculated for the 3D minus 2D endoscope, and reported alongside 95% confidence intervals (95% CI). The "n" column represents the number of participants in the studies that performed simulated tasks, or the number of procedures in those that report data for full procedures. Bold P-values are significant at P < .05. N/A = not applicable.

NR = not reported, ns = not significant.

**Study reported average times for 2D and 3D endoscopes as medians and interquartile ranges, from which the mean and standard deviation were estimated for analysis.*

***Reported as a mean, with no measure of variability, hence could not be included in the meta-analysis.*

Time taken to complete tasks

The most commonly reported outcome was the time taken for participants to complete tasks, the data for which are summarised in *Table 3*. After excluding the three studies that reported outcomes for full procedures, six pre-clinical trials were considered for inclusion in the analysis. Of these, Rampinelli et al. reported data for novice and experienced participants separately; hence these were treated as separate cohorts for analysis. Fraser et al. included two tasks which were each performed twice, with the first time using the 2D endoscope followed by the 3D endoscope, with the order reversed the second time. A large reduction in the average time taken was observed between the first and second round of tasks, likely due to a learning effect; hence only the second set of tasks were included in subsequent analysis. Finally, Shah et al. both reported no significant differences between the two endoscopes, but did not report measures of variability (e.g. SDs); hence, there was insufficient data to include this study in the meta-analysis model.

Of the remaining six cohorts, data relating to PEG transfers were reported for in four cases, which were combined to pool the average difference between 2D and 3D endoscopes (*Figure 2*). This found participants to be significantly faster when using 3D endoscopes (p=0.003), taking an average of 6.8 seconds less to complete the task than 2D endoscopes. Analysis of touch tasks included four cohorts, and found no significant difference in the time taken, with a pooled difference of 3.7 seconds (p=0.20). However, considerable heterogeneity was observed (I^2=63%), with Bickerton et al. reporting a significantly shorter task time with 3D endoscopes (median: 32 vs. 39 seconds, p=0.038), whilst Ten Dam et al. reported a non-significant increase in task times with the 3D endoscope (mean: 13.4 vs. 12.4 seconds).

Fraser et al. and Ten Dam et al. reported data for an additional two and four tasks, respectively. Pooling these found no significant difference between endoscopes, with a mean difference of less than one second (0.3 seconds, p=0.72).

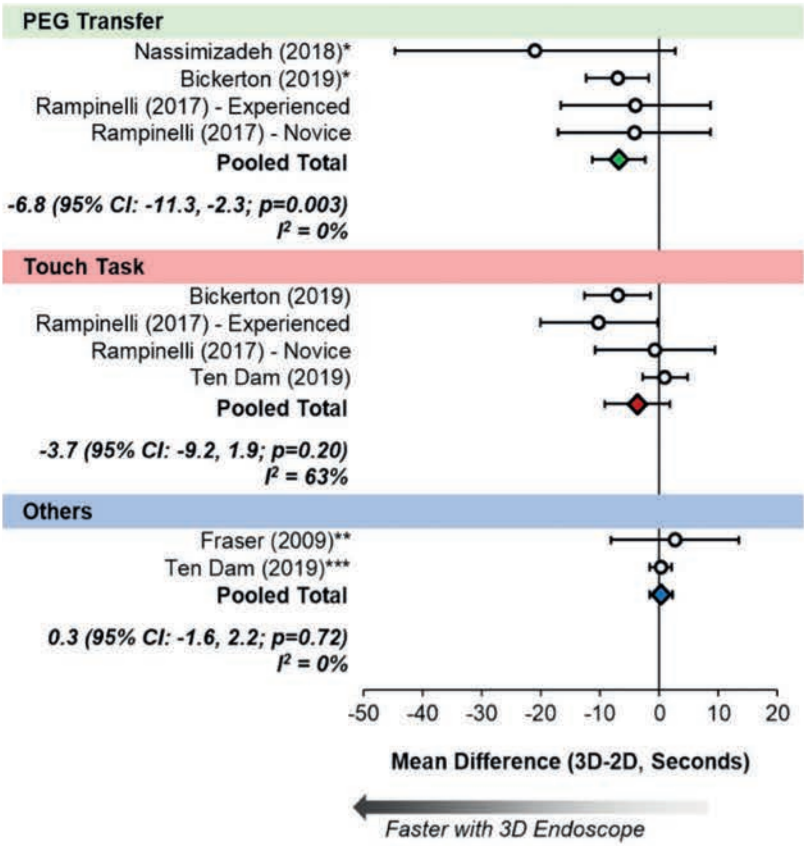

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Figure 2. Forest plot of times to complete tasks

**Study reported data as medians and interquartile ranges, from which the mean and standard deviations were estimated for analysis. **Pooled total of Tasks 3 and 4. ***Pooled total of tasks 1, 3, 4 and 5.*

Table 4. Other performance-related and subjective outcomes

			Endoscope		
Study	**Task**	**Statistic**	**2D**	**3D**	**p-Value**
Other Performance-Related Outcomes					
Adjustment Time (Seconds)					
Nassimizadeh (2018)	1) PEG Transfer	Median (IQR)	9 (5-13)	10 (5-19)	0.067
Bickerton (2019)	1) PEG Transfer	Median (IQR)	7 (4-11)	5 (3-8)	0.121
Past Pointing					
Nassimizadeh (2018)	1) PEG Transfer	Median (Range)	2 (0-5)	0 (0-2)	**0.025**
Number of Drops					
Nassimizadeh (2018)	1) PEG Transfer	Median (IQR)	2 (1-2)	1 (0-2)	0.501
Bickerton (2019)	1) PEG Transfer	Median (IQR)	3 (1.25-4)	2 (1-3)	**<0.001**
Number of Errors					
Bickerton (2019)	1) PEG Transfer	Median (IQR)	5 (3.25-6)	3 (2-4)	**<0.001**
Shah (2011)	Overall	Mean	2.27	1.33	0.26
Ten Dam (2019)	1) Identification Task	Mean ± SD	1.9 ± 2.6	2.0 ± 1.7	0.19
Ten Dam (2019)	2) Touch Task	Mean ± SD	0.7 ± 0.8	1.6 ± 1.4	**<0.001**
Ten Dam (2019)	3) Grasping and Retrieving	Mean ± SD	4.0 ± 3.2	2.6 ± 2.5	0.08
Ten Dam (2019)	4) Grasping and Retrieving	Mean ± SD	1.0 ± 1.3	1.0 ± 1.0	0.44
Ten Dam (2019)	5) Grasping and Retrieving	Mean ± SD	3.0 ± 1.7	2.4 ± 2.0	0.08
Task Failure					
Shah (2011)	Overall	Rate	8/15 (53%)	3/15 (20%)	0.13
		Subjective Outcomes*			
Depth Perception					
Nassimizadeh (2018)	Overall	Median (IQR)	4 (3-5)	8 (7-8)	**<0.001**
Bickerton (2019)	Overall	Median	4	7	**<0.001**
Ten Dam (2019)	Overall	Mean ± SD	5.8 ± 1.7	8.3 ± 1.2	**<0.001**
Albrecht (2016)	Overall	Mean ± SD	5.5 ± 2.25	8.92 ± 0.93	**<0.001**
Field of View					
Nassimizadeh (2018)	Overall	Median (IQR)	6 (5-7)	7 (5-8)	0.072
Ten Dam (2019)	Overall	Mean ± SD	7.4 ± 0.9	7.5 ± 0.7	0.35

Table 4. Other performance-related and subjective outcomes (continued)

			Endoscope		
Study	**Task**	**Statistic**	**2D**	**3D**	**p-Value**
Image Quality					
Nassimizadeh (2018)	Overall	Median (IQR)	6 (5-8)	8 (7-9)	**0.002**
Ten Dam (2019)	Overall	Mean ± SD	7.2 ± 0.9	8.0 ± 1.0	**<0.001**
Albrecht (2016)	Overall	Mean ± SD	7.95 ± 0.93	8.21 ± 1.24	ns
Manoeuvrability					
Nassimizadeh (2018)	Overall	Median (IQR)	7 (6-8)	7 (6-8)	0.247
Ten Dam (2019)	Overall	Mean ± SD	7.3 ± 1.1	7.5 ± 0.8	0.33
Comfort					
Albrecht (2016)	Overall	Mean ± SD	7.05 ± 1.17	8.18 ± 1.09	**0.025**

Bold p-values are significant at p<0.05. ns=not significant, but no p-value stated.
**Based on scores out of 10.*

Other performance-related outcomes

Details of other performance-related outcomes reported by studies are summarised in *Table 4*. For the PEG transfer tasks, two studies reported average adjustment times, with neither finding a significant difference between endoscopes. However, the single study that assessed past pointing found a significantly lower average in 3D endoscopes, and both studies that assessed the number of drops reported a lower average in 3D endoscopes, although only one of these was statistically significant. Of the studies reporting the number of errors, Bickerton found the average to be significantly lower in 3D endoscopes, whilst Shah reported no significant difference. Ten Dam assessed the number of errors separately for five different tasks, and found the results to vary by task, with 3D endoscopes tending to have fewer errors in the grasping and receiving tasks, but having significantly more errors in the touch task.

Table 5. Participants' preference

Study	N	Participants' Preference			Participants Preferring 3D Endoscope (%, 95% CI)	
		2D	3D	No Difference	Including "No Difference"	Excluding "No Difference"
Nassimizadeh (2018)	35	8	27	0	77% (60% - 90%)	77% (60% - 90%)
Bickerton (2019)	92	29	63	0	68% (58% - 78%)	68% (58% - 78%)
Rampinelli (2017) - Experienced	18	1	8	9	44% (22% - 69%)	89% (52% - 100%)
Rampinelli (2017) - Novice	50	9	36	5	72% (58% - 84%)	80% (65% - 90%)
Ogino-Nishimura (2015)	73	12	61	0	84% (73% - 91%)	84% (73% - 91%)
Fraser (2009)	33	6	25	2	76% (58% - 89%)	81% (63% - 93%)
				Pooled Total	72% (59% - 83%)	78% (68% - 85%)
				p-Value (vs. 50%)	**0.010**	**0.001**
				I^2	58%	24%

Percentages of participants preferring the 3D endoscope were calculated for the cohort as a whole, and after excluding from the denominator those who reported "no difference" between the scopes. The pooled totals are from intercept-only meta-regression models, with the p-value comparing this to a value of 50%. Bold p-values are significant at p<0.05.

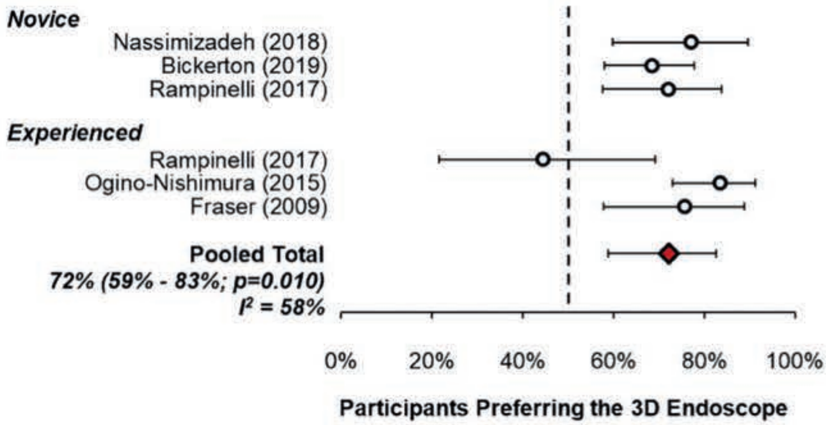

Figure 3. Forest plot of participants' preference

Results are as per the "including no difference" analysis in Table 5. Studies are split by the level of experience of participants, with Rampinelli (2017) included twice, as this included both a novice and experienced cohort. The results were not found to differ significantly by the level of experience (p=0.972); hence, the pooled total includes all studies, regardless of experience.

Participants' preference

Five studies asked participants which endoscope they preferred, yielding six cohorts for analysis, since Rampinelli et al. reported data for experienced and novice participants separately (*Table 5*). The proportion of participants reporting that they preferred the 3D endoscope ranged from 44% to 84% across the studies. Pooling this outcome yielded a rate of 72% (95% CI: 59%-83%), which was found to be significantly higher than 50% (p=0.010, *Figure 3*); hence, the majority of participants prefer the 3D endoscope to the 2D endoscope. Comparison between studies of novice vs. experienced participants found no significant difference in endoscope preference (p=0.972), although this was limited by the small number of studies. The analysis was also repeated after excluding those participants who reported "no difference" between the endoscopes, on the rationale that these did not give a conclusive preference; this gave consistent results.

Other subjective outcomes

In addition to asking about the overall preferred endoscope, some studies also asked participants to assign the endoscopes scores out of ten with regards to various subjective outcomes (*Table 4*). Participants gave considerably higher scores for depth perception with the 3D (vs. 2D) endoscope, with significant differences observed in all four studies that reported this outcome. In addition, 2/3 studies reported significantly better scores for image quality, and a single study reported significantly better comfort with the 3D endoscope. Two studies additionally reported participants' scores for field of view and maneuverability, neither of which found significant differences between endoscopes.

Risk of Bias

The risk of bias was not assessed for Barkhoudarian et al.,[24] as this was a retrospective case series. For the remaining n = 9 studies, the risk of bias assessment is reported in Supporting Tables S1 and S2 in the online version of this article. Blinding of participants was not possible for any of the included studies, due to the nature of the intervention; hence, this aspect was not considered in the risk of bias assessment. For the remaining aspects, the risk of bias was generally low, with the exception of selection and detection bias in Albrecht et al.[22] The risk of bias for Ogino-Nishimura et al.[19] and Tabaee et al.[25] was assessed differently to the other studies, as these were nonrandomized case series. No studies reported receiving funding, although Ten Dam et al.[21] stated that they received nonfinancial support.

Discussion

The principal idea that formed the advent of three-dimensional visualisation was to improve stereopsis. The Storz 3D endoscope incorporates dual 'chip-on-the-tip' technology, where two video chips create simultaneous images that are subsequently projected.[25] On the other hand, Visionsense utilises a fish-eye variation of this technology, granting a similar endpoint. Polarising glasses are required when looking at the screen for either input. These display systems can filter light output, thereby necessitating a dark background environment for optimal clarity.[17,21,26,27]

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There is currently a growing body of evidence advocating the use of 3D endoscopy, although these studies have limitations, including small numbers and the fact that a variety of different tasks, or even full procedures, are assessed. Regarding the first limitation, the current meta-analysis allowed for data to be pooled across studies, such that analysis was based on a larger number of cases. As for the variability of tasks, the meta-analysis focused on studies in a controlled pre-clinical environment, and attempted to pool like with like when assessing task performance-related outcomes.

On analysis of participant performance, 3D endoscopes were found to be associated with a significantly shorter time to complete PEG transfers, but not other task types, including touch tasks. Based on the quantitative and qualitative data available, we cannot come to a conclusion why there would be variance. Assuming that these improvements could translate to shorter operative times in clinical practice, this could potentially lead to a lower risk of postoperative complications, as well as increased levels of theatre productivity if 3D endoscopes were in common use.

This technology also potentially shortens the learning curve of novice surgeons. This would be vital on the basis that 90% of endoscopic surgical complications tended to occur in the first 30 patients of the learning curve, again reiterating the potential for improvement of surgical outcomes.[21,26,27,28]

Of the more subjective outcomes considered, participants consistently stated that they preferred the 3D endoscope to the 2D equivalent. Further assessment of these outcomes identified that participants particularly found depth perception and image quality to be superior on the 3D endoscope. In clinical practice, this may result in increased participant confidence with the endoscope, which could lead to improved patient outcomes.

However, any benefits of 3D endoscopes must be balanced against their drawbacks, including an initial higher purchase cost, although the cost difference appears to have diminished significantly with technological advances.[26]

The strengths of the current study are that several articles were identified for inclusion in the analyses, giving a sufficient sample size for analysis, and that a range of different outcomes were assessed. However, the study also has some limitations. In the analysis of the times taken to complete tasks, although the majority of studies reported outcomes using means and SDs, it was clear that several of these followed skewed distributions. For example, the mean ± SD time taken for novices to perform a PEG transfer with a 2D endoscope in Rampinelli et al. was 64 ± 36 seconds.[17] Assuming that the data were normally distributed, 95% of cases would be expected to be within the range: mean ± 1.96*SD. This would yield a negative lower bound in this case (i.e. -7 seconds), which is clearly impossible, implying that the data followed a non-normal distribution. Since meta-analysis models assume normality, this will have resulted in an overestimate of the variability in the data which, in turn, will have artificially increased the p-value. As such, the analyses may have underestimated the significance of the differences in the associated outcomes between 2D and 3D endoscopes. In addition, formal meta-analysis of the other performance-related and subjective outcomes was not possible, since there were too few studies reporting sufficient data for the majority of outcomes.

Our overall results suggest that three-dimensional technology seems to have some advantages when compared to traditional two-dimensional endoscopy, though there is the limit related to the number of participants and studies available.

Conclusion

As the use of the endoscope expands, with endoscopic sinus and skull base surgery, so does the requirement for advanced technology to improve surgical outcomes. There is a growing body of evidence seemingly in support of three-dimensional visualisation, and we have managed to amalgamate this into our study. We have demonstrated a significantly shorter time of performing simulated, reproducible and controlled tasks and a strong preference of participants towards the use of 3D endoscopy. This study provides the grounds for further evaluation of the technology, and the potential for a greater widespread use.

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PART 4

General Discussion and Summaries

9

General Discussion

General Discussion

Over the past two decades, there has been a significant transformation in surgical management of sinus related disease and anterior skull base surgery.[1,2] Having been initially introduced as a minimally invasive procedure to treat chronic rhinosinusitis, in patients whom medical management failed, endoscopic endonasal techniques have now expanded to treat orbital and skull base lesions, as well as both benign and complex malignant conditions.[3,4] This advancement has largely been propelled by improved endoscopic anatomical knowledge, new technology such as image guidance, high-powered debriders and angled instruments, as well as new surgical techniques.[1,4,5,6]

Key advantages of endoscopic endonasal operations include improved visualisation through magnified panoramic views, and reduction in removal of uninvolved structures, leading to improved overall morbidity. There is also decreased manipulation of neurovascular structures, avoidance of skin incisions and lower mortality.[6-13] Additional advantages include shorter operative duration, decreased postoperative hospital stay and improved quality of life.[6]

Despite improvements in visual quality, current endoscopic endonasal techniques still require the surgeon working in a two-dimensional (2D) environment, and with the lack of stereopsis there is an impairment in depth perception.[7] With highly variable sinonasal anatomy, anatomical knowledge and recognition through appropriate visualisation is paramount. While experienced surgeons mitigate the lack of stereopsis through experienced behaviours, these compensatory mechanisms can be misleading and are the primary cause of error.[8]

Part 1: Foundational Principles – Preliminary Work

Constant evolution of technology, techniques and a collaborative multidisciplinary team has reduced the complication rates of skull base surgery. However, it remains a challenging field with important risks. **Chapter 2** of this thesis evaluated the plethora of intra-operative and post-operative risks surrounding skull base surgery. Vascular complications in anterior skull base surgery primary affect the carotid within the sphenoid sinus. Variations, including sinus depth, increased septations and reduced intercarotid distance, heighten the risks of intra-operative injury.[9] Dehiscence rates of these vessels is as high as 93%.[10] The lack of appropriate vision can result in both vascular and neurological complications, as well as mortality. Cranial nerve injuries, such as the olfactory nerve, is common in ethmoidal tumours or meningiomas of the sphenoid ridge, as well as other tumours of the anterior skull base. Optic nerve injury can occur secondary to both protrusion and dehiscence, with over 30-70% population potentially having anatomical variations.[11] The oculomotor, trochlear and abducens nerves are adjacent to the cavernous sinus, and can result in ophthalmological complications. Similarly, elderly patients with fragile periorbital capillaries are at risk of similar sequalae. Post-operative complications such as haematoma, cerebrospinal fluid leak, infection, pneumocephalus and hydrocephalus are similar risks that require optimal conditions to mitigate.[12-14]

Chapter 2 provided an overview of unfavourable results typically related to learning curve and time taken to adapt to a two-dimensional (2D) environment.[15]

In addition to an evaluation of the risks of endoscopic endonasal approaches, **chapter 3** investigated current research and evidence within anterior skull base surgery and was the first review of randomised controlled trials (RCTs). The 14-year review analysed a total of 1785 patient participations, using the Consolidated Standards of Reporting Trials statement (CONSORT) and Jadad scale. The aim was to assess the current strength of skull base surgery reporting, and with it the foundation which we build our understanding of this field. The mean CONSORT score was found to increase significantly with larger sample size ($p=0.012$) and Jadad scores ($p=0.003$). Linear regression showed increased CONSORT scores by 0.36 for each additional 10 patients ($p=0.041$), and by 1.50 for each increase of one in the Jadad score ($p=0.002$). Overall, the reporting with regards to multiple aspects of the results and discussion of these papers was appropriate. When compared to other subject areas, RCTs in skull base surgery scored higher than other specialities.[16-18]

A combination of **chapters 2 and 3** together allowed the evaluation of current management and research strategies within this domain. It created a foundation that while current research into this field is appropriate, there continues to be scope for significant improvement in operative outcomes due to highly variable anatomy and deficiencies still present in traditional 2D endoscopes.

Part 2: Three-Dimensional Endoscopy – A Step Forward in Endoscopic Endonasal Management

In view of the preliminary work described above, the question was raised with regards to the next technological aid; namely the 3D endoscope. Certain factors persist, such as decreased manoeuvrability within narrow spaces, which cannot be addressed with 3D endoscopic techniques, but remain solely dependent on the skill and experience of the operating surgeon. However, the addition of stereoscopic surgery is a significant step forward. Before implementation of any technology, it is important to investigate the added value over the gold standard, and with it the benefits.

Chapter 4 described the initial operative experience, which highlighted no significant negative peri-operative or post-operative outcomes with the 3D endoscope. The image quality, which previously curbed enthusiasm at initial launch, had been improved to high-definition with each single lens comprised of numerous planes, similar to the eye of a fly. This improved lens led to better results in blood soiling, and image clarity. Acclimatisation to the equipment had shown to be time effective, cost efficient, safe and technically beneficial.[8,19]

In **chapter 5 and 6** there were two RCTs investigating the use of the 3D endoscope in a controlled, reproducible, validated model. While numerous studies have showed reduced time taken for tasks using the 3D endoscope, none reached the level of significance shown in **chapter 6**, principally due to smaller sample sizes.[20-23] The findings also showed a reduced error rate, also in agreement with preceding material.[20,22] It is important to consider that lower error rates during 3D endoscopic attempts may have played a large part in the reduction in time taken.

Both studies were accompanied by validated subjective questionnaires to complement the objective data. Across these trials there was statistically significant preference for 3D endoscopy. This was complemented by surrounding research which highlighted clinical comfort when opening the dura, improved visualisation of complex anatomy and higher rates of precision when removing tissue or understanding sinus anatomy.[24-27]

The work presented in **chapter 5 and 6** attributed the improvement of 3D technology solely to the form of visualisation, with differences between endoscope manoeuvrability, field of view and image resolution negated by using the same endoscope with 2D or 3D settings. The combination of objective and subjective results allowed the ability to theorise that with better depth perception, participants were likely to be more accurate and confident completing tasks, resulting in faster completion times alongside lower error rates. Depth perception helped spatial awareness, an important cognitive factor for co-ordinating movements in a given environment.[28]

These results were highly relevant when applied to clinical scenarios, as incremental effects of decreased time to complete tasks and reduced errors would result in quicker and more efficient operating times. Evidence has shown a potential 30-minute reduction in pituitary adenoma resection from the use of 3D endoscopy.[29] This improved efficiency and potential reduction in complications would offset the initial higher purchase costs of 3D technology, which is around £20,000 ($25,000) more expensive than 2D.

Chapter 5 and 7 also assessed more technical aspects of this technology, namely the field of view (FOV). Several authors had advocated that the FOV is reduced in 3D endoscopes compared to traditional technology.[30] While the 3D endoscope manufactured from VisionSense did have an approximately 10% reduction in field of view, the Storz endoscope was comparable to current technology. The basis of technology differs between the two manufacturers. While the VisionSense endoscope utilitses 'insect-eye' technology to produce a 3D image, with the interpupillary distance and reduced aperture diameter cited as other reasons for a reduced FOV, the Storz endoscope utilises dual-on-the-tip technology.[30-32] A reduced FOV proves to be an issues during the endonasal approach, where a wide range can improve surgical efficiency and the range of movement is more limited.[33] However, it is far less an issue for more intricate work, for example in the sella turcica where the image magnification of 3D technology is advantageous related to 2D.[30,34,35] It is also important to emphasise that the resolution of the image the most important factor of visualisation intra-operatively, and therefore the proportion of the FOV that exhibits good optical performance is paramount.[36]

Part 3: Amalgamation of Data Surrounding Three-Dimensional Endoscopy

As stated above, 3D endoscopic endonasal techniques provide an exciting new avenue for surgery, effectively addressing potential depth perception difficulties. In an attempt to provide a well-rounded evaluation, part 3 of this thesis focused on collating all available data in relation to this technology.

In **chapter 8**, all trials comparing 3D endoscope to traditional 2D endoscopes were combined. Despite the growing body of evidence advocating the use of 3D endoscopy, most studies were limited by small numbers, and therefore a meta-analysis allowed for data to be pooled across studies, such that analysis was based on a larger number of cases. The primary outcomes were those related to participant performance in controlled pre-clinical trials with reproducible outcomes, to minimise confounding factors. The secondary outcomes related to subjective impressions.

3D endoscopes were found to be associated with a significantly shorter time to complete PEG transfers, but not other task types, including touch tasks. Assuming these improvements could translate to shorter operative times in clinical practice, there could be increased productivity combined with decreased morbidity. Subjective outcomes showed a preference for the 3D endoscope, especially with regards to superior depth perception and image quality.

A combination of these factors can translate seamlessly into clinical practice, with increased levels of operative confidence. This is particularly poignant in novice surgeons, as it could potentially shorten the learning curve. This would be vital on the basis that 90% of endoscopic surgical complications tended to occur in the first 30 patients of the learning curve, again reiterating the potential for improvement of surgical outcomes.[24,37-39]

Concluding Remarks and Considerations for the Future

As the use of the endoscope expands, so does the requirement for advanced technology to improve surgical outcomes. This thesis provides research into novel technology which may yet shape the future of minimally invasive approaches.

There remain some shortcomings with 3D endoscopy, such as reports of vertigo and ergonomic issues.[37,38] While these reports have dwindled with newer technology, the theatre setup for the use of the 3D endoscope and screen is slightly different to conventional 2D, with the screen being placed further away for a better, more real experience and all members of the team must wear 3D glasses to appropriately visualise the screen.[40] These differences necessitate optimal space, training and experience with the technology prior to regular use. Other issues found in the literature, including bulky endoscope size, reduced field of vision and non-high-definition images have been addressed with newer technology and research found within this thesis.

While there are drawbacks to the current 3D system, it is comparable to the conception and advancement of the modern day television; from low pixelated, black and white images, to colour, followed by increased resolution prior to the introduction of high definition televisions, and the current surge of 3D functional systems. As a result, we believe 3D endoscopy not to be a revolution, but instead the next logical evolution in endoscopic surgery. The greatest advantage is for neurosurgeons who currently use the microscope for stereoscopic surgery on the skull base. As the 3D system retains stereopsis, this results in a far easier transition to endoscopic surgery than with conventional 2D endoscopy. In a similar vein, novice users seemingly adapt quicker to the 3D system, and would be another cohort to see huge benefits of widespread use. Experienced otolaryngologists on the other hand have used 2D images throughout training so the advantages are more subtle.

In summary, 3D endoscopic endonasal techniques provide an exciting new avenue for surgery, effectively addressing potential depth perception difficulties with current 2D systems. Outcomes and technology can however still be improved. In addition, future research should focus on clinical care and enhanced efficiency in hospital settings. Given the current evidence, these should ideally be multicentre studies to provide the number of patients and experienced surgeons required to demonstrate significance.

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9

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10

Summary

Summary

Since its first introduction in 1945, endoscopes transformed visualisation of the surgical field and allowed for minimally invasive surgery in previously major open procedures. Despite the obvious success of this technology, the specific drawbacks of working within a two-dimensional (2D) environment included impaired depth perception. This made the navigation of highly variable anatomical structures subjectively difficult. This limitation was addressed with a three-dimensional (3D) endoscope. The first part of this thesis (**chapter 2 and 3**) aimed to fill the knowledge gap concerning endoscopic endonasal surgery with regards to the skull base. The second part (**chapter 4, 5, 6, and 7**) evaluated the use of 3D technology within the field. This included the first uses of the endoscope clinically, reproducible pilot studies and randomised controlled trials, as well as technological assessments with traditional models. The last part of this thesis (**chapter 8**) focused on consolidating all the available information to provide an overall assessment of the new 3D endoscope.

Chapter 2 provided a comprehensive overview of skull base surgery and its associated complications. Intra-operative vascular complications are rare yet disastrous events which can lead to both vasospasm and cerebral infarction. Gentle handling of vessels using neurosurgical patties alongside low suction and frequent irrigation with isothermic saline are now mandatory operative techniques. Similarly, infiltration of vasoconstrictive agents pre-operatively lowers patient morbidity. Post-operative complications such as cerebrospinal fluid (CSF) leak can be managed with CSF lumbar drainage and antibiotic prophylaxis, and alongside early recognition of CSF rhinorrhoea, leads to a reduction of postoperative meningitis. In addition to this, a multidisciplinary approach in the management of skull base pathology ensures optimal patient outcome. Despite the evolution of surgical technique and technology which has improved patient care, it remains a challenging field of surgery. Skull base pathology is intimately linked to vital neurological structures such as cranial nerves, major arterial and venous supply, as well as the dura. These issues are compounded when managing pathology that directly invades important structures.

Chapter 3 assessed the quality of randomised controlled trials (RCTs) in skull base surgery. The quality of the RCTs were assessed using the Consolidated Standards of Reporting Trials statement (CONSORT) and Jadad scale as outcome measures. The results highlighted common omissions related to randomisation and blinding techniques, sample size calculations, and availability of protocols. The majority of RCTs scored below 18 when assessed alongside the CONSORT statement. While these issues may lead to questions regarding validity and reliability of these studies, when compared to other specialities, RCTs in skull base surgery scored higher on average. This review also highlighted the important advancements made within skull base surgery over the previous decade, with additional focus placed on patient-centred outcomes, such as quality of life measures. The purpose of this study was to provide valuable insights into the current quality of research, while providing a benchmark for research into 3D endoscopy.

Chapter 4 discusses the novel three-dimensional high definition (3D HD) endoscope in relation to endonasal approaches. Alongside a case series, there is a summary of current research into this new technology. Previous work into non-HD 3D endoscopic surgery concluded the technology to have poor image quality and difficulty navigating anatomical structures. The addition of HD to the 3D endoscope improved image quality and was similar to conventional two-dimensional high definition (2D HD) systems, while also addressing current depth perception difficulties. Despite limited evidence, no studies had shown significant peri or postoperative increases in morbidity when utilising the 3D HD endoscope, when compared with traditional 2D technology. This indicated that 3D HD endonasal approaches could be a safe and effective alternative to traditional techniques. This initial work provided an exciting new avenue for surgical techniques.

Chapter 5 investigated the benefits of 3D endoscopy for medical professionals using a prospective randomised study. While previous studies have focused on experienced surgeons with small sample sizes, this study targeted junior doctors and medical students with little to no endoscopic experience. Validated, standardised training models allowed for objective and subjective data collection using both 2D and 3D zero-degree 4mm Storz endoscopes. Statistical tests such as Wilcoxon's, Mann-Whitney, Kendall's tau, and Fisher's exact tests were used to compare variables. The participants performed better with the 3D endoscope. They completed the modified box trainer task faster and reported higher statistically significant scores on subjective measures of depth perception, field of vision, image clarity, and manoeuvrability with the 3D endoscope. The mean score for depth perception was 72.5 in the 3D group and 47.5 in the 2D group ($p<0.001$). Similarly, the mean score for image clarity was 70 in the 3D group and 50 in the 2D group ($p<0.001$). The evidence amalgamated showed that the technology improved depth perception and precision, even in individuals who are still developing their skillsets.

Chapter 6 expanded on the work previously described. 92 novice medical students completed two validated tasks using both 2D and 3D endoscopes, and objective performance was recorded. This included the time taken to complete the tasks and error rates, which were defined as any deviation from the correct path or damage caused to simulated tissue. 3D technology was significant fast, with a median time of 78 seconds (compared to 95 seconds for the 2D endoscope). The errors per task were also significantly lower for the 3D endoscope, with a median of three errors compared to five. Furthermore, Mann-Whitney tests were used to indicate there was no carryover effect dependant on which endoscope was used initially. 69% of participants also preferred the use of the 3D technology. With overall improvements in speed, accuracy and preference, the study highlighted that novice users may find 3D technology more intuitive and easier than traditional 2D endoscopes. This could lead to a smaller learning curve in surgical training, as well as increased precision.

Chapter 7 assessed the technological elements of the 3D endoscope, specifically the field of vision (FOV). Previous research had claimed the FOV in 3D endoscopes to be reduced and highlighted this as a potential limitation. The FOV of a conventional 2D endoscope was compared to two different 3D endoscopes and found no clinically significant differences. There was only a small, marginally miscalculated difference secondary to difficulties in achieving optimal lighting. This contradicted previous research, which had made implications for clinical practice and decision-making secondary to technological limitations. The intention of the study was to provide balance to the literature, as optical measurements from a single manufacturer cannot be generalised to all 3D endoscopes.

Chapter 8 amalgamated the information available surrounding 3D endoscopy, when compared to traditional techniques, using a 15-year systematic review. The primary outcome measured was participant performance, while the secondary outcome involved participant performance. Individuals who used the 3D endoscopes had overall performance increase in controlled pre-clinical trials. PEG transfer showed participants to be significantly faster (p=0.003), while participant preference leaned towards the 3D endoscope (p=0.01). The data followed a non-normal distribution, which resulted in an overestimate of variability. This created an artificial increase of the p-value and may have underestimated the significance of the associated outcomes. Formal analysis of several subjective outcomes was not possible due to insufficient data. Overall, this review suggested that 3D endoscopy may offer advantages over traditional 2D endoscopy.

The current thesis evaluated clinical and technical aspects of 3D endoscopy as a technological breakthrough with regards to endoscopic endonasal surgery and explored the remaining clinical challenges. The safety of improved anatomical identification and stereopsis of the newly developed technology is exciting, but still needs further investigation and critical appraisal. Additionally, future research would need to focus more on clinical outcomes in target patient groups, the efficiency within the care environment and appropriate implementation.

PhD Thesis Summary (Dutch)

Sinds de eerste introductie in 1945 hebben endoscopen de visualisatie van het operatiegebied getransformeerd en minimaal invasieve chirurgie mogelijk gemaakt bij voorheen grote open procedures. Ondanks het duidelijke succes van deze technologie waren er ook specifieke nadelen van werken binnen een tweedimensionale (2D) omgeving verbonden, nameljk een verminderde dieptewaarneming. Dit maakte herkenning van sterk variërende anatomische structuren subjectief moeilijk. Deze limitatie werd verbeterd met de komst van een driedimensionale (3D) endoscoop. Het eerste deel van deze scriptie (hoofdstuk 2 en 3) had tot doel de kennisleemte met betrekking tot endoscopische endonasale chirurgie met betrekking tot de schedelbasis aan te vullen. Het tweede deel (hoofdstuk 4, 5, 6 en 7) evalueerde het gebruik van 3D-technologie binnen dit veld. Dit omvatte de eerste klinische toepassingen van de endoscoop, reproduceerbare pilotstudies en gerandomiseerde gecontroleerde onderzoeken, evenals technologische beoordelingen met traditionele modellen. Het laatste deel van deze scriptie (hoofdstuk 8) richtte zich op het consolideren van alle beschikbare informatie om een algehele beoordeling van de nieuwe 3D-endoscoop te geven.

Hoofdstuk 2 gaf een uitgebreid overzicht van schedelbasischirurgie en de bijbehorende complicaties. Intra-operatieve vasculaire complicaties zijn zeldzame maar desastreuze gebeurtenissen die zowel vasospasmen als cerebraal infarct kunnen veroorzaken. Voorzichtige omgang met vaten door middel van neurochirurgische doeken, lage zuiging en frequente irrigatie met isothermische zoutoplossing zijn nu verplichte operatietechnieken. Evenzo vermindert de pre-operatieve infiltratie van vaatvernauwende middelen de morbiditeit van de patiënt. Postoperatieve complicaties zoals lekkage van cerebrospinale vloeistof (CSF) kunnen worden behandeld met CSF-lumbaaldrainage en antibioticaprofylaxe, en samen met vroege herkenning van CSF-rhinorroe leidt dit tot een vermindering van postoperatieve meningitis. Daarnaast zorgt een multidisciplinaire benadering van schedelbasispathologie voor een optimaal patiëntresultaat. Ondanks de evolutie van operatietechniek en technologie die de zorg voor patiënten heeft verbeterd, blijft het een uitdagend chirurgisch veld. Schedelbasispathologie is nauw verbonden met vitale neurologische structuren zoals hersenzenuwen, belangrijke arteriële en veneuze toevoer, evenals de dura. Dit geeft nog grotere risico`s bij pathologie die invadeert in deze belangrijke structuren. .

Hoofdstuk 3 beoordeelde de kwaliteit van gerandomiseerde gecontroleerde onderzoeken (RCT’s) in schedelbasischirurgie. De kwaliteit van de RCT’s werd beoordeeld aan de hand van de Consolidated Standards of Reporting Trials (CONSORT) en de Jadad-schaal als uitkomstmaten. De resultaten benadrukten veelvoorkomende weglatingen met betrekking tot randomisatie- en blinderingstechnieken, steekproef omvangberekeningen en beschikbaarheid van protocollen. De meerderheid van de RCT’s scoorde lager dan 18 bij beoordeling volgens de CONSORT-verklaring. Hoewel deze problemen vragen kunnen oproepen over de validiteit en betrouwbaarheid van deze studies, scoorden RCT’s in schedelbasischirurgie gemiddeld hoger in vergelijking met andere specialismen. Deze review benadrukte ook de belangrijke vooruitgang die het afgelopen decennium is geboekt in schedelbasischirurgie, met extra nadruk op patiëntgerichte uitkomsten, zoals kwaliteit van leven. Het doel van deze studie was om waardevolle inzichten te geven in de huidige kwaliteit van onderzoek, terwijl het tevens een uitgangspunt bood voor onderzoek naar 3D-endoscopie.

Hoofdstuk 4 bespreekt de nieuwe driedimensionale high definition (3D HD) endoscoop in relatie tot endonasale benaderingen. Naast een casusreeks is er een samenvatting van huidig onderzoek naar deze nieuwe technologie. Eerder onderzoek naar niet-HD 3D-endoscopische chirurgie concludeerde dat de technologie een slechte beeldkwaliteit had en dat het navigeren door anatomische structuren moeilijk was. De toevoeging van HD aan de 3D-endoscoop verbeterde de beeldkwaliteit en was vergelijkbaar met conventionele tweedimensionale high definition (2D HD) systemen, terwijl ook huidige dieptewaarnemingsmoeilijkheden werden verbeterd. Ondanks beperkt bewijs hadden geen studies significante peri- of postoperatieve verhogingen van morbiditeit aangetoond bij gebruik van de 3D HD-endoscoop, vergeleken met traditionele 2D-technologie. Dit gaf aan dat 3D HD-endonasale benaderingen een veilig en effectief alternatief konden zijn voor traditionele technieken. Hierdoor lag de weg vrij voor exploratie van nieuwe chirurgische technieken.

Hoofdstuk 5 onderzocht de voordelen van 3D-endoscopie voor medische professionals met behulp van een prospectieve gerandomiseerde studie. Terwijl eerdere studies zich hadden gericht op ervaren chirurgen met kleine steekproefomvang, richtte deze studie zich op junior artsen en medische studenten met weinig tot geen endoscopische ervaring. Gevalideerde, gestandaardiseerde trainingsmodellen maakten objectieve en subjectieve gegevensverzameling mogelijk met zowel 2D- als 3D-nulgraden 4mm Storz-endoscopen. Statistische tests zoals die van Wilcoxon, Mann-Whitney, Kendall's tau en Fisher's exacte tests werden gebruikt om variabelen te vergelijken. De deelnemers presteerden beter met de 3D-endoscoop. Ze voltooiden de aangepaste boxtrainer-taak sneller en rapporteerden significant hogere scores op subjectieve maten van dieptewaarneming, gezichtsveld, beeldhelderheid en manoeuvreerbaarheid met de 3D-endoscoop. De gemiddelde score voor dieptewaarneming was 72,5 in de 3D-groep en 47,5 in de 2D-groep ($p<0{,}001$). Evenzo was de gemiddelde score voor beeldhelderheid 70 in de 3D-groep en 50 in de 2D-groep ($p<0{,}001$). Het resultaten van deze studie toonden aan dat de technologie de dieptewaarneming en precisie verbeterde, zelfs bij individuen die nog hun vaardigheden aan het ontwikkelen zijn.

Hoofdstuk 6 breidde het eerder beschreven werk uit. 92 beginnende medische studenten voltooiden twee gevalideerde taken met zowel 2D- als 3D-endoscopen, en objectieve prestaties werden vastgelegd. Dit omvatte de tijd die nodig was om de taken te voltooien en foutpercentages, die werden gedefinieerd als elke afwijking van het juiste pad of schade aan gesimuleerd weefsel. Taken met 3D-technologie werden significant sneller uitgevoerd, met een mediane tijd van 78 seconden (vergeleken met 95 seconden voor de 2D-endoscoop). De fouten per taak waren ook significant lager voor de 3D-endoscoop, met een mediaan van drie fouten vergeleken met vijf. Bovendien werd met de Mann-Whitney-tests aangetoond dat er geen overloopeffect was afhankelijk van welke endoscoop aanvankelijk werd gebruikt. 69% van de deelnemers gaf ook de voorkeur aan het gebruik van de 3D-technologie. Met algehele verbeteringen in snelheid, nauwkeurigheid en voorkeur, benadrukte de studie dat beginnende gebruikers taken met de 3D-technologie intuïtiever en gemakkelijker kunnen uitvoeren dan met de traditionele 2D-endoscopen. Dit zou kunnen leiden tot een snellere leercurve in chirurgische training, evenals een verbeterde precisie.

Hoofdstuk 7 beoordeelde de technologische elementen van de 3D-endoscoop, met name het gezichtsveld (FOV). Eerder onderzoek had aangetoond dat het gezichtsveld in 3D-endoscopen verminderd was en benadrukte dit als een potentiële beperking. Het gezichtsveld van een conventionele 2D-endoscoop werd vergeleken met het gezichtsveld van twee verschillende 3D-endoscopen. Er werden geen klinisch significante verschillen gevonden. Er was slechts een klein, marginaal verkeerd berekend verschil als gevolg van moeilijkheden bij tot stand brengen van optimale verlichting. Dit stond in contrast met eerder onderzoek, dat implicaties had voor de klinische praktijk en besluitvorming vanwege technologische beperkingen. De bedoeling van de studie was om kritisch naar de literatuur te kijken , aangezien optische metingen van een enkele fabrikant niet gegeneraliseerd kunnen worden naar alle 3D-endoscopen.

Hoofdstuk 8 vergeleek de beschikbare informatie over 3D-endoscopie, met de traditionele technieken met behulp van een systematische review van 15 jaar. De primaire uitkomstmaat was de prestaties van deelnemers, terwijl de secundaire uitkomstmaat betrokken was bij de prestaties van deelnemers. Individuen die de 3D-endoscopen gebruikten, hadden een algehele prestatieverbetering in gecontroleerde preklinische onderzoeken. PEG-overdracht toonde aan dat deelnemers significant sneller waren ($p=0{,}003$), terwijl de voorkeur van deelnemers neigde naar de 3D-endoscoop ($p=0{,}01$). De gegevens volgden een niet-normale verdeling, wat resulteerde in een overschatting van de variabiliteit. Dit creëerde een kunstmatige verhoging van de p-waarde en kan de significantie van de bijbehorende uitkomsten hebben onderschat. Formele analyse van verschillende subjectieve uitkomsten was niet mogelijk vanwege onvoldoende gegevens. Over het algemeen suggereerde deze review dat 3D-endoscopie voordelen kan bieden ten opzichte van traditionele 2D-endoscopie.

Het huidige manuscript evalueert klinische en technische aspecten van 3D-endoscopie als een technologische doorbraak met betrekking tot endoscopische endonasale chirurgie en onderzocht de nog voorhanden klinische uitdagingen. De veiligheid van verbeterde anatomische identificatie en stereopsis van de nieuw ontwikkelde technologie is interessant , maar moet nog verder worden onderzocht en kritisch beoordeeld. Bovendien zal toekomstig onderzoek zich meer moeten richten op klinische uitkomsten in specifieke patiëntgroepen, de efficiëntie binnen de zorgomgeving en passende implementatie.

Appendices

Research Data Management,
List of Publications,
Currciulum Vitae,
Acknowledgments

Research Data Management

This thesis is based on the results of studies which were conducted according to guidelines for Good Clinical Practice. All studies were granted the relevant approval by the research and development committee of the University Hospitals Birmingham (UHB). None of the studies were subject to the medical research involving human subjects act (WHO).

Karl Storz (Germany) and Medtronic (Watford, England) supported the studies found in this thesis. No financial grants were given from either company. Data ownership from all included studies resides with UHB.

There are no actual or potential conflicts of interest including any financial, personal, or other relationships with people or organizations that could inappropriately influence, or be perceived to influence their results of all the published studies in this thesis. All data presented in this research was record, analysed, and interpreted by UHB independently. No persons or institution provided financial support to conduct or prepare research. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Prior to patient inclusion, written informed consent was obtained following UHB protocol. In studies that included demographics, outcome, surgical methodology and RFA data, these were recorded on paper case report forms. Furthermore, with regards to studies included, paper questionnaires were completed and stored securely within the ENT department sire file for update and reference.

On completion of each study this data was converted to electronic format in Excel and combined. This was stored with non-identifiable data and access was granted to only those individuals with a role in the project.

The privacy of participants in this thesis has been preserved by the allocation of individual identification numbers which corresponds to all data collected as well as consent documents and questionnaires.

All primary and secondary data that was obtained have been stored on secure computers with password encrypted access.

All data will be saved for 15 years after termination of the studies as per the research protocol and UHB research rules.

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Nassimizadeh A, Oca M, Kochar A, Karimi K. **Facelift Surgery** in: Cosmetic Facial Surgery by Joe Niamtu. 2023

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A

Currciulum Vitae

Abdul-Karim Nassimizadeh was born in Birmingham, UK on the 29th of July 1988, where he grew up with his parents and older brother. His childhood education was spent in the West Midlands where he attended King Edward VI Camp Hill School for Boys for his GCSE's and A-levels.

Following his schooling, he undertook his medical studies at the University of Birmingham Medical School. During his undergraduate degree, Abdul took time to also complete a Biomedical Sciences degree in Public Health and Population Sciences. This involved research around traditional Chinese customs and necessitated significant time spent immersing in the city of Guangzhou, China, as well as a variety of others. Abdul graduated BMedSci in 2011, and MBChB in 2012. Junior doctor training was undertaken in the West Midlands before entering an ENT themed core surgical training post in 2014. In 2016 Abdul successfully obtained a place on the ENT Higher Surgical Training Program.

During his 6 years of higher surgical training in Otolaryngology, Abdul gained broad experience in all aspects of ENT surgery, developing a specialty interest in Rhinology and Facial Plastic surgery at an early stage. This led to an involvement in research, formalised as an Honorary Research fellow at the University Hospitals Birmingham, under the privileged mentorship of Mr Shahzada Ahmed.

Abdul built upon this interest in Rhinology and Facial Plastic surgery and was awarded numerous regional, national and international prizes for his efforts. These included awards from the Midlands Institute of Otolaryngology (MIO), the British Association of Plastic & Reconstructive Surgery (BAPRAS), the British Nutrition Foundation, the Sir Arthur Thompson Trust, the Semon Club, the British Society of Otology (BSO), and recognition from the Royal Society of Medicine (RSM). He was also selected internationally for the Tarabichi-Stammberger Ear and Sinus Institute (TSESI) scholarship and was flown overseas to Dubai, United Arab Emirates.

In July 2023 Abdul successfully obtained his FRCS (ORL-HNS) at the Royal College of Surgeons, England. In the same year, he also completed his MD licensing for the United States of America. Upon completion, he took on a consultant role in the University Hospitals Birmingham Foundation Trust.

Abdul has been fortunate throughout his career to be surrounded by supportive mentors and excellent training opportunities. He has extensively published original peer-reviewed research, with over two hundred citations of his work worldwide, and presented on stage both nationally and internationally. He has written numerous book chapters alongside colleagues from the UK and the United States, as well as provided contributions towards International Consensus Statements for evolving patient care.

Alongside his accolades, Abdul continues his involvement in medical education. He is an Honorary Clinical Tutor at the University of Birmingham, with widespread involvement in undergraduate and postgraduate activities, electives and examinations.

Abdul lives with his wife, Yasmin, and two young children, Liyanna and Ali. His family are the cornerstones of his life, and the reason he continues to travelled the path taken.

Acknowledgments

During my career there have been a huge number of individuals – family and friends, as well as colleagues and mentors – who have supported me and without whom this thesis could not have been possible.

Mr Shahzada Ahmed who was the inspiration that drove me towards rhinology, as well as my mentor for over a decade. Thank you for believing in me, and evidently, being a bad judge of character so long ago. Without your support and motivation, I dread to think where I'd have ended up. You have been fundamental to any semblance of success I have achieved, and I will forever be indebted to you.

My parents, Hamid and Homa, who sacrificed their lives to provide for their children more than they could have dreamed of – a loving home, unwavering support, and role models to aspire to. If there is one wish I could have, it would be that my own children look at me someday the way I do you; real life superheroes.

My old brother, Mohammad, who spent every hard earned pound he had to show me the world. Who never felt ashamed that I stood by his side, and who carried me upon his shoulders so that I would stand tall. To my brother who took the pain of the world, and shielded others from its bitter taste, thank you.

My beautiful wife, Yasmin, thank you for supporting me through every hairbrained idea and dream I concocted. For taking the burdens that came with them – the difficult moves, the foldable beds, the toing and froing – and never allowing sadness to creep into our home. I have seen the world with you, but the day we agreed to walk this path together was when I truly received it. With you, I believe all things are possible, now and forever.

My children, Liyanna and Ali, who gave me the gift of fatherhood. My everything.

I will forever be grateful to my promotores – Prof. dr. M.K.S. Hol and Dr. A.G.W. Korsten-Meijer.

Prof. dr. Myrthe Hol, thank you for taking on the bulk of supporting this thesis, for co-ordinating a hundred different moving parts, and for your energy and guidance. I would never have thought as a student that this would be possible.

The financial support given for printing and editing of this thesis by the following organisations is gratefully acknowledge:

RijksUniversiteit Groningen

University Hospitals Birmingham

GetAhead Charity