

Evaluation and Management of Superior Canal Dehiscence Syndrome

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Evaluation and Management of Superior Canal Dehiscence Syndrome

Evaluatie en management van superieure kanaal dehiscentie
(met een samenvatting in het Nederlands)

Proefschrift

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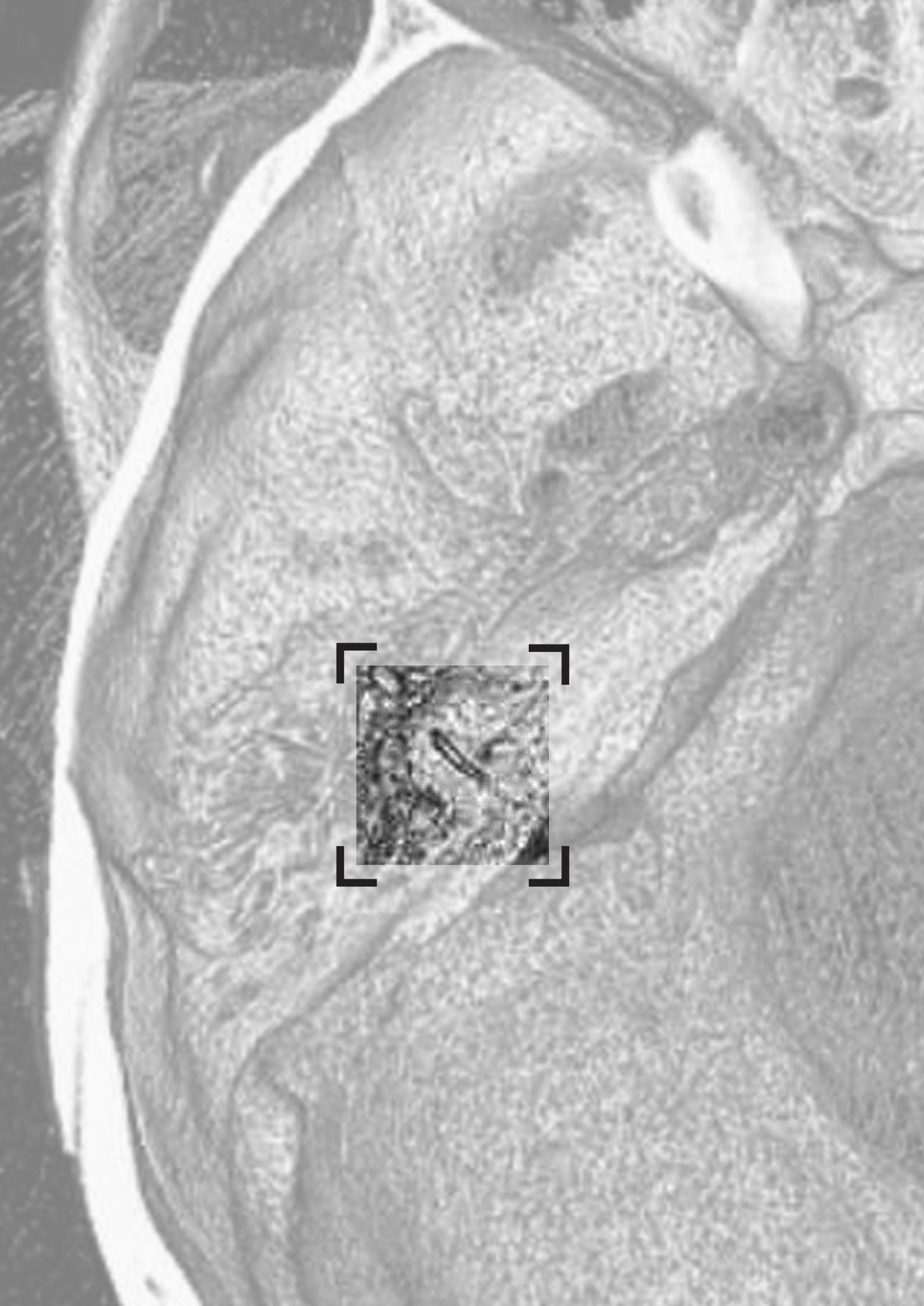
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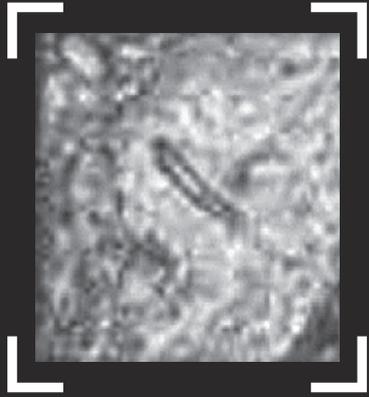
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Chapter 1

General Introduction

INTRODUCTION

Superior canal dehiscence (SCD) syndrome is a rare disorder involving the inner ear that was first described by Lloyd Minor in 1998 [Minor et al., 1998]. Patients with SCD syndrome can present with a range of auditory and/or vestibular signs and symptoms that are associated with a bony defect of one or both superior semi-circular canals. There have been over 300 publications on SCD since its discovery, but much is still not understood about this unusual clinical condition that can profoundly influence auditory and vestibular function in pediatric and adult patients. This doctoral thesis begins with a comprehensive review of auditory and vestibular anatomy and physiology, providing a foundation to the reader for a more detailed discussion of the clinical and radiologic features of SCD. What then follows is a series of clinical and scientific publications that give new insight into the clinical presentation, pathophysiology, and outcomes following surgical repair of SCD.

Anatomy of the auditory and vestibular system

The auditory function of the ear involves capturing sound waves via the outer ear, amplifying these vibrations across the ossicular chain of the middle ear and cochlear partition of the inner ear. These signals are then encoded into nerve impulses that are transmitted along the auditory nerve to the cochlear nucleus and the higher centres of sound processing found in the brain. The inner ear has an auditory and vestibular function. The paired auditory and vestibular organs are located on each side of the head within the temporal bone (Figure 1).

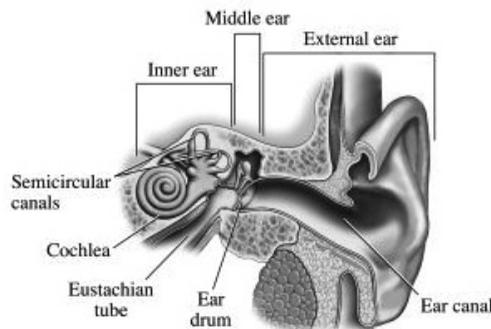


Figure 1. Overview of the external ear, middle ear and inner ear. Source: Scientific & Medical ART (SMART) Imagebase.

External ear

The outer ear consists of the auricle, formed by elastic cartilage covered by skin, and the external auditory canal. The auricle is placed around the opening of the

external auditory canal and is attached to the head with an angle of 30 degrees. The external auditory canal is approximately 3 to 4 centimetres long and 7 mm in diameter. The outer portion of the external auditory canal consists of cartilage covered with thick skin, hair cells and sebaceous glands producing wax, serving as a barrier and disinfectant, while the inner portion of the external auditory canal is covered in a thin layer of skin. The auditory canal has a slight bend at the transition from the cartilaginous component to the bony ear canal, which gives the ear canal a S-like shape contributing to the protection of the tympanic membrane [Alberti, 1995; Huizing, 2009; Lamore and Kapteyn, 2014].

The tympanic membrane divides the external ear from the middle ear. It is a cone shaped thin membrane (less than 1/10th of a millimetre) with the umbo directed inwards, creating a cone shaped opening of 135 degrees. It consists of 3 layers of which the outer layer is in continuity with the skin of the external auditory canal, the middle layer consists of fibrous material and the inner portion is in continuity with the thin respiratory epithelium covering the middle ear. The tympanic membrane is approximately 1 cm in diameter and is positioned in the ear canal within a corner of 60 degrees. A fibrous ridge surrounds the tympanic membrane [Alberti, 1995; Huizing, 2009; Lamore and Kapteyn, 2014].

Middle ear

The middle ear is filled with air and consists of the three middle ear ossicles, the malleus, the incus and the stapes, connecting the tympanic membrane with the stapes footplate covering the oval window and thereby aiding in the sound conduction. The malleus is embedded in the tympanic membrane and is positioned upward where it connects with the incus in the attic of the middle ear. The ossicles are suspended in the middle ear cavity by ligaments. The stapes consists of a footplate, positioned over the oval window, with an arch on top connected to the long process of the incus. The vertical dimension of the middle ear is 15 millimetres, while the horizontal dimension is only 7 millimetres, containing approximately 1cm³ of space. The lateral border of the middle ear is the tympanic membrane, the medial border is the cochlea, the posterior border is the antrum (the first air cell of the mastoid cavity), the anterior border is the Eustachian tube orifice, the superior border is the tegmen and the inferior border is the jugular bulb. The middle ear is laid with respiratory epithelium, which can secrete mucus and is innervated by the glossopharyngeal nerve (N IX) [Alberti, 1995; Huizing, 2009; Lamore and Kapteyn, 2014].

The middle ear contains two muscles, the tensor tympani and the stapedius muscles, innervated by the trigeminal nerve (V5) and facial nerve (V7), respectively.

The tensor tympani muscle pulls the tympanic membrane inwards, stretching the tympanic membrane and decreasing sound transmission (for low-frequency sounds). Loud sounds evoke stapedius muscle contraction, causing the stapes arch to move perpendicular to its normal motion, thereby decreasing sound transmission. Acoustic reflex testing can test this movement of the stapedius muscle [Jackler and Brackmann, 2005; Lamore and Kapteyn, 2014]. The Eustachian tube, a bony and cartilaginous thin tube connecting the middle ear and the nasopharyngeal space, regulates middle ear pressure. The facial nerve, innervating facial muscles, also passes through the middle ear, along the oval window, downwards in an angle of 90 degrees, exiting through the stylomastoid foramen. The chorda tympani nerve, one of the branches deriving from the facial nerve, crosses the middle ear to provide sense of taste to the anterior two-thirds of the tongue [Alberti, 1995; Huizing, 2009; Lamore and Kapteyn, 2014].

Cochlea

The inner ear consists of the cochlea and the vestibular labyrinth (Figure 2), which are in continuity with each other. Within the bony labyrinth, the membranous labyrinth, filled with endolymphatic fluid, is suspended with the aid of a small network of fibrous strands to the bony labyrinth and is surrounded by perilymphatic fluid. The perilymph originates from the subarachnoid space and arrives in the labyrinth through the perilymphatic duct. The membranous labyrinth is filled with endolymph, which is thought to be secreted by the stria vascularis in the cochlea and the dark cell area of the vestibular organs and resorbed in the endolymphatic sac [Huizing, 2009; Lamore and Kapteyn, 2014].

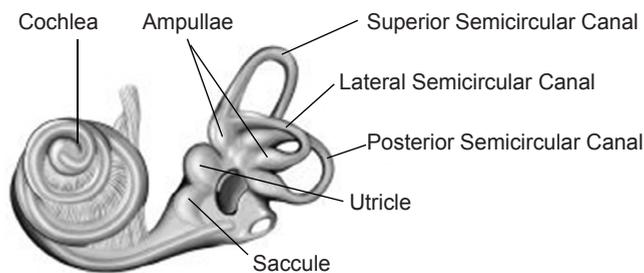


Figure 2. Overview of the inner ear with the cochlea and the vestibular labyrinth. Source: Scientific & Medical ART (SMART) Imagebase.

The cochlea, consisting of a canal shaped like the shell of a snail, is positioned in the temporal bone. It has 2 and 3/4 turns, with a total length of 35 mm and a cross-sectional of approximately 3mm². The cochlea contains three compartments: the scala vestibuli and the scala tympani, containing perilymph, surrounding the

scala media containing endolymph. The stapes footplate is positioned on the oval window of the scala vestibuli. Vibration of the stapes footplate sets the perilymph in scala vestibuli in motion. Since fluids are incompressible, the round window, positioned at the scala tympani compartment, moves simultaneously but in opposite phase of the oval window, allowing fluid flow. The round window lies inferior to the oval window in the middle ear. The scala vestibuli and scala tympani connect at the apex of the cochlea at the helicotrema. The scala media, located between the other two scalae, is separated from scala vestibuli by Reissner's membrane and from scala tympani by the basilar membrane. Thus perilymph is separated from endolymph. The lateral wall of the cochlea is the site of the stria vascularis, which aids in regulating the metabolism and ionic gradients within the cochlea [Alberti, 1995; Huizing, 2009; Lamore and Kapteyn, 2014].

The scala media houses the organ of Corti, which converts the mechanical sound waves into electrical signals. The organ of Corti consists of one row of inner hair cells (IHC) and three rows of outer hair cells (OHC), surrounded by supporting cells. Hair cells are named after typical hair-like protrusions, or stereocilia, at their apical membrane. The hair cells respond to the deflection of the stereocilia. The tunnel of Corti separates the outer and inner hair cells. When fluids are set in motion by sound vibrations delivered to the cochlea via the ossicular chain, displacement of the cochlear partition occurs and the rocking motion of the basilar membrane and organ of Corti causes hair cell motion. The tectorial membrane is a thin gelatinous layer, to which the IHCs have a loose connection, while the three rows of OHCs are strongly attached to the tectorial membrane. Because the hair cell stereocilia are attached to the tectorial membrane, movement of the hair cells due to sound causes deflection of the stereocilia, resulting in opening and closing of mechanically-gated ion channels. Changes in the membrane potential of the hair cells causes neurotransmitter release to stimulate the auditory nerve [Alberti, 1995; Lamore and Kapteyn, 2014].

The base of each hair cell is connected with one or more nerve fibres. In total, 15,000 such ganglion cells exist in each ear. Nerve fibres and hair cells do not have a one-on-one connection. Between 10 and 20 type 1 nerve fibres are connected with one IHC. The reverse accounts for the OHCs, of which numerous are connected with one nerve fibre. These type 2 nerve fibres assemble as the outer spiral bundle. The cell bodies of the fibres lie within the spiral ganglion. The nerve fibres travel through the axis of the cochlea, the modiolus, which is surrounded by the spiral ganglion. The central processes of the spiral ganglion cells form the cochlear nerve, which conducts impulses from the hair cells to the ventral

cochlear nucleus of the brainstem. In addition to this afferent pathway, efferent impulses from the brain are also sent to the cochlea, acting as an active feedback system. The cochlear nerve sends branches along both sides of the brain stem, to the hindbrain, the midbrain and to the cerebral cortex. The cochlear nerve and the adjacent vestibular nerve unite in the subarachnoid space and together form the vestibulocochlear nerve (N VIII) [Alberti, 1995; Huizing, 2009; Lamore and Kapteyn, 2014].

Vestibular labyrinth

Each vestibular organ consists of two orthogonally-oriented otolith organs, the utricle and saccule, and the three semicircular canals which are positioned at right angles to each other (Figure 3 and 4).

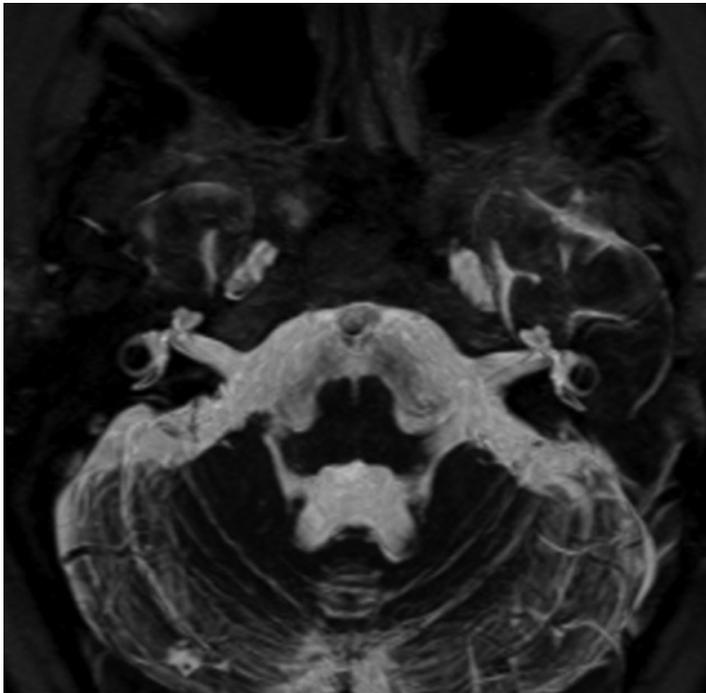


Figure 3. Overview of the location of the cochlea and vestibular labyrinth.



Figure 4. The vestibular labyrinth.

Utricle and saccule

The utricle and saccule (otolith organs) respond to linear acceleration, including movement with reference to gravity. The utricle is located superior to the saccule in the vestibule. The utricle has a dominantly horizontal position within the head, though its surface is slightly curved, whereas the saccule has a dominantly vertical orientation. The utricle and saccule each contain a sheet of neurosensory hair cells mixed with supporting cells called the macula [Cummings et al., 2005; Jackler and Brackmann, 2005]. Hair cells in the vestibular system have stereocilia (ten to hundreds per cell) and kinocilia (one per cell). When the bundle of stereocilia is deflected towards the single kinocilium by inertial movement of endolymph, the hair cell depolarizes (or hyperpolarizes when bending away from the kinocilium). Thus, each hair cell has a distinct direction in which it is sensitive to bending of the cilia; i.e., it is polarized. The cilia of the hair cells of the utricle and saccule are inserted in a gelatinous elastic mass, which lies directly on top of the maculae. On top of this mass is an otoconial membrane containing calcium carbonate crystals (otoliths), which are attached with fibrous strands to the gelatinous mass and add physical mass and weight to it. Because of this mass this layer resists acceleration and the entire complex lags behind when accelerated or keeps moving on when decelerated, causing bending of the stereocilia. The otolith organs do not respond to constant motion, because then the gelatinous layer is not displaced.

The hair cells of the macula are divided by the striola. The hair cells on each side of the striola are polarized in opposite directions. The striola of the utricle is C-shaped and the striola of the saccule is hooked. The kinocilia are always located away from the striola [Cummings et al., 2005]. This arrangement of cells in the macula of both the utricle and saccule leads to a complex pattern of excitation

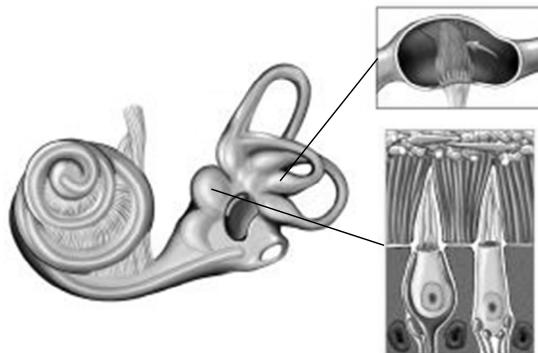


Figure 5. Overview of the inner ear with the vestibular labyrinth. Source: Scientific & Medical ART (SMART) Imagebase.

and inhibition. The elasticity of the gelatinous layers in the saccule and utricle allows them to return to the resting position soon after acceleration or deceleration.

The otolith organs can detect linear acceleration 500 times smaller than gravity. When the head is turned as compared to vertical, gravity causes displacement of the gelatinous otolithic membrane in the saccule. This inertial displacement of the otolithic membrane causes deflection of the vestibular hair cell stereocilia. The magnitude of the displacement of the stereocilia is therefore a measure of the position of our head as compared to gravity. There is a certain ambiguity associated with the interpretation of the activity patterns in utricle and saccule. The otolith organs cannot differentiate gravity from any other linear acceleration. The same pattern can be generated by a translational motion as by changing the position of the head in relation to gravity [Cummings et al., 2005; Huizing, 2009; Lamore and Kapteyn, 2014] (Figure 5).

Semicircular canals

Within each labyrinth there are three semicircular canals, the superior, posterior and horizontal canals, which are more or less positioned orthogonally with respect to each other [Cummings et al., 2005; Huizing, 2009]. Thus each canal plane is more or less perpendicular to the two other canal planes. The horizontal canals are actually tilted approximately 30 degrees above the horizontal plane. The semicircular canals from both labyrinths work in pairs that are in similar planes, therefore the superior canal of the left side is roughly coplanar with the posterior canal of the right side, forming a pair counteracting the movement of the other canal. When an angular head movement occurs in the shared plane of the left superior and right posterior canal, the endolymph of the left superior canal is for example moved to increase its neuronal firing rate, while the endolymph of the right posterior canal is moved in opposite direction and therefore has an equal but opposite inhibition rate. The same accounts for the paired right superior canal and left posterior canal and for both horizontal canals, which are roughly coplanar and therefore work as a pair [Cummings et al., 2005; Jackler and Brackmann, 2005]. A term borrowed from the aviation terminology is the movement along three orthogonal axes, namely “pitch, roll and yaw” or the vertical, lateral and longitudinal axis. The semicircular canals respond to these movements such that, in earth vertical position, both the superior and posterior canals are activated in pitch and roll movements of the head, while the horizontal canals are activated by yaw rotation (Figure 6).

The membranous canal is less than one-third of the cross-sectional area of the bony semicircular canal [Swartz et al., 1996]. The vestibular sense organ of a

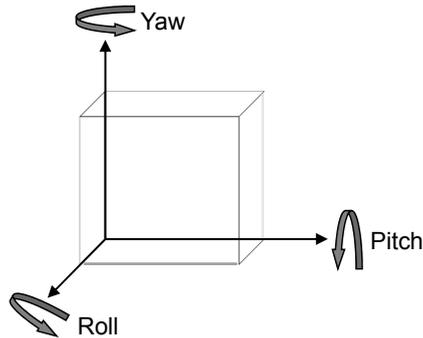


Figure 6. The semicircular canals sense motion of pitch, roll, and yaw.

semicircular canal is the crista ampullaris, which is located in the ampullated end (enlarged portion) of a semicircular canal. The crista ampullaris contains hair cells, each hair cell contains 30-200 stereocilia and one kinocilium. The stereocilia are covered by a ridge of gelatinous cupula composed of mucopolysaccharides. When angular acceleration of the head occurs, inertial movement of endolymph within the membranous canal causes the cupula and the stereocilia within the cupula to bend.

The endolymph stops moving within 2ms, due to friction with the membranous labyrinth and the resilience of the cupula in relation to the mass. The opposite occurs with angular deceleration. With constant rotation, the cupula bends back to its normal position within 20 seconds and the endolymph resumes its normal position as compared to the membranous canal [Huizing, 2009]. The movement of the endolymph reaches its maximum when the angular movement is in the plane of the canal. When the angular movement is in the plane perpendicular to the semicircular canal, displacement of endolymph does not occur. The left horizontal canal is most sensitive for rotation to the left, and the right horizontal canal is most sensitive for rotation to the right. The semicircular canals are most sensitive to acceleration between the frequencies of 0.5 Hz and 10 Hz. Thus, the vestibular system anatomy is optimized for detecting slow (i.e. low-frequency) movements [Huizing, 2009].

Vestibular nerve and vestibular nucleus

The hair cells of the saccule, utricle and the semicircular canals are connected through synapses with afferent fibres, which have their body in Scarpa's ganglion and are surrounded by cerebrospinal fluid in the internal auditory canal [Jackler and Brackmann, 2005]. From here the connections with mostly the vestibular nuclei and cerebellum are made. The vestibular nerve consists of approximately 18,000

neurons. The utricular nerve and the ampullary nerves each consist of around 3500 nerve fibres, while the saccular nerve consists of slightly less than 3000 nerve fibres [Jackler and Brackmann, 2005]. About 95% of these fibres are afferent; the remaining 5% are efferent. Vestibular nerve fibres have resting discharge rates from 10 to 100 spikes per second, but can reach spike frequencies of around 600 when optimally stimulated. The vestibular nerve is spontaneously active to allow bidirectional change (frequency up or down) depending on the deflection of the hair cell cilia in the end organs [Jackler and Brackmann, 2005]. The superior vestibular nerve communicates with the horizontal and superior semicircular canals and the utricle, and the inferior vestibular nerve communicates with the posterior semicircular canal and the saccule [Huizing, 2009].

The vestibular nuclei are positioned at the bottom of the fourth ventricle on both sides of the brainstem. There are four vestibular nuclei: the superior nucleus (Bechterew), the medial nucleus (Schwalbe), the lateral nucleus (Deiters) and the inferior nucleus (Roller), which integrate the information of the vestibular system with the information of the visual and proprioceptive systems. The vestibular nuclei send information to the cerebellum and to the oculomotor nucleus (oculomotor, abducens and trochlear nucleus), which control the eye movements by sending information to the six extra-ocular muscles.

Function of the auditory and vestibular systems

Auditory system

The main function of the auditory system is the processing of sound. Sound conduction occurs in the external and middle ear and sound transduction occurs in the inner ear. The cochlear nerve transports the sound to the auditory nuclei and auditory cortex.

External ear

The function of the outer ear is collection and localization of sound, mainly high frequency sounds, and conducting these sounds through the external auditory canal to the tympanic membrane. The auricle consists of a fairly large surface area, which collects sound for funnelling into the external auditory canal and blocks the sound from behind, aiding in directional hearing. In the mid frequencies, the head works as an obstacle and disturbs the free sound field by casting a sound shadow, changing the phase and time of arrival of sounds between ears. The pressure at the ear canal entrance is also influenced by the direction of sound. The arrival time of sound at the external auditory canal and the sound pressure at the entrance of the external auditory canal both influence our

directional hearing [Huizing, 2009; Jackler and Brackmann, 2005; Lamore and Kapteyn, 2014].

Due to the shape of the external auditory canal, resonance occurs at specific frequencies depending on the length of the ear canal, usually approximately around 3000 Hz (range 2000 to 5000 Hz). The effects of the head as an obstacle and the resonance of the ear canal together, cause a 15 dB (5 to 25 dB) gain in the frequencies 2000 to 5000 Hz [Jackler and Brackmann, 2005]. Sound sets the tympanic membrane in motion. This motion is passed to the middle and inner ear by the three middle ear ossicles [Alberti, 1995; Lamore and Kapteyn, 2014].

Middle ear

The middle ear works as an impedance transformer between the tympanic membrane and the stapes footplate, conducting sound from the tympanic membrane to the inner ear. Transmission of sound waves from air to fluid causes energy loss. Fluids have a high pressure (fluids are difficult to compress and thus hard to start a vibration) and a low velocity (the amplitude of the velocity is small), resulting in high impedance (pressure divided by velocity), while the impedance for air is relatively low, approximately 135 times smaller than the impedance of fluids. The ossicles aid in the transmission of low impedance substance (surrounding air) to high impedance substance (surrounding perilymph). Without the ossicles, only 3% of the sound energy would be passed to the perilymph and the remainder would be reflected [Alberti, 1995; Lamore and Kapteyn, 2014].

The first mechanism that aids in conduction of sound to the inner ear is the size of the tympanic membrane. Due to the large size difference of the surface area of the tympanic membrane and the stapes footplate, the surface area of the tympanic membrane is 17 times the surface area of the stapes footplate, hydraulic amplification occurs. The sound transduction is increased with 25 to 30 dB, varying with each frequency. The amount of sound that reaches the oval window by conduction through the ossicles, is therefore higher than the amount of sound that reaches the round window. This causes the fluids in the cochlea to be set in motion, causing improvement of sound transmission. The second mechanism that aids in the conduction of sound to the inner ear is the performance of the middle ear ossicles as a lever. The middle ear ossicles are not in a direct line with each other, leading to a rotational movement of each of the ossicles. Due to this rotational movement, 2 dB is added to the conducting mechanism. The third mechanism in the conduction of sound is the buckling of the tympanic membrane, which adds 6 dB to the conducting mechanism. These three mechanisms add approximately

33 dB to the sound conduction to the inner ear with [Huizing, 2009; Lamore and Kapteyn, 2014].

In order to transduce the sound properly, pressures on both sides of the tympanic membrane need to be similar, which is arranged by the Eustachian tube opening briefly by every 3rd or 4th swallow. In addition the mastoid air cells act as an air reservoir aiding in the regulation of middle ear pressure. If the Eustachian tube is closed for too long, air in the middle ear is absorbed by the respiratory epithelium, causing negative pressure. Consequently, negative pressure causes fluid secretion by the middle ear, causing a conductive loss. Multiple variables can influence the process of sounds transduction, e.g. a perforation in the tympanic membrane, a middle ear filled with fluids instead of air, lower air pressure in the middle ear as compared to the ambient pressure, disruption or stiffness of the ossicles [Jackler and Brackmann, 2005].

Inner ear

The cochlea contains sensory cells and has the ability to transduce the vibration of the travelling wave into a neural code. Sound travels via the tympanic membrane, along the middle ear ossicles to arrive at the oval window. Here, the mechanical energy is transformed by the stapes into a travelling wave (hydraulic energy). The travelling wave of the basilar membrane is set in motion by perilymph in scala vestibuli and tympani. The travelling wave starts at the base of the cochlea and continues to the apex of the cochlea. The mechanical characteristics of the basilar membrane change along the route to the apex. At the base of the cochlea the basilar membrane is relatively stiff and slender, due to the supporting cells, as it gets less stiff and wider towards the apex of the cochlea. In addition to the change in basilar membrane characteristics, the length of the hair cells increase towards the apex, while the diameter of the cells deteriorates. These mechanical changes result in frequency specific sensitivity along the course of the basilar membrane [Alberti, 1995; Lamore and Kapteyn, 2014].

The cochlea separates the different frequencies of sound. The tonotopy of the cochlea is arranged in such way that the basilar membrane resonates at the base of the cochlea for the higher frequencies and at the apex of the cochlea for the lower frequencies. Each travelling wave reaches its specific frequency on the basilar membrane. For example a frequency of 1000 Hz is reached halfway throughout the basilar membrane, therefore sounds below 1000 Hz have to travel further and sounds in frequencies higher than 1000 Hz travel less than half way through

the cochlea. The basilar membrane can separate the different frequencies in a complex sound.

The motion of the basilar membrane is a non-linear motion (logarithmic), contributing to the frequency selectivity of the cochlea [Jackler and Brackmann, 2005]. The normal range of hearing is 0 to 100 dB. To cope with this range of sound intensity, only the inner hair cells can transduce the sound vibrations to a nerve impulse. The inner edge of the basilar membrane, where the inner hair cells are located, is relatively immobile. Depending on the size of movement of the basilar membrane, the inner hair cells are stimulated. If the movement of the basilar membrane is small, the stimulated outer hair cells actively contract and shorten, amplifying the travelling wave because the outer hair cells are attached to both Reissner's membrane and the basilar membrane, and the inner hair cells respond to this amplification. When damage of the outer hair cells occur, which is more likely than damage of the inner hair cells, the outer hair cells cannot contract and amplify the travelling wave anymore, therefore the inner hair cells do not receive the necessary amplification for low intensity sounds, leading to a low intensity hearing loss. For the larger intensities, the inner hair cells are still directly stimulated. This is known as loudness recruitment. Due to the amplifying mechanism of the conducting mechanism at 3000 to 4000 Hz, the travelling wave at these frequencies is more intense, leading to more risk of damage at these frequencies.

Vestibular system

The main function of the vestibular system, consisting of the periphery (which we referred to as labyrinth above) and the central structures, is to sense head movements and counter them with reflexive eye movements and postural adjustments. In this way the system stabilizes our vision by stabilizing the image on our retina and keeps us from falling by maintaining our orientation in space [Cummings et al., 2005]. The labyrinth is located within the temporal bone and responds to both angular and linear head acceleration by sending information through the vestibular nerve to secondary vestibular neurons in the brainstem vestibular nuclei. The vestibular system also stabilizes and maintains body orientation in space by reflexes that act on the body, limb and extraocular muscles. Reflexive signs in vestibular disorders, such as eye movements or postural changes, can be explained by the brainstem's response to perceived rotation or tilting, even though the head does not move. The cerebellum plays a role in coordination and adaptation of vestibular reflexes when changes occur [Cummings et al., 2005; Huizing, 2009]. In addition to the vestibular system, other systems aid in maintaining body

and head orientation and equilibrium: the visual system, proprioception, the auditory system and the cerebellar function all contribute to our equilibrium [Huizing, 2009; Jackler and Brackmann, 2005]. Each system has its unique contribution, and interaction of these systems occurs mainly in the cerebellum and vestibular nuclei [Huizing, 2009].

Reflex mechanisms

There are three reflex mechanisms that are important for the vestibular system. The first is the vestibulo-ocular reflex (VOR), which helps us to stabilize our gaze [Cummings et al., 2005]. Our visual system can only process information of relatively static images, with an angular velocity of less than 3 degrees per second. Thus, the visual system alone is often too slow to stabilize the images when our head is moving. However, our vestibular system is fast enough. Our two labyrinths detect our head acceleration, and this information is sent to the vestibular nuclei and cerebellum. The oculomotor nucleus uses this information to control the ocular muscles. The ocular muscles ideally move with the same velocity but in opposite direction of our head velocity, which causes the image to be stabilized on our retina. Slow head movement can be stabilized by our visual system through its own feedback, but image stabilization associated with fast head movement (>1 Hz) mainly depends on our vestibular system. When being turned around, the compensatory opposite eye movement causes a nystagmus to occur, a rhythmical compensatory movement of the eye to stabilize the image, with a slow compensatory phase and a fast recovery phase [Huizing, 2009]. The primary reaction of the extraocular eye muscles work in the same planes as the planes of the pairs of semicircular canals. Therefore, an opposite reaction of the VOR in the same plane of the active semicircular canal stabilizes the gaze. In healthy subjects, the VOR can easily be suppressed by the visual system, an effect that we call fixation suppression [Cummings et al., 2005; Huizing, 2009].

The second reflex mechanism is the vestibulocollic reflex (VCR), which provides head stabilization in space. It cooperates with the cervicocollic reflex (CCR). Equilibrium depends on the postural muscle tone and on the position of our mass centre of gravity with reference to our supporting surface. The vestibular systems and the graviceptors detect our position as compared to gravity. The graviceptors are found throughout the body (e.g., graviceptors are located in the trunk). Detection of gravity causes stimulation of our vestibular nuclei, which causes tightening of muscles, resulting in increased muscle tone [Cummings et al., 2005].

The third reflex mechanism is associated with the vestibulospinal reflex (VSR), which is involved with regulation of postural stabilization and facilitates gait [Cummings et al., 2005]. Three VSR tracts exist: the medial vestibulospinal tract, the lateral vestibulospinal tract and the reticulospinal tract. Stimulation of the semicircular canals leads to fast contraction of neck muscles through the medial vestibulospinal tract (vestibulocollic reflex). The head is stabilized with regard to the plane of the semicircular canal that was stimulated. Stimulation of the otolith system causes excitation of the extensors and inhibition of the corresponding flexors in the ipsilateral limbs through the lateral vestibulospinal tract. The semicircular canals and the otolith organs form afferent fibres to the bulbar reticular formation, through the reticulospinal tract, to stimulate motor neurons in the lumbar spinal cord. These vestibulospinal tracts are regulated by the spinocerebellum, vestibulocerebellum, cortex and basal ganglia, to tune the posture of head and body with the motor tasks that need to be performed [Cummings et al., 2005; Huizing, 2009].

Hearing loss and dizziness

Hearing loss

Hearing loss can be sudden or gradual. Approximately 33% of elderly between 65 and 74 years of age and nearly 50% of those above 75 years of age have hearing loss (National Institutes of Health (NIH, U.S.) website). Hearing loss can impair oral communication skills, negatively impact learning, reduce work productivity and strain interpersonal relationships.

Audible sounds in human range between 16 and 32 Hz, to approximately 16,000 to 20,000 Hz. The sensitivity is highest from 128 Hz to about 4000 Hz. With increasing age, hearing sensitivity diminishes, especially for the higher frequencies [Alberti, 1995].

Many categories of hearing loss exist and these include 1) hereditary hearing loss (e.g. Pendred syndrome), 2) congenital hearing loss (e.g. sensorineural hearing loss from Connexin 26 mutation or maximal conductive hearing loss from canal atresia), 3) acquired conductive loss (e.g. middle ear effusion, ossicular fixation), 4) acquired sensorineural hearing loss, when the problem lies in the hair cells of the cochlea (e.g. noise exposure, ototoxic medication exposure, Ménière's disease) and 5) functional hearing loss (e.g. psychogenic) [Lamore and Kapteyn, 2014]. A combination of the above can also exist.

Dizziness

A disturbance in the vestibular system is characterized by vertigo, imbalance or gait instability, but not all dizziness is caused by inner ear pathology. Vestibular dysfunction is commonly encountered in the primary care or otolaryngology clinic, with 40% of patients seeking medical attention for dizziness at least once in their lifetime (National Institute of Deafness and Other Communication Disorders, NIDCD; a branch of the NIH in the U.S.) [Agrawal et al., 2009a; Kentala and Rauch, 2003]. Dizziness can in some cases lead to falls, which can lead to serious injuries. Falls is one of the major causes of accidental death in elderly, estimated at up to 50 percent [Kentala and Rauch, 2003; Schiller et al., 2007].

Dizziness can be divided into four categories: 1) vertigo, defined as hallucinations of movement involving oneself or the surrounding environment (e.g. Ménière's disease), 2) disequilibrium, a sensation of imbalance when standing or walking (e.g. sensory deficits), 3) impaired perfusion of the central nervous system or near syncope (e.g. orthostatic hypotension) and 4) psychogenic dizziness (e.g. anxiety disorder) [Froehling et al., 1994]. Vertigo in particular seems frequently associated with disturbances in the vestibular system. Light-headedness or feelings of imbalance can be vestibular-based but can just as easily be associated with other causes like blood pressure problems or muscle weakness. The cause of dizziness varies with age, but around 40 percent of dizzy patients have peripheral vestibular dysfunction, attributed to causes such as benign paroxysmal positional vertigo, vestibular neuritis or Ménière's disease. Of the remaining 60 percent, 10 percent have a central brainstem vestibular lesion, 15 percent have a psychiatric disorder, and 25 percent have other problems such as presyncope and disequilibrium. Some patients have multiple causes accounting for their dizziness. The diagnosis remains uncertain in approximately 10 percent of patients [Branch and Barton, 2012].

In the following thesis we aim to improve our understanding of superior canal dehiscence syndrome, an uncommon clinical condition that is associated with a disruption of the normal auditory and vestibular pathways as described above. Specifically, patients with SCD syndrome have a bony defect of the superior semicircular canal in one or both ears as seen on computed tomography (CT) and present with a range of vestibular and auditory signs and symptoms. This is a recently described condition and there are many unanswered questions that exist regarding pathophysiology, correlation of radiologic findings with signs and symptoms, and surgical management options and outcomes.

Superior canal dehiscence syndrome

Demographics

Superior canal dehiscence (SCD) is defined as a lack of bony covering over the superior semicircular canal (SSC). It was first described in 1998 by Minor et al. [Minor et al., 1998]. Patients can present with auditory symptoms, vestibular symptoms or a combination of both. The true incidence of SCD is not known. Temporal bone studies have reported an incidence of 0.5% to 2% of patients that have a thin (≤ 0.1 mm) or dehiscent SSC, of which 50 percent (6/12) of patients have bilateral SCD [Carey et al., 2000]. Three to nine percent of patients who have undergone CT imaging for other reasons have anatomic SCD (defined as a dehiscent SSC on CT scan) [Masaki, 2011; Williamson et al., 2003], and 17% to 46% of these patients are affected bilaterally [Belden et al., 2003; Williamson et al., 2003]. Some patients with a dehiscent SSC on imaging can present without SCD signs or symptoms and are defined as having an anatomic SCD. Patients who present with symptomatic SCD have SCD syndrome (SCDS).

Pathophysiology

Bony defects of the superior semicircular canals are more commonly seen than bony defects of the posterior or horizontal semicircular canals. This observation can be explained by the proximity of the SSC to surrounding anatomic structures that, for example, may result in incomplete ossification at the boundary between the SSC and middle fossa dura (arcuate eminence defect) or the superior petrosal sinus (defect of non-ampullated limb of SSC) [Carey et al., 2000; Chen et al., 2009; McCall et al., 2011; Minor, 2005]. The overwhelming majority of SCD cases involves the arcuate eminence and SCD ears are often associated with a low-lying dehiscence tegmen.

The development of SCD is not felt to be an arrest in the ossification process, as the bone surrounding the dehiscence is lamellar. Different theories on the onset of SCD signs and symptoms exist, including both congenital and acquired events. One theory is that there is a “first event” where some patients are born with thin or absent bone overlying the superior semicircular canal, and that a “second event” results in the onset of SCD signs and symptoms, perhaps due to the disruption of the exposed endosteum or membranous labyrinth in the region of the bony defect. Examples of a second event include head trauma, a Valsalva maneuver, or acoustic trauma. At the Massachusetts Eye and Ear Infirmary, a patient who was standing near the 2013 Boston Marathon bombing developed an abrupt onset of SCD symptoms (Lee et al, unpublished data). Imaging confirmed a bony defect of the arcuate eminence of the SSC in the symptomatic ear, and the patient underwent suc-

successful repair via a middle fossa craniotomy approach. Another theory to explain the pathogenesis of SCD is that dural pulsations over the arcuate eminence (and surrounding low-lying tegmen) result in progressive loss of bone. A third explanation is the progressive or abrupt disruption (second event) of the “autoplugging” by dura. Autoplugging of the dura is seen in large arcuate eminence defects during extradural dissection via middle fossa craniotomy [Carey et al., 2000] (Lee et al, unpublished observations). Theories that support progressive bone loss of the SSC are supported by observations that the prevalence of SCD increases among older populations [Nadgir et al., 2011]. In some patients, a combination of factors (thin bone over the superior canal, increased intracranial pressure, or a second event) may contribute to the development of SCDS.

Embryology

The semicircular canals arise as a budding from the membranous labyrinth of the otocyst. The superior canal develops first, followed by the posterior canal and finally the horizontal canal. When the membranous labyrinth nears adult size, ossification occurs. Before birth, the inner layer of endosteal bone develops around 6 months gestational age. At 2 months postnatal a middle layer of bone is added, and by 4 months the otic capsule thickens. By 10 months the bony covering over the SSC is formed. The bone overlying the SSC reaches its adult thickness by three years of age. Only after the age of three years can the bone overlying the superior canal be reliably detected on a CT-scan [Carey et al., 2000].

Pediatric SCD

SCD has been described in children. Recently one paper described SCDS in 7 patients between 5 and 10 years of age [Lee et al., 2011]. These children presented with auditory symptoms first, followed by vestibular symptoms. This finding is in contrast to adults, who can present with vestibular symptoms first. One out of 7 patients underwent surgical repair of the dehiscence and this 11-year-old patient showed good improvement of symptoms following surgical repair. Another paper described anatomic SCD in 14 out of 131 temporal bone CT-scans in children older than 3 years of age [Chen et al., 2009]. It is unknown why some dehiscence cases are symptomatic and others are not. Studies assessing the correlation between SCD size and clinical signs and symptoms show conflicting results. Some advocate that patients with a larger dehiscence show more vestibulocochlear symptoms [Pfammatter et al., 2010], while others found no correlation [Chien et al., 2012].

Radiology

SCD can be seen on temporal bone CT scans. Often reconstructions in the plane parallel (Pöschl view) and perpendicular (Stenvers view) to the semicircular canal are made [Belden et al., 2003]. Two major categories of SCDs are seen radiologically: 1) dehiscence of the arcuate eminence, which is most common (Figure 7), and 2) dehiscence located more in the region of the posterior-medial limb of the superior canal, with close approximation with the superior petrosal sinus (SPS). A dehiscence located in the region of the superior petrosal sinus is seen in approximately 9 percent (12 out of 131) patients [McCall et al., 2011]. Exertion-related symptoms were more common in these patients.

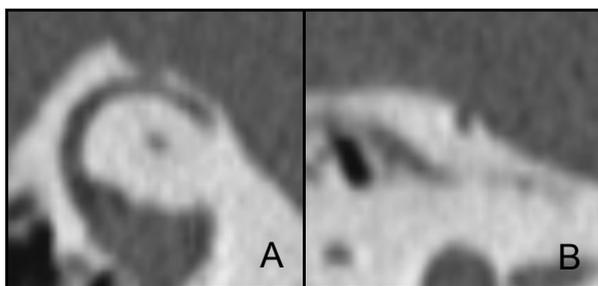


Figure 7. Reconstructions of CT-scan images in the plane parallel (Pöschl, A) to the superior semicircular canal (SSC) and in the plane perpendicular (Stenver, B) to the SSC.

Signs and symptoms

Sound- and pressure-induced dizziness are common complaints in patients with SCD syndrome. When a SCD is present, sound stimulation can result in decreased impedance at the stapes footplate, resulting in abnormal fluid motion through the defect of the SSC. This stimulation would result in ampullofugal excitation of the cupula and subsequent eye movement. On the other hand, lifting and straining can cause increase in cerebrospinal fluid pressure leading towards ampullopetal inhibition of the cupula [Rosowski et al., 2004].

Besides the vestibular complaints, SCD is often associated with complaints of hearing loss as well. Sound travels from the tympanic membrane, along the ossicles and reaches the cochlea. Normally no net flow through the superior canal exists because the pressure is the same at both ends of the SSC. A dehiscence in the superior canal is believed to act as a shunt path for the fluid motion. This shunting of fluid motion is thought to reduce transmission of the sound wave through the fluid that normally reaches the cochlea, and therefore reduces the stimulus that

activates hearing. In addition to this conductive hearing loss, a decrease in bone conduction threshold (that is, a hypersensitive bone conduction) is sometimes present at low frequencies. During bone conduction stimulation, the skull vibration results in fluid motion in the superior semicircular canal, which may increase the cochlear response to bone conduction stimulation [Rosowski et al., 2004].

Diagnosics

The diagnosis of SCD syndrome can sometimes be challenging because of the variety of signs and symptoms that are not necessarily unique to SCD, thus “mimicking” other diseases [Merchant et al., 2007]. For example, patients have undergone unnecessary stapes surgery for conductive hearing loss, and were later found to have SCD [Mikulec et al., 2004]. The diagnosis of SCD syndrome is based on a combination of factors: signs and symptoms, audiometric testing, cervical vestibular-evoked myogenic potential testing (cVEMP) and a temporal bone CT scan. Common auditory symptoms include conductive hyperacusis, autophony, aural fullness, hearing loss and/or pulsatile tinnitus. Vestibular symptoms include imbalance, and sound-, pressure- and/or exercise- associated dizziness. Nystagmus can be found when sound- (Tullio phenomenon) or pressure- (Hennebert sign) induced stimuli are provided. A mixed vertical-torsional nystagmus, with slow phase of the nystagmus directed upwards and away from the SSC, can be found [Basura et al., 2014]. Patients can present with auditory symptoms only, vestibular symptoms only, or a combination of auditory and vestibular symptoms.

Common findings on audiometric testing are a low-frequency conductive hearing loss and bone conduction thresholds better than normal, in the range -5 to -10 dB. This often leads to an air-bone gap (ABG) in the low frequencies, up to 1000 Hz. The stapedius reflex is usually preserved in SCD, in contrast to other etiologies of conductive hearing loss that block the stapedius reflex. Cervical vestibular-evoked myogenic potential (cVEMP) are a measure of saccular function evoked by acoustic stimuli and recorded in the ipsilateral sternocleidomastoid muscle. Patients with SCD syndrome typically have a dramatically enhanced response, i.e. lowered cVEMP thresholds and larger amplitudes, because of shunting of mechanical energy from to cochlea across the vestibule.

Management

Many SCD patients are asymptomatic or do not require treatment, and learning to avoid triggers (e.g., straining, nose blowing) can be effective. However, for SCD patients with debilitating symptoms, surgical repair has been helpful. Improvement

of sound- and pressure-induced vertigo, autophony, hyperacusis and hearing loss has been described. Most patients have some degree of disequilibrium for several weeks to several months after SCD repair; however, in some patients, the dizziness can persist. One study found that 38% (16/42) of patients who underwent SCD surgery had immediate vestibular hypofunction, and this was seen more commonly in patients with a larger defect [Agrawal et al., 2009b]. Aside from SCD size, no other factors associated with vestibular dysfunction or prolonged recovery following surgery have been described.

SCD can be treated via a middle fossa craniotomy or through a transmastoid approach. The most common method of treatment is plugging of the SCD, but resurfacing of the superior canal is also often used. Improvement of signs and symptoms is described. Surgical risks include facial nerve injury (due to a dehiscient geniculate ganglion), dural tear or cerebral spinal fluid leak, temporal lobe retraction injury, epidural hematoma, hearing loss, failure to find a defect and failure to alleviate hearing and/or balance symptoms [Limb et al., 2006].

Up until time of writing, only relatively few institutions have reported on case reports or small case series on SCD. Unresolved questions regarding the clinical and radiologic presentation and surgical outcomes exist. We made an attempt to address these unanswered questions in this relatively new condition.

OUTLINE OF THE THESIS

SCD Prevalence and Radiologic Confirmation

Chapter 2: Prevalence of superior canal dehiscence following failed stapes surgery

Rationale – Multiple case reports and small case series have described SCD in patients with no improvement in hearing following stapes surgery. We assessed the prevalence of SCD in patients with persistent hearing loss after stapes surgery. Prior to assessing the prevalence, we have validated the use of Stenver and Pöschl reconstructions at our institution for confirming SCD on CT scans.

SCD Length and location

Chapter 3.1: Superior canal dehiscence length and location influences clinical presentation, audiometric and cervical vestibular-evoked myogenic potential testing

Rationale – Patients with SCD present with a myriad of symptoms and do often not present with the classical signs on diagnostic testing. We determined if SCD length and location might influence clinical presentation as well as audiometric and VEMP testing results and therefore (partially) help explain the variability seen between SCD patients.

Chapter 3.2: The effect of superior canal dehiscence on intracochlear sound pressures

Rationale – Questions about the basic pathophysiology of SCD are addressed in this study in a human cadaveric temporal bone model. We measured the differential pressure along the cochlear partition (the cochlear drive) by making simultaneous measurements of basal intracochlear sound pressures in scala vestibuli (SV) and scala tympani (ST). The cochlear drive can be used as an estimate of hearing. We assessed the effect of small size dehiscences (up to 2 mm long) on conduction loss.

Chapter 3.3: Assessment of the effects on superior canal dehiscence location and size on intracochlear sound pressures

Rationale – In addition to the assessment of the effect of SCD length and location on hearing outcomes in our clinical study, we also assessed this effect in our human cadaveric temporal bone model. This study on larger SCD sizes and various SCD locations was performed, since patients usually present with larger dehiscences and the SCD various along the limbs of the SSC. We assessed the effect of larger size dehiscences and various SCD locations on the cochlear drive to be able to better understand the variation in hearing loss found on audiometric testing.

SCD Treatment

Chapter 4.1: Utility of cVEMPs in bilateral superior canal dehiscence syndrome

Rationale – Patients with bilateral SCD are sometimes unable to determine the more symptomatic ear prior to surgery. We therefore assessed a method to more objectively determine the worse ear prior to surgical repair to aid in surgical planning. If SCD symptoms are present following surgical repair, this might be due to either recurrence of symptoms in the operated ear, or unmasking of symptoms in the contralateral affected ear. We assessed VEMP and audiometric testing results to be able to provide better patient counseling in the pre- and post-operative period.

Chapter 4.2: Clinical factors associated with prolonged recovery in patients with superior canal dehiscence surgery

Rationale – Some patients have complete resolution of their dizziness following surgical repair, while other patients have a period of chronic imbalance. We examined factors that could influence the duration of disequilibrium after SCD surgery. In addition we analyzed the pre- and post-operative signs and symptoms in patients who underwent SCD repair to be able to better inform patients prior to surgery.

Chapter 4.3: Systematic review of outcomes following superior canal dehiscence surgery: determining best surgical candidates

Rationale – In the past years an increasing number of surgical repairs of SCD have been reported, by using different approaches and methods of SCD repair. Most studies provide information on relatively small patients groups. Therefore, a systematic review was done to provide more insight into the surgical results, complications and recurrence rates following SCD repair and to help determine which patients are the best surgical candidates.

Appendix I-III include studies that were also related to the thesis, but are small case series or case reports

Appendix I: Familial superior canal dehiscence

Rationale – The etiology involving SCD is not completely understood and multiple theories on the etiology exist. Genetic factors may play a role in the development of SCD, however familial SCD has only briefly been mentioned in the literature. We assessed the clinical and radiologic presentation of SCD in three pairs of first-degree relatives.

Appendix II: Radiologic and cVEMP progression in superior canal dehiscence syndrome

Rationale – Many patients describe SCD to be present for multiple years before diagnosis is made and often symptoms progress in time. We performed a retrospective review of 250 patients with SCD to assess the few patients with logged disease progression over time. We assessed the change in diagnostic test results, and have correlated these to the subjective change in SCD signs and symptoms.

Appendix III: Hearing your eyeballs move: superior canal dehiscence syndrome

Rationale – In patients with bilateral SCD, often unmasking of the less symptomatic ear following surgical repair occurs. This study discussed the surgical repair in patients with bilateral SCD.

REFERENCES

Agrawal Y, Carey JP, Della Santina CC, Schubert MC, Minor LB: Disorders of balance and vestibular function in US adults: Data from the national health and nutrition examination survey, 2001-2004. *Arch Intern Med* 2009a;169:938-944.

Agrawal Y, Migliaccio AA, Minor LB, Carey JP: Vestibular hypofunction in the initial post-operative period after surgical treatment of superior semicircular canal dehiscence. *Otol Neurotol* 2009b;30:502-506.

Alberti PW: The anatomy and physiology of the ear and hearing. World Health Organization 1995.

Basura GJ, Cronin SJ, Heidenreich KD: Tullio phenomenon in superior semicircular canal dehiscence syndrome. *Neurology* 2014;82:1010.

Belden CJ, Weg N, Minor LB, Zinreich SJ: CT evaluation of bone dehiscence of the superior semicircular canal as a cause of sound- and/or pressure-induced vertigo. *Radiology* 2003; 226:337-343.

Branch WT, Barton JJS: Approach to the patient with dizziness. Up to date 2012.

Carey JP, Minor LB, Nager GT: Dehiscence or thinning of bone overlying the superior semicircular canal in a temporal bone survey. *Arch Otolaryngol Head Neck Surg* 2000;126:137-147.

Chen EY, Paladin A, Phillips G, Raske M, Vega L, Peterson D, Sie KC: Semicircular canal dehiscence in the pediatric population. *Int J Pediatr Otorhinolaryngol* 2009;73:321-327.

Chien WW, Janky K, Minor LB, Carey JP: Superior canal dehiscence size: Multivariate assessment of clinical impact. *Otol Neurotol* 2012;33:810-815.

Cummings CW, Haughey BH, Thomas RJ. *Cummings Otolaryngology: Head and Neck surgery*. Elsevier Mosby 2005:321.

Froehling DA, Silverstein MD, Mohr DN, Beatty CW: The rational clinical examination. Does this dizzy patient have a serious form of vertigo? *JAMA* 1994;271:385-388.

Huizing EH, Snow GB: Keel-neus-oorheelkunde en hoofd-halschirurgie. Bohn Stafleu Van Loghum 2009:456.

Jackler RK, Brackmann DE: *Neurotology*. Mosby, Incorporated 2005:1411.

Kentala E, Rauch SD: A practical assessment algorithm for diagnosis of dizziness. *Otolaryngol Head Neck Surg* 2003;128:54-59.

Lamore J, Kapteyn T: *Nederlands leerboek audiologie*. Nederlandse vereniging van Audiologie, Revisie 2014.

Lee GS, Zhou G, Poe D, Kenna M, Amin M, Ohlms L, Gopen Q: Clinical experience in diagnosis and management of superior semicircular canal dehiscence in children. *Laryngoscope* 2011; 121:2256-2261.

Limb CJ, Carey JP, Srireddy S, Minor LB: Auditory function in patients with surgically treated superior semicircular canal dehiscence. *Otol Neurotol* 2006;27:969-980.

Masaki Y: The prevalence of superior canal dehiscence syndrome as assessed by temporal bone computed tomography imaging. *Acta Otolaryngol* 2011;131:258-262.

McCall AA, McKenna MJ, Merchant SN, Curtin HD, Lee DJ: Superior canal dehiscence syndrome associated with the superior petrosal sinus in pediatric and adult patients. *Otol Neurotol* 2011;32:1312-1319.

Merchant SN, Rosowski JJ, McKenna MJ: Superior semicircular canal dehiscence mimicking otosclerotic hearing loss. *Adv Otorhinolaryngol* 2007;65:137-145.

Mikulec AA, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.

Minor LB: Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:1717-1727.

Minor LB, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998;124:249-258.

Nadgir RN, Ozonoff A, Devaiah AK, Halderman AA, Sakai O: Superior semicircular canal dehiscence: Congenital or acquired condition? *AJNR Am J Neuroradiol* 2011;32(5):947-9.

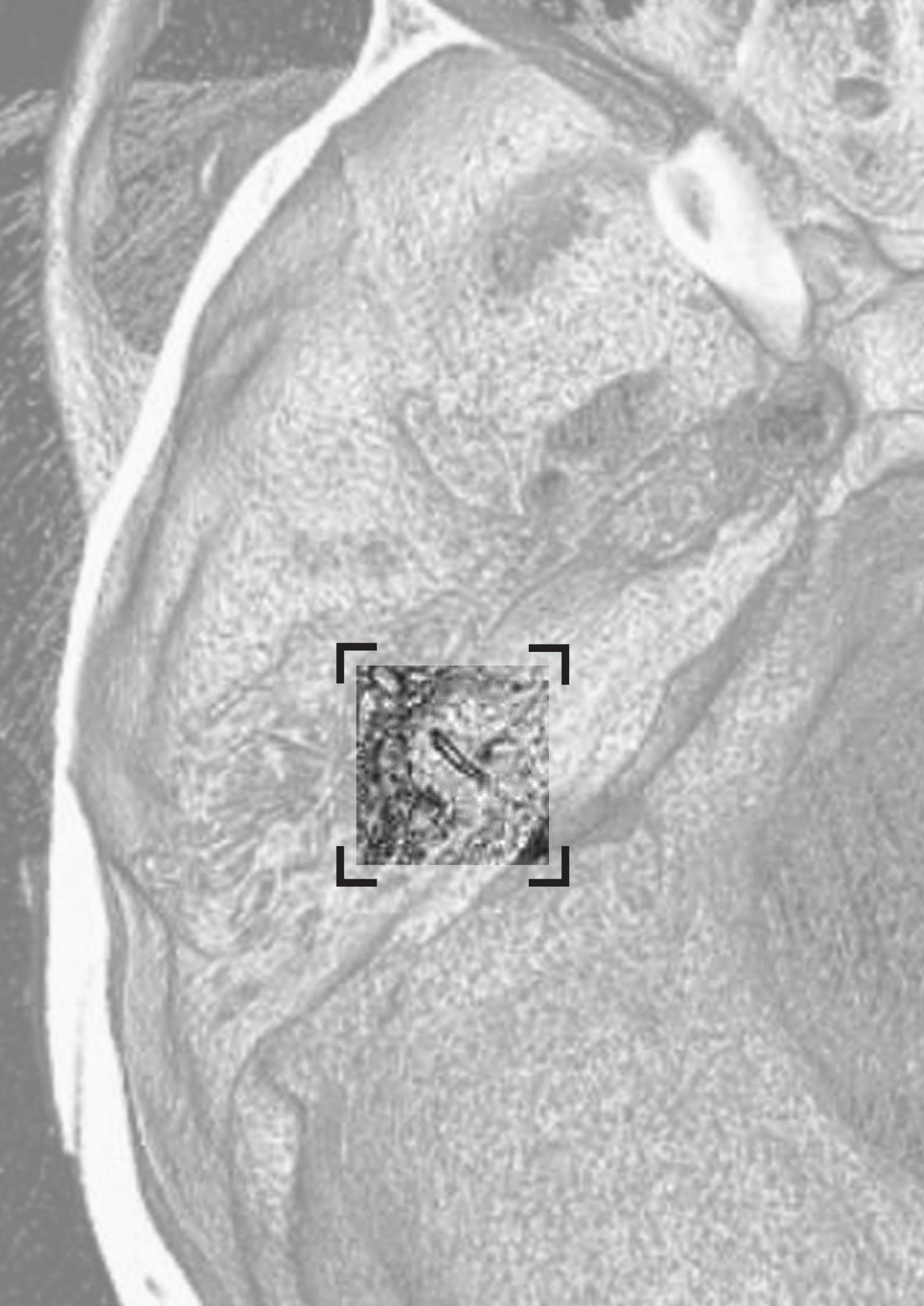
Pfammatter A, Darrouzet V, Gartner M, Somers T, Van Dinther J, Trabalzini F, Ayache D, Linder T: A superior semicircular canal dehiscence syndrome multicenter study: Is there an association between size and symptoms? *Otol Neurotol* 2010;31:447-454.

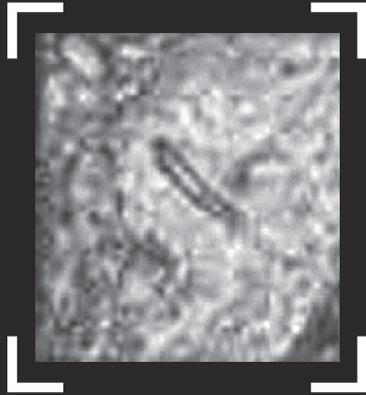
Rosowski JJ, Songer JE, Nakajima HH, Brinsko KM, Merchant SN: Clinical, experimental, and theoretical investigations of the effect of superior semicircular canal dehiscence on hearing mechanisms. *Otol Neurotol* 2004;25:323-332.

Schiller JS, Kramarow EA, Dey AN: Fall injury episodes among noninstitutionalized older adults: United States, 2001-2003. *Adv Data* 2007:1-16.

Swartz JD, Daniels DL, Harnsberger HR, Shaffer KA, Mark L: Balance and equilibrium, i: The vestibule and semicircular canals. *AJNR Am J Neuroradiol* 1996;17:17-21.

Williamson RA, Vrabec JT, Coker NJ, Sandlin M: Coronal computed tomography prevalence of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2003;129:481-489.





Chapter 2

Prevalence of superior canal dehiscence following failed stapes surgery

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Submitted

ABSTRACT

Objective: To validate our method for confirming superior canal dehiscence (SCD) on computed tomography scan (CT-scan) and to assess the prevalence of SCD in patients with otosclerosis with a persistent air-bone gap (ABG) following primary stapes surgery

Study Design: Retrospective cohort study.

Setting: Tertiary care referral center.

Patients: We analyzed CT-scans in 30 ears with or without SCD. In addition we assessed 131 ears (129 patients) that underwent primary stapes surgery.

Intervention: Temporal bone CT-scan reconstructions and primary stapes surgery

Main Outcome Measures: 1) Assessment of 30 CT-scan reconstructions for absence or presence of SCD in the plane parallel (Pöschl) and perpendicular (Stenver) to the superior semicircular canal (SSC). 2) The prevalence of SCD using CT-scan reconstructions in patients with an ABG of >20 dB following stapes surgery assessed by two independent observers.

Results: Inter-observer agreement showed a percent agreement of 90% (CI: 73.5%-97.9%) and a Cohen's kappa of 0.831 (CI: 0.7-1.0). Seventeen of the 131 ears that underwent primary stapes surgery had a post-operative ABG >20 dB and 10 of these patients had a CT-scan available. CT-scan reconstructions revealed no SCD.

Conclusion: We found that: 1) Assessing absence or presence of SCD on CT-scan reconstructions in the planes parallel and perpendicular to the SSC in addition to the standard axial and coronal view is a reliable method 2) In our cohort of patients with a persistent post-operative ABG following stapes surgery, no patients with SCD were found. We therefore would not recommend CT-scan testing following stapes surgery solely for diagnosis of SCD.

INTRODUCTION

Otosclerosis is characterized by disordered bone remodeling in the region of the otic capsule, located primarily between the cochlea and the vestibule and just anterior to the footplate of the stapes [Menger and Tange, 2003; Schrauwen and Van Camp, 2010]. Stapes surgery is a treatment option for hearing loss resulting from otosclerosis and has proved to be an effective and safe intervention [de Bruijn et al., 2001; Kisilevsky et al., 2010; Kisilevsky et al., 2009; Lippy et al., 1997; Vincent et al., 2006]. However, in some cases hearing loss does not improve after primary stapes surgery. Vincent et al. reported that out of 4508 primary stapes operations, 652 surgeries resulted in a revision [Vincent et al., 2010]. Common reasons for failure of stapes surgery are incus erosion and prostheses dislocation [Vincent et al., 2010]. In a number of patients no reason for failure could be found. In the past years, several case reports have described unimproved hearing following stapes surgery due to superior canal dehiscence (SCD) [El Kohen et al., 2007; Halmagyi et al., 2003; Hope and Fagan; Lehmann et al.; Li et al.; Mikulec et al., 2004; Minor et al., 2003].

Superior canal dehiscence is a condition of the inner ear [Minor et al., 1998]. A defect in the bony covering of the superior semicircular canal (SSC) can cause vestibular and/or auditory symptoms [Minor, 2005]. Patients with SCD do not always present with vestibular symptoms and can have auditory complaints only. Therefore, they can mimic patients with otosclerosis [Lehmann et al.; Li et al.; Mikulec et al., 2004; Teszler et al., 2008]. Although we know that SCD can mimic other otologic diseases such as otosclerosis, SCD is not always considered in patients with no post-operative improvement following stapes surgery. Because of this, patients with a missed diagnosis of SCD may undergo unnecessary (revision) stapes surgery. However, the prevalence of SCD in patients with failure of stapes surgery is unknown.

Since multiple case reports on “unmasked” SCD following unsuccessful stapes surgery have been described (Table 1), we have assessed the prevalence of anatomic SCD on CT-scan reconstructions in patients with a post-operative hearing loss following stapes surgery. Prior to these measurements we performed an internal validation of our method for assessing presence or absence of SCD on the CT-scan reconstruction.

Table 1. Overview of studies describing patients with SCD who underwent previous stapes surgery

Study	Age (yrs)	Gender	Signs at presentation	Stapes surgery	Change HL	SCD
Lehmann 2011	48	F	HL, vertigo	3x Left	No	Left
Li 2010	36	F	HL, tinnitus, ETD, mild disequilibrium*	1x Right	No	Right
	56	M	HL, episodic disequilibrium	2x Left	No	Left
	53	M	HL, tinnitus	1x Left	No	Left
Hope 2009	30	M	HL, post-op vertigo, imbalance, tinnitus	1 x Bilateral	Yes	Left
Mikulec 2004	27	F	HL, pressure IV	1x Right	No	Right
	52	M	HL	1x Left	No	Bilateral
	49	M	HL	1 x Right	No	Bilateral
Halmagyi 2003	65	M	HL, hyperacusis, sound IV, pressure IV	3 x Left	No	Bilateral
Minor 2003	36	F	HL, post-op pressure IV	2 x Right	No	Right
	67	M	HL	2 x Right	No	Right
	47	M	HL, exercise IV, pressure IV, imbalance	2 x Right	No	Right

Yrs = years; F = female; M = male; HL = hearing loss; ETD = Eustachian tube dysfunction; * = with rapid head motion; IV = induced vertigo; post-op = post-operative; Change HL = post-operative improvement in hearing loss; SCD = superior canal dehiscence.

METHODS

Patient selection

For validation of our CT-scan reconstruction method, we used thirty ears of patients with conductive hearing loss from our tertiary referral center. These thirty CT-scans included fifteen patients with a suspicion of an anatomic SCD on temporal bone CT-scans (without reconstructions). In addition 15 temporal bone CT-scans of patients with a conductive loss (without a clinical suspicion of SCD) were included.

To assess the prevalence of SCD in patients with a persistent ABG following stapes surgery, we performed a retrospective cohort study among all patients that underwent primary stapes surgery between January 1, 2010 and December 31, 2011 at our center (this is a different patient group than the patients used for validation of the method). Exclusion criteria included: patients that underwent previous stapes surgery on the same ear, patients under the age of 18 years and patients with additional ear problems that might influence air conduction thresholds, such as tympanic membrane perforation or cholesteatoma. Most patients underwent

a stapedotomy by using the micropick technique as described by Marquet et al. [Somers et al., 1994] or by using a potassium titanyl phosphate laser. Two experienced surgeons from our institution performed the surgical procedure.

Audiometric testing

Audiometric evaluation included pre- and post-operative ABG, air-conduction (AC) thresholds, and bone-conduction (BC) thresholds. Only AC and BC results that were obtained at the same time post-operatively were used for calculation of ABG and pure-tone averages (PTAs). We used an average PTA at 250-4000 Hz for AC and BC thresholds. Audiometric testing was reported according to the American Academy of Otolaryngology—Head and Neck Surgery guidelines [1995], except for thresholds at 3 kHz, which were substituted in all cases with those at 4 kHz.

The surgical procedure was considered to be successful if the mean post-operative ABG for the frequencies 250-4000 Hz was ≤ 20 dB. When the mean pre-operative ABG was < 20 dB, post-operative improvement > 5 dB was found to be successful. Patients with otosclerosis underwent pre- and post-operative audiometric testing. Post-operative follow-up data were collected after at least 1 month following stapes surgery, in patients with multiple post-operative tests; the latest audiometric test was used.

CT-scan analyses

The temporal bone CT-scans were reviewed by two of the authors independently (F.P and M.N.), both experienced in reviewing CT-scans for SCD. In addition to the standard axial and coronal images, reconstructions in the plane parallel (Pöschl) to the SSC and in the plane perpendicular (Stenver) to the SSC were made [Belden et al., 2003]. An illustration of this method is shown in figure 1. A three-point scale was used to assess for absence or presence of SCD. We used the following criteria: 1) "SCD present", 2) "SCD: unclear" and 3) "SCD absent". Consensus of any discrepancies between the two authors was reached by discussing these cases together.

Statistical analyses

We used SPSS 20.0 for our statistical analysis. For validation of our method for assessing presence or absence of SCD on CT-scan reconstructions, we calculated the percent agreement (95% confidence interval (CI)) and the chance corrected agreement between raters (Cohen's kappa, 95% CI). After we validated our method, we assessed the prevalence of SCD in patients with a persistent ABG following stapes surgery (so in a different group of patients than used for validation of the method)

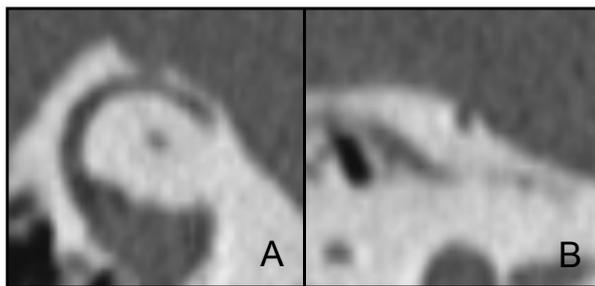


Figure 1. Reconstructions of CT-scan images in the plane parallel (Pöschl, A) to the superior semicircular canal (SSC) and in the plane perpendicular (Stenver, B) to the SSC.

with a mean four-frequency ABG (for the frequencies 0.5, 1, 2 and 4 kHz) of >20 dB following primary stapes surgery.

RESULTS

CT-scan analysis – Validation of method

Two independent observers assessed 30 CT-scan reconstructions for absence or presence of SCD in the plane parallel (Pöschl) and perpendicular (Stenver) to the superior semicircular canal (SSC), in addition to the standard axial and coronal projections. Table 2 shows an overview of the results. In 7 cases both observers rated the CT-scan as “SCD present”, in 4 cases both observers rated the CT-scan as “unclear” and in 16 cases both observers rated the CT-scan as “SCD absent”. In 3 cases discrepancy between both observers was found, in all cases consensus was reached by discussion. The percent agreement was 90% (CI: 73.5%-97.9%), with a chance corrected agreement (Cohen’s kappa) of 0.831 (95% CI: 0.7-1.0) (Table 2).

Table 2. Validation of CT-scan reconstruction method

Inter-observer agreement	SCD present	SCD: unclear	SCD absent	Total
SCD present	7 (23%)	1 (3%)	0 (0%)	8 (27%)
SCD: unclear	1 (3%)	4 (13%)	1 (3%)	6 (20%)
SCD absent	0 (0%)	0 (0%)	16 (53%)	16 (53%)
Total	8 (27%)	5 (17%)	17 (57%)	30

Inter-observer agreement between two independent observers, who assessed 30 CT-scan reconstructions for absence or presence of SCD in the plane parallel (Pöschl) and perpendicular (Stenver) to the superior semicircular canal (SSC), in addition to the standard axial and coronal projections, in 15 patients with SCD and 15 patients with conductive hearing loss and no SCD. The chance corrected agreement between raters is 0.831 (Cohen’s kappa, 95% CI).

Prevalence of SCD following failed stapes surgery

129 patients (131 ears) with pre-operative audiometric data underwent primary stapes surgery, 127/131 ears had a pre-operative ABG >20 dB (for the frequencies 0.25 to 4 kHz) prior to stapes surgery. Seventeen of the 127 ears (13%) had a post-operative ABG of >20 dB, of which 12 ears showed a partial improvement and 5 ears showed no improvement. The mean pre-operative ABG of these ears was 41 dB (27-55 dB) and the mean post-operative ABG of these ears was 30 dB (21-63 dB). Of these 17 patients with an ABG > 20 dB, ten patients had a CT-scan available for analysis. Two of the 127 ears presented with a post-operative sensorineural hearing loss in the frequencies >1 kHz, therefore the average ABG could not be calculated and CT-scan analysis was observed to assess for SCD. There were four patients with a pre-operative ABG <20 dB, of which 2 did not show post-operative improvement. One of these two patients had a CT-scan available for analysis (Figure 2).

Two observers (F.P. and M.N.) independently rated the 13 CT-scans for “SCD present”, “unclear” or “SCD absent”. In 12/13 (92%) cases, both observers rated the CT-scans as “SCD absent” and both observers did not rate any of the CT-scans as “SCD present”. One case (1/13) was rated as “unclear” by one observer and “SCD absent” by another observer (Table 3). After discussing the case, both observers agreed to rate the case as “unclear”. Both observers also rated the contralateral

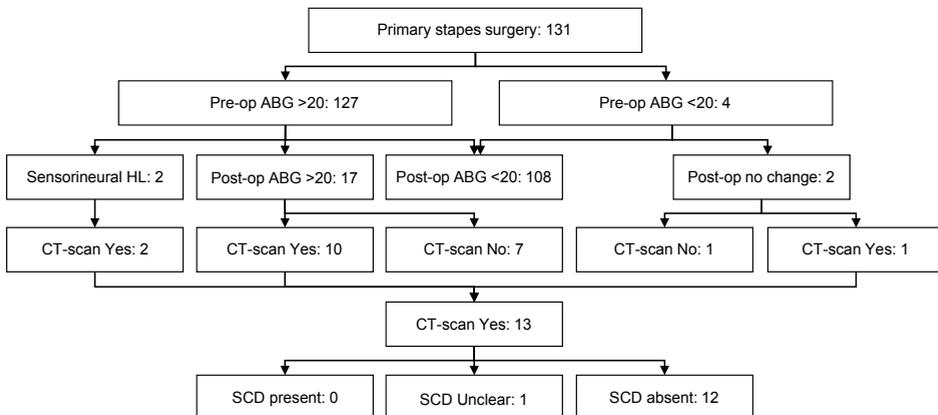


Figure 2. Flowchart for patient selection. 131 ears with pre-operative audiometric data underwent primary stapes surgery. 17/127 ears had a mean five-frequency air-bone gap (ABG) >20 dB (0.25, 0.5, 1, 2 and 4 kHz) following stapes surgery and 10 of these patients had a CT-scan available for analyses. Two ears with a pre-operative ABG of <20 dB had no improvement, of which one had a CT-scan available for analysis. Two ears presented with high frequency sensorineural hearing loss post-operatively and both had a CT-scan available for analysis. None of the 13 ears with an available CT-scan was diagnosed with superior canal dehiscence (SCD). Pre-op = pre-operative; Post-op = post-operative, ABG = air-bone gap; HL = hearing loss, SCD = superior canal dehiscence.

Table 3. Prevalence of SCD in patients with an ABG >20 dB following stapes surgery

Post-operative ABG >20 dB	SCD present	SCD: unclear	SCD absent	Total
SCD present	0 (0%)	0 (0%)	0(0%)	0 (0%)
SCD: unclear	0 (0%)	0 (0%)	0 (0%)	0 (0%)
SCD absent	0 (0%)	1 (7%)	12 (93%)	13(100%)
Total	0 (0%)	1 (7%)	12 (93%)	13

Inter-observer agreement between two independent observers, who assessed 13 CT-scan reconstructions for absence or presence of SCD in the plane parallel (Pöschl) and perpendicular (Stenver) to the superior semicircular canal (SSC), in addition to the standard axial and coronal projections, in patients with a persistent ABG following stapes surgery.

ears and all 13 ears were diagnosed as no SCD. The percent agreement was 93% (64.0%-99.8%). In the group of patients with a persistent ABG following stapes we have not found any patients with a definite anatomic SCD on the CT-scan reconstructions, therefore the prevalence of SCD does not seem to be raised in patients with post-operative hearing loss following stapes surgery.

DISCUSSION

Our results show that assessing absence or presence of SCD on CT-scan reconstructions in the planes parallel and perpendicular in addition to the standard axial and coronal view is a reliable method. Secondly, in our cohort of patients with a persistent post-operative ABG following stapes surgery, no patients with SCD were present.

Multiple small case series and case reports have been published describing patients with conductive hearing loss that underwent stapes surgery without post-operative hearing improvement and turned out to have SCD [Halmagyi et al., 2003; Hope and Fagan; Lehmann et al.; Li et al.; Mikulec et al., 2004; Minor et al., 2003]. The exact prevalence of SCD in patients with a persistent ABG following stapes surgery has not been described yet. However, due to the existence of multiple reports on SCD in this patient group we would have expected that the prevalence of SCD would have been raised.

The prevalence of SCD in patients undergoing temporal bone CT-scan testing has been described in previous reports and ranged from 3% to 9% [Masaki, 2011; Williamson et al., 2003]. Based on this prevalence, we could have expected one patient with SCD in our population, without having a raised prevalence of SCD in the

group of patients with persistent ABG following stapes surgery. Since we have not found any patients with a definite anatomic SCD, SCD could not explain the persistent hearing loss following primary stapes surgery in patients with otosclerosis.

Some possible limitations should also be discussed. We assessed a relatively small number of patients with a persistent ABG following stapes surgery. This is the result of a retrospective study design with incomplete CT-scan data available. Missing data could lead to bias and we should therefore be careful with the interpretation of these data. However, in retrospect, with the low prevalence of SCD found in this group it does not seem feasible to summon these patients for CT-scan testing. It could be anticipated that more patients should be included to assess the prevalence of SCD in a larger population.

Based on our findings that SCD was not present in the group of patients with a persistent hearing loss following stapes surgery, a CT-scan solely for the purpose of excluding SCD in patients with a persistent ABG following stapes surgery would not be recommended.

CONCLUSION

Assessing absence or presence of SCD on CT-scan reconstructions in the planes parallel and perpendicular to the SSC in addition to the standard axial and coronal view is a reliable method. By using this method, none of the otosclerosis patients without hearing improvement following primary stapes surgery turned out to have SCD.

REFERENCES

Committee on hearing and equilibrium guidelines for the evaluation of results of treatment of conductive hearing loss. American academy of otolaryngology-head and neck surgery foundation, inc. *Otolaryngol Head Neck Surg* 1995;113:186-187.

Belden CJ, Weg N, Minor LB, Zinreich SJ: CT evaluation of bone dehiscence of the superior semicircular canal as a cause of sound- and/or pressure-induced vertigo. *Radiology* 2003; 226:337-343.

de Bruijn AJ, Tange RA, Dreschler WA: Efficacy of evaluation of audiometric results after stapes surgery in otosclerosis. II. A method for reporting results from individual cases. *Otolaryngol Head Neck Surg* 2001;124:84-89.

Halmagyi GM, Aw ST, McGarvie LA, Todd MJ, Bradshaw A, Yavor RA, Fagan PA: Superior semicircular canal dehiscence simulating otosclerosis. *J Laryngol Otol* 2003;117:553-557.

Hope A, Fagan P: Latent superior canal dehiscence syndrome unmasked by stapedotomy for otosclerosis. *J Laryngol Otol* 2010;124:428-430.

Kisilevsky VE, Bailie NA, Halik JJ: Bilateral hearing results of 751 unilateral stapedotomies evaluated with the glasgow benefit plot. *J Laryngol Otol* 2010;124:482-489.

Kisilevsky VE, Dutt SN, Bailie NA, Halik JJ: Hearing results of 1145 stapedotomies evaluated with amsterdam hearing evaluation plots. *J Laryngol Otol* 2009;123:730-736.

Lehmann M, Ebmeyer J, Upile T, Sudhoff HH: Superior canal dehiscence in a patient with three failed stapedectomy operations for otosclerosis: A case report. *J Med Case Reports* 2011;3:5:47.

Li PM, Bergeron C, Monfared A, Agrawal S, Blevins NH: Superior semicircular canal dehiscence diagnosed after failed stapedotomy for conductive hearing loss. *Am J Otolaryngology* 2011;32(5):441-4.

Lippy WH, Burkey JM, Schuring AG, Rizer FM: Stapedectomy in patients with small air-bone gaps. *Laryngoscope* 1997;107:919-922.

Masaki Y: The prevalence of superior canal dehiscence syndrome as assessed by temporal bone computed tomography imaging. *Acta Otolaryngol* 2011;131:258-262.

Menger DJ, Tange RA: The aetiology of otosclerosis: A review of the literature. *Clin Otolaryngol Allied Sci* 2003;28:112-120.

Mikulec AA, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.

Minor LB: Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:1717-1727.

Minor LB, Carey JP, Cremer PD, Lustig LR, Streubel SO, Ruckenstein MJ: Dehiscence of bone overlying the superior canal as a cause of apparent conductive hearing loss. *Otol Neurotol* 2003;24:270-278.

Minor LB, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998; 124:249-258.

Schrauwen I, Van Camp G: The etiology of otosclerosis: A combination of genes and environment. *Laryngoscope* 2010;120:1195-1202.

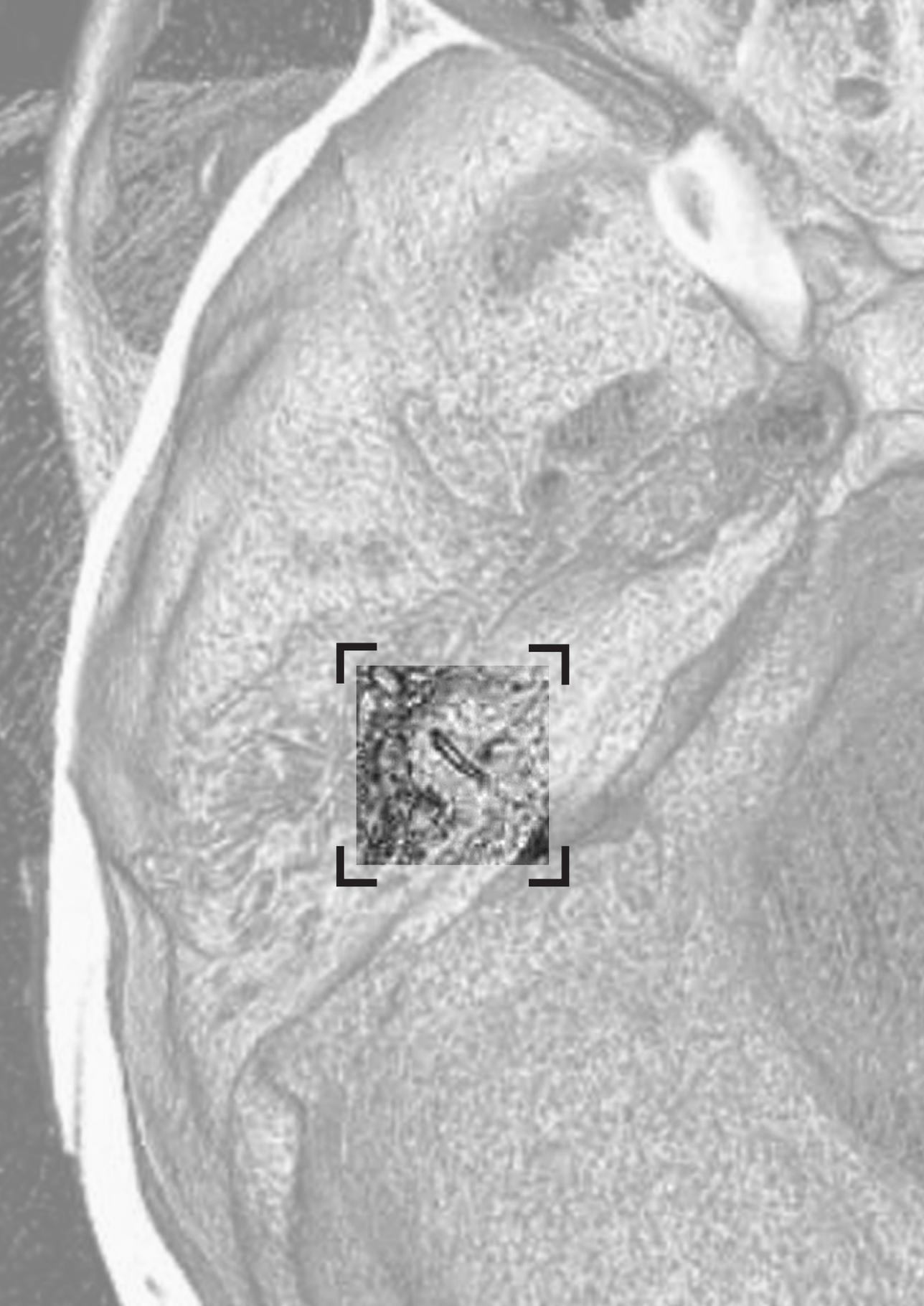
Somers T, Govaerts P, Marquet T, Offeciers E: Statistical analysis of otosclerosis surgery performed by Jean Marquet. *Ann Otol Rhinol Laryngol* 1994;103:945-951.

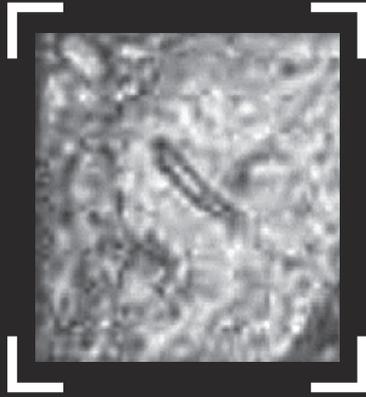
Teszler CB, Daval M, Altabaa K, Williams MT, Ayache D: Computed tomography-based workup of conductive hearing loss with normal middle ear: Don't forget superior semicircular canal dehiscence. *Int Tinnitus J* 2008;14:53-56.

Vincent R, Rovers M, Zingade N, Oates J, Sperling N, Deveze A, Grolman W: Revision stapedotomy: Operative findings and hearing results. A prospective study of 652 cases from the otology-neurotology database. *Otol Neurotol* 2010;31:875-882.

Vincent R, Sperling NM, Oates J, Jindal M: Surgical findings and long-term hearing results in 3,050 stapedotomies for primary otosclerosis: A prospective study with the otology-neurotology database. *Otol Neurotol* 2006;27:S25-47.

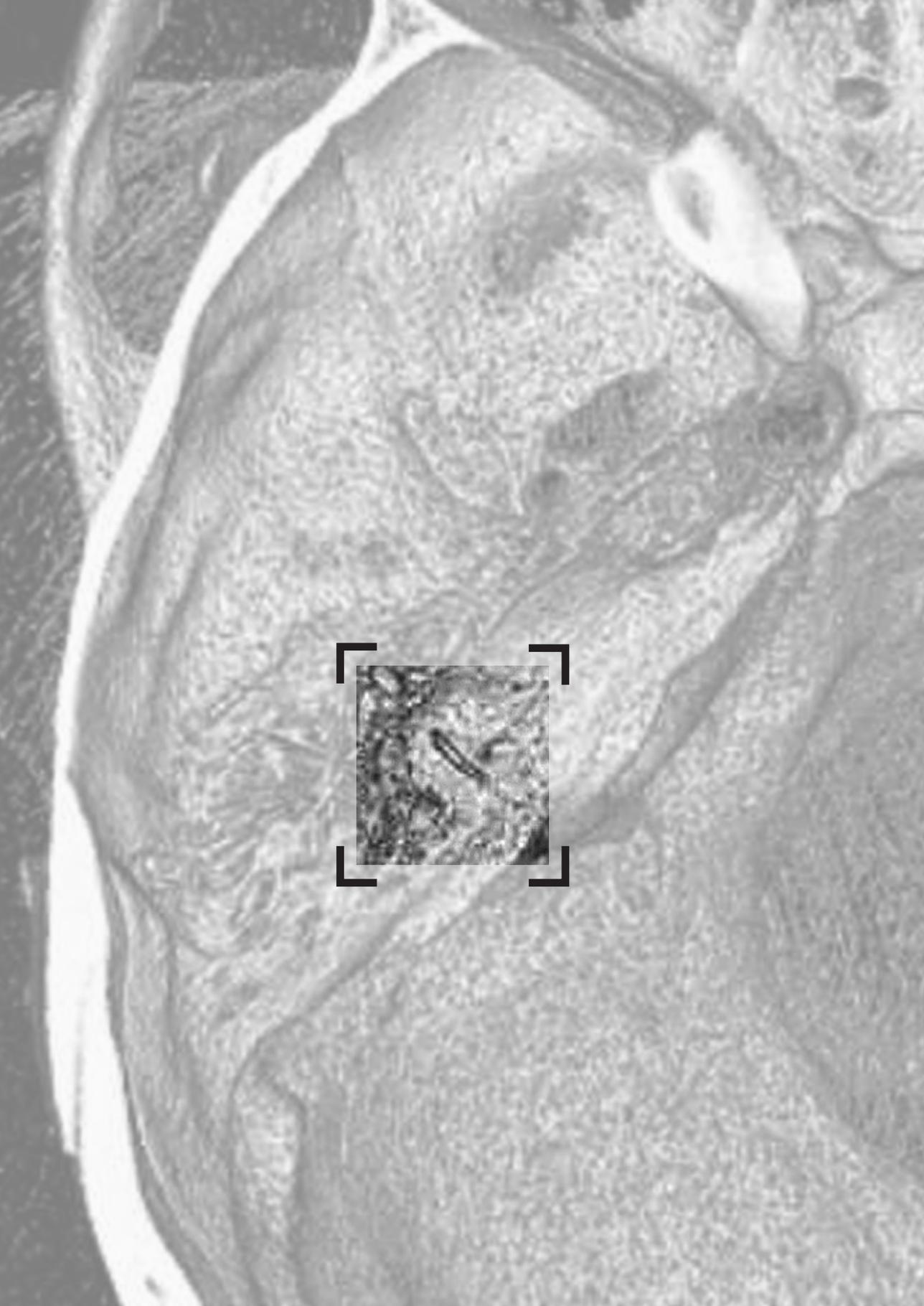
Williamson RA, Vrabec JT, Coker NJ, Sandlin M: Coronal computed tomography prevalence of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2003;129:481-489.

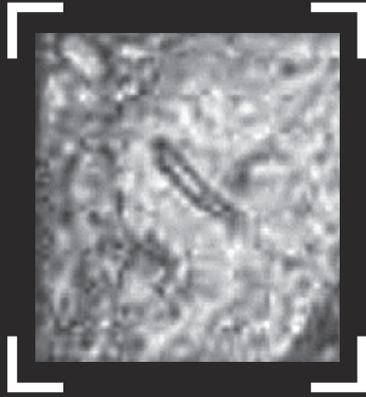




Chapter 3

SCD Length and Location





Chapter 3.1

Superior canal dehiscence length and location influences clinical presentation and audiometric and cervical vestibular-evoked myogenic potential testing

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ABSTRACT

Superior canal dehiscence (SCD) is caused by an absence of bony covering of the arcuate eminence or posteromedial aspect of the superior semicircular canal. However, the clinical presentation of SCD syndrome varies considerably, as some SCD patients are asymptomatic and others have auditory and/or vestibular complaints. In order to determine the basis for these observations, we examined the association between SCD length and location with: (1) auditory and vestibular signs and symptoms; (2) air conduction (AC) loss and air-bone gap (ABG) measured by pure-tone audiometric testing, and (3) cervical vestibular-evoked myogenic potential (cVEMP) thresholds. 104 patients (147 ears) underwent SCD length and location measurements using a novel method of measuring bone density along 0.2-mm radial CT sections. We found that patients with auditory symptoms have a larger dehiscence (median length: 4.5 vs. 2.7 mm) with a beginning closer to the ampulla (median location: 4.8 vs. 6.4 mm from ampulla) than patients with no auditory symptoms (only vestibular symptoms). An increase in AC threshold was found as the SCD length increased at 250 Hz (95% CI: 1.7–4.7), 500 Hz (95% CI: 0.7–3.5) and 1,000 Hz (95% CI: 0.0–2.5), and an increase in ABG as the SCD length increased at 250 Hz (95% CI: 2.0–5.3), 500 Hz (95% CI: 1.6–4.6) and 1,000 Hz (95% CI: 1.3–3.3) was also seen. Finally, a larger dehiscence was associated with lowered cVEMP thresholds at 250 Hz (95% CI: –4.4 to –0.3), 500 Hz (95% CI: –4.1 to –1.0), 750 Hz (95% CI: –4.2 to –0.7) and 1,000 Hz (95% CI: –3.6 to –0.5) and a starting location closer to the ampulla at 250 Hz (95% CI: 1.3–5.1), 750 Hz (95% CI: 0.2–3.3) and 1,000 Hz (95% CI: 0.6–3.5). These findings may help to explain the variation of signs and symptoms seen in patients with SCD syndrome.

INTRODUCTION

Superior canal dehiscence (SCD) syndrome is caused by an absence of bony covering of the superior semicircular canal (SSC) and was first described by Minor et al. [1998]. Patients with SCD syndrome typically present with auditory and/or vestibular complaints, low-frequency air-bone gap (ABG) and lowered cervical vestibular-evoked myogenic potential (cVEMP) thresholds. The clinical presentation of SCD syndrome varies widely, from auditory symptoms only (hyperacusis, autophony, aural fullness, hearing loss and/or pulsatile tinnitus) to vestibular symptoms only (imbalance, and sound-, pressure- and/or exercise-associated dizziness), to a combination of auditory and vestibular symptoms. It has been theorized that the 'third window' created by SCD alters the inner ear fluid flow, causing auditory and vestibular complaints. Vestibular symptoms are thought to be caused by the entrainment of the cupula due to SSC fluid motion elicited by sound [Carey et al., 2004]. Hearing loss may be related to the shunting of acoustic energy away from the cochlea, resulting in a reduction of the stimulus to the hearing mechanism. Rosowski et al. [2004; Songer and Rosowski, 2007] hypothesized that the magnitude of the ABG is influenced by SCD length and location. Our group has recently characterized the effect of SCD length on air conduction (AC) loss in a human temporal bone model [Pisano et al., 2012].

The literature is conflicting regarding the association of SCD length with signs and symptoms of SCD syndrome. A larger defect has been shown to correlate with vestibulocochlear manifestations in one study [Pfammatter et al., 2010], while other studies did not find an association between SCD length and clinical presentation [Martin et al., 2009; Chi et al., 2010; Chien et al., 2012]. The ABG increased with a larger SCD in two studies [Yuen et al., 2009; Chien et al., 2012], while other studies found no correlation between SCD length and degree of hearing loss [Mikulec et al., 2004; Chi et al., 2010]. Relatively small sample sizes and varied methods of measuring SCD length might explain these conflicting results. Research in chinchillas and in a human temporal bone model suggests that the correlation of dehiscence length with hearing sensitivity is more complicated than a monotonic relationship. For example, Pisano et al. [2012] showed that the smallest dehiscence had the largest effects, consistent with more mid-frequency hearing loss, in some ears. Furthermore, the effect of SCD length appears to reach a maximum once the dehiscence has reached a certain length [Songer and Rosowski, 2007; Niesten et al., 2013a]. Recent reports that examined SCD location and clinical presentation were limited by varied methods of measuring the defect and a relatively small sample size [Martin et al., 2009; Pfammatter et al., 2010]. To resolve these contradictory

findings, we performed a detailed analysis on a large cohort of SCD patients using a novel method for measuring SCD length and location by high-resolution CT. Specifically, we sought to determine the association of SCD length and location with auditory and vestibular signs and symptoms, magnitude of the ABG and cVEMP thresholds.

METHODS

Selection of patients, patient characteristics and signs and symptoms

This study was approved by the Human Studies Committee of the Massachusetts Eye and Ear Infirmary (Protocol No. 09-08-088; principal investigator: D.J.L.). We identified 147 ears from 104 patients with SCD syndrome that underwent high-resolution temporal bone CT (HR-CT) at the Massachusetts Eye and Ear Infirmary between 2000 and 2011. The presence of an anatomical SCD was based on HR-CT of the temporal bone without contrast. The diagnosis of SCD syndrome was based on clinical signs and symptoms with complementary audiometric and vestibular testing. A chart review was performed to collect demographic patient data and to assess various clinical signs and symptoms, including auditory signs and symptoms (hyperacusis, autophony, aural fullness, report of hearing loss and/or tinnitus) and vestibular signs and symptoms (imbalance; sound-, pressure- and exercise-associated dizziness; Tullio's phenomenon and/or Hennebert's sign). It is important to note that 'auditory signs and symptoms' are subjective findings reported by the patient and are not always associated with abnormalities on audiometric measurements.

Audiometric data

Audiometric testing was done at the Massachusetts Eye and Ear Infirmary as part of the patients' clinical evaluation as described in Niesten et al. [2013b]. If multiple audiograms were performed, the test closest in time to the HR-CT was used for analysis. AC and bone conduction (BC) thresholds were measured at 250, 500, 1,000, 2,000, 4,000 and 8,000 Hz (for BC up to 4,000 Hz). The ABG was calculated as a difference between the AC threshold and the BC threshold from 250 to 4,000 Hz.

Cervical vestibular-evoked myogenic potential (cVEMP) data

cVEMP testing is a standard procedure at our institution to aid in diagnoses of SCD syndrome. cVEMP thresholds were determined at 250, 500, 750 and 1,000 Hz, and converted from normal hearing level to peak sound pressure as described by Rauch et al. [2004].

Radiology

CT imaging was performed in a multidetector row CT scanner (Somatom Sensation 40; Siemens Healthcare, Erlangen, Germany) by using a standardized temporal bone CT protocol. Radiologic assessment of the superior canal was performed by HR-CT, available on our picture archiving and communication system (Synapse). The settings were as follows: 120 kVp tube voltage, 320 mAs effective tube current and a helical scanning mode with a pitch factor of 0.55. Axial, Pöschl and Stenvers views were reconstructed at 0.5-mm intervals separately for the left and right ears by using a 0.6-mm image thickness, 10-cm reconstruction field-of-view and an ultra-high-resolution kernel (U70u).

Curved reconstruction of the superior canal

Voxar 3D (Toshiba) was used to view the oblique multiplanar reformatted images while making a curved reconstruction of the SSC, which was divided into approximately 80 radial sections of 0.2 mm in width (Figure 1). Measurements of

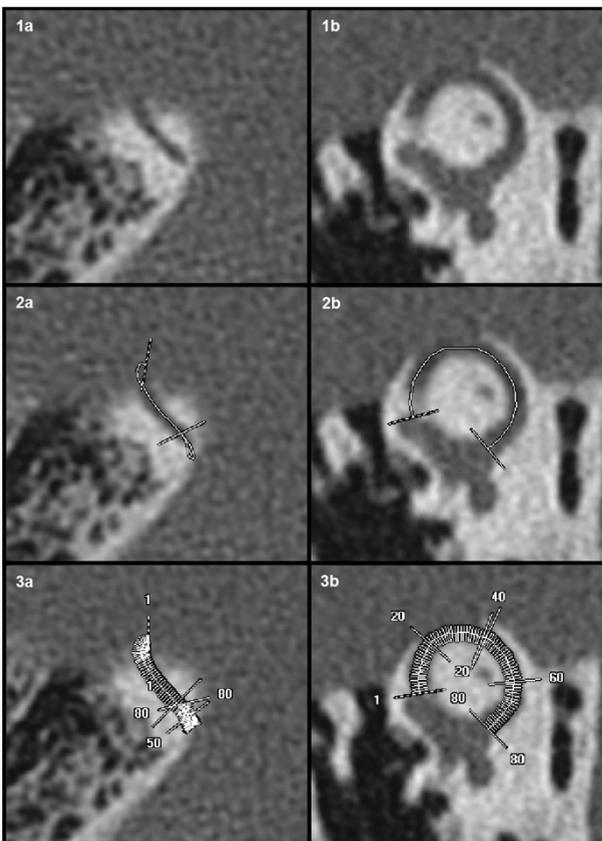


Figure 1. Reconstruction of an oblique multiplanar reformatted CT image in the plane axial and parallel through the semicircular canal (1a and 1b) of the left ear of a patient. Images 2a and 2b show the lines drawn through the semicircular canal, starting at the side of the ampulla and ending toward the common crus. Images 3a and 3b show the reconstruction divided into radial sections with a thickness of 0.2 mm, perpendicular to the bony covering of the superior canal, on which density measurements were performed.

bone density around the SSC were used to identify a dehiscence on radial sections. Specifically, the density profile along the radial dimension of each section (based on a straight line beginning at the temporal bone, through the center of the canal, passing through the SSC and ending in the brain) was plotted in Hounsfield units (HU) using ImageJ software (National Institutes of Health) [Schneider et al., 2012]. To determine the bone density in intact superior canals, we made measurements in 8 patients (16 ears) who (1) did not have a bony dehiscence or (2) had an intact but thin bone covering the SSC. We measured the thinnest part of the bony covering of the intact superior canal (mean = 1,130 HU; SD = 267 HU). To minimize the risk of diagnosing intact bone as a dehiscence, an HU value below 300 (less than the mean value of the bone minus 3 SD) was selected as a threshold below which the HU values were assumed to indicate an absence of the bony covering of the SSC (Figure 2).

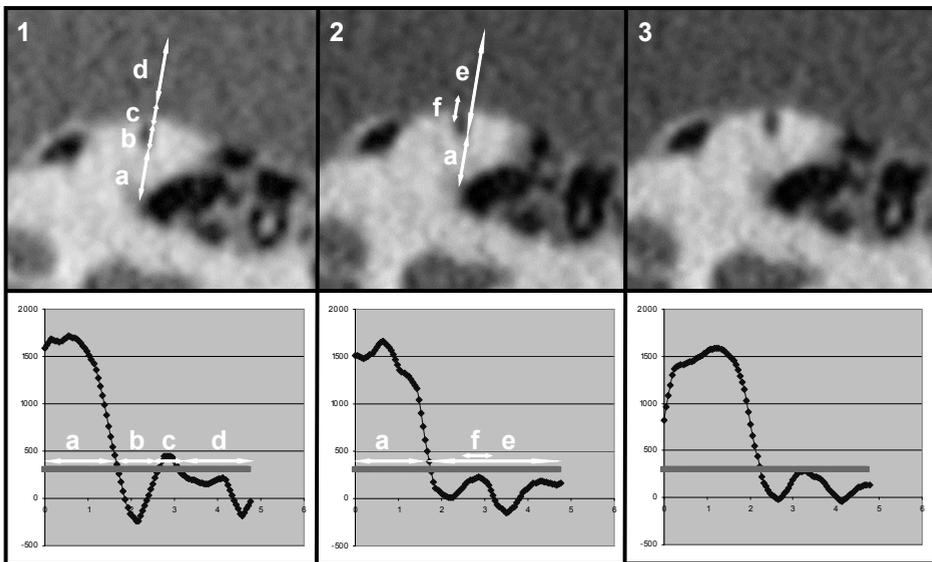


Figure 2. Density measurements made in three 0.2-mm-thick radial CT images through the SSC taken at different positions in a single patient. The radiodensity of the SSC was measured by drawing a line through the semicircular canal (a–d). Density measurements below 300 HU (horizontal line in the plot) indicate an absence of bone overlying the semicircular canal. Y-axis: HU; x-axis: length of the line that is drawn, in millimeters. The length and location of each dehiscence can be determined by counting the number of sections showing a dehiscence and the number of sections between the ampulla and the start of the SCD, respectively. In the figure, lines are drawn slightly off centre to show the dehiscence or thin bony covering in this figure. 1: Example of a thin bony covering of the SSC. Arrow a: temporal bone; arrow b: lumen of the canal; arrow c: bony covering of the SSC; arrow d: brain. 2: Example of an SCD. Arrow e: lumen of the SSC and the brain; arrow f: lack of bony covering (the density measurement stays just below 300 HU, confirming a dehiscence). 3: Similar to B but the dehiscence is less obvious; however, the density measurements show thresholds below 300 HU, indicating a dehiscence.

The length of a dehiscence was calculated by multiplying the number of radial sections in which the dehiscence was found with the thickness of the radial section (0.2 mm). If multiple dehiscences were present (with bone covering the SSC between two dehiscent sections), the total SCD length was the sum of the thickness of multiple sections. SCD location was determined by counting the number of radial sections from the ampulla to the start and end of the SCD, and by multiplying this by the thickness of the radial sections. In our later descriptions of SCD location, we use the start of the SCD in millimeters from the ampulla, because we did not find any statistically significant correlation between any of our variables and the end of the SCD. Independent measurements of dehiscence length and location were performed by two of the authors; one author measured them in the first 46 patients, and another author in the remaining 58 patients. To determine consistency between these two authors, 5 patients were measured by both authors, and the mean difference in SCD length was 0.24 mm and the mean difference in SCD starting location was 0.2 mm, i.e. the differences between authors were at the limit of the imaging resolution.

Data analysis

Statistical software (SPSS version 15.0) was used to analyze the data. We assessed the strength of the relationship between SCD length and location and patient characteristics (as well as the presence of a sign or symptom) by calculating the 'effect size' (<0.3 indicates a small effect). We analyzed whether differences in SCD length and location existed by: gender; patient age (patients younger or older than the median age of 45 years); duration of complaints until CT scanning (shorter or longer than the median period of 18 months); or the presence or absence of a second event preceding the onset of symptoms. A 'first event' is considered to be congenital thinning of the bone overlying the SSC. In some patients, the onset of SCD symptoms is associated with a 'second event', an activity that dramatically affects inner ear pressure (such as head trauma, excessive straining, coughing or child birth [Watters et al., 2006]). We also assessed the strength of the relationship between the presence of a sign or symptom (for each sign separately) and SCD length and location, by using effect size. In the case of a bilateral dehiscence, the more symptomatic ear in each patient was used for analysis.

We divided the SCD patients into three groups: (1) those with only auditory signs and symptoms, such as hyperacusis, autophony, aural fullness, hearing loss and/or tinnitus; (2) those with only vestibular signs and symptoms, such as imbalance, sound-, pressure- and exercise-associated dizziness, Tullio's phenomenon and/or Hennebert's sign, and (3) those with both auditory and vestibular signs and

symptoms. Because the distribution of SCD location data in these patients barely met the criteria for a normal distribution, we used nonparametric statistics [that do not assume a particular distribution, e.g. median, interquartile ranges (IQRs) and Mann-Whitney U tests] to compare for differences in SCD length and location among the three different groups. In each case we compared the difference between one group and the two other groups combined, to determine whether a difference exists between these patients and the remainder of the group.

We compared AC and BC thresholds and the ABG with SCD length and location (due to a significant correlation between SCD length and location) by using linear regression, reported as the 95% CI around the slope. In patients with bilateral dehiscence, both ears were used for audiometric testing as the pure-tone average could be measured for each ear individually. Similarly, cVEMP thresholds were analyzed by linear regression analysis for both SCD length and location, reported as the 95% CI around the slope. Regression analyses were done on ears without a history of ear disease or ear surgery, because these conditions could affect the pure-tone average and cVEMP threshold data independently of the SCD status.

RESULTS

Selection of patients

From our database of 146 patients diagnosed with SCD between 2000 and 2011, 104 patients (147 ears) with SCD syndrome underwent temporal bone HR-CT imaging at our institution. Out of the 104 patients, 34 (33%) had left SCD, 27 (26%) had right SCD, and 43 (41%) had bilateral SCD. The median SCD length was 4.4 mm (IQR: 2.8–5.4 mm) and the median SCD starting location was 5.0 mm (IQR: 4.2–6.0 mm) from the ampulla. Patient characteristics and signs and symptoms were analyzed for 104 ears (only the more symptomatic ear of the 104 patients). Audiometric data were available for 146 ears, and cVEMP data for 76 ears. After exclusion of ears with a history of ear disease or surgery, we analyzed the audiometric data on 118 ears and cVEMP data on 66 ears. See Figure 3 for the flowchart showing patient selection.

Patient characteristics and signs and symptoms

The mean age of the patients was 47 years (range: 15–85 years), and 58 of the 104 patients (56%) were female. The presence of a second event prior to the onset of SCD symptoms was noted in 25 out of the 50 patients that were specifically asked this question based on their medical record. We did not find a strong correlation

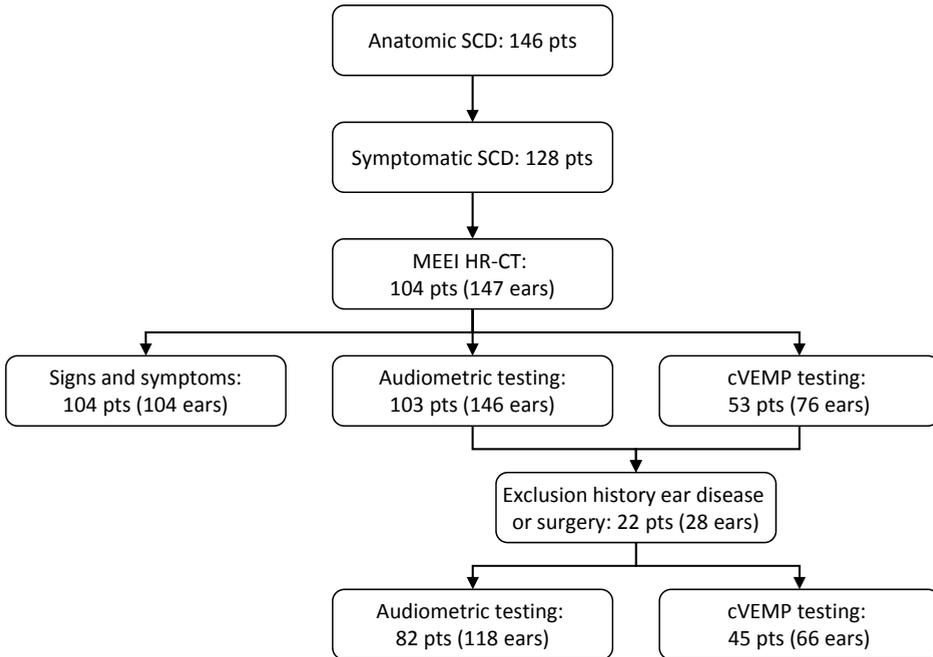


Figure 3. Patient selection flowchart. From our database of 146 patients with SCD, 128 had symptomatic SCD. Of these 128 patients, 104 underwent CT scanning at the Massachusetts Eye and Ear Infirmary (MEEI). Signs and symptoms were analyzed in all 104 patients. Audiometric and cVEMP testing was performed on ears without a history of ear surgery.

of gender, age, duration of complaints and the presence or absence of a preceding second event with SCD length or location (effect size: <0.15).

Signs and symptoms were correlated separately with SCD length and location, and included hyperacusis, autophony, aural fullness, tinnitus, imbalance and sound- and pressure-associated dizziness. These variables individually did not show a significant correlation with SCD length or location.

We then divided the SCD patients into three groups based on signs and symptoms, as described in the methods section: (1) auditory signs and symptoms only; (2) vestibular signs and symptoms only, and (3) both auditory and vestibular signs and symptoms. We compared each group with the other two groups combined. Our data indicate that a larger dehiscence starting closer to the ampulla was found in patients with auditory symptoms (with or without vestibular symptoms) as compared with the group that had no auditory symptoms (vestibular symptoms only; Mann-Whitney U test for SCD length = 0.03, and for SCD location = 0.004; Figure 4 ; Table 1).

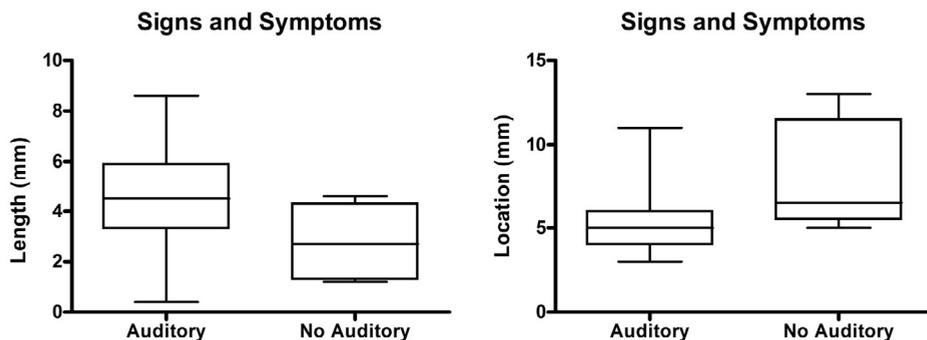


Figure 4. Box-and-whisker plots showing the association of signs and symptoms with SCD length (left) and SCD location (right) in millimeters from the ampulla. Box: median and IQR; whiskers: range; auditory: audiometric complaints (hyperacusis, autophony, aural fullness, report of hearing loss and/or tinnitus) with or without vestibular complaints; no auditory: vestibular complaints only (imbalance, sound-, pressure- or exercise-induced dizziness, Tullio's phenomenon and/or Hennebert's sign). The group with auditory complaints had 98 patients (94%), the group with no auditory (only vestibular) symptoms had 6 patients (6%). Significant differences between the auditory group and the 'no auditory' (vestibular only) group were found for both length (Mann-Whitney $p = 0.03$) and location (Mann-Whitney $p = 0.004$).

Table 1. Relationship between SCD length and location with signs and symptoms

	Group	Median (IQR)	Comparison group	Median (IQR)	MW
Length	Auditory only	4.4 (3.4-5.4)	vestibular only and auditory + vestibular	4.4 (2.9-5.9)	0.821
	No auditory (Vestibular only)	2.7 (1.4-4.2)	auditory only and auditory + vestibular	4.5 (3.4-5.9)	0.030
	Audio + Vest	4.6 (3.2-6.2)	auditory only and vestibular only	4.2 (3.0-5.1)	0.382
Location	Auditory only	4.8 (4.0-6.0)	vestibular only and auditory + vestibular	5.0 (4.1-5.7)	0.838
	No auditory (Vestibular only)	6.4 (5.7-10.7)	auditory only and auditory + vestibular	4.8 (4.0-5.6)	0.004
	Auditory + Vestibular	5.0 (4.0-5.6)	auditory only and vestibular only	5.0 (4.1-6.3)	0.209

Values in parentheses denote IQR. Auditory only = auditory signs and symptoms only; no auditory (vestibular only) = vestibular signs and symptoms only; auditory and vestibular = auditory and vestibular signs and symptoms; MW = Mann-Whitney test.

Data analysis – Audiometric testing

We analyzed AC and BC thresholds and the ABG in 118 ears with SCD. Twenty-eight out of 147 ears were excluded due to a history of ear disease or ear surgery (severe sensorineural hearing loss, prolapse of the dura abutting the ossicular chain, mastoidectomy, atticotomy, stapes surgery, glomus tympanicum, acoustic neuroma removal and middle fossa craniotomy). Audiometric data were not available for 1 patient. By linear regression analysis, we found that a larger dehiscence

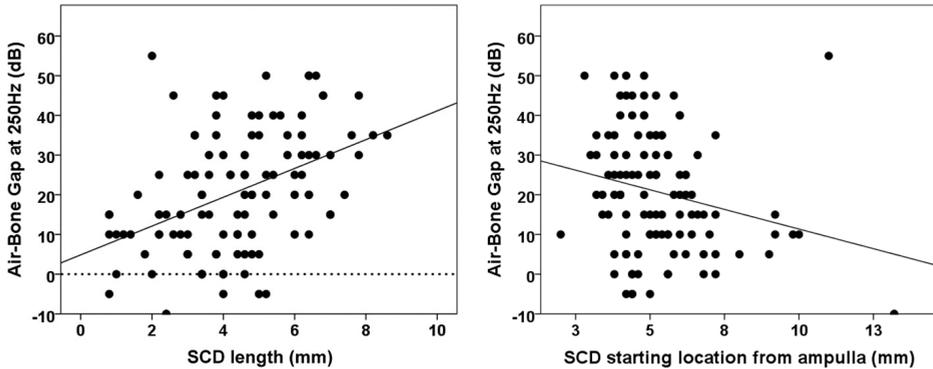


Figure 5. Scatter plots correlating ABG with SCD length (left) and location (right) in patients with data on the ABG (excluding 28 patients with a history of ear disease; $n = 118$). Each graph shows the linear regression line. When both length and location are used in two-factor linear regression ($R^2 = 0.19$, $F = 12.6$), SCD length shows the 95% CI around the slope of 2.0–5.3 ($p < 0.001$), and SCD location shows the 95% CI around the slope of –1.7 to 1.8 ($p = 0.954$). A Intercept = 4.9; slope = 3.6; $R^2 = 0.19$; $F = 25.4$ ($p < 0.001$). B Intercept = 31.1; slope = –2.0; $R^2 = 0.05$; $F = 5.8$ ($p = 0.018$).

showed significantly more AC loss at 250 Hz (95% CI: 1.7–4.7), 500 Hz (95% CI: 0.7–3.5) and 1,000 Hz (95% CI: 0.0–2.5) and a significantly larger ABG at 250 Hz (95% CI: 2.0–5.3), 500 Hz (95% CI: 1.6–4.6) and 1,000 Hz (95% CI: 1.3–3.3). No correlation with SCD length was found for AC loss or the ABG for frequencies above 1,000 Hz, as well as for BC loss.

Finally, linear regression analyses showed a statistically significant relationship of SCD length and location with ABG. After adjusting for this correlation, we did not observe a statistically significant relationship between SCD location and AC loss, BC loss or ABG. Figure 5 shows a scatter plot of the association of ABG at 250 Hz with SCD length and location.

Data analysis – cVEMP testing

We analyzed cVEMP testing in 66 ears with SCD. On 80 ears, cVEMP testing results were not available, and 10 patients were excluded due to a history of ear disease or surgery. Linear regression analyses showed a statistically significant relationship of SCD length and location with cVEMP thresholds. After adjusting for this relationship, lowered cVEMP thresholds were seen with a larger dehiscence at 250 Hz (95% CI: –4.4 to –0.3), 500 Hz (95% CI: –4.1 to –1.0), 750 Hz (95% CI: –4.2 to –0.7) and 1,000 Hz (95% CI: –3.6 to –0.5) and a starting location closer to the ampulla at 250 Hz (95% CI: 1.3–5.1), 750 Hz (95% CI: 0.2–3.3) and 1,000 Hz (95% CI: 0.6–3.5). These data can be found in Figure 6. Exclusive of SCD length, the location of the dehiscence did not significantly correlate with cVEMP thresholds at 500 Hz (95% CI: –0.4 to 2.5).

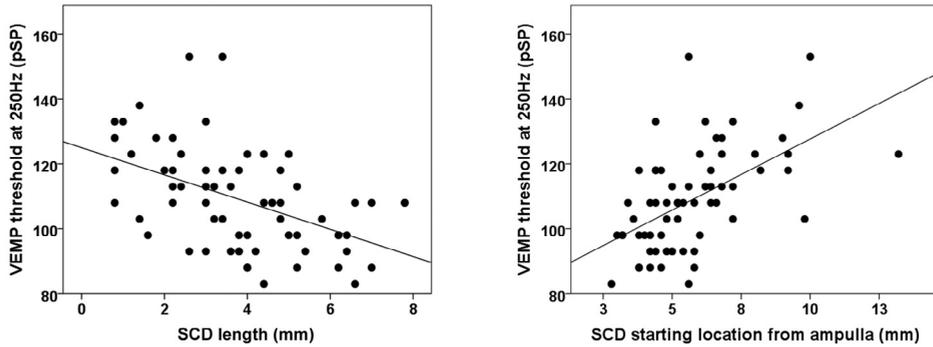


Figure 6. Scatter plots correlating cVEMP with SCD length (left) and location (right) in patients with cVEMP testing (excluding 10 patients with a history of ear disease; $n = 66$). Each graph shows the linear regression line. When both length and location are used in two-factor linear regression ($R^2 = 0.36$, $F = 17.4$), SCD length shows the 95% CI around the slope of -4.4 to -0.3 ($p = 0.024$), and SCD location shows the 95% CI around the slope of 1.3 – 5.1 ($p = 0.001$). pSP = peak sound pressure. A Intercept = 125.0; slope = -4.2 ; $R^2 = 0.23$; $F = 19.9$ ($p < 0.001$). B Intercept = 83.9; slope = 4.4; $R^2 = 0.30$; $F = 27.6$ ($p < 0.001$).

DISCUSSION

Our radiologic study of 104 patients with SCD syndrome showed that (1) a larger dehiscence located closer to the ampulla was associated with auditory symptoms, with or without vestibular symptoms; (2) a larger ABG was associated with a larger dehiscence and not associated with SCD location, and (3) a lower cVEMP threshold was associated with a larger dehiscence located closer to the ampulla. Differences in length and location of the bony defect may help to explain the varied clinical presentation of SCD syndrome.

Signs and symptoms in SCD

Patients without auditory symptoms (only vestibular symptoms, such as imbalance, sound-, pressure- or exercise-associated dizziness, Tullio's phenomenon and/or Hennebert's sign) demonstrated less spread in the length and location of their SCD than patients with auditory symptoms (hyperacusis, autophony, aural fullness, report of hearing loss, tinnitus). The smaller sample size of the 'vestibular only' group might contribute to these findings. When auditory signs and symptoms were present, the dehiscence was usually located near the ampulla of the SSC (and thus closer to the cochlea), whereas when auditory signs and symptoms were not present (vestibular symptoms only), the dehiscence was located further from the ampulla. Auditory symptoms were usually associated with a larger bony defect, whereas no auditory symptoms (vestibular symptoms only) were associated with a small dehiscence.

Differences in measurement techniques and patient selection may help to explain why our data are not in agreement with other recent reports. One study correlated intraoperative SCD length with clinical findings, audiometric testing and cVEMP testing [Chien et al., 2012], but because only patients who underwent surgical repair were included, patients with mild symptoms or with only auditory symptoms may not have been adequately represented. We included all symptomatic SCD patients (whether or not they underwent surgery) that had imaging available for detailed analysis, allowing us to study a wide range of SCD lengths and locations to correlate with signs and symptoms. Although we observed a range of symptoms across a number of patients who had a variety of defect sizes and locations, larger dehiscences closer to the ampulla were rather associated with auditory (with or without vestibular) symptoms than with vestibular symptoms alone. Such information is clinically valuable and helps to explain why, for example, a patient with a small bony defect located distant from the ampulla may not have auditory symptoms.

Audiometric testing in SCD

Rosowski et al. [2004] suggested that the impedance through a superior canal defect will vary according to length and location; thus a larger dehiscence would theoretically lead to lower impedances and more low-frequency conductive loss. Pisano et al. [2012] examined the effect of SCD length on intracochlear pressure measurements in fresh human cadaveric temporal bones and computed the differential pressure across the cochlear partition. This differential pressure measurement is related to sound input to the cochlea, and provides an estimate of hearing in a human temporal bone model. They showed that acoustic input to the cochlea was reduced monotonically with an increase in length of the SCD at low frequencies (below 1 kHz). Surprisingly, at higher frequencies (above 1 kHz), sometimes the smallest SCD (<0.5 mm diameter, generally below the resolution of CT) showed more reduction in cochlear input than the larger SCD [Pisano et al., 2012]. Our clinical data are in accordance with these low-frequency findings in the temporal bone model: patients with a larger SCD have higher AC thresholds (and larger ABG) across three frequencies. SCD location, however, does not significantly contribute to AC thresholds or the magnitude of the ABG. This final observation will need to be validated in our temporal bone model.

cVEMP in SCD

The cVEMP measures the function of the saccule and the inferior vestibular nerve, and low thresholds and large amplitudes are often seen in symptomatic SCD ears [Brantberg et al., 1999; Streubel et al., 2001; Belden et al., 2003; Curtin, 2003; Roditi

et al., 2009]. The bony defect is felt to create a ‘third window’ or low-impedance fluid pathway, resulting in enhanced vestibular sensitivity. One study reported lower cVEMP thresholds in patients with larger canal defects [Pfammatter et al., 2010], but another study showed no association with intraoperative SCD length and VEMP thresholds [Chien et al., 2012]. The influence of SCD location on cVEMP thresholds, however, has not been described before. We theorize that an SCD located closer to the saccule (and thus closer to the ampulla of the SSC) creates a lower fluid impedance pathway shunting energy through this third window, leading to lower cVEMP thresholds (as shown by our data). In future studies we will examine the SSC fluid flow in temporal bones and in computational models to better assess these anatomic relationships. However, cVEMP thresholds can be affected by multiple variables (e.g. sternocleidomastoid muscle mass, otosclerosis or middle ear disease) and are found to be lowered in other third-window conditions such as large vestibular aqueduct syndrome [Merchant et al., 2007].

Limitations of this study

Most studies that have assessed SCD length used linear CT scanning measurements of the curved superior canal. We developed a method of assessing SCD length taking the curvature of the superior canal into account by making an oblique reconstruction of the SSC. However, recent studies have described the risk of overestimation of the SCD length by using CT scans [Sequeira et al., 2011; Tavasoliev et al., 2012]. Risk of overestimation and false-positive diagnoses of SCD have especially been described for patients with a small dehiscence (<3 mm) [Sequeira et al., 2011]. To minimize the risk of (1) overestimating SCD length or (2) missing a very thin layer of bone due to the partial volume averaging effect, we determined a conservative HU cutoff point (less than the mean HU value for bone minus 3 SD) for the bone to be defined as absent. In addition, SCD size on CT scanning measurements can be correlated with the intraoperative measurements. However, precise measurements of the dehiscence are difficult to obtain intra-operatively due to (1) angulation of the defect relative to the measuring instrument; (2) blood and occasionally cerebrospinal fluid in the field; (3) the need to continuously immerse the field with irrigation fluid to reduce injury to the labyrinth, and (4) the desire to repair the dehiscence in a timely manner to minimize prolonged exposure of the membranous labyrinth. Finally, we used radial measurements in this study, and the measurement during surgery is linear. A more precise and efficient way to measure these defects intra-operatively needs to be developed, perhaps incorporated into the microscope or endoscope (which provides a superior and high-magnification view of the defect [Carter et al., 2014] as a superimposed heads-up display scale bar that could be rotated to conform to the defect.

While we describe significant correlations of SCD length and location with the magnitude of the ABG and cVEMP thresholds, these relationships only explain about 20–30% (R^2 of 0.19 and 0.36, respectively; Figure 5, 6) of the variability in ABG and cVEMP thresholds. Other factors that might influence these outcomes need to be further studied, such as the effect of natural plugging or ‘autoplugging’ of the dura and/or brain on SCD signs and symptoms, as recently described [Brandolini and Modugno, 2012].

Clinical implications

When a patient presents with signs and symptoms suspicious for SCD syndrome, high-resolution CT imaging with Stenvers and Pöschl reformats are used to confirm the presence of a bony defect of the superior canal. Audiometric and VEMP testing are used to support the diagnosis and determine the ‘worse ear’, but not all patients present with classical test results (e.g., low-frequency ABG, lower cVEMP thresholds). Our data help explain why normal cVEMP thresholds or no ABG are seen in some patients with positive SCD symptoms and CT findings and provide important information in the surgical counseling of patients with SCD.

CONCLUSION

We found that: (1) patients with auditory symptoms (with or without vestibular symptoms) have a larger dehiscence located closer to the ampulla; (2) a larger ABG is associated with a larger SCD, while dehiscence location did not influence the AC threshold or ABG, and (3) lower cVEMP thresholds are found in patients with a larger dehiscence located closer to the ampulla. We believe that both SCD length and location are important features to assess in the evaluation of temporal bone CT imaging in patients with SCD syndrome. Our findings help explain why symptomatic patients with a smaller SCD located further away from the ampulla may not present with an ABG or with lowered cVEMP thresholds.

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REFERENCES

Belden CJ, Weg N, Minor LB, Zinreich SJ: Ct evaluation of bone dehiscence of the superior semicircular canal as a cause of sound- and/or pressure-induced vertigo. *Radiology* 2003; 226:337-343.

Brandolini C, Modugno GC: Do signs of natural plugging of superior semicircular canal dehiscence exist? *Am J Otolaryngol* 2012;33:268-271.

Brantberg K, Bergenius J, Tribukait A: Vestibular-evoked myogenic potentials in patients with dehiscence of the superior semicircular canal. *Acta Otolaryngol* 1999;119:633-640.

Carey JP, Hirvonen TP, Hullar TE, Minor LB: Acoustic responses of vestibular afferents in a model of superior canal dehiscence. *Otol Neurotol* 2004;25:345-352.

Carter MS, Lookabaugh S, Lee DJ: Endoscopic-assisted repair of superior canal dehiscence syndrome. *Laryngoscope* 2014;124(6):1464-8

Chi FL, Ren DD, Dai CF: Variety of audiologic manifestations in patients with superior semicircular canal dehiscence. *Otol Neurotol* 2010;31:2-10.

Chien WW, Janky K, Minor LB, Carey JP: Superior canal dehiscence size: Multivariate assessment of clinical impact. *Otol Neurotol* 2012;33:810-815.

Curtin HD: Superior semicircular canal dehiscence syndrome and multi-detector row ct. *Radiology* 2003;226:312-314.

Martin C, Chahine P, Veyret C, Richard C, Prades JM, Pouget JF: Prospective radiological study concerning a series of patients suffering from conductive or mixed hearing loss due to superior semicircular canal dehiscence. *Eur Arch Otorhinolaryngol* 2009;266:1175-1181.

Merchant SN, Nakajima HH, Halpin C, Nadol JB, Jr., Lee DJ, Innis WP, Curtin H, Rosowski JJ: Clinical investigation and mechanism of air-bone gaps in large vestibular aqueduct syndrome. *Ann Otol Rhinol Laryngol* 2007;116:532-541.

Mikulec AA, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.

Minor LB, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998; 124:249-258.

Nielsen MEF, Lee DJ, Stieger C, Rosowski JJ, Grolman W, Nakajima HH: Assessment of superior canal dehiscence location and size on intracochlear sound pressures. Association for Research in Otolaryngology, 36th MidWinter Meeting, February 16-20, 2013, Baltimore, Maryland 2013.

Nielsen MEF, McKenna MJ, Herrmann BS, Grolman W, Lee DJ: Utility of cvemps in bilateral superior canal dehiscence syndrome. 2012;In Press.

Pfammatter A, Darrouzet V, Gartner M, Somers T, Van Dinther J, Tralbalzini F, Ayache D, Linder T: A superior semicircular canal dehiscence syndrome multicenter study: Is there an association between size and symptoms? *Otol Neurotol* 2010;31:447-454.

Pisano DV, Niesten ME, Merchant SN, Nakajima HH: The effect of superior semicircular canal dehiscence on intracochlear sound pressures. *Audiol Neurootol* 2012;17:338-348.

Rauch SD, Zhou G, Kujawa SG, Guinan JJ, Herrmann BS: Vestibular-evoked myogenic potentials show altered tuning in patients with meniere's disease. *Otol Neurotol* 2004;25:333-338.

Roditi RE, Eppsteiner RW, Sauter TB, Lee DJ: Cervical vestibular-evoked myogenic potentials (cvemps) in patients with superior canal dehiscence syndrome (scds). *Otolaryngol Head Neck Surg* 2009;141:24-28.

Rosowski JJ, Songer JE, Nakajima HH, Brinsko KM, Merchant SN: Clinical, experimental, and theoretical investigations of the effect of superior semicircular canal dehiscence on hearing mechanisms. *Otol Neurotol* 2004;25:323-332.

Schneider CA, Rasband WS, Eliceiri KW: Nih image to imagej: 25 years of image analysis. *Nature Methods* 2012;9:671-675.

Sequeira SM, Whiting BR, Shimony JS, Vo KD, Hullar TE: Accuracy of computed tomography detection of superior canal dehiscence. *Otol Neurotol* 2011;32:1500-1505.

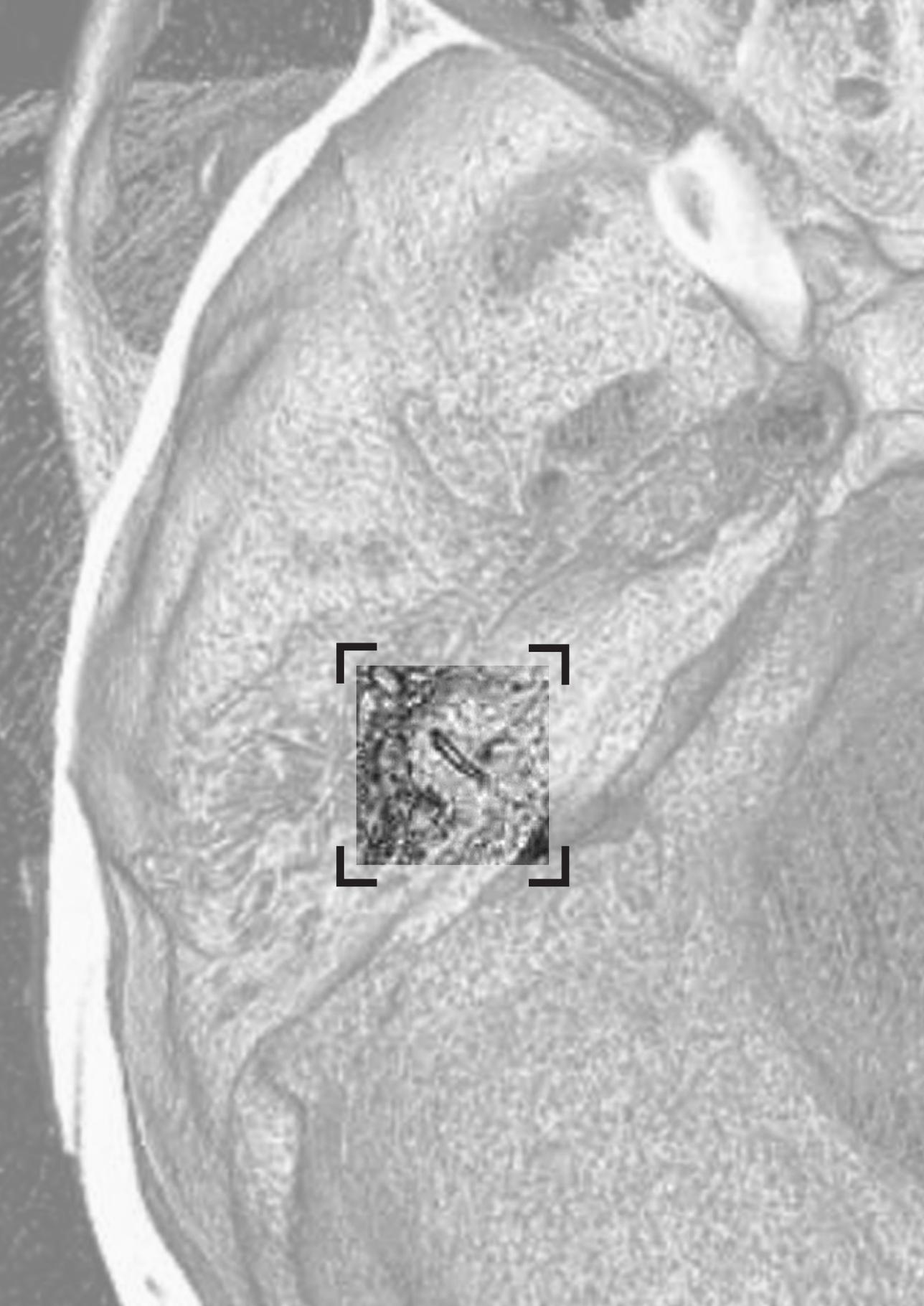
Songer JE, Rosowski JJ: A mechano-acoustic model of the effect of superior canal dehiscence on hearing in chinchilla. *J Acoust Soc Am* 2007;122:943-951.

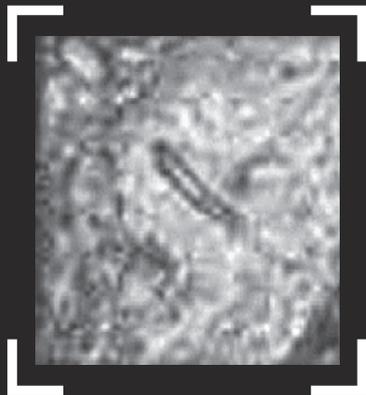
Streubel SO, Cremer PD, Carey JP, Weg N, Minor LB: Vestibular-evoked myogenic potentials in the diagnosis of superior canal dehiscence syndrome. *Acta Otolaryngol Suppl* 2001;545:41-49.

Tavassolie TS, Penninger RT, Zuniga MG, Minor LB, Carey JP: Multislice computed tomography in the diagnosis of superior canal dehiscence: How much error, and how to minimize it? *Otol Neurotol* 2012;33:215-222.

Watters KF, Rosowski JJ, Sauter T, Lee DJ: Superior semicircular canal dehiscence presenting as postpartum vertigo. *Otol Neurotol* 2006;27:756-768.

Yuen HW, Boeddinghaus R, Eikelboom RH, Atlas MD: The relationship between the air-bone gap and the size of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2009;141:689-694.





Chapter 3.2

The effect of superior semicircular canal dehiscence on intracochlear sound pressures

Dominic V. Pisano, Marlien E.F. Niesten, Saumil N. Merchant, Hideko H. Nakajima

ABSTRACT

Semicircular canal dehiscence (SCD) is a pathological opening in the bony wall of the inner ear that can result in conductive hearing loss. The hearing loss is variable across patients, and the precise mechanism and source of variability are not fully understood. Simultaneous measurements of basal intracochlear sound pressures in scala vestibuli (SV) and scala tympani (ST) enable quantification of the differential pressure across the cochlear partition, the stimulus that excites the cochlear partition. We used intracochlear sound pressure measurements in cadaveric preparations to study the effects of SCD size. Sound-induced pressures in SV and ST, as well as stapes velocity and ear-canal pressure were measured simultaneously for various sizes of SCD followed by SCD patching. Our results showed that at low frequencies (<600 Hz), SCD decreased the pressure in both SV and ST, as well as differential pressure, and these effects became more pronounced as dehiscence size was increased. Near 100 Hz, SV decreased about 10 dB for a 0.5 mm dehiscence and 20 dB for a 2 mm dehiscence, while ST decreased about 8 dB for a 0.5 mm dehiscence and 18 dB for a 2mm dehiscence. Differential pressure decreased about 10 dB for a 0.5 mm dehiscence and about 20 dB for a 2 mm dehiscence at 100 Hz. In some ears, for frequencies above 1 kHz, the smallest pinpoint dehiscence had bigger effects on the differential pressure (10 dB decrease) than larger dehiscences (less than 10 dB decrease), suggesting larger hearing losses in this frequency range. These effects due to SCD were reversible by patching the dehiscence. We also showed that under certain circumstances such as SCD, stapes velocity is not related to how the ear can transduce sound across the cochlear partition because it is not directly related to the differential pressure, emphasizing that certain pathologies cannot be fully assessed by measurements such as stapes velocity.

INTRODUCTION

Simultaneous measurement of basal intracochlear pressures in scala vestibuli (P_{sv}) and scala tympani (P_{st}) in human cadaveric temporal bones enables determination of the differential pressure across the cochlear partition. Differential pressure is the stimulus that excites the partition [Nakajima et al., 2009; Voss et al., 1996; Wever and Lawrence, 1950]. We use intracochlear pressure measurements to study superior semicircular canal dehiscence (SCD), an additional opening in the bony wall of the inner ear that does not exist in normal ears. This pathological third window provides an alternative path through which the stimulus-induced fluid displacement of the oval window can flow. SCD can result in conductive hearing loss, but the precise mechanism is presently not well understood.

It has been demonstrated previously that the induction of SCDs in chinchillas [Songer and Rosowski, 2006] and human temporal bones [Chien et al., 2007] produces sound-induced motion of the lymph in the semicircular canal and results in increases in ossicular velocity at frequencies less than 1 kHz. It has also been demonstrated in chinchilla that SCDs produce decreases in the low-frequency sound-induced cochlear potentials measured near the round window in response to wide-band chirps [Songer and Rosowski, 2005]. These results have led to the suggestion that SCD acts to reduce the sound pressure in the cochlear vestibule as well as the sound pressure difference across the cochlear partition [Songer and Rosowski, 2007]. The present study presents a test of those hypotheses via direct measurements of the sound pressures in scala vestibuli and tympani of human cadaveric temporal bone preparations before and after induced SCDs. These direct measurements of the mechanical consequences of SCD on the hearing process also help shed light on why the severity of hearing loss varies among individuals with SCD.

A subset of the results presented here was the subject of a presentation at the 2011 Mechanics of Hearing Meeting, and was included in a proceedings manuscript [Nakajima et al., 2011].

METHODS

Temporal Bone Preparation

Temporal bones were removed by an intracranial approach [Nadol, 1996] during autopsy within 24 hours of death, after permission was granted to obtain speci-

mens for research. Immediately after removal, the specimens were stored in 0.9% normal saline and refrigerated. Only a brief description of our temporal bone preparation is presented here as details are available in Nakajima et al. [2009]. The bony ear canal was shortened to a length of about 1 cm, a mastoidectomy performed and the facial recess opened widely for middle- and inner-ear access. The stapedial tendon was removed to allow access to the area surrounding the oval window. The promontory was thinned near the oval and round windows where the pressure sensors were to be inserted. The epitympanic region was opened to access the superior semicircular canal from the lateral transmastoid approach. A 2-3 mm length of the bone overlying the superior semicircular canal near the arcuate eminence was thinned where the superior semicircular canal is adjacent to the temporal lobe of the middle fossa.

The temporal bone was positioned such that the tympanic ring of the tympanic membrane was roughly horizontal. This position allowed for easy immersion of the inner-ear compartment in saline during the cochleostomy procedure and during the opening of the dehiscence. To seal the pressure transducers in the cochleostomies, the fluid around the inner ear was lowered so that a meniscus of saline surrounded the cochleostomy and the inserted transducer; then Jeltrate® dental impression material was applied. This procedure ensured that air was not introduced into the cochlea.

The transmastoid (lateral) approach for the SCD was chosen to enable the dehiscence to remain immersed in saline throughout the preparation and measurement procedure. The region of the superior semicircular canal dehiscences was kept slightly lower than the area where stapes velocity measurements were made (thus the SCD dehiscence always had about 1mm fluid above the hole and the posterior crus of the stapes was above fluid). The SCDs were made facing laterally (transmastoid approach), enabling the same general direction of the SCD opening as the cochleostomy openings for the pressure sensors. There are likely no differences in intracochlear pressure effects between slight directional differences of the dehiscence (about 90 degree difference, facing laterally versus superiorly along the same section of the semicircular canal arc). Because our goal in this study was to determine whether hole size affected hearing – as long as parameters except size were generally kept consistent, and the effects were reversible – our goal was reached.

Sound Stimulation, Ear Canal Pressure, Ossicular Velocity

Sound stimuli, velocity measurements and pressure recordings were performed in the manner described by Nakajima et al. [2009] and illustrated in Figure 1. Sound stimulation was presented to the sealed ear canal via an earphone (Radio Shack 40-1377) coupled to the canal with flexible tubing. Ear-canal sound pressure (P_{EC}) was recorded with a calibrated probe tube microphone (Etymotic ER-7C) with the tip of the flexible probe tube positioned approximately 1-2 mm from the umbo of the tympanic membrane. Velocities for Stapes (V_{Stap}) and round window were measured with a laser Doppler vibrometer (Polytec CLV700) aimed at 0.2 mm² reflectors (consisting of polystyrene micro beads) placed on the posterior crus of the stapes and the round window membrane. All measured velocities were referenced by the simultaneously measured P_{EC} and are reported as such with units of m·s⁻¹·Pa⁻¹. Phase comparison between V_{Stap} and round-window velocity was made to ensure a ½ cycle difference below 500 Hz; such a phase difference indicates that air was not introduced into the inner ear and that a pre-existing third window was not present.

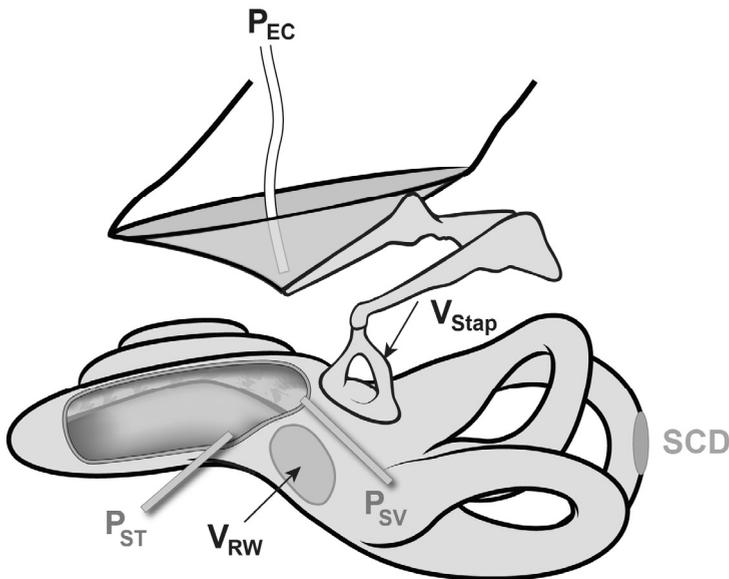


Figure 1. Illustration of a left ear demonstrating a superior semicircular canal dehiscence (SCD) along with measurements made. Measurements included sound pressure in the ear canal (P_{EC}) with a probe-tube microphone, stapes velocity (V_{Stap}) and round-window velocity (V_{RW}) with laser Doppler vibrometry and sound pressures in scala vestibuli (P_{SV}) and scala tympani (P_{ST}) measured simultaneously with micro-optical pressure transducers. For illustration purposes only, the scalae are shown opened (cut-out area to the left of the round window) to show the placement of the transducers within the two perilymphatic scalae.

Pressure Sensors

Intracochlear sound pressures were measured in scala vestibuli (P_{SV}) and scala tympani (P_{ST}) simultaneously with micro-optical pressure sensors developed by Olson [1998], along with P_{EC} and V_{stap} . Figure 1 illustrates the various measurements made. The pressure sensors were inserted through ($\sim 200 \mu\text{m}$ diameter) cochleostomies drilled in the bony promontory into scala vestibuli and tympani [Nakajima et al., 2009]. The sensors were placed approximately 100-200 μm deep into the scalae. During drilling and sensor insertion, the regions surrounding the cochleostomies were immersed in saline. The sensors were sealed to the surrounding cochlear bone with dental alginate impression material (Jeltrate, L.D. Caulk Co.) to prevent release of fluid from the cochlea, and to prevent air leaking into the cochlea. Repeated calibrations of the sensitivity of the pressure sensors [Olson, 1998; Nakajima et al., 2009] were performed just before intracochlear placement and after removal of the sensors from the cochlea. The similarity of the calibrations made before placement and after removal of the sensors (differences of less than 2 dB) was an important constraint on the quality of our results.

Superior canal dehiscence

The superior semicircular canal was accessed by the lateral transmastoid approach where various sizes of dehiscences (from small to large) were made consistently near the arcuate eminence interfacing the middle cranial fossa. CT scans of the temporal bones after the experiment showed that the location (center of the SCD along the arc of the superior semicircular canal) varied approximately between 4–5 mm from the ampulla. Starting with a pinpoint hole of approximately 0.5 mm diameter, the dehiscence was enlarged in length to 1 mm and then 2 mm with constant widths of approximately 0.5 mm. Simultaneous recordings of P_{SV} and P_{ST} , as well as V_{stap} and P_{EC} were made before and after each increase in dehiscence size. We then attempted to reverse the effects of the SCD by patching the dehiscence with dental impression material or dental cement.

Generally, dental impression material placed over the dehiscence reversed the effect of the SCD on V_{stap} , P_{SV} , and P_{ST} . Dental cement was less effective. It is possible that the dental impression material (which is water soluble before drying) sealed the hole completely, while the dental cement, which requires a dry substrate, did not always completely seal the dehiscence.

Summary of Specimens Used

Summary of the specimens used are shown in Table I. Experiments were conducted on twenty five human temporal bones for this study. The first three bones

Table I. Summary of Specimens

Number	Comment Complication	SV sensor Stable	ST sensor Stable	P_{sv} SCD reversed	P_{st} SCD reversed	V_{stap} SCD reversed
1 (036)	Development					
2 (038)	Development					
3 (047)	Development					
4 (067)	Air					
5 (069)	Low V_{stap}					
6 (071)		X	X	X	X	X
7 (073)			X		X	X
8 (075)	Trauma					
9 (076)		X	X	X		X
10 (078)	Air					
11 (079)		X	X			X
12 (080)	Air					
13 (081)			X		X	X
14 (082)		X		X		X
15 (083)						
16 (084)	Air					
17 (085)			X		X	X
18 (086)						
19 (087)	Low V_{stap}					
20 (088)						
21 (089)	Trauma					
22 (090)	Low V_{stap}					
23 (091)						
24 (092)		X	X	X	X	X
25 (093)		X	X	X	X	X

V_{stap} = stapes velocity; SV = scala vestibuli; ST = scala tympani, P_{sv} = scale vestibuli pressure; P_{st} = scale tympani pressure.

were used to develop techniques. In nine bones, complications occurred such as: air introduced into the inner ear, abnormally low middle-ear motion, or trauma to the preparation. In three bones, both scala vestibuli and scala tympani pressure sensors became unstable (i.e. calibration at the end of the experiment differed from the beginning by over 2 dB). Of the remaining ten temporal bones, six ears provided P_{sv} results with stable sensors (five with reversal of SCD effect after patching, and one with incomplete reversal), eight ears provided P_{st} results with stable sensors (six with reversal of SCD effect after patching, and two with incomplete reversal), and three ears had both P_{sv} and P_{st} sensors that were stable with good reversal of SCD effects.

RESULTS

Stapes Velocity (V_{Stap})

Stapes velocity relative to ear-canal pressure measured before and after creating dehiscences in the superior semicircular canal of various sizes showed that changes in V_{Stap} due to SCD varied across ears. Figure 2 shows three representative examples of $V_{\text{Stap}}/P_{\text{EC}}$ magnitude and phase for the initial state (black solid lines), after various SCD sizes, and after patching the SCD (black dashed lines). The three examples show variations in the amount and frequency range of the SCD-induced change in V_{Stap} across ears and that these changes were reversible by patching the SCD.

In general, an increase in SCD size resulted in an incremental increase in the magnitude of V_{Stap} over some range of frequencies; however, the frequency range of the effect as well as the amount of change varied across ears. In Figure 2A, there is a wide frequency range (up to 7 kHz) where there is a monotonic relationship between magnitude and dehiscence size. In contrast, Figure 2B shows an example where an incremental increase in V_{Stap} with dehiscence size only occurs below 1 kHz, while between 1 to 2 kHz, V_{Stap} magnitude actually decreases as dehiscence size increases. Another example of how dehiscence size can affect V_{Stap} in a complicated manner is shown in Figure 2C, where only the pinpoint dehiscence (~0.5 mm diameter) resulted in an increase in stapes velocity below 600 Hz. Between 1 to 2 kHz the pin-hole dehiscence actually produced a decrease in V_{Stap} magnitude

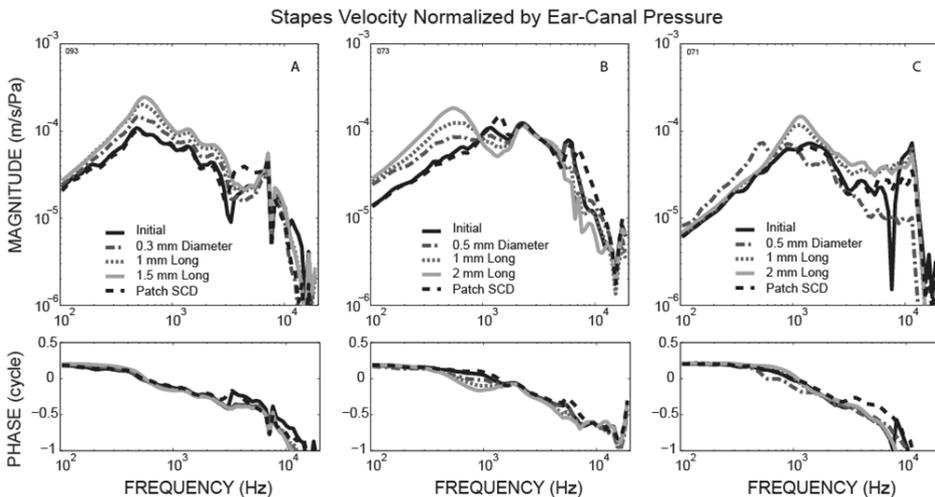


Figure 2. Three (A, B, C) representative examples of stapes velocity relative to ear-canal pressure including the magnitude and phase for the initial state, after inducing SCD of various sizes, and after patching the SCD.

(instead of an increase as seen in the larger dehiscences). Overall, for dehiscences of approximately 2 mm, V_{stap} increased in magnitude over varying frequency ranges (below 4 kHz for 4 ears, below 1 kHz for 4 ears, 0.8 to 6 kHz for 2 ears). All 10 ears showed reversal of these increases in V_{stap} after patching the SCD. SCD induced increases in V_{stap} has been reported earlier in temporal bones [Chien et al., 2007] and animal studies [Songer et al., 2006; Rosowski et al., 2004].

The stapes velocity results are generally consistent with the idea that the SCD shunts the fluid flow evoked by oval-window motion, allowing increased freedom of stapes motion due to the decrease in the acoustic impedance of the inner ear. However, the frequency range of these effects varies. Notably, as shown by the representative example in Figure 2C, the effect of dehiscence size on V_{stap} can be complicated, especially for smaller dehiscences. This is because V_{stap} is affected by the overall inner-ear input impedance, including the impedance within the vestibule, the impedances of the individual scalae compartments, as well as the impedance of the dividing cochlear partition. Because of these complexities, V_{stap} is not always well correlated with the sound pressure across the cochlear partition, and therefore is not a good indicator of how hearing is affected by SCD.

Pressure in Scala Vestibuli (P_{sv})

The effect of SCD on scala vestibuli pressure varied across ears, and generally two types of effects were seen. Figure 3 illustrates representative examples of the two

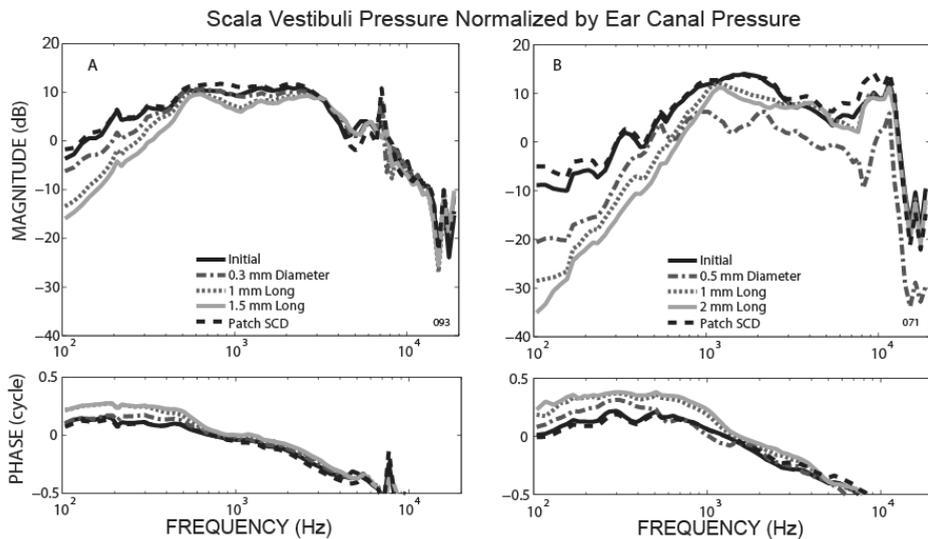


Figure 3. Representative example of scala vestibuli pressure relative to ear canal pressure for the initial state, after various SCD sizes, and after patching the SCD.

response types. Plotted in the figure is scala vestibuli pressure relative to ear-canal pressure (P_{sv}/P_{ec}) in the initial state (black solid lines), after various SCD sizes, and after patching the SCD (black dashed lines). Figure 3A plots an example of a simple monotonic relationship where P_{sv} magnitude decreased and the phase changed to the leading direction with increase in SCD size for a wide frequency range (<3 kHz). Patching the SCD resulted in reversal of the effects of SCD on P_{sv} in this preparation with stability of the pressure sensor calibration within 2 dB. The trend of incremental decreases in P_{sv} with increases in SCD size was seen in 4 out of 6 ears where the P_{sv} sensors were stable and the SCD effects were reversible in all except one where the SCD was not completely reversed by patching with dental cement.

Figure 3B shows a representative ear showing a more complicated effect of SCD size on P_{sv}/P_{ec} . In the low frequency region (<500 Hz), the magnitude decreased and the phase showed an increased lead as SCD size was increased, similar to the effect seen in 3A. However, for frequencies above 1 kHz, the smallest dehiscence (0.5 mm diameter) yielded the biggest decrease in magnitude (compared to the larger dehiscences) and the phase generally remained the same. The larger dehiscences (1 and 2 mm long) affected the magnitude and phase of P_{sv} in a manner similar to the behavior in the low frequency region and to the example of 3A for all frequencies. The pressure sensor was stable to within 1 dB during the experiment and the effect of SCD was reversible. Two ears out of 6 had this complicated relationship where the smallest pinpoint dehiscence had the largest effect on P_{sv} in the mid-to-high frequencies; both ears had pressure measurements that were reversible after patching the SCD. The ears that had the complicated P_{sv} effect due to the smallest dehiscences, were also the same ears that showed the complicated relationship in the V_{step} (as in Figure 2C) mentioned earlier.

Pressure in Scala Tympani (P_{st})

As illustrated in representative examples in Figure 4, SCD had two types of effect on scala tympani pressure relative to ear-canal pressure (P_{st}/P_{ec}). In both types, increases in SCD size decreased the magnitude and changed the phase to the leading direction for low frequencies (below 400-700 Hz). The difference between the two types of effects occurred in the higher frequencies (above 400-700 Hz). In one type of SCD effect, shown in the representative example of Figure 4A, P_{st} at higher frequency did not change significantly (the pressure sensor calibration in this case remained within 1 dB). Four of the 8 P_{st} data had this simple relationship with SCD size, and the SCD effects were reversible except one ear with the SCD patched with dental cement which did not show complete reversal of the SCD. In

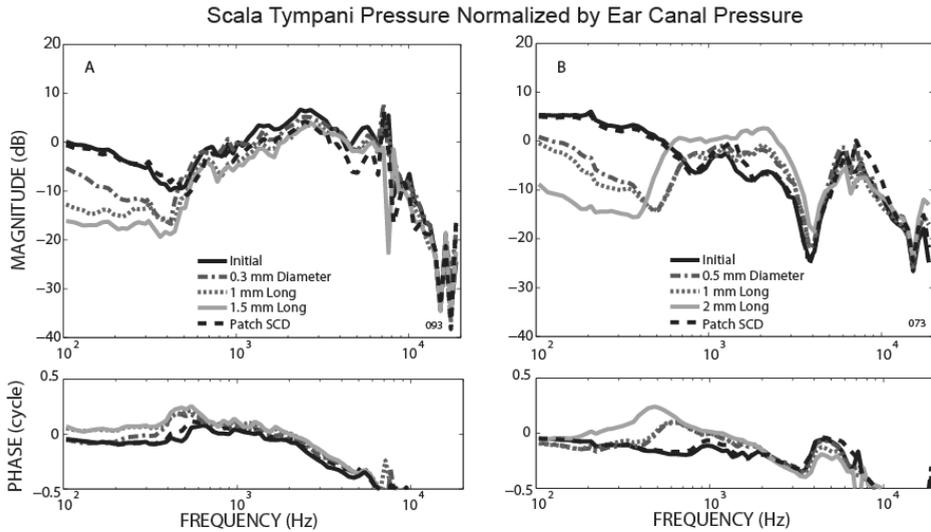


Figure 4. Representative example of scala tympani pressure relative to ear canal pressure for the initial state, after various SCD sizes, and after patching the SCD.

the other type of SCD effect, shown in Figure 4B, P_{ST} increased in magnitude with increasing size of SCD in the mid-to-high-frequency range (the pressure sensor calibration in this case remained within 1 dB). The phase was either slightly in the leading direction compared to the initial state, or changed little with the SCD. This second type of effect was seen in 4 out of 8 P_{ST} measurements, and all 4 had stable pressure sensors and 3 had reversibility of the SCD effects. Five of the 8 ears with stable P_{ST} pressure sensors also had stable P_{SV} pressure sensors. There did not appear to be a relationship between the type of SCD effect on P_{SV} (Figure 3 A or B) and the type of effect on P_{ST} (Figure 4 A or B).

Average Change in Intracochlear Pressures Due to SCD

To illustrate the general effect of SCD, the average change in intracochlear pressure was calculated for scala vestibuli and scala tympani pressures. Figure 5 plots the geometric mean and standard deviation of the magnitude (error bars) and arithmetic mean and standard deviation of the phase for changes in P_{SV} and P_{ST} due to various sizes of SCD (represented by different colors). The averages included five P_{SV} (Figure 5A) and six P_{ST} (Figure 5B) measurements, where all of the included experiments exhibited stable pressure sensor calibrations and the reversing of SCD effects by patching. Below 600 Hz, the magnitude of both P_{SV} and P_{ST} monotonically decreased and the phase shifted towards the leading direction with increases in SCD size. These general changes in intracochlear pressures below 600 Hz and their monotonic relationship with SCD size were consistent for

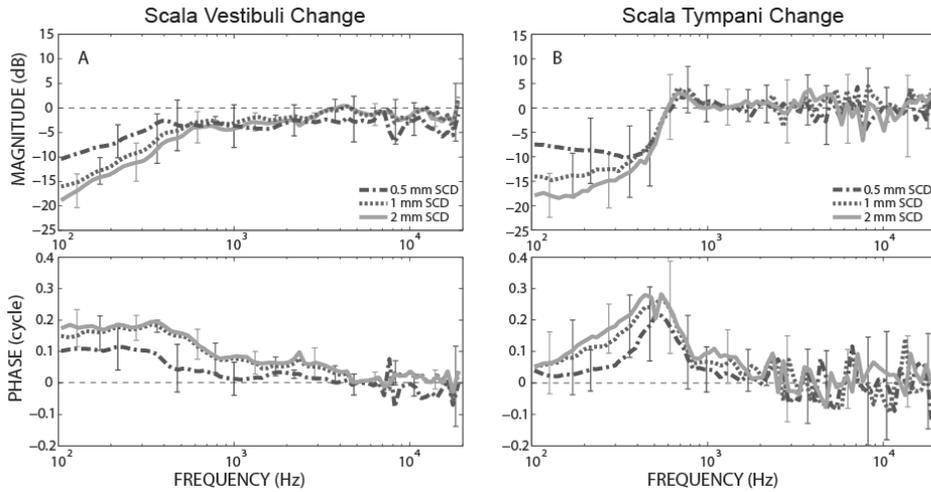


Figure 5. Changes in scala pressures due to various sizes of SCD, represented with geometric mean and standard deviation (error bars) for magnitudes and linear mean and deviations for phase. (A) Change in P_{SV} ($N=5$), (B) Change in P_{ST} ($N=6$).

all temporal bones. However, across ears, there were variations in the absolute amount of pressure change induced by a given dehiscence size as illustrated by the large error bars. Calculations of correlation coefficients for P_{SV} magnitude showed statistical significance (p -values between 0.002 to 0.01) below 200 Hz with R^2 between 0.41 and 0.52. P_{ST} magnitude also showed statistical significance (p -values between 0.01 to 0.036) below 200 Hz with R^2 between 0.246 and 0.350. The lower R^2 and poor statistical significance at higher frequencies describes a significant variation in the effects of the SCD across ears and also reflects the relatively small sample size in our study.

Differential Pressure Across the Cochlear Partition

The differential pressure ($P_{SV} - P_{ST}$) across the partition of the basal section of the cochlea (where the differences of the real and imaginary parts of the pressures are linearly subtracted) is thought to represent the final acoustic input to the cochlea. Thus, this difference can predict how various pathologies, such as SCD, affect hearing function when the sensory apparatus of the inner ear is unaltered, and we can use our measurements of this difference in our cadaveric preparations to estimate how SCD might affect hearing in live humans.

Representative examples of two types of SCD effects on the differential pressure relative to ear-canal pressure, $(P_{SV} - P_{ST})/P_{EC}$, are illustrated in Figure 6. Both examples illustrate similar low-frequency (below 600-700 Hz) changes with SCD size: differential pressure magnitude decreased and the phase increased mono-

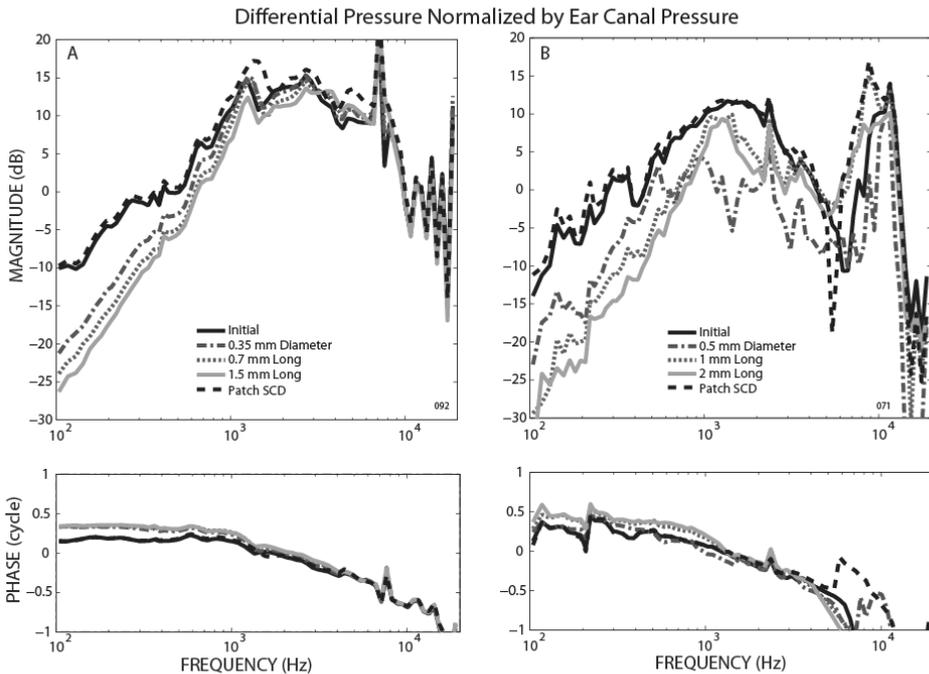


Figure 6. Representative examples of the differential pressure across the cochlear partition relative to ear canal pressure, $(P_{SV} - P_{ST})/P_{EC}$, for the initial state, after various SCD sizes, and after patching the SCD.

tonically towards the leading direction with increases in SCD size. The mid-to-high frequency changes owing to SCD varied across ears. In one type of SCD effect, shown in Figure 6A, the differential pressure changed insignificantly for frequencies above ~ 600 Hz (both P_{SV} and P_{ST} pressure sensors were stable within 1 dB). In the other type of high-frequency SCD effect, shown in Figure 6B, the smallest pinpoint SCD had the greatest effect: it decreased differential pressure magnitude more than did larger dehiscences, and it altered the phase of the pressure difference in a direction opposite to the changes produced by the larger dehiscences (both P_{SV} and P_{ST} pressure sensors were stable within 1 dB). Only three experiments succeeded in having both pressure sensors in scala vestibuli and scala tympani stable in calibration throughout the experiment, as well as exhibiting full reversal of both P_{SV} and P_{ST} pressures after patching the SCD. Two ears had the type of SCD effect shown in Figure 6A, while one ear had the effect shown in Figure 6B. The ear that had the complicated behavior of differential pressure due to a pinpoint dehiscence (Figure 6B) also had a similarly complicated behavior in P_{SV} (Figure 3B). Furthermore, this ear had V_{Stap} that showed more effect due to the pinpoint dehiscence at low frequencies (<1 kHz) (Figure 2C) than the larger dehiscences.

DISCUSSION

Measurements of intracochlear sound pressures in scala vestibuli and scala tympani in cadaveric temporal bones enabled experimental evaluation of how SCD can affect hearing. The effects of SCD on intracochlear pressures in scala vestibuli and scala tympani were reversible by patching the dehiscence. This ensured that the effects observed were solely due to the various manipulations made at the superior semicircular canal. As discussed in the Methods section, patching the SCD with dental impression material was superior to dental cement, likely due to the impression material enabling a tight fluid seal versus the cement that may have allowed a small leak.

The results showed that both low-frequency (below 400-700 Hz) P_{SV} and P_{ST} magnitudes decreased and their phases shifted to the leading direction due to SCD. For low frequencies (< 600 Hz) the effects on P_{SV} and P_{ST} were more pronounced with an increase in SCD size. This monotonic relationship of magnitudes decreasing and phases increasingly leading with increasing SCD size sometimes held true for all frequencies in P_{SV} . However, for some ears (2/6 ears) at frequencies above 1 kHz, the smaller pinpoint dehiscence (~0.5 mm diameter) produced the largest decreases in P_{SV} magnitude as compared to larger dehiscences. In these same ears, P_{ST} increased with increasing SCD size or had little change for frequencies above 400-700 Hz.

Calculations of the differential pressure across the partition showed that increase in SCD size resulted in decreased differential pressure for frequencies below 600 Hz. This would be interpreted as more conductive hearing loss with increased SCD size for frequencies below 600 Hz. These low-frequency decreases in the differential pressure for an SCD around 2 mm long were between 10-20 dB, similar to the amount of conductive hearing loss seen in patients with SCD of about 2 mm. However, an interesting finding is that above 1 kHz, the smallest pinpoint hole in the superior semicircular canal sometimes resulted in more differential pressure decrease, representing more conductive hearing loss than the larger dehiscence sizes.

When the differential pressure decreased more at frequencies above 1 kHz due to the smallest SCD dehiscence (compared to the larger dehiscences), P_{SV} also had a similar pattern. However, there did not appear to be a correlation with unusual differences in P_{ST} at the higher frequencies. Interestingly, the V_{stap} response was also unusual, but in a non-predictable manner. Although the low-frequency P_{SV}

and P_{ST} , as well as the differential pressure, decreased in a monotonic relationship with SCD size, the V_{Stap} increase was not monotonic with SCD size as might be expected, but instead, the smallest size SCD resulted in the biggest increase in V_{Stap} (Figure 2C). For the higher frequencies, the smallest dehiscence resulted in the most decrease in P_{SV} and the differential pressure, however instead of an expected V_{Stap} increase (as was seen in the larger dehiscences), V_{Stap} decreased. V_{Stap} is related to the impedance presented by the whole inner ear at the oval window. Under certain circumstances such as SCD, V_{Stap} is not related to how the ear can transduce sound across the cochlear partition because it is not directly related to the differential pressure. Thus comparisons of V_{Stap} and differential pressure emphasize that inner-ear pathologies, such as third-window effects, cannot be fully assessed by measurements such as V_{Stap} .

The observed non-monotonic effect of SCD size on hearing across frequency may explain why most of the clinical studies trying to correlate the size of SCD to various symptoms have not shown consensus. For example, no correlation between SCD size and air-bone gaps were found in multiple clinical studies [Pfammater et al., 2010; Chi et al., 2010; Martin et al., 2009; Mikulec et al., 2004]. However Yuen et al. [2009] did find correlation between the dehiscence size and low-frequency (500-2000 Hz) air-bone gap in patients with 3 mm or larger SCDs (18 ears).

The approach taken in this study has some limitations in regard to direct comparison with clinical findings. In our experiments, the dehiscence was surrounded by fluid to prevent air from entering the semicircular canal and to keep the static pressure of the fluid at the interface of the dehiscence consistent across the various sizes. In a patient, an SCD would be in contact with cerebral spinal fluid, dura and/or brain. The static pressure at the SCD interface in patients would differ from our experimental condition. Many other variables can differ across patients even if – as determined radiologically – the length and location of the bony dehiscence may be similar; for example, the adherence of the dura to the edges of the dehiscence can vary, and how much the overlying brain and/or dura pushes into the dehiscence can vary. This may explain why some patients with incidental findings of SCD on imaging have no symptoms, and why some patients experience symptoms acutely.

Although the condition surrounding the SCD in our experiment differs slightly from the clinical situation, details regarding the effect of SCD on hearing can be better understood in this present study than in clinical studies, especially because various sizes of SCD can be induced in the same ear without changing other vari-

ables, and reversal of the SCD can ensure that the pressures return to the pre-SCD baseline measurements.

The experiments in which the smallest SCD resulted in the largest conductive hearing loss might be explained by the effects of the hole size on resistance to fluid flow through the hole and resulting absorption of acoustic energy. For no hole, there is no shunt connection from the scala vestibuli compartment. For a large hole the sound flow through the dehiscence depends on the shunt impedance that is probably dominated by the inertance associated with flow through the canal remnant as well as the input impedance of the compartment to which fluid flows (Songer and Rosowski 2007). For very small holes, however, the resistance to fluid flow through the opening may become important, and the damping it provides may have a broadband effect on scala vestibuli pressure.

Furthermore, the effect of SCD on V_{stap} can be complicated and show little relationship to the differential pressure across the partition. Again, this is likely due to the impedance that is presented at the oval window, which can be influenced by various factors such as the balance between the effect of the annular ligament surrounding the stapes footplate in relationship to the impedances of the inner-ear structures. Thus, V_{stap} may have no simple relationship to the size of the dehiscence, the effect on intracochlear pressures, the differential pressure across the partition, and most importantly no unique relationship to how the ear transduces sound across the cochlear partition. This example demonstrates the importance of understanding the mechanical effect of pathologies on hearing by measuring the differential pressure across the partition, and that measurements such as V_{stap} do not necessarily determine the effect of pathology on hearing.

Future studies will focus on modeling the inner ear impedances to simulate the effect of SCD in humans to aid in the explanation of these findings. Furthermore, larger sized SCD (larger than 2 mm) occur clinically as do variation in SCD location, thus these parameters will be topics of future study. From model predictions of Songer and Rosowski (2007), it would be expected that the effect of SCD will not continue to increase with increase in SCD size after exceeding a certain SCD size. Additionally, in some patients, low-frequency hypersensitive bone conduction has been observed (Minor 2000; Minor et al. 2003; Mikulec et al. 2004). Our intracochlear pressure measurements have the potential to illuminate how bone conduction transduces sound to the cochlea. This is a topic that we certainly plan to take up. After learning some of the basics regarding bone conduction mechanism by intracochlear pressure measurements, we plan to study the effect of SCD on

bone conduction using our methodology. SCD would be expected to have different effects on the air-conduction and bone-conduction mechanisms that produce the pressure difference across the cochlear partition.

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REFERENCES

Chi FL, Ren DD, Dai CF: Variety of audiologic manifestations in patients with superior semicircular canal dehiscence. *Otol Neurotol* 2010;31:2-10.

Chien W, Ravicz ME, Rosowski JJ, Merchant SN: Measurements of human middle- and inner-ear mechanics with dehiscence of the superior semicircular canal. *Otol Neurotol* 2007;28:250-7.

Martin C, Chahine P, Veyret C, Richard C, Prades JM, Pouget JF: Prospective radiological study concerning a series of patients suffering from conductive or mixed hearing loss due to superior semicircular canal dehiscence. *Eur Arch Otorhinolaryngol* 2009;266:1175-1181.

Mikulec AA, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.

Minor LB: Superior canal dehiscence syndrome 2000;21:9-19.

Minor LB, Carey JP, Cremer PD, Lustig LR, Streubel SO, Ruckenstein MJ: Dehiscence of bone overlying the superior canal as a cause of apparent conductive hearing loss. *Otol Neurotol* 2003;24:270-8.

Nadol JB: Techniques for human temporal bone removal: Information for the scientific community. *Otolaryngol Head Neck Surg* 1996;115:298-305.

Nakajima HH, Dong W, Olson ES, Merchant SN, Ravicz ME, Rosowski JJ: Differential Intracochlear Sound Pressure Measurements in Normal Human Temporal Bones. *J Assoc Res Otolaryngol* 2009;10:23-36.

Nakajima HH, Pisano DV, Merchant SN, Rosowski JJ: The effect of superior semicircular canal dehiscence on intracochlear sound pressures; in Shera CA, Olson ES (eds); *What Fire is in Mine Ears: Progress in Auditory Biomechanics*, Proceedings of the 11th International Mechanics of Hearing Workshop. American Institute of Physics, 2011;pp110-115.

Olson ES: Observing middle and inner ear mechanics with novel intracochlear pressure sensors. *J Acoust Soc Am* 1998;103:3445-3463.

Pfammatter A, Darrouzet V, Gärtner M, Somers T, Van Dinther J, Trabalzini F, Ayache D, Linder T: A superior semicircular canal dehiscence syndrome multicenter study: is there an association between size and symptoms? *Otol Neurotol* 2010;31:447-454.

Rosowski JJ, Songer JE, Nakajima HH, Brinsko KM, Merchant SN: Clinical, experimental, and theoretical investigations of the effect of superior semicircular canal dehiscence on hearing mechanisms. *Otol Neurotol* 2004;May;25:323-332.

Songer JE, Rosowski JJ: The effect of superior canal dehiscence on cochlear potential in response to air-conducted stimuli in chinchilla. *Hear Res* 2005;210:53-62.

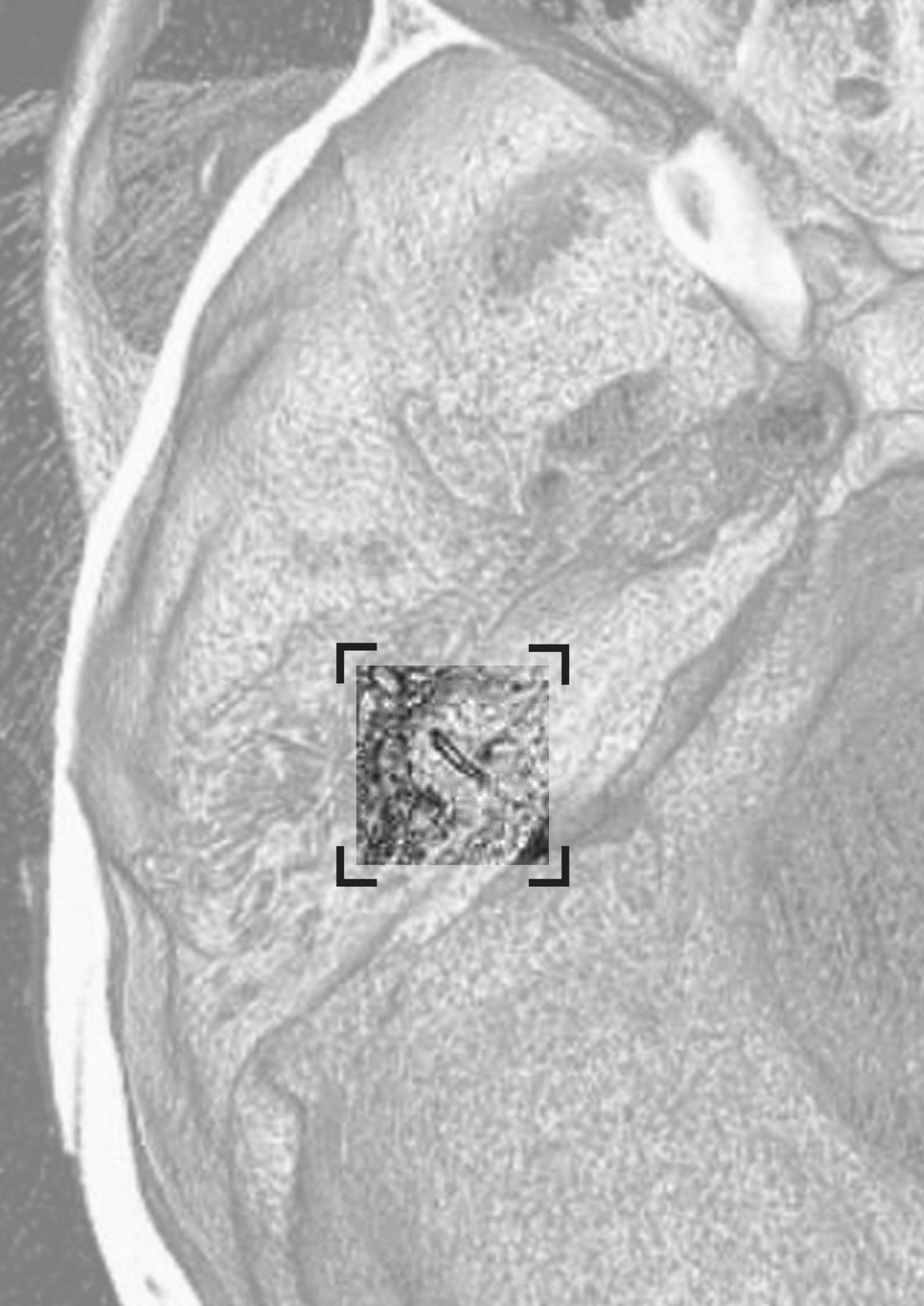
Songer JE, Rosowski JJ: The effect of superior-canal opening on middle-ear input admittance and air-conducted stapes velocity in chinchilla. *J Acoust Soc Am* 2006;120: 258-269.

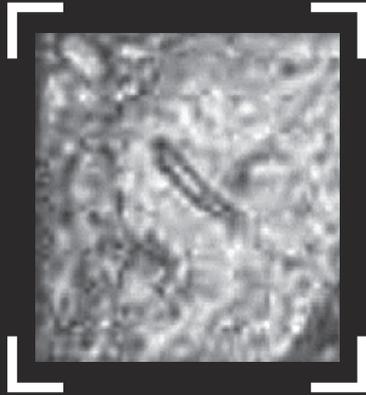
Songer JE, Rosowski JJ: A mechano-acoustic model of the effect of superior canal dehiscence on hearing in chinchilla. *J Acoust Soc Am* 2007;122:943-51.

Voss SE, Rosowski JJ, Peake WT: Is the pressure difference between the oval and round windows the effective acoustic stimulus for the cochlea? *J Acoust Soc Am* 1996;100:1602-1616.

Wever EG, Lawrence M: The acoustic pathways to the cochlea. *J Acoust Soc Am* 1950;22:460-467.

Yuen HW, Boeddinghaus R, Eikelboom RH, Atlas MD: The relationship between the air-bone gap and the size of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2009;141:689-694.





Chapter 3.3

Assessment of the effects of superior canal dehiscence location and size on intracochlear sound pressures

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ABSTRACT

Superior canal dehiscence (SCD) is a defect in the bony covering of the superior semicircular canal. Patients with SCD present with a wide range of symptoms, including hearing loss, yet it is unknown whether hearing is affected by parameters such as the *location* of the SCD. Our previous human cadaveric temporal bone study, utilizing intracochlear pressure measurements, generally showed that an increase in dehiscence size caused a low-frequency monotonic decrease in the cochlear drive across the partition, consistent with increased hearing loss. This previous study was limited to SCD sizes including and smaller than 2 mm long and 0.7 mm wide. However, the effects of larger SCDs (>2 mm long) were not studied, although larger SCDs are seen in many patients.

Therefore, to answer the effect of parameters that have not been studied, this present study assessed the effect of *SCD location* and the effect of *large-sized SCD* (>2 mm long) on intracochlear pressures. We used simultaneous measurements of sound pressures in scala vestibuli and scala tympani at the base of the cochlea to determine the sound-pressure difference across the cochlear partition – a measure of the cochlear drive in a temporal bone preparation – allowing for assessment of hearing loss. We measured the cochlear drive before and after SCDs were made at different locations (e.g., closer to the ampulla of the superior semicircular canal or closer to the common crus), and for different dehiscence sizes (including larger than 2 mm long and 0.7 mm wide). Our measurements suggest that: 1) Different SCD locations result in similar cochlear drive; 2) Larger SCDs produce larger decreases in cochlear drive at low frequencies. However, the effect of SCD size seems to saturate as the size increases above 2-3 mm long and 0.7 mm wide. Although the monotonic effect was generally consistent across ears, the quantitative amount of change in cochlear drive due to dehiscence size varied across ears. Additionally, the size of the dehiscence above which the effect on hearing saturated, varied across ears. These findings show that the location of the SCD does not generally influence the amount of hearing loss and that SCD size can help explain some of the variability of hearing loss in patients.

INTRODUCTION

Abnormal absence of bone between the superior semicircular canal and the intracranial space, called superior canal dehiscence (SCD), can cause a range of symptoms – SCD syndrome – including hearing loss [Minor et al., 1998]. Normally, sound produces motion of the oval and round windows, allowing for the development of a pressure difference between scala vestibuli (SV) and scala tympani (ST). This input differential pressure across the partition at the base of the cochlea – the cochlear drive – is an estimate of hearing in a human temporal bone preparation [Nakajima et al., 2009]. Previously, we described a method to simultaneously measure the intracochlear sound pressures in SV and ST (P_{SV} and P_{ST}) in order to determine the cochlear drive [Nakajima et al., 2009]. We then studied the effect of SCD on intracochlear pressures [Pisano et al., 2012], finding that SCD resulted in decreased P_{SV} and P_{ST} due to fluid motion shunting through an alternative low-impedance SCD pathway. Across the cochlear partition, the cochlear drive was also found to be lower with SCD, consistent with the hearing loss observed in patients with SCD [Pisano et al., 2012].

Patients with SCD syndrome present symptoms ranging from no hearing loss to a large low-frequency conductive loss. It is yet unknown whether differences in the location of the SCD affect differences in hearing. Clinically, dehiscences vary in location along the arc of the semicircular canal. Williamson et al. [2003] described that 36% of their patients had an SCD located at the arcuate eminence; the remainder had an SCD located at the posterior (36%) or anterior (28%) aspect of the superior semicircular canal. In addition, McCall et al. [2011] described a series of 12 patients (from a database of 131 patients) who had a more posterior-located SCD due to contact of the superior semicircular canal with the superior petrosal sinus. Furthermore, some clinical studies have found that an increase in SCD size is associated with increased hearing loss [Chien et al., 2012; Niesten et al., 2013], while others have observed no association [Chi et al., 2010; Mikulec et al., 2004]. Our previous human cadaveric temporal bone study showed results consistent with size-related hearing loss: an increase in dehiscence size (from 0.3 mm diameter pin-point to 2 mm long and 0.7 mm wide) caused a low-frequency monotonic decrease in the cochlear drive. Effects of larger SCDs (>2 mm long) were not assessed in our previous temporal bone studies, although many SCD patients have a dehiscence larger than 2 mm. The computational model predictions of Songer and Rosowski [2007] indicated that the low-frequency effect of the SCD size might reach a plateau after a certain size. Furthermore, another complicating matter is that above 1 kHz, it has been observed in cadaveric preparations that a

small dehiscence (0.3-0.5 mm diameter) can sometimes produce a larger decrease in cochlear drive than larger dehiscences [Pisano et al., 2012]. In this present study, we study yet unanswered questions: assess the effect of SCD location and the effect of large-sized SCD on intracochlear sound pressures.

METHODS

Summary of specimens

We used 12 temporal bones from donors ranging in age from 22 to 81 years old, including 6 females and 6 males. In one experiment, we only studied the effect of SCD size, and in all other experiments we studied the effect of the SCD location as well. From the 12 temporal bones, 6 were excluded due to complications such as low stapes velocity (due most likely to ossicular stiffness or partial disarticulation), presence of air in the cochlea, trauma that occurred during the experiment, or sensor calibrations that differed by more than 3 dB in both SV and ST. Table 1 shows an overview of the 6 remaining preparations. Five bones resulted in experiments with stable sensors in which the effects of SCD on PSV could be reversed by patching, and 3 of these 5 experiments also included reversal of the SCD effects in PST by patching. The stapes velocity obtained in 6 temporal bones was initially normal, changed when the SCD was created, and reversed on patching.

Table 1. Summary of Specimens

Number	Comment	P_{SV} reversed	P_{ST} reversed	V_{Stap} reversed
(108)	SCD size only	X		X
(112)		X	X	X
(115)		X		X
(118)				X
(124)		X	X	X
(125)		X	X	X

V_{Stap} is stapes velocity. P_{SV} and P_{ST} are pressures in scala vestibuli and scala tympani. Xs indicate whether the changes in the various measurements due to SCD were successfully reversed by patching the dehiscence.

Temporal bone preparation

We prepared the temporal bones as described in Nakajima et al. [2009] and Pisano et al. [2012]; therefore, only a brief description of the preparation will be given. We used fresh human cadaveric temporal bones and previously frozen temporal bones that were removed within 24 hours of death by the method described in

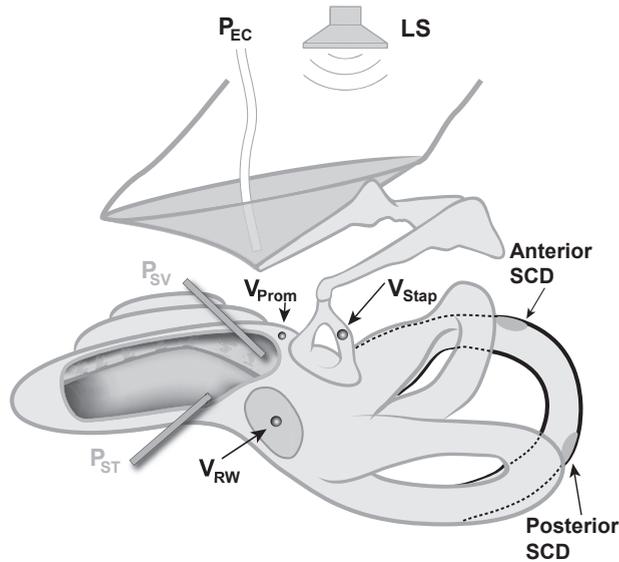


Figure 1. Illustration of the temporal bone preparation showing the anterior and posterior dehiscence locations along the superior semicircular canals. P_{SV} = scala vestibuli pressure, P_{ST} = scala tympani pressure, P_{EC} = ear canal pressure, V_{Prom} = promontory velocity, V_{Stap} = stapes velocity, V_{RW} = round window velocity, SCD = superior canal dehiscence, LS = loudspeaker. Note: the opening shown in the cochlea is for illustration purposes only.

Nadol et al. [1996]. During temporal bone preparation, we opened the facial recess, thinned the area of the cochlear promontory where SV and ST sound pressure sensors would later be inserted, and removed the stapes tendon. In addition, we thinned (blue-lined) the bone overlying the superior semicircular canal along a length of 10 mm through the lateral transmastoid approach.

After placing a speaker at the ear-canal opening and probe-tube microphone 1-3 mm from the umbo, the ear canal was sealed. Under fluid, we drilled 200 μ m diameter cochleostomies in SV and ST, near the oval and round windows, into which we inserted two micro-optical sound pressure sensors of the type developed by Olson et al. [1998]. The sensors were sealed with a dental impression material, Jeltrate (L.D. Caulk Co.), so as to prevent air from entering the inner ear and fluid from leaking out. With laser Doppler vibrometry (Polytec CLV) and reflectors on the stapes posterior crus and round-window membrane, we confirmed stability of stapes and round-window velocities before and after making cochleostomies and pressure-sensor insertions. We also evaluated if a half-cycle phase difference was present between the oval and round window motion in order to confirm that no air was introduced in the cochlea. Before and after insertion, the sensors were calibrated to ensure their stability within 3 dB. See Figure 1 for a schematic of our temporal bone preparation.

Experimental approach

Before and after the creation of an SCD under fluid (to prevent entrance of air into the inner ear), we measured the pressures in SV, ST and the ear canal, as well as the stapes velocity for frequencies between 100 Hz and 10 kHz. In each temporal bone, we created dehiscences slowly with a diamond burr in two different locations: a more anterior SCD between the ampullated end and the arcuate eminence, and a more posterior SCD between the arcuate eminence and the common crus (Figures 1 and 2). After each measurement with an SCD, we patched the SCD with dental impression material to ensure a reversal of the SCD effects and to confirm that the values were similar to the baseline. Then an SCD was created in the other location, measurements made, then the SCD was patched and measurements were again made to ensure reversal to the initial state after patching the second SCD. In half of the experiments, we created the anterior SCD first, and in the other half, we created the posterior SCD first. By keeping the SCD size similar for both locations (~1.3 mm long and 0.7 mm wide) and ensuring reversal of the SCD effects, the SCD location was therefore the only variable that changed during measurements. From our previous experiments [Pisano et al. 2012], we know that an SCD length between 1 and 1.5 mm shows a considerable change in pressure and that the effect is reversible with patching.

Patching in this study was modified with respect to our earlier study of Pisano et al. [2012]. Unlike previously, where only Jeltrate was applied [Pisano et al. 2012], we initially layered a piece of writing paper approximately the size of the dehiscence, then applied the Jeltrate over the paper; this was done to prevent Jeltrate from entering the semicircular canal. Throughout this procedure, we were careful not to introduce air into the semicircular canal.

After completing intracochlear sound pressure measurements for both SCD locations separately, we removed the Jeltrate and paper from the SCDs and measured the intracochlear pressures with both SCDs open. It was noted that upon removal of the paper and Jeltrate, the Jeltrate likely did not obstruct the lumen, and the contents of the lumen did not appear traumatized. In addition, we drilled away the bone between the anterior and posterior SCDs to create one large dehiscence of around 4 mm long and 0.7 mm wide, which is approximately the median SCD size found in a study assessing SCD size and location in 104 patients clinically [Niesten et al., 2012]. We patched the different SCDs after each measurement to ensure reversal of the effects. Figure 2 shows photographs of the preparation, with sensors inserted in the cochlea and an anterior and a posterior dehiscence in the superior semicircular canal.

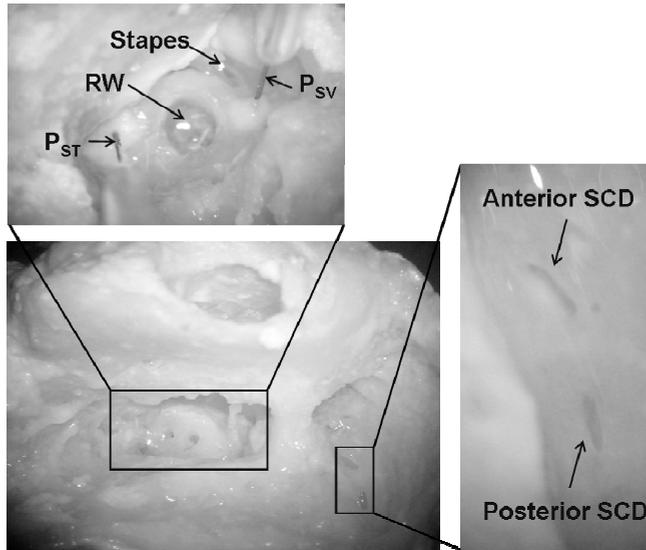


Figure 2. Images of a temporal bone during and after an experiment. The large picture in the center shows an open facial recess and epitympanic space. Cochleostomies were made for the pressure sensors, and two dehiscences were created in the semicircular canal. In the top image, pressure sensors are shown inserted in scala vestibuli and scala tympani. The image on the right shows a magnified version of the dehiscences. P_{SV} = scala vestibuli pressure, P_{ST} = scala tympani pressure, RW = round window, SCD = superior canal dehiscence.

Sound Pressure measurements

Measurements of P_{SV} , P_{ST} , and the ear canal sound pressure (P_{EC}) are represented as complex numbers (indicating both magnitude and phase) and can be used to calculate the differential pressure (ΔP), the cochlear drive, where $\Delta P = (P_{SV} - P_{ST}) / P_{EC}$ as described in Nakajima et al. [2009] and Stieger et al. [2013]. This measurement of the cochlear drive is used in our estimate of hearing loss in the human cadaveric temporal bone model. We determined the effect of the varying SCD locations and the effect of varying SCD size (including larger than 2 mm-long SCDs) on measurements of stapes velocity, P_{SV} , P_{ST} and ΔP .

RESULTS

Stapes Velocity

In all six temporal bones, the velocity of the stapes changed when an SCD was made, and reversed back to the initial value after the dehiscence was patched (similar to Pisano et al., 2012). In all but one experiment, the stapes velocity increased at varying frequencies after creating a dehiscence. This has been explained by the idea of the fluid motion shunting through the SCD, allowing for

larger movement of the stapes [Chien et al., 2007; Pisano et al., 2012].) However, in one experiment, the stapes velocity did the opposite: it decreased following SCD and reversed back to its initial velocity following patching. These results were similar to that found in Pisano et al. [2012], where it was found and described that the changes in stapes velocity due to SCD varied across ears and was unrelated to the cochlear input drive. The impedance at the oval window (influencing stapes velocity) is likely influenced by relative impedances of various structures in the inner ear to the impedance of the annular ligament between the footplate and cochlea. Therefore, stapes velocity serves as a poor indicator of the effects of SCD on hearing.

Effects of SCD Location – Scala vestibuli pressure (P_{sv})

Four experiments had stable sensors in scala vestibuli and reversal of the SCD effects after patching. In 2 experiments we created the anterior SCD first, and in the 2 others we created the posterior SCD first. The first SCD was patched before the second SCD was created, with confirmation of reversals in pressures to the initial

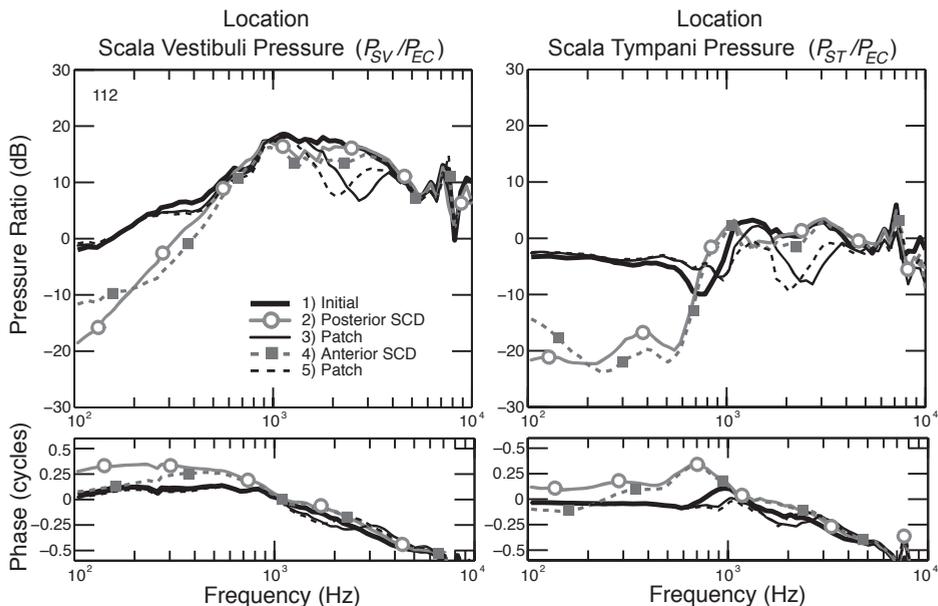


Figure 3. Data of a representative experiment demonstrating the effect of dehiscence location on intracochlear pressures. Figure on the left shows the scala vestibuli pressure normalized to ear-canal pressure (P_{sv}/P_{EC}) and figure on the right shows the scala tympani pressure normalized to ear-canal pressure (P_{sv}/P_{EC}). Upper panels represent magnitudes and lower panels phases. Five sequential measurements in the same temporal bone were performed: 1) initial (thick solid black line), 2) posterior SCD (thin solid line with circle), 3) patched (thin solid black line), 4) anterior SCD (thin dashed line with square), 5) patched (thin dashed black line).

values; therefore, results were not influenced by which SCD location was created first (anterior or posterior). In each ear, the anterior and posterior SCDs were about the same size (0.7 mm wide) and approximately the same length (within 0.2 mm). Across ears, the length varied between 1.2 and 1.5 mm long.

Figure 3 illustrates a representative example showing a similar drop in P_{SV} for the anterior and posterior SCD. For each specimen, similar decreases in P_{SV} resulted with anterior and posterior SCD, (within 0 to 4 dB, except for experiment 112 shown in Figure 3 were the lowest frequency of 100 Hz had a difference of 6.8 dB). However, as shown in Figure 4, the magnitude of change in pressure due to SCD varied among the four temporal bones, ranging from 8 to 18 dB, similar to variations seen across bones in Pisano et al. [2012]. The effects of SCD were mainly present in the low frequencies, up to 1 kHz. In the mid to high frequencies (1-2 kHz) we either found a slight increase or decrease in P_{SV} , or we did not see an effect. In one temporal bone, we found a slight increase in P_{SV} between 1 and 2 kHz.

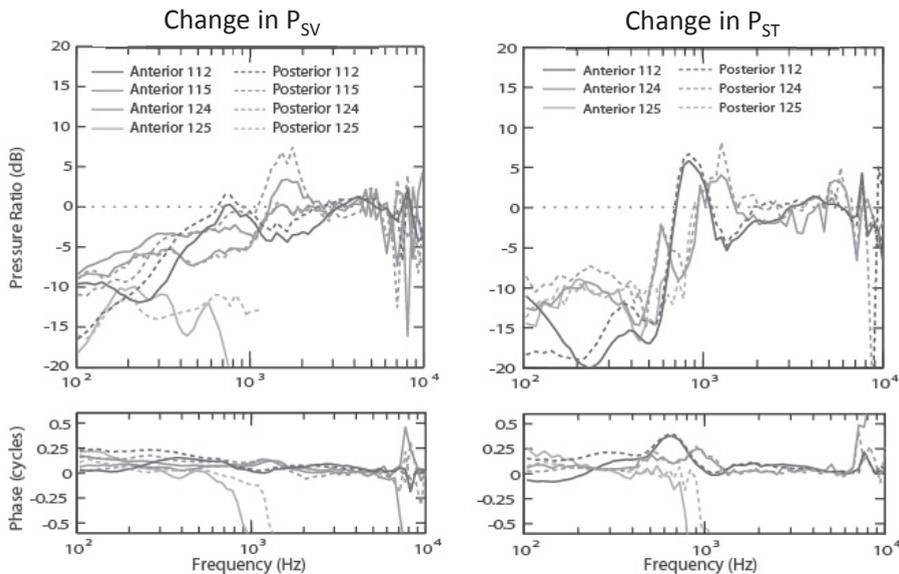


Figure 4. Overview effect of SCD location: change in pressure in scala vestibuli P_{SV} for four temporal bones (left plot) and scala tympani P_{ST} for three temporal bones (right). The sizes for both locations were similar: 112 – anterior 1.3 mm and posterior 1.4 mm, 115 – anterior 1.35 mm and posterior 1.5 mm, 124 – anterior and posterior 1.2 mm, 125 – anterior and posterior 1.4 mm. Pressure measurements for experiment 125 are only plotted below 1 kHz because the magnitudes dropped to the noise level at frequencies above 1 kHz after dehisces were made. Generally, anterior and posterior dehisces resulted in similar changes in scalae pressures across specimens.

Effects of SCD Location – Scala tympani pressure (P_{ST})

Three temporal bones had stable sensors in scala tympani and reversal of the SCD effects after patching. Figure 3 shows an example of P_{ST} before and after anterior and posterior SCDs were made for a representative experiment. The drop in P_{ST} was similar for both SCD locations, ranging from 0 to 4 dB within each temporal bone (except for experiment 112: at 100 Hz there was a difference of 6.9 dB between the anterior and posterior SCD). Similar to Pisano et al. [2012], the change in P_{ST} across temporal bones varied and ranged from 8 to 17 dB, as shown in Figure 4. The effects were mainly present up to 600-800 Hz. In the high frequencies, P_{ST} remained similar or changed slightly, similar to Pisano et al. [2012]. For one experiment (#125), the measurements were close to the noise level at high frequencies.

Effects of SCD Location – Cochlear drive (ΔP)

Three experiments had stable sensors and reversal of the SCD effects on both SV and ST pressures, for which we were able to calculate ΔP . Figure 5 shows two examples of ΔP . In addition to the low-frequency decrease in P_{SV} and P_{ST} , we found a decrease in ΔP after creation of an SCD. We found a similar low-frequency decrease in differential pressure for the anterior and posterior SCD, indicating that

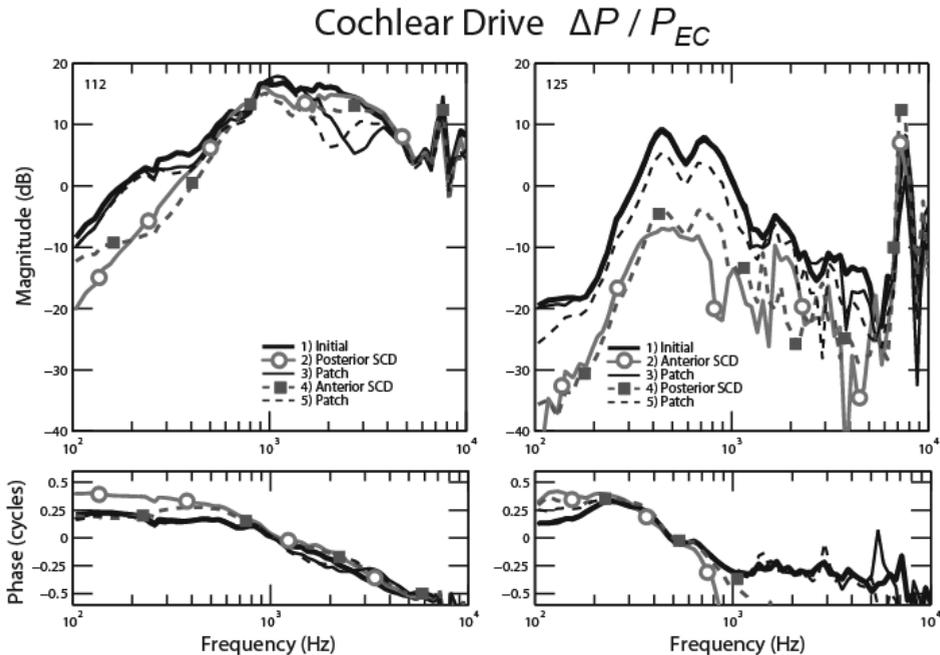


Figure 5. Differential pressure before and after creation of an anterior and posterior SCD for two representative experiments. The sequential measurements are described in Figure 4.

the location of the SCD does not influence the differential pressure. This would correspond clinically with similar hearing loss for patients with an SCD located either more anteriorly or more posteriorly. The decrease in ΔP ranged from 10 to 20 dB up to 600 and 800 Hz. Since the magnitude of P_{SV} was generally larger than P_{ST} , the cochlear drive is mostly influenced by P_{SV} changes (as discussed in Stieger et al. [2012]), and can be appreciated by comparing experiment #112 in Figure 5 and Figure 3.

Effects of large SCD size – Scala vestibuli pressure (P_{SV})

In 4 temporal bones we had stable sensors and a reversal of SCD effects on P_{SV} for various SCD sizes. Figure 6 shows a representative example of the different SCD sizes, starting with an SCD length of 0.6 mm, a larger SCD of 1.2 mm, then a 2.4 mm, and finally an SCD length of 3.0 mm. The width was around 0.5 mm for the small SCDs and around 0.7 mm for the larger SCDs. In the low frequencies, and primarily at 100 Hz, we found a larger decrease in P_{SV} when the dehiscence size increased. As illustrated in Figure 6, the smaller SCD of 0.6 mm seemed to cause less decrease in pressure up to 1000 Hz, which is consistent with data from Pisano et al. [2012]. Above 200-300 Hz, not much variation exists in the amount

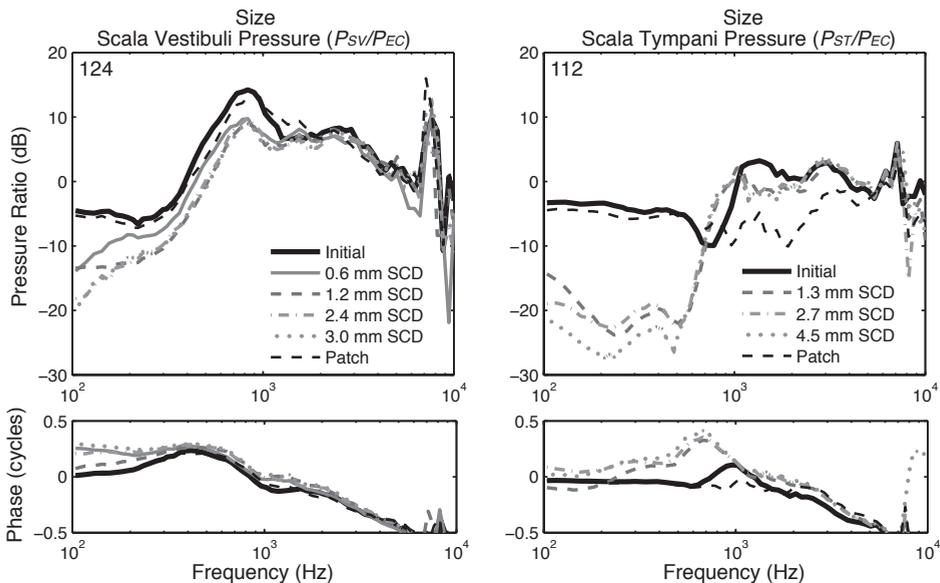


Figure 6. Effect of dehiscence size: The left figure shows the change in scala vestibuli pressure magnitude and phase and the right figure shows the change in scala tympani pressure magnitude and phase, after the creation of different sizes of SCD in two different experiments. The black solid line shows the initial intracochlear sound pressure; the other lines show the decrease in pressure as different SCD sizes are created. At the end of the experiment, the SCD was patched, as indicated by the thin dashed black line.

of pressure drop for the larger (1.2-3.0 mm) SCDs. Generally, P_{SV} decreased monotonically when the SCD size increased, ranging from 2-8 dB within each temporal bone. The effect of SCD size was more prominent for smaller SCDs (<1.5 mm) and seemed to saturate as the size increased above approximately 2-4 mm long and 0.7 mm wide (with the size for which saturation of SCD effects occurred varying across ears). Because large dehiscence sizes (>2 mm length) were studied in this study, as compared to Pisano et al. (2012, where <2 mm lengths were studied), we were able to determine that the size effect saturated. In the high frequencies, the intracochlear sound pressures were similar or slightly decreased due to the dehiscence. This amount of decrease in pressure was variable across different temporal bones.

Effects of large SCD size – Scala tympani pressure (P_{ST})

We had 2 bones with successful reversal of SCD effects in P_{ST} due to different SCD sizes. Figure 6 shows a representative example of P_{ST} , where we made intracochlear sound pressure measurements for SCD lengths of 1.3, 2.7, and 4.5 mm. The figure illustrates that pressure decreased with an increase in SCD size, up to 500-600 Hz. Generally, the P_{ST} decreased further as SCD size increased, ranging from 2-7 dB drop within each temporal bone. The effects of SCD size on P_{ST} were generally similar as in SV in that after an increase in dehiscence length of over 1.5-3 mm, the incremental decrease in ST pressure were less pronounced, though saturation was not always reached (as shown in Figure 6). Magnitude variation of the pressure drop across ears existed for P_{ST} as well.

Effects of large SCD size – Cochlear drive (ΔP)

Pisano et al. [2012] showed that ΔP decreases as the SCD size increases up to approximately 2 mm. The magnitude of ΔP is similar to the magnitude of P_{SV} as shown above, because P_{SV} is generally much larger in magnitude than P_{ST} , that is, $\Delta P = (P_{SV} - P_{ST}) \approx P_{SV}$ (Stieger et al. [Stieger et al., 2012]). Reversal of the effects in both scalae became more challenging as the SCD size increased, especially for SCDs around 3-4 mm. While we did not have an experiment with perfect reversal of both P_{SV} and P_{ST} after large SCDs of 4 mm, the saturation seen in P_{SV} with increase in dehiscence size would predict a similar sized saturation in ΔP .

DISCUSSION

Our measurements suggest that: 1) differences in SCD location do not affect changes seen in intracochlear pressures, and 2) larger SCDs produce larger de-

creases in cochlear drive at low frequencies, but this effect seems to saturate as size increases (though varying across ears) above 2-4 mm long and 0.7 mm wide. The results of this present study for small dehiscences are consistent with those of Pisano et al. (2012). However, in Pisano et al. (2012) the location of the dehiscence was held constant and the sizes were less than 2mm long. In this study, we were able to show the saturation of the effect of SCD for dehiscences greater than approximately 2 mm. The magnitude of pressure change for similarly-sized SCD varied across ears as well as the size of dehiscence to result in the saturation of the SCD effects.

Effect of SCD Location

To study the effect of SCD location, all variables (such as the length, shape, and width of the SCD) were kept constant and only variations in SCD location were made. Different SCD locations resulted in similar decreases in low-frequency pressures, as shown in Figure 4. In two experiments (#124 and #125), each ear had anterior and posterior SCDs of the same length resulting in the same decrease (within 2 dB) in cochlear drive. In two other experiments, there was a slight difference in SCD length (within 0.2 mm) between the two locations, resulting in a slight difference in the decreases of pressures (within 5 dB).

When we compare our outcomes with our clinical study that assessed the effect of SCD size and location on hearing, we find similar results. The clinical study also showed that the location of the SCD did not correlate with the amount of hearing loss [Nielsen et al., 2013]. Predictions in an animal model hypothesized that an SCD closer to the ampulla would show slightly more effect on hearing than an SCD further away from the ampulla, but that the SCD location could not account for large differences in hearing [Rosowski et al., 2004]. It could be theorized that the fluid flow may divide preferentially towards the amputated end of the semicircular canal or to the common crus, depending on where the dehiscence is located, and therefore diversion of fluids through a dehiscence located more medially/posteriorly may be just as easy as through a dehiscence located more anteriorly/laterally. To clarify this mechanism, and to investigate the direction of fluid flow when an SCD is created, sound pressure measurements in the semicircular canal itself might help to address this question in the future.

Effect of SCD Size

In this study we found that when all factors were kept similar and only variations in the SCD size were made, a larger SCD caused a larger drop in pressure, but that this effect seemed to saturate as the SCD size increased beyond a critical point

(approximately 2 mm in length). A theory that might explain this phenomenon is that increasing SCD size results in lowered impedance through the SCD, but at some point, other limits dominate and further increase in size does not appreciably continue to lower the inner-ear impedance. Our results correspond with an animal computational modeling study predicting that the effect of SCD size will not continue to influence hearing outcomes after a certain size is reached [Songer and Rosowski, 2007]. They proposed that the magnitude of hearing loss is affected by the increase in dehiscence size, but that this loss is maximal once the SCD size exceeds the diameter of the canal in the chinchilla. However, our human temporal bone experiments showed that the length of SCD to result in saturation was approximately twice the diameter of the semicircular canal.

Some clinical studies report that a larger SCD tends to correlate with larger ABG [Chien et al., 2012; Niesten et al., 2012; Yuen et al., 2009] or that no correlation between SCD size and hearing loss exists [Chi et al., 2010; Martin et al., 2009; Mikulec et al., 2004]. The large variation in cochlear pressure drop across the different ears for similar sized SCDs in temporal bone preparations might help explain the results from these clinical studies, and the number of patients in some of these clinical studies might also have been too small to study the effect of SCD size on hearing, due to this large variability among ears. Furthermore, in some ears, cochlear pressures in temporal bones were affected even more by very small SCD than large SCDs at frequencies above 1 kHz, also complicating the effects that SCD size has on inner ear pressures, hearing, balance and other symptoms (Pisano et al., 2012).

Limitations of the study

It has been shown that differential pressure ΔP can be used to make an estimate of hearing in a human cadaveric temporal bone preparation (assuming the neurosensory system is intact) because it estimates the input drive across the partition despite changes in cochlear impedances. It is a good method to assess the effect of one variable in a controlled setting by keeping the other variables constant within the same ear by ensuring that effects are reversible. However, although this method provides insight into hearing in live humans, it is still difficult to determine the influences of factors that are different in the clinical situation.

Isolated temporal bone preparations do not include soft tissues such as the dura and brain above the superior semicircular canal. In some cases, the dura and brain could seal or plug the SCD. It is possible that natural plugging by the dura and brain can prevent symptoms despite having anatomical SCD diagnosed by CT

(Brandolini and Modugno 2012). Natural plugging or patching by soft tissue could also explain why many patients report a “second event”, a trauma, “unmasking” SCD symptoms, and why patients present with a myriad of signs and symptoms. Adding pressure at the dehiscence with a column of fluid, as well as patching the dehiscence with dura has been shown to result in decreased mechanical effect of SCD (Luers et al., 2014). In our experiments we find that resurfacing the SCD with dental cement (which dries to a hard substance, but requires a dry surface to set well) often does not reverse the effects of SCD, likely due to a persistent small leak. However, resurfacing with dental impression material (Jeltrate, which dries to a soft material, but can set in a wet environment) usually reverses the effect of SCD, thus producing a tight water-seal for the dehiscence. In the future, studies with whole head specimens could investigate the effect of dura and brain on SCD (Stieger et al., 2012).

In some experiments with stable sensors, we could not achieve full reversal of the effects of a large SCD after patching the dehiscence. Patching a larger dehiscence was more challenging than patching a smaller dehiscence (up to 2 mm). We also found that with our method of “resurfacing” the dehiscence with paper and dental impression material, slight leakage of the dental impression material into the superior canal sometimes occurred. Still, in most cases, the resurfacing material was easily removed in one piece without notable trauma to the lumen of the canal.

Clinical implication and future directions

We found an effect of SCD on cochlear pressure predominantly in the low frequencies, but the magnitude of the effect varied among different ears. At low frequencies near 100 Hz, some specimens showed a large effect, while others showed only a small decrease in pressure at this frequency. The frequency range in which the effect of an SCD is visible seems to vary among ears. This could help explain the variation among patients in conductive hearing loss across the different frequencies. We also suspect the effect of SCD to be larger in frequencies below 100 Hz, and we plan to assess this in our future studies. In addition, in patients with SCD syndrome, bone conduction thresholds are increased [Mikulec et al., 2004; Minor et al., 2003], and similar results have been found in an animal model studying SCD [Rosowski et al., 2004; Songer and Rosowski, 2007]. We plan to study the effect of SCD on bone conduction in our temporal bone model in the future.

CONCLUSION

The location of the dehiscence in the superior canal does not seem to affect the severity of hearing loss. However, the large clinical variation in hearing loss can be partly explained by a difference in SCD size: a larger SCD seems to correspond with a larger drop in pressure within each ear below 1 kHz, but this effect seems to saturate as the SCD size increases. Nevertheless, across ears, the magnitude of the SCD effect appears to vary.

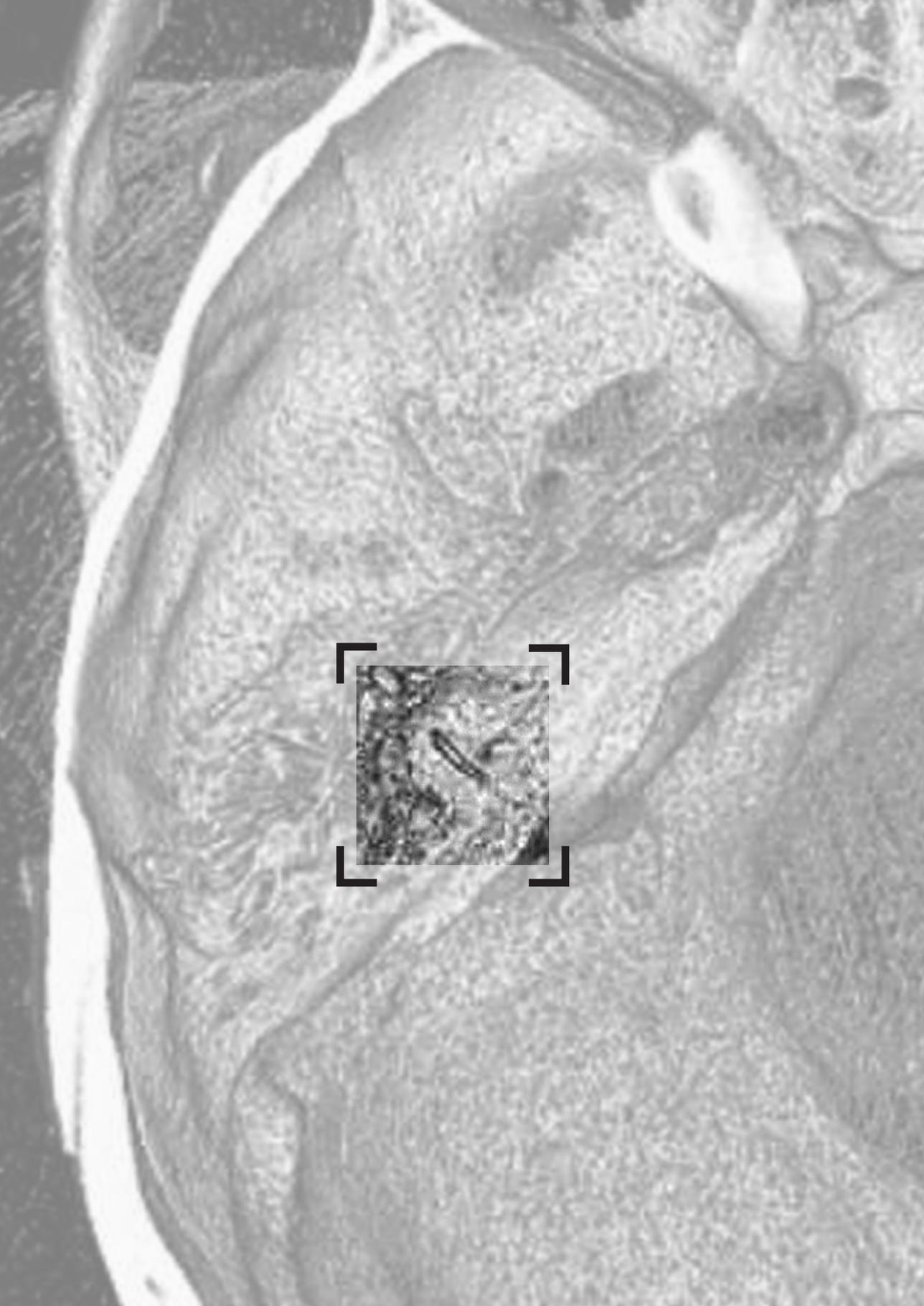
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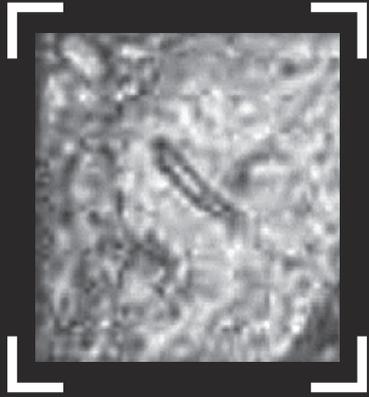
We thank Mike Ravicz, Melissa McKinnon, Diane Jones, and Sarah Lookabaugh for their contributions. Research reported in this publication was supported by the National Institute on Deafness and Other Communication Disorders of the National Institutes of Health under award number R03DC011158 and R01DC013303.

REFERENCES

- Chi FL**, Ren DD, Dai CF: Variety of audiologic manifestations in patients with superior semicircular canal dehiscence. *Otol Neurotol* 2010;31:2-10.
- Chien W**, Janky KL, Minor LB, Carey J: Superior canal dehiscence size: Multivariate assessment of clinical impact. *Otology & Neurotology* 2012;33:810Y815.
- Martin C**, Chahine P, Veyret C, Richard C, Prades JM, Pouget JF: Prospective radiological study concerning a series of patients suffering from conductive or mixed hearing loss due to superior semicircular canal dehiscence. *Eur Arch Otorhinolaryngol* 2009;266:1175-1181.
- Mikulec AA**, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.
- Minor LB**, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998;124:249-258.
- Nadol JB, Jr.**: Techniques for human temporal bone removal: Information for the scientific community. *Otolaryngol Head Neck Surg* 1996;115:298-305.
- Nakajima HH**, Dong W, Olson ES, Merchant SN, Ravicz ME, Rosowski JJ: Differential intracochlear sound pressure measurements in normal human temporal bones. *J Assoc Res Otolaryngol* 2009;10:23-36.
- Nielsen MEF**, Hamberg L, Silverman J, Lou K, McCall AA, Windsor A, Curtin HD, Herrmann BS, Grolman W, Nakajima HH, Lee DJ: Association of size and location of superior canal dehiscence with clinical presentation, audiometric and vestibular testing. *Abstr Assoc Res Otolaryngol* 2012;35.
- Olson ES**: Observing middle and inner ear mechanics with novel intracochlear pressure sensors. *J Acoust Soc Am* 1998;103:3445-3463.
- Pisano DV**, Nielsen ME, Merchant SN, Nakajima HH: The effect of superior semicircular canal dehiscence on intracochlear sound pressures. *Audiol Neurootol* 2012;17:338-348.
- Rosowski JJ**, Songer JE, Nakajima HH, Brinsko KM, Merchant SN: Clinical, experimental, and theoretical investigations of the effect of superior semicircular canal dehiscence on hearing mechanisms. *Otol Neurotol* 2004;25:323-332.
- Songer JE**, Rosowski JJ: A mechano-acoustic model of the effect of superior canal dehiscence on hearing in chinchilla. *J Acoust Soc Am* 2007;122:943-951.
- Stieger C**, Rosowski JJ, Nakajima HH: Comparison of forward (ear-canal) and reverse (round-window) sound stimulation of the cochlea. *Hear Res* 2013;301:105-14.
- Williamson RA**, Vrabec JT, Coker NJ, Sandlin M: Coronal computed tomography prevalence of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2003;129:481-489.

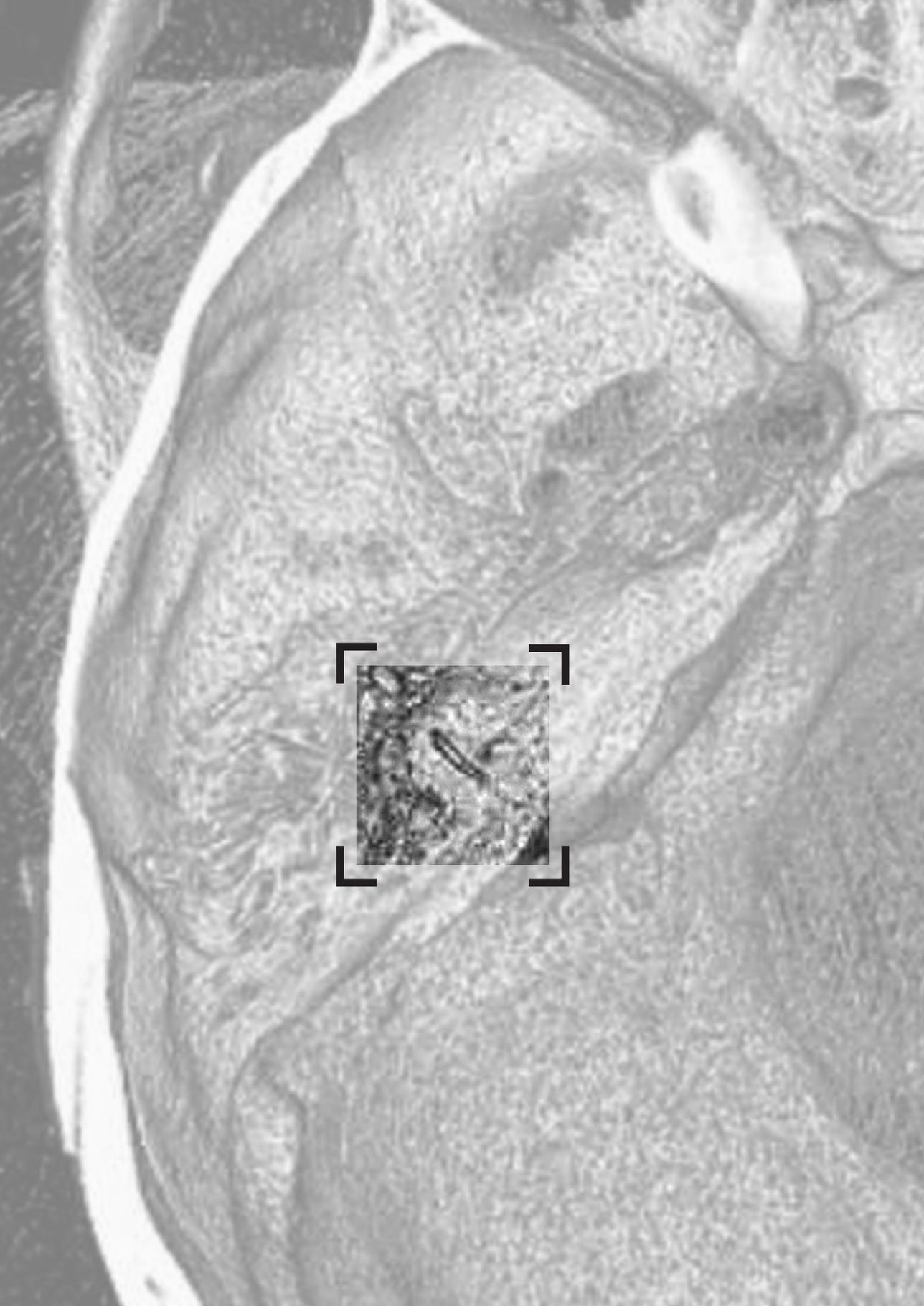
Yuen HW, Boeddinghaus R, Eikelboom RH, Atlas MD: The relationship between the air-bone gap and the size of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2009;141:689-694.

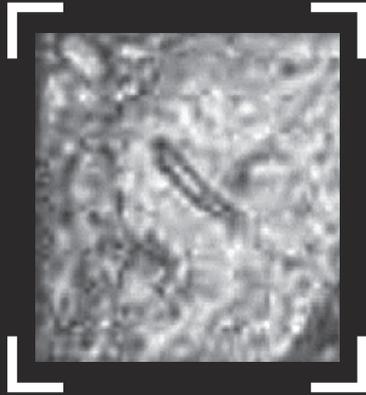




Chapter 4

SCD Treatment





Chapter 4.1

Utility of cVEMPs in bilateral superior canal dehiscence syndrome

Marlien E.F. Niesten, Michael J. McKenna, Barbara S. Herrmann,
Wilko Grolman, Daniel J. Lee

ABSTRACT

Objective: To determine the utility of cervical vestibular-evoked myogenic potential (cVEMP) thresholds in the surgical management of bilateral superior canal dehiscence syndrome (SCDS).

Study design: Retrospective review.

Methods: We identified patients who underwent surgical treatment for SCDS from our database of 147 patients diagnosed with superior canal dehiscence (SCD) between 2000 and 2011 at our institution. The diagnosis of SCDS was based on clinical signs and symptoms, audiometric and cVEMP testing and high-resolution computed tomography.

Results: We identified 38 patients who underwent SCD surgery in 40 ears (2 bilateral). In seven patients with bilateral SCD, the more symptomatic ear had lower cVEMP thresholds, a larger air bone gap and a lateralizing tuning fork. In 13 patients with peri-operative cVEMP testing, thresholds increased in 12 patients following primary repair and no threshold shift was seen in one patient with persistence of symptoms after revision surgery. Audiometric data showed a significant mean decrease of the low-frequency air-bone gap and a mild (high-frequency) bone conduction loss after surgical repair.

Conclusions: We found that 1) pre-operative cVEMP thresholds, the magnitude of the air bone gap and tuning fork testing are important to confirm the worse ear in patients with bilateral SCD 2) elevation of cVEMP thresholds following surgery correlates with improvement of symptoms and underscores the importance of post-operative testing in patients with bilateral disease or recurrence of symptoms and 3) SCD plugging is associated with a partial closure of the air-bone gap and a mild (high-frequency) sensorineural hearing loss.

INTRODUCTION

Superior canal dehiscence syndrome (SCDS) is caused by a bony defect of the superior semicircular canal (SSC) and is associated with a range of auditory and vestibular signs and symptoms. The condition was first described by Minor et al. in 1998 [Minor et al., 1998] and two major categories of SCDS are seen radiologically: 1) dehiscence of the arcuate eminence or 2) medially in the region of the superior petrosal sinus [McCall et al., 2011] and both types have been associated with a “third window” phenomenon. A “third window” of the inner ear is theorized to lower the cochlear impedance experienced by the stapes footplate resulting in 1) the shunting of fluid flow preferentially to the dehiscent SSC causing dizziness and 2) the reduction of pressure difference across the cochlear partition resulting in hearing loss [Rosowski et al., 2004]. The diagnosis of SCDS is based on clinical signs and symptoms, audiometric and cervical vestibular-evoked myogenic potential (cVEMP) testing and high resolution computed tomography (HR-CT) imaging [Belden et al., 2003]. Vestibular findings include imbalance, sound- and pressure associated dizziness and typically lowered cVEMP thresholds [Brantberg et al., 1999; Minor, 2000; Minor et al., 1998; Watson et al., 2000]. cVEMPs are an indirect measure of otolith function, measured through sound and vibration responses recorded in the ipsilateral sternocleidomastoid muscle. Auditory findings include autophony, aural fullness, tinnitus and hearing loss. Supranormal bone conduction thresholds (–5 to –10 dB) can be seen in SCDS [Mikulec et al., 2004] and may be due to increased cochlear responses associated with increased difference in scalae impedances across the cochlear partition [Rosowski et al., 2004]. Both the air conduction loss and/or supranormal bone conduction thresholds contribute to an air-bone gap seen in the majority of SCDS patients [Limb et al., 2006; Mikulec et al., 2004; Minor, 2000; Minor et al., 1998].

The prevalence of SCDS is not known, but histopathological studies demonstrate that 0.5-2% of patients have a thin (≤ 0.1 mm) or dehiscent SSC, of which 50% (6/12) of patients have bilateral superior canal dehiscence (SCD) [Carey et al., 2000]. Three to 9% of patients who have undergone CT imaging for other reasons have anatomic SCD (defined as a dehiscent SSC on CT-scan) [Masaki, 2011; Williamson et al., 2003] and 17% to 46% of these patients are affected bilaterally [Belden et al., 2003; Williamson et al., 2003]. Many patients with bilateral SCD undergoing surgical repair present with unilateral or mild contralateral symptoms [Carey et al., 2007; Friedland and Michel, 2006; Minor, 2005]. However, a subset of patients who present with significant SCD symptoms in both ears may not always be able to report which ear is worse based on symptoms. Sequential bilateral SCD plugging

may be a reasonable management option, as shown by a recent report examining clinical outcomes in five patients who underwent bilateral SCD repair [Agrawal et al., 2012]. If surgical intervention is indicated in a patient with bilateral SCDS, the worse ear should be repaired first. However, some bilateral SCD patients are unable to report the subjectively worse ear, and methods to more objectively determine the more affected ear pre-operatively have not been well described. Our study hypothesis is that cVEMP thresholds, the air-bone gap and tuning fork testing can help to confirm the clinical worse ear in patients with bilateral SCDS. In this context, we performed a retrospective review of our patients who underwent surgical repair of SCD at our institution. Specifically, we correlated cVEMP thresholds and the ABG of both ears in patients with bilateral SCDS and compared these with our unilateral SCDS cohort. In addition, we examined the association between vestibular and auditory signs and symptoms with cVEMP thresholds as well as presenting a detailed analysis of audiometric outcomes following SCD surgery. These data will help provide valuable information that will aid in surgical planning and counseling in patients with unilateral or bilateral SCDS.

METHODS

Selection of patients

We identified patients who underwent surgical treatment for SCDS from a database of 147 SCD patients diagnosed between 2000 and 2011 at our institution. SCDS diagnosis was based on clinical signs and symptoms, pure-tone audiometry, cVEMP testing and high resolution temporal bone computed tomography (HR-CT) without contrast (Stenver and Pöschl) [Belden et al., 2003]. Diagnosis of bilateral SCD was based on an anatomic SCD seen on CT-scan testing in both ears and diagnosis of bilateral SCDS was made when signs and symptoms were present bilaterally. We offered surgical SCD repair only if incapacitating vestibular and/or auditory signs and symptoms existed, such as autophony, aural fullness, tinnitus and sound-, pressure- and/or exercise associated dizziness. If bilateral SCDS was present, we plugged the more “symptomatic” ear, confirmed by clinical findings and cVEMPs as summarized in the results.

Cervical Vestibular-Evoked Myogenic Potentials (cVEMP)

Determination of the otolith function using cVEMP testing was also done as part of the clinical evaluation for SCDS. The clinical procedure recorded cVEMP responses from the ipsilateral sternocleidomastoid muscle (SCM) using surface electrodes while the patient sat in an upright position and contracted the SCM using a head

turn [Rauch, 2004]. Responses were recorded to tone bursts (Blackman window, 2 cycle rise/fall, TDH 49 Telephonics earphones) at the center frequencies 250, 500, 750 and 1000 Hz. cVEMP threshold was determined by identifying the presence of the cVEMP at a high level (typically 123 dB peak sound pressure or 90 dB HL) and reducing the stimulus level in 10 dB steps until no response was identified. Subsequently the stimulus was increased in 5 dB steps to find the response threshold. When no response threshold was found, 10 dB was added to the maximum stimulus level used which corresponded to the stimulus level limit of the equipment. The post-operative change in cVEMP thresholds was reviewed only in patients undergoing both pre- and post-operative cVEMP testing. We did not analyze the change in cVEMP amplitudes (only the cVEMP thresholds). Twenty-seven out of twenty-eight patients undergoing cVEMP testing were tested at MEEI, one patient underwent pre-operative cVEMP testing at an outside facility.

Audiometric Data

All audiometric testing was done at MEEI as part of the patient's clinical evaluation, which included pure tone thresholds and speech recognition (W-22 Auditec or CNC House Ear Institute), tympanometry and acoustic reflexes. All testing was done in accordance to ANSI standards and calibration (ANSI S3. 21, ANSI S3.5 and S3.6). Air-conduction (AC) for frequencies of 250, 500, 1000, 2000, 4000 and 8000 Hz and bone-conduction (BC) thresholds for the frequencies 250, 500, 1000, 2000 and 4000 Hz were collected for analysis from the pre-operative and post-operative evaluations. Pre- and post-operative air-bone gaps (ABGs) were calculated from threshold data. Masked BC thresholds were elevated if they were better than 0 dB (in the range of -5 to -10 dB) and we used the term supranormal bone conduction for these findings.

Surgical Technique

Plugging of the SCD was performed through a middle fossa craniotomy (MFC) or transmastoid (TM) approach. In the MFC approach, the dehiscence was exposed after extradural dissection and plugging was performed using bone wax. In the TM approach, labyrinthotomies were made to expose the endosteum of the anterolateral and posteromedial limbs of the superior canal and then these defects were plugged with bone wax. In one patient, resurfacing of the SCD was performed through a MFC approach. These surgical techniques are described in detail in previous papers [McCall et al., 2011; Mikulec et al., 2005].

Analysis of data

We included the results of pure-tone audiometry and cVEMP testing from the last pre-operative and first post-operative measurement. Statistical analysis of pure-

tone average results was done by using SPSS 15.0. Two-sided paired T-Tests were used to analyze changes in air conduction thresholds, bone conduction thresholds, ABG and cVEMP thresholds, for each of the frequencies separately. Because multiple t-tests were done, a stricter criterion for significant change was applied (99% Confidence Interval). cVEMP thresholds were converted to peak sound pressure (pSP) thresholds, by applying the criteria set in Rauch et al. 2004 [Rauch, 2004].

Human Subjects

This clinical study was approved by the Human Subjects Committee of the Massachusetts Eye and Ear Infirmary (Protocol # 09-08-088, PI: Daniel J. Lee, M.D.)

RESULTS

Patient characteristics and symptoms

Thirty-eight patients (40 operated ears, 37% male, mean age=44 years) with unilateral or bilateral SCDS who underwent surgical management were identified from our database of 147 patients diagnosed with SCD. Of this subset of patients (38/147, 26%), eighteen patients underwent left-sided surgery, eighteen patients underwent right-sided surgery and two patients underwent sequential bilateral surgery. Of the thirty-seven patients who underwent primary surgical repair of the SSC through a MFC, thirty-six patients underwent SSC plugging and one patient underwent SSC resurfacing. In one patient the SSC was plugged through a TM approach. Three patients required revision surgery.

cVEMP - Pre-operative results in bilateral SCD patients

Eleven out of thirty-eight (29%) patients had anatomic bilateral SCD. For determining the subjective worse ear we assessed vestibular and auditory signs and symptoms such as: imbalance, sound- and pressure associated dizziness, dizziness and/or nystagmus provoked by Tullio's phenomenon or Hennebert's sign, autophony, aural fullness, hearing loss and tinnitus. Nine out of eleven patients had both vestibular signs or symptoms (such as imbalance and sound- or pressure associated dizziness) and auditory signs and symptoms. One patient had only vestibular signs and symptoms and one patient had only auditory signs and symptoms. In 21/27 patients with unilateral SCD who underwent cVEMP testing, the mean pre-operative cVEMP threshold was 96 dB pSP in the SCD ear and 117 dB pSP in the contralateral not affected ear. In 7/11 patients with bilateral SCD who underwent cVEMP testing, the mean cVEMP threshold of the worse SCD ear was 100 dB pSP and a mean of 119 dB pSP was found in the contralateral less

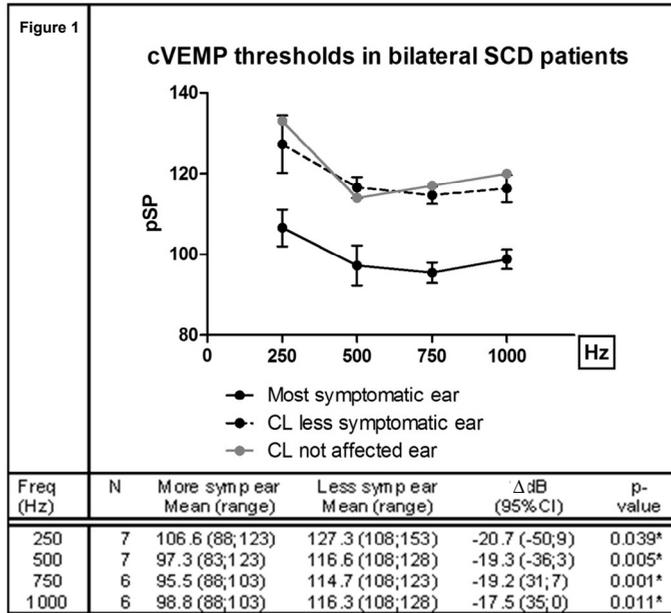


Figure 1. Pre-operative cervical vestibular-evoked myogenic potential (cVEMP) thresholds in patients with bilateral superior canal dehiscence (SCD) in our cohort. The figure shows the mean and standard error of the mean. * indicates a significant difference in cVEMP thresholds between the more symptomatic and the contralateral less symptomatic SCD ear, as calculated with a paired t test with confidence interval (CI) of 95%. pSP = peak sound pressure, Hz = Hertz, Freq = frequency, CL = contralateral, N = number of patients, symp ear = symptomatic ear, D = difference between the more symptomatic and contralateral ear and dB = decibel.

symptomatic ear. The mean cVEMP threshold for the worse ear was on average 19 dB lower in all frequencies. The contralateral ear showed values comparable with the not affected ear in patients with unilateral SCD, which are within normal limits [Rauch, 2004] (Figure 1).

Four of these seven patients with anatomic bilateral SCD had symptoms in both ears (bilateral SCDS), and the ear in which they experienced the most severe vestibular and auditory symptoms had lower cVEMP thresholds compared with the other ear (Table 1). Three patients with bilateral SCD had unilateral complaints, two of these patients showed lower thresholds in the SCDS ear. In the one patient with unilateral SCDS and bilateral anatomic SCD, the cVEMP thresholds were equal during his initial testing but patient ultimately developed progressive SCD symptoms on the second side 4.5 years later. These results show that the cVEMP threshold corresponded with the ear with most severe vestibular and auditory signs and symptoms in our patients with bilateral SCDS.

Table 1. Patients with bilateral SCD

Case	2	3*	8	9*	14	15	17	19	26	28	30
Age/Sex	35 F	36 F	40 M	61 F	35 F	58 F	31 F	37 F	60 F	55 F	67 F
Side	L R	L R	L R	L R	L R	L R	L R	L R	L R	L R	L R
Autophony	-	+	+	+	+	-	-	+	+	-	+
Aural Fullness	+	-	+	+	+	+	-	+	+	+	-
Report of hearing loss	-	-	+	-	+	+	-	-	+	-	+
Tinnitus	+	-	-	-	+	+	-	-	+	+	+
Imbalance	+	-	-	-	+	+	-	-	+	+	-
Pressure associated dizziness	+	+	+	+	+	+	+	+	+	+	-
Sound associated dizziness	+	-	+	-	+	-	+	+	+	+	-
Hennebert's sign	+	-	+	+	+	+	+	-	-	+	-
Tullio's sign	+	-	+	-	+	-	+	-	+	+	-
Weber lateralization	Left	X	X	X	X	Left	Left	Right	Left	Right	X
Av ABG 250-1000Hz >10 dB	+	-	-	-	+	+	-	-	+	+	+
Audio ABG 250-1000Hz	16.7	5	5	1.7	33.3	8.3	23.3	-1.6	5	10	1.7
Δ ABG 250-1000Hz	11.7	3.3	3.2	10	25	25	5	13.3	23.3	8.3	16.7
cVEMP 500Hz (pSP)	103	113	X	X	88	113	98	113	93	118	128
Δ cVEMP 500Hz (pSP)	10	X	0	X	25	15	25	35	X	25	X
(First) operated ear	+	-	+	-	+	+	+	-	+	-	+

Overview of signs and symptoms, the magnitude of the air-bone gap (ABG), and cervical vestibular-evoked myogenic potential (cVEMP) thresholds in patients with bilateral superior canal dehiscence (SCD). X, data was not available. * Case 3 and case 9 underwent bilateral sequential SCD surgery; case 3 underwent left sided surgery 1.5 years after primary right-sided surgery, and case 9 underwent repair of the left SCD 3 years following primary right SCD surgery. Case 8 presented with bilateral anatomic SCD with symptoms only on the left side. 4.5 years after his left surgery, patient developed symptoms on the right side as well, but did not require right-sided surgical repair. F = female, M = male, L = left, R = right, + = presence of a sign or symptom, - = absence of a sign or symptom.

Audiometric findings - Pre-operative results in bilateral SCD patients

The pre-operative ABG was measured in 24/27 patients with unilateral SCD. The mean ABG of the frequencies 250, 500 and 1000 Hz was >10 dB in 20/24 of the SCD ears and in 5/24 of the contralateral not affected ears. Eight out of eleven patients with bilateral SCD had a mean ABG of the frequencies 250, 500 and 1000 Hz >10 dB in the worse ear. In two of these patients the ABGs were >10 dB in both ears but the ABG was larger in the more symptomatic ear. Three patients with bilateral SCD did not have an ABG. Finally, six bilateral SCD patients who had documented pre-operative tuning fork testing showed lateralization to the more symptomatic ear. See Table I for the results. This shows that in addition to the cVEMP thresholds, the laterality of the 512Hz tuning fork test and a mean ABG at 250-1000 Hz of >10dB also corresponded with the more symptomatic ear in our patients with bilateral SCD.

cVEMP - Post-operative cVEMP thresholds in our cohort

Thirteen out of thirty-eight patients underwent pre- and post-operative cVEMP testing. Twelve patients underwent cVEMP testing following primary SCD repair and 1 patient underwent post-operative cVEMP testing after revision surgery. Clinically all twelve patients had improvement of their vestibular and auditory SCD signs and symptoms after primary repair. In all twelve patients who underwent primary SCD repair, cVEMP thresholds were elevated in the operated ear, with a mean improvement of 24 dB (Figure 2). The post-operative improvement in cVEMP threshold seems to correspond with the clinical improvement of signs and symptoms in these patients.

One patient presented with pressure- and sound associated dizziness, balance problems, autophony, aural fullness and a positive Tullio's sign and Hennebert's phenomenon. She had pre-operative cVEMP thresholds of 88, 83, 83, 88 dB pSP at 250, 500, 750 and 1000 Hz respectively. After primary repair of the left SCD, she had an initial improvement in her pressure-induced dizziness. In the months following surgery her pressure- and sound associated dizziness autophony and aural fullness recurred. Revision plugging did not improve clinical complaints. Patient underwent post-operative cVEMP testing after revision surgery. Her cVEMP testing following revision surgery showed thresholds that were similar to her initial pre-operative lowered thresholds (post-operative 88, 83, 83, 93 pSP at 250, 500, 750 and 1000 Hz respectively). In this patient the lack of improvement in her clinical signs and symptoms was associated with no shift in the cVEMP thresholds post-operatively.

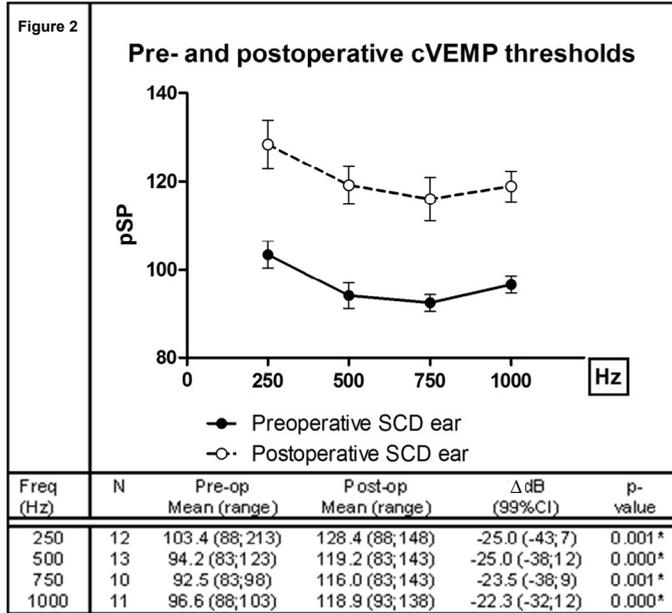


Figure 2. Post-operative cervical vestibular-evoked myogenic potential (cVEMP) thresholds in our patient cohort. The figure shows the mean and standard error of the mean. * indicates a significant difference in cVEMP thresholds between the pre-operative and post-operative SCD ear, as calculated with a paired t test with confidence interval (CI) 99%. pSP = peak sound pressure, Hz = Hertz, Freq = frequency, N = number of patients, Pre-op = pre-operative threshold, Post-op = post-operative threshold, Δ = difference between pre- and post-operative values and dB = decibel.

Audiometric Results - Post-operative audiometric testing results in our cohort

Pre-operative audiometric testing was performed in all thirty-eight patients and post-surgical results were available for thirty-four patients. Pure-tone average testing results are shown in Figure 3. The pre-operative air conduction thresholds were highest in the low frequencies, with an average threshold of 24 dB and 22 dB at 250 Hz and 500 Hz respectively. Post-operatively air conduction thresholds improved significantly by 8 dB (99% CI = 3.8;11.8) at 250 Hz and 5 dB (99% CI = 1.1;8,6) at 500 Hz (Figure 3). Mean air conduction thresholds in the high frequencies were higher after SCD repair with an average increase of 7 dB at 4000 Hz (99% CI = -12.7;-0.8) and 10 dB at 8000 Hz (99% CI = -16.7;-3.3), indicating a mild high frequency sensorineural hearing loss (SNHL) in these cases following surgery. The post-operative word recognition scores (WRS) were at or above 90% in all patients, with the exception of one patient with a WRS of 58% (pre-operative score of 90%, Case 30) at three weeks following surgery. This patient had a pre-operative asymmetric sensorineural hearing loss in the ear that was plugged.

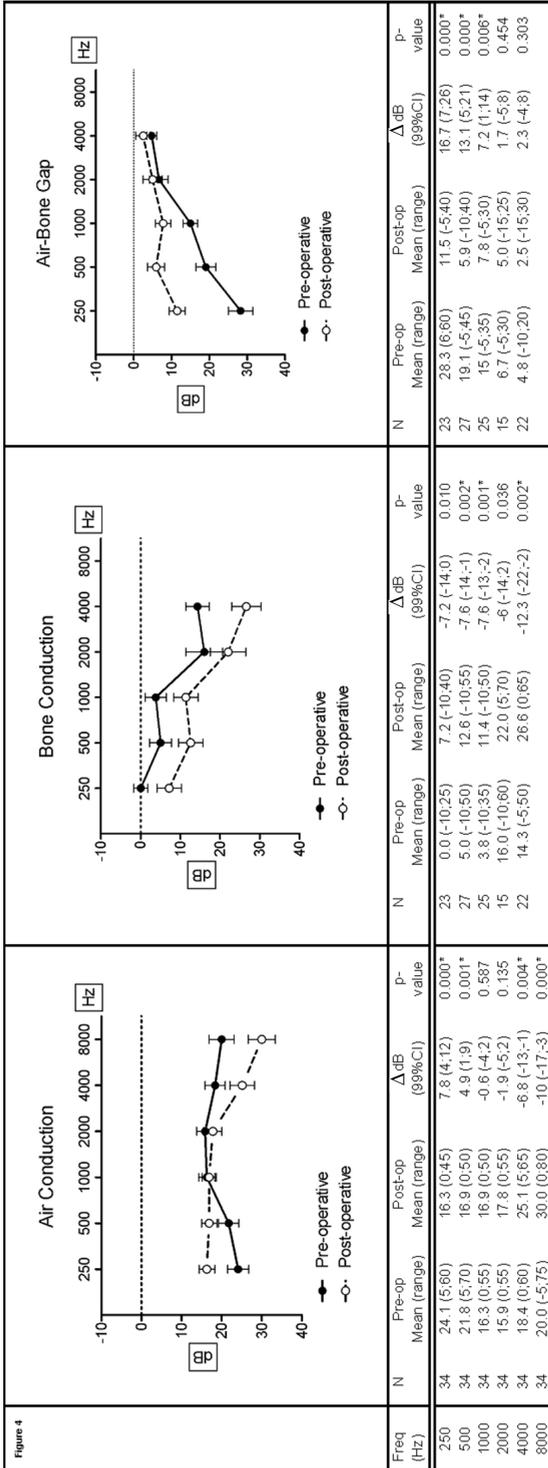


Figure 4

Figure 3. Post-operative audiometric testing results in our patient cohort. The figure shows the mean and standard error of the mean. * indicates a significant difference in pure-tone average threshold between the pre-operative and the post-operative SCD ear, as calculated with a paired t test with confidence interval (CI) 99%. dB = decibel, Hz = Hertz, Freq = frequency, N = number of patients, Pre-op = pre-operative threshold, Post-op = post-operative threshold Δ = difference between pre- and post-operative values.

Pre- and post-operative bone conduction thresholds were measured in 30 patients at one or more frequencies. Supranormal bone conduction thresholds (<0 dB) were seen in nine patients at 250 Hz, eleven patients at 500 Hz, ten patients at 1000 Hz, two patients at 2000 Hz and in one patient at 4000 Hz. Following surgery supranormal bone conduction thresholds were seen in six patients at 250 Hz, five patients at 500 Hz and in four patients at 1000 Hz. The mean bone conduction thresholds post-operatively were elevated by 8 dB (99% CI = -13.7;-1.4) at 500 Hz, 8 dB (99% CI = -13.3;-1.9) at 1000 Hz and 12 dB (99% CI = 22.4;-2.2) at 4000 Hz (Figure 3). Following surgery 10/30 (33%) patients had a mean elevation of bone conduction thresholds of ≥ 10 dB as measured over all frequencies (an additional six patients had elevation of bone conduction thresholds of ≥ 10 dB at 2000 and 4000 Hz). The maximum average bone conduction threshold shift was 34 dB, as measured three weeks post-operatively in case 30 (with post-operative WRS of 58%).

Twenty-four out of twenty-nine (83%) patients had a pre-operative ABG of more than 10 dB at an average of 250, 500 and 1000 Hz. The overall change in ABG (Figure 3) shows a mean closure of the ABG at all frequencies, with a significant improvement of 17 dB at 250 Hz (99% CI = 7.0;26.5), 13 dB at 500 Hz (99% CI = 5.0;21.3) and 7 dB at 1000 Hz (99% CI = 0.5;13.9).

Three patients underwent revision surgery. The first patient, a 31-years old woman, underwent revision surgery through a TM approach and experienced a 15-20 dB sensorineural hearing loss at all frequencies starting at 500 Hz. The second patient who underwent revision plugging through a TM approach was a 36-year-old male. His hearing remained stable at all frequencies. The third patient, a 34-year-old woman, underwent revision plugging of the SSC through a MFC approach with stable hearing and normalization of her supranormal bone conduction thresholds. Our series had only one patient who underwent primary plugging of the SSC through a TM approach, and this patient experienced an improvement of the low frequency air conduction thresholds of 10 dB and no SNHL.

DISCUSSION

In our subset of SCD patients with incapacitating symptoms who underwent surgical repair (38/147, 26%), lower cVEMP thresholds, a larger ABG and tuning fork lateralization was associated with the worse ear in patients with bilateral SCD. The value of cVEMP testing in the diagnosis of SCD has been reported previously in patients with an anatomic bilateral SCD [Arts et al., 2009]. Aguirre et al. made

a suggestion based on a case report to identify the side of which the symptoms originate by looking at the side with the lowest cVEMP threshold [Aguirre et al., 2007]. Welgampola et al. described unilateral lowered cVEMP thresholds in three patients with bilateral SCD on CT-scan and unilateral symptoms. They also described bilateral lowered cVEMP thresholds in three patients with bilateral SCDS [Welgampola et al., 2008]. We found that cVEMP thresholds may be important in confirming which ear to operate on first in patients with bilateral SCDS, as there seems to be an association between the severity of symptoms in patients with bilateral symptoms and cVEMP thresholds (even if thresholds are lowered bilaterally). Our data showed that in patients with bilateral SCDS, the cVEMP threshold in the less symptomatic SCD ear showed similar values to the not affected ear in patients with unilateral SCD. Lateralization of tuning fork testing and a mean ABG of >10 dB seem to confirm which ear is worse in our patient cohort.

In addition to the use of cVEMP thresholds in confirming the worse ear in patients with bilateral SCDS, they also have an important role following surgery. Post-operative cVEMP testing has been described to “normalize” following surgical SCD repair in smaller studies [Arts et al., 2009; Brantberg et al., 2001; Phillips et al., 2010; Welgampola et al., 2008; Zhou et al., 2007]. In our patient cohort post-operative cVEMP thresholds correlated with clinical presentation in all twelve patients with improvement of symptoms after primary repair, and they correlated with our one patient showing no shift in cVEMP thresholds after non-successful revision surgery. These findings are important in the counseling of patients with bilateral SCDS who remain symptomatic following surgery in determining if symptoms are due to 1) persistence of symptoms in the operated ear or 2) unmasking of symptoms in the contralateral affected ear, as shown in a recent study of bilateral SCDS surgical outcomes [Agrawal et al., 2012].

A third window from SCD can cause air conduction threshold shift and supranormal bone conduction thresholds. Surgical repair can eliminate this third window leading to a closure of the ABG. In our patient cohort we found a post-operative (partial) closure of the low-frequency ABG [Limb et al., 2006; Wilkinson et al., 2008] in most patients and normalization of the supranormal bone conduction thresholds in about 50% of patients, comparable with previous studies. In addition, we found a mild sensorineural hearing loss, predominantly in the high frequencies. Multiple studies showed cases in which high frequency sensorineural hearing loss after SSC repair was present [Hillman et al., 2006; Kirtane et al., 2009; Mikulec et al., 2005; Minor, 2005], with a prevalence of hearing loss varying from 12% to 30% [Agrawal and Parnes, 2008; Chi et al., 2010]. Association between MFC and

post-operative SNHL has been described previously [Limb et al., 2006; Minor, 2005], however an overall risk of mild sensorineural hearing loss has not been previously determined.

Limitations of the study

The findings of our research are limited by the retrospective chart review design and the relatively small number of patients. Previous studies have described a risk of overestimation of diagnosis of anatomic SCD based on CT-scan testing and in addition patients with SCD signs and symptoms with intraoperative thin bony covering of the SSC have been described. We diagnosed SCDS when signs and symptoms, the ABG and cVEMP thresholds showed evidence for SCDS in addition to a dehiscence seen on CT-scan. Some of our patients with unilateral SCDS presented with normal cVEMP thresholds and improved symptomatically following surgical repair. This suggests that SCDS can be present even when cVEMP thresholds are normal. One explanation for normal cVEMP thresholds could be due to SCD characteristics. Specifically, our data showed that the SCD size and location can influence cVEMP thresholds [Niesten et al., 2012]. In patients with bilateral anatomic SCD and bilateral symptoms, an explanation for the normal cVEMP thresholds in the “better” ear could be due to SCD size and location and we plan to more carefully study this possible association with a larger patient cohort.

Established hearing and vestibular handicap indices were not used to assess peri-operative signs and symptoms. Audiometric and cVEMP testing was not performed in all surgical patients and one patient underwent cVEMP testing at an outside facility. Large variation in VEMP testing between different facilities exists, which could influence testing results in this one patient. Other factors such as lack of normalization of sternocleidomastoid muscle function, difference in muscle mass, fatigue and lack of artifact rejection can influence cVEMP results as well. A comprehensive prospective analysis of SCDS outcomes that include peri-operative auditory and vestibular testing will be useful to help validate our observations in this study.

CONCLUSION

In our subset of SCDS patients with incapacitating vestibular and/or auditory symptoms undergoing surgical management, we found that 1) in patients with bilateral SCDS the more symptomatic ear showed lower cVEMP thresholds, a larger ABG when present and lateralization of 512 Hz tuning fork testing, 2) post-operative

elevation of cVEMP thresholds corresponds with the clinical improvement of signs and symptoms in patients with SCDS and 3) plugging of SCD results in closure of the ABG as well as an associated mild sensorineural hearing loss. These findings provide valuable information for surgical counseling as they help to determine which ear to operate on first in patients with bilateral SCD syndrome as well as to highlight the potential improvement of the air bone gap and the risks of a mild hearing loss. Finally, post-operative cVEMP testing should become a routine test performed after SCD repair as an objective measure to assess outcomes, much like an audiogram after middle ear surgery.

REFERENCES

- Agrawal SK**, Parnes LS: Transmastoid superior semicircular canal occlusion. *Otol Neurotol* 2008;29:363-367.
- Agrawal Y**, Minor LB, Schubert MC, Janky KL, Davalos-Bichara M, Carey JP: Second-side surgery in superior canal dehiscence syndrome. *Otol Neurotol* 2012;Jan;33(1):72-77.
- Aguirre MSB**, Migliaccio A, Carey J: Characterization of bilateral superior canal dehiscence. *Acta Otorrinolaringol Esp* 2007;437-439.
- Arts HA**, Adams ME, Telian SA, El-Kashlan H, Kileny PR: Reversible electrocochleographic abnormalities in superior canal dehiscence. *Otol Neurotol* 2009;30:79-86.
- Belden CJ**, Weg N, Minor LB, Zinreich SJ: CT evaluation of bone dehiscence of the superior semicircular canal as a cause of sound- and/or pressure-induced vertigo. *Radiology* 2003; 226:337-343.
- Brantberg K**, Bergenius J, Mendel L, Witt H, Tribukait A, Ygge J: Symptoms, findings and treatment in patients with dehiscence of the superior semicircular canal. *Acta Otolaryngol* 2001; 121:68-75.
- Brantberg K**, Bergenius J, Tribukait A: Vestibular-evoked myogenic potentials in patients with dehiscence of the superior semicircular canal. *Acta Otolaryngol* 1999;119:633-640.
- Carey JP**, Migliaccio AA, Minor LB: Semicircular canal function before and after surgery for superior canal dehiscence. *Otol Neurotol* 2007;28:356-364.
- Carey JP**, Minor LB, Nager GT: Dehiscence or thinning of bone overlying the superior semicircular canal in a temporal bone survey. *Arch Otolaryngol Head Neck Surg* 2000;126:137-147.
- Chi FL**, Ren DD, Dai CF: Variety of audiologic manifestations in patients with superior semicircular canal dehiscence. *Otol Neurotol* 2010;31:2-10.
- Friedland DR**, Michel MA: Cranial thickness in superior canal dehiscence syndrome: Implications for canal resurfacing surgery. *Otol Neurotol* 2006;27:346-354.
- Hillman TA**, Kertesz TR, Hadley K, Shelton C: Reversible peripheral vestibulopathy: The treatment of superior canal dehiscence. *Otolaryngol Head Neck Surg* 2006;134:431-436.
- Kirtane MV**, Sharma A, Satwalekar D: Transmastoid repair of superior semicircular canal dehiscence. *J Laryngol Otol* 2009;123:356-358.
- Limb CJ**, Carey JP, Srireddy S, Minor LB: Auditory function in patients with surgically treated superior semicircular canal dehiscence. *Otol Neurotol* 2006;27:969-980.
- Masaki Y**: The prevalence of superior canal dehiscence syndrome as assessed by temporal bone computed tomography imaging. *Acta Otolaryngol* 2011;131:258-262.
- McCall AA**, McKenna MJ, Merchant SN, Curtin HD, Lee DJ: Superior canal dehiscence syndrome associated with the superior petrosal sinus in pediatric and adult patients. *Otol Neurotol* 2011;32:1312-1319.

Mikulec AA, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.

Mikulec AA, Poe DS, McKenna MJ: Operative management of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:501-507.

Minor LB: Superior canal dehiscence syndrome. *Am J Otol* 2000;21:9-19.

Minor LB: Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:1717-1727.

Minor LB, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998;124:249-258.

Nielsen MEF, Hamberg L, Silverman J, Lou K, McCall AA, Windsor A, Curtin HD, Herrmann BS, Grolman W, Nakajima HH, Lee DJ: Association of size and location of superior canal dehiscence with clinical presentation, audiometric and vestibular testing. *Abstr Assoc Res Otolaryngol* 2012;35.

Phillips DJ, Souter MA, Vitkovic J, Briggs RJ: Diagnosis and outcomes of middle cranial fossa repair for patients with superior semicircular canal dehiscence syndrome. *J Clin Neurosci* 2010;17:339-341.

Rauch SD: Vestibular-evoked myogenic potentials (vemps) show altered tuning in patients with meniere's disease. *Otology and NeuroOtology* 2004;25:333-338.

Rosowski JJ, Songer JE, Nakajima HH, Brinsko KM, Merchant SN: Clinical, experimental, and theoretical investigations of the effect of superior semicircular canal dehiscence on hearing mechanisms. *Otol Neurotol* 2004;25:323-332.

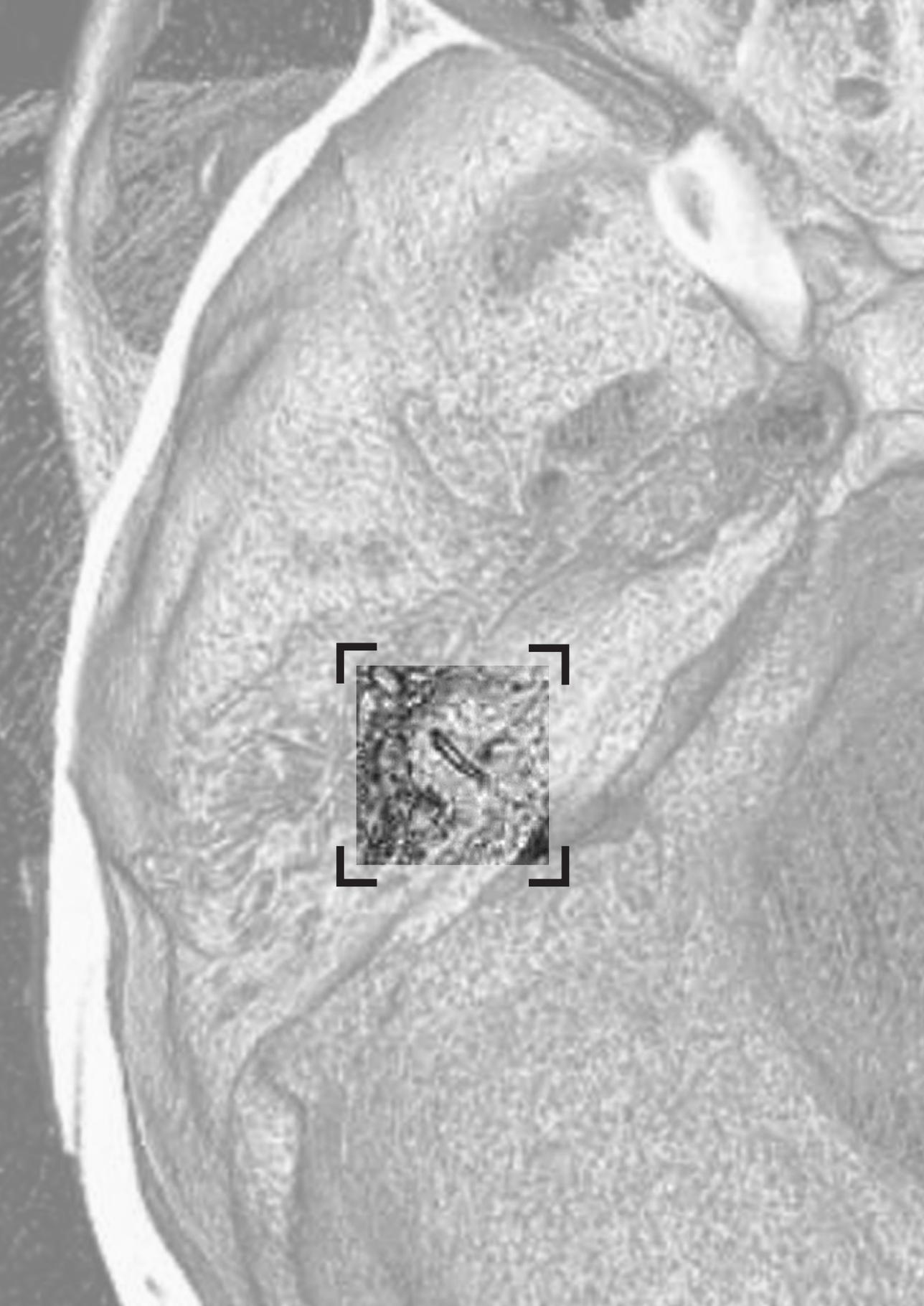
Watson SR, Halmagyi GM, Colebatch JG: Vestibular hypersensitivity to sound (tullio phenomenon): Structural and functional assessment. *Neurology* 2000;54:722-728.

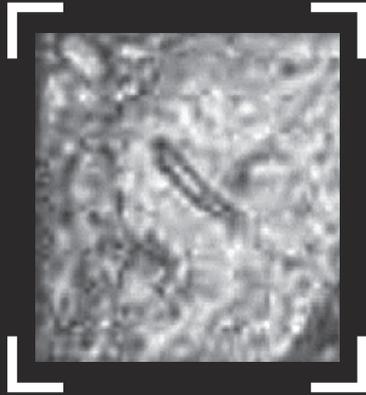
Welgampola MS, Myrie OA, Minor LB, Carey JP: Vestibular-evoked myogenic potential thresholds normalize on plugging superior canal dehiscence. *Neurology* 2008;70:464-472.

Wilkinson EP, Liu GC, Friedman RA: Correction of progressive hearing loss in superior canal dehiscence syndrome. *Laryngoscope* 2008;118:10-13.

Williamson RA, Vrabec JT, Coker NJ, Sandlin M: Coronal computed tomography prevalence of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2003;129:481-489.

Zhou G, Gopen Q, Poe DS: Clinical and diagnostic characterization of canal dehiscence syndrome: A great otologic mimicker. *Otol Neurotol* 2007;28:920-926.





Chapter 4.2

Clinical factors associated with prolonged recovery after superior canal dehiscence surgery

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ABSTRACT

Objective: To identify clinical factors associated with prolonged recovery following superior canal dehiscence surgery.

Study design: Retrospective review.

Setting: Tertiary care academic medical center.

Patients: Thirty-three patients that underwent surgery for SCDS were identified from a database of 140 patients diagnosed with SCD (2000-2010) at the Massachusetts Eye and Ear Infirmary (USA). The diagnosis of SCDS was based on clinical signs and symptoms, audiometric and vestibular testing and high-resolution temporal bone computed tomography.

Intervention: For the primary repair, the superior canal was plugged in thirty-one patients through a middle fossa craniotomy approach and in one patient through a transmastoid approach. In one patient the SCD was resurfaced through a middle fossa craniotomy approach.

Main Outcome Measures: Post-operative clinical signs and symptoms and factors that may influence duration of disequilibrium following surgery.

Results: Thirty-three patients (15 to 71 years, mean=43 years) underwent surgery for SCDS on 35 ears (2 bilateral). Mean follow-up was 28.7 months (range 3 months to 10 years). 33/33 (100%) patients experienced initial improvement of the chief complaint. Three patients required revision surgery, improving symptoms in two patients. Six patients had dizziness lasting more than 4 months post-operatively and all had bilateral SCD, migraines and a dehiscence of ≥ 3 mm.

Conclusion: Surgical plugging of SCD is an effective management option to provide long-term improvement of the chief complaint in SCDS patients. Patients with bilateral SCD, a history of migraines and larger defects may be at risk of prolonged recovery and should be appropriately counseled.

INTRODUCTION

Superior canal dehiscence syndrome (SCDS) was first described by Minor et al. in 1998 and is caused by a bony defect of the superior semicircular canal [Minor et al., 1998]. This can lead to a range of auditory and vestibular symptoms, notably autophony, aural fullness, hearing loss, tinnitus, chronic imbalance and sound- and pressure induced vertigo. It is theorized that a third window (in addition to the oval and round windows) is created by a dehiscence of the superior canal, reducing inner ear impedance. Loud sounds or abrupt alterations in middle ear pressure that result in the shunting of inner ear fluids to the dehiscence (or intracranial pressure changes that transmit energy into the dehiscence) can alter the neuronal firing rates of the superior semicircular canal (SSC) ampulla [Hirvonen et al., 2001; Minor et al., 2001], causing dizziness and vertigo. A decrease in cochlear input impedance and increase in bone-conduction cochlear-evoked potentials is also seen in these patients, causing hearing loss or conductive hyperacusis [Merchant et al., 2007; Minor et al., 2003; Rosowski et al., 2004]. In some patients, the onset of SCD symptoms is associated with a “second event”, an activity that dramatically affects inner ear pressure (head trauma, excessive straining, coughing or child birth) [Watters et al., 2006]. The first event is considered to be congenital thinning of the bone overlying the SSC [Watters et al., 2006].

The diagnosis of SCDS is based on clinical signs and symptoms, audiometric and vestibular testing and high resolution computed tomography (HR-CT). Most SCD patients are asymptomatic or do not require treatment [Minor, 2000] and avoidance of triggers (e.g. straining, nose blowing) can be effective [Brantberg et al., 2001]. However, for SCD patients with incapacitating symptoms surgical repair is a reasonable option [Minor, 2000; Vlastarakos et al., 2009]. Improvement of sound- and pressure-induced vertigo, autophony and hearing loss has been described [Crane et al., 2009; Mikulec et al., 2004; Mikulec et al., 2005; Minor, 2005]. Most patients have some degree of disequilibrium for several weeks to several months following SCD repair; however in some patients the dizziness can persist. One study found that 38% (16/42) of patients who underwent SCD surgery had immediate vestibular hypofunction and this was seen more commonly in patients with a larger defect [Agrawal et al., 2009]. Aside from SCD size no other factors associated with vestibular dysfunction or prolonged recovery after surgery have been described.

In this retrospective study of our experience from 2000-2010, we examine the factors that may influence the duration of disequilibrium after surgery. In this

context, we performed a detailed analysis of pre- and post-operative signs and symptoms in thirty-three consecutive patients who underwent SCD repair. Our results are based on a large surgical SCD patient series assessing clinical signs and symptoms, with a mean follow-up period of more than two years.

METHODS

Selection of patients

Patients who were diagnosed with SCD at the Massachusetts Eye and Ear Infirmary (MEEI) between 2000 and 2010 and underwent surgical treatment were identified. Diagnosis of anatomic SCD was based on HR-CT of the temporal bone without contrast. Reconstructions were made in the Stenver (perpendicular to SSC) and Pöschl (parallel to SSC) planes, in addition to the standard axial and coronal projections [Belden et al., 2003]. The diagnosis of SCDS was made when clinical signs and symptoms, audiometric and vestibular testing were referable to the side of dehiscence. Pure-tone average showing an air-bone gap in the low frequencies and/or bone conduction thresholds in the range above 0 dB (–5 or –10 dB) was used to help confirm SCDS, as well as cVEMP testing showing lowered thresholds.

Surgical repair was offered to patients only if they had debilitating vestibular and/or auditory complaints and was not offered if the SCD diagnosis was based on imaging alone. In patients with bilateral dehiscence, the more symptomatic ear was plugged, based on signs, symptoms, and lower cVEMP thresholds.

Collection and analysis of data

A chart review was performed to collect demographic patient data, to assess for clinical signs and symptoms and the presence of a second event. Auditory and vestibular complaints that were assessed included autophony, aural fullness, subjective hearing loss, pulsatile tinnitus, imbalance, vertigo, sound- and pressure associated dizziness and dizziness provoked by physical activity. Physical exam findings were reviewed for: 1) subjective and objective Tullio's phenomenon by using a 512Hz tuning fork and a Barany noise box 2) Hennebert's sign provoked by pneumatic otoscopy, tragal compression and Valsalva maneuver against pinched nostrils. If a sign was present during one point in time pre-operatively this sign was marked positive, likewise for a negative sign. If no information on the sign was available, this was documented as unknown. In our assessment of outcomes, a change in signs and symptoms was reviewed for each patient using the longest follow-up period possible. In addition the duration of recovery was associated with

variables such as comorbid factors (e.g. history of migraines, seizures), bilateral SCD or the size of the dehiscence. Due to the small patient cohort, no statistical analysis was performed on the factors associated with prolonged recovery. All patients underwent audiometric and cVEMP testing, and a detailed analysis of these data will be presented in a separate manuscript.

Surgical Technique

Plugging of the SCD was performed through a middle fossa craniotomy (MFC) or transmastoid (TM) approach. These surgical techniques have been described [McCall et al., 2011; Watters et al., 2006]. To summarize, when the MFC approach was used the SCD was directly plugged with bone wax and then any associated tegmen defects were repaired with temporalis fascia and split calvarial bone graft. One patient underwent primary plugging of the SSC with temporalis fascia through a MFC approach. Bone pate and calvarial bone graft wrapped in fascia were placed on top of the plug covering the SSC. In another case the SCD was resurfaced by using bone graft. When performing the TM approach, both limbs of the SSC were plugged after labyrinthotomies were made on either side of the dehiscence (the defect was not directly addressed). All patients received intravenous corticosteroids prior to incision and post-operatively, followed by an oral prednisone taper on discharge. Intraoperative facial nerve monitoring was used in all cases. A pressure bandage was applied over the wound for 2-5 days to prevent post-operative hemorrhage.

Human Subjects

This study was approved by the Human Subjects Committee of the Massachusetts Eye and Ear Infirmary (Protocol # 09-08-088, PI: Daniel J. Lee, M.D.)

RESULTS

Patient characteristics

From a database of 140 patients diagnosed at MEEI with SCD, asymptomatic SCD was present in 19 patients and 121 patients had SCDS. Thirty-three patients (33/121, 27%) underwent surgery for SCDS (67% female, mean age=43 years, range 15 to 71 years). 11/33 (33%) patients presented with bilateral SCD. Patient characteristics are given in Table 1. A "second event" preceding onset of symptoms was seen in 6/18 patients (33%), ranging from head trauma to childbirth. In fifteen patients information on the presence or absence of a second event was not logged. The left ear was plugged in 14/33 (42%), the right ear was plugged in 18/33 (55%).

Table 1. Patient Characteristics

Case	Age/ Sex	Second event	History	SCD on CT	Operative side	Operative type	Repair type	Adverse Event	Side Effect	FU (months)	SCD Size (mm)
1	31 F	None	None	R	R 2x	MFC, TM	Plug	None	Hardware removal	31	6.0
2	35 F	U	Chiari T1 malformation	B	L	MFC	Plug	None	None	28	3.6
3	36 F	U	None	B	R, L	MFC Bilateral	Plug	None	None	49	5.0
4	41 F	None	None	R	R	MFC	Plug	None	None	70	6.2
5	49 F	U	U	R	R	MFC	Plug	HB grade IV/VI, free gracilis transfer	None	52	1.6
6	35 M	U	U	L	L	MFC	Plug	None	None	3	6.2
7	36 M	U	U	L	L	MFC	Plug	None	None	62	7.0
8	40 M	U	U	B	L	MFC	Plug	None	None	68	3.8
9	61 F	U	None	B	R, L	MFC Bilateral	Plug*	None	None	36	6.4
10	42 F	U	None	L	L	MFC	Plug	Epidural hematoma, evacuation	None	8	5.4
11	40 F	U	U	L	L	MFC	Plug	None	None	52	4.4
12	34 F	None	None	L	L 2x	MFC 2x	Plug	None	Delayed HB grade III/ VI, now grade I/VI	11	4.0
13	15 F	None	None	R	R	TM	Plug	None	None	8	1.4
14	35 F	Child birth	None	B	L	MFC	Plug	None	None	24	5.2
15	58 F	TIA	Seizures, meningitis	B	L	MFC	Plug	Post OR seizure, managed with med	None	16	7.8
16	43 F	U	Previous MFC	R	R	MFC	Plug	None	None	3	0.6
17	31 F	None	None	B	L	MFC	Plug	None	None	10	3.0

Table 1. Patient Characteristics (continued)

Case	Age/ Sex	Second event	History	SCD on CT	Operative side	Operation type	Repair type	Adverse Event	Side Effect	FU (months)	SCD Size (mm)
18	42 M	U	T-mastoidectomy	R	R	MFC	Plug	None	None	26	2.0
19	37 F	None	None	B	R	MFC	Plug	None	None	7	3.0
20	43 F	U	None	L	L	MFC	Plug	None	None	7	4.4
21	52 F	MVA	Tympanoplasty TI	R	R	MFC	Plug	None	None	60	2.6
22	36 M	U	U	L	L 2x	MFC, TM	Plug	None	None	132	X
23	30 F	U	None	R	R	MFC	Plug	None	None	3	4.6
24	44 M	MC	Otoplasty surgery	L	L	MFC	Plug	None	None	4	2.8
25	26 M	None	None	R	R	MFC	Res	None	None	21	0.4
26	60 F	None	Tympanotomy	B	L	MFC	Plug	CSF-L, 72 hours LD, resolution	None	22	3.8
27	71 M	None	None	R	R	MFC	Plug	None	None	21	4.2
28	55 F	None	None	B	R	MFC	Plug	None	None	13	3.2
29	43 M	MBT face	Ossiculoplasties	R	R	MFC	Plug	None	None	3	3.0
30	67 F	Head trauma	None	B	R	MFC	Plug	None	None	88	5.2
31	46 F	None	None	R	R	MFC	Plug	None	None	3	3.2
32	62 M	None	None	R	R	MFC	Plug	None	None	3	3.8
33	59 M	Hammer	None	R	R	MFC	Plug	None	None	3	5.0

F = Female, M = Male, U = Unknown, TIA = Transient Ischemic Attack, MVA = Motor Vehicle Accident, MC = Multiple Concussions, MBT = Mild Blunt Trauma, Hammer = Onset of complaints after use of a hammer, Chiari T1 malformation = Chiari Type 1 malformation, T-mastoidectomy = Tympanomastoidectomy, Tympanoplasty TI = Tympanoplasty Type I, L = Left, R = Right, B = Bilateral, MFC = Middle Fossa Craniotomy, TM = Transmastoid, Plug = Plugging, Res = Resurfacing, HB = House Brackmann, OR = Operation, CSF-L = Cerebrospinal fluid leak, LD = Lumbar drainage, FU = Follow-up. * Case 9 underwent resurfacing of the left SCD during second-sided surgery.

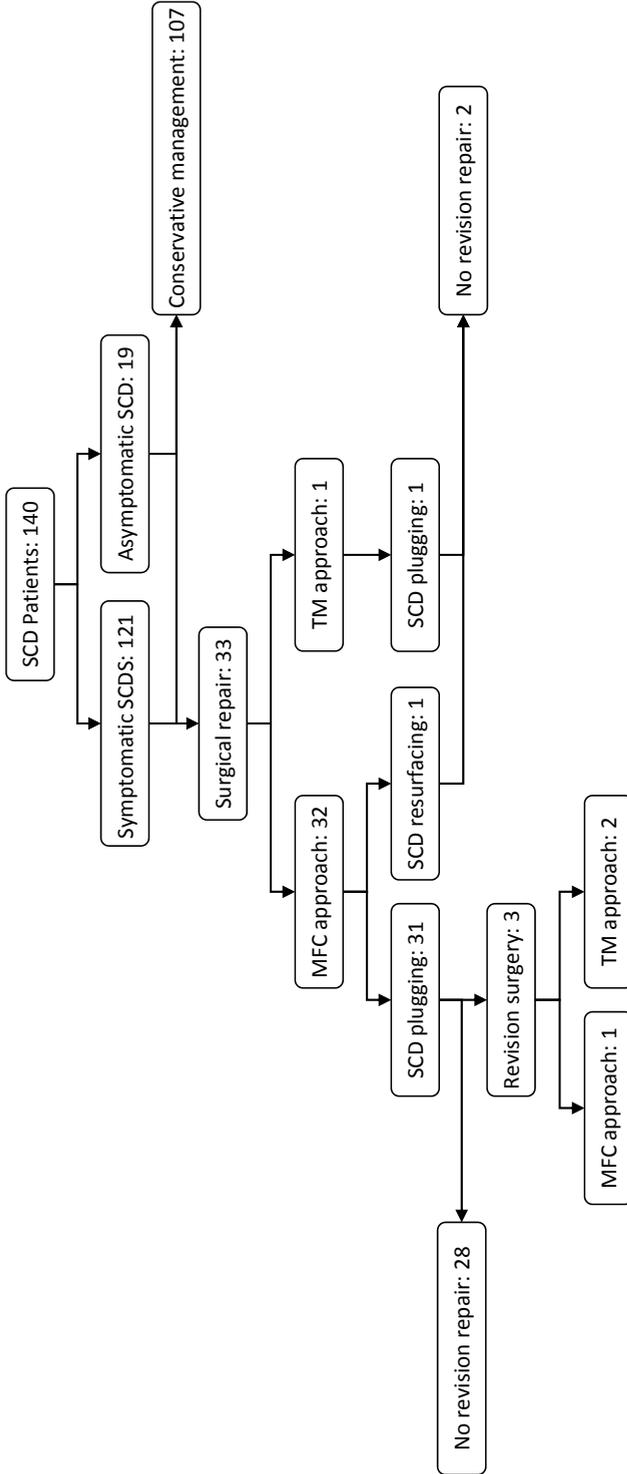


Figure 1. Flowchart of SCD management for our total cohort of patients, divided for management, surgical approach, method of repair of the SSC and revision surgery. MFC = Middle Fossa Craniotomy, TM = Transmastoid.

Two patients underwent bilateral sequential SCD surgery, 1.5 years and 3 years apart. For primary repair a MFC approach was performed in thirty-two patients, thirty-one patients underwent plugging and one patient underwent resurfacing of the SSC. In one patient the SCD was plugged through a transmastoid approach (Figure 1). A mean post-operative follow-up of 28.7 months (median 21 months, range 3 months to 10 years) was found.

Signs and symptoms

Table 2 summarizes the presenting signs and symptoms in our cohort. The following symptoms were found: autophony 25/33 (76%), aural fullness 25/33 (76%), subjective hearing loss 20/33 (61%), imbalance 20/33 (61%), sound associated dizziness 21/33 (64%), pressure associated dizziness 24/33 (73%), exercise associated dizziness 8/33 (24%), migraines 15/33 (45%), tinnitus 19/33 (58%) of which 14/19 (74%) patients had pulsatile tinnitus. All patients (33/33, 100%) undergoing primary plugging or resurfacing of the SSC had an improvement or resolution of the chief complaint. Symptoms still present post-operatively by last follow-up were: aural fullness 3/33 (9%), subjective hearing loss 6/33 (18%), imbalance 3/33 (9%) and tinnitus 6/33 (18%).

Factors associated with prolonged recovery

Clinical factors

Most patients experienced a period of imbalance or dizziness in the first several weeks to months following SCD repair. Vestibular physical therapy was recommended to 8/33 (24%) patients following primary surgical repair. Six female patients (all with a migraine history and bilateral SCD) had a prolonged recovery period, defined by balance problems, dizziness or vertigo for a period of four or more months following surgery. In addition to these six cases, one female patient (Case 16) with a history of migraines who underwent a previous MFC experienced a prolonged recovery after revision MFC. Improvement of the SCD related signs and symptoms was seen in all six patients.

Size of dehiscence

All six patients with prolonged recovery had bilateral SCD and a dehiscence of at least 3 mm or larger (mean 4.6, range=3-7.8 mm). The remainder of the cohort had a smaller mean size of dehiscence (3.9, range=0.4-7 mm) and 7 patients in this group had a defect <3mm. Statistical analysis was not performed due to small sample size.

Table 2. Pre- and Post-operative Signs and Symptoms (continued)

Case	Pre-operative Signs and Symptoms													Post-operative Signs and Symptoms													Notes
	Autophony	Aural Fullness	Reports HL	Imbalance	Sound	Pressure	Exercise	Tinnitus	Pulsatile	Migraine	Tullio's	Hennebert's	Total	Autophony	Aural Fullness	Reports HL	Imbalance	Sound	Pressure	Exercise	Tinnitus	Pulsatile	Tullio's	Hennebert's	Total		
19	■	●	●	○	●	●	□	●	●	●	●	●	10	○	○	○	●	○	○	○	○	○	□	○	1	Prolonged recovery	
20	●	●	○	□	■	●	○	●	○	○	●	□	7	○	○	○	□	○	○	○	○	○	□	○	0	BPPV resolved	
21	●	■	○	□	●	●	●	○	○	○	○	●	5	○	○	○	□	○	○	○	○	○	○	○	1		
22	●	□	○	□	■	□	□	□	□	□	□	○	3	□	□	□	□	○	○	○	○	□	○	○	0		
23	□	●	○	●	■	□	□	□	□	□	●	○	5	□	●	○	○	○	○	○	○	□	○	○	2		
24	□	●	○	○	○	○	○	○	○	○	●	○	5	□	□	○	○	○	○	○	○	□	○	○	1	BPPV resolved	
25	●	●	●	●	●	■	□	○	○	○	●	○	8	○	○	○	○	○	○	○	○	○	○	○	0		
26	●	●	■	●	●	●	□	●	●	●	●	○	10	□	○	○	●	□	○	○	□	□	○	○	1	Prolonged recovery	
27	■	●	●	●	○	○	○	□	□	□	○	○	5	○	●	○	○	○	○	○	○	□	○	○	3		
28	●	●	●	●	●	■	●	○	○	○	●	●	11	○	○	○	○	○	○	○	○	○	○	○	○	0	
29	■	●	●	●	○	○	○	□	□	□	○	○	4	○	○	○	○	○	○	○	○	□	○	○	1		
30	●	□	●	■	○	○	○	□	□	○	○	○	4	○	□	○	○	○	○	○	○	□	○	○	1		
31	●	●	●	●	●	●	■	○	□	○	○	●	10	○	○	○	○	○	○	○	○	○	○	○	0		
32	●	●	●	■	●	○	○	□	□	□	○	○	9	○	○	□	○	○	○	○	○	○	□	○	1		
33	●	●	●	●	●	■	○	●	●	●	○	○	10	○	□	○	○	○	○	○	○	○	□	○	0		
Total	25	25	20	20	21	24	8	19	14	15	17	21	229	0	3	6	4	0	0	0	7	1	0	0	21		

● = symptom is present pre-operatively or did not improve post-operatively, ○ = symptom is absent or improved post-operatively, ■ = chief complaint, □ = no information, HL = Hearing Loss, Sound = Sound associated dizziness, Pressure = Pressure associated dizziness, Exercise = Exercise associated dizziness, Pulsatile = Pulsatile tinnitus, Tullio's = Tullio's sign, Hennebert's = Hennebert's sign, BPPV = Benign Paroxysmal Positional Vertigo.

Cases with prolonged recovery period

The first patient (Case 2) reported imbalance and disequilibrium after left SCD repair. She had minor drop attacks and migraines and received medical management and vestibular physical therapy. Two years post-operatively she reported no dizziness.

The second patient (Case 9) noted disequilibrium and gait instability following right SCD surgery. Her migraine medication was adjusted. One year following her right surgery she reported improvement in balance but difficulty when walking in the dark or when turning her head while walking, as well as worsening of left-sided SCD symptoms. Two years following right SCD surgery patient underwent left SCD resurfacing using bone cement. She reported partial improvement in her balance and experienced less severe disequilibrium following the second-sided surgery as compared to her first SCD repair (at one week post-operatively).

The third patient (Case 15) had a history of viral meningitis, tonic-clonic seizures and migraines, for which she was treated with anti-epileptics. She experienced several seizures after her left SCD repair while an inpatient that were managed medically and was discharged on post-operative day 6. Due to her gait instability and the need of a walker, patient underwent vestibular physical therapy and at 17 months post-operatively she can walk without assistance and drive.

The fourth patient (Case 17) reported gait instability following SCD repair. She noted a mild off-balance sensation when using the stairs or a treadmill but had resumed most of her normal activities at ten months following surgery.

The fifth patient (Case 19) presented with persistence of gait instability after repair, was given migraine medications and vestibular therapy. At seven months post-operatively her symptoms are still improving.

The sixth patient (Case 26) underwent left MFC with meningoencephalocele repair and left SSC plugging. Her post-operative course was complicated by CSF leak necessitating lumbar drainage for 72 hours, which resulted in resolution of the leak. Due to her balance problems and migraines she underwent vestibular physical therapy and received migraine prophylaxis and at 22 months post-operatively she continues to show improvement.

Case presentations – (Serious) Adverse events

A 49-year-old healthy woman (Case 5) with sound-induced dizziness as her chief complaint underwent plugging of the right SSC through a MFC approach. The geniculate ganglion was not dehiscent with normal facial nerve function immediately post-operatively. Three weeks after surgery, she presented with an acute onset of right facial paralysis, managed with oral steroids and antiviral medication. She recovered to House Brackmann grade IV/VI and underwent a free gracilis transfer three years after onset.

A 42-year-old woman (Case 10) with a history of migraines presented with a five year history of episodes of dizziness and imbalance, presenting as a rapid shift in visual field and a sense of moving. After MFC approach for plugging of the left SSC, patient required return to the operating room to evacuate an epidural hematoma and control of a meningeal vessel bleed that developed acutely in the PACU. Patient recovered fully, as well as her vestibular symptoms.

Case presentations – Side effects

Four patients (12%) developed transient benign paroxysmal positional vertigo (BPPV), which recovered following the Epley maneuver. Case 12 experienced a delayed House-Brackmann III/VI facial nerve palsy that resolved completely. This will be discussed under revision surgery.

Revision Surgery

Three patients underwent revision surgery after primary plugging of the SCD through a MFC approach. The first patient (Case 12) presented with a chief complaint of pressure- and sound associated dizziness. She awoke with normal facial nerve function but several days post-operatively developed a left facial palsy (House Brackmann grade III/VI). After treatment with corticosteroids and anti-viral medication the facial palsy resolved completely. Three months after MFC, patient developed recurrence of symptoms and a revision MFC approach with plugging of the SSC was performed eight months following primary surgery. Patient received antiviral medication one week prior to repair and one week following her surgery. Facial nerve function was normal following revision surgery. However, her symptoms have persisted.

The second patient (Case 1) is a healthy 31-year-old female patient and presented with autophony as chief complaint. All complaints improved after plugging of the right SCD through a MFC approach. Due to discomfort over the operated area, a craniotomy plate was removed 9 months after primary MFC. Patient experienced

recurrence of symptoms after an episode of severe bronchitis eighteen months after the initial SCD repair. She underwent revision plugging of the SCD through a TM approach. Post-operatively she improved with vestibular physical therapy.

The third patient (Case 22) is a 36-year-old male who presented with sound- and pressure associated dizziness. He underwent repair of the left SCD after which symptoms resolved. Ten years later, patient presented with similar symptoms but less severe. Recurrence of left SCD symptoms was managed through revision plugging of the SSC through a TM approach, which improved his vestibular complaints.

Nondehiscent case

Case 25 - A 26-year-old healthy male patient who presented with autophony, aural fullness, hearing loss, imbalance, sound- and pressure induced dizziness and a positive Tullio's sign. Diagnostic work-up supported SCDS of the right ear. HR-CT showed right SCD, dehiscence of the right tegmen and dura abutting the ossicles. During the MFC the SSC was intact but blue-lined, indicating a thin bony covering. The SSC was resurfaced using fascia and bone chips. All signs and symptoms resolved following surgery.

DISCUSSION

In our cohort, all patients (33/33 or 100%) that underwent plugging or resurfacing of the SCD showed improvement in their chief complaint. Similar results are found in previous studies [Agrawal et al., 2009; Brantberg et al., 2001; Mikulec et al., 2005; Minor, 2005]. The strength of our study is 1) identification of factors associated with a prolonged recovery, 2) the size of our surgical cohort (33 patients) in which clinical signs and symptoms were reviewed and 3) the mean follow-up period of 28.7 months. The largest single institution series assessing the change in clinical signs and symptoms comprised twenty patients and the mean follow-up was not mentioned [Minor, 2005]. In a meta-analysis of SCD surgery outcomes in 64 patients, the longest follow-up was up to six months in 60 patients and 6 to 23 months in 4 patients [Vlastarakos et al., 2009].

Three factors were associated with prolonged recovery in six female patients in our cohort: a history of migraines, bilateral SCD and a larger dehiscence. 15/33 (45%) of our patients suffered from migraines, a higher prevalence than the general population (6.0% of men, 17.2% of woman) [Lipton et al., 2002]. Co-morbidity between migraines and cochleovestibular disorders, with both dizziness and ver-

tigo occurring in 54% of patients with migraines, has been associated with other conditions such as Ménière's disease and BPPV [Baloh, 2004; Casani et al., 2009; Furman et al., 2005; Kayan and Hood, 1984]. We hypothesize that migraines may reduce the central compensation mechanisms following SCD repair.

The second factor associated with delayed recovery is the presence of a contralateral dehiscence. In our series, 11/33 patients presented with bilateral dehiscence. Six of these patients experienced a recovery period of greater than four months. To our knowledge, no information on the association of bilateral SCDS on the duration of recovery following unilateral repair has been described. Cases with persistence of SCDS symptoms in the contralateral ear after unilateral SCD repair have been described [Hillman et al., 2006; Phillips et al., 2010]. It is possible that repair of one ear results in the unmasking of symptoms in the contralateral ear with SCDS and may help to explain the persistent dizziness and prolonged recovery in these patients.

A third factor possibly influencing recovery is the size of the dehiscence. We observed that all six patients with a prolonged recovery period had a dehiscence of 3 mm or larger. Smaller dehiscences were observed in the remainder of the cohort. A study examining vestibular function following SCD surgery showed a mean SCD of 4.9 mm in the patient group with immediate post-operative vestibular hypofunction, compared to 3.4 mm in the group of patients without post-operative hypofunction [Agrawal et al., 2009]. Future studies that formally assess vestibular function pre- and post-operatively in a greater number of patients will help to determine whether the size of the defect and acute vestibular dysfunction after surgery affects the duration of recovery independent of other variables, such as migraine history.

Two patients in our cohort that underwent surgery developed delayed facial nerve palsy. Anderson et al. showed that 4/110 (3.6%) patients undergoing MFC and temporal lobectomy for epilepsy developed a delayed facial nerve palsy, of which one patient developed the facial nerve palsy on the contralateral side of the surgery [Anderson et al., 1991]. Patients with trigeminal neuralgia undergoing a MFC approach experienced immediate facial palsy in 16/553 (2.9%) patients and delayed facial palsy in 21/553 (3.8%) patients [Peet and Schneider, 1952]. Mechanisms proposed to cause delayed facial palsy are reactivation of a latent viral infection present in the geniculate ganglion (occurring after induction of a stress response on the immune system) [Cohen et al., 2010; Guthikonda et al., 2010], traction on the greater superficial petrosal nerve, thermal injury caused by the

use of electrocautery in the region of the geniculate ganglion or mechanical injury to an underlying dehiscent geniculate ganglion [Anderson et al., 1991; Isaacson and Vrabec, 2007; Morello et al., 1971; Stookey, 1959; Wilkins, 1966]. A dehiscent geniculate ganglion is more commonly seen in patients with SCD compared to a cohort without SCD (38.1% versus 11.4% in a total of 365 sides analyzed), theoretically increasing the risk of facial nerve injury when manipulating the middle cranial fossa floor [Isaacson and Vrabec, 2007].

The complications we encountered after MFC have been described before. Fukamachi et al. described 16 epidural hematomas after 1055 intracranial operations (2%), requiring surgical management in 10 cases (1%). In 4/10 the epidural hematoma site was regional, caused by incomplete hemostases of the bone or dura mater in all four patients [Fukamachi et al., 1986]. Kvam et al. reported that 23/538 (4%) patients who underwent craniotomy had a seizure following surgery and that the most common reason was inadequate anticonvulsant prophylaxis [Kvam et al., 1983]. Yamakami et al. described 8/64 (13%) patients with a CSF leak following cranial base surgery. 5/8 of these CSF leaks were successfully managed by lumbar drainage [Yamakami et al., 1996].

Three of our patients required revision surgery. Friedland et al. described similar recurrence of symptoms following an upper respiratory tract infection with persistent coughing in a patient who underwent resurfacing through a MFC approach [Friedland and Michel, 2006]. Other cases of revision surgery are described in the literature and have been ascribed to the resorption or slippage of the bone graft [Friedland and Michel, 2006; Limb et al., 2006]. We performed a revision TM approach in 2/3 cases. Our institution uses the MFC approach in most cases as the defect is directly visualized, the tegmen is often low-lying and the deficient can be easily repaired, and we have no cases of moderate, severe or profound hearing loss with this technique [data not published]. We reserve the transmastoid approach for cases where the defect is medial (due to the superficial petrosal sinus) [McCall et al., 2011] and for revision surgery if access to the limbs of the SSC is available.

Limitations of our study

The major limitation is our study design - retrospective analysis of patient charts. In addition, four surgeons performed SCD surgery in our cohort and the reporting of symptoms varied. Several symptoms were not logged, introducing the risk of information bias. To minimize the impact of these missing data, we focused on the improvement or resolution of the chief complaint as this was found in all patient charts. We did not perform any statistical analyses on our patient cohort,

due to the fact that the cohort is too small for statistical analysis. Future work will include the use of established instruments pre- and post-operatively (e.g. dizziness handicap inventory (DHI)). Going forward, we plan to perform a prospective study using these questionnaires to formally track auditory and vestibular signs and symptoms and to prospectively analyze factors possibly contributing to a prolonged recovery period.

CONCLUSION

Our study found that repair of SCDS improved the chief complaint in all patients after initial surgery. We also found factors associated with a prolonged recovery, including 1) a history of migraines, 2) bilateral SCD and 3) a dehiscence ≥ 3 mm. Surgery for SCDS was associated with a low rate of adverse events and side effects. Careful patient selection and counseling of surgical risks is imperative. Prospective studies on a larger cohort of SCDS patients using established surveys and pre- and post-operative vestibular testing will allow us to better quantify vestibular, auditory and quality of life outcomes in addition to factors associated with prolonged recovery following SCD surgery.

REFERENCES

- Agrawal Y**, Migliaccio AA, Minor LB, Carey JP: Vestibular hypofunction in the initial post-operative period after surgical treatment of superior semicircular canal dehiscence. *Otol Neurotol* 2009;30:502-506.
- Anderson J**, Awad IA, Hahn JF: Delayed facial nerve palsy after temporal lobectomy for epilepsy: Report of four cases and discussion of possible mechanisms. *Neurosurgery* 1991; 28:453-456.
- Baloh RW**: Superior semicircular canal dehiscence syndrome: Leaks and squeaks can make you dizzy. *Neurology* 2004;62:684-685.
- Belden CJ**, Weg N, Minor LB, Zinreich SJ: CT evaluation of bone dehiscence of the superior semicircular canal as a cause of sound- and/or pressure-induced vertigo. *Radiology* 2003; 226:337-343.
- Brantberg K**, Bergenius J, Mendel L, Witt H, Tribukait A, Ygge J: Symptoms, findings and treatment in patients with dehiscence of the superior semicircular canal. *Acta Otolaryngol* 2001; 121:68-75.
- Casani AP**, Sellari-Franceschini S, Napolitano A, Muscatello L, Dallan I: Otoneurologic dysfunctions in migraine patients with or without vertigo. *Otol Neurotol* 2009;30:961-967.
- Cohen M**, Balaker A, Kirsch C, Mendelsohn A, Ishiyama A: Magnetic resonance imaging findings in delayed facial palsy after stapes surgery. *Otol Neurotol* 2010;31:1153-1156.
- Crane BT**, Lin FR, Minor LB, Carey JP: Improvement in autophony symptoms after superior canal dehiscence repair. *Otol Neurotol* 2009;31:140-146.
- Friedland DR**, Michel MA: Cranial thickness in superior canal dehiscence syndrome: Implications for canal resurfacing surgery. *Otol Neurotol* 2006;27:346-354.
- Fukamachi A**, Koizumi H, Nagaseki Y, Nukui H: Postoperative extradural hematomas: Computed tomographic survey of 1105 intracranial operations. *Neurosurgery* 1986;19:589-593.
- Furman JM**, Sparto PJ, Soso M, Marcus D: Vestibular function in migraine-related dizziness: A pilot study. *J Vestib Res* 2005;15:327-332.
- Guthikonda B**, Pensak ML, Theodosopoulos PV: Delayed facial palsy after the anterior petrosal approach: Case report and review of the literature. *Neurosurgery* 2010;66:E845-846; discussion E846.
- Hillman TA**, Kertesz TR, Hadley K, Shelton C: Reversible peripheral vestibulopathy: The treatment of superior canal dehiscence. *Otolaryngol Head Neck Surg* 2006;134:431-436.
- Hirvonen TP**, Carey JP, Liang CJ, Minor LB: Superior canal dehiscence: Mechanisms of pressure sensitivity in a chinchilla model. *Arch Otolaryngol Head Neck Surg* 2001;127:1331-1336.
- Isaacson B**, Vrabcic JT: The radiographic prevalence of geniculate ganglion dehiscence in normal and congenitally thin temporal bones. *Otol Neurotol* 2007;28:107-110.
- Kayan A**, Hood JD: Neuro-otological manifestations of migraine. *Brain* 1984;107 (Pt 4):1123-1142.

Kvam DA, Loftus CM, Copeland B, Quest DO: Seizures during the immediate postoperative period. *Neurosurgery* 1983;12:14-17.

Limb CJ, Carey JP, Srireddy S, Minor LB: Auditory function in patients with surgically treated superior semicircular canal dehiscence. *Otol Neurotol* 2006;27:969-980.

Lipton RB, Scher AI, Kolodner K, Liberman J, Steiner TJ, Stewart WF: Migraine in the united states: Epidemiology and patterns of health care use. *Neurology* 2002;58:885-894.

McCall AA, McKenna MJ, Merchant SN, Curtin HD, Lee DJ: Superior canal dehiscence syndrome associated with the superior petrosal sinus in pediatric and adult patients. *Otol Neurotol* 2011;32:1312-1319.

Merchant SN, Rosowski JJ, McKenna MJ: Superior semicircular canal dehiscence mimicking otosclerotic hearing loss. *Adv Otorhinolaryngol* 2007;65:137-145.

Mikulec AA, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.

Mikulec AA, Poe DS, McKenna MJ: Operative management of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:501-507.

Minor LB: Superior canal dehiscence syndrome. *Am J Otol* 2000;21:9-19.

Minor LB: Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:1717-1727.

Minor LB, Carey JP, Cremer PD, Lustig LR, Streubel SO, Ruckenstein MJ: Dehiscence of bone overlying the superior canal as a cause of apparent conductive hearing loss. *Otol Neurotol* 2003;24:270-278.

Minor LB, Cremer PD, Carey JP, Della Santina CC, Streubel SO, Weg N: Symptoms and signs in superior canal dehiscence syndrome. *Ann N Y Acad Sci* 2001;942:259-273.

Minor LB, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998;124:249-258.

Morello G, Bianchi M, Migliavacca F: Combined extra-intradural temporal rhizotomy for the treatment of trigeminal neuralgia. Results in 409 patients. *J Neurosurg* 1971;34:372-379.

Peet MM, Schneider RC: Trigeminal neuralgia; a review of six hundred and eighty-nine cases with a follow-up study of sixty five per cent of the group. *J Neurosurg* 1952;9:367-377.

Phillips DJ, Souter MA, Vitkovic J, Briggs RJ: Diagnosis and outcomes of middle cranial fossa repair for patients with superior semicircular canal dehiscence syndrome. *J Clin Neurosci* 2010;17:339-341.

Rosowski JJ, Songer JE, Nakajima HH, Brinsko KM, Merchant SN: Clinical, experimental, and theoretical investigations of the effect of superior semicircular canal dehiscence on hearing mechanisms. *Otol Neurotol* 2004;25:323-332.

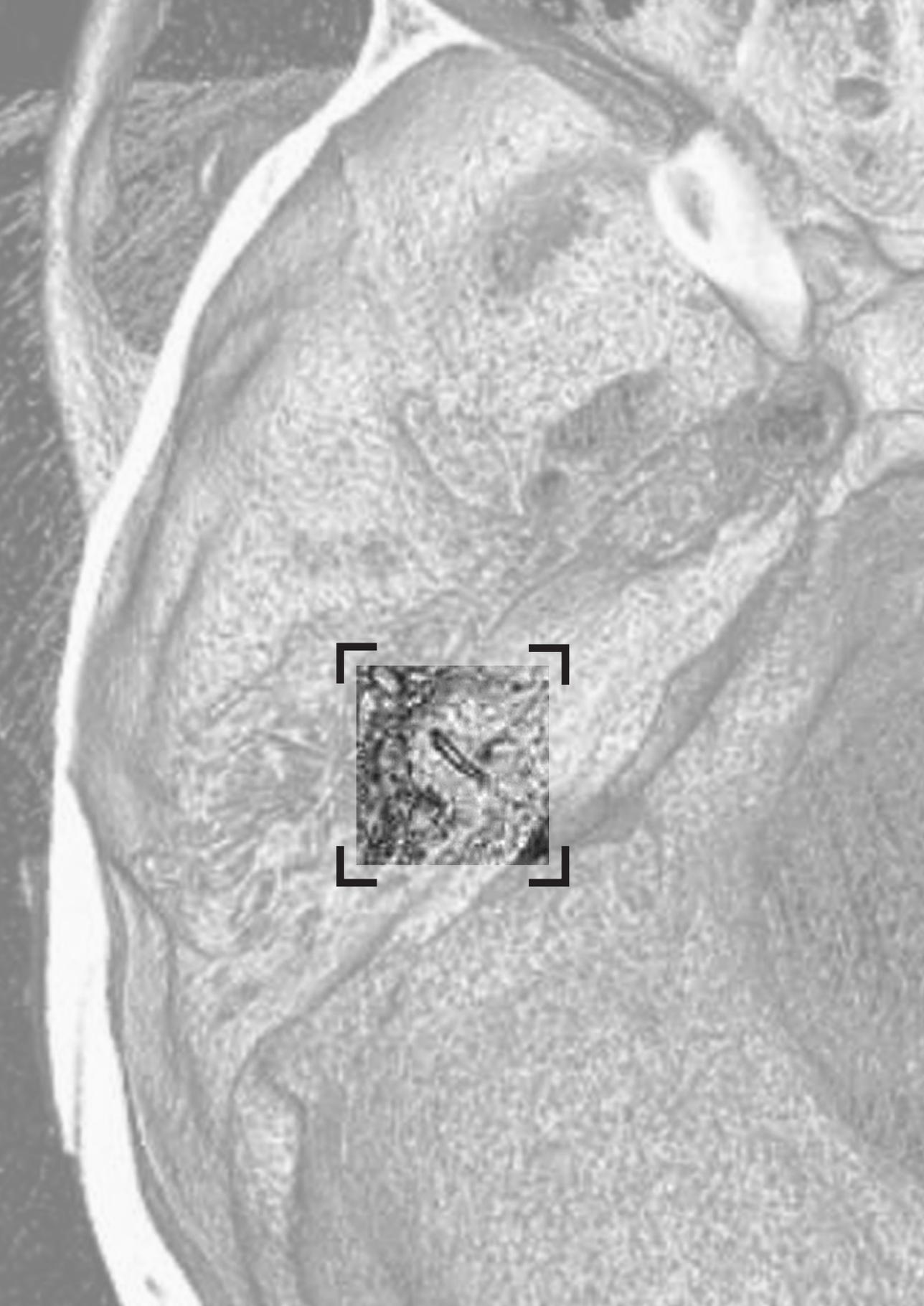
Stookey BP, Ransohoff J: Trigeminal neuralgia. Its history and treatment. Springfield 1959.

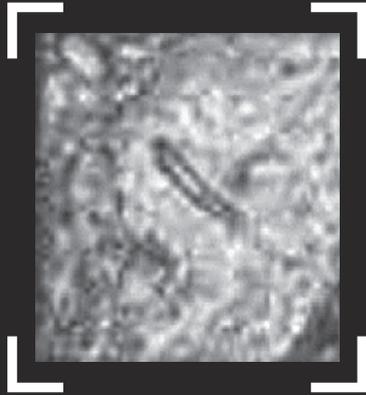
Vlastarakos PV, Proikas K, Tavoulari E, Kikidis D, Maragoudakis P, Nikolopoulos TP: Efficacy assessment and complications of surgical management for superior semicircular canal dehiscence: A meta-analysis of published interventional studies. *Eur Arch Otorhinolaryngol* 2009;266:177-186.

Watters KF, Rosowski JJ, Sauter T, Lee DJ: Superior semicircular canal dehiscence presenting as postpartum vertigo. *Otol Neurotol* 2006;27:756-768.

Wilkins H: The treatment of trigeminal neuralgia by section of the posterior sensory fibers using the transdural temporal approach. *J Neurosurg* 1966;25:370-373.

Yamakami I, Serizawa T, Yamaura A, Nakamura T: Cerebrospinal fluid leak after cranial base surgery. *No Shinkei Geka* 1996;24:29-33.





Chapter 4.3

Systematic review of outcomes
following superior canal dehiscence
surgery: determining best surgical
candidates

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Submitted

ABSTRACT

Objective: To determine the change in reported signs and symptoms, hearing outcomes and vestibular-evoked myogenic potential (VEMP) thresholds following surgery for superior canal dehiscence (SCD) syndrome, to help determine which patients are best surgical candidates.

Data Sources: Systematic review using the PubMed and Embase databases.

Review Methods: We performed a systematic search by retrieving studies with original data and assessed these on relevance and risk of bias. Data was extracted on SCD signs and symptoms, audiometric testing, VEMP testing and recurrence of symptoms.

Results: A total of 247 unique studies were retrieved. Nineteen studies were included following screening on title and abstract, full-text screening and cross-reference checking. One study with, according to our definition, low relevance was excluded. Fourteen studies reported an initial improvement of post-operative SCD signs and symptoms in 223/233 patients (96%, range 91-100%). Pre-operative average air-bone gap (ABG) of 18dB (range 14-26dB) improved post-operatively to an 11dB average ABG (range 6-21dB). Two studies showed deterioration of bone conduction thresholds ≥ 10 dB following surgical repair in 25-33% of patients. Pre-operative VEMP thresholds (range 61-73 dB nHL) were elevated to 80-88dB nHL following SCD repair.

Conclusion: Surgical repair of SCD is associated with improvement of auditory and/or vestibular signs and symptoms (especially autophony and sound- and pressure-induced vertigo) and reversal of diagnostic indicators. Large heterogeneity in 1) description of surgical repair methods and 2) reporting of outcomes was found among the studies. A more standardized reporting approach utilizing prospective data collection is needed to better understand the long-term outcomes.

INTRODUCTION

First described in 1998 by Minor et al, superior canal dehiscence (SCD) is a lack of bony covering of the superior semicircular as seen on high resolution computed tomography (CT) [Minor et al., 1998]. Patients with SCD syndrome can present with auditory symptoms (conductive hyperacusis, autophony, hearing loss or pulsatile tinnitus) and/or vestibular symptoms (sound-, pressure- and/or exercise-induced vertigo, chronic disequilibrium or imbalance). Typical findings include an air-bone gap (ABG) in the low frequencies on audiometric testing and cervical vestibular-evoked myogenic potential (cVEMP) responses that are low in threshold and high in amplitude.

It is hypothesized that SCD causes auditory and vestibular signs and symptoms through a “third window” phenomenon that lowers the cochlear impedance experienced by the stapes footplate. Consequently, this third window shunts inner ear fluids towards the SCD, causing vestibular symptoms such as dizziness. In addition, a reduction in the pressure across the cochlear partition and an increase in bone-conducted cochlear-evoked potentials can lead to hearing loss or conductive hyperacusis [Modugno et al., 2005].

Multiple groups have assessed the effect of SCD surgery on signs and symptoms, hearing outcomes and VEMP testing. However, SCD is a rare condition, and thus, only small patient groups are often studied. One review from 2009 assessed outcomes following surgical repair but only included multiple case reports and studies with small patient populations [Vlastarakos et al., 2009]. Subsequent studies have reported on surgical outcomes with larger patient groups that utilize varying approaches and methods for SCD repair. However, there does not seem to be consensus between the higher volume centers on the preferred surgical approach. Continued research is needed to 1) determine which patients are the best candidates to opt for a surgical treatment, and 2) compare outcomes using different surgical techniques.

In this study, we conducted a rapid systematic review drawing from the latest reported clinical series to analyze SCD outcomes as measured by change in SCD patient reported signs and symptoms, audiometric testing and vestibular-evoked myogenic potential testing.

METHODS

Retrieving studies

A rapid systematic search was conducted in the PubMed and Embase databases. A clinical librarian assisted in the search. The search terms used were “superior canal dehiscence” and its synonyms and “surgery” and its synonyms (date of last search was October 31st 2013), see Table 1 for the complete syntax. Following this systematic search, two reviewers (M.E.F.N. and I.S.) removed all duplicates and also independently screened the papers for inclusion based on title and abstract. Original studies describing patients with superior canal dehiscence undergoing surgical repair of the SCD were included. Exclusion criteria were systematic reviews, animal studies, laboratory studies, opinion papers, poster presentations and case reports describing less than 10 patients. Following the title-abstract screening, the remaining studies were fully assessed by the same two reviewers using the same in- and exclusion criteria. The references of the remaining papers

Table 1. Search for studies on surgical outcomes of SCD

Database	Search	Hits
PubMed	((("Semicircular Canals"[Mesh] OR ((superior[Title/Abstract] OR anterior[Title/Abstract] OR semicircular[Title/Abstract] OR "semi circular"[Title/Abstract]) AND (canal[Title/Abstract] OR canals[Title/Abstract]))) AND (dehiscence[Title/Abstract] OR dehiscences[Title/Abstract] OR dehiscent[Title/Abstract])) AND ((“Surgical Procedures, Operative”[Mesh] OR “Otologic Surgical Procedures”[Mesh] OR “surgery”[Title/Abstract] OR “surgical”[Title/Abstract] OR “surgically”[Title/Abstract] OR “treatment”[Title/Abstract] OR “treated”[Title/Abstract] OR “management”[Title/Abstract] OR “manage”[Title/Abstract] OR “managed”[Title/Abstract] OR “managing”[Title/Abstract] OR “repair”[Title/Abstract] OR “repaired”[Title/Abstract] OR “repairing”[Title/Abstract] OR “plugging”[Title/Abstract] OR “plugged”[Title/Abstract] OR “plug”[Title/Abstract] OR “cap”[Title/Abstract] OR “capping”[Title/Abstract] OR “capped”[Title/Abstract] OR “resurfacing”[Title/Abstract] OR “resurfaced”[Title/Abstract] OR “occlusion”[Title/Abstract] OR “occlude”[Title/Abstract] OR “occluding”[Title/Abstract] OR “occluded”[Title/Abstract] OR “craniotomy”[Title/Abstract] OR “transmastoid”[Title/Abstract]))	230
Embase	((superior:ti,ab OR anterior:ti,ab OR semicircular:ti,ab OR 'semi circular':ti,ab) AND (canal:ti,ab OR canals:ti,ab) AND (dehiscence:ti,ab OR dehiscences:ti,ab OR dehiscent:ti,ab)) AND ('surgery':ti,ab OR 'surgical':ti,ab OR 'surgically':ti,ab OR 'treatment':ti,ab OR 'treated':ti,ab OR 'management':ti,ab OR 'manage':ti,ab OR 'managed':ti,ab OR 'managing':ti,ab OR 'repair':ti,ab OR 'repaired':ti,ab OR 'repairing':ti,ab OR 'plugging':ti,ab OR 'plugged':ti,ab OR 'plug':ti,ab OR 'cap':ti,ab OR 'capping':ti,ab OR 'capped':ti,ab OR 'resurfacing':ti,ab OR 'resurfaced':ti,ab OR 'occlusion':ti,ab OR 'occlude':ti,ab OR 'occluding':ti,ab OR 'occluded':ti,ab OR 'craniotomy':ti,ab OR 'transmastoid':ti,ab)	227

Overview of syntax used in the PubMed and Embase libraries. Date of last search: 31-10-2013.

were hand-searched for relevant missing references, as were related reviews and meta-analyses.

Assessing studies

Included papers were critically appraised by studying the relevance and risk of bias by the aforementioned reviewers using predefined criteria (see Table 2 for the criteria). The relevance of each study included patient domain (patients with SCD), surgical treatment and surgical outcome. The surgical outcome was divided in three categories: assessment of signs and symptoms, assessment of audiometric outcomes and assessment of VEMP testing outcomes. Each item was either reported as satisfactory or unsatisfactory. When the grading was unsatisfactory for all surgical outcomes, the study was excluded. In addition, the follow-up period was extracted. The risk of bias was assessed as satisfactory, moderately satisfactory or unsatisfactory using the Cochrane Collaboration's tool [Higgins and Green, 2011] and studied the selection of patients, the standardization of treatment, outcome assessment and the completeness of reported data for the primary outcome. Initial discrepancies between the two independent reviewers were resolved by discussion and consensus was reached in all cases.

Data extraction

Analysis of data was done for post-operative change in signs and symptoms, audiometric testing results and cVEMP testing results separately. Studies describing signs and symptoms were assessed on the change in pre- and post-operative SCD signs and symptoms. Audiometric outcomes studied the effect of surgical repair on the change in ABG. The change in bone conduction threshold was noted as well. VEMP testing compared the pre- and post-operative thresholds in the different studies. The follow-up period, surgical approach, and method of SCD repair was extracted from the studies. In addition, all studies were assessed based on complications, recurrence rate and, in the studies using a middle fossa craniotomy approach, the non-dehiscent cases were also reviewed.

RESULTS

Retrieving studies

A total of 457 studies were retrieved based on the above mentioned search terms; 230 papers were found in PubMed and 227 papers were found in Embase. After removal of duplicates, 261 unique studies remained. By using the in- and exclusion criteria, we had 33 papers left after performing a search on title and abstract.

Table 2. Study assessment of studies on surgical outcomes of SCD

Study (year)	Number of operated ears	Study design	Relevance					Risk of Bias					
			Patients	Treatment	Symptoms	Outcome		Patient selection	Standardization (T)	Signs and symptoms Standardization (O)	Audio and VEMP testing Standardization (O)	Complete data	
						Audiometric testing	VEMP testing						Follow-up
Beyea et al 2012	16	RCS	●	●	●	○	○	-	●	●	○	-	●
Bogle et al 2013	20	RCS	●	●	●	○	○	4 months	●	●	●	-	○
Carey et al 2007	19	PCS	●	●	●	○	○	≥ 6 weeks	●	○	○	-	○
Hillman et al 2006	13	RCS	●	●	●	○	○	≥ 3 months	●	○	○	-	○
Lundy et al. 2011	37	RCS	●	●	●	○	○	≥ 3 months	●	●	○	-	●
Minor 2005	20	RCS	●	●	●	○	○	≥ 3 months	●	○	○	-	●
Nielsen et al 2012	33	RCS	●	●	●	○	○	≥ 3 months	●	○	○	-	●
Tavassolie et al. 2012	34	RCS	●	●	●	○	○	-	●	●	○	-	●
Mikulec et al. 2005	11	RCS	●	●	●	●	○	≥ 1 month	●	○	○	●	○
Zhao et al. 2012	11	RCS	●	●	●	●	○	≥ 3 months	○	○	○	○	●
Crane et al 2010	19	RCS	●	●	●	●	●	3 months	●	●	●	●	●
Saliba et al. 2013	28	PCS	●	●	●	●	●	≥ 2 months	●	●	●	●	○
Crane et al 2008	19	RCS	●	●	●	○	●	≥ 3 months	●	●	●	●	●
Welgampola et al. 2008	12	RCS	●	●	●	○	●	≥ 3 months	○	○	○	●	●
Nielsen et al 2013	38	RCS	●	●	○	●	●	≥ 3 months	●	○	-	●	○
Janky et al 2012	20	PCS	●	●	○	●	○	≥ 6 weeks	○	●	-	●	●
Limb et al. 2006	29	RCS	●	●	○	●	○	-	●	○	-	●	●
Ward et al. 2012	43	RCS	●	●	○	●	○	≥ 1 month	●	●	-	●	○
Agrawal et al 2009	42	RCS	●	●	○	○	○	≥ 6 weeks	●	●	-	●	○

Nineteen papers were found to be eligible, following the full-text screening and a cross-reference check in answering our clinical questions (Figure 1) [Agrawal et al., 2009; Beyea et al., 2012; Bogle et al., 2013; Carey et al., 2007; Crane et al., 2010; Crane et al., 2008; Hillman et al., 2006; Janky et al., 2012; Limb et al., 2006; Lundy et al., 2011; Mikulec et al., 2005; Minor, 2005; Nielsen et al., 2012; Nielsen et al., 2013; Saliba et al., 2013; Tavassolie et al., 2012; Ward et al., 2012; Welgampola et al., 2008; Zhao et al., 2012].

Number of operated ears: Number of ears included in each study that underwent surgical repair of SCD (superior canal dehiscence). *Study Design*: PCS = prospective cohort study; RCS = retrospective cohort study. *Directness of evidence*: Patients: ● = patients with superior canal dehiscence; ○ = other. Treatment: ● = superior canal dehiscence repair; ○ = other. Outcome symptoms: ● = change in SCD signs and symptoms; ○ = other. Outcome audiometric testing: ● = change in hearing results; ○ = other. Outcome VEMP testing: ● = change in VEMP thresholds; ○ = other. Follow-up: minimal follow-up duration in weeks or months. *Risk of bias* Patient selection: ● = description on how patients with SCD were selected and use of same patients pre- and post-operatively; ◐ = partly described on how patients with SCD were selected and use of same patients pre- and post-operatively; ○ = no description on how patients with SCD were selected or use of different patient groups pre- and post-operatively. Standardization (T) of treatment of SCD repair: ● = similar approach and method of dehiscence repair were used; ◐ = two or more approaches or methods of repair were used; ○ = not described which approach or method of repair was used. Standardization (O) of outcome is divided in signs and symptoms and audiometric and VEMP testing outcomes: ● = outcome was assessed in an objective manner; ◐ = outcome was assessed in a subjective manner, but similar in all patients; ○ = assessment of outcome was not described or was not performed similar in all patients. Completeness of outcome data for primary outcome: ● = <10% missing data; ◐ = <90% of operated patients were included in outcome assessment and reason of missing data was described; ○ = <90% of operated patients were included in outcome assessment, but no reason for missing data was described.

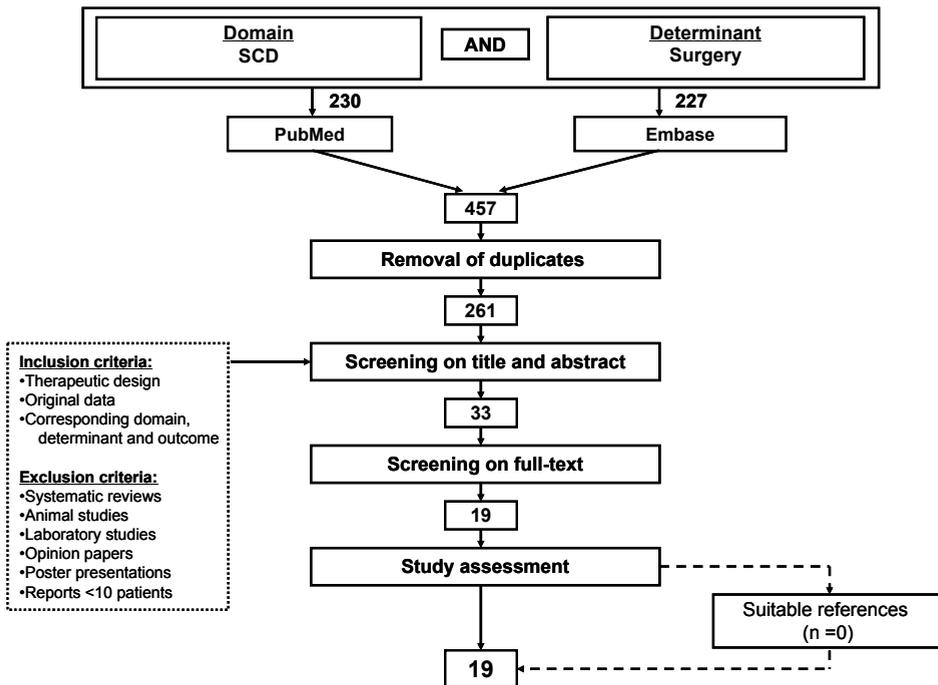


Figure 1. Flow chart for patient selection. All papers from the PubMed and Embase libraries up to October 31st 2013 were added. After removal of duplicates, screening on title and abstract by using the in- and exclusion criteria, screening on full-text and study assessment, 19 papers remained for critical appraisal.

Assessing studies

Of the final 19 papers we assessed on relevance and risk of bias, 14 papers reported surgical outcomes of improvement of signs and symptoms of SCD, 8 papers reported surgical outcomes on audiometric testing and 5 papers reported post-operative VEMP outcomes. One paper was excluded on relevance, since it did not describe outcomes on SCD signs and symptoms, audiometric testing or VEMP testing. The remaining 18 (out of 19) studies were included in the results section. No studies were excluded based on risk of bias (Table 2). Patient selection was unsatisfactory if different patients were used pre- and post-operatively. This was done in 2 studies. Patients that used two or more different methods of surgical approach or SCD repair had a moderately satisfactory outcome on treatment standardization. Because of the heterogeneity of data, no meta-analyses could be performed.

Patient Characteristics

An overview of patient characteristics is given in Table 3. In total surgery was performed on 422 ears. Twelve papers described characteristics on side of surgical repair and showed that 165 out of 313 (53%) of patients were operated on the left side and 149 out of 313 (47%) of patients were operated in the right side. Twelve studies described patients with bilateral SCD, and 90 out of the 286 (31%) patients included in those studies had bilateral SCD. Six of these studies described if the patients with bilateral SCD were symptomatic on both sides. Out of the 48 patients with bilateral SCD included in those six studies, 18 (38%) patients had bilateral symptomatic SCD. The average age of patients was 46 years, with a range of 15 to 93 years. Eleven studies described gender, showing 163 out of 288 (57%) females.

Signs and Symptoms

Fourteen of the nineteen studies described outcomes on signs and symptoms, either on change in signs and symptoms (11 studies) or change in questionnaire scores (3 studies), see Table 4. These studies showed the following pre-operative auditory signs and symptoms: hyperacusis (69%, range 57-89%), autophony (72%, range 44-100%), aural fullness (64%, range 38-93%) and tinnitus (54%, range 23-82%). The following pre-operative vestibular signs and symptoms were described: imbalance or chronic disequilibrium (63%, range 20-100%), sound-induced vertigo (77%, range 64-85%), pressure-induced vertigo (74%, range 68-80%), Tullio phenomenon (54%, range 24-72%) and pressure-induced vertigo either by Valsalva, or tragal pressure or Hennebert sign (50%, range 22-73%). The most common pre-operative auditory sign was autophony, and the most common vestibular sign was sound-induced vertigo.

Table 3. Patient Characteristics

Study (year)	Number of ears	Side Surgery		Side SCD		Age		Gender	
		Left	Right	Bil SCD	Bil Symptoms	Mean	Range	Female	Male
Beyea et al 2012	16	-	-	-	-	-	-	-	-
Bogle et al 2013	20	8	12	6	-	48*	36-80	14	6
Carey et al 2007	19	-	-	11	7	-	-	-	-
Crane et al 2010	19	11	8	7	1	48	29-66	9	10
Crane at al 2008	29	-	-	11	1	49	34-66	-	-
Hillman et al 2006	13	-	-	5	2	-	-	-	-
Janky et al 2012	20	10	10	-	-	47	28-61	-	-
Limb et al. 2006	19	-	-	4	-	44*	27-64	14	15
Lundy et al. 2011	37	16	21	10	-	56	35-93	26	11
Mikulec et al. 2005	11	10	1	4	-	39	33-57	2	9
Minor 2005	20	13	7	3	0	-	27-64	9	11
Nielsen et al 2012	33	14	19	11	-	43	15-73	22	11
Nielsen et al 2013	38	18	20	11	7	44	-	24	14
Saliba et al. 2013	28	17	11	7	-	44	27-60	13	15
Tavassolie et al. 2012	34	19	15	-	-	46	30-66	-	-
Ward et al. 2012	43	22	21	-	-	44	-	24	19
Welgampola et al. 2008	12	-	-	-	-	43	-	-	-
Zhao et al. 2012	11	7	4	-	-	52	31-76	6	4
Total	422	53%	47%	31%	38%	46	15-93	57%	43%

Overview of patient characteristics. The first column is the number of ears that underwent surgical repair of SCD (superior canal dehiscence). Twelve studies described side of SCD and surgery. Of the twelve studies that described the number of patients with bilateral SCD, six studies described the percentage of patients with bilateral SCD symptoms. Fourteen studies described the age of patients, the average age (and age range) is shown in the column, except for two studies with an *, indicating the median age. Eleven studies described the distribution between males and females. When no information on a characteristic was given, this is reported by "-". Bil = bilateral.

All studies (those using a middle fossa craniotomy (MFC) and transmastoid repair (TM)) reported an average initial improvement or complete resolution of symptoms in 96% (223/233) of patients (range between studies 91 to 100%). Seven studies also reported the number of patients who had total resolution of symptoms: of the 150 patients assessed from those studies, 107 patients had total resolution (72%, range between studies 40 to 93%). Most common observed post-operative signs and symptoms included: chronic imbalance/disequilibrium and tinnitus. Signs

Table 4. Overview of the change in pre- and post-operative signs and symptoms in twelve studies

Study	Pre-operative										Post-operative										
	Auditory					Vestibular					Auditory					Vestibular					
	Hyperacusis	Auto-phony	Ear Fullness	Tinnitus	Imbalance	Sound IV	Pressure IV	Tullio	Fistula sign	Number of included ears	Hyperacusis	Auto-phony	Ear Fullness	Tinnitus	Imbalance	Sound IV	Pressure IV	Tullio	Fistula sign	Total resolution	
Beyea 2012	-	44%	38%	50%	-	-	-	63%	32%	16	-	-	-	-	-	-	-	-	-	94%	-
Carey 2007	-	-	-	-	-	-	-	-	-	19	-	-	-	-	-	-	-	-	-	100%	-
Hillman 2006	-	-	-	23%	-	-	-	-	-	13	-	-	-	8%	-	-	-	-	-	93%	93%
Lundy 2011	-	54%	49%	-	100%	-	24%	22%	-	37	-	-	-	-	-	-	-	-	-	92%	78%
Mikulec 2005	-	45%	-	-	36%	-	64%	73%	-	11	-	-	-	-	27%	-	-	9%	9%	91%	55%
Minor 2005	60%	-	-	-	60%	85%	80%	70%	60%	20	-	-	-	-	-	-	-	-	5%	95%	75%
Nielsen 2012	-	76%	76%	58%	61%	64%	73%	52%	64%	33	-	0%	9%	18%	9%	0%	0%	0%	0%	100%	61%
Saliba 2013	57%	100%	93%	82%	89%	-	57%	46%	-	28	-	-	-	-	-	-	-	-	-	97%	-
Tavassolie 2012	89%	97%	-	81%	73%	83%	68%	72%	53%	34	0%	9%	3%	3%	12%	0%	0%	-	-	97%	62%
Welgampola 2008	-	-	-	-	-	-	-	-	-	12*	-	0%	-	0%	8%	0%	0%	-	-	92%	-
Zhao 2012	-	90%	-	30%	20%	-	30%	-	-	10	-	0%	-	20%	40%	-	-	0%	-	100%	40%
Total (average)	69%	72%	64%	54%	63%	77%	74%	54%	50%	233	69%	72%	64%	54%	63%	77%	74%	54%	50%	223/233 (96%)	107/150 (72%)

The pre- and post-operative signs and symptoms are divided in auditory and vestibular signs and symptoms. For each separate signs or symptom, the percentage of patients presenting with this symptom is shown. Imbalance = chronic imbalance or disequilibrium; IV = induced vertigo; Tullio consists of sound induced vertigo e.g. with the use of a Barony noise box, Fistula sign consists of Valsalva manoeuvre, tragal pressure or pneumatic otoscopic pressure. If multiple fistula signs were reported, the sign with the highest percentage is reported in the table. The column with improvement shows the average initial improvement on post-operative signs and symptoms. The last column shown the percentage of patients with total resolution of symptoms. Recurrence of symptoms is not taken into account in this table. * Different pre- and post-operative groups of patients are used, therefore only the post-operative results of the patients are shown (since the pre-operative results relate to different patients). When no information on a sign was given, this is reported by “-”.

and symptoms that were observed less commonly were autophony, sound- and pressure-associated dizziness, Tullio signs and Hennebert sign.

Three studies used objective measures to assess the change in dizziness and autophony symptoms [Bogle et al., 2013; Crane et al., 2010; Crane et al., 2008], of which one study found a significant improvement in dizziness handicap inventory (DHI) score [Crane et al., 2008], while the other study did not find a significant improvement in DHI [Bogle et al., 2013]. A separate study found a decrease in autophony index of 89% in 19 patients following surgical repair [Crane et al., 2010].

Audiometric testing results

Table 5 shows the audiometric testing results. Eight studies assessed the effect of SCD surgery on the change in ABG. The average pre-operative ABG changed from 18 dB (range between studies 14 to 26 dB) to an average of 11 dB (range between

Table 5. Pre- and post-operative audiometric testing

Study	Number surgeries	Pre-operative							Post-operative							Significance		
		Air-Bone Gap					Average ABG	PTA	Speech	Air-Bone Gap					Average ABG		PTA	Speech
		250	500	1000	2000	4000				250	500	1000	2000	4000				
Crane 2010	18	-	-	-	-	-	26	-	-	-	-	-	-	-	16	-	-	-
Janky 2012*	20^	28	15	14	5	8	16	-	-	13	5	7	5	6	8	-	-	No
Limb 2006	19^	20	17	13	4	3	14	-	97%	24	13	17	7	5	15	-	97%	No
Mikulec 2005	11^	28	23	19	2	4	18	-	-	13	10	10	1	6	9	-	-	-
Niesten 2013	34	28	19	15	7	5	17	-	-	12	6	8	5	3	8	-	-	Yes
Saliba 2013	28	25	16	12	-	-	18	22	90%	10	2	7	-	-	6	16	92%	Yes
Ward 2012	43	-	-	-	-	-	16	8	99%	-	-	-	-	-	8	16	93%	Yes
Zhao 2012	11	26	24	20	14	22	21	35	-	25	24	20	14	23	21	36	-	-

Eight studies reported on the change in pre- and post-operative hearing loss. The average ABG was calculated for the available frequencies. If data on the ABG was available on all frequencies, the average ABG from 250 to 2000 Hz was calculated. ABG = air-bone gap; PTA = pure tone average; Speech = speech discrimination scores. Significance: yes = studies reported a significant change in ABG, no = studies reported no significant change in ABG. When no information on a variable was given, this is reported by “-”. In the study marked with *, different groups are used pre- and post-operatively. ^ = data is extracted from a figure by two of the authors separately.

studies 6 dB to 21 dB) following surgical repair. Three studies reported that this improvement in magnitude of the ABG was significant, one study reported a non-significant improvement in magnitude of the ABG and one study reported no significant change in ABG. Three studies did not report significant, two of these studies showed a post-operative ABG improvement and one study showed stable ABG thresholds.

Mean bone conduction loss was reported in three studies, which reported statistical difference (deterioration) between bone conduction thresholds pre- and post-operatively at one or more frequencies [Limb et al., 2006; Niesten et al., 2013; Ward et al., 2012]. Two studies showed a deterioration of bone conduction thresholds of 10 dB or more following surgical repair in 25-33% of patients [Niesten et al., 2013; Ward et al., 2012]. In addition, four studies described sensorineural hearing loss in one or two patients following primary SCD repair [Janky et al., 2012; Lundy et al., 2011; Mikulec et al., 2005; Welgampola et al., 2008].

Four studies reported sensorineural hearing loss following SCD repair in several patients that underwent previous ear surgery or previous SCD repair [Limb et al., 2006; Mikulec et al., 2005; Niesten et al., 2013; Ward et al., 2012]. In these patients increases in bone conduction thresholds and/or lower speech discrimination scores were found.

VEMP testing results

Five studies reported outcomes on the change in VEMP thresholds (Table 6). All studies used different cut-off points for an abnormal threshold, which makes it hard to compare these studies with each other, but low pre-operative thresholds are seen in 89% [Crane et al., 2008] up to 100% [Crane et al., 2010; Welgampola et al., 2008] of patients. Overall, an increase (or normalization) in VEMP thresholds in patients following surgical repair was found. These five studies had three different outcome measures (nHL, pSP, SPL). In normal hearing level (nHL) the mean pre-operative thresholds ranged from 61 to 73 dB nHL [Crane et al., 2008; Crane et al 2010; Saliba et al., 2013] and the mean post-operative VEMP thresholds ranged from 80 to 88 dB nHL [Crane et al., 2010; Saliba et al., 2013]. Low post-operative VEMP thresholds in patients with recurrence of symptoms were described in two studies [Niesten et al., 2013; Welgampola et al., 2008].

Non-dehiscent cases

Five studies reported a total of eight cases that had a SSC that appeared to be non-dehiscent during surgical repair. Intra-operative non-dehiscence can only

Table 6. Pre- and post-operative VEMP testing

Study	Number of ears	Outcome measure	Pre-operative		Post-operative		Significance
			Mean	Abnormal thresholds	Mean	Abnormal thresholds	
Crane 2010	8	nHL	69 (55-75)	100%	88 (75-100)	13%	-
Crane 2008	11	nHL	73 (60-90)	89%	-	9%	-
Nielsen 2013	13	pSP	97 (83-123)	-	121 (83-148)	-	Yes
Saliba 2013	24	nHL	61 (50-80)	96%	80 (65-90)	54%	Yes
Welgampola 2008*	12	SPL	84	100%	110	-	Yes

Number of ears = number of ears with pre- and post-operative cervical vestibular-evoked myogenic potential (cVEMP) thresholds. All results are given for the air conducted cVEMP thresholds. These five studies used three different outcome measures for the VEMP thresholds: nHL = normal hearing level; pSP = peak sound pressure; SPL = sound pressure level. Abnormal thresholds = the percentage of patients with a thresholds lower than the cut-off limit as defined by each institution. The cut-off values for normal and abnormal differ between institutions and even within an institution over time. For Saliba et al, outcomes are reported in dB, it is assumed that they used nHL as well. In the study marked with *, different groups are used pre- and post-operatively.

be determined in studies using the middle fossa craniotomy approach, since this approach allows the surgeon to directly view and repair the dehiscent area. In two of the eight patients, there was no attempt to repair the canal and thus no change in symptoms [Hillman et al., 2006]. In another two patients the blue-lined SSC was resurfaced, with no change in symptoms in one patient [Mikulec et al., 2005], while the other patient described improvement of symptoms [Nielsen et al., 2012]. In the final four patients the canal was opened and plugged. Two of these patients reported improvement of symptoms [Tavassolie et al., 2012], but the results for the other two patients were not described [Carey et al., 2007].

Recurrence of SCD

Recurrence of subjective SCD symptoms is described in five different studies (Table 7) [Carey et al., 2007; Hillman et al., 2006; Minor, 2005; Nielsen et al., 2012; Tavassolie et al., 2012]. All five studies used a MFC approach for surgical repair. Four of these studies reported recurrence of symptoms following plugging of the SCD and four studies reported recurrence following resurfacing of the defect (in three studies, outcomes on both plugging and resurfacing was described). In addition, three studies included patients that had undergone previous SCD repair, but they did not report on the recurrence of symptoms in the patients they describe in these studies [Limb et al., 2006; Ward et al., 2012; Welgampola et al., 2008]. In the remaining nine studies no information of recurrence of symptoms was provided.

Table 7. Overview of method of surgical repair, recurrence rate and adverse events

Study (year)	Surgery				Recurrence	Adverse events
	Approach	plugging	Resurfacing	Occlusion		
Beyea et al 2012	TM	-	-	16	-	2 pts small dural tear
Bogle et al 2013	TM+MC	-	-	20	-	3 pts BPPV
Carey et al 2007	MFC	18	1	-	0/19	1 pt epidural hematoma, 1 pt cellulites, 1 pt transient diabetes insipidus
Crane et al 2010	MFC	19	-	-	-	-
Crane at al 2008	MFC	19	-	-	-	-
Hillman et al 2006	MFC	-	13	-	1/13	-
Janky et al 2012	MFC	20	-	-	-	-
Limb et al. 2006	MFC	13	6	-	2/29*	-
Lundy et al. 2011	TM+MC	-	-	37	-	-
Mikulec et al. 2005	MFC	10	1	-	-	1 pt small seroma, 1 pt small hematoma, 2 pts BPPV
Minor 2005	MFC	9	11	-	1/9, 4/11	-
Nielsen et al 2012	MFC, TM	32	1	-	3/33	2 pts facial paralysis, 1 pt epidural hematoma, 4 pts BPPV
Nielsen et al 2013	MFC, TM	37	1	-	-	-
Saliba et al. 2013	MFC	28	-	-	-	-
Tavassolie et al. 2012	MFC	34	-	-	1/34	-
Ward et al. 2012	MFC	43	-	-	4/43*	-
Welgampola et al. 2008	MFC	12	-	-	2/12*	-
Zhao et al. 2012	TM	11	-	-	-	1pt BPPV

In the second column the method of surgical repair is described, MFC = middle fossa craniotomy approach; TM = transmastoid approach, MC = mini craniotomy approach. The next columns describe the method of SCD repair divided in plugging, resurfacing or occlusion of the dehiscence. Two studies used a combined mastoid and tegmen mini-craniotomy approach. Recurrence rates are described in 5 studies following surgical repair. Studies with * mention how many of the included patients are a revision surgery, they do not mention how many patients in the follow-up period of their study had recurrence of symptoms. Adverse events are described in six different studies, pt = patient; pts = patients, BPPV = benign paroxysmal positional vertigo. When no information was given, this is reported by “-”.

In 119 patients absence or presence of recurrence of symptoms is described. Ten of these patients (8.4%) presented with recurrence of symptoms. Recurrence was reported in 5/93 patients (5.4%) following SCD plugging [Carey et al., 2007; Minor, 2005; Nielsen et al., 2012; Tavassolie et al., 2012] and 5/26 (19.2%) patients following SCD resurfacing [Carey et al., 2007; Hillman et al., 2006; Minor, 2005]. Reported adverse events are also shown in Table 7.

DISCUSSION

Since SCD had first been described, multiple studies have reported on SCD outcomes following surgical repair in relatively small patient cohorts. This systematic review shows large heterogeneity in outcome measures and methods used in studies assessing SCD in ten or more patients. Because of this heterogeneity, no hard conclusions can be drawn, though in general, an improvement or resolution of SCD signs and symptoms, (partial) closure of the ABG and normalization of VEMP threshold is seen in most patients undergoing primary SCD repair. We found that autophony, sound- and pressure-associated dizziness showed good post-operative symptom improvement, while chronic imbalance and tinnitus were found to improve less in patients post-operatively. Due to the chance of complications and recurrence of symptoms, the risks and benefits of surgery must be considered in each patient separately; best post-operative symptom relief is expected in those patients with autophony, sound- and/or pressure-associated dizziness, therefore patients with these pre-operative complaints are likely to be good surgical candidates.

Overall, a high post-operative improvement or resolution of SCD signs and symptoms was found in the reviewed literature. Symptoms such as autophony, sound- and pressure-associated dizziness were observed to show good post-operative symptom relief. This indicated that patients with autophony, sound and/or pressure-associated dizziness as chief complaint are expected to show better post-operative symptom relief. Nevertheless, similar post-operative symptoms remaining in some patients following surgical repair were reported by the included studies (using MFC approach as well as TM approach), including mild chronic imbalance, aural fullness and tinnitus. Post-operative imbalance might be explained by vestibular hypofunction, found to be present in the weeks following surgical repair [Agrawal et al., 2009], however, this is likely to improve in the long-term follow-up period. In the first post-operative days to weeks, aural fullness may be explained due to a hemotympanum or middle ear effusion [Ward et al., 2012]. Improvement of the aural fullness would be expected after the middle ear problems have dissipated. Pulsatile tinnitus is often seen in patients pre-operatively, theoretically because the dural pulsations enter the labyrinth through the dehiscence. Post-operatively, it could be expected that the tinnitus would improve since the dehiscence is repaired, however tinnitus remained in a substantial amount of patients. One study reported vertigo and/or oscillopsia relieve in 100% of patients, however, this study did not provide any details on this number or reports on the pre-and post-operative signs and symptoms or on other SCD signs and symptoms [Carey et al., 2007].

A previous review reported that resurfacing was less effective in relieving SCD signs and symptoms than plugging or capping of the superior canal [Vlastarakos et al., 2009]. The results in this literature study differ from Vlastarakos et al., since we found an improvement on sign and symptom relief following resurfacing, plugging and capping of the SCD. The number of included studies and thus patients might help explain for these differences.

The large spread in reported results necessitates a more standardized manner to objectively describe SCD repair outcomes. We have developed a SCD questionnaire (Figure 2), which includes the most common SCD signs and symptoms. Currently, this questionnaire is in the process of validation.

Although a pre-operative ABG is often seen in SCD patients, and this ABG can even be a pitfall in differentiating with middle ear abnormalities such as otosclerosis, we do not consider hearing loss as an indication for SCD surgery. In addition to the (partial) closure of the ABG, an overall mild (high frequency) sensorineural hearing loss, without affecting speech discrimination, is described. This mild bone conduction loss is similar to outcomes described in different otologic studies (e.g., following stapes surgery [Vincent et al., 2006]), which may be explained by a loss of perilymph that causes the mild sensorineural hearing loss to exist. Sensorineural hearing loss is described in patients who have undergone previous otologic surgeries before their SCD repair. The exact mechanism remains unclear, but it can be theorized that damage to the inner ear causes this sensorineural hearing loss.

There is a striking difference in outcome measures of VEMP thresholds. In addition, different cut-off values are used, even over time at the same institution [Crane et al., 2010; Crane et al., 2008]. These differences in VEMP testing methods and different cut-off points make it challenging to compare VEMP threshold outcomes among studies. All studies did show a “normalization” of the VEMP thresholds post-operatively. VEMP testing is a relatively new vestibular test, which was upcoming in the nineties and one of the pioneers were Colebatch and Halmagyi [Colebatch and Halmagyi, 1992]. In 1994 they already described abnormally low thresholds of click-evoked responses in patients with Tullio phenomenon [Colebatch et al., 1994]. Awareness of SCD and VEMP testing was upcoming more or less in the same time period and one of the first to describe VEMP testing in SCD patients was Brantberg et al [Brantberg et al., 1999]. They found low VEMP thresholds in SCD patients, especially in the low frequency range. Since the upcoming of VEMP testing, multiple outcomes on VEMP testing in SCD patients have been reported. Various institutions use the VEMP test, but disadvantages such as lack of standardization (for e.g.

Superior Semicircular Canal Dehiscence Questionnaire						
Signs and symptoms	Questions	Answer:	If yes: indicate left, right or both			
Second event	When did your symptoms start?					
	Did your symptoms start suddenly?	Yes No	Left	Right	Both	
	If sudden, was there head injury? Illness? Loud sound? Heavy lifting or exertion?	Yes No	Left	Right	Both	
History	Do you have a history of prior ear surgery / infections	Yes No	Left	Right	Both	
Aural fullness	Do you have ear blockage or ear fullness?	Yes No	Left	Right	Both	
Hyperacusis	• Do you hear your own voice echo in your ear?	Yes No	Left	Right	Both	
	• Do you hear your footsteps?	Yes No	Left	Right	Both	
	• Do you hear your own eyeballs	Yes No	Left	Right	Both	
	• Does brushing your hair or shaving sound too loud?	Yes No	Left	Right	Both	
	• Do sounds seem too loud?	Yes No	Left	Right	Both	
Hearing loss	Do you have hearing loss?	Yes No	Left	Right	Both	
Vertigo	Do you have vertigo / dizziness / spinning sensation?	Yes No	Left	Right	Both	
	• Do loud sounds cause dizziness or vertigo?	Yes No	Left	Right	Both	
	• Does blowing your nose/sneezing/coughing cause dizziness/vertigo?	Yes No	Left	Right	Both	
	• Does heavy lifting or straining (e.g. bathroom) cause dizziness/vertigo?	Yes No	Left	Right	Both	
	• Does exercise or physical activity cause dizziness/vertigo?	Yes No	Left	Right	Both	
Chronic imbalance	Do you have a feeling of imbalance?	Yes No	Left	Right	Both	
Tinnitus	Do you hear a ringing sound / tinnitus in the ear?	Yes No	Left	Right	Both	
	If yes to tinnitus, is this sound timed to your heartbeat?	Yes No	Left	Right	Both	
Migraine	Do you suffer from migraines?	Yes No	Left	Right	Both	
	Do you have a history of seizures?	Yes No	Left	Right	Both	
Signs	Tullio's phenomenon? Subjective/objective?	Yes No	Left	Right	Both	
	Hennebert's phenomenon? Subjective/objective?	Yes No	Left	Right	Both	
	Does tragal compression cause dizziness/vertigo? Subjective/objective?	Yes No	Left	Right	Both	
	Does Valsalva maneuver cause dizziness/vertigo? Subjective/objective?	Yes No	Left	Right	Both	

Figure 2. Superior Semicircular Canal Dehiscence Questionnaire.

threshold cut-off values or reporting measures such as nHL, SPL, pSP), differences in muscle mass and fatigue are not taken into account and background noise can disturb outcome measures. Despite these disadvantages, VEMP testing has been shown to be helpful in diagnosing SCD syndrome and in helping to determine in patients with bilateral SCD and post-operative symptoms, if these symptoms are due to recurrence of symptoms in the operated ear, or (unmasking of) symptoms in the contralateral SCD ear. Standardization of VEMP testing would make it easier to compare pre- and post-operative VEMP outcome between institutions.

Studies using the MFC have a clear view of the bony covering of the SSC and thus of the dehiscence. Five studies have described a thin, but intact, blue-lined SSC instead of a frankly dehiscent SSC. These findings show the difficulty in surgical diagnosis of SCD diagnosis. A false positive SCD diagnosis on the CT scan can be due to the volume averaging effect: the SSC can look dehiscent on a temporal bone CT, while a thin bony covering actually remains. A recent study described outcomes in ten patients with a near dehiscent SSC [Ward et al., 2013] and showed an improvement of SCD signs and symptoms following SCD resurfacing or plugging, similar to the studies included in this review which showed that resurfacing or opening and plugging the thin bony covering could relieve SCD signs and symptoms.

Recurrence of SCD signs and symptoms was described in 8.4% of patients. However, 8.4% is a minimum percentage of patients in which SCD recurred, since multiple papers reviewed included patients with previous SCD repair, either from their institution or from an outside institution [Limb et al., 2006; Ward et al., 2012; Welgampola et al., 2008]. Recurrence in patients that underwent SCD resurfacing was reported more frequently as compared to recurrence following plugging of the SCD. This observation is in line with the study from Vlastarakos et al, which reported that resurfacing was (significantly) less effective than plugging or capping [Vlastarakos et al., 2009]. However, it is important to note that multiple studies did not report their recurrence rate, therefore these results are based on a small number of studies and no hard conclusions can be drawn.

Multiple adverse events of SCD repair have been reported, most of which were only temporary and improved in time. However, the risks and benefits of surgical repair must be considered on a case-by-case basis.

Surgical approaches

Most studies performed the MFC approach. The major advantage of a MFC approach is enhanced visualization of the SSC defect, allowing for direct repair. The main disadvantage is that it involves invasive surgery with retraction of the dura and manipulation of the defect. The TM approach has been used in a smaller number of patients. The advantages of a TM approach are that the approach is less invasive by avoiding a craniotomy and temporal lobe retraction, no manipulation of the defect, and the approach is familiar to many otolaryngologists. In addition, if the SSC defect is located more medial, beyond a prominent ridge of tegmen (data not published at time of submission), and/or in close approximation of the superior petrosal sinus [McCall et al., 2011], it may be more challenging to visualize through a MFC approach using traditional binocular microscopy. A TM approach allows repair of the defect without direct visualization. There are two different methods of SCD repair when using a TM approach. The first is by making two labyrinthotomies in both limbs of the SSC and plugging both labyrinthotomies. The defect of the SSC remains untouched, but shunting of energy through the dehiscence is not possible anymore, since both limbs of the SSC are plugged. The second method of SCD repair by using a TM approach is to remove a small area of tegmen in close approximation of the arcuate eminence of the SSC, which allows elevation of the dura to create space for placement of a cartilage cap over the SCD. The location of the removal of a small area of tegmen is determined pre-operatively with the use of a CT-scan. Both methods of TM repair do not allow for visualization of the defect, which prevents direct manipulation, but which has as a disadvantage that the SSC is capped without seeing the defect. In addition, the TM approach is more challenging in ears with a low-lying tegmen, since the space to reach the limbs of the SSC is limited in patients with such topographical distinctions, with the risk of causing damage to the tegmen and/or dura [Beyea et al., 2012]. The report on outcomes either through a MFC or a TM approach varies between studies, and thus comparison between different surgical approaches and methods of repair is yet another challenge. Newer techniques are also developing. A modification to the MFC approach has been described by introducing the endoscope [Carter et al., 2013].

Limitations

This systematic literature review compared the post-operative change of SCD signs and symptoms, the change in ABG and VEMP thresholds. Due to the large variation in reported outcomes, no reliable meta-analysis could be performed. The reported outcomes of the different studies (approaches and methods of repair) were mostly descriptive. In addition, almost all studies were retrospective,

diminishing the quality of results since retrospective studies have a larger risk of bias and missing or incomplete data. Prospective studies can better objectify the post-operative change in signs and symptoms. However, none of the prospective studies compared the outcomes of the different surgical methods and approaches. Furthermore, most studies used the MFC approach and plugging of the SCD, and thus it is challenging to draw definitive conclusions on outcomes comparing MFC versus TM approach and plugging versus resurfacing.

CONCLUSION

Surgical repair of SCD is associated with improvement of auditory and/or vestibular signs and symptoms in the majority of patients as well as reversal of diagnostic indicators such as the air bone gap and low cVEMP thresholds. We observed that tinnitus and chronic imbalance showed less improvement following SCD repair, while autophony and sound- and pressure induced vertigo showed good post-operative improvement, indicating that patients with these symptoms as chief complaint would show better post-operative symptom relief. Large heterogeneity in 1) description of surgical repair methods and 2) reporting of outcomes was found among the studies included in this analysis. A more standardized reporting approach utilizing prospective data collection is needed to better understand the long-term outcomes in a larger cohort of patients who have undergone SCD repair.

REFERENCES

- Agrawal Y**, Migliaccio AA, Minor LB, Carey JP: Vestibular hypofunction in the initial post-operative period after surgical treatment of superior semicircular canal dehiscence. *Otol Neurotol* 2009;30:502-506.
- Beyea JA**, Agrawal SK, Parnes LS: Transmastoid semicircular canal occlusion: A safe and highly effective treatment for benign paroxysmal positional vertigo and superior canal dehiscence. *Laryngoscope* 2012;122:1862-1866.
- Bogle JM**, Lundy LB, Zapala DA, Copenhaver A: Dizziness handicap after cartilage cap occlusion for superior semicircular canal dehiscence. *Otol Neurotol* 2013;34:135-140.
- Brantberg K**, Bergenius J, Tribukait A: Vestibular-evoked myogenic potentials in patients with dehiscence of the superior semicircular canal. *Acta Otolaryngol* 1999;119:633-640.
- Carey JP**, Migliaccio AA, Minor LB: Semicircular canal function before and after surgery for superior canal dehiscence. *Otol Neurotol* 2007;28:356-364.
- Carter MS**, Lookabaugh S, Lee DJ: Endoscopic-assisted repair of superior canal dehiscence syndrome. *Laryngoscope* 2014;124(6):1464-8.
- Colebatch JG**, Halmagyi GM: Vestibular-evoked potentials in human neck muscles before and after unilateral vestibular deafferentation. *Neurology* 1992;42:1635-1636.
- Colebatch JG**, Rothwell JC, Bronstein A, Ludman H: Click-evoked vestibular activation in the tullio phenomenon. *J Neurol Neurosurg Psychiatry* 1994;57:1538-1540.
- Crane BT**, Lin FR, Minor LB, Carey JP: Improvement in autophony symptoms after superior canal dehiscence repair. *Otol Neurotol* 2010;31:140-146.
- Crane BT**, Minor LB, Carey JP: Superior canal dehiscence plugging reduces dizziness handicap. *Laryngoscope* 2008;118:1809-1813.
- Higgins J**, Green S: *Cochrane handbook for systematic reviews of interventions version 5.1.0* The Cochrane Collaboration 2011;www.cochrane-handbook.org.
- Hillman TA**, Kertesz TR, Hadley K, Shelton C: Reversible peripheral vestibulopathy: The treatment of superior canal dehiscence. *Otolaryngol Head Neck Surg* 2006;134:431-436.
- Janky KL**, Zuniga MG, Carey JP, Schubert M: Balance dysfunction and recovery after surgery for superior canal dehiscence syndrome. *Arch Otolaryngol Head Neck Surg* 2012;138:723-730.
- Limb CJ**, Carey JP, Srireddy S, Minor LB: Auditory function in patients with surgically treated superior semicircular canal dehiscence. *Otol Neurotol* 2006;27:969-980.
- Lundy L**, Zapala D, Moushey J: Cartilage cap occlusion technique for dehiscent superior semicircular canals. *Otol Neurotol* 2011;32:1281-1284.
- McCall AA**, McKenna MJ, Merchant SN, Curtin HD, Lee DJ: Superior canal dehiscence syndrome associated with the superior petrosal sinus in pediatric and adult patients. *Otol Neurotol* 2011;32:1312-1319.

Mikulec AA, Poe DS, McKenna MJ: Operative management of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:501-507.

Minor LB: Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:1717-1727.

Minor LB, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998;124:249-258.

Modugno G, Brandolini C, Savastio G, Ceroni AR, Pirodda A: Superior semicircular canal dehiscence: A series of 13 cases. *ORL J Otorhinolaryngol Relat Spec* 2005;67:180-184.

Nielsen ME, McKenna MJ, Grolman W, Lee DJ: Clinical factors associated with prolonged recovery after superior canal dehiscence surgery. *Otol Neurotol* 2012;33:824-831.

Nielsen ME, McKenna MJ, Herrmann BS, Grolman W, Lee DJ: Utility of cvemps in bilateral superior canal dehiscence syndrome. *Laryngoscope* 2013;123:226-232.

Saliba I, Maniakas A, Benamira LZ, Nehme J, Benoit M, Montreuil-Jacques V: Superior canal dehiscence syndrome: Clinical manifestations and radiologic correlations. *Eur Arch Otorhinolaryngol* 2013, Epub ahead of print.

Tavassolie TS, Penninger RT, Zuniga MG, Minor LB, Carey JP: Multislice computed tomography in the diagnosis of superior canal dehiscence: How much error, and how to minimize it? *Otol Neurotol* 2012;33:215-222.

Vincent R, Sperling NM, Oates J, Jindal M: Surgical findings and long-term hearing results in 3,050 stapedotomies for primary otosclerosis: A prospective study with the otology-neurotology database. *Otol Neurotol* 2006;27:S25-47.

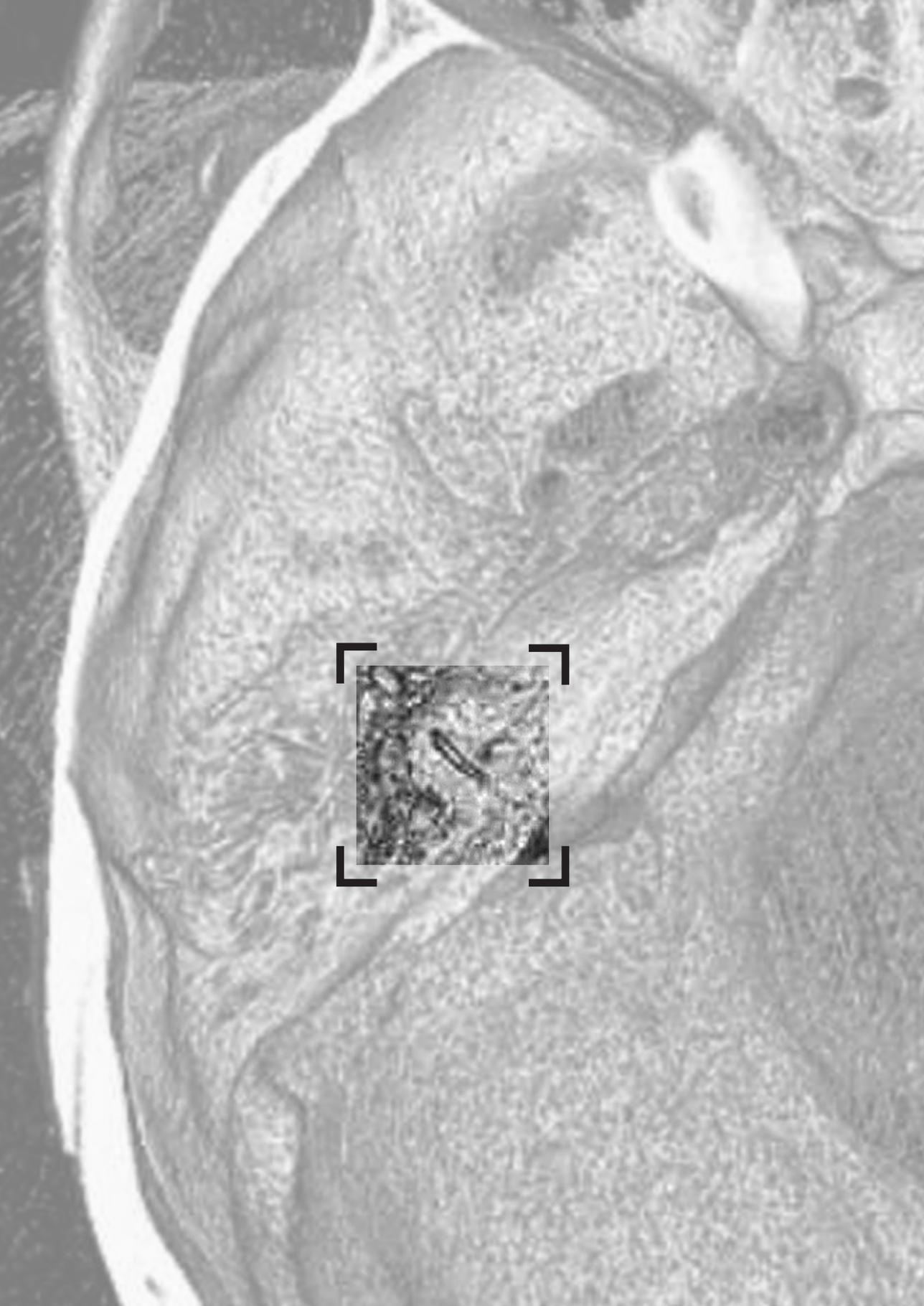
Vlastarakos PV, Proikas K, Tavoulari E, Kikidis D, Maragoudakis P, Nikolopoulos TP: Efficacy assessment and complications of surgical management for superior semicircular canal dehiscence: A meta-analysis of published interventional studies. *Eur Arch Otorhinolaryngol* 2009;266:177-186.

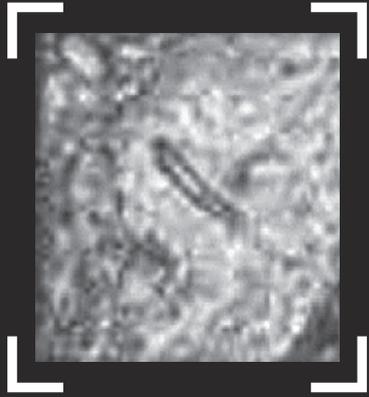
Ward BK, Agrawal Y, Nguyen E, Della Santina CC, Limb CJ, Francis HW, Minor LB, Carey JP: Hearing outcomes after surgical plugging of the superior semicircular canal by a middle cranial fossa approach. *Otol Neurotol* 2012;33:1386-1391.

Ward BK, Wenzel A, Ritzl EK, Gutierrez-Hernandez S, Della Santina CC, Minor LB, Carey JP: Near-dehiscence: Clinical findings in patients with thin bone over the superior semicircular canal. *Otol Neurotol* 2013;34:1421-1428.

Welgampola MS, Myrie OA, Minor LB, Carey JP: Vestibular-evoked myogenic potential thresholds normalize on plugging superior canal dehiscence. *Neurology* 2008;70:464-472.

Zhao Y, Somers T, van Dinther J, Vanspauwen R, Husseman J: Transmastoid repair of superior semicircular canal dehiscence. *Journal of Neurological Surgery* 2012;73:225-229.





Chapter 5

Discussion and Summary

DISCUSSION AND SUMMARY

This thesis has focused on the evaluation and management of superior canal dehiscence (SCD) and examined the outcomes following surgical repair. We have explored unresolved issues regarding the variability in clinical presentation of SCD using a human temporal bone model as well as a large cohort of patients with SCDS.

We answered questions regarding the effect of length and location of the dehiscence. We found that a larger SCD and a location closer to the ampullated end of the superior semicircular canal (SSC) appeared to correspond with auditory signs and symptoms, a larger air- bone gap (ABG) and lower cervical vestibular-evoked myogenic potential (cVEMP) thresholds. This can partially help explain why patients with SCD signs and symptoms and radiologically confirmed anatomic SCD present with different results and show different outcomes on diagnostic testing. The clinical findings that a larger SCD corresponds with a larger ABG and that the location of the SCD does not influence the magnitude of the ABG are in accordance with the results from our human cadaveric temporal bone model. In addition, we found in our temporal bone model a large spread in hearing loss for similar SCD sizes between ears. This observation supports our clinical findings that the magnitude of the ABG does vary among patients with bony defects of the superior canal that are similar in size.

We determined the management of patients with bilateral SCD. In patients with bilateral SCD, lateralization of tuning fork testing, the size of the ABG and VEMP thresholds help to determine the more affected ear. Comparison of pre- and post-operative signs and symptoms showed an overall reduction following surgical repair of the dehiscence. Post-operative audiologic testing demonstrates a normalization of the ABG and cVEMP thresholds. However, decreased bone-conduction sensitivity and risk of surgical complications were also found. The decreased bone-conduction sensitivity was likely due to two different mechanisms: low-frequency changes likely due to mechanical effects of plugging the dehiscence and high-frequency effects due to sensorineural hearing loss (SNHL). In patients with post-operative recurrence of symptoms (e.g. sound- and pressure-associated dizziness), VEMP thresholds are found to be helpful in diagnosing its cause. This testing helps to discriminate between a recurrence and persistence of the SCD in the surgically repaired ear and unmasking of symptoms in the contralateral SCD ear.

Our systematic review of the literature revealed a large heterogeneity on reporting of the surgical outcomes. We conclude that there is a need for more prospective data reporting which would ultimately help us to provide better patient counseling and surgical planning.

Methodological considerations per chapter

The methodological design of clinical studies greatly influences the risk of introducing bias and thereby the value of the research findings. Healthcare studies face numerous challenges influencing the methodological considerations. The goal of medical research is improvement of health care. Economics have an important role in choice of study design, since experimental studies, such as large clinical trials, are often associated with high costs and funding is not always available. Certain diseases or syndromes are rare, thus only a small number of patients may be available for research. Thus choice of study design can be influenced by disease prevalence. For example observational studies might be favoured above experimental studies when a limited number of patients are available. Multiple factors influence the methodological considerations in medical research and for this reason we critically appraised the following chapters.

In this thesis a relatively large cohort of patients with SCD syndrome is studied for which various methods are included; retrospective studies, prospective studies, a systematic review of literature and human cadaveric temporal bone studies. For each of the above-described methods, a different level of evidence accounts and the advantages and disadvantages of each of these methods and study designs will be discussed below.

SCD has an estimated prevalence of 0.5 to 2 percent of patients with a thin or dehiscent SSC as described in a temporal bone study [Carey et al., 2000]. SCD was first described 16 years ago [Minor et al., 1998], and up to time of writing many clinical questions remain unanswered. Clinical relevant questions need to be answered with the best evidence available and since this is a relatively new and uncommon syndrome, many clinical questions can be addressed with retrospective studies. In chapter 4.1 and 4.2 we performed a retrospective review on surgical outcomes in patients undergoing SCD repair between 2000 and 2011. These studies were performed to help us determine the more symptomatic ear in patients with bilateral SCD prior to surgical repair and to assess which factors might influence the duration of the recovery period following SCD repair. Both retrospective studies on surgical outcomes (chapter 4.1 and 4.2) have a level of evidence of 4 [Phillips, 2009]. One of the disadvantages of retrospective observational studies is that the

chance on bias and missing data is higher than in prospective or experimental studies. A bias is “a systematic error in the design, conduct or analysis of a study that results in a mistaken estimate of an exposure’s effect on the risk of disease” [Schlesselman and Stolley, 1982].

The limitations of these studies are found in the risk of information bias and selection bias. Information bias can be present due to interviewer or reporting bias. For example the patients undergoing surgical repair were seen in clinic by four different otolaryngology attendings, all logging information on pre- and post-operative SCD signs and symptoms in various ways. This induces the risk of information bias. The surgeons were not blinded for the intervention since they performed the surgical repair, which could have also influenced the post-operative reporting of outcomes. The risk of information bias was reduced for the audiometric and VEMP testing results, since these data were collected through a standardized protocol performed by other clinicians than the surgeon. Selection bias can be present in the inclusion of patients: a study design such as a randomized controlled trial (RCT) can prevent selection bias. Due to the retrospective assessment of clinical data in these two studies, a RCT design was not possible. To minimize selection bias, we have clearly defined the inclusion criteria – including all eligible patients who underwent consecutive SCD surgical repair from 2000 until 2011. Selection bias can also be present due to loss to follow-up. Follow-up duration varied among the patients, which could possibly bias results. For example, if a patient experiences recurrence of symptoms and presents at a different clinic, results can look more favourable. Overall, we had a significant time to follow-up, minimizing selection bias due to loss to follow-up.

Missing data is common in retrospective studies, since the data is collected for other purposes than the study outcome [Burton and Altman, 2004]. Non-random missing data may lead to possible bias. That leads to the next limitation of the study in Chapter 4.2, where several symptoms were not registered, leading to possible bias. To reduce the bias of missing data, we have focused on the chief complaint of each patient, since information on this symptom was present pre- and post-operatively in all patients. In Chapter 4.1 missing data was present because not all patients had undergone audiometric and cVEMP testing (or they had undergone VEMP testing at an outside facility). VEMP testing is a relatively new diagnostic tool and has not been performed routinely post-operatively until a couple of years ago. Mainly the first surgical candidates had missing data on post-operative VEMP testing, so lack of post-operative VEMP results is independent of change in surgical outcomes in these patients.

In total only thirty-eight patients were included in these studies, therefore statistical analysis on the improvement of signs and symptoms could not be performed. We observed that certain factors were more common in six patients with a prolonged recovery period. This patient number was too small to use in a prediction model, and only our observed results were described in these patient. We recommend the development of a prediction model in a larger patient cohort in a prospective setting, to understand which characteristics might delay recovery.

These studies included a relatively large patient group (considering SCD being a rare disease) and costs of performing retrospective analysis were relatively low. Both studies helped us determine where to focus on in future prospective studies. The first step will be to use a more standardized approach of data collection, assessing which patients are likely to show most improvement following surgical repair and assessment of the different methods and approaches of SCD repair.

In chapter 4.3 we performed a systematic review on change in SCD signs and symptoms, audiometric testing and VEMP testing following SCD repair. This study was performed, because multiple studies that have reported on surgical outcomes following SCD repair did not result in a consensus on ideal surgical approach and determination of best surgical candidates. We reviewed the literature to perform a quality assessment of current literature on this topic. Nineteen articles on surgical outcomes fulfilling our inclusion criteria were included and critically appraised. Due to the large spread in different surgical outcomes, a meta-analysis could not be performed. All studies that were relevant (thus included data on post-operative signs and symptoms, audiometric testing and/or VEMP testing) were included (18/19), regardless of the risk of bias. The consideration for this approach was that large differences on the level of evidence or study design were not present and most studies were retrospective, with the above-mentioned known risks of bias.

Most studies described inclusion of patients with debilitating SCD signs and symptoms as surgical candidates. However, studies did often not describe to what degree patients must suffer from their signs and symptoms to be classified as debilitating. A striking finding was a lack of standardization in methods of surgical repair and outcome measure. Various methods and approaches of SCD repair were used. The majority of studies performed a middle fossa craniotomy approach and repair of the dehiscence with plugging of the defect. The use of different approaches and methods of repair made it challenging to draw definite conclusions on outcomes. Outcome measures were often also not standardized, assessment of outcome measures mostly consisted of description of the subjective change in symptoms.

Since SCD is a relatively new and rare disease and guidelines of the evaluation of a patient with (suspicion of) SCD do not exist. In addition, standardization in the work-up and management is not present. This systematic review provided an overview of the existing literature, in which a large number of patients were included, and described the advantages and disadvantages for surgical repair. It provided practical recommendations on how to improve future research.

In chapter 2 the prevalence of SCD in patients with a persistent ABG following stapes surgery is also assessed with the use of a retrospective study design. This study was performed because SCD is described to mimic other diseases such as otosclerosis. Multiple studies have described case reports on patients with a persistent ABG following stapes surgery that turned out to have SCD [Halmagyi et al., 2003; Hope and Fagan; Lehmann et al.; Li et al.; Mikulec et al., 2004; Minor et al., 2003]. However, the exact prevalence of SCD in the group of patients with persistent hearing loss following stapes surgery was not known. We have included 131 ears that underwent primary stapes surgery of which 13 patients with a CT-scan available had persistent post-operative hearing loss. CT-scan analysis did not reveal SCD in any of these 13 ears.

The above-described disadvantages of retrospective studies including risk of inducing bias and higher possibility of missing data also account for the study conducted in chapter 2 on the prevalence of SCD in patients with persistent ABG following stapes surgery. A limitation is the missing data. Not all patients included in the study underwent CT-scan testing and therefore in these patients the presence or absence of SCD could not be assessed. This missing data could lead to bias, however seen the low prevalence of SCD in the patients that had a CT-scan available for assessment, it does not seem feasible to summon these patients without a CT-scan back to clinic to undergo CT-scan testing. If SCD had been present in a larger percentage of patients with a persistent ABG following stapes surgery (as compared with the normal population), we would have expected to find at least one patient with a definite SCD in the group of patients that did undergo CT-scan testing.

Again, despite the level of evidence of 4, we used the best available evidence to answer that the prevalence of SCD is not higher in the patient group with persistent hearing loss following stapes surgery. The answer to this clinical relevant question might prevent patients with persistent hearing loss following stapes surgery to undergo a CT-scan for the sole purpose of excluding SCD as a possible cause of surgical failure.

In the same study we prospectively validated the method to determine presence or absence of SCD on radiologic images. The use of CT-scan reconstructions has been described in literature as a reference measure to assess if SCD is present on a temporal bone CT-scan (Belden et al). To assure that the findings described in Chapter 2, on absence or presence of SCD in the patient cohort with persistent ABG following stapes surgery, are not due to misjudgement of CT scan assessment, two experienced clinicians validated the method to establish absence or presence of SCD on CT-scans at UMC Utrecht. Methodologically, the inter-observer agreement can be calculated with the use of a percent agreement or Cohen's kappa. Cohen's kappa determines the inter-observer agreement between two independent observers, by taking the agreement suspected by chance into account (which is not taken into account by a percent agreement). If a rater (radiologist) is well trained and not likely to guess the outcome, a percent agreement could be used as an alternative to determine inter-observer agreement. A limitation of the use of Cohen's kappa is that it makes assumptions on rater independence. We included both outcomes, on percent agreement and on Cohen's kappa, to take the advantages and disadvantages of both methods into account when showing the inter-observer agreement. This validation showed that the use of reconstructions in the plane parallel and perpendicular to the SSC indeed is a reliable and universal method to judge the presence or absence of anatomical SCD with CT-scans.

Chapter 3.1 assessed the effect of SCD length and location on signs and symptoms, audiometric and VEMP testing in a large cohort of clinical patients. This study was performed to help explain the variation in clinical presentation. Patients with SCD can present with a myriad of signs and symptoms, ranging from auditory symptoms only, vestibular symptoms only, or a combination of auditory and vestibular symptoms. To assess the length and location of the dehiscence in a precise manner, we developed a new 3D reconstruction method where the density of the bone (or missing bone) of the SSC was measured in Hounsfield Units (HU).

To minimize the risk of selection bias, all patients diagnosed with SCD syndrome between 2000 and 2011 were included. We standardized our inclusion by only including patients who had a Massachusetts Eye and Ear Infirmary (MEEI) CT-scan available for analysis. However, this induced the risk of selection bias, by excluding patients whom underwent diagnostic work-up at outside facilities prior to presentation at MEEI. It could be theorized that specifically patients with debilitating symptoms are referred to a tertiary care centre and this group of patients with a CT-scan from an outside institution was not taken into account.

The potential risk of overestimation of SCD length or false diagnosis of SCD is a possible limitation in CT-scan studies. The risk of missing a thin layer of bony covering of the SSC exists due to the partial volume averaging effect, whereby the average volume of a pixel is taken into account. Considering this risk, we have developed a new 3D reconstruction method, minimizing the risk of the partial volume averaging effect. First we made a 3D scan reconstruction of the SSC. Next the density of the bone overlying SSC was measured in Hounsfield Units (HU). It was a challenge to determine the appropriate HU cut-off point. If your cut-off limit is too high, the risk exists that a very thin layer of bone is missed because the average HU of that pixel is below the cut-off point. Therefore a conservative HU cut-off point of 300 HU was taken (the mean HU of the thinnest part of bony covering of the SSC minus 3 times the standard deviation, as determined in 8 patients without a dehiscent SSC).

Another possible limitation in our study design is that our CT-scan measurements were not compared with intra-operative measurements, which could support the accuracy of the CT-scan measurements. There are several reasons why we did not compare the CT-scan measurements with the intra-operative measurements: intra-operatively a linear measurement is performed, while there is an angulation of the defect relative to the measurement. In addition blood, cerebrospinal fluid and irrigation in the field (to reduce the injury to the labyrinth) make the measurements more challenging. Also, measuring the SCD length takes time while exposure of the labyrinth needs to be reduced. An advantage of our design is that the curvature of the SSC is taken into account by making oblique reconstructions of the SSC. Conventional methods for measuring the SCD length all used linear measurements. Finally, we also included the conservatively managed patients, therefore intra-operative measurements would not have been available for all patients.

Correlation between each SCD sign and symptom separately and SCD length and location was assessed. Because multiple comparisons induce the chance on finding a statistic significant difference by chance, we used the effect size to assess the correlation between the signs and symptoms and SCD length and location. This gave a good overview of the different correlations and showed that no separate sign correlated with SCD length or location. In addition we divided patients into 3 groups, one group with auditory signs only, one group with vestibular signs only and one group with both auditory and vestibular signs and symptoms. These groups were then assessed by correlating SCD length and location. The effects of SCD length and location on audiometric and VEMP thresholds were analyzed with

linear regression, since these variables were continuous and normally distributed and therefore parametric tests could be used.

The advantages of this study are that a large patient group was studied and all necessary patient charts and CT-scan testing was available. Also multiple outcomes were assessed; namely the effect of SCD length and location on signs and symptoms, audiometric testing and VEMP testing. We found that the effect of SCD length and location only explained 20-30 percent of the variability of the myriad of SCD signs and symptoms in patients. We found similar results of the effect of SCD length and location in this clinical study as compared to our human cadaveric temporal bone model studies described next.

Chapter 3.2 and 3.3 studied the effect of SCD size and location on hearing loss in a human cadaveric temporal bone model. A human cadaveric temporal bone model is a unique model, which can be used to estimate hearing. Simultaneous measurements of intracochlear sound pressures in scala vestibuli and scala tympani enable quantification of the differential pressure (the cochlear input drive). This study was conducted to help explain the variation of hearing loss among different patients, since clinical studies do not agree on outcomes regarding the effect of SCD size and location on the magnitude of the ABG. The cochlear drive assessed in temporal bones afforded controlled changes in variables such as SCD size and location.

Methodological considerations in developing a human cadaveric temporal bone model are made by assessing the variables in clinical patients. In clinical patients, fluid continuously surrounds a dehiscence of the SSC. Similarly, fluid covered the dehiscence during our experiments, preventing air from entering the labyrinth. The static pressure of the fluid at the interface of the dehiscence was kept consistent across various SCD sizes and locations. However, the static pressure in patients with SCD would differ from our temporal bone experiments, since in patients the SCD is in contact with the cerebrospinal fluid, dura and/or brain. The dura might adhere to the edges of the SCD and might provide “autoplugging” of the dehiscence. This variability in the amount of autoplugging, possibly explains why some patients present with only an anatomical SCD and why other patients present with SCD syndrome. In our temporal bone model, we did not simulate the possible effect of the dura or brain on the SCD, which is a possible limitation in comparing these results with clinical patients.

In our clinical patients with SCD, the median length of the dehiscence was 4.4 mm (Chapter 3.1). In our first human cadaveric temporal bone study, we assessed the effect of small dehiscences on the cochlear drive. Therefore we had an indication of the effect of SCD size on the cochlear drive, but limited to about 2 mm. Since most patients with SCD syndrome present with larger SCDs, our second temporal bone study assessed the effect of larger size dehiscences. When comparing the effect of different locations in our temporal bone model, it was challenging to make two dehiscences of exactly the same length on different locations of the superior canal. A small difference in size may influence the change in differential pressure, while most accurate results are found when only one variable, in this case the SCD location, is changed.

In clinical patients, dehiscences are repaired by a variety of approaches and methods or repair. We repaired the SSC in our temporal bone model comparable to a transmastoid approach. However the dehiscences were located more to the lateral side of the limb as compared to an arcuate eminence defect often seen in clinical patients. The patching of larger SCDs was more challenging, since it was not always possible to get a full reversal of the effect of SCD. We developed a new method to patch these larger dehiscences with the use of a piece of paper.

In patients, multiple unknown factors can contribute to the outcomes when assessing the effect of SCD size and location. A main advantage of the human cadaveric temporal bone model is that it gives us a good understanding of the effects of SCD size and location on hearing, since one variable at a time can be modified. In these experiments all variables can be kept similar, while the effect of SCD length and/or location can be assessed in a single temporal bone. Because the effects of the SCD on the differential pressure were reversed, the changes in differential pressure were attributable to this one variable (size or location) that changed.

OVERVIEW OF CHAPTERS

Chapter 2: SCD Prevalance and Radiologic Confirmation

Chapter 2: Prevalence of superior canal dehiscence following failed stapes surgery

The exact prevalence of SCD is not known and estimates vary from 0.5% to 2% of patients having a thin or dehiscent SSC in temporal bone studies, up to 3% to 9% of patients with an anatomic SCD seen on CT-scans [Carey et al., 2000; Masaki,

2011; Williamson et al., 2003]. Multiple case reports have described that SCD was found in patients with persistent ABG following stapes surgery. We assessed the prevalence of SCD in patients with otosclerosis without hearing improvement following primary stapes surgery, but first we validated our method for confirming SCD on CT-scan testing. Assessment of 30 CT-scan reconstructions for absence or presence of SCD in the plane parallel (Pöschl) and perpendicular (Stenver) to the superior semicircular canal (SSC) was performed by two independent clinicians. Inter-observer agreement showed a good percent agreement and a good chance corrected agreement, the Cohen's Kappa, between raters. This indicated that our method for determining absence or presence of SCD is reliable. CT-scan reconstruction revealed no SCD in thirteen CT-scans assessed of patients with no post-operative improvement or a persistent ABG of >20dB. Therefore we would not recommend a CT-scan following persistent hearing loss after stapes surgery solely for diagnosis of SCD

Chapter 3: Effect of SCD Size and Location

Chapter 3.1: Superior canal dehiscence length and location influences clinical presentation and audiometric and cervical vestibular-evoked myogenic potential testing

Patients with SCD syndrome can present with a variety of symptoms, which makes clinical diagnosis more challenging. For instance, a patient with debilitating symptoms can sometimes lack the “typical” SCD findings on audiometric and VEMP testing. To determine the association of SCD length and location with auditory and vestibular signs and symptoms, magnitude of the ABG and cVEMP thresholds, a large clinical cohort of 104 patients with SCDS underwent SCD length and location measurements. This was done using a novel method of measuring bone density along 0.2-mm radial CT sections with the use of 3D reconstructions. We found that a larger dehiscence located closer to the ampullated end of the SSC was associated with auditory symptoms (with or without vestibular symptoms), rather than with vestibular symptoms alone. The location of the SCD did not influence the magnitude of the air conduction loss or the ABG, while patients with a larger SCD had more air conduction loss and a larger ABG in the low frequencies. A large dehiscence was also associated with cVEMP thresholds as well as a location closer to the ampullated end of the SSC. These findings may partially (20-30%) help explain the variation of signs and symptoms seen in patients with SCD syndrome, for example a patient with a small bony dehiscence located at the medial-posterior limb might not present with auditory symptoms, an ABG or lower VEMP thresholds.

Chapter 3.2: The effect of superior semicircular canal dehiscence on intracochlear sound pressures

Hearing loss is variable across patients, and the precise mechanism and source of variability are not fully understood. Clinical studies showed no consensus on the effect of SCD size on hearing thresholds, therefore we assessed the effect of SCD size on the conductive loss on a human cadaveric temporal bone model. Simultaneous sound pressure measurements in the scala vestibuli and scala tympani were made, allowing for estimation of the differential pressure across the cochlear partition. The differential pressure is related to sound input to the cochlea and provides an estimate of hearing in a human temporal bone model. The experiments showed that a larger sized dehiscence reduced the low-frequency pressures in scala vestibuli and scala tympani, as well as the differential pressure across the cochlear partition. This agrees with a decrease of input to the cochlea for around 10 to 20 dB. In addition we showed that sometimes the smallest dehiscence (<0.5mm diameter) caused the largest decrease in intracochlear pressures in scala vestibuli at frequencies above 1000 Hz. This variation is also seen in clinical patients, where patients can have classic SCD signs and symptoms despite a very thin layer of bone (where multiple microscopic holes may sum to a small hole). These effects due to SCD were reversible by patching the dehiscence. We also showed that under certain circumstances such as SCD, stapes velocity is not related to how the ear can transduce sound across the cochlear partition because it is not directly related to the input drive across the cochlear partition, emphasizing that certain pathologies cannot be fully assessed by measurements such as stapes velocity.

Chapter 3.3: Assessment of the effects of superior canal dehiscence location and size on intracochlear sound pressures

Patients with SCD can present with a large range of conductive losses. In addition to the various SCD sizes present in the clinical population, the location of the SCD also varies among patients, ranging from a location near the arcuate eminence to a more lateral or medial (superior petrosal sinus) located dehiscence. Patients also often present with a SCD larger than the 2 mm length, (study in a chapter 3.1 showed an average of approximately 4 mm). We therefore assessed the effect of SCD location and of larger sized SCDs on the cochlear drive. We found that indeed the pressure difference across the partition decreased for larger sized dehiscences, however this effect seemed to saturate when the dehiscence was 2-3 mm long and 0.7 mm wide. In addition the magnitude of change in cochlear pressure due to an SCD varied across ears and the SCD length by which saturation of the effect was seen varied across ears as well. Different SCD locations showed a similar cochlear drive, indicating no effect of location. The temporal bone findings that dehiscence

size positively correlated to the effect on cochlear drive, and varying the SCD location had no effect on cochlear drive, agree with our clinical study showing a larger conduction loss being associated with a larger SCD size and no change in air conduction or magnitude of the ABG for the different SCD locations. In patients, as well as in our temporal study, similar sized dehiscences resulted in different magnitudes of conduction loss (cochlear drive) across ears.

Chapter 4: SCD Treatment

Chapter 4.1: Utility of cVEMPs in bilateral superior canal dehiscence syndrome

Some patients with bilateral SCD, present in 46% of our surgically repaired patients, cannot localize symptoms to one ear. In these patients it is essential to localize the ear causing the most significant complaints. We found that tuning fork lateralization, a larger ABG and lower pre-operative cVEMP thresholds can help determine the worse ear prior to SCD surgery. Following surgical repair, the change in cVEMP thresholds seemed to correspond with the clinical improvement in the thirteen patients assessed. In twelve patients with improvement of clinical signs and symptoms, normalization of cVEMP testing was found while no shift in cVEMP threshold was found in one patient in whom post-operative complaints remained. The post-operative cVEMP thresholds can be used to help determine if the symptoms are due to unsuccessful surgery in the operated ear or due to unmasking of symptoms in the contralateral SCD ear. A post-operative (partial) closure of the ABG in the low frequencies was found. This is due to an improvement in air conduction thresholds as well as a deterioration or normalization (decrease) of the supra normal bone sensitivity. In addition we found a sensorineural hearing loss, mainly in the high frequencies. This is important information to share with patients when counselling for surgical repair.

Chapter 4.2: Clinical factors associated with prolonged recovery after superior canal dehiscence surgery

Often patients have some degree of disequilibrium for several weeks to several months following SCD repair. However, in some patients the dizziness can persist. With this study we have identified possible clinical factors that could be associated with prolonged recovery after superior canal dehiscence surgery. In addition we have assessed the change in post-operative clinical signs and symptoms. Thirty-three patients that mainly underwent plugging of the dehiscence through a middle fossa craniotomy approach were identified from a database of 140 patients diagnosed with SCD. We found that in all patients, the chief complaint improved following surgical repair. Following surgical repair, six patients (out of 34) had

dizziness lasting more than 4 months (usually recovery is seen within the first couple of weeks to months). We observed that these six patients with a prolonged recovery were female patients with bilateral SCD, a history of migraines and dehiscence length of 3mm or longer. This study showed that surgical plugging of SCD is an effective management option to provide long-term improvement of the chief complaint in SCD syndrome patients. However, patients with bilateral SCD, a history of migraines and larger defects may be at risk of prolonged dizziness after surgery and should be appropriately counseled.

Chapter 4.3: Systematic review of outcomes following superior canal dehiscence surgery: determining best surgical candidates

The effect of SCD surgery on signs and symptoms, audiometric outcomes and VEMP testing has been assessed in various studies. However, there has been no consensus to determine which patients are the best candidates for surgery and in comparing different surgical approaches and methods of SCD repair. We performed a systematic search by retrieving 247 unique studies, including 422 patients, with original data on surgical outcomes of SCD. After screening on title and abstract, full-test screening and critical appraisal, eighteen studies were assessed on post-operative outcomes. Different surgical approaches such as a middle fossa craniotomy and transmastoid approach (in some cases combined with a mini-craniotomy approach) were used. Method of SCD repair varied from plugging, resurfacing or recapping. Initial subjective improvement of post-operative SCD signs and symptoms was described in most patients (96%, however recurrence of symptoms was found in some of these patients with initial improvement). We found that overall autophony and sound- and pressure associated dizziness showed best post-operative improvement. Reversal of diagnostic indicators was also found, including an improvement of the pre-operative average ABG and post-operative normalization of cVEMP thresholds. In addition, bone conduction sensitivity decreased (normalization in low frequency, but deterioration at high frequency). Recurrence of SCD signs and symptoms was only described in a few studies and was slightly more common following SCD resurfacing as compared to SCD plugging. Twenty adverse events were described of which most were transient. The most striking observation found was lack of standardization on report of SCD outcomes. Large heterogeneity in description of surgical repair methods and reporting of outcomes was found among these studies. A more standardized reporting approach utilizing prospective data collection is needed to better understand the long-term outcomes in a larger cohort of patients who have undergone SCD repair.

Appendices: Small case series and case reports

Appendix I: Familial superior canal dehiscence

The etiology of superior canal dehiscence (SCD) involving the arcuate eminence is not completely understood, but genetic factors may play a role. One hypothesis is that patients are born with a defect of the superior canal, and an acute event (such as head trauma) or progressive loss of bone (e.g., due to dural pulsations) may result in the onset of SCD symptoms. From our database of more than 200 SCD patients, 3 families that each had 2 members with SCD syndrome were identified. We found that first-degree relatives presented with similar complaints and that temporal bone computed tomography scans between relatives showed very similar skull base topography and anatomic SCD defects. This suggests that genetics may play a role in the etiology of SCD.

Appendix II: Radiologic and cVEMP progression in superior canal dehiscence syndrome

The paucity of information in the literature about disease progression and long-term outcomes makes it difficult for clinicians to provide patients with answers to these important questions regarding SCD. A retrospective review of 250 patients with SCDS showed two patients with disease progression over time. Both patients initially presented with minor symptoms and years later progression of SCD signs and symptoms were observed. Audiometric testing showed development of a small ABG and even lower VEMP thresholds. Repeated CT-scan testing showed an increase in dehiscence size on one affected ear in both patients. These patients showed that disease progression, as subjectively described by a patient, can be objectively observed and monitored with diagnostic testing. We therefore think that it is important to perform a full evaluation at time of initial presentation to follow the disease course over time.

Appendix III: Hearing your eyeballs move: superior canal dehiscence syndrome

Patients with bilateral SCD sometimes warrant bilateral sequential SCD repair. Only patients with intractable symptoms in both ears should be considered for surgery, and a more conservative approach should be used for bilateral SCD patients with mild symptoms in the unrepaired ear. The study discussed showed that second-side surgery is safe and effective, however it can cause temporary or permanent oscillopsia, and patients must be counseled to expect a prolonged recovery period. The risks and benefits should be considered carefully for each patient before deciding to pursue a second-side SCD repair. Finally, comprehensive vestibular testing (such as VEMPs and calorics) should be performed to assess residual balance function prior to consideration of bilateral sequential SCD

repair to reduce the risk of chronic oscillopsia and dizziness after second ear surgery.

CONCLUSIONS AND RECOMMENDATIONS

1) CT-scan reconstructions in the planes of Stenver and Pöschl are reliable in detecting SCD. SCD is not more common in patients with persistent ABG following stapes surgery and therefore a CT-scan solely for diagnosis of SCD is not recommended in these patients.

2) A study on SCD length and location demonstrates that: a) patients with auditory symptoms have a larger dehiscence located closer to the ampulla; b) a larger ABG is associated with a larger SCD, while dehiscence location does not influence hearing results c) lower cVEMP thresholds are found in patients with a larger dehiscence located closer to the ampulla.

3) Our human cadaveric temporal bone studies showed that a) SCD decreases the differential pressure across the cochlear partition, with the effects being more prominent in larger dehiscences; b) saturation of the effect of SCD size in SCDs occurs above the size of 2-3 mm long and 0.7 mm wide; c) the amount of change in cochlear drive varies across ears for different SCD sizes; d) different SCD locations result in similar effects on cochlear drive.

4) In patients with bilateral SCD, pre-operative cVEMP thresholds, the magnitude of the air-bone gap and tuning fork testing are important to confirm the worse ear. Following surgical repair we found a) improvement of chief complaint in all patients; b) a partial closure of the air-bone gap and a mild (high-frequency) sensorineural hearing loss; c) elevation of cVEMP thresholds, correlating with improvement of symptoms and underscoring the importance of post-operative testing in patients with bilateral disease or recurrence of symptoms. Patients with bilateral SCD, a history of migraines and larger defects may be at risk of prolonged recovery.

5) Surgical repair of SCD is associated with improvement of auditory and/or vestibular signs and symptoms (especially autophony and sound- and pressure-induced vertigo) as well as reversal of diagnostic indicators. Large heterogeneity in description of surgical repair methods and reporting of outcomes was found.

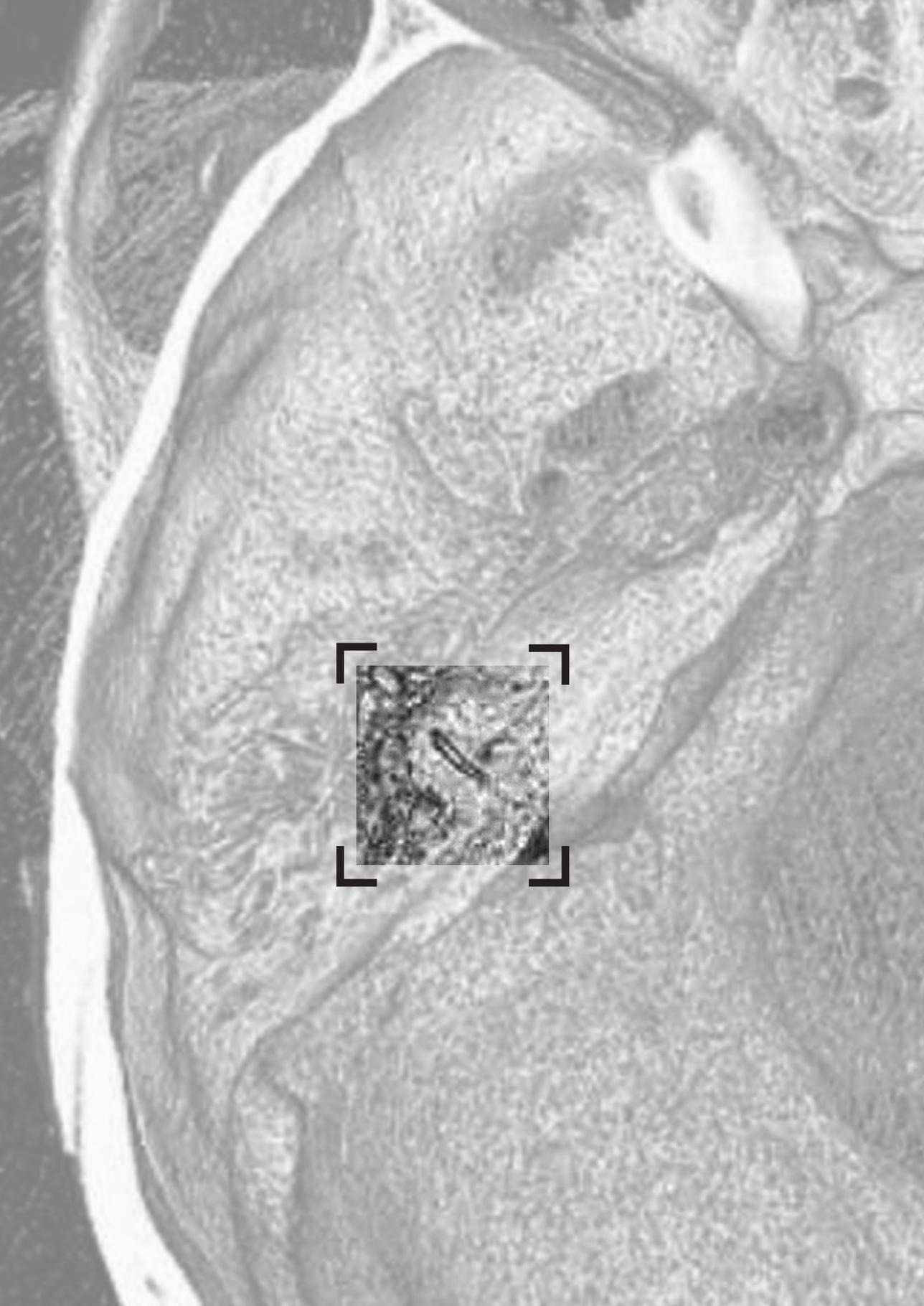
These studies raise new questions about SCD. The advantages and disadvantages of study designs as used in these investigations are discussed in the above section. Since most studies assessing surgical effects are retrospective, a prospective study with a more standardized approach using objective data collection to assess which SCD signs and symptoms would aid in the diagnosis and treatment of SCD. We have proposed a SCD questionnaire (including common SCD signs and symptoms) to objectively log the change in pre-and post-operative signs and symptoms. Future plans include validation of this questionnaire in the SCD population and in the population of patients undergoing workup for absence or presence of SCD. In addition this questionnaire might aid in determining in which patients to expect better outcomes following surgical repair.

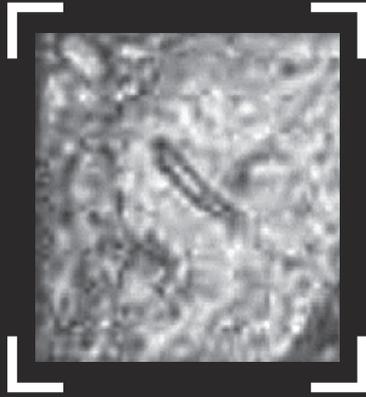
To diagnose SCD, presence of SCD on a CT-scan (reconstruction) is used as reference standard. Patients with SCD syndrome can present with a myriad of clinical signs and symptoms and results on audiometric and VEMP testing can show large spread in outcomes among these patients. This variation in clinical presentation and diagnostic measurements make it more challenging to diagnose SCD in clinical patients. A screening tool for diagnosis of SCD such as power reflectance measurements could possibly contribute in diagnosing SCD. Power reflectance measurements are inexpensive and relatively simple in use. It is the complex ratio between the reflected pressure wave and the incident pressure wave of the ear canal. Future research assessing the possibilities of the use of power reflectance as a screening tool for SCD diagnosis would be useful.

What are not fully understood are the ideal assessment tools needed to determine when a patient's symptoms are debilitating enough to warrant surgery and which surgical approach and method of repair are most effective. New surgical methods and approaches for SCD repair are developing; minimal-invasive approaches such as endoscopic SCD repair or round window patching have recently been described. The effects of different materials and methods of SCD repair can be studied by using a more standardized reporting approach utilizing prospective data collection. Radiologic landmarks would be useful in deciding which approach to choose for each patient. In addition the effects of different materials and methods of repair can be assessed in our human cadaveric temporal bone model, since one variable can be analyzed separately in a controlled setting. Standardizing reporting of patient symptoms, defect length and location, and surgical repair methods will greatly enhance our understanding of this rare condition and improve our ability to predict which patients with SCD will benefit most from surgery.

REFERENCES

- Burton A**, Altman DG: Missing covariate data within cancer prognostic studies: A review of current reporting and proposed guidelines. *Br J Cancer* 2004;91:4-8.
- Carey JP**, Minor LB, Nager GT: Dehiscence or thinning of bone overlying the superior semicircular canal in a temporal bone survey. *Arch Otolaryngol Head Neck Surg* 2000;126:137-147.
- Halmagyi GM**, Aw ST, McGarvie LA, Todd MJ, Bradshaw A, Yavor RA, Fagan PA: Superior semicircular canal dehiscence simulating otosclerosis. *J Laryngol Otol* 2003;117:553-557.
- Hope A**, Fagan P: Latent superior canal dehiscence syndrome unmasked by stapedotomy for otosclerosis. *J Laryngol Otol*;124:428-430.
- Lehmann M**, Ebmeyer J, Upile T, Sudhoff HH: Superior canal dehiscence in a patient with three failed stapedectomy operations for otosclerosis: A case report. *J Med Case Reports*;5:47.
- Li PM**, Bergeron C, Monfared A, Agrawal S, Blevins NH: Superior semicircular canal dehiscence diagnosed after failed stapedotomy for conductive hearing loss. *Am J Otolaryngol*.
- Masaki Y**: The prevalence of superior canal dehiscence syndrome as assessed by temporal bone computed tomography imaging. *Acta Otolaryngol* 2011;131:258-262.
- Mikulec AA**, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.
- Minor LB**, Carey JP, Cremer PD, Lustig LR, Streubel SO, Ruckenstein MJ: Dehiscence of bone overlying the superior canal as a cause of apparent conductive hearing loss. *Otol Neurotol* 2003;24:270-278.
- Minor LB**, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998; 124:249-258.
- Phillips B**, Ball C, Sackett D, Badenoch D, Straus S, Haynes B, Dawes M: Centre of evidence based medicine. www.cebm.net 2009.
- Schlesselmann JJ**, Stolley PD: Case-control: Design, conduct, analysis. New York: Oxford University Press 1982.
- Williamson RA**, Vrabec JT, Coker NJ, Sandlin M: Coronal computed tomography prevalence of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2003;129:481-489.





Chapter 6

Dutch Summary - Nederlandse Samenvatting

OPBOUW VAN DIT PROEFSCHRIFT

Dit proefschrift beschrijft de evaluatie en het management van superieure kanaal dehiscentie (SCD). SCD is een relatief nieuwe en zeldzame aandoening, voor het eerst beschreven in 1998 [Minor et al., 1998]. Het betreft het ontbreken van de benige bedekking van het superieure semicirculaire kanaal (SSC). Indien SCD is vastgesteld middels een os petrosum computertomografie scan (CT-scan), is er sprake van een anatomische SCD. Indien zich ook symptomen voordoen, spreken we van SCD syndroom (SCDS). De variatie in klinische presentatie verschilt sterk. Patiënten kunnen zich presenteren met audiologische symptomen (zoals gehoorverlies, autophonie, hyperacusis, een vol gevoel in de oren en/of tinnitus), met vestibulaire symptomen (zoals geluid- of druk geïnduceerde vertigo, inspanningsgerelateerde vertigo en/of een gevoel van onbalans) of met een combinatie van beide. Ook kan nystagmus worden geobjectiveerd indien geluidsgeïnduceerde (Barony muziekdoos) of drukgeïnduceerde (Valsalva manoeuvre, pneumatische otoscopie) stimuli worden toegediend.

Als referentie standaard voor het vaststellen van anatomische SCD wordt een os temporalis CT-scan gebruikt, zo nodig met reconstructies in het vlak parallel (Pöschl) en loodrecht (Stenver) op het SSC [Belden et al., 2003]. Audiologische en vestibulaire testen kunnen de diagnose SCD syndroom ondersteunen. Typische bevindingen op het audiogram zijn een laagfrequent conductief verlies en een beengleiding die beter is dan de normale drempelwaarden (-5 of -10 dB). Dit leidt samen vaak tot een air-bone gap (ABG) in de lage frequenties (tot 1000 Hz) [Minor, 2005]. Een veel gebruikte vestibulaire test, de cervicale “vestibulair evoked myogenic potential” (cVEMP), is een maat van de functie van de sacculus uitgelokt door acoustische stimulatie en waargenomen in de ipsilaterale musculus sternocleido-mastoideus. Patiënten met SCD syndroom hebben typisch lagere drempelwaarden en grotere amplitudes [Brantberg et al., 2001].

Veel patiënten met SCD zijn asymptomatisch of behoeven geen operatieve behandeling, aangezien het leren vermijden van uitlokkende momenten (zoals tillen of snuiten) effectief kan zijn in het voorkomen van de vertigo klachten. Voor SCD patiënten met invaliderende symptomen kan chirurgisch ingrijpen effectief zijn, waarvan goede verbetering van de auditieve en vestibulaire symptomen is beschreven. Wel hebben patiënten post-operatief frequent een kortdurend gevoel van onbalans. Het SSC kan benaderd worden via een middel fossa craniotomie (MFC) benadering, of via een transmastoidale (TM) benadering. Hierbij wordt het SSC meestal geplugd, echter het afdekken van het SSC is ook een mogelijkheid.

HOOFDSTUK 2: SCD PREVALENTIE EN RADIOLOGISCHE BEVESTIGING

Hoofdstuk 2: Prevalentie van superieure kanaal dehiscentie in patiënten met persisterend gehoorverlies na stapes chirurgie

Meerdere case reports beschrijven SCD bij patiënten met een persisterend gehoorverlies na stapes chirurgie, echter de incidentie van SCD in deze patiënt groep is niet bekend [Mikulec et al., 2004; Minor et al., 2003]. De exacte incidentie van SCD in het algemeen is niet conclusief: bij patiënten beoordeeld in een os temporalis studie varieert het percentage dun of dehiscent SSC van 0.5% tot 2% [Carey et al., 2000]. Studies naar de radiologische incidentie van SCD laten incidenties van 3% tot 9% zien [Masaki, 2011; Williamson et al., 2003]. Om meer inzicht te krijgen in de incidentie van SCD bij patiënten met persisterend gehoorverlies na stapes chirurgie, hebben wij de incidentie van SCD in patiënten met otosclerose zonder verbetering van het gehoor (of met enige verbetering maar een persisterende ABG) in kaart gebracht. Hiervoor werd eerst de methode voor het vaststellen van aan- of afwezigheid van SCD op CT-scans gevalideerd. 30 CT-scans met reconstructies in het vlak parallel (Pöschl) en loodrecht (Stenver) op het SSC zijn door twee onafhankelijke beoordelaars beoordeeld op aan- of afwezigheid van SCD. Hierbij werd een goede Cohen's kappa, overeenkomst gecorrigeerd voor kans, gevonden voor het vaststellen van aan- of afwezigheid van SCD. Deze methode is vervolgens toegepast op 13 CT-scans, die zijn beoordeeld van patiënten zonder verbetering van het gehoor of een persisterende ABG van >20 dB na stapes chirurgie. In deze groep patiënten werd geen SCD vastgesteld. Daarom zouden wij alleen voor het uitsluiten van SCD geen post-operatieve CT-scan voor persisterend gehoorverlies na stapes chirurgie aanraden.

HOOFDSTUK 3: EFFECT VAN SCD GROOTTE EN LOCATIE

Hoofdstuk 3.1: Superieure kanaal dehiscentie beïnvloedt klinische presentatie, audiometrische en cervicale “vestibular-evoked myogenic potential” test uitkomsten

Patiënten met SCD syndroom kunnen zich met een scala aan klachten presenteren, wat het vaststellen van de diagnose SCD tot een uitdaging kan maken. Daarom hebben we de grootte en de locatie van de SCD gecorreleerd aan klinische symptomen en diagnostische parameters, zoals de grootte van de ABG en cVEMP drempelwaardes. Hiervoor hebben we bij een grote groep van 104 klinische SCD patiënten, de grootte en de locatie van de SCD gemeten waarvoor een nieuwe meetmethode is gebruikt. In deze methode worden eerst 3D reconstructies van

het SSC gemaakt, welke worden verdeeld in 0.2 mm radiale CT-scan secties. Vervolgens wordt van elke radiale sectie de botdichtheid van de benige bedekking over het SSC gemeten in Hounsfield Units (HU). Indien de botdichtheid kleiner dan 300 HU is, wordt het als een dehiscentie geïdentificeerd.

Met deze methode werd de SCD grootte en de SCD locatie bepaald. Vervolgens werd dit gecorreleerd aan klinische symptomen en diagnostische parameters, met de volgende conclusies: een grotere dehiscentie dicht bij de ampulla zijde van het SSC gelegen, werd geassocieerd met auditieve symptomen (met of zonder vestibulaire symptomen), in plaats van met alleen vestibulaire symptomen. Tevens werd bij patiënten met een grotere SCD meer conductief verlies en een grotere ABG in de lage frequenties gevonden. De SCD locatie had geen invloed op het conductieve verlies of de ABG. Een grotere SCD en een locatie dicht bij de ampulla zijde van het SSC werden tevens geassocieerd met lagere cVEMP drempelwaardes. Deze resultaten dragen voor 20-30% bij in het verklaren van het klinische verschil in presentatie. De uitkomsten kunnen bijvoorbeeld mede verklaren waarom een patiënt met een kleine benige dehiscentie gelegen in het mediaal-posterieure been van het SSC zich niet presenteert met vestibulaire klachten, een ABG of met verlaagde cVEMP drempelwaardes.

Hoofdstuk 3.2: Het effect van superieure kanaal dehiscentie op intracochleaire geluidsdrukken

De mate van gehoorverlies varieert tussen patiënten met SCD. Het precieze mechanisme en de oorsprong van de variatie van de mate van verlies wordt niet volledig begrepen. Klinische studies laten geen consensus zien over het effect van SCD grootte op de conductieve drempelwaardes. Om die reden hebben we het effect van SCD grootte op het conductieve verlies in een humaan kadaver os temporalis model beoordeeld. Met behulp van simultane geluidsdrukmetingen in scala vestibuli en scala tympani werd het drukverschil over de cochleaire partitie benaderd. Het drukverschil is verbonden aan de input van geluid van de cochlea en is een benadering van het gehoor in een humaan os temporalis model. Na het creëren van een SCD in ons os temporalis model werd een drukvermindering (voornamelijk in de lage frequenties) in scala vestibuli en scala tympani waargenomen. Dit komt overeen met een afname van het drukverschil over de cochleaire partitie, welke vergelijkbaar is met een vermindering van de cochleaire input van 10 tot 20 dB. Hiernaast werd gevonden dat soms de kleinste dehiscentie de grootste afname van intracochleaire druk in scala vestibuli voor de frequenties >1000 Hz tot gevolg had. Klinisch worden vergelijkbare effecten geobserveerd, een kleinere SCD in de ene patiënt kan een groot conductief verlies tot gevolg kan hebben,

terwijl een grotere SCD in een andere patiënt, minder gehoorverlies tot gevolg kan hebben. Alle effecten van die gecreëerd werden met een dehiscentie, konden worden omgekeerd door het afdichten van het SSC. Hiernaast hebben we gevonden dat de stapes beweeglijkheid onder bepaalde omstandigheden zoals bij SCD, niet direct gerelateerd is aan de omzetting van geluid over de cochleaire partitie, omdat de stapes niet direct gerelateerd is aan het drukverschil over de cochleaire partitie. Hiermee willen we benadrukken dat niet alle pathologieën volledig met stapes beweeglijkheid kunnen worden beoordeeld.

Hoofdstuk 3.3: Het effect van locatie en grootte van superieure kanaal dehiscentie op intracochleaire geluidsdrukken

Naast de verschillende groottes van SCD waarmee klinische patiënten zich kunnen presenteren, kan de locatie van de SCD ook variëren tussen patiënten. Dit kan uiteenlopen van een defect van de eminentia arcuata tot een defect meer lateraal/mediaal gelokaliseerd (ter plaatse van de sinus petrosus superior). Patiënten met SCD hebben meestal een dehiscentie die groter is dan de 2 mm welke gebruikt werd in het vorige hoofdstuk (de gemiddelde grootte in onze klinische studie van rond de 4 mm). Daarom hebben we in dit hoofdstuk het effect van SCD locatie en grotere SCD lengtes op het drukverschil over de cochleaire partitie beoordeeld. Het drukverschil over de cochleaire partitie verminderde inderdaad voor grotere dehiscenties, maar dit effect bleek af te vlakken voor dehiscenties groter dan 2-3 mm lang en 0.7 mm breed. In ieder preparaat werd een vergelijkbaar effect van SCD grootte op de intracochleaire geluidsdrukken gezien, echter de verschillende preparaten lieten een verschillende grootte van de effecten van een zelfde SCD grootte zien (dus een dehiscentie van bijvoorbeeld 3 mm had in het ene preparaat een grotere effect op de intracochleaire geluidsdrukken dan in een ander preparaat). Tevens varieerde de grootte van de dehiscentie waarop het effect van verzadiging optrad tussen de verschillende preparaten (maar het effect was wel in ieder preparaat aanwezig). De verschillende SCD locaties toonden vergelijkbare intracochleaire drukveranderingen, wat een effect van SCD locatie op de intracochleaire drukken uitsluit. Deze resultaten laten een afname van het drukverschil voor grotere dehiscenties zien en tonen geen effect van SCD locatie. Dit komt overeen met onze klinische resultaten waarbij patiënten met een grotere SCD gemiddeld een grotere ABG hadden terwijl de locatie van de SCD geen effect op de ABG had. Tevens werden in de verschillende preparaten waarbij een vergelijkbare SCD grootte werd gecreëerd, een verschillende mate van afname van de intracochleaire geluidsdrukken waargenomen. Dit komt overeen met de variatie in veranderingen van conductief verlies voor dezelfde grootte van de dehiscentie tussen verschillende patiënten.

HOOFDSTUK 4: SCD BEHANDELING

Hoofdstuk 4.1: Gebruik van cVEMPs in patiënten met het bilaterale superieure kanaal dehiscentie syndroom

Sommige patiënten met bilaterale SCD kunnen de symptomen niet aan één zijde toekennen. Indien deze patiënten chirurgische behandeling willen ondergaan, is het essentieel om het meest symptomatische oor te identificeren. Wij hebben gevonden dat de meest aangedane zijde zich kenmerkt door 1) lateralisatie van de stemvorkproef (Weber), 2) een grotere ABG en 3) een lagere cVEMP drempelwaarde, hierdoor kunnen deze parameters helpen bij het identificeren van de meest symptomatische zijde in patiënten met bilaterale SCD. In de 13 patiënten met pre- en post-operatieve cVEMP drempelwaardes, werd een normalisatie van de drempelwaardes gevonden in twaalf patiënten die tevens een verbetering van de klinische symptomen lieten zien. In één patiënt met post-operatief persisterende klachten, werd geen verschuiving van de cVEMP drempelwaardes gevonden. De post-operatieve cVEMP drempelwaardes kunnen worden gebruikt om vast te stellen of post-operatieve symptomen aanwezig zijn door niet succesvolle chirurgie in het geopereerde oor of door het ontmaskeren van symptomen in het contralaterale SCD oor. Hiernaast werd post-operatieve (gedeeltelijke) sluiting van de ABG in de lage frequenties gevonden, te verklaren door een verbetering van het conductieve verlies en een normalisatie of verslechtering van de supranormale beengeleiding. Tevens werd een perceptief verlies gevonden, voornamelijk in de hoge frequenties. Dit is belangrijke informatie om met patiënten te delen in de begeleiding tijdens het pre-operatieve traject.

Hoofdstuk 4.2: Klinische factoren geassocieerd met een verlengde hersteltijd na superieure kanaal dehiscentie chirurgie

Patiënten hebben vaak een mild gevoel van onbalans gedurende enige weken tot maanden na SCD chirurgie. Bij sommige patiënten kan dit gevoel van onbalans echter persisteren. Wij hebben factoren geobserveerd die mogelijk een bijdrage kunnen leveren aan deze verlengde herstel periode. Hiernaast hebben we de post-operatieve verandering van klinische symptomen geobjectiveerd. Drieëndertig patiënten die voornamelijk pluggen van het superieure kanaal via de MFC benadering ondergingen werden geïdentificeerd uit een database van 140 patiënten met SCD. In alle 33 patiënten werd een goede post-operatieve verbetering van de hoofdklacht gevonden. Zes (6/33) patiënten hadden post-operatieve klachten van duizeligheid of een gevoel van onbalans die langer dan 4 maanden persisterden. We hebben geobserveerd dat dit vrouwelijke patiënten met bilaterale SCD waren, met een voorgeschiedenis van migraine en allen een dehiscentie van 3 mm of lan-

ger. Met deze studie hebben we aangetoond dat SCD een effectieve management optie is om een goede en langdurige verbetering van de hoofdklacht te geven in patiënten met SCDS. De groep patiënten met bilaterale SCD, een voorgeschiedenis van migraine en een groter defect, zou een grotere kans op een langdurige hersteltijd kunnen hebben en moet daarom goed worden voorgelicht.

Hoofdstuk 4.3: Systematische review van uitkomsten van chirurgie van superieure kanaal dehiscentie: het bepalen van de beste chirurgische kandidaten

Het effect van SCD chirurgie op de verandering van symptomen, audiologische uitkomstmaten en VEMP drempelwaardes zijn in verschillende studies bestudeerd. Echter is er geen consensus over welke patiënten de beste chirurgische kandidaten zijn. Tevens is er geen consensus wat de beste chirurgische benaderingswijze en methode van herstel zijn. Wij hebben een systematische zoekopdracht uitgevoerd, waarbij we 247 unieke studies (422 patiënten) hebben geïncludeerd met originele data en uitkomsten van SCD chirurgie. Na screening op titel, samenvatting en full-tekst en na de critical appraisal, werden achttien studies beoordeeld op post-operatieve uitkomsten. Verschillende chirurgische benaderingswijzen zoals de MFC en TM (in sommige gevallen in combinatie met een mini-craniotomie benaderingswijze) werden gebruikt. De methode van SCD herstel varieerde van het pluggen van de dehiscentie tot verschillende methodes van het afdichten van de SCD. Initiële subjectieve verbetering van de post-operatieve symptomen werd in de meeste patiënten gevonden (96%, waarbij een aantal van deze patiënten in een later stadium een recidief heeft ontwikkeld). Met name de symptomen zoals autophonie en geluids- en druk- geïnduceerde vertigo lieten een goede verbetering zien. Hiernaast werd een omkering van de diagnostische indicatoren gezien, inclusief een verbetering van de gemiddelde pre-operatieve ABG en post-operatieve elevatie van cVEMP drempelwaardes. Echter een verslechtering van de beengeluidsdrempels werd ook gevonden. Recidief van SCD symptomen was maar in een relatief klein aantal studies beschreven en liet een enigszins hoger recidief percentage zien na afdekken van de SCD in vergelijking met het pluggen van de dehiscentie. Twintig complicaties werden beschreven, waarvan de meeste tijdelijk waren. De meest imponerende bevinding was gebrek aan standaardisatie in rapportage van uitkomsten. Grote heterogeniteit werd gevonden in de beschrijving van de chirurgische benaderingswijzen en methodes van SCD herstel en tevens in de rapportage van uitkomsten. Een meer gestandaardiseerde wijze van rapportage, gebruik makend van prospectieve data collectie, is noodzakelijk om de lange termijn uitkomsten in een grote groep patiënten die SCD chirurgie hebben ondergaan beter te interpreteren.

APPENDICES: KLEINE CASE SERIES EN CASE REPORTS

Appendix I: Familiale superieure kanaal dehiscentie syndroom

De etiologie van superieure kanaal dehiscentie, gelokaliseerd ter plaatse van de eminentia arcuata van het superieure kanaal, is niet geheel begrepen. Mogelijk spelen genetische factoren een rol. Hypothetisch gezien kunnen patiënten geboren worden met een dunne benige bedekking van het SSC en kan een acute gebeurtenis (zoals trauma capites) of langzaam progressief verlies van benige bedekking (zoals door durale pulsaties) resulteren in SCD symptomen. Uit onze database met meer dan 200 SCD patiënten werden 3 families met elk 2 leden met SCD syndroom geïdentificeerd. De eerstegraads familie leden bleken zich met hetzelfde klachtenpatroon te presenteren en de os temporalis CT-scans toonden vergelijkbare schedelbasis topografie en anatomische defecten van SCD.

Appendix II: Radiologische en cVEMP progressie in het superieure kanaal dehiscentie syndroom

De schaarste aan informatie in de literatuur betreffende ziekte progressie en lange termijn uitkomsten maken het uitdagend om patiënten goed over de prognose van SCD voor te lichten. Een retrospectieve review van 250 SCD patiënten, toonden 3 patiënten met bilaterale SCD en subjectieve ziekte progressie in de loop der jaren. Alle drie de patiënten hadden milde klachten bij initiële presentatie en presenterden zich jaren later met subjectieve toename van de klachten. Audiometrisch onderzoek en cVEMP onderzoek toonden toename van de typische SCD karakteristieken. Herhaling van de CT-scan liet een toename van de SCD grootte zien in alle patiënten. Met behulp van deze patiënten is aangetoond dat ziekte progressie, zoals subjectief door een patiënt beschreven, objectief kan worden vastgesteld met behulp van diagnostische testen. Om deze reden denken wij dat het belangrijk is om een volledige evaluatie (inclusief audiogram en VEMP test) te verrichten bij initiële presentatie, om zo de ziekte progressie objectief te kunnen vervolgen.

Appendix III: Het horen bewegen van je oogbollen: superieure kanaal dehiscentie syndroom

Patiënten met bilaterale SCD ondergaan soms sequentiële bilaterale SCD chirurgie. Alleen patiënten met sterk invaliderende symptomen in beide oren zouden voor bilaterale sequentiële SCD chirurgie overwogen moeten worden. Een meer conservatieve benaderingswijze zou geadviseerd worden voor patiënten met bilaterale SCD en milde symptomen aan de niet geopereerde zijde. De bediscussieerde studie liet zien dat bilaterale sequentiële SCD chirurgie veilig en effectief is, echter post-operatieve oscillopsia kan tijdelijk of blijvend geïnduceerd worden. Hiernaast

moeten patiënten worden begeleidt in de post-operatieve herstel periode, welke mogelijk verlengd is na bilaterale SCD chirurgie. De voor- en nadelen moeten zorgvuldig voor iedere patiënt worden afgewogen indien bilaterale sequentiële SCD chirurgie overwogen wordt.

CONCLUSIES

Dit proefschrift heeft zich primair gericht op de diagnostische tests en het management van superieure kanaal dehiscentie (SCD). Eerst hebben we het vaststellen van de aan- of afwezigheid van SCD op CT-scan reconstructies in het vlak parallel (Pöschl) en loodrecht (Stenver) gevalideerd. De incidentie van SCD is niet bekend, maar verschillende studies hebben SCD beschreven in patiënten met persisterend gehoorverlies na stapes chirurgie. Wij hebben de incidentie van SCD in deze groep patiënten die over een periode van 2 jaar zijn geopereerd geobjectiveerd en hebben hierbij geen patiënten met SCD gevonden.

De presentatie van patiënten met SCD varieert sterk, patiënten kunnen zich presenteren met alleen auditieve symptomen, alleen vestibulaire symptomen of een combinatie van beide. Het effect van SCD grootte en locatie op deze klinische presentatie hebben we met behulp van een grote klinische studie en een humaan kadaver os temporalis model in kaart gebracht. Hierbij werd in de klinische studie gevonden dat een grotere SCD en een locatie meer richting de ampulla zijde van het superieure semicirculaire kanaal, geassocieerd is met audiologische symptomen (met of zonder vestibulaire symptomen) en lagere cVEMP drempelwaardes. In zowel de klinische studie als in het temporalis model werd een grotere dehiscentie geassocieerd met een groter geleidingsverlies en werd geen effect van de SCD locatie gevonden. Dit kan helpen verklaren waarom patiënten met SCD symptomen en een bevestigde anatomische SCD op CT-scans zich niet met de klassieke kenmerken op audiometrische en VEMP testen presenteren. Hiernaast werd in ons os temporalis model een grote spreiding in mate van conductief verlies gevonden voor dezelfde groottes van de SCD in verschillende preparaten. Dit ondersteunt onze klinische bevindingen dat de grootte van de ABG kan variëren tussen patiënten met een zelfde grootte van de dehiscentie.

Wij hebben gevonden dat de meest aangedane zijde zich kenmerkt door 1) lateralisatie van de stemvorkproef (Weber), 2) een grotere ABG en 3) een lagere cVEMP drempelwaardes. Hierdoor kunnen deze parameters helpen bij het identificeren van de meest symptomatische zijde in patiënten met bilaterale SCD. Bij patien-

ten in wie conservatief management niet meer voldoende was, liet chirurgische interventie een goede algehele reductie in post-operatieve symptomen zien. Daarnaast werd een (partiële) sluiting van de ABG en een normalisatie van de cVEMP drempelwaardes gevonden. Echter een (voornamelijk hoogfrequent) verlies in de beengeleiding en een risico op complicaties werd ook gevonden. In patiënten met bilaterale SCD met post-operatieve SCD symptomen kan de cVEMP drempelwaarde bruikbaar zijn in het beoordelen of de symptomen komen door recidief van symptomen in het geopereerde oor of door het ontmaskeren van symptomen aan de contralaterale SCD zijde. De systematische review sluit aan op bovenstaande resultaten. De meest imponerende bevinding was een grote heterogeniteit in het rapporteren van post-operatieve uitkomsten en het gebruik van verschillende methodes en materialen voor SCD chirurgie. Meer gestandaardiseerde wijze van rapportage gebruik makend van prospectieve data collectie is noodzakelijk om de lange termijn uitkomsten in een grote groep patiënten die SCD chirurgie hebben ondergaan beter te interpreteren.

AANBEVELINGEN

Multipale vragen zijn met dit proefschrift beantwoord, echter deze studies hebben ook nieuwe vragen en overwegingen opgeworpen. De voor- en nadelen van de verschillende studie methodes zijn in de discussie uitgebreid besproken. De meeste studies die de chirurgisch effecten beoordelen zijn retrospectief. Derhalve zou een prospectieve studie met een meer gestandaardiseerde benadering en gebruikmakend van objectieve data collectie voor het verzamelen van informatie over SCD symptomen, helpen in het diagnostische proces en de behandeling van SCD. Wij hebben een SCD vragenlijst ontwikkeld (met de meest voorkomende SCD symptomen) om objectief de verandering in SCD symptomen te vervolgen. In toekomstige studies zal deze vragenlijst worden gevalideerd in de SCD (en voor SCD verdachte) populatie. Hiernaast is er nog mogelijk een rol weggelegd in het beoordelen van de beste chirurgische kandidaten.

In het diagnostische proces van SCD wordt de aanwezigheid van SCD op een CT-scan als referentie standaard gebruikt. Patiënten met SCD kunnen zich met een scala aan klachten presenteren en audiometrische en VEMP testen laten een grote spreiding in uitkomsten zien. Deze variatie in symptomen en spreiding in diagnostische uitkomsten maakt het stellen van de diagnose van SCD uitdagend. Een screeningstest in de diagnostiek van SCD zoals “power reflectance” metingen zou een mogelijke optie zijn om in het diagnostische proces van SCD te gebruiken.

“Power reflectance” is goedkoop en relatief eenvoudig in gebruik. Het is de complexe ratio tussen de gereflecteerde drukgolf en de eigen drukgolf van de meatus acousticus externa. Toekomstig onderzoek om de mogelijkheden van het gebruik van “power reflectance” als een screeningstest voor SCD in kaart te brengen zou een goede toegevoegde waarde hebben.

In het management van SCD blijven meerdere vragen onbeantwoord, zoals wanneer de symptomen invaliderend genoeg zijn om op te wegen tegen de operatie risico's en welke chirurgische benaderingswijzen en methode van herstel van de dehiscentie het beste gebruikt kan worden. Nieuwe benaderingswijzen en methodes van herstel zijn zich aan het ontwikkelen: minimaal-invasieve benaderingswijzen zoals endoscopisch SCD herstel of het afdichten van het ronde venster zijn recent beschreven. De effecten van de verschillende materialen en methodes van chirurgisch herstel zouden bestudeerd moeten worden door gebruik te maken van een gestandaardiseerde manier van rapportage, gebruik makend van prospectieve data collectie. Hiernaast zouden dit beoordeeld kunnen worden in ons humaan of temporalis model. Tevens zouden radiologische landmarks praktisch kunnen zijn bij het bepalen van de juiste chirurgische benaderingswijze per patiënt. Meer gestandaardiseerde rapportage van symptomen, standaardisatie in het meten van de grootte en locatie van de SCD en rapportage van chirurgische herstel methodes, zou ons begrip van deze zeldzame aandoening aanzienlijk vergroten.

REFERENTIES

Belden CJ, Weg N, Minor LB, Zinreich SJ: CT evaluation of bone dehiscence of the superior semicircular canal as a cause of sound- and/or pressure-induced vertigo. *Radiology* 2003; 226:337-343.

Brantberg K, Bergenius J, Mendel L, Witt H, Tribukait A, Ygge J: Symptoms, findings and treatment in patients with dehiscence of the superior semicircular canal. *Acta Otolaryngol* 2001; 121:68-75.

Carey JP, Minor LB, Nager GT: Dehiscence or thinning of bone overlying the superior semicircular canal in a temporal bone survey. *Arch Otolaryngol Head Neck Surg* 2000;126:137-147.

Masaki Y: The prevalence of superior canal dehiscence syndrome as assessed by temporal bone computed tomography imaging. *Acta Otolaryngol* 2011;131:258-262.

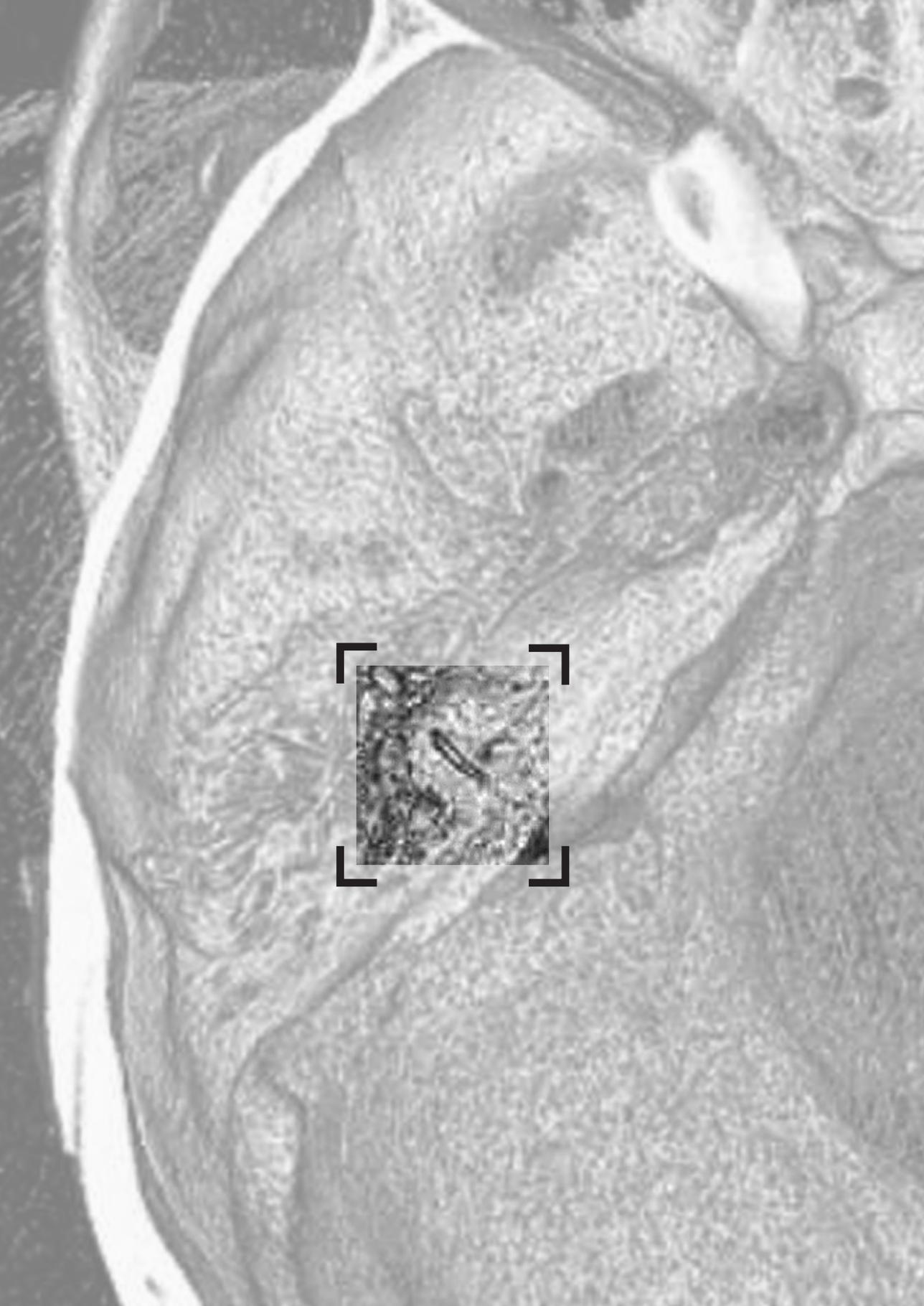
Mikulec AA, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.

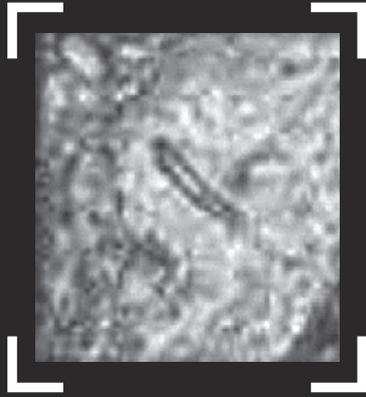
Minor LB: Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:1717-1727.

Minor LB, Carey JP, Cremer PD, Lustig LR, Streubel SO, Ruckenstein MJ: Dehiscence of bone overlying the superior canal as a cause of apparent conductive hearing loss. *Otol Neurotol* 2003;24:270-278.

Minor LB, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998; 124:249-258.

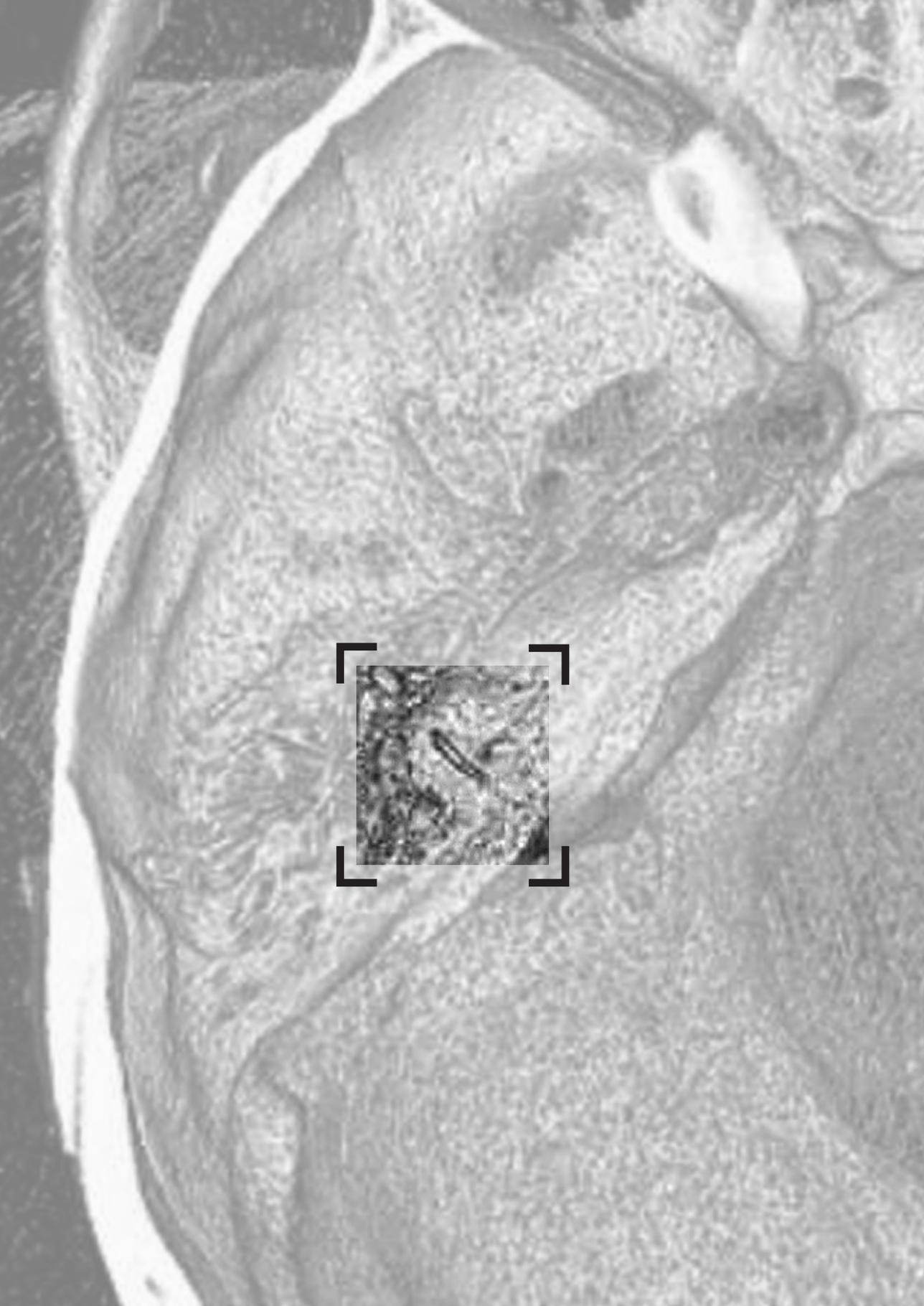
Williamson RA, Vrabec JT, Coker NJ, Sandlin M: Coronal computed tomography prevalence of superior semicircular canal dehiscence. *Otolaryngol Head Neck Surg* 2003;129:481-489.

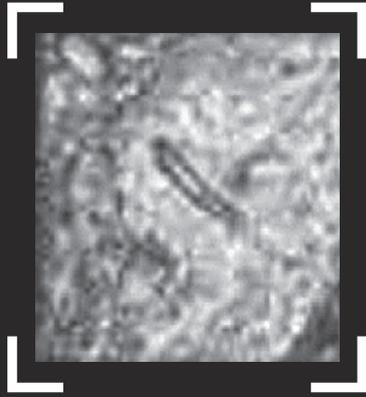




Appendices

Small case series and case report





Appendix I

Familial superior canal dehiscence syndrome

Marlien E.F. Niesten, Sarah Lookabaugh, Hugh Curtin, Saumil N. Merchant, Michael J. McKenna, Wilko Grolman, Daniel J. Lee

ABSTRACT

Importance: The etiology of superior canal dehiscence (SCD) involving the arcuate eminence is not completely understood, but genetic factors may play a role. One theory is that patients are born with thin bone overlying the superior canal, and an acute event (such as head trauma) or progressive loss of bone (e.g., due to dural pulsations) can cause dehiscence of the superior semicircular canal (SSC). A combination of the above factors could also result in SCD. Familial SCD has only been briefly mentioned in the literature to date.

Observations: In this study we report three families that each had two members with superior canal dehiscence syndrome (SCDS). We found that first-degree relatives presented with similar complaints, and that temporal bone computed tomography (CT) scans between relatives showed very similar skull base topography and anatomic SCD defects.

Conclusion: The presence of symptomatic SCD amongst first-degree relatives and similar skull base topography suggests that genetics may play a role in the etiology of SCD. We recommend an audiogram, cVEMP, and temporal bone CT scans (with both Pöschl and Stenver views) to be included in the work-up of all patients suspected to have SCD.

INTRODUCTION

Superior canal dehiscence syndrome (SCDS), or Minor Syndrome can present with a myriad of auditory and/or vestibular symptoms that are associated with a bony defect of the superior canal [Minor et al., 1998]. High-resolution computed tomography (CT) demonstrates a dehiscence area of bone in the region of the arcuate eminence (in contact with temporal lobe dura) or the medial (non-ampullated) limb associated with the superior petrosal sinus (SPS-SCD) [McCall et al., 2011].

The pathogenesis of SCDS is not completely understood, and both congenital and acquired events could contribute to its etiology. One theory is that some patients are born with thin bone overlying the superior semicircular canal [Carey et al., 2000], [Hirvonen et al., 2003], [Minor, 2005; Zhou et al., 2007], and that a “second event” (e.g., skull base trauma, a Valsalva maneuver, or intense acoustic exposure) causes an abrupt dehiscence of the arcuate eminence. Another theory is that dural pulsations over the arcuate eminence (located higher than the surrounding tegmen) result in progressive loss of bone over the superior canal. This latter theory is supported by observations that the prevalence of SCD increases among older populations. In some patients, a combination of factors (thin bone over the superior canal, increased intracranial pressure, or a second event) may contribute to the development of SCDS. In the case of SPS-SCD, the close proximity between the superior petrosal sinus and the medial limb of the superior canal is a relationship likely present at birth.

There have been brief mentions in the literature of SCDS occurring in family members [Brantberg et al., 2001; Mikulec et al., 2004]; however, these studies did not discuss the role of genetics in the context of SCD etiology. Hildebrand et al. described a cochlin (COCH) gene mutation (C-to-T base change in exon 3 at DFNA9 locus) in a single SCD patient with familial hearing loss [Hildebrand et al., 2009]. COCH is the most highly expressed protein in the human inner ear and may be responsible for either structural integrity or antimicrobial activity. Though the genetics of SCD are not known, Hildebrand et al. proposed that SCD may be present in other DFNA9-mutated patients (DFNA9 mutations lead to progressive hearing loss and vestibular impairment). More recently, SCD was described in ten children aged 5-11 years, which does support a congenital etiology in these cases [Lee et al., 2011].

To better understand the characteristics of SCDS among family members, we performed a retrospective review of over 200 SCDS patients from our institution

and identified three sets of first-degree relatives. The following is a retrospective case review of these patients.

Family 1 – Two brothers with hearing loss and suspected otosclerosis

A healthy man in his 40s (brother 1) presented in 2000 with progressive hearing loss. The patient had no vestibular signs or symptoms (Table 1). His mother and brother both had hearing loss, with no official diagnosis. Rinne was positive bilaterally, and Weber lateralized to the right. Audiometric testing showed a bilateral conductive hearing loss (right > left) with an air-bone gap (ABG) of 60dB at 250 Hz (Figure 1A). No acoustic reflexes, cVEMP (cervical vestibular-evoked myogenic potential), or imaging were obtained prior to surgery. Due to suspicion of bilateral otosclerosis, the patient underwent right stapedectomy in July 2001. Post-operatively, pure tone measurements showed no improvement in right-sided conductive hearing loss (CHL), and acoustic reflexes were absent bilaterally. CT imaging demonstrated bilateral SCD (Figs. 2A-B). cVEMP testing was also performed, showing low thresholds on the right and elevated thresholds on the left. The patient was managed conservatively, and amplification was offered. The patient has since been lost to follow-up.

The brother of the aforementioned patient presented in 2001 as a healthy man in his 50s (brother 2) with a history of bilateral progressive hearing loss, greater on the left side. He denied vertigo or disequilibrium. His otoscopic exam was normal. Rinne was positive bilaterally, and Weber was midline. Audiometric testing demonstrated a low frequency ABG of 40dB at 250 Hz and bilateral mixed hearing loss, with more loss on the left (Figure 1B). Acuity for conversational speech was diminished bilaterally. No acoustic reflexes, cVEMP, or imaging were obtained.

Table 1. Overview of symptoms reported for each relative

	Family 1		Family 2		Family 3	
	Brother 1	Brother 2	Mother	Daughter	Mother	Daughter
Side	Bilateral	Bilateral	Bilateral	Left	Bilateral	Left thin SSC
Autophony/hyperacusis	-	-	+	+	+	+
Hearing loss	+	+	+	+	+	-
Dizziness	-	-	+	+	+	+
ABG at 250Hz	60 dB	40 dB	40-50 dB	25 dB	30 dB	10 dB
cVEMP	Low [†]	Low [†]	X	≤ 60 dB	≤ 65 dB	X

+ = presence of a symptom, - = absence of a symptoms, X = no data available, ABG = Air-bone gap, cVEMP = cervical vestibular-evoked myogenic potential. [†]= cVEMP thresholds were low by report, but specific values were unavailable to authors.

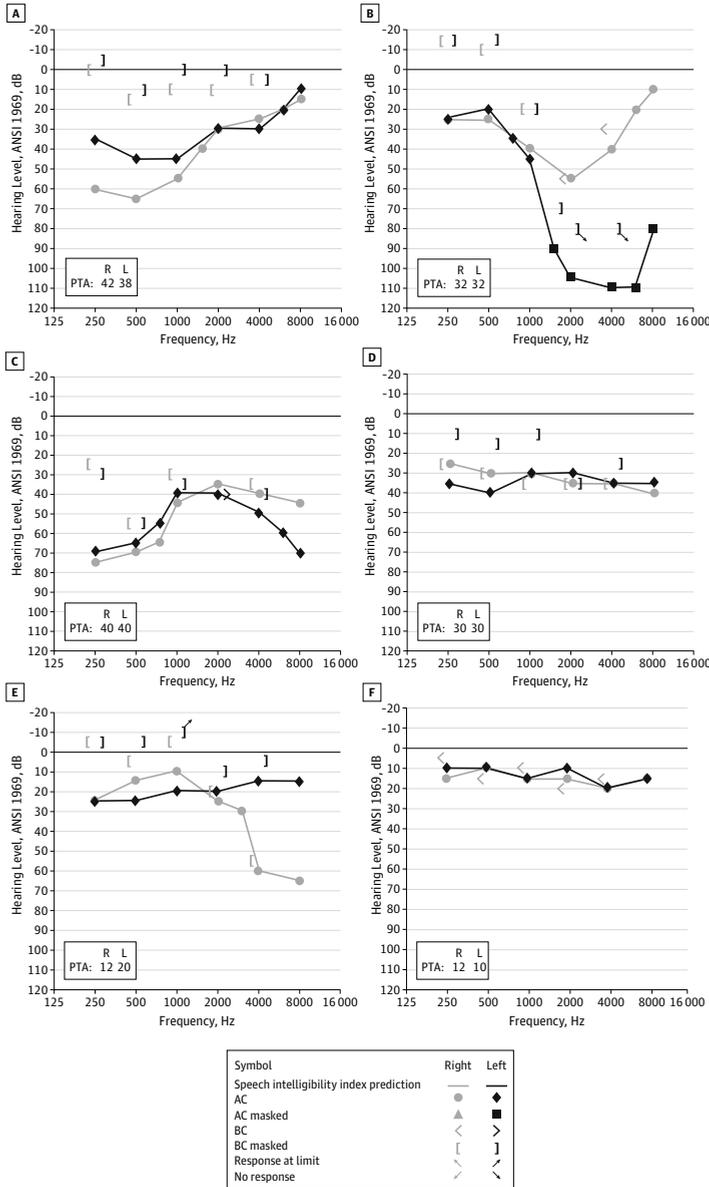


Figure 1. A = Family 1 (brother 49 yrs), B = Family 1 (brother 52 yrs), C = Family 2 (mother 74 yrs), D = Family 2 (daughter 48 yrs), E = Family 3 (mother 55 yrs), F = Family 3 (daughter 30 yrs). Despite similarities in symptom presentation, audiograms between family members vary considerably. Family 1 (A and B) has significant air-bone gaps at all frequencies, but the magnitude of the air-bone gaps differ. B also has supranormal conduction (bone conduction around -10dB at 250 Hz and 500 Hz) while A does not. Family 2 (C and D) has largely symmetric hearing loss in both relatives. However, C has a moderate to severe mixed hearing loss, while D only has a mild mixed hearing loss. Finally, Family 3 (E and F) share very little in common on audiogram. E shows air-bone gaps at all frequencies, while F does not show an air-bone gap. E also has moderate hearing loss in the high frequencies (60dB at 4kHz and 65dB at 8kHz) while F has normal hearing.

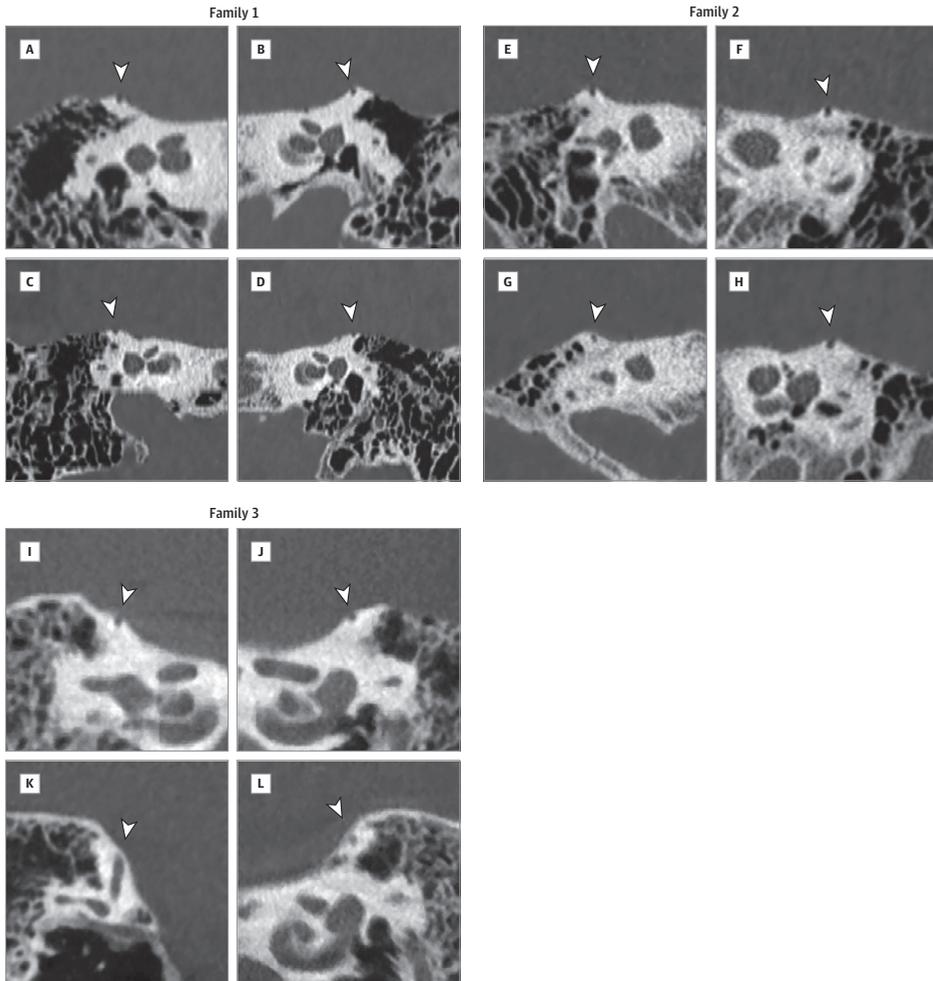


Figure 2. Temporal bone computed tomography (CT). A & B= Family 1 (brother 49 yrs), C & D= Family 1 (brother 52 yrs); E & F= Family 2 (mother 74 yrs), G & H= Family 2 (daughter 48 yrs); I & J= Family 3 (mother 55 yrs), K & L= Family 3 (daughter 30 yrs). All images are shown in Stenver view. Images in left-hand column are of RIGHT ears (i.e., A, C, E, G, I, K), and images in right-hand column are of LEFT ears (i.e., B, D, F, H, J, L). In Figs. A and B, CT scan revealed defects of the medial arcuate eminence bilaterally (arrows) and well-aerated mastoids. Likewise, Figs. C and D show well-aerated mastoid bones and SCD defects in the same location as defects in A and B. Both brothers also had right-sided tegmen defects without dural herniation (not shown). In Figs. E and F, the defects involve the peak of the arcuate eminence (arrows). The anatomic location of the defect in Figure H is similar to the anatomic location of the defect in Figure F. Though Figure G reveals a near-dehiscence on the right side, it is in the same location as the defects in Figure E. Images E through H also reveal well-aerated mastoid bones. The temporal bones in all images for Family 3 (Figs. I through L) show a severe downsloping tegmen that extends medially. These downsloping defects (arrows) have important surgical ramifications as intraoperative visualization of the defect can be difficult or impossible using binocular microscopy (and would necessitate excessive temporal lobe retraction). In such cases, we have found that a rigid angled endoscope is useful for direct visualization and repair of the entire bony defect via mini-craniotomy (data not published).

Diagnosis of bilateral otosclerosis was made, and this patient underwent a left stapedectomy in September 2001. Post-operatively, the audiogram showed no change in the air-bone gap, cVEMP thresholds were low, and imaging confirmed bilateral SCD (Figs. 2C-D). Amplification was offered to the patient. Unfortunately, he was lost to follow-up.

Family 2 – Mother and daughter with auditory and vestibular symptoms

A woman in her 70s presented with decreased hearing, autophony, aural fullness, and pressure-associated and sound associated dizziness (Table). Family history was significant for paternal hearing loss. Audiometric testing showed bilateral mixed hearing loss with a bilateral ABG of 40-50dB at 250 Hz (Figure 1C). Acoustic reflexes were present bilaterally, but tuning fork tests and cVEMP were not obtained. Dizziness was not evoked through tragal compression, pneumatic otoscopy or Valsalva maneuver. CT confirmed the diagnosis of bilateral SCD, with a larger arcuate eminence defect on the left (Figs. 2E-F). Management was conservative, but the patient was subsequently lost to follow-up.

A woman in her 40s, the daughter of the aforementioned patient, presented in 2010 with progressive hearing loss that had started 8 years prior. She had experienced vertigo in the past and had mild dizziness during migraine headaches (from which she no longer suffered at time of presentation) (Table 1). Rinne was positive bilaterally, and Weber lateralized to the left ear. Audiometric testing showed a 25dB low frequency ABG at 250 Hz (Figure 1D), and acoustic reflexes were present bilaterally. cVEMP testing showed lowered thresholds on the left side (55, 55, 50 and 60dB nHL at 250, 500, 750 and 1000 Hz, respectively) and non-responsive (NR) thresholds on the right (90(NR), 100(NR), 100 and 100(NR)dB nHL at 250, 500, 750 and 1000 Hz, respectively). No dizziness or nystagmus were evoked through tragal compression, pneumatic otoscopy or Valsalva maneuver. Temporal bone CT revealed left SCD and a thin, but intact, right SSC (Figs. 2G-H). Management was conservative, but the patient has been subsequently lost to follow-up.

Family 3 – Mother and daughter with auditory and vestibular symptoms

A woman in her 50s presented in 2011 with a 5-year history of dizziness provoked by sound, pressure, and exercise. She also reported aural fullness, autophony, conductive hyperacusis, right-sided pulsatile tinnitus and bilateral hearing loss (right>left) (Table 1). A previous diagnosis of a Type 1 Chiari malformation was not thought to be the cause of her symptoms. Her otoscopic exam was unremarkable. The Rinne was positive bilaterally, and Weber was midline. Audiometric testing showed a mixed hearing loss in the right ear (the patient had previously lost her

high tone hearing in the right ear). The left ear showed an ABG of 60dB at 4kHz and bone conduction thresholds above 0dB (Figure 1E). Acoustic reflexes were not obtained pre-operatively, but cVEMP thresholds were low bilaterally (60-65dB nHL). Pneumatic otoscopy and Valsalva caused nystagmus. Temporal bone CT showed bilateral SCD (Figs. 2I-J). The patient underwent right-sided middle fossa craniotomy with occlusion of her right-sided defect with bone wax.

One year after the initial operation, the patient underwent a second middle fossa craniotomy with occlusion, this time on the left (one year after the initial operation). Post-operatively, she noticed improvement in autophony, conductive hyperacusis and dizziness, while hearing remained stable bilaterally. cVEMP thresholds were also within normal limits bilaterally. She continues to be symptom-free one year following her second surgery.

A woman in her 30s, the daughter of the aforementioned patient, presented with dizziness and headaches in 2011. The daughter's complaints started during pregnancy (one year prior to presentation). She had similar symptoms as her mother, but less severe. The patient reported imbalance, dizziness provoked by sound, pressure, and exercise, aural fullness, hyperacusis, pulsatile tinnitus and headaches. She reported no hearing loss (Table 1). Rinne was positive bilaterally, and Weber lateralized to the right. Audiometric testing showed a 10dB ABG at 250 Hz on the right (Figure 1F). Acoustic reflexes were not obtained, but cVEMP testing showed normal thresholds bilaterally. Temporal bone CT showed a very thin but intact left superior canal and intact right canal (Figs. 2K-L). This patient has been managed conservatively with migraine medications.

DISCUSSION

In this case report we present three families with symptomatic SCD amongst first-degree relatives. These findings suggest that genetics may play a role in the etiology of SCD for some patients (in the absence of head trauma or skull base fracture). Interestingly, first-degree relatives present with similar complaints: the two brothers experienced only conductive hearing loss, while both mothers and daughter sets experienced vestibular and auditory symptoms. Furthermore, temporal bone CT scans between relatives showed very similar skull base topography and anatomic SCD defects. It is possible that skull base structure and anatomic location of SCD is passed down genetically to offspring, which may explain the resemblance of symptoms in first-degree relatives. A larger cohort is needed to

formalize a radiologic classification system based on the anatomic characteristics of the canal defect and the surrounding skull base topography.

Although similar symptoms were reported, both mothers presented with more severe complaints than their daughters. In all cases symptom onset occurred during adulthood, and symptoms seemed to progress with age. Worsening of symptoms in adulthood has been described before; Hegemann et al. describe a patient who reported initial SCD symptoms at age ten with progressively worsening symptoms until surgical repair at age 40 [Hegemann and Carey, 2011]. They hypothesize that the dehiscence began to transmit more pressure between the inner ear and intracranial space as the patient aged. On the other hand, Nadgir et al. speculate that SCD is an acquired condition with an increased prevalence in older populations [Nadgir et al., 2011]. The study found no association between temporal bone thinning and aging, and also no association of thinning with contralateral dehiscence (i.e., thinning occurs independently of dehiscence development). Based on the current study, we agree with Hegemann et al. and additionally hypothesize that an increase in bony defect size over time may correlate with symptom progression. Nevertheless, more research is needed to further elucidate the pathophysiology of such processes.

Of note, the mother of Family 3 had an established diagnosis of a Type 1 Chiari malformation (CM-I) before she was given the diagnosis of SCD. Kuhn et al. have shown that the prevalence of CM-I is increased in patients with SCD compared to the prevalence of CM-I in the general population, 23% vs. 0.6%–1%, respectively [Kuhn and Clenney, 2010]. The pathogenesis of CM-I has been attributed to neuroectodermal developmental abnormalities and overcrowding of the hindbrain by an underdeveloped posterior cranial fossa [Nishikawa et al., 1997]. As a result, the cerebellum obliterates the cerebrospinal fluid (CSF) space surrounding the cervicomedullary junction, and exaggerated CSF pressure waves may have a cumulative erosive effect on the surrounding bone. As neurotologic symptoms tend not to occur until adulthood, this slow, bony erosive process may affect a preexisting developmental bony abnormality, thus leading to the development of SCD in patients with CM-I. However, the authors suggest that it may be premature to have all SCD patients undergo magnetic resonance imaging (MRI) to detect underlying CM-I.

Finally, the daughter of Family 3 had very thin bone over the SSC rather than a frank dehiscence. Nevertheless, the patient did present with auditory and vestibular symptoms suggestive of SCD. Vertigo can be seen in one out of ten

patients with thinning of the SSC [Carey et al., 2000]. In addition, patients with a “near-dehiscence” and signs and symptoms of SCD have recently been described [Ward et al., 2013]. The authors surgically managed these patients by plugging and/or resurfacing the SSC, and improvements in SCD signs and symptoms were reported. Additional studies are needed to determine the benefit of surgery in this unique group of patients with SCD, as well as an objective, validated methodology for defining “thin” bone.

CONCLUSION

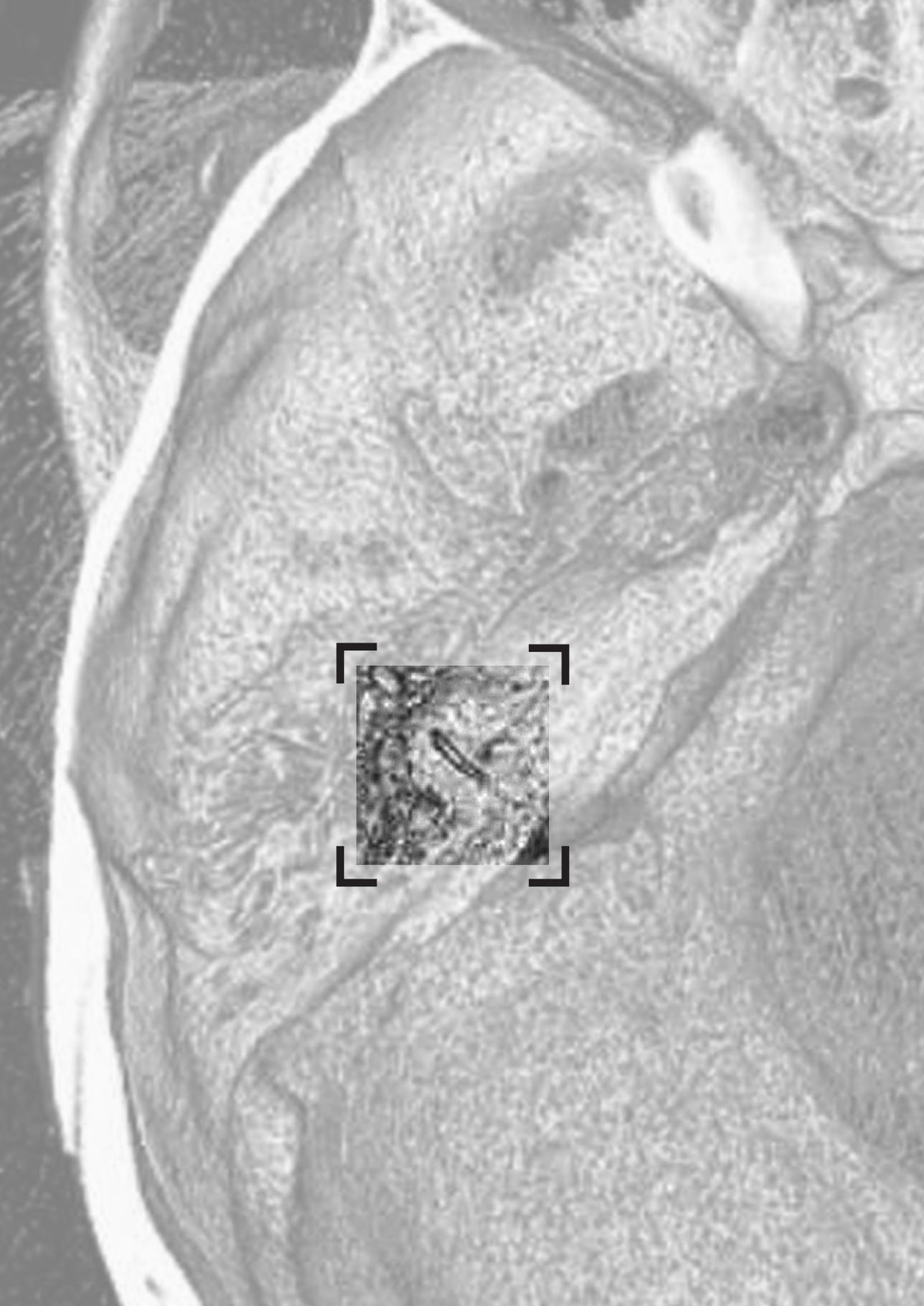
Our observations suggest that: 1) the presentation of SCD signs and symptoms in members of the same family were similar, 2) the topography of the skull base relative to the bony defect of the superior canal was similar amongst first-degree relatives with SCD and 3) symptoms seemed to be more pronounced with older patients (mothers) compared to their younger counterparts (daughters). Although SCD etiology is still debated, a genetic basis seems plausible. Additional genetic and cohort studies are needed to examine potential contributions for this condition.

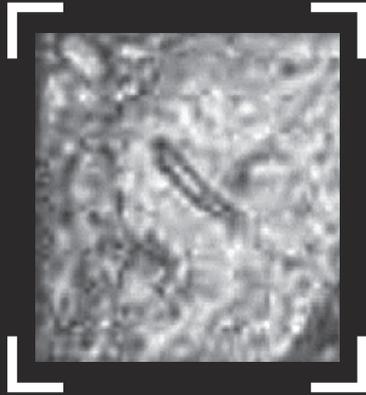
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REFERENCES

- Brantberg K**, Bergenius J, Mendel L, Witt H, Tribukait A, Ygge J: Symptoms, findings and treatment in patients with dehiscence of the superior semicircular canal. *Acta Otolaryngol* 2001; 121:68-75.
- Carey JP**, Minor LB, Nager GT: Dehiscence or thinning of bone overlying the superior semicircular canal in a temporal bone survey. *Arch Otolaryngol Head Neck Surg* 2000;126:137-147.
- Hegemann SC**, Carey JP: Is superior canal dehiscence congenital or acquired? A case report and review of the literature. *Otolaryngol Clin North Am* 2011;44:377-382, ix.
- Hildebrand MS**, Tack D, Deluca A, Hur IA, Van Rybroek JM, McMordie SJ, Muilenburg A, Hoskinson DP, Van Camp G, Pensak ML, Storper IS, Huygen PL, Casavant TL, Smith RJ: Mutation in the coch gene is associated with superior semicircular canal dehiscence. *Am J Med Genet A* 2009;149A:280-285.
- Hirvonen TP**, Weg N, Zinreich SJ, Minor LB: High-resolution CT findings suggest a developmental abnormality underlying superior canal dehiscence syndrome. *Acta Otolaryngol* 2003; 123:477-481.
- Kuhn JJ**, Clenney T: The association between semicircular canal dehiscence and Chiari type I malformation. *Arch Otolaryngol Head Neck Surg* 2010;136:1009-1014.
- Lee GS**, Zhou G, Poe D, Kenna M, Amin M, Ohlms L, Gopen Q: Clinical experience in diagnosis and management of superior semicircular canal dehiscence in children. *Laryngoscope* 2011; 121:2256-2261.
- McCall AA**, McKenna MJ, Merchant SN, Curtin HD, Lee DJ: Superior canal dehiscence syndrome associated with the superior petrosal sinus in pediatric and adult patients. *Otol Neurotol* 2011;32:1312-1319.
- Mikulec AA**, McKenna MJ, Ramsey MJ, Rosowski JJ, Herrmann BS, Rauch SD, Curtin HD, Merchant SN: Superior semicircular canal dehiscence presenting as conductive hearing loss without vertigo. *Otol Neurotol* 2004;25:121-129.
- Minor LB**: Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:1717-1727.
- Minor LB**, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998; 124:249-258.
- Nadgir RN**, Ozonoff A, Devaiah AK, Halderman AA, Sakai O: Superior semicircular canal dehiscence: Congenital or acquired condition? *AJNR Am J Neuroradiol* 2011;32:947-949.
- Nishikawa M**, Sakamoto H, Hakuba A, Nakanishi N, Inoue Y: Pathogenesis of chiari malformation: A morphometric study of the posterior cranial fossa. *J Neurosurg* 1997;86:40-47.
- Ward BK**, Wenzel A, Ritzl EK, Gutierrez-Hernandez S, Della Santina CC, Minor LB, Carey JP: Near-dehiscence: Clinical findings in patients with thin bone over the superior semicircular canal. *Otol Neurotol* 2013;34(8):1421-8.
- Zhou G**, Ohlms L, Liberman J, Amin M: Superior semicircular canal dehiscence in a young child: Implication of developmental defect. *Int J Pediatr Otorhinolaryngol* 2007;71:1925-1928.





Appendix II

Radiologic and cVEMP progression in superior canal dehiscence syndrome

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†= Both authors contributed equally to this manuscript

Submitted

ABSTRACT

Objective: To observe and assess the change in hearing, vestibular function and size of superior canal dehiscence in patients with superior canal dehiscence syndrome (SCDS) over time.

Patients: Two patients with SCDS identified with symptomatic and objective progression of this syndrome, shown by repeated audiometric testing, cervical vestibular-evoked myogenic potentials (cVEMP) and computed tomography (CT) scans.

Intervention: Audiometric testing, cVEMP testing and temporal bone CT scans were performed twice on patients with high clinical suspicion of disease progression.

Main Outcome Measure: Audiometry (magnitude of the air-bone gap), cVEMP (magnitude of the thresholds) and CT scans (size of the superior canal dehiscence) were reviewed. Symptoms were assessed at each clinical visit and prior to repeat testing.

Results: Retrospective review of 250 patients with SCDS showed three patients with disease progression over time. All patients initially presented with minor symptoms, air-bone gaps (ABG) on audiometry, low cVEMP thresholds and small dehiscences. Eight, six and four years later, progression of SCD signs and symptoms was seen in all patients. Audiometry showed development of larger ABGs and even lower VEMP thresholds. Repeated CT scanning showed an increase in dehiscence size on one affected ear in all patients.

Conclusions: Progression of SCD signs and symptoms, as subjectively described by a patient, can be objectively observed and monitored with diagnostic testing. We think that it is important to perform a full evaluation at time of initial presentation, including audiometric testing, cVEMP testing and a temporal bone CT scan, to follow the disease course over time.

INTRODUCTION

Superior canal dehiscence syndrome (SCDS) was first characterized by Minor et al. in 1998, and patients can present with a myriad of auditory and/or vestibular symptoms associated with a bony defect of the superior canal [Minor et al., 1998]. The pathogenesis of SCDS is not completely understood, and both congenital and acquired events may contribute to its etiology. For this reason, and the relative infancy of its discovery, the natural course of this condition has yet to be determined. As such, it is of the utmost importance to the SCDS patient whether or not they can expect their condition to improve, worsen or remain the same over time. Furthermore, the prognosis becomes even more significant to the patient who is trying to determine the best course of management, i.e., conservative or surgical, as either course is not without associated risks.

The paucity of information in the literature about disease progression and long-term outcomes makes it difficult for clinicians to provide patients with answers to these important questions. Zhou et al. presented a single pediatric SCDS case in which the patient experienced a decline in hearing both subjectively and audiometrically over a 5 year period [Zhou et al., 2007]. Audiometry showed increased air-bone gaps (ABG) and supranormal bone conduction in the low frequencies over this time frame. Computed tomography (CT) scans were taken at intervals as well, all showing the dehiscent superior canal, but measurements of defect size were not reported. Likewise, Wilkinson et al. showcased an adult SCDS patient with a decline in hearing (increase in ABGs) with symptomatic progression over time [Wilkinson et al., 2008]. However, neither study reported any changes in cVEMP thresholds or physical enlargement of the actual defect based on CT exam.

To better understand and assess the progression of SCDS, we performed a retrospective review of over 250 SCDS patients from our institution and identified three patients that showed disease progression based on audiometry, cVEMP testing, and temporal bone CT scans. The following is a review of these patients.

PATIENTS

Patient 1

A 51 year-old male presented to our clinic in 2004 with mild symptoms of hearing loss, autophony and conductive hyperacusis that began suddenly in the right ear two years prior with no inciting event. His otoscopic exam was normal, with

Weber lateralizing to the right. Audiometry showed a -5 dB air-bone gap (ABG) on the right at 500 Hz (Figure 1A). However, low cervical vestibular-evoked myogenic potential (cVEMP) thresholds were seen in both ears (Table 1). High-resolution

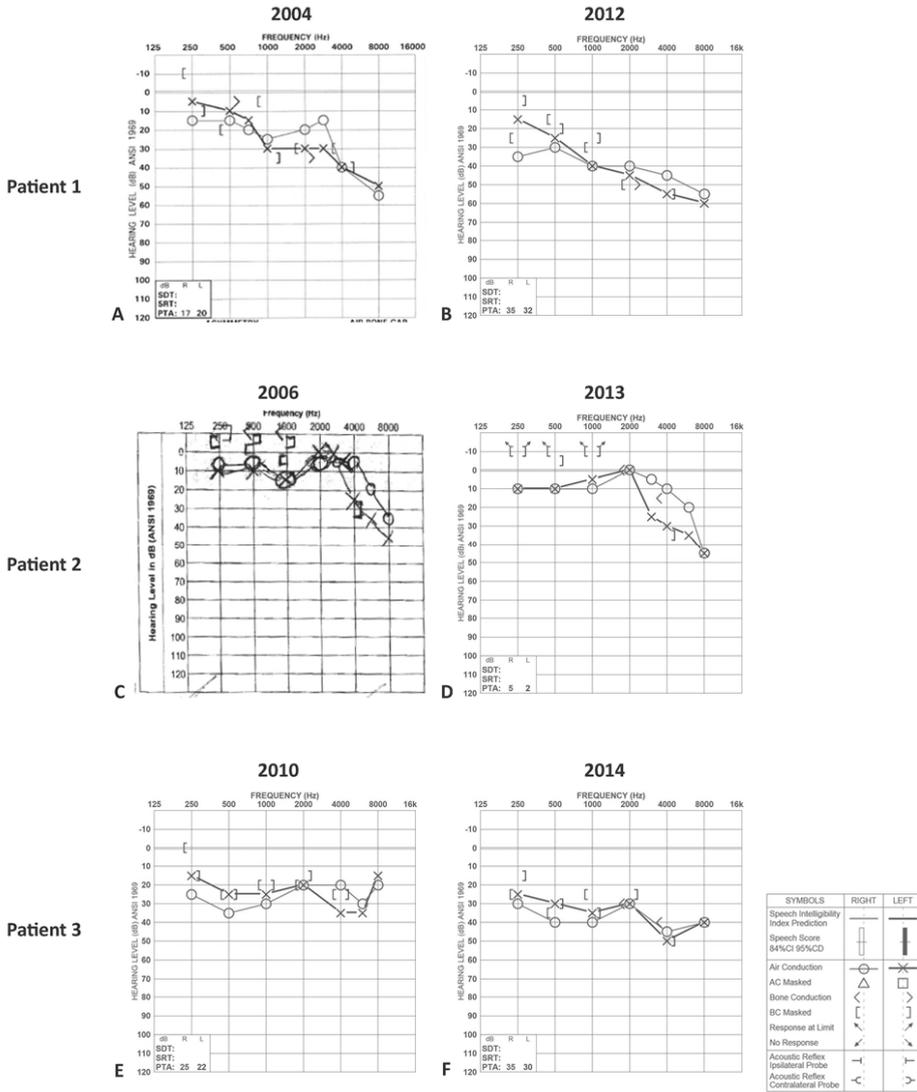


Figure 1. Audiometric testing. Patient 1- (A) and (B). Patient 1 - had an increase in his air-bone gap (ABG) at 500 Hz on the right side from 2004 (-5 dB) to 2012 (15 dB); he also had increase in ABG on the left side in the low frequencies during this period. Patient 2 - (C) and (D). Patient 2 showed supra-normal bone conduction and ABGs at 250, 500, and 1000 Hz in both ears in 2006 and 2013. However, the ABGs are increased on the right from 2006 to 2013 at the same frequencies. Patient 3 - (E) and (F). Patient 3 showed a new 10 dB ABG on the left in 2010 compared to no ABG at 250 Hz in 2010. This patient also had right-sided SCD repair prior to the 2014 testing, and thus the ABGs at 250 and 500 Hz are much smaller in 2014.

temporal bone computed tomography (CT) scan revealed bony defects of the superior semicircular canal (SSC) bilaterally near the arcuate eminence. At this time, the patient chose conservative management with avoidance of stimuli.

Eight years after his initial diagnosis, this patient presented with progressive signs and symptoms of SCD, including oscillopsia with loud sounds, pulsatile tinnitus and worsened hearing loss. Otoscopic exam was again normal, and Weber still lateralized to the right side. Audiometric testing showed an increased ABG at 500 Hz of 15 dB on the right side (Figure 1B). The patient showed bilateral lower thresholds on repeat cVEMP testing as compared to the initial test eight years prior (Table 1). Temporal bone CT was also repeated, and showed an increased defect of the SSC on the right side- from a 32° dehiscence in 2004 to 62° in 2012 (Figure 2) (all measurements were made using the angle measurement tool on our institution's picture archiving and communication system (PACS) (Synapse version 4.2, Fujifilm, Tokyo, Japan). As the patient presented with debilitating symptoms at this juncture, he decided to undergo a right-sided middle fossa craniotomy (MFC) with SCD repair by the senior author (DJL). Subsequently, this patient elected to have the contralateral side surgically repaired via middle fossa craniotomy, and he is doing well with significant improvement of all previous symptoms.

Patient 2

A 55 year-old male presented in 2006 with autophony, aural fullness and pulsatile tinnitus (left ear worse than right) with no inciting event. These symptoms started nine years prior to presentation. Otoscopic exam was normal, and audiometry showed supranormal bone conduction bilaterally in the lower frequencies (Figure

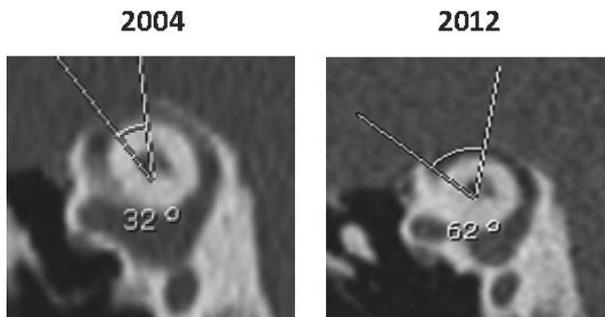


Figure 2. Temporal bone computed tomography (CT) scans of Patient 1. Comparison of the right superior canal on the CT scans of 2004 and 2012 on the Pöschl view (parallel to the semicircular canal). The right ear shows an approximate 32° angle of dehiscence on the 2004 scan. The same ear in 2012, however, shows a 62° angle of dehiscence; almost double the measurement from 2004. (All measurements taken using the angle measurement tool on our institution's PACS system- Synapse version 4.2, Fujifilm, Tokyo, Japan).

Table 1. Overview of cVEMP data.**A**

Patient 1		
Left cVEMP	2004	2012
250 Hz	70	55
500 Hz	65	55
750 Hz	75	60
1000 Hz	80	65
Right cVEMP		
250 Hz	50	40
500 Hz	55	55
750 Hz	55	55
1000 Hz	60	60

B

Patient 2		
Left cVEMP	2006	2013 [†]
250 Hz	55	80
500 Hz	60	80
750 Hz	-	85
1000 Hz	60	85
Right cVEMP		
250 Hz	60	45
500 Hz	70	65
750 Hz	-	65
1000 Hz	70	60

C

Patient 3		
Left cVEMP	2010	2014*
250 Hz	100	55
500 Hz	95	75
750 Hz	90	70
1000 Hz	95	75
Right cVEMP		
250 Hz	65	90
500 Hz	60	100
750 Hz	65	100
1000 Hz	65	100

cVEMP= cervical vestibular-evoked myogenic potential; all thresholds reported in dB HL. (A) Patient 1 showed decreased thresholds in the left ear at all frequencies between 2004 and 2012, and showed a decreased threshold at 250 Hz in the right ear during this time frame; (B) Patient 2 revealed decreased thresholds in the left ear at all tested frequencies in 2006, and a decreased threshold at 250 Hz in the right ear at this time. By 2013, all thresholds had further decreased on the right side; (C) Patient 3 also showed decreased thresholds in the left ear at all frequencies between 2010 and 2014. †= By the time of the second VEMP test in late 2013, Patient 2 had already undergone superior canal dehiscence repair on the left side only, hence the normalization of thresholds on the left side. *= Patient 3 had also already had a right-sided repair performed by the time of the second VEMP test in 2014; “-” = not tested.

1C). cVEMP testing revealed low thresholds bilaterally, left lower than right (Table 1). Temporal bone CT scan showed a dehiscence on the medial downslope of the superior canal bilaterally. The patient did not feel his symptoms warranted surgical treatment at this time, and chose conservative management instead.

Six years later, this patient presented in 2012 with worsened autophony, hyperacusis, aural fullness, pulsatile tinnitus and pressure- and sound-induced vertigo. Otoscopic exam was again normal. Although the patient subjectively reported worse symptoms on the left, audiometric testing showed larger ABGs on the right versus left at 500 Hz and bilateral supranormal bone conduction (Figure 1C and D). Temporal bone CT was repeated and showed an increase in defect size on the right from a 22° dehiscence in 2006 to a 34° dehiscence in 2012 (Figure 3). At this time the patient felt that his symptoms severely impacted his daily life and chose to undergo a MFC with repair of the left SCD by the senior author. cVEMP testing was repeated after the left-sided repair and showed an even lower threshold on the right than in 2006 (Table 1). As with the first patient, Patient 2 had bilateral disease and underwent a second repair via MFC for the right ear and is doing well in his post-operative course.

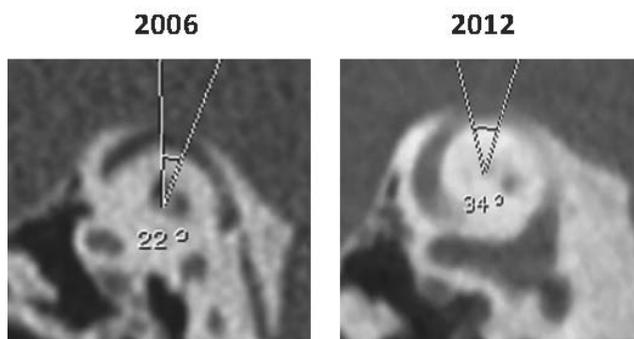


Figure 3. Temporal bone computed tomography (CT) scans of Patient 2. Comparison of the right superior canal on the CT scans of 2006 and 2012 on the Pöschl view (parallel to the semicircular canal). The right ear shows an approximate 22° angle of dehiscence on the 2006 scan. The same ear six years later in 2012 shows a 34° angle of dehiscence. (All measurements taken using the angle measurement tool on our institution's PACS system- Synapse version 4.2, Fujifilm, Tokyo, Japan).

Patient 3

A 57 year-old female presented to our clinic in 2010 with autophony, pulsatile tinnitus and aural fullness (right worse than left). She also complained of sound- and pressure-induced dizziness. These symptoms started several years prior to presentation. Otoscopic exam was normal, with Weber lateralizing to the right. Audiometric testing revealed a 25 dB ABG on the right at 250 Hz, and no ABG on the left at 250 Hz (Figure 1E). She showed low cVEMP thresholds in the right ear and normal thresholds on the left (Table 1). Temporal bone CT scan showed a dehiscence on the medial downslope of the superior canal bilaterally. The patient decided to undergo right-sided surgical repair via MFC by the senior author, and experienced improvement in all pre-operative symptoms.

Four years after the initial diagnosis, this patient presented with worsened autophony, hyperacusis, aural fullness, and pressure- and sound-induced vertigo, left worse than right. Otoscopic exam was again normal, but Weber lateralized to the left. Audiometric testing showed a new 10 dB ABG at 250 Hz on the left (Figure 1F). Repeat cVEMP testing now showed decreased thresholds on the left (Table 1). Repeat CT showed an increase in defect size of the left SSC from a 28° dehiscence in 2010 to 47° in 2014 (Figure 4). The patient is currently considering SCD repair for the left side.

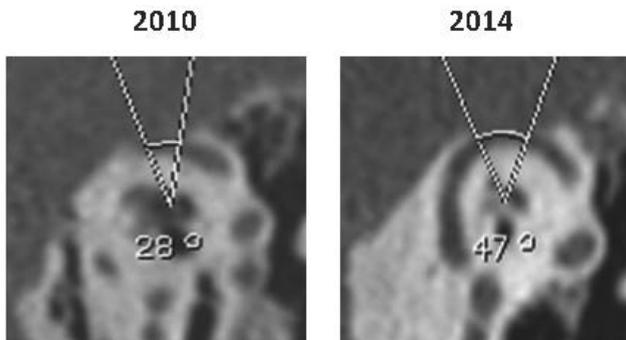


Figure 4. Temporal bone computed tomography (CT) scans of Patient 3. Comparison of the left superior canal on the CT scans of 2010 and 2014 on the Pöschl view (parallel to the semicircular canal). The left ear shows an approximate 28° angle of dehiscence on the 2010 scan. In 2014, the same ear shows a 47° angle of dehiscence- a 19° difference in just four short years. (All measurements taken using the angle measurement tool on our institution's PACS system- Synapse version 4.2, Fujifilm, Tokyo, Japan).

DISCUSSION

Patients often present to clinic after SCD signs and symptoms have been present for years, often after a long, frustrating search for an appropriate diagnosis. In these patients VEMP thresholds and CT measurements are usually not made at the onset of symptoms for a variety of reasons (e.g., misdiagnosis, lack of knowledge about SCD). Consequently, a change in VEMP thresholds or increase in SCD size over time cannot be adequately studied without these preliminary results.

In this unique case report, we were able to objectively measure and observe lower cVEMP thresholds and a larger SCD several years after initial presentation, which seemed to correspond with the subjective progression of SCD symptoms that two of the patients experienced. Reasons for the worsening of symptoms may be explained by the exact objective measures we observe, in that a larger defect size or location influences the clinical presentation. In another paper from our institution, we examined the association between SCD length and location with auditory and vestibular symptoms, ABG on audiometry, and cVEMP thresholds in 104 patients [Nielsen et al., 2014]. We found that patients with auditory symptoms had a larger dehiscence on CT scan than patients with vestibular symptoms only. We also saw that ABGs increased as the SCD length increased, and that a larger dehiscence was associated with even lower cVEMP thresholds. Finally, our study showed that hearing loss increased with increased SCD size in one temporal bone as well. This observation may help explain why the patients in the current study experienced a progression of symptoms because their actual defect enlarged as well.

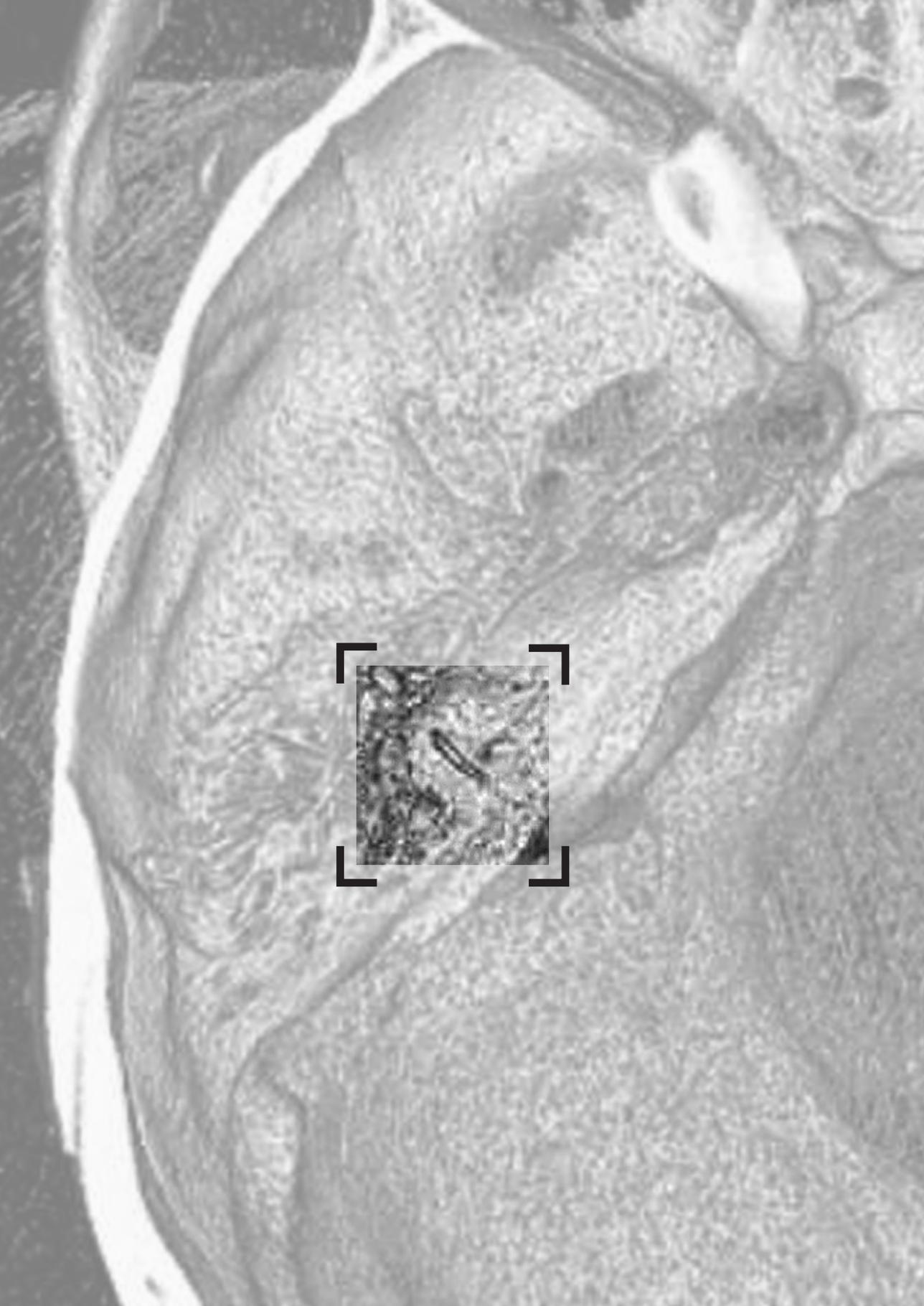
In the above cases, all patients reported improvement of symptoms after surgical intervention. In addition, these patients demonstrated decreased or closure of ABGs on repeat audiometric testing and normalization of cVEMP thresholds. Previous studies have shown the resolution or improvement of patients' symptoms and normalization of audiograms or VEMP thresholds after surgery as well [Beyea et al., 2012; Limb et al., 2006; McCall et al., 2011; Minor, 2005; Wilkinson et al., 2008]. The combination of these subjective and objective results suggests that disease progression may at least be stalled, if not improved or halted altogether. However, without knowing the etiology of this condition, it may be difficult to truly determine the prognosis for patients. Further studies are needed to determine the natural progression and long-term outcomes of SCDS for those patients that are managed conservatively and/or surgically.

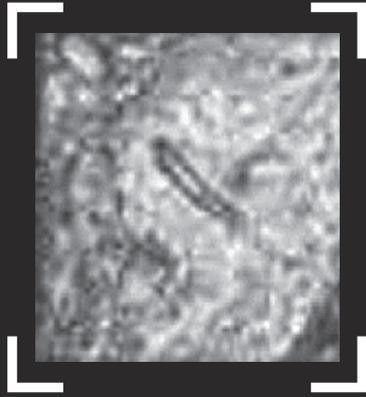
CONCLUSION

Progression of SCD signs and symptoms, as subjectively described by a patient, can be objectively observed and monitored with diagnostic testing. We believe it is important to perform a full evaluation at time of initial presentation, including audiometric testing, cVEMP testing and a temporal bone CT scan, to follow the disease course over time.

REFERENCES

- Beyea JA**, Agrawal SK, Parnes LS: Transmastoid semicircular canal occlusion: A safe and highly effective treatment for benign paroxysmal positional vertigo and superior canal dehiscence. *Laryngoscope* 2012;122:1862-1866.
- Limb CJ**, Carey JP, Srireddy S, Minor LB: Auditory function in patients with surgically treated superior semicircular canal dehiscence. *Otol Neurotol* 2006;27:969-980.
- McCall AA**, McKenna MJ, Merchant SN, Curtin HD, Lee DJ: Superior canal dehiscence syndrome associated with the superior petrosal sinus in pediatric and adult patients. *Otol Neurotol* 2011;32:1312-1319.
- Minor LB**: Clinical manifestations of superior semicircular canal dehiscence. *Laryngoscope* 2005;115:1717-1727.
- Minor LB**, Solomon D, Zinreich JS, Zee DS: Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. *Arch Otolaryngol Head Neck Surg* 1998; 124:249-258.
- Nielsen ME**, Hamberg LM, Silverman JB, Lou KV, McCall AA, Windsor A, Curtin HD, Herrmann BS, Grolman W, Nakajima HH, Lee DJ: Superior canal dehiscence length and location influences clinical presentation and audiometric and cervical vestibular-evoked myogenic potential testing. *Audiol Neurootol* 2014;19:97-105.
- Wilkinson EP**, Liu GC, Friedman RA: Correction of progressive hearing loss in superior canal dehiscence syndrome. *Laryngoscope* 2008;118:10-13.
- Zhou G**, Ohlms L, Liberman J, Amin M: Superior semicircular canal dehiscence in a young child: Implication of developmental defect. *Int J Pediatr Otorhinolaryngol* 2007;71:1925-1928.





Appendix III

Hearing your eyeballs move: superior canal dehiscence syndrome

Daniel J. Lee and Marlien E.F. Niesten

Has a patient ever told you he can hear his eyeballs moving or his heart beating in his ear? Has anyone ever said his voice sounds too loud when he speaks? Has a patient ever reported dizziness with loud sounds, heavy lifting, or blowing his nose?

These peculiar symptoms can be associated with an unusual condition of the inner ear called superior canal dehiscence (SCD) syndrome. Lloyd Minor, MD, in 1998 described a series of patients with vestibular and auditory symptoms caused by a defect or dehiscence of the bony covering of the superior semicircular canal. The superior canal is part of the inner ear, and is one of three pairs of balance organs that detect angular head acceleration.

Patients with SCD syndrome can present with a wide range of clinical signs and symptoms that include ear (aural) fullness, sensitivity to self-generated sounds such as swallowing or speaking (autophony), hearing loss, pulsatile tinnitus, dizziness, and vertigo. Patients with SCD syndrome are often misdiagnosed with more common otologic conditions such as Eustachian tube dysfunction, otosclerosis, Ménière's disease, and benign paroxysmal positional vertigo. Some patients with intractable symptoms seek psychiatric care.

The diagnosis is based on presenting signs and symptoms, the absence of external or middle ear pathology on otoscopic examination, 512-Hz tuning forks lateralizing to the more severely affected ear, nystagmus triggered by loud, low-frequency sound stimuli or a Valsalva maneuver, and computed tomography imaging confirming a bony defect of the semicircular canal. Additional testing used to confirm SCD syndrome includes audiometric threshold testing demonstrating a low-frequency air-bone gap (conductive hearing loss), bone-conduction thresholds better than 0 dB (in the range of -5 to -10 dB, called supranormal bone conduction).

Tympanometry and stapedial reflex testing are generally normal, excluding a middle ear or ossicular abnormality as a possible cause of the patient's symptoms. A few patients, however, do have co-existing SCD and either ossicular fixation or Eustachian tube dysfunction. A sensitive measure of an active SCD is the cervical vestibular-evoked myogenic potential (cVEMP) test that measures inhibitory responses of the sternocleidomastoid, a neck muscle. The cVEMP tests the integrity of the saccule (one of two balance organs that detect linear acceleration) and inferior vestibular nerve. Most patients with symptoms associated with SCD will have low-threshold cVEMPs compared with the better ear.

Two types of SCD are seen based on CT imaging: dehiscence of arcuate eminence (top of the superior semicircular canal) and dehiscence associated with the superior petrosal sinus, a vein that runs in a bony groove along the ridge of the temporal bone. (Otol Neurotol 2011;32[8]:1312; Figure.) The pathologic process, or first event, by which SCD may occur includes congenital bone-thinning over the superior semicircular canal with low-lying skull base (arcuate eminence defect) or a close anatomic relationship between the superior petrosal sinus and the medial limb of the superior semicircular canal. Twenty to 30 percent of SCD patients re-

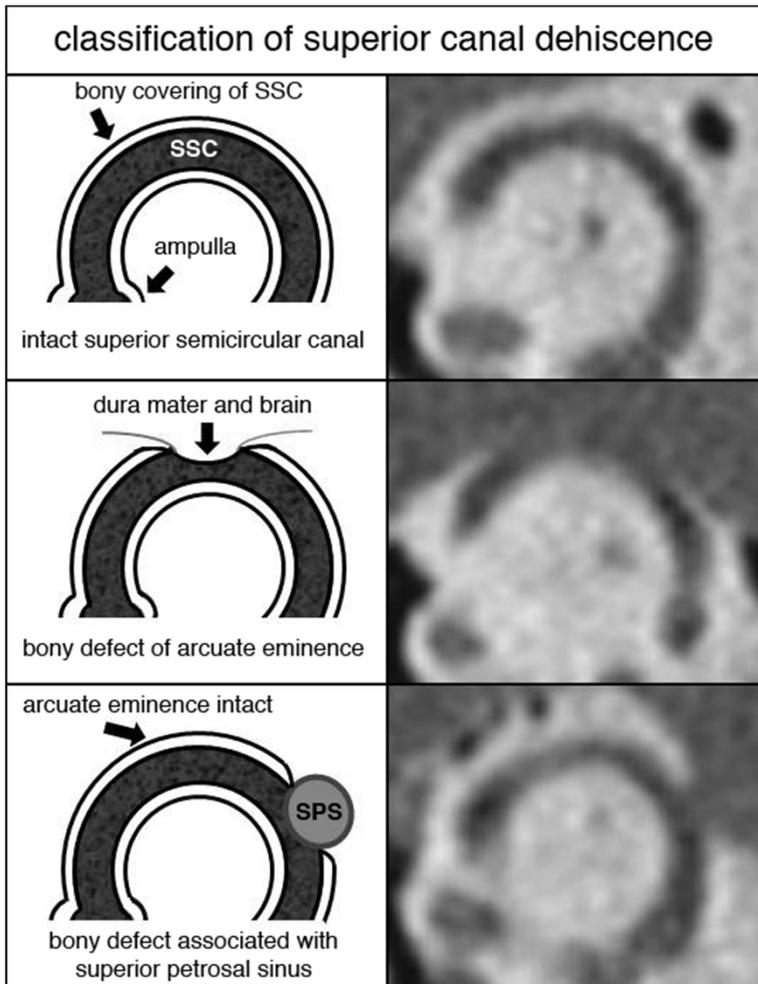


Figure. Classification of superior canal dehiscence (SCD) based on location with schematic and correlating computed tomography image (Pöschl view, parallel to the superior canal). A, intact bony covering of the superior semicircular canal; B, dehiscence at the arcuate eminence where most SCDs (around 90%) are found; C, dehiscence due to a vein called the superior petrosal sinus. SSC, superior semicircular canal; SPS, superior petrosal sinus.

port a second event that triggered symptoms, resulting from a loud sound, heavy lifting, or childbirth.

Surgical repair, either by plugging or resurfacing the defect, is successful in the majority of patients who have intolerable symptoms associated with SCD in one ear. The approach can be done using a middle fossa craniotomy to visualize and repair the SCD directly (arcuate eminence defect). Mastoidectomy can also be used to repair the SCD indirectly (superior petrosal sinus associated defect). Surgery is generally safe and effective. Complications are not common and include hearing loss, dizziness, facial nerve injury, and brain fluid leakage. As vestibular dysfunction in the operated ear is a known risk (or even expected outcome) after SCD repair, patient selection and choice of which ear to operate on is important, especially in patients with bilateral SCD. Most patients with bilateral SCD seen on CT have symptoms in only one ear, but managing patients with symptoms of SCD from both ears is more challenging. Findings from our institution suggest that a larger conductive loss and lower cVEMP thresholds correlate with the worse ear in patients with bilateral SCD. (*Otol Neurotol* 2012;33[5]:824.) A recent study provides new insight on outcomes in patients who underwent surgical repair of bilateral SCD syndrome.

Second-Side Surgery in Superior Canal Dehiscence Syndrome

Agrawal Y, Minor LB, et al. Otol Neurotol. 2012;33[1]:72

The symptom profile of adult patients with bilateral SCD syndrome who underwent second-side surgery was examined, and the effects of surgery on dizziness and quality of life were assessed. Five patients underwent second-side SCD repair, with reported results on four patients. One patient did not have post-operative follow-up at the time of publication. Follow-up ranged from three to 34 months. All patients received a middle fossa craniotomy with plugging of the bony defect; none experienced major surgical complications.

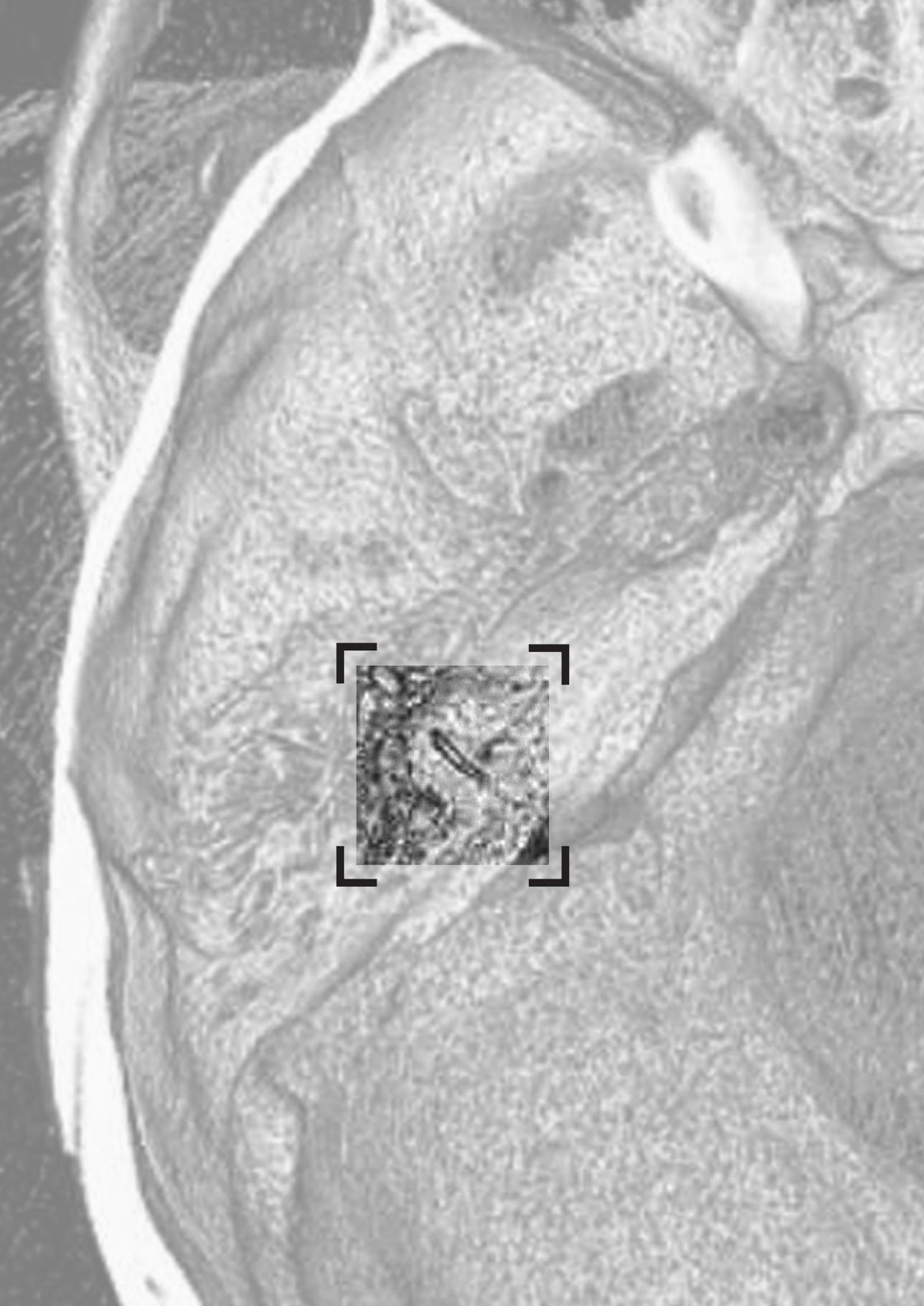
Symptoms were present after the first SCD repair in the contralateral ear immediately after surgery in three of five patients. The remaining two patients developed progressive symptoms of the other ear following repair of the first ear. The symptoms that prompted patients to pursue second-side surgery were autophony and sound- and pressure-induced dizziness. All five patients reported severe symptoms caused by the contralateral SCD ear; their daily activities were impaired, and they were on disability. Symptoms resulted in falls that caused a fracture in one case.

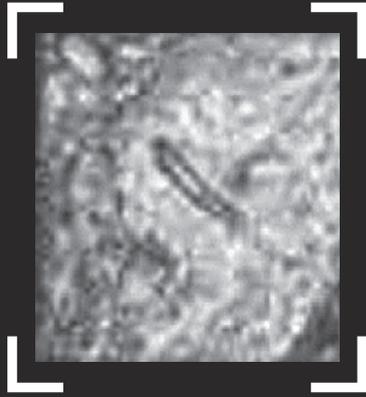
Questionnaire scores on dizziness and quality of life were measured in two patients before and after second-side SCD surgery. Patients were also asked to rate their satisfaction on a scale ranging from zero (very happy) to 10 (very unhappy). One patient said his dizziness lessened, but he reported little improvement in quality of life (score 2/10) and was happy that he underwent surgery. The second patient described increased dizziness and worse quality of life (0/10) following her second surgery, and was also very happy. All four patients with post-operative outcome data reported an improvement of symptoms following surgery.

Research in patients who have had SCD surgery has shown that the function of superior canal is reduced, but what happens to the vestibular system following bilateral SCD surgery? Vestibular testing was performed after second-side surgery in one patient. He underwent dynamic visual acuity testing, which assesses the ability to see an object precisely during head movements; it was within normal limits for both of the surgically repaired superior semicircular canals as well as for the other semicircular canals.

These findings suggest that compensation for the loss in peripheral function of both superior canals occurs following surgery. This patient, however, reported a sensation that objects were moving back and forth in his visual field (oscillopsia). The other three patients with post-operative outcome data reported oscillopsia as well, which resolved in two of the patients, and all patients reported that they were happy to have undergone second-side SCD repair.

What do these findings mean for patients with bilateral SCD syndrome? Should they all undergo bilateral surgical repair? This study showed that second-side SCD repair is safe and effective but that the risk of dizziness following surgery mandates careful patient selection. Only those with intractable symptoms in both ears should be considered for surgery, and a more conservative approach should be taken for bilateral SCD patients with mild symptoms in the unrepaired ear. This study also suggested that the ear and brain can compensate for reduced function of the semicircular canals even when the function was decreased in both canals. Second-side surgery, however, can cause temporary or permanent oscillopsia, and patients must be counseled to expect a prolonged recovery period. The results of this small patient cohort are promising, but the risks and benefits should be considered carefully for each patient before deciding to pursue a second-side SCD repair.





List of publications

LIST OF PUBLICATIONS

Marlien E.F. Niesten, Michael J. McKenna, Wilko Grolman, Daniel J. Lee. Clinical factors associated with prolonged recovery after superior canal dehiscence surgery. *Otology Neurotology* 2012 Jul;33(5):824-31.

Dominic V. Pisano, **Marlien E.F. Niesten**, Saumil N. Merchant, Hideko H. Nakajima. The Effect of Superior Semicircular Canal Dehiscence on Intracochlear Sound Pressures. *Audiology Neurotology*. 2012 Jul;17(5):338-48.

Marlien E.F. Niesten, Michael J. McKenna, Barbara S. Herrmann, Wilko Grolman, Daniel J. Lee. Utility of cVEMPs in bilateral superior canal dehiscence syndrome. *Laryngoscope*. 2013 Jan;123(1):226-32.

Daniel J. Lee, **Marlien E.F. Niesten**. Hearing your eyeballs move: superior canal dehiscence syndrome. *Hearing Journal Club*, Sept 2012, Vol 65, NO. 9.

Puram SV, Roberts DS, **Marlien E.F. Niesten**, Dilger AE, Lee DJ. Cochlear implant outcomes in patients with superior canal dehiscence. *Cochlear Implants International*, 2013 Nov 25.

Carlijn E.L. Hoekstra, Huib Versnel, Sebastiaan F.W. Neggers, **Marlien E.F. Niesten**, Gijsbert A. van Zanten. Bilateral low-frequency repetitive transcranial magnetic stimulation of the auditory cortex in tinnitus patients is not effective: a randomized controlled trial. *Audiology Neurotology* 2013;18(6):362-73

Marlien E.F. Niesten, Leena Hamberg, Joshua B. Silverman, Kristina V. Lou, Andrew A. McCall, Alanna Windsor, Hugh D. Curtin, Barbara S. Herrmann, Wilko Grolman, Hideko H. Nakajima, Daniel J. Lee. Superior canal dehiscence length and location influences clinical presentation and audiometric and cervical vestibular-evoked myogenic potential testing. *Audiology Neurotology*. 2014 Jan;19(2):97-105.

Marlien E.F. Niesten, Sarah Lookabaugh, Hugh Curtin, Saumil N. Merchant, Michael J. McKenna, Wilko Grolman, Daniel J. Lee. Familial superior canal dehiscence syndrome. *JAMA Otolaryngology Head Neck Surgery* 2014 Apr 1;140(4):363-8.

Gabrielle R. Merchant, Christof Rösöli, **Marlien E.F. Niesten**, Mohamad A. Hamade, Daniel J. Lee, Melissa L. McKinnon, Cagatay H. Ulku, John J. Rosowski., Saumil N.

Merchant, Hideko H. Nakajima. Power reflectance as a screening tool for the diagnosis of superior semicircular canal dehiscence. *Otology Neurotology*, In press.

Inge Wegner, **Marlien E.F. Niesten**, Cornelis H. van Werkhoven, Wilko Grolman. Rapid systematic review of the Epley maneuver versus vestibular rehabilitation for benign paroxysmal positional vertigo. *Otolaryngology–Head and Neck Surgery*, 2014 May, Epub.

Marlien E.F. Niesten, Christof Stieger, Daniel J. Lee, Julie P. Merchant, Wilko Grolman, John J. Rosowski, Hideko H. Nakajima. Assessment of the effects of superior canal dehiscence location and size on intracochlear sound pressures. Submitted.

Marlien E.F. Niesten, Inge Stegeman, Sarah Lookabaugh, Vedat Topsakal, Daniel J. Lee, Wilko Grolman. Systematic review of outcomes following superior canal dehiscence surgery: determining best surgical candidates. Submitted.

Marlien E.F. Niesten, Arnold JN Bittermann, Frank Pameijer, Wilko Grolman. Prevalence of superior canal dehiscence following failed stapes surgery. Submitted.

Sarah Lookabaugh[†], **Marlien E.F. Niesten**[†], Maryanna Owoc, Wilko Grolman, Daniel J. Lee. Radiologic and cVEMP progression in superior canal dehiscence syndrome. Submitted.

Sarah Lookabaugh, Hillary R. Kelly, Margaret S. Carter, **Marlien E.F. Niesten**, Michael J. McKenna, Hugh Curtin, Daniel J. Lee. Radiologic Classification of Superior Canal Dehiscence: Submitted.

PRESENTATIONS

Marlien E.F. Niesten, Michael J. McKenna, Wilko Grolman, Daniel J. Lee. Surgical Repair of Superior Canal Dehiscence Syndrome. Dutch Society of Otorhinolaryngology and Head & Neck Surgery 218th meeting, Utrecht, the Netherlands, April 7-8, 2011.

Marlien E.F. Niesten. Diagnosis and Treatment of Superior Canal Dehiscence: Hearing your eyeballs move. Dutch-Belgian Vestibular Society, Utrecht, the Netherlands, November 24, 2011.

Marlien E.F. Niesten, Michael J. McKenna, Wilko Grolman, Daniel J. Lee. Audiometric and cVEMP Outcomes following Surgery for Superior Canal Dehiscence Syndrome. 115th Annual Combined Otolaryngology Spring Meeting, Triological Society, San Diego, California, USA, April 18-22, 2012.

Marlien E.F. Niesten. Focus Talk, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts, USA, July 26, 2012.

Marlien E.F. Niesten, Daniel J. Lee, Christof Stieger, Saamil N. Merchant, Wilko Grolman, Hideko H. Nakajima. Effect of round window stimulation on intracochlear pressure for superior canal dehiscence. 7th International Symposium on Objective Measures in Auditory Implants, Amsterdam, the Netherlands, September 21, 2012.

Marlien E.F. Niesten, Leena M. Hamberg, Barbara S. Herrmann, Hideko H. Nakajima, Daniel J. Lee, Wilko Grolman. Effect of Superior Canal Dehiscence Length and Location on Clinical Presentation, Audiometric and Vestibular testing. Dutch Society of Otorhinolaryngology and Head & Neck Surgery 221th meeting, Utrecht, the Netherlands, November 8-9, 2012.

Marlien E.F. Niesten, Christof Stieger, Daniel J. Lee, Wilko Grolman, John J. Rosowski, Hideko H. Nakajima. Evaluation of location and length of superior canal dehiscence on intracochlear sound pressure. Dutch Society of Otorhinolaryngology and Head & Neck Surgery 222th meeting, Utrecht, the Netherlands, April 25-26, 2013.

POSTERS

Marlien E. F. Niesten, Leena Hamberg, Joshua B. Silverman, Kristina V. Lou, Andrew A. McCall, Alanna Windsor, Hugh D. Curtin, Barbara S. Herrmann, Wilko Grolman, Hideko H. Nakajima, Daniel J. Lee. Correlation of Size and Location of Superior Canal Dehiscence with Clinical Presentation, Audiometric and Vestibular Testing. 36th Annual MidWinter Research Meeting of the Association for Research in Otolaryngology, San Diego, California, USA, February 25-29, 2012.

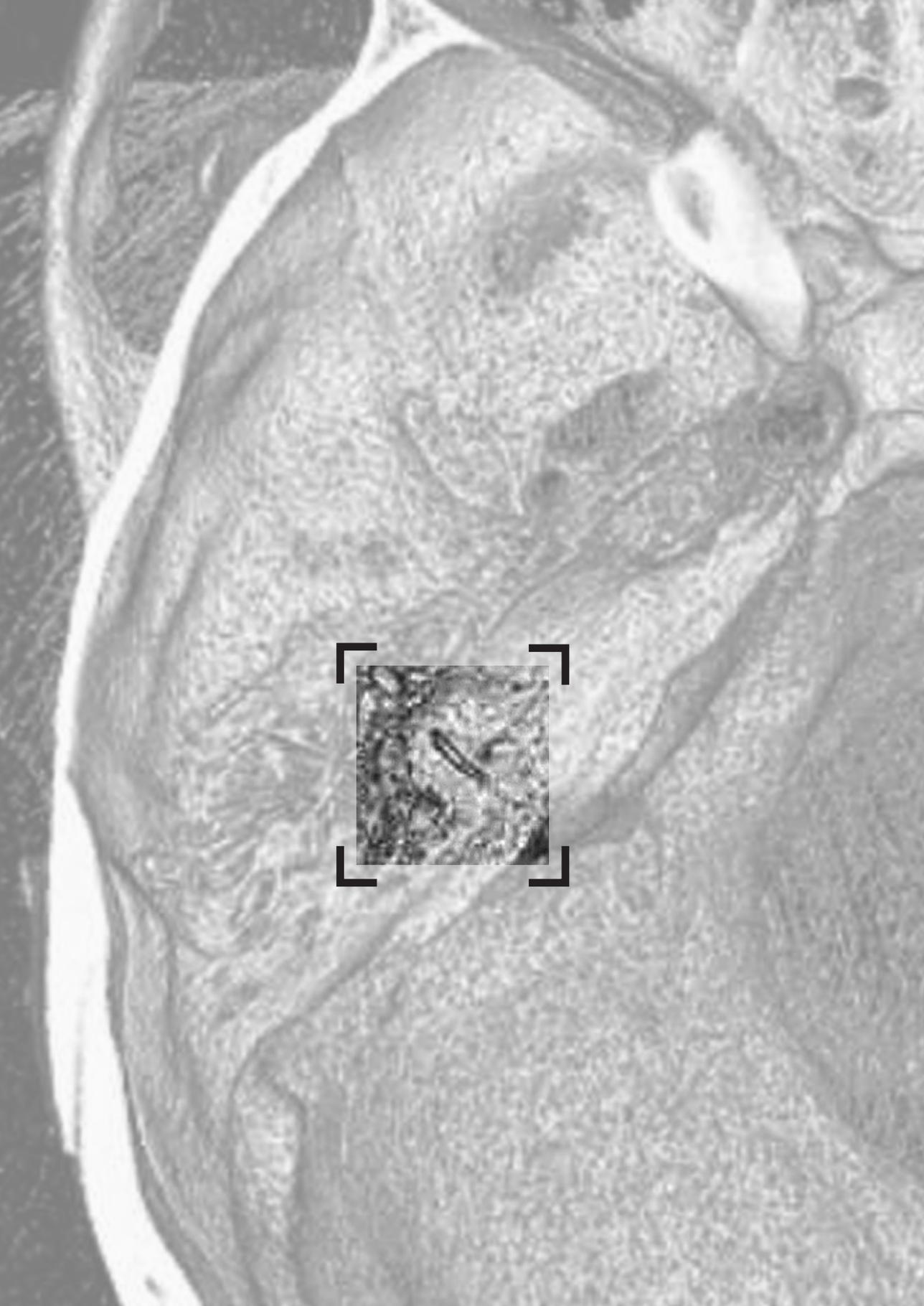
Daniel S. Roberts, **Marlien E.F. Niesten**, Barbara S. Herrmann and Daniel J. Lee. Cochlear implant outcomes in patients with superior canal dehiscence. The 12th International Conference on Cochlear Implants and other Implantable Auditory Technologies, Baltimore, Maryland, USA, May 3-5, 2012.

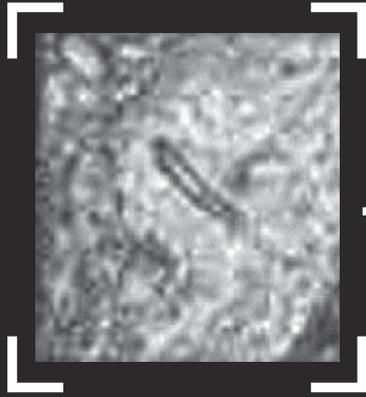
Gabrielle R. Merchant, Christof Rösli, **Marlien E. F. Niesten**, Mohamad A. Hamade, Daniel J. Lee, John J. Rosowski, Saumil N. Merchant, Hideko H. Nakajima. Effect of Superior Semicircular Canal Dehiscence on Ear-Canal Reflectance and Umbo Velocity. The 6th International Symposium on Middle-ear Mechanics in Research and Otolaryngology, Daegu, Korea, June 27-July 1, 2012.

Marlien E. F. Niesten, Christof Stieger, Daniel J. Lee, Julie P. Merchant, Wilko Grolman, John J. Rosowski, Hideko H. Nakajima. Assessment of the effects of superior canal dehiscence location and size on intracochlear sound pressures. 37th Annual MidWinter Research Meeting of the Association for Research in Otolaryngology, Baltimore, Maryland, USA, February 16-20, 2013,

AWARDS

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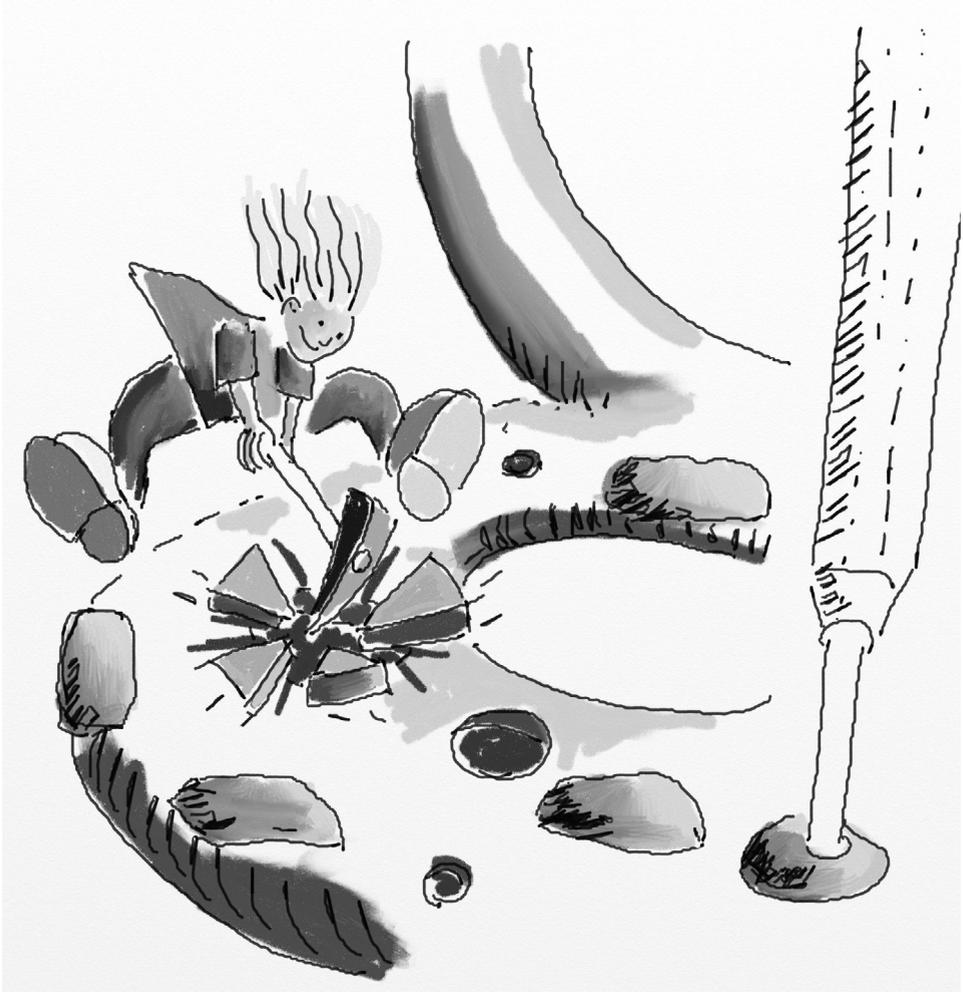
Lieve Rieky en Theo, vanaf dag 1 hebben jullie als oppas aan mijn wieg gestaan. Tot op de dag van vandaag nemen jullie een belangrijke plek in in mijn leven.

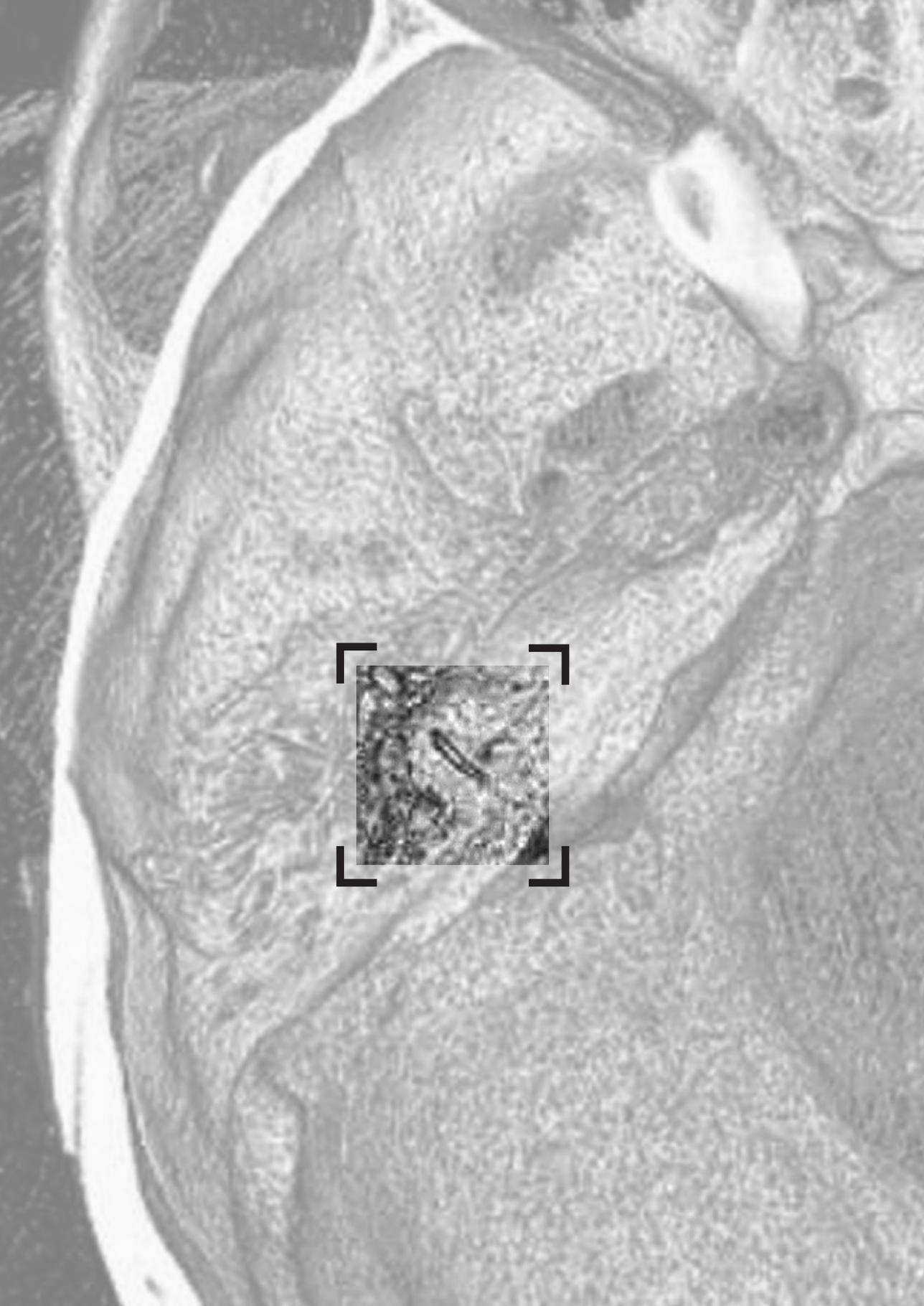
Lieve Margaret, Fons, Rogier, Henk-Joost, Sarah en kleine Yva: dank dat jullie me zo thuis laten voelen in de familie Crooijmans. Jullie toonden altijd weer interesse in mijn onderzoek.

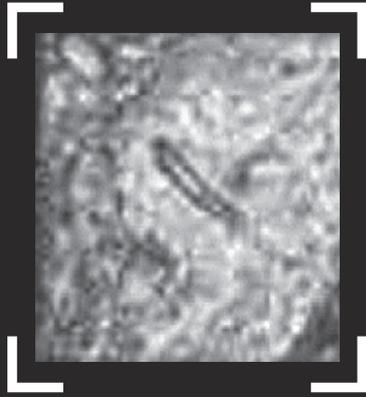
Lieve Pepijn, Floor en Mil, wat een geluk heb ik met drie zulke broers. We hebben samen mooie dingen meegemaakt en ik weet dat jullie er altijd voor me zullen zijn. Pap, dank voor de gezellige etentjes de afgelopen jaren, dit waren mooie momenten om samen bij te kletsen.

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Curriculum Vitae

Marlien Niesten was born on April 30th 1985 in Eindhoven, the Netherlands. She lived in Greeneville and Knoxville Tennessee, USA, from 1987 until 1992. She graduated from the Lorentz Casimir Lyceum in Eindhoven. During that time she played field hockey being part of the South Netherlands Team for multiple years. In 2003 she started Medical School at the Utrecht University. During medical school she followed an internship Obstetrics and Gynaecology at the Lyell McEwin Hospital in Adelaide, Australia in 2008. After having studied Spanish in 2006 in Granada, Spain, she participated in an internship at the department of Otorhinolaryngology at the Hospital Nivel IV Adolfo Guevara Valesco - Essalud in Cuzco, Peru in 2009. She undertook an intensive course in ENT anatomy at the anatomy department and continued this by teaching anatomy to fellow students. During her medical school she participated in a team of eight female rowers in the "Ringvaart", a 100 km rowing contest.

After graduating from medical school in 2010, she started research on superior canal dehiscence at the Massachusetts Eye and Ear Infirmary and Harvard Medical School Boston, USA. This research developed into a PhD program at the University Medical Center Utrecht, under supervision of prof. dr. W. Grolman. Part of the research was performed as a research fellow at the Massachusetts Eye and Ear Infirmary and Harvard Medical School under supervision of Daniel J. Lee and Hideko H. Nakajima. During this period several chapters of this thesis have been published in international peer-reviewed journals as well as presented at national and international conferences. In addition she won a travel award for the 36th Annual MidWinter Research Meeting of the Association for research in Otolaryngology in San Diego, California, USA. Parallel to doing SCD research, she became a resident at the Department of Otorhinolaryngology and Head and Neck Surgery of the University Medical Center Utrecht (prof. dr. W. Grolman) in January 2013. During the final months of her thesis, a rotation was done at the Amphia Hospital Breda (supervisor: dr. G.K. van Wermeskerken).