Tissue Banking for Auditory Research: Current Practice and Perspectives from Aotearoa New Zealand

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Abstract

Background: Diseases with pathology in the inner ear, such as the majority of sensorineural hearing loss and peripheral vestibular disorders, are difficult to treat due to our lack of understanding about their disease mechanisms. To understand the underlying pathology and develop novel treatments for these conditions, research using human inner ear samples is critical. The challenge is that the inner ear is embedded in the temporal bone, hindering access in living patients, leaving post-mortem tissue collection as the primary option. In Aotearoa New Zealand (NZ), we currently do not have resources allocated to support ear tissue banking dedicated to post-mortem collection of the temporal bone to support our understanding of inner ear disease in the NZ population.

Aims: To inform future ear tissue banking in NZ nationwide, this thesis explores: current practices in existing NZ tissue banks to identify points of consideration specific to an ear tissue bank (Part I) and; perspectives from otologists and neurotologists towards such ear tissue bank as a resource (Part II).

Methods: In Part I, a semi-systematic search using an approach similar to a scoping review was conducted to identify existing tissue banks in NZ to extract information from key cultural and donor information practices. In Part II, semi-structured qualitative interviews were conducted to gain insight into clinician perceptions about ear tissue banking in NZ.

Results: Nine existing NZ tissue banks were identified, and four provided donor information packages and donor consent forms for subsequent analysis, which identified unique constraints in tissue banking in NZ regarding cultural safety considerations. There were seven interview participants, and four themes were identified: perceived roles, perceived benefits, perceived barriers, and collaborative efforts in relation to ear tissue banking in NZ.

Conclusion: The present study identified overall positive attitudes from clinicians towards tissue banking to support otologic research and how an ear tissue bank would follow key practices of currently operating tissue banks. It also identified some challenges specific to temporal bone collection and interest in intraoperative methods. Strategies to address these barriers were identified in current tissue banks' practices, but investigation into how they would be modified to specifically suit ear tissue banking should be explored to facilitate clinician engagement, as an ear tissue bank in NZ would foster expansion of otology as a subspeciality.

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List of Abbreviations

ARB	Auckland Regional Biobank
ATBB	Australian Temporal Bone Bank
CANVAS	Cerebellar ataxia with neuropathy and vestibular areflexia syndrome
CHL	Conductive hearing loss
CI	Cochlear implant
CLSM	Confocal laser scanning microscopy
CSTB	Cancer Society Tissue Bank
CT	Computed tomography
EAC	External auditory canal
EH	Endolymphatic hydrops
ENU	N-ethyl-N-nitrosourea
HAL	Human Anatomy Lab
IHCs	Inner hair cells
MD	Ménière's Disease
MEEI	Massachusetts Eye and Ear Infirmary
MRI	Magnetic resonance imaging
NIDCD	National Institute on Deafness and Other Communication Disorders
NZ	Aotearoa New Zealand
NZBS	NZ Blood Service
NZIER	New Zealand Institute of Economic Research
NZNEB	NZ Eye National Bank
ODNZ	Organ Donation NZ

OHCs	Outer hair cells
Pākehā	European New Zealanders
PCR	Polymerase chain reaction
PIS	Participant Information Sheet
Registry	Hearing and Balance Pathology Resource Registry
SEM	Scanning electron microscopy
SGNs	Spiral ganglion neurons
SNHL	Sensorineural hearing loss
Tauiwi	Non-Māori people of New Zealand
TEM	Transmission electron microscopy
TM	Tympanic membrane

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Preface

In our daily life, multiple senses help us create meaningful interactions with our environment. Hearing and balance are two such senses, and the disturbance or loss of their function can cause significant distress and uncertainty. Herein lies the importance of auditory and vestibular research: to not just understand the mechanisms behind normal and abnormal function, but also to understand how to address and treat these discrepancies.

What senses of hearing and balance have in common is that the peripheral sensory organs for hearing (cochlea) and balance (vestibular labyrinth) share a small space within the temporal bone of the skull, referred to as the inner ear. As the inner ear's location is deep inside the skull, it is very difficult to collect biopsies from the inner ear to understand any pathological changes that occurs in the cochlea or vestibular system. Clinical diagnostic tools such as computerised tomography or magnetic resonance imaging do not provide enough resolution to understand cellular changes in the inner ear. For this reason, histopathological analysis of human inner ear tissue collected post-mortem has been an essential component thus far towards understanding auditory and vestibular function, and how it changes in disease states.

However, we currently do not have this capability in Aotearoa New Zealand (NZ) to collect and perform oto-histopathology in NZ. This is a hindrance to understanding the pathology of hearing and balance disorders that may be unique to NZers, including Māori. Our research group have an ambitious long-term goal to establish such a capability in collaboration with clinical colleagues and those affected by hearing and balance disorders in NZ. This thesis aims to lay the foundation for how we might be able to approach this endeavour in NZ.

The literature review will first cover basic anatomy and function of the inner ear, with some specific examples of how human tissue analysis has contributed to our overall understanding of inner ear pathology. Following that, an overview of some current NZ practices in tissue banking will be explored in two parts:

Part I of the study intends to understand the current practices for biobanking in general in existing NZ tissue banks, with particular focus on consenting and culturally safe protocols that are important to collecting and using human tissues for research. Part II investigates the perceptions of prospective stakeholders towards a potential ear tissue bank in NZ, focusing on clinicians as the population of interest due to their involvement in inner ear disease and the key roles they may play in otologic tissue banking. The outcome from this thesis provides

fundamental knowledge in our field of research that has had little exploration in NZ, towards establishing a sustainable and ethical pathway to facilitate otologic research and understanding hearing and balance disorders affecting NZers.

1 Literature Review

1.1 Hearing and vestibular systems and disorders

To help navigate the world around us, our auditory system is responsible for the sense of hearing, while our vestibular system processes our sense of balance. These two systems share something in common; the peripheral organ for hearing (cochlea) and vestibular function (vestibular labyrinth) are housed within the inner ear, sharing similar sensory transduction elements and fluid compartments (Phillips et al., 2020). The auditory system is the means by which living organisms detect, process, and comprehend sounds within the environment. It plays an important role in transforming external sound waves into neural signals. This information is then integrated with other sensory information, facilitating behavioural responses, orientation, and communication (Peterson et al., 2023). The vestibular system plays an important role in proprioception and equilibrium, integrating orientation and acceleration of the head with appropriate eye movement and posture changes (Casale et al., 2023). Exploration into the vestibular system has revealed that it also has contributions to consciousness, and dysfunctions in the system have the potential to cause cognitive deficits in relation to spatial memory, learning, and navigation (Casale et al., 2023).

When pathological changes occur in the inner ear, hearing and vestibular disorders are the most common clinical presentations. Hearing losses can be categorised as conductive, sensorineural, or mixed. Conductive hearing loss (CHL) occurs when issues involving the tympanic membrane and middle ear arise. Sensorineural hearing loss (SNHL) encompasses pathologies that occur in the cochlea and auditory neurons (Anastasiadou & Khalili, 2023). A mixed hearing loss is classified as when there are both conductive and sensorineural components occurring simultaneously. SNHL is a diverse disorder, with a wide range of causes. Presbycusis, otherwise known as age-related SNHL, has been attributed to degeneration of the cochlea over time. Genetic variability in certain genes can cause SNHL at birth (congenital SNHL) or cause early-onset progressive SNHL. Some viral infections such as measles, mumps, and rubella and ototoxic medication such as aminoglycosides can cause SNHL. Finally, excessive noise exposure is a major cause of noise induced SNHL (Mackenzie & Smith, 2009). Sources of excessive noise can be occupational or recreational, but the risk of causing permanent hearing damage may be mitigated by the use of hearing protection or strategies to reduce exposure (Mackenzie & Smith, 2009).

Vestibular dysfunction occurs when there is an insult to the peripheral and/or central vestibular system. Common symptoms include vertigo, nausea, vomiting, unsteady gait, imbalance, and clinical presentation of nystagmus (Dougherty et al., 2023). Vestibular dysfunction is broadly categorised into peripheral and central causes, though symptoms of either can often overlap. Peripheral vestibular dysfunction refers to pathology of the vestibular structures within the inner ear plus the vestibular portion of the eighth cranial nerve. Examples of this include endolymphatic hydrops (EH) and Ménière's Disease (MD). Central vestibular dysfunction involves the vestibular pathways in the brainstem, from the vestibular cochlear nucleus to the vestibulocerebellum, thalamus, and vestibular cortex areas in the temporoparietal cortex (Strupp et al., 2023).

Hearing loss is often considered a hidden disability due to how it is not immediately apparent to others. An effect of this is perpetual limited understanding of hearing loss among the community, creating miscommunication and misunderstanding. The impact of unaddressed hearing impairment is not limited to the individual; rather, it extends to the community and country (Mackenzie & Smith, 2009; Manrique et al., 2023). In NZ, the prevalence of hearing loss was estimated to be 10.3% of the population in 2022, which is predicted to rise due to the ageing population over the next fifty years, as reported by the New Zealand Institute of Economic Research (NZIER) in 2023. Economically, the cost of hearing loss is high from both healthcare and the lost productivity due to hearing loss contributing to early retirement, reduced learning ability and labour productivity, employment rates, and revenue. According to the NZIER, productivity increases in workers with hearing loss can lead to a growth of between $718 million and $924 million in annual real gross domestic product. On the level of the individual, hearing impairments have been thought to have strong implications on cognition as they can significantly impact quality of life, subsequently causing social isolation, depression, and loss of self-esteem (Koh et al., 2015). Furthermore, research has suggested that hearing loss is a major modifiable risk factor of dementia. While the exact link between hearing loss and dementia are not clear, it has been theorised that decreased auditory stimulation negatively affects social interaction, therefore reducing cognitive function (Lin et al., 2012).

The risk of vestibular disorders and falling increases with age, leading to financial burden, decreased quality of life, and stress on families taking care of the individual at risk (Kowalewski et al., 2018). It has been estimated that 30% of individuals over the age of 65 have had at least one fall, and 20% of individuals have fallen more than once within one year (Manrique et al., 2023). It is thought that around 90% of vestibular symptoms are due to

disturbances in the peripheral vestibular system (Lui et al., 2023). Research has suggested that there is an association between hearing loss and vestibular disorders, where older adults with hearing loss have poorer reactive balance and slower gait speed compared to young and older adults with normal hearing, and that the greater the degree of hearing loss, the more likely the occurrence of a fall (Carpenter & Campos, 2020; Kowalewski et al., 2018). Because the auditory and vestibular systems share the same fluid compartments and sensory transduction elements, pathology that occurs to one often impacts the other, leading to a combined loss of function (Koh et al., 2015; Phillips et al., 2020). However, the mechanisms that explains why hearing loss is linked to greater risk of falls and imbalance are not yet well-established. The complex interaction between hearing impairment, vestibular disorders, and cognition suggests that a multifactorial approach is needed to understand these conditions, prompting the need for further research to determine potential causes and possible assessment and treatment strategies.

1.1.1 The auditory system

The peripheral auditory structures are comprised of the outer, middle, and inner ear. They are involved in the collection, filtering, amplification and conversion of sound energy into electrical energy for transmission to the central auditory system for further processing (Rowe & O'Leary, 2014). The outer ear consists of the pinna and the external auditory canal (EAC), ending where it meets the tympanic membrane (TM). The pinna's asymmetrical shape and forward orientation creates spectral characteristics to incoming sound energy that is used for sound localization (Rowe & O'Leary, 2014). The first third of the EAC is cartilaginous, and the remaining two thirds are bony. The TM is located at the medial end of the EAC, consisting of three layers: an outer epithelial layer continuous with the skin of the EAC, a middle fibrous layer, and an inner mucosal layer (Rowe & O'Leary, 2014). Sound pressure is transferred from the external ear to the middle ear via vibration of the TM. The middle ear is located behind the TM and contains the three ossicles: the malleus, incus, and stapes. The middle ear transfer function describes the process by which the middle ear matches the impedances between the air-filled cavity and the fluid-filled cochlea to minimise the reduction of sound energy (Zhao et al., 2009). Vibrational energy that travels through the ossicles from the TM is transferred to the oval window, which vibrates in response, propagating waves throughout the cochlea (White et al., 2023). A summary of these structures is depicted in Figure 1.

The cochlea is tonotopically organised, with the base sensitive to detecting higher frequencies and the apex sensitive to lower frequencies. The cochlea contains three fluid-filled compartments: the scala vestibuli, scala media, and scala tympani (Rowe & O'Leary, 2014). The basilar membrane separates the scala tympani from the scala media, and Reissner's membrane separates the scala media from the scala vestibuli (Rowe & O'Leary, 2014). Within the scala media is the organ of Corti, within which there are two types of sensory hair cells that are responsible for sound transduction (Ricci & Kachar, 2007). Outer hair cells (OHCs) mechanically amplify the auditory stimulus by increasing the deflection of the basilar membrane in response to sound, while inner hair cells (IHCs) transduce the mechanical movement of the basilar membrane into electrical signals, which are conveyed to the spiral ganglion neurons (SGNs; Fettiplace, 2017). SGNs are primary afferent neurons that transmit electric signals from the IHCs down the central auditory pathway (Wang et al., 2022).

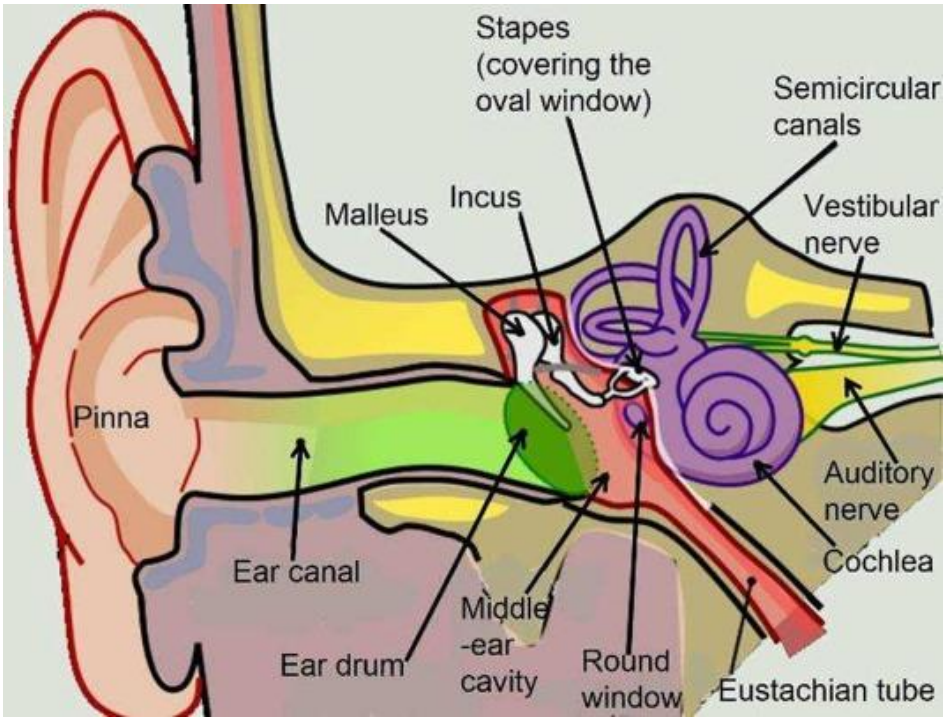

Figure 1. Diagram of the peripheral auditory system. Reprinted from Kunchur (2023) with permission from Elsevier. The outer ear comprises of the pinna, EAC, and TM. The middle ear consists of the structures contained between the TM and oval window. The inner ear comprises the cochlea and the semicircular canals.

The projection from the auditory neurons travels via the vestibulocochlear nerve, otherwise known as cranial nerve VIII (Figure 2), which leaves the cochlea and ascends to the ipsilateral cochlear nuclei at the pontomedullary junction (Staecker & Thompson, 2013). Most nerve fibres then cross over to the contralateral superior olivary complex, while some synapse on the ipsilateral superior olivary complex. Nerve fibres then ascend to the ipsilateral and contralateral lateral lemniscus, followed by the inferior colliculus, before projecting to the medial geniculate body within the dorsal thalamus (Peterson et al., 2023). From there, the nerve fibres project to the primary auditory cortex of the temporal lobe for further processing.

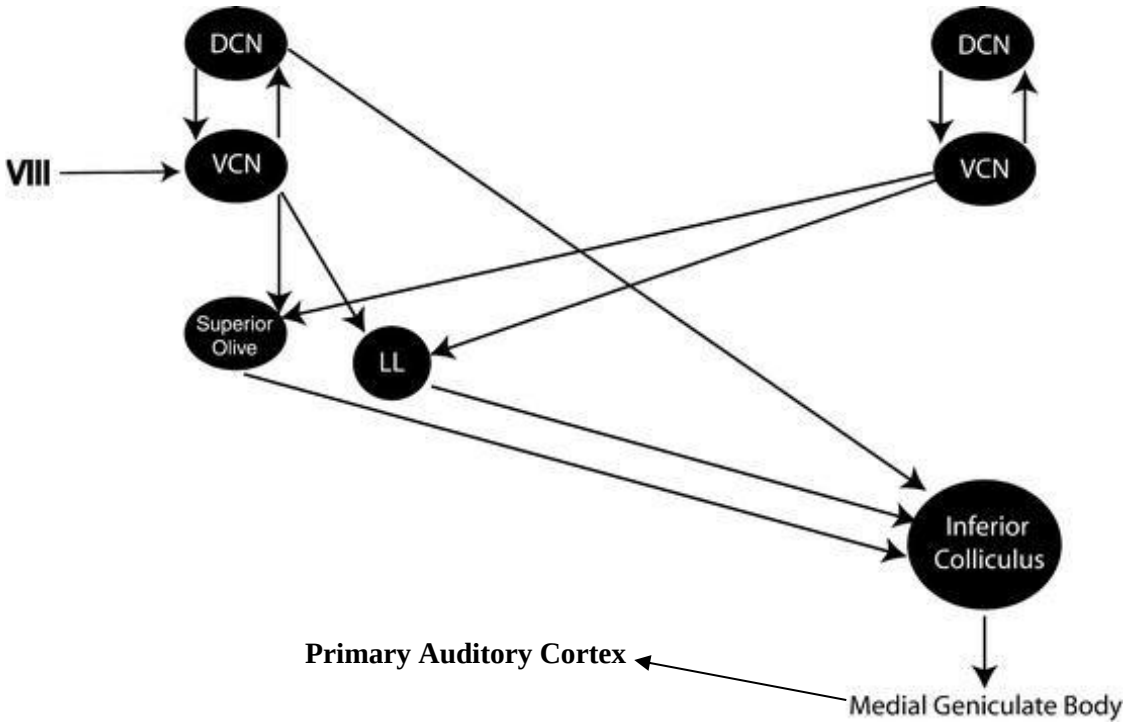

Figure 2. A schematic diagram showing the pathways of the central auditory system (CAS). Adapted from H. Staecker and J. Thompson (2013) with permission from Springer Nature. VIII = vestibulocochlear nucleus, DCN = dorsal cochlear nucleus, VCN = ventral cochlear nucleus, LL = lateral lemniscus.

1.1.2 The vestibular system

The vestibular system is responsible for the maintenance of stance, posture, proprioception, and equilibrium. It detects the position and movement of the head in space, which is used to coordinate and compensate for movement (Casale et al., 2023). The inner ear contains five organs that constitute the vestibular system: the three semicircular canals (superior, posterior, lateral), and two otolith organs (utricle and saccule). The semicircular canals detect rotational accelerations of the head. At the end of each semicircular canal near the opening to the utricle is a structure called the ampulla, which contain sensory hair cells to detect motion (Casale et al., 2023). These hair cells sit on a bed of crista and extend into a gelatinous mass called the cupula, which is submerged in endolymph. Angular acceleration causes longitudinal movement of the endolymph, and the resulting inertia exerts force on the cupula, deflecting the stereocilia of the hair cells (Casale et al., 2023). This leads to depolarisation of the hair cell population on one side but hyperpolarisation on the other, causing a difference in excitatory and inhibitory activity. Each semicircular canal is paired with another on the opposite side of the head, and the hair cells in that canal are aligned oppositely (Casale et al., 2023). The lateral canals are

paired while the superior canal is paired to the posterior canal on the other side. During head rotation, one canal of the pair will be excited whilst the other will be inhibited, giving rise to a total combination of six signals that are further processed to determine the physical characteristics of the movement (Walker, 2016).

The utricle and saccule detect linear head accelerations (Casale et al., 2023). The utricles are involved in the detection of head movement in the horizontal plane while the saccules are responsive to movements in the vertical plane (Dieterich & Brandt, 2015). Each organ contains a sensory epithelium and the macula. The macula is composed of the vestibular system's sensory hair cells and their associated supporting cells. A gelatinous layer overlies the hair cell bundles, and above that, is the otolithic membrane, which contains calcium carbonate crystals known as otoconia (Dieterich & Brandt, 2015). During linear accelerations, gravity causes the otolithic membrane to shift relative to the sensory epithelium, and the shearing motion displaces the hair bundles (Dieterich & Brandt, 2015). When the hair bundles are displaced, a receptor potential is generated. The hair cells are organised relative to the striola, such that the hair cells on opposite sides have opposing polarisations mirroring each other. Consequently, tilts along the striola's axis would excite the hair cells on one side while at the same time inhibiting the hair cells on the opposing side (Casale et al., 2023). The utricular macula is oriented vertically while the macula of the saccule possesses a horizontal orientation. As the utricular and saccular maculae on one side are mirror images of the ones on the other side of the head, it follows the same conventions of semicircular canal stimulation, where the excitation of one side corresponds with inhibitory activity on the opposite side (Dieterich & Brandt, 2015). Upon depolarisation of the hair cell, neurotransmitters are released across the synaptic cleft, inducing nerve transmission to the vestibular ganglion before travelling across the vestibular portion of the vestibulocochlear nucleus (Casale et al., 2023).

Several relay nuclei and pathways compose the central vestibular system. The vestibular nerve separates into two branches as it enters the brainstem at the pontomedullary junction, with the majority of the primary afferents synapsing on the vestibular nuclear complex while the rest ascend to the cerebellum (Jones et al., 2009). The vestibular nuclear complex is the site of neural integration from multiple sensory, motor, and cognitive systems, the purpose of which is to form the appropriate output signals for eye, head, and body movements, alongside contributing to autonomic control, attention and cognition, and learning and memory (Jones et al., 2009). The cerebellum modulates reflexive movements involved in motor coordination, and contains three functional divisions, one of which is called the vestibulocerebellum

(Dieterich & Brandt, 2015). This structure is thought to play an important role in predicting spatial environments and thus compensating for vestibular deficits (Barmack & Yakhnitsa, 2013).

1.2 Approaches to hearing and vestibular research: Animal models versus human tissue

In order to develop novel treatment, management, and rehabilitation strategies for people affected by inner ear disorders that have become widely prevalent within the community, we need to understand the underlying pathology. To date, auditory and vestibular research in human and animal models has advanced our understanding of SNHL and peripheral vestibular diseases that have pathological origins in the inner ear and its associated central nervous structures (Hamid et al., 2009). Here, some examples of such research efforts will be reviewed.

1.2.1 Animal models to understand SNHL pathology

Analysis of the human inner ear is challenging (discussed later in 2.3.4). Many animal models have been used in the past to drive our understanding of SNHL. Several advantages have been posed for using animal models over human tissue in research pertaining to the inner ear. Invasive methods that are not appropriate for humans can be conducted, the history and aetiology of the individual models used can be controlled, and experimental tools that range from behavioural to molecular can be applied (Brozoski & Bauer, 2015).

The dominant animal model used are laboratory mice due to their anatomical and physiological similarities to the human cochlea and vestibular labyrinth (Kikkawa et al., 2012; Ohlemiller et al., 2016; Reis et al., 2017). Laboratory mice have been a traditional animal model used in studying hearing and vestibular function due to several advantages offered over many alternative models: shorter maturational period, a shorter lifespan to provide a lifetime's worth of data over a relatively short span of time, and high rates of reproductivity (Ohlemiller et al., 2016).

The anatomy and function of the cochlea and vestibular labyrinth of rodents are comparatively similar to that of humans (Lin et al., 2021), and they can be used as viable equivalent baseline models in auditory research. Further, genes and proteins responsible for hearing and vestibular function are relatively well conserved among mammalian species including human and mouse, allowing the exploration of pathological conditions involving inner ear structures under controlled conditions (Ohlemiller et al., 2016; Reis et al., 2017). Thus, laboratory mice have been specifically used to re-model human genetic deafness. Currently, over 100 causative genes have been identified to induce hearing loss, and an additional 300 loci have been linked to hereditary hearing loss (Early et al., 2022; Shearer et al., 2023). In mice, mutations in

approximately 180 different genes have been identified as contributors to SNHL (Chatterjee & Lufkin, 2011). Forty-four of those genes have been linked to human hereditary hearing loss (Chatterjee & Lufkin, 2011). Typically, the degree of hearing loss in these mouse models is assessed using auditory brainstem response to establish phenotypic characterisation of hearing for known genetic conditions. Patterns of pathology could also be revealed through histopathology of inner ear structures, allowing us to link genotype with cellular and molecular changes (Early et al., 2022; Reis et al., 2017).

In addition to knockout mice and mutant mice being generated through genetic modifications, several inbred mouse strains with hearing impairment of variable degree and onset time have been identified and used to study age-related hearing loss in humans (Bowl & Dawson, 2015; Kikkawa et al., 2012). For example, the C57BL/6J (B6) strain has been well-documented as an animal model to explore progressive sensorineural hearing loss, as this particular strain presents with early-onset high-frequency hearing loss at 3-6 months of age, progressing to severe-profound at 9-15 months old (Kikkawa et al., 2012; Suzuki et al., 2020). Recent advancement in gene manipulation techniques have enabled researchers to improve the degree of control implemented in designing genetically modified mice to recreate human gene variants associated with hearing impairments. CRISPR-Cas9 techniques have led to the creation of knock-in mouse strains possessing specific mutations identified in human hereditary hearing loss (Carlson & Avraham, 2022; Wang et al., 2019). N-ethyl-N-nitrosourea (ENU) mutagenesis screening is a tool in which treatment of the chemical can generate mutations within the genome at particular sites (Stottmann & Beier, 2014). In addition, additional novel mouse models of deafness can be identified using ENU mutagenesis, which has the added benefit of further understanding how different pathogenic phenotypes caused by mutations in different sites of the same gene (Kikkawa et al., 2012). The importance of this lies in that pathogenic phenotypes of hearing impairment can also vary in people of the same family with the same mutation, and so strategies to reflect this would prove beneficial in understanding hereditary hearing loss in humans.

Although laboratory mice are the most popular animal model used in auditory research, large animal models such as sheep have an advantage in that researchers can test surgical procedure, drug administration methodologies, and medical imaging (Lue et al., 2023). Because these procedures are constrained by size, they are not possible to conduct on small animals. The use of large animal models compensates for this shortcoming, while bridging the gap between small animal models and humans, due to their closer developmental and maturational

similarities to humans (Lue et al., 2023). Large animal models also have the additional benefit of closer size and anatomical resemblance of the auditory system to humans than small animal models, allowing more translational data than can be provided by rodents for clinical research (Lue et al., 2023). With these factors in mind, it may very well be a combined approach that would prove most sound. Small animal models have proven their efficacy with their shorter gestational and maturational periods while remaining relatively cost-effective (Lue et al., 2023; Ohlemiller, 2019). Genetic manipulation would also be easier to carry out on rodent models. In contrast, large animal models have potential for studying developmental risk factors and clinical applications. As such, the combined use of both types of models could increase the pace of current research in the field.

1.2.2 Animal models to study the vestibular system

Research has established that the vestibular system is preserved across vertebrate species, yielding the ability to draw general conclusions across species in regard to neuronal components throughout the vestibular pathways (Straka et al., 2016). In the present study, focus will be placed on peripheral vestibular dysfunction. Consideration would still need to be applied when selecting animal models: differing locomotor dynamics may influence relative contributions of sensory inputs between bipeds versus quadrupeds; otolith organs serve auditory function alongside vestibular in fish, frogs, and birds; and fish and amphibians only possess type II hair cells (Corneil & Camp, 2018; Straka et al., 2016). The majority of vestibular research done on animal models consist of electrophysiology recordings, including the vestibulo-ocular reflex and vestibular evoked myogenic potentials (Corneil & Camp, 2018; Madoux et al., 2022; Yang et al., 2020). Histological methods have been implemented in animal models that mimic pathophysiological processes in humans via lesions induced by surgical, excitotoxic, or chemical means to give insight into the molecular, cellular, and physiological basis of hearing loss and vestibulopathies (Maudoux et al., 2022; Tighilet et al., 2022).

1.2.3 Limitations of animal models and the need to study the human inner ear

Despite the wide range of animal models available for use in research, any animal model is only an approximation to human tissue. Not all human genetic mutations may have an equivalent that can be found in animal models, and the functional roles of the resulting proteins may differ between animal models and humans for the ones that do (Ohlemiller, 2019).

Humans have much longer lifespans than most animal models, and many pathologies are age-related, hence to study age-related hearing loss, animal models may not be suitable (Kujawa & Liberman, 2019). Identifying key genes and whether their function changes in different stages of the human life cycle becomes important when considering the phenotypes that may be presented with different genetic variants. Modelling disease states at specific points within the life cycle may be required to grasp the full picture of a particular condition (Reilly & Rossor, 2020). In vestibular research, the relative contributions of different sensory inputs may differ from humans, such as a heavier reliance on olfaction rather than vision for rodents, leading to implications when comparing the neural circuitry of the vestibular system across species (Corneil & Camp, 2018; Ohlemiller et al., 2016; Straka et al., 2016).

Diagnostic issues such as the lack of ease in obtaining biopsy or images of the inner ear due to its size and location creates challenges in understanding human inner ear pathology. Computed tomography (CT) and magnetic resonance imaging (MRI) can identify gross anatomic defects but have limited resolution of intracochlear microanatomy due to the surrounding density of the otic capsule (Bommakanti et al., 2022). Figure 3 shows a human temporal bone to give an idea of the additional challenges posed by the size and location of the inner ear. The human inner ear is a small organ embedded in the petrous portion of the temporal bone (Figure 3). Due to the highly ossified nature of the inner ear, both the collection of inner ear tissue and histological analyses are technically challenging (Figure 3). Of around 200 genes associated with causing deafness, only 22 have had reported histopathological findings, opening many areas of potential research (Sagi et al., 2023). An additional benefit of having human inner ear tissue includes the potential of receiving postoperative information to help further shape current practices in otologic surgery, such as in refining surgical techniques during cochlear implant (CI) placement (Sagi et al., 2023). Studying human inner ear pathology is a different challenge to studying the human inner ear, which will be discussed in the next section.

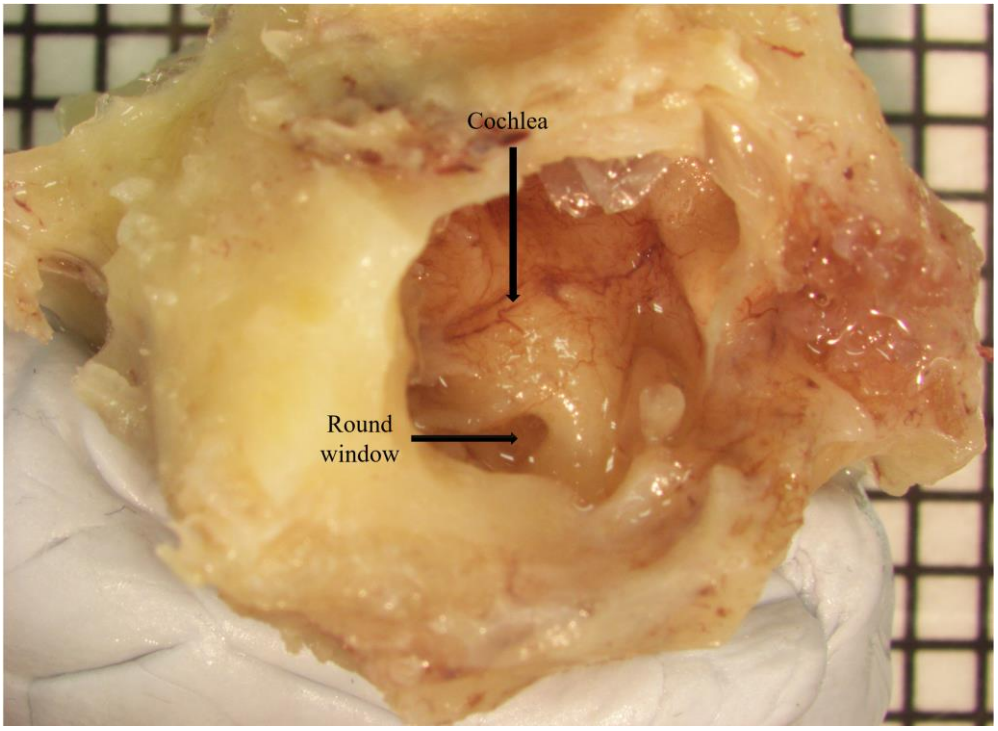

Figure 3. Photo of a human temporal bone with round window and cochlea exposed. Scale: one grid represents 2 mm. Image kindly provided by S. Han, University of Auckland, 2024.

1.2.4 Methodologies and challenges of studying human inner ears post-mortem

Analysing human inner ear tissue is predominantly performed post-mortem, as routine biopsies cannot be performed in the inner ear of living individuals. There are several ways of studying human inner ears bones, each differing in the ease of use and the information that can be obtained. Imaging techniques are most commonly utilised. Light microscopy has had a long history of use that spans centuries, particularly in visually documenting pathologic changes via comparison between normal and diseased tissue. Light microscopy imaging has since been improved by the implementation of transmission electron microscopy (TEM) and scanning electron microscopy (SEM), which significantly enhances the resolution of microscopic examination. SEM has been used to define normal variation of cilia numbers per hair cells in humans, which helped researchers quantify hair cell bundles of OHCs and IHCs in disease states, while TEM has been used to quantify and study morphology of synapses on IHCs and OHCs (Nadol, 2019). An advancement for SEM is energy-dispersive X-ray spectroscopy by scanning electron microscopy, which can identify elemental composition of samples (Mutalib et al., 2017). An example of its use is in studying immunologic response to CI electrodes in human cochlear tissue to examine if they can be correlated with variable outcomes after cochlear implantation (Nadol et al., 2014; O'Malley et al., 2017). Confocal laser scanning microscopy (CLSM) utilises optical sectioning to reconstruct 3D structures using multiple 2D

images. In a study on hidden hearing loss by Viana et al. (2015), this technique was used to analyse normal human temporal bones and found that cochlear synaptopathy and cochlear nerve peripheral axon degeneration could be an important factor in presbycusis despite normal or near-normal hair cell populations. Mass spectrometry has been previously used to assess the distribution of chemotherapeutic agents that were taken in life in human temporal bone specimens, giving insight into the retention period and differential distribution within the cochlea and vestibular peripheral organs (Breglio et al., 2017; Rauch, 2006). Immunostaining and proteomic analysis have played a hand in elucidating the role of gene function within the inner ear and how they contribute to pathogenesis of hearing and vestibular disorders (Merchant et al., 2008; Robertson et al., 2006). Immunohistochemistry involves the detection and localisation of specific antigens within cells and tissue via specific binding between an antibody and an antigen, while proteomic analysis refers to the identification and quantification of the entire protein complement expressed by a genome, cell, or tissue (Al-Amrani et al., 2021; Magaki et al., 2019). Examples of their use is the localisation of aquaporins throughout the human inner ear (Lopez et al., 2007), and comparison of cochlin levels between normal inner ears and genetic SNHL-affected inner ears in humans and mice (Robertson et al., 2006). The study of nucleic acids within human temporal bones is also possible via polymerase chain reaction (PCR), where DNA can be extracted from temporal bone sections to undergo amplification of genomic DNA for sequences of interest, such as the GJB2 gene. This gene's mutations are well-known for causing congenital hearing loss (Jun et al., 2000; Wackym et al., 1998).

Due to the scarcity of human temporal bone specimens available in the research space and the difficulty in accessing and collecting human temporal bones, a fine balance between obtaining human temporal bones and preserving their use must be maintained, hence continued development in analytical techniques. 3D models of the human inner ear from histologic and radiologic data have proved to be a valuable tool in establishing a database that may be accessible by teaching and research circles internationally and are one such way of maximising the use of donated temporal bones (Wang et al., 2006). This has been done by a combination of ionising radiation and micro-slicing of the human temporal bone to reconstruct 3D models capturing anatomic variation amongst unique individuals (Sieber et al., 2019). Another strategy to employ greater use of donated temporal bones is to develop non-destructive techniques, as histopathological methods are destructive, limiting future use of the tissue and inhibiting studies that may require the temporal bone's 3D structure. (Bommakanti et al., 2022).

Reversible iodine staining for microCT is a method that has been proposed for high-resolution visualisation of the human inner ear, particularly as the structural integrity of the temporal bone would be maintained for further analysis post-destaining (Bommakanti et al., 2022; Sagi et al., 2023).

1.2.5 Specific examples of human inner ear study 1: MD

Human inner ear analysis in combination with animal studies have advanced our understanding of MD. MD is a pathology of the inner ear and is characterised by episodic vertigo, fluctuating hearing loss, tinnitus, and aural fullness. In the initial stages, MD is usually localised to one ear, but may affect both in later stages. It is a chronic condition that has been estimated to affect around 190 per 100,000 people in the United States (Alexander & Harris, 2010). MD is typically progressive in nature with an average onset at 40 years of age (da Costa et al., 2002). There are several challenges posed in the study of MD. The complexity of the inner ear structures, where the cochlear and vestibular end organs share connections, means that their respective contribution to the disease varies, giving rise to differing presentations of hearing loss and vestibular symptoms (Seo & Brown, 2020). In the study of temporal bones obtained from humans, the histopathologic finding of idiopathic EH is characteristic of MD. EH describes the distension of the structures bounding the endolymphatic space due to the enlargement of endolymphatic volume (Salt & Plontke, 2010). In MD, this is often seen as a distension of Reissner's membrane into the scala vestibuli, with potential displacement of other membrane-bound structures within the inner ear, such as the saccule, utricle, and ampullae of the semicircular canals (Rauch, 2001). The endolymphatic sac is thought to play an important role in ion homeostasis and regulation of endolymphatic fluid volume along with some potential involvement in inner ear immune response and removal of cellular debris and otoconia (Kim et al., 2019). It has been theorised that when there are disturbances in the endolymphatic sac (such as inflammation), ion transport could be affected such that ion homeostasis and fluid volume regulation are disrupted, leading to the formation of EH and impacts on hearing and vestibular function (Kim et al., 2019). Past cadaveric studies have supported this, as loose connective tissue, capillaries, and villi were found to surround the endolymphatic sac, suggesting a role in resorption of endolymphatic fluid (Kim et al., 2019). The correlation between EH and MD is not straightforward, with histopathological studies from temporal bone donors who had early-stage MD showing essentially normal sensory and supporting cells morphology (Salt & Plontke, 2010). Close examination of temporal bones

from patients who had a clinical diagnosis of MD revealed the presence of EH in at least one ear, but there was also a proportion of patients who were found to have EH but did not exhibit the classical symptoms of MD (Merchant et al., 2005). At the same time, there is also a proportion of patients who had exhibited the symptoms of MD in life but had no evidence of EH observed upon post-mortem histopathology (Kim et al., 2019; Merchant et al., 2005; Takeda et al., 2020).

Other examples of how human temporal bones have been utilised in research include the implementation of PCR and immunohistochemistry to examine the inner ear for evidence of inflammatory and immune-mediated causes of MD, which has been a standing theory in the pathophysiology behind the disease. It has since been found that sites of focal inflammation within the endolymphatic sac were more likely to test positive for cytomegalovirus, herpes simplex virus, and varicella zoster virus compared to human inner ears from disease-free subjects, offering credibility to the theory in addition to highlighting the importance of having human inner ears to study specific conditions, as risk factors and potential management strategies could then be inferred for future approaches (Arenberg et al., 2006; Kumagami, 1996).

As the symptoms of MD have generally been attributed to EH, the animal models that have been developed to study MD are designed to reflect this. EH has been induced by surgical methods via ablation of the endolymphatic duct and endolymphatic sac, thus inducing malabsorption of endolymph to produce EH (Seo & Brown, 2020). However, a limitation of this is the development of secondary EH, which differs from the spontaneous EH produced in MD, in addition to inconsistent presentation of vestibular symptoms (Wick et al., 2014). Medication methods are also one such way of inducing EH by administration of hormones such as aldosterone too increase the production of endolymph, or toxins such as cholera toxin to induce an immune response or inflammation within the inner ear to disrupt fluid homeostasis (Takeda et al., 2020). Alternatively, genetic methods have given rise to the Phex murine mouse model, carrying a defective phosphate-regulating gene with homology to endopeptidases located on the X chromosome (*PHEX*). Although the *PHEX* mutation has not been observed in MD patients, this mouse model has been found to be a suitable model due to the presentation of spontaneous, progressive hearing loss and vestibular impairment, as is seen in MD (Megarian et al., 2010). Although several methods are in development to assess MD in animals, a significant consideration to keep in mind is that despite efforts in visualising EH during the animal's life, confirmation of EH remains largely reliant on sectioning of the cochlea, which

is by then already in late-stage disease. This points towards the potential in live imaging studies such as optical coherence tomography, which can be used to produce 2D images of internal tissue microstructures, thus allowing observation of functional changes within the inner ear after induction of EH (Kakigi et al., 2020). Further research is needed to fully understand this disease, but inner ear pathology has contributed to making links between EH and MD.

1.2.6 Specific examples of human inner ear study 2: CANVAS

A second example where human inner ear analysis coupled with clinical assessment of human patients has helped us understand disease status is in the study of cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS). CANVAS is an autosomal recessive disease that typically presents later in life with inner ear pathology localised to the vestibular system. Its symptoms include progressive imbalance, oscillopsia, somatosensory impairment, chronic cough, and autonomic dysfunction (Thieme et al., 2022), with the most common complaint being progressive imbalance, often made worse in the dark (Cortese et al., 2022). CANVAS is suggested to have more than one causative gene and is thought to have wide phenotypic heterogeneity with a complex pattern of inheritance (Szmulewicz et al., 2016). Biallelic repeat expansions in the replication factor C subunit 1 (RFC1) gene has been identified as the causative agent for a large proportion of CANVAS cases (Ronco et al., 2023; Thieme et al., 2022). RFC1 encodes for the production of replication factor C, which has a role in DNA replication and repair by coordinating synthesis of both DNA strands (Thieme et al., 2022; Ronco et al., 2022). Due to the relatively recent identification of this disease, current work into researching CANVAS prominently features histopathology of donated temporal bones from patients who have had CANVAS. Otopathology of the temporal bones have revealed that while there was preservation of vestibular hair cells, there was also significant loss of Scarpa's ganglion cells and severe atrophy of vestibular nerve axons and dendrites (Ishai et al., 2021). Coupled with examination of the brainstem, the preservation of the vestibular nuclei indicated that the vestibular dysfunction experienced by patients in life originates from peripheral vestibular structures, marking this condition as a vestibular neuronopathy (Ishai et al., 2021; Szmulewicz et al., 2014). Temporal bone histopathology of several CANVAS patients has also revealed degeneration of the trigeminal and facial ganglia, with preservation of the auditory ganglion cells and auditory nerves, consistent with findings of normal (for age) hearing in CANVAS patients (Ishai et al., 2021; Yacovino et al., 2019).

Research using animal models for CANVAS have yet to be undertaken, with the development of a suitable model still underway. There are several challenges posed in this endeavour; alongside limited protein turnover, neurons are also unable to replicate, which means that the ability to efficiently repair damage is vital to maintain its functionality (Mathieson et al., 2018). Because research has suggested that a loss-of-function mechanism underpins CANVAS, this means that the complete loss of RFC1 may not be compatible with live animal models (Ronco et al., 2022). An additional challenge in developing an animal model for CANVAS is that anatomical differences may have greater implications in studying neuropathies than for auditory dysfunction. For example, the relationship between the height of the organism and the inherited neuropathy in question could limit understanding of the pathogenesis, as the height of a human defines the length of the nerves (Reilly & Rossor, 2020). Additionally, as CANVAS is a disease that presents later in life, large animal models may be required to accurately reflect human developmental stages. With these factors in mind, the importance of having both human and animal tissue for research is once again highlighted, especially with how many aspects of CANVAS disease research are still in development.

1.3 Enabling inner ear research through human tissue donation and tissue banking

As discussed previously, the study temporal bones post-mortem has been critical in advancing our understanding of inner ear disease. The acquisition of human tissue for research is dependent on ethical and effective practices. Here, we will discuss the practical aspects of tissue donation and tissue banking.

Tissue banking has a long history, spanning from human cadaveric dissection by the Greek school of medicine in Alexandria during the 3rd century BC to medical schools in the 21st century (Ghosh, 2015). Throughout this time, many changes occurred in the landscape of anatomical examination. Changing religious beliefs in the Middle Ages prohibited the dissection of human bodies before its revival in the 14th century, but shortages of human bodies led to acts of grave robbing and body snatching (Ghosh, 2015). No legislation regarding legally permitted use of human body tissue was established until the 18th and 19th centuries, though unethical practices continued to persist as anatomical research and education continued without the consideration of human rights and autonomy (Ghosh, 2015). In 1949, the United States Navy Tissue Bank was established at the Naval Medical Center in Bethesda, Maryland for the purposes of collecting bone samples for use as allografts (Strong, 2000). This was revolutionary to the practice of tissue banking, as it was the first institution to establish formal and legal standards and protocols in the processes of tissue donation. That is, it documented donor criteria, retrieval and processing methods, donor registration, and evaluation of received tissue for stored records (Narayan, 2012). Since then, advancements in technology and legal regulations have been made to improve strategies in preserving collected tissue, as well as expanding the types of tissue that may be collected in an appropriate manner. The capacity of tissue banks has also expanded, with more calls towards collaboration between both national and international tissue banks, along with the potential of virtual banks to increase access and ease of sharing information (Beaton et al., 2017). Local engagement with the wider community has also become prominent in order to promote active participation as well as address issues and concerns such as ignorance, fears surrounding retrieval of tissues from the deceased, religious beliefs, and bereavement (Narayan, 2012). Because tissue banking covers a wide range of tissue types and populations, from normal, healthy tissue from the general population to specific diseased tissues from individuals identified during clinical intervention (Bevilacqua et al., 2010), the importance of examining the specifics of the procedures involved becomes evident during the establishment of a culturally and ethically appropriate tissue bank.

In NZ, the utility of tissues can be categorised into therapeutic and non-therapeutic. Therapeutic use of human tissues encompasses the utilisation of tissues or organs in allograft transplantation, while non-therapeutic use includes research, education, audit, and anatomical examination of human tissue. When collecting human tissue for any purpose, informed consent must be given by the donor before any procedures involved in tissue donation may be permitted. Informed consent encapsulates the provision of sufficient information for an individual to make a knowledgeable decision (Health and Disability Commissioner Act, 1996), and serves to uphold an individual's autonomy. In the context of human tissue research, consent for use of the tissue sample in 'specified research' must be distinct from consent for the collection of human tissue for 'future unspecified research' purposes. Future unspecified research purposes describe the storage and distribution of tissue samples to researchers for an unspecified research project that has obtained the appropriate ethical approval (Guidelines for the Use of Human Tissue for Future Unspecified Research Purposes, 2007), and is a feature commonly undertaken by tissue banks (Beaton et al., 2017).

1.3.1 The Human Tissue Act (2008) of New Zealand

During the years of the National Socialist regime in Germany from 1933 to 1945, many bodies were procured from deceased psychiatric patients, prisoners, people who committed suicide, and victims of mass execution, leading to an ethical transgression of human rights that has since left its mark in history (Hildebrandt, 2021). To prevent such breaches in human rights and dignity again, the process of tissue donation therefore requires strict regulation and governance to ensure tissue banking is carried out appropriately. Establishment and maintenance of tissue banks within NZ is legally governed by the Human Tissue Act of 2008, which forms the basis of many of the procedures that the tissue banks must abide by. There are multiple purposes of this Act, such as ensuring that collection and use of human tissue is carried out with proper recognition and respect on behalf of the individual, and that it is done with inclusion of the cultural and spiritual needs, values, and beliefs of the individual's immediate family (Human Tissue Act 2008).

According to the Human Tissue Act (2008), human tissue is defined as below:

"(1) Human tissue or tissue means material that –

> (a) is, or is derived from, a body, or material collected from a living individual or from a body; and

(b) is or includes human cells; and

(c) is not excluded, for the purposes of some or all of the provisions of this Act, by subsection (2) or (3).

(2) A human embryo or human gamete is not human tissue for the purposes of any provision of this Act.

(3) Cell lines derived from human cells are human tissue for the purposes of the following sections, but not for the purposes of any other provisions of this Act:

(a) standards for collection or use of human tissue for non-therapeutic purposes):

(b) standards, etc, for export and import of human tissue."

Human tissue may be collected from living individuals or post-mortem. In the context of post-mortem donation, should the individual give informed consent prior to their death, the consent framework gives it legal standing, preventing others from vetoing the donor's consent. However, there is yet to be a provision that consent is registered in a legally binding manner upon death (Howard, 2013). Other people such as nominee(s), immediate family, or close relatives are allowed to consent or object on the individual's behalf so long as the individual had not expressed objection or had allowed a nominee to make the decision on their behalf (Human Tissue Act, 2008). It should be noted that even if a potential donor had given consent in life, individuals who are entitled to give informed consent (e.g. immediate family) possess the right to express their views to the person proposing to collect and use the tissue, and that person may decide to not proceed with the collection and use of tissue (Human Tissue Act, 2008). An example depicting the workflow from obtaining appropriate consent to collection of post-mortem tissue for research is represented in Figure 4.

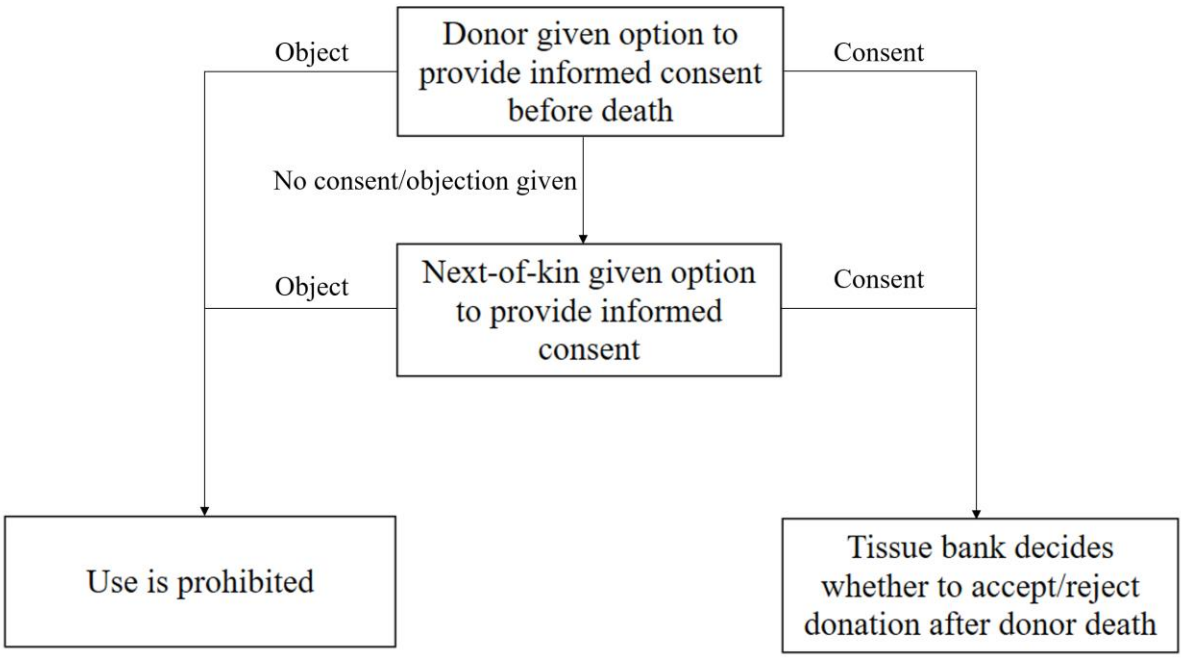

Figure 4. Workflow of consent to collection process. The flow diagram depicts an overview of the events that occur from donor consent to collection of human tissue for post-mortem non-therapeutic use. Adapted from Human Tissue Act 2008, s 5(1), *Overviews of use for certain purposes of certain tissue.*

1.3.2 Attitudes towards tissue donation in NZ

The introduction of the Human Tissue Act 2008 was an effort to increase organ donation rate by introducing new consent arrangements for organ collection from deceased donors, as NZ, much like elsewhere, have more people in need of organ transplants than there are available organs. Organ donation rates in NZ are considered low amongst the OECD, with an estimated rate of deceased organ donation at 15.2 donors per million per year, compared to European countries, where some have >30 donors per million per year (Douglas & Douglas, 2009; Harbour et al., 2015; Shaw & Webb, 2021). Although the rate for tissue donation for therapeutic purposes has been estimated, the rate of tissue donation for non-therapeutic purposes is unknown. While the scope of this thesis project does not address organ donation for transplantation, there is still significant overlap in terms of the strategies that may be implemented to increase public awareness and approach the act of collecting tissue with appropriate sensitivity and consideration of all factors.

There is currently no single organisation within NZ that places a sole focus on improving public awareness or engagement around post-mortem tissue donation for therapeutic or non-

therapeutic purposes, nor are there any programmes or campaigns to coordinate consistent engagement with media surrounding information pertaining to tissue donation (Increasing Deceased Organ and Transplantation: Towards a National Strategy, 2017). As a result, several studies have attempted to gauge the awareness, knowledge, and perceptions of tissue donation in different demographics within NZ. When assessing the attitudes and knowledge of young adult populations (age range 18-24) within NZ towards organ and tissue donation, findings have indicated that there is a high level of support in favour of donating, citing benefits on both societal and personal levels (Cornwall et al., 2015). In addition, no significant dissent was found when asked about giving consent to donating organs or tissues from a loved one if the individual had previously indicated a desire to donate (Cornwall et al., 2015), suggesting the importance of communication between an individual and their immediate family to prevent any risk of miscommunication. Separate interviews with NZ medical students have also indicated strong support towards organ donation, although the majority did not feel they were confident enough to discuss donation with patients in depth (Harbour et al., 2015). Overall, it appears that there is a general positive attitude towards tissue and organ donation, but the low organ donation rates that persist suggest that public campaigns and increased media coverage may help tie the positive attitudes into action. From the clinician side, the population of medical students that have been interviewed indicate that although there is a willingness to support organ donation, basic knowledge about the donation process may be lacking, which could discourage clinician facilitation on the topic when interacting with patients.

1.3.3 Māori attitudes and values in tissue donation

In addition to ethical concerns in NZ, tissue banking must also address the cultural needs for Māori and adhere to the principles of Te Tiriti o Waitangi. Hearing is taonga (precious item) for Māori (Manuel et al., 2021) and health inequity currently exists in hearing healthcare for Māori (Digby et al., 2014). It is crucial that our research activities related to hearing and balance research in NZ have responsiveness to Māori. In the context of tissue banking, it is critically important to weigh the risk and benefit to ensure that tissue banks will effectively address Māori concerns about human tissue research and that whatever benefits which may come out of it would work to better public health and aid Māori health development. If we cannot be inclusive to Māori for human tissue-based research, there is a significant risk that we do not advance our understanding of hearing and balance in the Māori population, affecting future treatments and therapies being delivered to Māori. Although the scope of this thesis project

does not extensively cover Māori spiritual beliefs in relation to tissue donation, an effort will be made to recognise some of the most prominent traditional beliefs, and to acknowledge the importance of engaging with these values when considering the process of tissue banking with Māori. It has been found that post-mortem donation rates for Māori are proportionately lower in comparison to Pākehā. Shaw and Webb (2021) examined qualitative interviews conducted with 15 Māori and 42 Pākehā individuals on their views on organ donation and transplantation and found that a potential explanation for lower post-mortem donation rates for Māori is that they did not perceive high approachability of healthcare providers and felt uncertainty about receiving culturally competent service. This has important implications for discussing tissue donation with Māori. If Māori do not feel that they are receiving clear communications or being included in the process, it may decrease their willingness to engage with tissue banking. To increase Māori engagement with tissue banking, cultural and spiritual values would need to be incorporated in Tikanga Māori (Māori protocols and practices; Hudson et al., 2016).

Whakapapa has been used to traditionally describe ancestral lineage and connection, embodying a responsibility for past and future generations, and is represented by the DNA of a person (Hudson et al., 2016). Disruptions to the body, a physical manifestation of whakapapa, would mean affecting an individual's sense of belonging (Shaw & Webb, 2021). Thus, the importance of ensuring the protection, accessibility, and usage of the tissue in question becomes paramount to uphold in relation to whakapapa (Hudson et al., 2016; Lewis & Pickering, 2003). Wairua, the spirit, may also be impacted in different ways in the event of post-mortem donation. During life, the body houses the wairua, meaning that the removal of tissue from the body may be interpreted as an act of disrespect to the body (Kennedy et al., 2015; Webb & Shaw, 2011). In the context of collecting and storing human tissue, the tissue itself, DNA, and associated genomic or clinical data are viewed as a taonga, which is considered tapu (sacred) and may come with rules and prohibitions, therefore leading to restrictions in its use (Beaton et al., 2017; Lewis & Pickering, 2003). One reservation concerning post-mortem donation held by Māori concerns the spiritual belief that not burying the individual whole breaks the cycle of life back to Papatūānuku (the earth mother), as returning someone to the earth with tissue or organs missing introduces unfulfillment between the time of birth and death, which in turn affects tapu (Lewis & Pickering, 2003). This means that without the appropriate practice to collect the taonga while preserving and respecting the tapu imbued in them, it would be prohibited to collect human tissue for any use. To address the spiritual anxieties surrounding the process of tissue banking, a karakia conducted by cultural

experts has been recommended to dispel these worries (Hudson et al., 2016). Communication with the donor is the first and foremost aspect to cultivating a relationship between them and the researchers requesting to use their tissue. In the physical dimension of upholding Māori values in wellbeing, Hudson et al. (2016) suggests that donor information sheets and consent forms should inform the donor of the use of the tissue, the research that may be involved in it, conditions of consent, what benefits come out of it, and how the tissue sample would be governed and used in the future. These practices should be communicated in a way that all parties involved can easily understand what would be involved. An additional consideration is that some Māori believe that donating parts of a body affects both the tūpāpaku (dead body) and the whānau (extended family; Douglas & Douglas, 2009). As such, there could be strong opposition from the family/whānau to retrieving tissue or organs from deceased Māori. It would therefore be in the tissue bank's best interest to recommend and offer facilitation in discussing donor wishes to donate tissue with the family/whānau.

These beliefs are not prevalent among all Māori and are not always uniform in nature, as the final decision ultimately rests upon one's own individualistic beliefs. In addition, beliefs are dynamic, and while the traditional Māori beliefs remain a prominent aspect in NZ culture, many Māori in the current space have deviated or upheld variations of the same beliefs (Sibley & Houkamau, 2013; Webb & Shaw, 2011). In addition, Māori individuals have commented that attitudes and perceptions of tissue donation have and can change within families over time, and that first-hand experience in involving themselves in donation have shifted opinions within their whānau (Webb & Shaw, 2011).

1.3.4 Examples of international temporal bone banks

As previously mentioned, the importance of human temporal bone studies includes developing rationale for treatments in diseases of the ear and improving strategies for treatment for hearing and vestibular disorders. There are currently no official facilities for the processing of human ear tissue in NZ, though international temporal bone banks can serve as an example and offer insight to the inner workings of one. In the United States, both temporal bone banks and laboratories have been established throughout the years, more so post-World War II, when technology and research was massively expanded in medical specialties, including otology (Schuknecht, 1984). The Massachusetts Eye and Ear Infirmary (MEEI) is an institution affiliated with the National Temporal Bone, Hearing and Balance Pathology Resource Registry (Registry), which had been established in 1992 by the National Institute on Deafness and Other

Communication Disorders (NIDCD). The purpose of the Registry is to oversee temporal bone donation, providing a resource for the public and researchers associated with hearing, balance, and the facial nerve. From the work that has been done in the MEEI and other temporal bone laboratories throughout the United States, several factors have been identified to enhance the efficiency and effectiveness of a temporal bone bank. This includes using histologic technicians skilled in temporal bone preparation, in conjunction with animal research, and clinically oriented directors. It also includes a register that stores medical and otologic history, diagnostic data, and a summary of findings for the associated temporal bone (Schuknecht, 1984). The MEEI has been a participant in international collaboration, for example, with the Australian Temporal Bone Bank (ATBB). The ATBB is the first temporal bone bank to be established in Australia and one of the few internationally that specialize in vestibular disorders in addition to hearing disorders. Located in the Royal Victorian Eye and Ear Hospital, the ATBB works in conjunction with the Department of Otolaryngology at the University of Melbourne, with research interests in histopathological analysis for vestibular disorders and CIs. With these international temporal bone banks to serve as examples, we hope to translate any insight offered into an NZ context in the future.

2 Thesis Aims

The overarching goals of this thesis project were to identify key considerations for establishing an ear tissue bank in NZ. To achieve this, two approaches were taken: the first was to investigate tissue banks currently in operation in NZ and identify what relevancies and adjustments may be necessary for an ear tissue bank, and the second was to investigate the perceptions clinicians involved in management of the inner ear currently hold towards an ear tissue bank as a potential resource for research purposes. From these goals, specific sub-aims were:

i. To identify existing tissue banks in NZ and survey information about their operations.

ii. Using an approach similar to a scoping review, to extract information on key cultural safety and donor involvement practices and make comparisons across these tissue banks.

iii. To design and conduct an explorative study to investigate clinician attitudes and opinion towards an ear tissue bank in NZ.

iv. To conduct thematic analysis to the interview data to identify clinician perceptions from a NZ lens.

3 Methodology

3.1 Methods Part I: Identification and investigation of existing NZ tissue banks

3.1.1 Documentation collection from NZ tissue banks

In order to obtain a better understanding of the roles and responsibilities that tissue banks in NZ must abide by, it was important to investigate the current practices undertaken by NZ tissue banks. To undertake this systematically, an approach similar to a scoping review was used to first determine how many tissue banks were currently operating in NZ, and then to extract the information of interest from documentation that we received from the tissue banks. A scoping review uses a systematic approach to identify and retrieve literature or evidence that is relevant to a given topic (Mak & Thomas, 2022; Munn et al., 2018). Munn et al. (2018) suggested that some indications of a scoping review included wanting to identify what types of evidence were available in a given field, to examine how research or practices are conducted in a specific field, and to identify the key characteristics or factors that are related to a concept of interest. Our aim of extracting information from current practices related to tissue banks fulfilled these indications, and we subsequently decided to employ similar methods to a scoping review to explore NZ's landscape in tissue donation.

3.1.2 Identification of existing tissue banks in NZ

The first step was to create a list of NZ tissue banks that are currently in operation. This list was generated by inputting the search terms "NZ tissue bank", "NZ biobanks", "NZ tissue donation", "NZ human tissue research", and "NZ human tissue laboratory" into the Google search engine and applying a time range from 1st January 2008 to 1st June 2023. The year 2008 was chosen as it was the year the Human Tissue Act 2008 was enacted. To determine if the tissue bank was eligible for analysis, the tissue bank needed to:

1) Be currently active in the community
2) Possess a website that offers public information
3) Have an active role in the collection of tissue (i.e. is not solely administrative).

Applying the same search terms into scientific databases such as PubMed and Scopus yielded results pertaining to only a select few tissue banks. This was because not all tissue banks generated and/or published research. Therefore, Google was used as the search engine of choice as it would host the public pages relevant to the NZ tissue banks.

3.1.3 Information collection about the tissue banks

All tissue banks that were identified through Google search were contacted. Initial investigation into the tissue banks were conducted through email, inquiry forms, and in-person communications to establish contact and request their donor information package and donor consent form. In-person communications additionally involved individual interviews to gain insight into the procedures and functioning of the tissue bank, and to obtain their perspectives of ear tissue banking in NZ.

General information such as the tissue bank's time of establishment, location, the type of tissue(s) collected, their objectives, and affiliations were also collected. This was summarised with following descriptions specific to each tissue bank in Table 1.

3.1.4 Information extraction from received donor information packages and donor consent forms

Donor information packages and donor consent forms were the chosen documentation to conduct data extraction from, as they are the documents that the prospective donor and donor's family are required to read and confirm to have read in the consent forms. In the data extraction phase, Mak and Thomas (2022) suggest that extraction categories vary as they are dependent on the research question and purpose. As we were interested in the current practices undertaken by tissue banks in relation to the donor, questions were formed to explore two domains: 1) cultural safety and considerations NZ tissue banks have in place, and 2) how tissue banks frame the relationship between research and the donor and/or donor's family/whānau.

The generated questions are as follows:

1. Is there any mention of cultural safety and/or Māori customs/procedures in the donor information package or donor consent form?
2. Are there any options to request specific cultural considerations during the collection process?

3. Is there a way for research outcomes related to the donated tissue to be released back to donor/family?
4. Are recommendations put in place to discuss potential donation with family/whānau?
5. Does the tissue bank provide any motivations for participating in tissue donation?

Once the questions were generated, they were then systematically applied to all eligible banks. As the tissue banks applied similar but variable methods of abiding by the requirements of the Human Tissue Act (2008), information from each question was summarised in individual tables. The tables were then grouped by similar concepts, and a more specific explanation of the abridged notes was then summarised after each grouping.

3.2 Methods Part II: Interviews with clinicians and reflexive thematic analysis

The purpose of the interviews was to explore clinician attitudes and opinions towards a potential ear tissue bank within NZ. Studies have been conducted on general population attitudes and opinions on tissue banking, but little work has been done on exploring clinician attitudes. The interviews were intended to allow clinicians to discuss their thoughts on primarily post-mortem donation of the inner ear, and their ideas of how it would be beneficial to them and in relation to the people of NZ. Qualitative methodology has the advantage of exploring and understanding complex human experiences that cannot be captured by quantitative analysis (Cleland, 2017). As one of the overarching research aims is to investigate clinician attitudes and opinions towards an ear tissue bank, qualitative interviews allow deeper exploration of multiple viewpoints to gain insight into an ear tissue bank's feasibility from the perspective of a clinician based in NZ. This exploratory study was approved by the University of Auckland Human Participants Ethics Committee on 16th October 2023 (reference number AHREC25973).

3.2.1 Participant recruitment

Due to the specific nature of this research project, the desired participants were clinicians who were involved in managing inner ear disease. Eligibility to participate was therefore limited to otologists and neurotologists currently practicing in NZ. A combined approach of purposeful sampling and snowball sampling was used to recruit participants. Purposeful sampling was initially used, as it identified and selected individuals with specific attributes, such as having experience or being especially knowledgeable about a phenomenon of interest (Palinkas et al., 2015). Snowball sampling, which is when participants provide referrals to other eligible candidates, was then employed over the course of the study as the target population of otologists and neurotologists was difficult to reach due to the small community (Parker et al., 2024).

Potential participants were invited to participate in an interview via email advert with an attached participant consent form and participant information sheet (PIS) through the NZ Society of Otolaryngology Head and Neck Surgery (NZSOHNS) and contact lists through conferences. The participants were given the option of meeting in-person at a public space, over the phone, or over Zoom to conduct the interview.

3.2.2 Interview process

All interviews were conducted by the student researcher. Recording devices such as in-built recording software on Zoom or mobile recording apps were used to capture audio for later transcription. Before starting the interview, verbal consent to record the ensuing interview was obtained.

Participants who agreed to take part in the interview were sent the participant information sheet (PIS), participant consent form, and a copy of the core questions to be asked to allow them to prepare before the interview. The interview was semi-structured so that participants were able to bring up other topics of interest or relevance. Follow-up questions were asked at the discretion of the interviewer to ensure adequate discussion of the current topic or to clarify any discussion points. The interview questions were not necessarily asked in chronological order, as the topic of current discussion would sometimes lead to a more relevant question that is not in sequential order.

The recorded interviews were then transcribed in preparation for data analysis. Following transcription, the transcripts were returned to the participant, and the participant was given a two-week period in which they could review the transcript and request for any amendments that they felt were necessary. After the two-week period, the transcript was then de-identified to undergo data analysis. De-identification was carried out by assigning each participant a representative number, and personal names or names of workplaces were redacted.

3.2.3 Reflexive thematic analysis

Reflexive thematic analysis was chosen to closely examine the interview data, as it is an interpretive approach that facilitates the identification and analysis of the patterns in the dataset (Byrne, 2021). As this was an explorative study, the goal was to identify ideas about clinicians' perceptions that emerged from the data rather than applying pre-conceived ideas to the data. The process of reflexive thematic analysis followed the recommended phases outlined by Braun and Clarke (2006):

- Phase One involved familiarisation of the data (Braun & Clarke, 2006). Transcription of the interview simultaneously gave the opportunity to begin familiarisation and interpretation of the data. Transcription required two phases: a first-round preliminary

transcription of the audio recording, and a second-round review of the transcript, which consisted of a full readthrough and revision of the syntax (Braun & Clarke, 2006).

- Phase Two was to generate the initial codes to apply to the interview transcripts. Codes identify meaningful features of data which capture any common topics throughout the full dataset (Braun & Clarke, 2006). This process was carried out using a qualitative data analysis computer software called NVivo, where sections of text were tagged with a relevant code. Coding was performed systematically by conducting multiple sweeps to ensure no additional amendments were required, whether by adding, removing, or revising existing codes (Braun & Clarke, 2006).
- In Phase Three, themes were generated. Themes encompass the abstract patterns and processes that explain a phenomenon or concept (Mishra & Dey, 2022). Codes that had common meanings were grouped together into potential overarching themes along with their associated data extracts. This phase ended with a set of candidate themes in preparation for evaluation.
- Phase Four was to re-evaluate the themes to ensure they were distinct from one another in meaning. Themes that had distinctly overlapping features were combined, and themes that had broad subsets were broken down into separate themes (Braun & Clarke, 2006). The refinement of themes was carried out in two levels. The first level of re-evaluation was to revise the themes to check if they formed a coherent pattern. This was done by reading through the collated extracts under each theme to ensure they matched the theme's meaning (Braun & Clarke, 2006). The second level of re-evaluation was to ascertain that the themes were representative of the entire dataset. Additional data that had not been coded in the initial stages were incorporated into the themes as fit until no substantial adjustments were needed (Braun & Clarke, 2006).
- Phase Five involved the defining and naming of the themes formed in Phase Four. The key point for each theme was identified, ensuring they captured an aspect of interest from the collated data extracts (Braun & Clarke, 2006). The names of the themes were worded to be succinct yet also contained enough detail to immediately give a sense of what it was about.
- Phase Six encompasses the final analysis and write-up to produce a report that conveys the story formed from the data (Braun & Clarke, 2006). To support the identified themes,

quotes that demonstrated the essence of the theme were extracted and embedded in the write-up.

4 Results

4.1 Results Part I: Identification and investigation of existing NZ tissue banks

4.1.1 Analysis using scoping review methodology: National tissue banks

A total of nine tissue banks that are currently active in NZ were identified through Google database search conducted between 1st January 2008 to 1st June 2023 using search terms specified in the methodology (Chapter 3.1.2). General information such as the name of the tissue bank, their location within NZ, the type of tissue they collect, the primary purpose of the collected tissue, whether they are a public or private institution, and a link to their public page was collected and summarised in Table 1.

Table 1. Summary of current active tissue banks in *NZ*.

Name of Tissue Bank	Location	Tissue Collected	Purpose(s)	Public/ Private	Public Website
Human Anatomy Lab	Auckland	Whole Body Donation	Education, research	Public	Link
NZ National Eye Bank	Auckland	Cornea, sclera	Transplantation, research	Private	Link
Otago Body Bequest Programme	Dunedin	Whole body donation	Education, research	Public	Link
NZ Blood Service	Nationwide	Blood, plasma, other tissues, organs	Transplantation, research	Public	Link
Malaghan Institute of Medical Research Immune Tissue Bank	Wellington	Cells, blood, tissue	Research	Private	Link
Auckland Regional Biobank	Auckland	Tissue	Research	Public	Link
Neurological Foundation Human Brain Bank	Auckland	Brain	Research	Private	Link
Cancer Society Tissue Bank	Christchurch	Cancer tissue	Research	Private	Link
Gillies McIndoe Research Institute Tissue Bank	Wellington	Blood, cancer tissue	Research	Private	Link

Transplantation falls under the category of therapeutic use of human tissue. Research purposes refer to non-therapeutic use of human tissue.

4.1.2 General summary of each national tissue bank identified

The tissue banks identified were contacted to collect information about the nature of the tissue bank and their operation. The following information was extracted from available public pages associated with the tissue bank, making inquiries via email, and inquiry in-person.

1. The Human Anatomy Lab (HAL) is a facility at the University of Auckland's Faculty of Medical and Health Sciences that receives cadaver donations for teaching and training purposes. The donation of bodies is facilitated by the Human Body Bequest Programme, which has been administered by the Department of Anatomy and Medical Imaging since the opening of the Medical School in 1968. Users include undergraduate and postgraduate medical and science students, researchers, surgeons, and other health professions with an involvement in anatomical study. The Human Body Bequest Programme operates under geographical constraints, where registrations are generally only accepted from within an area of approximately three hours' drive from Auckland.

2. The NZ National Eye Bank (NZNEB) was established in 1991 and is a non-profit organisation that provides donated corneal and other tissues such as sclera and amniotic membrane to treat blindness. The facility is based in the University of Auckland and is involved in the collection, storage, and distribution of tissues throughout NZ. Although the primary purpose of the NZNEB is to oversee tissue donations for transplantation, it has contributions to clinical research, particularly pertaining to corneal transplantation and its scope in NZ.

3. Under the Department of Anatomy at the University of Otago is the Otago Body Bequest Programme, which operates similarly to the HAL at the University of Auckland. With the first official bequest to the Medical School in 1943, it has since been overseeing the registration and processing of bodies from altruistic donations from the late 1950s onwards. The main purpose of the programme is to provide cadavers for teaching anatomy to medical and science students, although research may be carried out using the bequeathed bodies as well, with approval from the University of Otago (Health) Ethics Committee. Geographically, the programme accepts donations from greater Dunedin, Invercargill, Christchurch, and Nelson/Marlborough.

4. The NZ Blood Service (NZBS) is a well-established service in NZ that oversees the performance of functions of donated blood and other controlled human substances such as plasma. The NZBS was established in 1998 under the NZ Public Health and Disability Act 2000 and is additionally classified as a Public Benefit Entity. The primary objective of the NZBS is to manage the collection, processing and supplying of blood, controlled human substances, and other related services. The Blood Bank operates nationwide, with 34 banks around the country to prepare donations for transfusions. The NZBS is also involved in accepting tissue and organ donation, for example hip bones, tissues such as cornea and sclerae, heart valves, and skin. Organ donation is in collaboration with Organ Donation NZ (ODNZ), which is a part of the NZBS and is responsible for coordinating donated organs and tissues from deceased donors for transplant units and tissue banks.

5. The Malaghan Institute of Medical Research is based in Wellington and was first established in 1979 as the Wellington Cancer and Medical Research Institute before being renamed in 1986. In 2018, the Institute established the Immune Tissue Bank for the purpose of storing blood, cell and tissue samples for future research. The samples were donated by participants who had been involved in certain studies or clinical trials conducted or coordinated by the Malaghan Institute. The primary use of the collected samples is for research into the immune system function in health and disease, alongside the development of novel treatments.

6. The Auckland Regional Biobank (ARB) is a facility that stores a collection of donated tissue samples from patients. The Biobank was originally started in 2010 at Middlemore Hospital, Auckland, before relocating to the University of Auckland's Faculty of Medical and Health Sciences in 2016. With a partnership between the University of Auckland and all three Auckland Metropolitan District Health Boards (Auckland, Waitemata, Counties-Manukau), the ARB collects, processes, and stores tissue samples for distribution to researchers for use in ethically approved research projects. Examples of tissue that may be collected includes solid tumours, bone marrow, or blood during biopsies or blood tests.

7. The Neurological Foundation Human Brain Bank, located at the University of Auckland, began in 1994 when the Neurological Foundation granted the University of Auckland the

funding to purchase a freezer for the purpose of storing brain tissue. Since them, the Brain Bank has expanded into an extensive collection of human brain tissue with the purpose of researching neurological conditions such as Alzheimer's disease, Parkinson's disease, and more. The Brain Bank can collect nationwide, though this operates on the stipulation that the brain can be received within 24 hours after death.

8. The Cancer Society Tissue Bank (CSTB) is a private charity located in Christchurch that works in collaboration with the University of Otago, Canterbury District Health Board, and the Canterbury/West Coast division of the Cancer Society NZ. Established in 1996, the CSTB works to collect and provide human cancer tissue samples and clinical data for the purposes of research. The CSTB has made a significant impact on cancer research in NZ, with over 9,000 donors since its establishment and over 10,000 samples having been accessed by researchers.

9. The Gillies McIndoe Research Institute Tissue Bank in Wellington is a private charity that opened in 2013 and has since collected over 3,000 tissue and blood samples through collaboration with Hutt Hospital, Wellington Regional Hospital, and Boulcott Hospital. These samples are stored for use in research into cancer, vascular birthmarks, and fibrotic conditions in the hopes of furthering knowledge in these conditions and developing new treatments that are less invasive and more available to the general population.

Of the nine tissue banks identified, four were based in Auckland, not including the NZBS, which has centres around the country. The majority (five out of nine) of the tissue banks are also privately owned but have affiliations with public universities and/or District Health Boards. Five tissue banks out of the nine are involved in post-mortem tissue collection (HAL, NZNEB, Otago Body Bequest Programme, NZBS, Brain Bank), while the rest were involved in collecting tissue from living donors. All tissue banks had a function in research, even if it was not their primary purpose.

The oldest tissue bank identified was the Otago Body Bequest Programme (est. 1943) and the newest was the Gillies McIndoe Research Institute Tissue Bank (est. 2013). The tissue bank that had the most similar operations to what an NZ ear tissue bank would have is the Brain Bank, due to their involvement with post-mortem skull-based tissue with a focus on collecting for non-therapeutic use.

4.1.3 Information extraction from tissue bank documentation

Of the nine tissue banks found and summarised in Table 1, four tissue banks responded to our requests for donor information packages and donor consent forms. These are: the HAL, Otago Body Bequest Programme, Malaghan Institute, and ARB. Information extracted from both forms are summarised as follows:

Table 2. Summary of cultural safety measures

Tissue Bank	Mention of cultural safety measures (Yes/No)	Mention of Māori customs (Yes/No)	Additional Notes
HAL	Yes	No	No mention of specific Māori customs in documents given to donor
Otago Body Bequest Programme	Yes	Yes	Poroporoaki[1] at the end of the teaching year
Malaghan Institute	Yes	Yes	Offer of a karakia[2] before the disposal of tissue or before sample is sent overseas
ARB	Yes	Yes	Offer of a karakia before the disposal of tissue

This is in response to the question: "Is there any mention of cultural safety and/or Māori customs/procedures mentioned in the donor information package or donor consent form?"

[1] Poroporoaki – eulogies for the dead.
[2] Karakia – prayers.

Table 3. Summary of cultural consideration options for donors

Tissue Bank	Option for donor and their family to request specific cultural considerations (Yes/No)	Additional Notes
HAL	No	No option available in information package or consent forms
Otago Body Bequest Programme	No	Unable to make special arrangements for donors
Malaghan Institute	No	No other option available beyond providing contact details for Māori Liaison Officer
ARB	No	No other option available beyond provided contact for Māori consultation

This is in response to the question: "Are there any options for donors and their family to request specific cultural considerations during the collection process?"

Table 2 and Table 3 investigated how NZ tissue banks addressed donor cultural safety and if there were any differences in their individual practices. All donor information packages received from the tissue banks state that cultural safety and competence measures have been considered. Although the HAL did not mention specific Māori customs in the documents, the HAL are able to discuss body bequests on a per individual basis due to the small operational size and donor numbers. The other tissue banks also made a note of this, suppling contacts to coordinators who can guide the donor through the process. This highlights the importance of the role tissue bank coordinators play in engaging potential donors and ensuring that they are well-informed of the consenting framework. In-person communications with the HAL also revealed that they were responsible for coordinating the poroporoaki, which included a karakia, on an annual basis when human tissue was to be disposed of in the University of Auckland. Poroporoaki is a direct address to the deceased, with the belief that the individual's spirit is present and can hear what is being said, bidding the deceased to begin their journey towards their ancestors, and signifying the closure of an encounter (Irwin, 2022; Minton et al., 2022). At the HAL, the poroporoaki is overseen by a Māori elder. The Malaghan Institute and the ARB offer a karakia prior to the disposal of human tissue, and in the case of the Malaghan Institute, before a tissue sample is sent overseas, provided consent had been obtained.

Although Māori and Pasifika cultural considerations have been mentioned by the tissue banks, there is currently no option in the donor information packages or consent forms to request non-Māori cultural customs or considerations. Specifically, no option has been provided by the HAL, while the donor information package for the Otago Body Bequest Programme state that special arrangements were unable to be made for donors upon completion of the cadaver's study, and the Malaghan Institute and ARB provided the contact details for a Māori Liaison Officer should the donor and their family/whānau wish to discuss more about donation, storage, and disposal of the collected tissues.

The HAL and Otago Body Bequest Programme also bring up funeral service considerations due to the post-mortem nature of their function. Funeral directors notify and liaise with the tissue banks to arrange transportation of the body to separate embalming facilities under the tissue banks.

Table 4. Summary of donor information return options

Tissue Bank	Option for donor/family to receive information about sample's use (Yes/No)	Additional Notes
HAL	No	No autopsies are performed and there is no pathway for family/ whānau to receive specific details of the research conducted with the tissue
Otago Body Bequest Programme	No	No option available for family/ whānau to receive specific information about sample's use
Malaghan Institute	Yes	No pathway for donor to receive specific details of the research conducted with their tissue, but donors may opt to be notified about incidental findings
ARB	Yes	No pathway for donor to receive specific details of the research conducted with their tissue, but donors may opt to be notified about incidental findings

This is in response to the question: "Is there a way for research outcomes related to the donated tissue to be released back to donor/family?"

Table 5. Summary of discussion recommendations with family/whānau

Tissue Bank	Recommendations to discuss donation with family/whānau (Yes/No)	Additional Notes
HAL	Yes	Donors encouraged to discuss participation with next-of-kin and family
Otago Body Bequest Programme	Yes	Consent from immediate family member required, involving agreement that all reasonably practicable steps have been taken to consult members of the immediate family
Malaghan Institute	Yes	Donors encouraged to discuss participation with family/whānau
ARB	Yes	Donors encouraged to discuss participation with family/whānau

This is in response to the question: "Are recommendations put in place to discuss potential donation with family/whānau?"

These questions (Table 4 and Table 5) were to investigate what involvement a donor and their family/whānau may have with the tissue bank as part of the tissue donation process. All four tissue banks specify in their donor information sheet that they are unable to return information about findings related to specific tissue samples. This is to protect personal information as divulging specific research outcomes from studies involving the donor's tissue to the donor or their family would risk breaching confidentiality.

However, the Malaghan Institute and the ARB may be able to return information that is considered an incidental finding. Incidental findings describe information that was discovered during research of the donated tissue that may have an impact on the donor and/or has relevance to the donor's medical care. As these two tissue banks are involved in collecting pathologic tissue from living donors for research, researchers may have ethical approval to return this information to the donor. Being able to provide information about incidental findings in this case is important as it may involve genetic information that would apply to the family as well. These two institutions achieve this ethically by having an additional, separate consent pertaining to donor approval of return of this information if they wish to have it.

Donor information packages from all tissue banks encouraged discussion with the donor's family/whānau prior to donating. In the cases of the HAL and Otago Body Bequest Programme, additional consent was required from the next-of-kin or member of the immediate family. This is because these two tissue banks accept post-mortem body donation. It is important to discuss with the family/whānau to ensure that they are made aware of the donor's intentions and come to a consensus. Family/whānau support is also important after the death of the donor so that the tissue bank is notified and proper arrangements to transport the body can be made. Although the ARB is not involved in post-mortem tissue collection, their donor consent form contained a blank section for the purposes of recording discussions with the family/whānau about donating tissue.

Table 6. Summary of provided motivations for donor participants

Tissue Bank	Motivations outlined for tissue donation (Yes/No)	Additional Notes
HAL	Yes	Importance is placed on teaching anatomy with the possibility of use in research
Otago Body Bequest Programme	Yes	Importance is placed on teaching anatomy with the possibility of use in research
Malaghan Institute	Yes	Primary purpose is for research. Samples may be sent overseas, which requires separate consent
ARB	Yes	Primary purpose is for research. Samples may be sent overseas, which requires separate consent

This is in response to the question: "Does the tissue bank provide any motivations for participating in tissue donation?"

The HAL and Otago Body Bequest Programme emphasise the importance cadavers play in the teaching and training of doctors and health professionals. The Malaghan Institute explains that donated tissue samples are a useful resource for immune system research that can further knowledge about the immune system and how it could help treat disease. Finally, the ARB describes how donated tissue can allow better understanding of medical conditions and disease for the improvement of care for future patients. All these motivations appear to focus on community benefit rather than immediate benefit.

4.1.4 Summary of Part I

In summary, nine existing tissue banks in NZ were found in total. The four tissue banks that were eligible for information extraction were the HAL, Otago Body Bequest Programme, Malaghan Institute, and the ARB. The questions that were applied to these tissue banks showed that cultural safety and donor involvement practices were dependent on the nature of the tissue collected. Post-mortem tissue had additional Māori customs arranged in the form of a poroporoaki at the time of disposal. All tissue banks communicated to the donors that a karakia is offered for any tissue donation (Table 2). The karakia addressed the cultural and spiritual state of the given tissue. It is used as part of whakawātea, which refers to the process in which a restriction is removed before a state of tapu is returned (Hudson et al., 2016). Living donors were given the additional option of requesting the return of incidental findings, as it may have impact on their medical care in life. The motivations to donate tissue that were supplied by the tissue banks centred around the betterment of future patients and training of new medical professionals.

4.2 Results Part II: Interviews with clinicians and reflexive thematic analysis

There were seven interview participants in total. Each interview took approximately 30 minutes. There were five male participants and two female participants. All participants came from a non-Māori cultural background. These demographics are likely reflective of the current makeup of this highly specialised workforce.

Table 7. Participant demographic information

Variables	Number of participants
Occupation	
Otologists	6
Neurotologists	1
Gender	
Male	5
Female	2
Cultural background	
Tauiwi[3]	7
Māori/Pasifika	0

The interview questions investigated the clinicians' attitudes and opinions towards an ear tissue bank in NZ. Through reflexive thematic analysis, four themes were generated from the interview data. These are: 1) *Perceived roles:* the clinician's perception of their role in an ear tissue bank; 2) *Perceived benefits:* how an ear tissue bank benefits the community at large; *3) Perceived barriers:* challenges in sustaining the ear tissue bank and otologic research; and 4) *Collaborative efforts:* the importance of professional collaboration. These themes, along with their associated codes, are summarised in Figure 5.

[3] Tauiwi – non-Māori New Zealanders

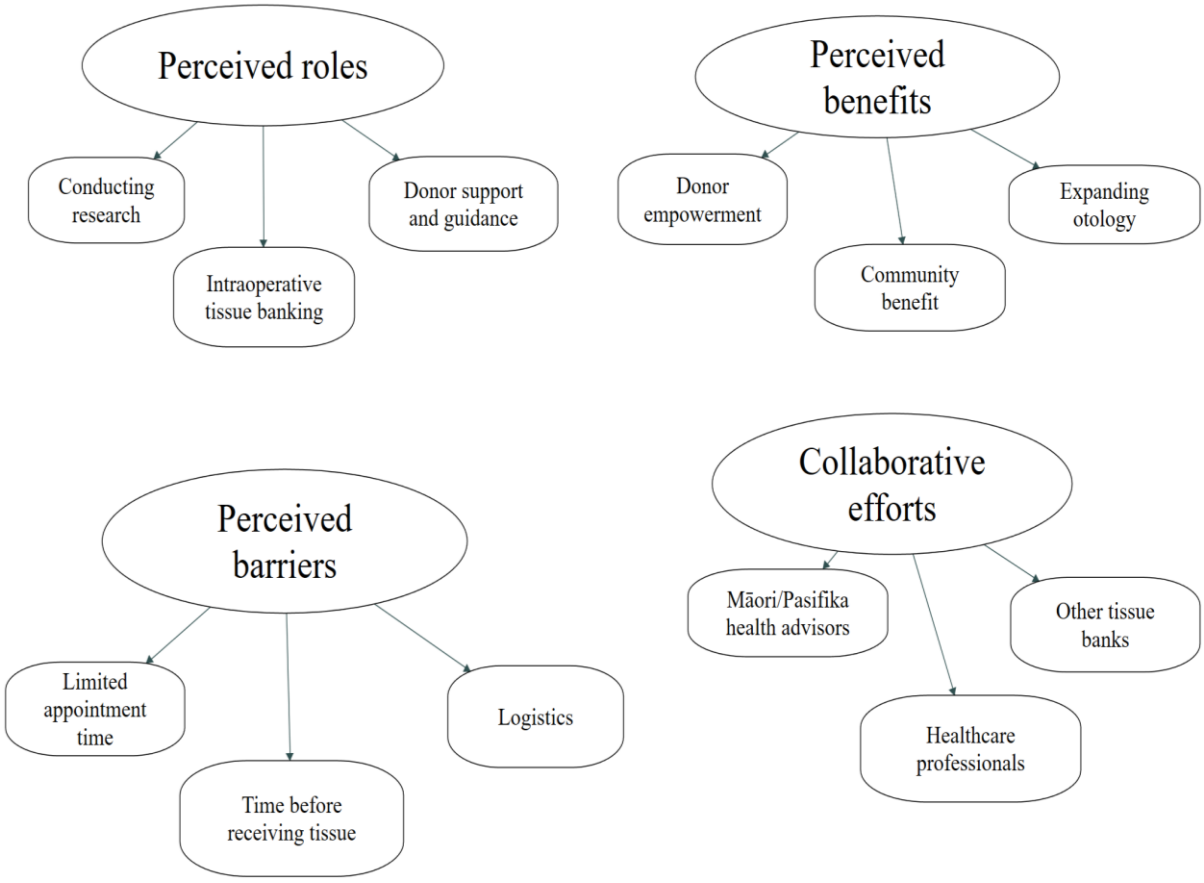

Figure 5. Thematic map of generated themes. This map depicts the four themes relating to the attitudes and opinions of otologists and neurotologists towards a potential ear tissue bank in NZ.

4.2.1 *Perceived benefits:* The benefits from the procedures and outcomes of an ear tissue bank

This theme was formed when participants identified and discussed various ways in which an ear tissue bank and how the research that comes out of it could benefit different groups, from an individual to a community level.

Most participants acknowledged that although donors would not be able to see the research outcomes from future studies on their condition, the act of donation would be able to give them a sense of empowerment.

> "I think making a difference can be a huge thing for patients. They might think, "I was just one of the lot," but seeing that it's actually important and their help can be very useful is beneficial and empowering." – *P2*

> "I think patients like to think that in some way, that their, for want of a better word, suffering, might help. (…) it does potentially give someone some satisfaction." – *P6*

The majority of participants brought up that most of the benefits associated with an ear tissue bank would be for the communities involved in inner ear pathology. The initial benefit would be for the research and clinician community to further their understanding of inner ear diseases, but benefits will also reach future patients and people potentially affected by hearing or vestibular disorders. Emphasis was placed on the betterment of future patients by providing them evidence-based practice and more options in treatment or management. The participants believed that this information was important for the donor and their family to know prior to donating, and that there would be no financial gain resulting from their act of altruism.

> "So it won't empower them directly. But because I'm just thinking, you know, genetic stuff, you won't really be able to pass that on temporal bones. Because it's more like blood samples. But they will give them more information on some conditions that they may have. But it's down the line, it's the youngest generations." – *P1*

> "I think people like to be able to give back, particularly if they've been helped, or if there's something which is not clear. And I think knowledge for a lot of people is very empowering. And even if they don't get the knowledge themselves, knowing that they're contributing to helping other people understand things, particularly someone in their family, that they can contribute to family knowledge, like genetic stuff going on, I think that's very empowering. (…) So for individual patients, probably not so much. But it's more empowering community understanding. Community contribution is probably more relevant than individual patients, I suspect." – *P4*

Some participants thought that another benefit of an ear tissue bank could be how resulting scientific findings could lead to the expansion of otology as a subspeciality, especially because otology compared to many other disciplines does not have as significant a presence in literature. One participant considered rhinology as a comparison, citing that many other subspecialities have seen significant expansion within their field in contrast to the progress in otology.

> "I think basic science, studying the inner ear of abnormal ears and people with hearing loss, all the way to learning something about what we actually do. You know, what happens when you put a CI in 20, 30 years down the line? What happens to the nerve? What happens to the inner ear? You know, all those interesting topics." – *P2*

> "… just increasing our ability to have basic science research in otology, it'd be really quite a powerful thing to have. At the moment, like I said, our rhinology colleagues are probably quite a step ahead of us in how they are progressing with their research. So I think it would be great for us as a subspecialty." – *P5*

4.2.2 *Perceived roles:* The clinician's perception of their role in an ear tissue bank

This theme encompasses the perceived roles clinicians believed they would be able to carry out should they have an involvement in the ear tissue bank. Ideas surrounding potential roles were varied, as the participants considered multiple individual factors that could affect their participation, such as their own personal interest in research and their clinical workload.

The first role to be discussed is a role in personally conducting research. All participants indicated an interest in conducting research using human tissue samples and expressed interest in both basic science research and clinical research, with a focus on how it would increase their knowledge of specific conditions and diseases inclusive of both hearing and vestibular, and the treatment strategies from research findings that they could implement in clinic. This suggests that the establishment of an ear tissue bank may foster engagement in research amongst clinicians and open more opportunities for NZ-based otology research.

> "… I don't know if you've heard about eustachian tube dilation, but I'm doing some work on that. But you know, on the ground. And there's actually not that many published data on the sizes and the orientation of the eustachian tube. In adults, we know the approximate length. So it would be quite interesting if we had post-mortem ones, we could do a bit more anatomy in order to improve the shape and the sizes of the balloons." – *P1*

> "… other things that would be interesting to see would be balance disorders, for instance, to look at some of the anatomy, particularly around the valve of Bast, looking to see if we can see associations, perhaps between BPPV with otoconia, and the semicircular canals, and possibly whether there's otoconia in other parts of the inner ear as well, particularly around the valve of Bast and the vestibular system. Or, you know, what happens when otoconia get into the cochlea? What prevents otoconia from getting into the cochlea, all those sorts of questions might be interesting to explore from a pathological perspective." – *P4*

> "It [human tissue research] would open up a few more options for some of the middle ear diseases, and even the ear canal diseases that I still don't have good answers for. So even something simple like exostoses; I was talking to some registrars the other day and saying we get the most exostoses in the world, probably. And we still don't know why some people get exostoses and some people don't. Being able to study that at a basic science level would be pretty good." – *P5*

Donor support and guidance were also discussed in the interviews. Most participants felt that they could be involved in donor recruitment in the clinic, although the scope of their involvement would be limited to passing on external contact details to potential donors should they wish to find out more. Several clinicians expressed that they perceived their role in research to be more so along the lines of providing clinical support, such as supplying clinical

information about specific donors over the course of their treatment, or providing cases for specific conditions should any potential research be undertaken with them, provided that the appropriate consent had been obtained.

> "And if somebody asked me, "Oh, well, how does it [tissue donation] work? What are you going to do and blah, blah, blah," it would take a lot of time. So I'm happy to give them a contact of somebody who can call them, or that they can call and discuss that in more detail. That's what I see as my involvement." – *P1*

> "… there are obviously a lot of inner ear disorders that are unknown at the moment. And so I guess if there was something that looks like a genetic inner ear disorder that you can identify within my own clinic or with other people, then you could look to see if some of those people would be willing to donate. But it would be more of the clinical presentation type of research. The second part of it is if there was a drive from somewhere to learn more about a particular condition, whether we had patients that would be willing to donate. I guess what my strength would be is providing the clinical information." – *P7*

The possibility of intraoperative tissue banking was brought up and discussed with most clinicians. Intraoperative tissue banking refers to the collection of tissue from a living donor during a surgical procedure. The clinicians noted that it would be a viable option to obtain tissue samples as they would be obtained from living donors, ensuring that the tissue is collected in its diseased state. Some examples given of specific tissue that can be collected included middle ear mucosa and vestibular schwannoma samples. Participants noted that during surgical procedures on the inner ear, collecting ear tissue at the same time would not cost much more additional time. Participants also agreed that fresh tissue may be easier to obtain than post-mortem tissue as the waiting time between receiving donor consent and harvesting post-mortem tissue would be avoided. One participant added that patient recovery must be considered, in that the process of intraoperative tissue collection would not affect patient outcome. Furthermore, clinicians also stated that intraoperative tissue banking would give the opportunity to collect not just from the inner ear, but also from the outer and middle ear, expanding research opportunities.

> "… as long as it's [intraoperative tissue banking] not something where you jeopardise the patient's ultimate outcomes. It adds a little bit of time, but not much. It'll be perfectly fine. Although, I've seen research where people sample from the inner ear. I'm not sure how ethical that is, because there are a whole lot of problems around that in terms of affecting healing and scarring. Acoustic neuroma surgery is quite destructive to the inner ear anyway. You're essentially removing normal inner ear tissue, why not collect it?" – *P2*

> "You could do intraoperative tissue banking, that perhaps is a better way than waiting for people to die. And that perhaps is a really good way of getting samples of tissue in the ear that will otherwise be destroyed. We will drill out, for example, acoustic neuromas.

> Should be asked about this, I mean, a part of the operation is drilling out the labyrinth, for example. Tissue from the labyrinth, the cochlea, no use, it should be removed as well, so I think there can be tissue that can be gained if you're looking at middle ear mucosa, middle ear ossicles, that can be done intraoperatively. You don't have to wait for post-mortem." – *P3*

> "Yeah, so skull base surgery is probably the classic one. They're not often performed, but you occasionally remove the inner ear, or portions of it on your way in to access tumours around the brain. And it's certainly technically possible to get some tissue on the way in." – *P6*

4.2.3 *Perceived barriers:* Challenges in sustaining the ear tissue bank and otologic research

This theme was formed when participants were asked about potential barriers to their personal involvement if they were to work with the tissue bank. The challenges that were brought up pertained to both themselves and to their interactions with potential donors.

All participants felt that they would not have sufficient time during the appointment to discuss post-mortem tissue donation with the patient. The sensitivity of the subject was consistently brought up, and some participants felt that patients would prefer to already have a degree of closeness and familiarity with the clinician before the discussion could be held, which would indicate having spent a relatively extensive amount of time with the patient beforehand, which may not be feasible with the time afforded by a typical appointment timespan.

> "In the clinical setting, we're a bit time pressured, so I wouldn't have the time to discuss that with them. From my point of view, I would be happy to say, "Look, this exists." There are always patients who want to contribute to research." – *P1*

> "I think it's quite difficult, but you'd probably want to discuss it with somebody you know well and have known for a while, and someone who trusts you. (…) But I think with the right person and in the right setting, you probably could have the chat." – *P7*

Another concern brought up by the participants was the wait time between receiving consent and being able to collect post-mortem tissue, as it could mean that certain studies would not be able to be carried out in addition to the difficulty in following up with the potential donor over a long period of time.

> "I also don't know how I personally know how to approach and keep the follow up. I mean, what do you do if somebody consents age 30 and dies at age 90? Keep on reminding them? I don't know if there are ways around that." – *P2*

> "People with conditions right now, for example, such as Ménière's patients, the ones that are going to be really good for tissue banks, you're going to have wait 30, 40 years for them to die." – *P3*

Several aspects of logistics were mentioned by the participants when asked about barriers that could limit their involvement in an ear tissue bank. Some concerns surround funding for the ear tissue bank and geographical barriers that may make clinician participation difficult. Most participants (five out of seven) said that time would be the biggest barrier for them if they were to involve themselves in the ear tissue bank, as they felt their clinical work would not allow them much time to conduct research using the tissue bank as a resource.

> "I think I would be interested in using it [the ear tissue bank] as part of a team. I don't think I'll be organised enough or have enough time to start a huge research project by myself, but certainly as part of the team under someone else." – *P2*

> "Yeah, because a lot of people will be very metro-focused, but there's a huge proportion of our patients who aren't living in big cities, and a lot of us surgeons that live outside of the big cities that would still want to be involved. That's always an issue." – *P5*

> "I think probably the main challenge is really funding. That's probably the biggest thing. (…) It's also in a busy clinical practice, getting time and then remembering to ask people about things like that as well, is also a bit of a challenge." – *P6*

4.2.4 *Collaborative efforts:* The importance of professional collaboration.

In relation to the previous theme, *(Perceived barriers)*, questions were also asked about how clinician involvement with the ear tissue bank could be made easier for the participants. The answers that the participants gave led to the formation of the fourth theme, which involved perspectives on collaborative efforts. Professional collaboration refers to the cooperation between key stakeholders that contribute professional expertise in different areas.

When asked about their thoughts on the cultural considerations that need to be undertaken, some clinicians cautioned that they would be careful about their answers as they were Pākehā and could not answer in-depth on behalf of indigenous populations. Several participants suggested that consultation with Māori and Pasifika health advisors would be prudent for ensuring that tissue donation would be discussed in an appropriate manner for Māori and Pasifika patients. One participant added that it would also be important to keep in mind that individuals of Māori and Pasifika descent may not necessarily uphold traditional perspectives.

> "I think it will be good to talk with Pasifika or Māori health advisors like we have in the hospital just to see, because I come from a Pākehā culture and from a medical point of view. I don't know all the subtleties. They will probably be able to tell you better, or, you know, what they think, how this should be presented to those patients. Because, obviously, culturally, when people are not aware that you can donate your tissues, and they don't know what the temporal bone is, it will be good to talk to them. I think they will give you better answers than I would. But from that point of view." – *P1*

> "That [post-mortem tissue collection for Māori donors] would need to be carefully thought-out when going through the ethics committees. I think you usually have to meet up with local Māori people involved in research for most kind of research anyway, so you end up having to do that and get some advice around that." – *P7*

Involving and consulting other healthcare professionals were mentioned by several participants when discussing how certain conditions could be studied using the ear tissue bank as a resource. The addition of other important parties would maximise donor safety and benefits that can come out of human tissue study. Some participants mentioned collaboration with genetic counsellors as they can offer input on known genetic conditions that cause hearing and vestibular disorders. The involvement of neurologists would aid in the study of vestibular disorders. For example, neurologists can provide insight into central vestibular dysfunction, such as in the potential presentation of episodic vertigo after a stroke. Other healthcare professionals brought up included general practitioners (GPs) and audiologists to obtain a donor's medical information relevant to hearing or vestibular assessments.

> "Yeah, so the bigger thing is trying to tie everything together. Geneticists, neurologists, if there's neurology in particular. For balance disorders, it depends on the local centre whether that's ENT or whether it's neurology, or actually much of it's been driven by vestibular physiotherapists as well." – *P4*

> "The GP will have some stuff, but I think it'd be more useful - it depends on the patient - but it's likely to be more useful from an otologist, or an audiologist, or a CI programme. It's going to be much easier to sift through for researchers. I mean, retrospective clinical information is notoriously poor in answering all the questions you want, but it should be more concise and more accurate if it's collected from someone who's an ear specialist." – *P5*

In response to potential strategies that could address some of the logistical challenges mentioned in the previous theme, participants thought that collaboration with other tissue banks would ease some of the pressures that could pose difficulty in the running of an ear tissue bank. For example, working with another tissue bank that is already involved with harvesting post-mortem tissue to make the process of collection easier.

> "I think we'd be happy to just jump on board with brain research. If they get consent, there's no way that a patient would say, "Well, don't take the temporal bone, but you can have my brain."" – *P2*

> "I think if you did it as part of tissue donation for people who are donating for example, to the medical school, they've got the cadavers there, then that becomes very easy." – *P3*

5 Discussion

5.1 Summary of findings

This thesis was undertaken to identify key considerations for establishing an ear tissue bank in NZ, and to explore clinician attitudes and opinions towards such bank. In Part I, nine existing tissue banks in NZ were identified and it was found that all nine tissue banks were involved in research, even if it was not their primary purpose. Four were eligible to be analysed in detail based on the information provided using an approach similar to a scoping review methodology. It was found that cultural safety was a prominent aspect of the documentation and that it was conveyed in the practices of the tissue bank, particularly for disposal/return of tissue. This was part of the information communicated to potential donors and their family/whānau alongside provided motivations as to why their contributions matter.

In Part II, semi-structured interviews were designed and conducted with six otologists and one neurotologist on their attitudes and opinions towards an ear tissue bank in NZ. Reflexive thematic analysis revealed four themes: perceived roles, perceived benefits, perceived barriers, and collaborative efforts. Clinicians were supportive of the ear tissue bank and were interested in participating in research using it as a resource. Several practical barriers as well as some additional factors for consideration to maximise potential improvements such as including different people and collaboration were identified. While the focus of the interviews was initially on the post-mortem collection of the inner ear, one unexpected finding from the interviews was the interest and support of clinicians towards intraoperative tissue banking.

5.2 Limitations

It should be acknowledged that for the purpose of this study, only formal institutions involved in tissue banking within NZ were covered. Smaller research groups operating solely for specified research were not considered. There was no publicly available source that listed all existing tissue banks in NZ, so identification of the tissue banks was only viable through Google search. Additionally, although every effort was made to contact and follow up with the tissue banks currently operating in NZ, documentation was received from only four of the nine, resulting in a small number for Part I, hence the outcome should be interpreted with caution. The reason for lack of response from the remaining five tissue banks was not provided despite a number of attempts to contact them.

For Part II, the sample size of the study was relatively small with only seven participants, due to the limited number of otologists and neurotologists that are currently practising in NZ. A report released by the Medical Council of New Zealand indicated that in 2023, there were 132 otologists practising in NZ (The New Zealand Medical Workforce, 2023). As neurotologists only represent a small subset of otologists in NZ, exploration of their perspectives was limited to a select few individuals. However, only clinicians that were in NZ were of interest as the ear tissue bank will be for local operation. Furthermore, otologists and neurotologists experience constant pressure under heavy workloads all year round, with high demand for their services. Because of the smaller sample size and the small workforce, the data should be interpreted with caution. Nevertheless, all participants possessed similar opinions and outlooks.

There was a limitation with the methodology as a qualitative approach was used to analyse the interview data. This may have introduced some bias as all the research team members involved in the analysis and revision of the data came from a position of personal investment into a potential ear tissue bank, which may have influenced the interpretation of the data (Anderson, 2010). Because of the pilot nature of this work, future studies could embark on more systematic studies rather than studies of an explorative nature.

5.3 Clinician attitudes and opinions towards an ear tissue bank

The outcome from Part II identified a positive attitude from clinicians and interest in using the ear tissue bank as a resource, whether it be in conducting studies themselves, being notified for new findings on conditions or fields of interest, or both. This aligns with the international trend; a meeting organised by the American Academy of Otolaryngology-Head and Neck Surgery Foundation in 2005 discussed research opportunities amongst 158 registrants representing 33 otolaryngology departments and came to the consensus that otologist-involved research was crucial for the preservation and enhancement of otology as a subspeciality, especially in translating advances in basic science to medial application in the clinic (Grandis et al., 2006). Similarly, a survey conducted by Eyigör and Kara (2021) in Turkey on 119 otolaryngology residents found that almost all participants believed that research was important throughout their careers as it promoted evidence-based medical practice, provided life-long learning, and aided in supporting critical-thinking skills. What was found in the present study is that many of the tissue banks in NZ are involved in clinical research (see Chapter 4.1.1), which implicates that NZ tissue banks have factored clinician contribution into their functions. Clinical research requires a degree of clinician input, which emphasises the need for otologist and neurotologist contribution in an ear tissue bank, and in turn, the ear tissue bank would be able to offer the benefits discussed by Grandis et al. (2006) and Eyigör and Kara (2021), thus promoting an ongoing collaborative relationship between clinicians and researchers.

The interview participants also identified the main challenges posed for clinicians wishing to partake in research. These were: limited dedicated time for research participation, research funding, and geographical barriers. The most common barrier brought up by the participants was the question of time, where almost all clinicians remarked that they would find direct involvement in conducting research difficult to integrate into their demanding workloads. Participants also identified that funding was an issue that may limit their participation, as underfunded research projects could restrict their access to resources. These are international barriers not limited to NZ, as found by Fournier et al. (2019), who conducted a survey that recruited 928 otologists and residents during the 2017 International Federation of Otolaryngological Societies (IFOS) meeting. Fournier et al. (2019) found that although otologists and residents considered research to be a worthwhile experience, there were distinct factors that limited their participation. Limited dedicated time towards conducting research was the most considerable barrier, followed by limited financial support in the form of research

grants, and a perceived lack of research education, which could lead to uncertainty in undertaking data analysis. However, there was an additional factor that participants identified in the present study that had not been mentioned by Fournier et al. (2019) and other studies. Geographical barriers were identified as an additional constraint, as most tissue banks in NZ appear to only operate from a central location, with only the NZBS having multiple branches across the country. In Part I of the current study, it was found that some tissue banks such as the HAL and Otago Body Bequest Programme are only able to accept donations within a specific geographic range. Should this also be the case for the ear tissue bank, the pool of prospective donors may become further restricted. This is important to consider as it was evident that NZ clinicians were keen to involve themselves, but the capacity to create a viable process to allow this must first be established.

When asked about how participation in an ear tissue bank could be made easier for clinicians, many participants believed that working in a team alongside researchers who can provide laboratory support would greatly reduce the workload and time that a clinician would need to spend otherwise. This support could be in conducting basic science research or even having someone available to collect tissue samples from theatre. An opinion piece by Brauer et al. (2007) from the University of Queensland in conjunction with the Princess Alexandra Hospital and the Prince Charles Hospital suggested that another advantage in working with a research group is that it could help clinicians better understand research processes. In Part II, several participants noted that they felt more confident with conducting clinical research than basic science. Clinicians collect clinical data as part of their assessments, such as audiometric testing and diagnostic tests (CT and MRI scans), while basic scientists conduct lab-based analysis of post-mortem or intraoperative tissues using experimental laboratory techniques, such as molecular biology and histology, and the combination of both elucidates pathophysiology of inner ear disease (see Chapter 1.3.4). As demonstrated in Part I, most existing tissue banks in NZ possess clinical research as either their primary or secondary purpose (Table 1), suggesting cooperative relationships between clinicians and academics are a long-standing facet of a tissue bank's operations in the country. By implementing the same strategies and offering administrative or laboratory support via collaboration with academics within the tissue bank, this may bolster clinician confidence in research involvement. Another strategy that the interview participants mentioned included having third-party contacts on hand to give to prospective donors who may be interested in participating in the ear tissue bank. As found in Part I, NZ tissue banks typically provided contact details for a coordinator, whose role may

include discussing tissue donation with the donor and/or their family, providing support to the family during the donation process in the case of post-mortem donation, and organising the logistics around the collection phase.

5.4 The potential of intraoperative tissue banking

An unexpected finding in this study was the interest from clinicians for intraoperative tissue banking as an appealing opportunity, which had not been considered in the initial development of this project. The concept of intraoperative tissue banking was brought up in several of the conducted interviews, with most participants who had discussed it having had past experience in harvesting tissue during surgery (Chapter 4.2.2). To date, no study has been conducted exploring otologist/neurotologist attitudes and opinions on intraoperative tissue banking, highlighting the gap in knowledge about this topic. The participants believed that there were multiple advantages to intraoperative tissue banking. It is an opportunity to collect tissue in its disease state, as there were concerns about post-mortem temporal bones not reflecting the active disease process upon collection. Another reason was how harvesting fresh tissue may be easier than collecting post-mortem tissue due to the reduced wait time.

Because intraoperative tissue banking opens opportunities to collect from all parts of the ear (outer, middle, inner), several participants had alluded that they would have more interest in outer and middle ear research as it has higher relevancy to their current clinical practice. An outer ear condition that was specifically brought up by participants in Part II is exostoses. Otherwise known as Surfer's Ear, exostoses are benign growths of bone that extend into the EAC, with risk factors including exposure to cold water and wind (Simas et al., 2019). A study conducted by Simas et al. (2019) aimed to identify the lifetime prevalence of exostoses in NZ surfers by surveying 1376 individuals, of which approximately 15% were Māori. Simas et al. (2019) reported a prevalence of nearly 30%, suggesting that nearly 100,000 surfers could be affected by exostoses in NZ. If intraoperative sampling of exostoses was undertaken, it may lead to research that could allow us to better understand the interactions between the NZ environment and our local population. In NZ, the prevalence of middle ear disease is also high. For example, incidence rates of acute otitis media (infection of the middle ear) in children under five years of age have been reported to be 27.3% in NZ (Gribben et al., 2012). One participant reported anecdotally that they tended to see a high number of Māori patients for cholesteatoma, which is a benign cystic lesion that grows into the middle ear space from behind the TM as a result of damage or perforation of the TM that can cause CHL in the early stages, followed by vestibular issues and facial nerve palsy in later stages (Agrup et al., 2007; Kuo et al., 2015). Although its prevalence in NZ is unknown, the international annual incidence of acquired cholesteatoma has been estimated to range from 9 to 14 cases per 100,000 adults and from 3 to

15 cases per 100,000 children (Kuo et al., 2015; Yang et al., 2023). One example of how intraoperatively collected middle ear tissue has been used to study cholesteatoma is a study conducted by Yang et al. (2023), who excised cholesteatoma and normal, healthy middle ear mucosa samples from patients to perform autofluorescence testing, with the idea that an imaging system can be developed to enhance the visibility of cholesteatoma tissue and margins, which provides image-guided assistance during cholesteatoma removal surgery. As participant 5 puts it, "36% of our population here [North Island region] are Māori. Most of my cholesteatoma cases are Māori (…)". This suggests a need to understand how specific conditions could impact the indigenous population as there appears to be a higher prevalence of cholesteatoma in Māori groups, alongside investigating why that might be the case. However, for a similar study to be conducted on NZ's indigenous population, it must be done with the incorporation of cultural safety.

With regard to intraoperative tissue collection from the inner ear, two participants discussed how they had previously been involved in collecting perilymph from the cochlea, which is one of the fluids that fills the inner ear. Compared to other tissues (including outer and middle ear) that can be collected intraoperatively, biopsies or live tissue sampling are particularly difficult to obtain from the inner ear due to its position in the temporal bone (Figure 1) (Peter et al., 2022; van Dieken et al., 2022). Opportunities to sample from the inner ear is limited in NZ, as the interview participants identified that more uncommon procedures such as cochlear implantation and skull-base surgeries were the windows of opportunity to allow the collection of inner ear tissues when prompted about the feasibility of intraoperatively collecting inner ear tissue. Some participants suggested that tissue samples from vestibular schwannomas could be collected during surgical procedures to remove it. This has been done before, as demonstrated by a study by Nickl et al. (2024), who explored the research applications of intraoperatively collected samples of vestibular schwannomas from 16 patients. Nickl et al. (2024) found that slices taken from the tissue sample could be cultured for use as a 3D tumour slice model for pharmacological testing. As discussed in Chapter 1.3.3, this method of studying human tissue could address the gap between animal and human studies. Even with the different challenges imposed by intraoperative tissue banking, fresh samples from the inner ear could complement post-mortem tissue collection. Nadol and Burgess (1985) found that post-mortem sampling has an additional limitation in that there was rapid degradation of DNA, RNA, and proteins in samples drawn from cadavers, which may limit molecular analysis. Intraoperative tissue

sampling from the inner ear could add a different dimension to inner ear research, thereby potentially bridging the gap between post-mortem findings and fresh tissue research.

As one of the participants discussed, intraoperative tissue sampling should only be carried out if it did not risk patient outcome (see Chapter 4.3.2). In the past, there had been concerns that opening the inner ear would be a major risk of hearing loss. However, current practice in procedures such as hearing preservation cochlear implantation and stapedectomy have shown that manipulation of the inner ear with minimal or no loss of residual hearing is now possible (Pillsbury et al., 2018; Schmitt et al., 2017). Schmitt et al. (2017) demonstrated this by assessing the effects of intraoperative perilymph sampling on post-operative outcomes during cochlear implantation surgery and found no significant differences in the residual hearing and speech perception in patients who underwent both cochlear implantation surgery and perilymph sampling compared to patients who had the cochlear implantation surgery only. Additional risks that may be associated with intraoperative tissue banking would need to be considered, mostly as intraoperative tissue banking is performed on a living donor, compared to the post-mortem collection of the temporal bone. From the clinician's perspective, they would need to consider if the process of sampling would affect patient outcome. From the side of the ear tissue bank, intraoperative tissue banking would mean that next-of-kin consent would not need to be obtained, as the patient can consent for themselves, as opposed to post-mortem tissue donation (Table 5). Ultimately, as with donation of any tissue, the final decision on whether to collect or not rests on the patient. The need to consider these three viewpoints highlights that communication between the researcher, clinician, and patient to achieve appropriate ethics and informed consent is essential for intraoperative banking in NZ.

5.5 Points of consideration for ear tissue banking

Taking together Part I and Part II, the present study identified some key points for consideration towards establishing ear tissue banking in NZ.

Māori responsiveness and Tikanga Māori:

There is a clear need to have Māori stakeholders involved in co-designing the communication, operations, and purposes to donors, such as in the donor information package, shaping the process of consenting, and to include Tikanga Māori (e.g. poroporoaki and karakia) in tissue collection/handling. Indigenous and ethnic minority often experience inequities in healthcare, and this applies to Māori in NZ (Curtis et al., 2019), leading to further inequities such as less willingness to participate or share in decision-making, and less awareness of services or rights to which they may be entitled. Social and cultural values are even more intimately intertwined with one's decision-making when considering donating parts of one's own body such as for tissue banking. This study showed that NZ-based clinicians recognised the importance of cultural values and procedures involved in tissue banking, however, they did not feel that they could speak about Māori and Pasifika values with confidence, believing that Māori or Pasifika health officers would be more suited to play the role. The present study also showed that current practice from tissue banks in NZ tries to address this issue by having specifics on the release of clinical information, sending tissue overseas, and returning information about incidental findings all requiring separate consent from the donor (Chapter 4.1.3). Beaton et al. (2017) investigated Māori perspectives on tissue donation and found that Māori were willing to participate in tissue banking if it was communicated that it would address specific health issues of importance to Māori. Both the scope and specificity of the consent along with the return of research outcomes were important considerations for Māori, and consent for unspecified future use was acceptable with effective Māori representation within the governance structures of the tissue bank (Beaton et al., 2017). Requiring informed consent for every use of the donor's tissue actively involves the donor by informing them of what would happen to their tissue sample beyond the point of collection and gives them an opportunity to permit how they would like their tissue to be used.

Existing tissue banks had implemented Māori customs, namely a poroporoaki and karakia, during the disposal and/or return of donated tissue (Chapter 4.1.3). Implementations of a karakia and poroporoaki are critical considerations for an ear tissue bank, as post-mortem collection of the inner ear would call for addressing the donor's tapu (Chapter 1.3.3). By

including Tikanga Māori processes within the pathway to collect and use the human tissue sample, the tissue's imbued tapu would be retained. It should be noted that the use of a karakia was not limited to the disposal or return of tissue, but was also signified in the transfer of responsibility, appointing a kaitiaki (guardian) to make decisions about the use of the taonga such as in the distribution of the tissue sample for different research projects (Table 1; Hudson et al., 2016). This appointment of responsibility ensures that the spirit of the gift is maintained (Hudson et al., 2016). The observation of these customs expresses respect for the taonga bestowed, contributing to the maintenance of cultural safety, which is a vital aspect within healthcare. Our future ear tissue bank would need to abide by these values to maintain cultural safety and ensure that the opportunities and benefits of an ear tissue bank alongside subsequent otologic research are presented to Māori.

Identification of key players and collaborative teamwork across disciplines:

This explorative study identified many roles associated with the practical implementation of tissue banking that involve key stakeholders outside of otologists and neurotologists, including pathologists, non-clinical scientists, tissue bank coordinators, Māori coordinators or board members, and funeral directors. Our future ear tissue bank will need to identify and work with these players to ensure ethical, safe, effective, and sustainable operation.

Otologists and neurotologists: Otologists and neurotologists play an important role in providing thorough otologic and neurotologic documentation across a disease's progression throughout a patient's life. NZ-based clinicians described one of their perceived roles to be the supplier of clinically relevant information for specific tissue samples, provided the appropriate consent had been obtained. The Malaghan Institute and the ARB requested donor consent for the release of clinically relevant information to researchers using their tissue samples. This should be incorporated in an ear tissue bank as well, since records of auditory and vestibular function that can be correlated with laboratory findings would significantly enhance the value of the procured tissue sample (Nadol et al., 1996), and enable clinicians to collect such information.

Pathologists and non-clinical scientists: While the acquisition of post-mortem inner ear tissue can be carried out by otologists, trained pathologists can also carry out the procedures or offer input for proper removal techniques that would not mutilate the body or damage the sample, as well as how to store the sample (Nadol et al., 1996). Pathologists can identify the sample's nature and origin to determine what should be stored in the tissue bank, along with provide

information associated with a specific sample before it is processed and distributed to researchers (Bevilacqua et al., 2010). Pathologists may bridge the gap or have overlapping roles with clinicians and non-clinical scientists, (Suh et al., 2013). As the interview participants expressed a desire for help in undertaking non-clinical work, non-clinical scientists can fulfil this role, working in parallel with clinicians to provide basic science outcomes that clinicians may draw from.

Tissue bank coordinators: Tissue bank coordinators play diverse roles in the process of obtaining donor consent, collecting otologic tissue, and coordination of efforts across different institutions.

Māori coordinators or board members: Māori representation is needed to facilitate incorporation of appropriate cultural safety practices, as discussed earlier.

Funeral directors: The HAL and the Otago Body Bequest Programme outlined that funeral directors were one of the contacts to notify when wishing to donate the whole body. Funeral directors support the donation process by liaising with the tissue bank to arrange transportation of the body. Because temporal bone harvesting requires post-mortem dissection of the skull, communication with the funeral director is vital to identify any issues that may arise should the tissue donation process interfere with their services. For example, whether the extent of dissection would create additional difficulty in cosmetic restoration. Funeral directors would therefore need to make special considerations for post-mortem temporal bone removal, such as specific stitching patterns, specific glues, and additional packing material to prevent the cavity from collapsing after the temporal bone is removed. It is essential that the ear tissue bank and funeral homes maintain strong communication and cooperate with each other to uphold the donor and their family's wishes for donation, while at the same time considering the appearance of the body post-collection.

Nationwide institutional collaboration to address practical considerations:

A nationwide collaborative approach with local hospitals, research institutions, and other tissue banks should be explored when considering how to sustainably operate an ear tissue bank in collaboration with key players identified earlier throughout NZ. Most of the current NZ-based tissue banks, whether public or private, were affiliated with other institutions, commonly hospitals and universities (Table 1). Hospitals and universities may provide an infrastructure for operations. NZ-based clinicians also observed that the sustainability of a tissue bank may

be reliant on working with other institutions rather than remaining as a sole enterprise. Hospitals are likely to be the primary centres for donor identification, and they also hold the medical records of the donor which provides context and critical information for investigators collecting human tissues for research (Dhir et al., 2008; Li et al., 2021). Alongside local hospitals, affiliations with local universities could provide research facilities such as laboratories and data servers that may be otherwise difficult to maintain and fund independently (Patel et al., 2006). A partnership between a university and local hospitals would be an opportunity to form a collaborative relationship between clinicians and academics, in that there would be a pathway to transfer ear tissue samples from the hospital to appropriate research facilities. The collaborative approach will help address the time and resource constraints expressed by NZ-based clinicians that may restrict their involvement (Chapter 4.2.3). Collaborative efforts amongst local institutions are important for the harmonisation of policies and minimising disruption in the recruitment of potential donors, obtaining informed consent, providing information to donors and their families, and ensuring that standard procedures lead to the procurement of high-quality tissue samples (Brauer et al., 2004).

Until this study, there has been no formal summary of existing tissue banks and their practices in NZ. Furthermore, there is currently no formal association to create a collaborative network specific to tissue banks. Both parts of the present study identified that collaborating with national tissue banks would be a viable strategy of managing the logistics associated with running the ear tissue bank. These can include establishing donor registration procedures and creating partnerships for joint research projects. From the otology perspective, the Brain Bank could be a significant aid in the collection of otologic tissue as access to the inner ear requires post-mortem dissection of the skull, which the Brain Bank carries out to collect the brain (Table 1). Part I of this study identified that several NZ tissue banks already work together; for example, tissue banks that are closely affiliated with the University of Auckland such as the HAL, ARB, NZNEB, and Brain Bank, collectively organise human tissue disposal, which is coordinated by the HAL, and that this arrangement has been beneficial. For sustainable operation, an ear tissue bank in the current NZ environment would find it essential to build collaborative partnerships with tissue banks within the nation.

Considerations to include international collaboration:

Additional considerations should be made about the ethics and benefits of international collaboration. NZ has a comparatively small demographic to other countries such as the United States, which would mean that we would have a smaller number of potential tissue samples to study. Some rare diseases such as CANVAS represent an extremely small margin of the NZ population. It would be difficult to conduct the research with enough sample size from NZ alone, therefore working with international researchers would have the benefit of being part of larger studies. The most important caveat in working with overseas collaborators is the data sovereignty and appropriate consenting for human tissue to be sent overseas. Human tissues once sent overseas are no longer under NZ sovereignty and are under the jurisdiction and protocols of the recipient country. As a result, NZ ethics committees would have significantly reduced, if any, control over the tissue samples that have been sent offshore. This may carry risks such as the potential use of NZ tissue samples for commercial reasons, and the lack of security in ensuring that Māori tissue samples would be stored, used, and discarded with culturally appropriate protocols (Guidelines on the Use of Human Tissue for Future Unspecified Research Purposes, 2007). The Malaghan Institute and the ARB were identified to be involved in sending human tissue samples overseas, but they have achieved this by having separate consent from the donor to send their tissue samples overseas, with the donor information packages communicating that these samples were not under NZ sovereignty and would therefore be subjected to international protocols. In this way, the autonomy of the donor is upheld so long as the donor understands and accepts this before giving their consent. We hope that this may be employed in an ear tissue bank to contribute to otologic research both locally and internationally and overall help expand otology as a subspeciality. In addition, working collaboratively with overseas may also help with the resource issue we face in NZ with our small clinical population of otologists, neurotologists, and researchers. Merit also lies in collaborating with overseas clinicians and researchers to expand the scope of otologic research in NZ.

5.6 Future direction

This is the first study to have collated information from NZ tissue banks about their practices and explored NZ-based clinician perceptions towards an ear tissue bank. Future studies should build on the current study to next approach broader stakeholders, such as opinions on ear tissue donation from potential donors. However, this study did not cover patient opinions on ear tissue donation and family/whānau. Their opinions would add great value towards understanding how an ear tissue bank would impact the donor community. Further studies using qualitative or quantitative methods could be conducted to assess how Māori and Tauiwi patients and their family/whānau would perceive donation of otologic tissues to help validate what is currently being done, and to form the foundation of the future practice co-planned with Māori values.

Subsequent steps could also include investigating methods by which clinicians and researchers could work together to sustain otologic research in NZ. Operational practice guidelines will need to be established for the temporal bone collection, use and data sovereignty, along with appropriate ethics approval for both tissue banking and intended research projects. We hope that this, along with active work on corroborating appropriate practices in all facets of establishing and maintaining a tissue bank could lead to the establishment of an ear tissue bank in NZ that will help expand otology as a subspeciality. In the future, we hope that research from the ear tissue bank will lead to better understanding of hearing and vestibular disorders as well as make headway into the development of novel treatment strategies in NZ and globally.

6 Conclusion

This study is the first to collate the main existing tissue banks in NZ to form a cohesive picture of the current scope of tissue donation in the country. Overall, this study also identified several benefits and challenges specific to ear tissue banking in NZ. From the information extracted on cultural safety and donor information practices, we found that Māori values served as a prominent guideline to procedures conducted by the tissue bank. In general, clinicians had great interest in utilising the ear tissue bank as a resource even with the present challenges, and that this drive may be a precipitating factor towards furthering the progress of otologic research.

Throughout this entire research project, from investigating NZ tissue bank protocols to interviewing otologists and neurotologists, we have come to appreciate that an ear tissue bank does not only represent a facility to collect and study human tissue, but it is also representative of many other facets from empowering patients through the act of donation to raising awareness and expanding otology as a subspeciality. We hope that in time, this banding together of multiple communities across the country and those overseas will lead to a future of greater knowledge and novel treatment strategies.

Appendices

Appendix A: Auckland Health Research Ethics Committee Approval Letter

AUCKLAND HEALTH RESEARCH ETHICS COMMITTEE (AHREC)

16/10/2023

Dr Haruna Suzuki-Kerr

Physiology

Re: Application for Ethics Approval (Our Ref. AH25973): Approved

The Committee considered your application for ethics approval for the study entitled "**Attitude Towards Biomedical Research To Develop Novel Therapeutic Device for Hearing Loss**".

We are pleased to inform you that ethics approval has been granted.

The expiry date for this approval is **16/10/2026**.

Locality approval: Before starting your research, ensure that all the required locality approvals have been obtained. If one or more DHBs will be a locality, please contact their Research Office(s) to determine the locality approval requirements of the DHB(s).

Final report: In order that up-to-date records are maintained, you must notify the Committee once your project is completed and submit a final report.

Amendments to the approved project: Should you need to make any changes to the approved project, please follow the steps below:

- Send a request to the AHREC Administrators to unlock the application form (using the Correspondence tab in Ethics RM).
- Make all changes to the relevant sections of the application form and attach revised documents (as appropriate).
- Change the Application Type to "Amendment request" in Section L.
- Add a summary of the changes requested in the text box.
- Submit the amendment request (PI/Supervisors only to submit the form).

If the project changes significantly, you are required to submit a new application.

Funded projects: If you received funding for this project, please provide this approval letter to your local Faculty Research Project Coordinator (RPC) or Research Project Manager (RPM) so that the approval can be notified via a Service Request to the Research Operations Centre (ROC) for activation of the grant.

The Chair and the members of AHREC would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the AHREC Ethics Administrators at ahrec@auckland.ac.nz in the first instance.

Additional information:

- Do not forget to fill in the 'approval wording' on the PISs, CFs and/or advertisements, using the date of this approval and the reference number, before you use the documents or send them out to your participants.

All communications with the AHREC regarding this application should indicate this reference number: **AH25973**.

AHREC Administrators

Auckland Health Research Ethics Committee

Appendix B: Participant Information Sheet

Participant Information Sheet

Department of Physiology,
School of Medical Sciences
Blg 502 Room 401
30 Park Avenue, Grafton, 1023
Auckland, New Zealand
T+64 9 373 7599
W www.auckland.ac.nz
The University of Auckland
Private Bag 92019
Auckland 1142 New Zealand

PARTICIPANT INFORMATION SHEET

Project title:

Attitude Towards Biomedical Research To Develop Novel Therapeutic Device for Hearing Loss.

Research team:

Dr. Haruna Suzuki-Kerr: Principle investigator. Co-supervisor, Research fellow (University of Auckland, section of Physiology) and researcher for Eisdell Moore centre.

Professor Peter Thorne: Co-supervisor, Professor (University of Auckland, section of Audiology and Physiology), Director of Eisdell Moore centre and co-director of the Brain Research NZ.

Yu-Ting (Judy) Lai: Student researcher, enrolled in Master of Audiology student (University of Auckland, section of Audiology)

What is the aim of this study?

In Aotearoa, New Zealand, almost 800,000 people are affected by hearing loss.
Currently, the main treatments for hearing loss are prosthetic devices like hearing aids

and cochlear implants. This is because there are no FDA-approved drug-based therapies to prevent or slow down the progression of hearing loss. Our research group is developing a special device platform that can diagnose the cause of hearing loss and help deliver drugs for treating hearing loss. To move our project forward, we need more information about variability in the human ear and what is happening in human sensorineural hearing loss. To gain that information, we require the capability in New Zealand to work with human ear tissues for research. This study aims to evaluate how these specialists feel about using human ear tissues for research purposes in Aotearoa, New Zealand.

This research project is part of a Master's thesis and will be undertaken by Yu-Ting Judy Lai, a second year Master of Audiology student under the guidance of Dr. Haruna Suzuki-Kerr and Prof. Peter Thorne.

What does the study involve?

You are being contacted about this study because you are a clinical specialist working with patients who may have inner ear diseases. There is currently a very limited capacity in Aotearoa, New Zealand, to conduct research involving human inner ear tissues. We are interested in hearing your view towards establishing such capabilities in Aotearoa, New Zealand, how it may help your future practice and research as a clinician, and how it could lead to overall benefit for your patients.

Participation in this study is completely voluntary. You are free to decline to participate or to withdraw from the study at any point without experiencing any disadvantage.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep. If we perform an interview via Zoom or phone call, we will ask you to provide your signature via e-signature on a document and send it back to us via email, or we will send the printed consent form for you to sign and return.

As participants, you will be invited to an individual or whaanau semi-structured interview. The interview can take up to an hour. The interview will take place through a Zoom call, in person or over the phone. In-person interviews will be done on a public site that is convenient for your reach with your input, and you are welcome to bring a support person/whaanau member.

We will provide you with questions we would like to ask you prior to the interview. Some questions are about your thoughts towards research that has not happened yet in Aotearoa, New Zealand. You may experience and may cause discomfort by not knowing how to answer some of our questions. You do not have to answer all or any of the questions if you do not wish to.

What happens to the results and information?

The interview will be video recorded for the purpose of transcription, which will be conducted by the student researcher. Transcription will be done by the student researcher. Transcription will be done after the recording has been de-identified.

The student researcher and the research team listed will view the data for the purpose of analysis. Data will be de-identified and securely stored on the access-restricted data server at the University of Auckland.

As the participant, you will be given an opportunity to review and edit transcriptions of their audio recordings or remove/withdraw some information. We will provide you with the

transcript and ask you to review the information within two weeks after receipt of the transcript.

Benefits and risks

The outcome of this study will inform us about the views of the clinicians toward the future research capability we are trying to develop. The outcome of the research will also provide us with some feedback on how clinical experts view it. From a wider perspective, we believe this is an opportunity to drive the research with input from clinical experts towards driving research to improve for people affected by inner ear disorders.
We understand that some participants might feel uncomfortable not being sure how to answer some of our questions. To make sure they feel supported, we will let them know what questions we plan to ask beforehand. You do not have to answer all questions. We highly value whatever perspective you can share about your experience and thoughts. You are welcome to bring a support person/whaanau if you wish. Māori cultural support is available with our Māori collaborator listed below, so please let us know if you would like.

Who pays for the study?

Participation to this study will not cost you anything. As an expression of gratitude and to compensate for the time and effort you have taken to participate in this research, we are offering a token of gratuity of a $40 Countdown voucher for everyone who has engaged in the interview process. This is offered regardless of whether you withdraw from the interview after it has commenced or withdrawal data at a later stage. The voucher will be sent via post, if you could provide us your postal address. Research funding to cover the cost is supported by the School of Population Health and School of Medical Sciences, University of Auckland.

Rights of the participant(s)

Participation is voluntary:

- Participation to this study is completely voluntary and you will not be at disadvantage if you decide not to participate.

Withdrawal from participation and withdrawal of data:

- You have the right to withdraw from participation to this study at any time without any disadvantage.
- You have the right to withdraw without giving a reason anytime between providing the consent to the interview.
- We will provide you with the transcript of your interview data. You have two weeks following the receipt of transcripts to edit, remove or withdraw information. You have the right to request withdrawal of your data from the research up two weeks after you have been provided the transcript.

Confidentiality and anonymity:

- The interview will be conducted and transcribed by the student researcher and members of the research team.
- Any personal information (name, contact details etc.) will be removed and data will be de-identified by the student researcher during analysis.
- Transcribed data will be de-identified prior to analysis and will not be linked back to personal information.

- Information that are necessary for the analysis of data, such as your age group, your hospital location, your experience as clinician, gender and ethnicity will be retained.
- The information you provide during the interview will be analysed using qualitative research methodology.
- Analysis of data is done using secure research tool (NVivo) and stored on the secure server managed by the University of Auckland.

What will happen after the study

The consent form will be stored for six years. Research data will be stored in a secure network drive managed by the University of Auckland. Access to a secure network drive is restricted to the research team. Data will be stored for ten years and then deleted. The time for storage is to allow sufficient time for analysis and publication and sharing of data arising from this study.

Upon the completion of the study, you have the option to receive a report that contains the main findings from this study, either through mail or email. This will happen approximately 3- 6 months after the completion of this study. If you wish to receive the report, please indicate it in your consent form.

You can also request an electronic copy of the thesis from this research. This will become available after the thesis has been examined, corrected, and deposited into the University of Auckland library. Please contact the research supervisor if you wish to receive a copy of the thesis.
For further enquiries regarding the research, or if you have any concerns, please feel free to contact people below.

Student researcher:
Ms. Yu-Ting Judy Lai
Email: yu-ting.judy.lai@auckland.ac.nz

Supervisors:
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Academic Head:
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Ph: 09-373-7599
Address: Building 503-401L, 85 Park Road, GRAFTON, AUCKLAND1023

If you require Māori cultural support, talk to your whānau in the first instance. You may also contact our collaborator, Whaea Misty Edmonds, at the Iwi United Engaged by emailing misty@iue.net.nz, telephoning027-4890-804 or from their website https://www.iue.net.nz/contact/ to discuss any questions or complaints about the study.

For concerns of an ethical nature, you can contact the Chair of the Auckland Health Research Ethics Committee at: Email: ahrec@auckland.ac.nz
Phone: 09-373 7599 x 83711, Auckland Health Research Ethics Committee, The University of Auckland, Private Bag 92019, Auckland 1142.

Approved by the Auckland Health Research Ethics Committee on 16/October/2023 for three years. Reference number [AHREC25973].

Appendix C: Participant Consent Form

MEDICAL AND
HEALTH SCIENCES

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W www.auckland.ac.nz
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Auckland 1142 New Zealand

CONSENT FORM

THIS FORM WILL BE HELD FOR A PERIOD OF 6 YEARS

Project title:

Attitude Towards Biomedical Research To Develop Novel Therapeutic Device for Hearing Loss.

Research team:

Dr. Haruna Suzuki-Kerr: Principle investigator. Co-supervisor, Research fellow (University of Auckland, section of Physiology) and researcher for Eisdell Moore centre.

Professor Peter Thorne: Co-supervisor, Professor (University of Auckland, section of Audiology and Physiology), Director of Eisdell Moore centre and co-director of the Brain Research NZ.

Yu-Ting (Judy) Lai: Student researcher, Master of Audiology student (University of Auckland, section of Audiology)

I have read, or have had read to me in my first language, the Participant Information Sheet. I have been given sufficient time to consider whether or not to participate in this study and to ask questions, and was offered support from whānau/family or a friend to help me understand what the study involves. I am satisfied with the answers given to me, I understand the nature of the research and why I have been invited to participate.

I agree to take part in this research.

- I understand my participation is voluntary.
- I understand that the time needed is 1 hour.
- I understand I am free to withdraw any data traceable to me up to for two weeks following the receipt of transcripts without giving a reason.
- I understand that my participation in this study is confidential and that no material which could identify me personally will be used in any reports on this study.
- I agree / do not agree to be recorded (please circle one).
- Even if I agree to be recorded, I understand that I can ask for the recording to be stopped at any time without giving a reason.
- I wish / do not wish to have my recordings returned to me (please circle one).
- I understand that the researcher themselves or a third party who has signed a confidentiality agreement will transcribe the tapes.
- I understand that I have opportunity for two weeks following the receipt of transcripts to review the transcript and withdraw any content.
- I understand that data will be kept for 10 years and separate from the Consent Forms, after which they will be destroyed.
- I agree / do not agree that information collected about me up to the point when I withdraw may continue to be processed if I decide to withdraw from the study (please circle one).
- I consent to the research staff collecting and processing my information.
- I wish / do not wish to receive the summary of findings (please circle one).
  Email/postal address: _____
- I know who to contact if I have any questions about the study in general.

Name _____

Signature _____ Date _____

Approved by the Auckland Health Research Ethics Committee on 16/October/2023 for three years. Reference number [AHREC25973].

Appendix D: Question Guide

AHREC25973_part3_questions

1. What do you know of an ear tissue bank?

2. Would you be interested in involving yourself in research if this resource was made available?

3. What kind of research would you be interested in if this resource was made available?

4. How do you think we should approach discussing tissue donation with prospective donors?

5. What information do you think would be important for the patient and patient's family to know before donating their tissue?

6. Would you be willing to provide resources to clients about tissue donation? E.g. Placing brochures in the clinic space?

7. An ear bank can also be used to educate and train medical students or provide justification to the government for funding, such as for cochlear implants. Would this be of interest to you?

8. What do you think are the major barriers in the implementation of an ear tissue bank if it was to work in collaboration with you?

9. Would you be willing to provide medical history/rehabilitation notes for research that makes use of the tissue bank?

10. What are your thoughts around the cultural safety and considerations that would need to be undertaken?

11. Do you think having the ear bank as a resource could empower patients? For example, by having a better understanding of the pathology behind a hereditary hearing loss.

12. If you were to involve yourself in the ear bank, how could we make this easier for you?

Appendix E: Example of Code Assignment

> "I think we'd be happy to just jump on board with brain research. If they get consent, there's no way that a patient would say, "Well, don't take the temporal bone, but you can have my brain." So I think it's a matter of just, "Would you be interested? Yes, you are." And I know that the Hearing House, for example, already asks whether families will be happy to take part in research. Not specific, nothing specific, not post-mortem. But potentially, you can just add that on. But I think it's not a simple question of asking the patients, and you know, you need to be looking at a young person, you're asking them to donate 30, 40, 50, 60 years down the line, things change. But it's getting the initial consent, then getting back to the families." – *P2*

Code list:

- Conducting research
- Donor support and guidance
- Time before receiving tissue

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