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● *Original Contribution*

LISTENING TO THE COCHLEA WITH HIGH-FREQUENCY ULTRASOUND

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Abstract—We have developed a high-frequency pulsed-wave Doppler ultrasound probe as a promising minimally-invasive technique for measuring intracochlear mechanics without damaging the cochlea. Using a custom high-frequency ultrasound system, we have measured dynamic motion of intracochlear structures by recording the pulsed-wave Doppler signal resulting from the vibration of the basilar and round window membranes. A 45 MHz needle-mounted Doppler probe was fabricated and placed against the round window membranes of eight different fresh human temporal bones. Pulsed-wave ultrasonic Doppler measurements were performed on the basilar membrane and round window membrane during the application of pure tones to the external ear canal. Doppler vibrational information for acoustic input frequencies ranging from 100–2000 Hz was collected and normalized to the sound pressure in the ear canal. The middle ear resonance, located at approximately 1000 Hz, could be characterized from the membrane velocities, which agreed well with literature values. The maximum normalized mean velocity of the round window and the basilar membrane were 180 μm/s/Pa and 27 μm/s/Pa at 800 Hz. The mean phase difference between the membrane displacements and the applied ear canal sound pressure showed a flat response almost up to 500 Hz where it began to accumulate. This is the first study that reports the application of high frequency pulsed wave Doppler ultrasound for measuring the vibration of basilar membrane through the round window. Since it is not required to open or damage the cochlea, this technique might be applicable for investigating cochlear dynamics, *in vivo*. (E-mail: z.torbatian@dal.ca)

Key Words: **High-frequency ultrasound, Pulsed-wave Doppler, Basilar membrane, Round window membrane, Mechanics of the cochlea.**

INTRODUCTION

At present, there are no effective diagnostic techniques available in clinical settings for imaging inside the cochlea in living patients due to the cochlea's small size and sensitivity to damage if invasive procedures are attempted. Noninvasive imaging using magnetic resonance imaging (MRI) and computed tomography (CT) does not have the spatial or temporal resolution to properly visualize the anatomy or dynamics of the inner ear. The availability of an *in vivo* probe capable of making anatomical and functional measurements inside the cochlea has the potential to revolutionize diagnostics in otolaryngology.

Across its width, the cochlea is separated into three ducts: the scala vestibuli, scala media and scala tympani. The scala media and scala tympani are separated by the basilar membrane (BM), upon which sit the inner and outer hair cells that are responsible for, respectively, auditory transduction (Moller 2006) and somatic motility (Lagarde et al. 2008). The scala media is separated from the scala vestibuli by Reissner's membrane. When the eardrum and ossicles of the middle ear vibrate, the stapes footplate is pushed into the scala vestibuli, and the resulting pressure difference across the BM causes it to vibrate, setting up a travelling wave. Wave motion on the BM is dispersive and the BM exhibits a varying stiffness along its length so that each point along the basilar membrane has a local resonant frequency for which the vibration amplitude is higher. The response of the BM rapidly decays to zero at points past the resonance. The point directly below the round window membrane has a resonance of approximately 18 kHz. Basilar membrane motion drives inner hair cell deflections, opening ion channels in the hair cells and releasing

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neurotransmitters. Because vibrations are carried by slow-moving waves on the basilar and tympanic membranes and because of the stiffnesses and inertia of the ossicles, significant phase shifts can accumulate between the ear canal sound pressure and the motion of various parts of the auditory system at acoustic frequencies.

Many forms of sensorineural hearing loss are associated with changes in basilar membrane motion in response to sound. Examples include the loss of cochlear nonlinear amplification/compression when outer hair cells are lost (common in many disorders) or changes to BM vibration characteristics (*i.e.*, Meniere's Disease [Kim et al. 1994]). Therefore, direct measurement of basilar membrane vibration could be an important diagnostic tool for assessing and diagnosing hearing disorders (Robles and Ruggero 2001).

Intra-cochlear vibration measurements have been made in live animals and human cadaveric temporal bones using stroboscopic optical microscopy, laser Doppler interferometry, the Mossbauer technique and Doppler optical coherence tomography (DOCT) (Robles and Ruggero 2001; Dong and Olson 2009; Lukashkin et al. 2005; Kossl and Russell 1995; Khanna 1991; Ren et al. 2002; Khanna and Leonard 1981; Nuttall et al. 1991; Ren 2002; Oversteert et al. 2002; Cooper 1999; Stenfelt et al. 2003; Johnstone and Boyle 1967; Rhode 1971; Gundersen et al. 1987; Wang and Nuttall 2010; Choudhury et al. 2008; Hung and Freeman 2006; Chen et al. 2011; Gao et al. 2011). None of these techniques have so far allowed *in vivo* monitoring of the human BM due to their invasiveness, as any fenestration made into the cochlea carries an unacceptable risk of hearing and vestibular loss. Since both optical and ultrasonic techniques are unable to see through the thick, boney otic capsule surrounding the cochlea, noninvasive measurement with these modalities must be performed through the round window membrane (RWM), the only accessible soft-tissue window into the cochlea. The RWM is an approximately 3 mm diameter membrane at the basal turn of the cochlea that acts to relieve pressure in the scala tympani when stapes footplate moves (Moller 2006). From this access point, only the basal turn of basilar membrane can be monitored. The passive tuning of the cochlea/BM, which is governed by the membrane stiffness is such that the local basilar membrane resonance directly under the RWM with the highest stiffness, is around 18 kHz (Stakhouskaya et al. 2007). The basilar membrane has a nonlinear compressive amplification response about its local resonance frequency that is essential to expand the hearing dynamic range up to 120 dB (Robles and Ruggero 2001).

Since the 1980s, heterodyne laser Doppler vibrometry (LDV) has been the preferred method of measuring BM motion in animal models (Robles and Ruggero 2001). Standard LDV does not provide axial sectioning and, therefore, all reflected light contributes to the LDV signal. When measuring the BM through the RWM, the strength of reflected light from the RWM is much stronger than that from the BM, so that a hole is usually made in the cochlea to measure BM motions. A few groups have developed optical sectioning methods for LDV, notably confocal microscopy (Dong and Olson 2009) and self-mixing laser interferometry combined with a high numerical aperture lens (Lukashkin et al. 2005; Kossl and Russell 1995; Khanna 1991) that have allowed BM velocity measurements through the RWM in animal models. More recently, optical coherence tomography, which combines optical sectioning with high lateral and axial resolution, has been used for cochlear visualization and vibrometry in animal studies (Wang and Nuttall 2010; Choudhury et al. 2008; Hung and Freeman 2006; Chen et al. 2011; Gao et al. 2011). However, these measurements have been done through an opening in the cochlea to access the basilar membrane. Although OCT offers very high resolution, its depth of penetration through scattering tissue is very low. To our knowledge, OCT has not yet been used to measure the BM through the RWM in human temporal bones.

All optical techniques suffer from some common problems. The index of refraction of the BM is nearly identical to that of water, resulting in a very weak reflection of 0.0039–0.033% (Khanna et al. 1989) that must be detected in the presence of stronger reflections from the RWM and the cochlear wall. The human round window differs from that of animals typically used for hearing research, by being much thicker than in most animals (Roeser et al. 2007) and often covered by optically dense soft tissue "folds" that cause large optical reflection and scattering losses. Finally, any optical technique requires a direct line of sight between a microscope, the RWM and the BM, which is much harder to achieve under surgical conditions in humans than in small animals as the bony round window niche often covers the RWM (Goycoolea 2001).

The goal of proposed study was to develop an effective technique for measuring the vibration of basilar membrane without damaging the cochlea with the potential for development into a clinical tool. To this end, we have developed a new approach, high-frequency pulsed-wave ultrasound Doppler vibrometry for studying the intra-cochlear dynamics through the round window. This technique has the advantages that pulsed ultrasound reflectometry automatically gives axial sectioning, suffers only a small loss at the soft tissue folds and RWM and generates a large acoustic reflection (on the order of 30% [Brown et al. 2009]) from the BM through the round window. Furthermore, the cochlear ultrasound