Monitoring the Effects of Cholesteatoma Treatment Utilizing Auditory Brainstem Response Testing

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Introduction

Background: Cholesteatomas are cyst-like growths in the middle ear that result in hearing loss, ear drainage, facial nerve paralysis, and meningitis. Oncolytic virotherapy is a treatment that is emerging with potential of shrinking cholesteatoma (Lipschitz, et al., 2020). This treatment is currently being tested in a gerbil model of cholesteatoma. Monitoring hearing sensitivity throughout the treatment requires the use of a technique called auditory brainstem response (ABR).

Objective: This study piloted bone conduction ABR as a method to bypass the middle ear and assess the inner ear directly in a gerbil model of cholesteatoma.

Computed Tomography of Gerbil Model

Figure 1. The Computed Tomography (CT) images to the right show the ear anatomy of gerbils. The anatomy of the gerbil ear is similar to that of the human ear. In the top image of Fig.1, a control gerbil with no cholesteatoma is shown. In the bottom image of Fig.1, the highlighted image shows the right (red) and left (blue) anatomy of a gerbil whose middle ears were affected by cholesteatoma growth. The CT imaging is utilized throughout the oncolytic virotherapy regimen to monitor the size of the cholesteatomas.

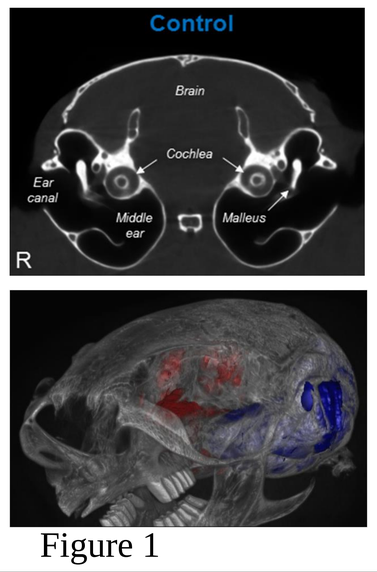
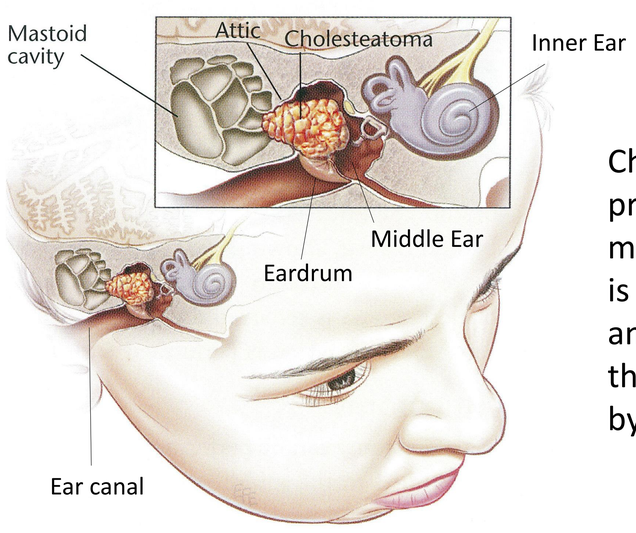
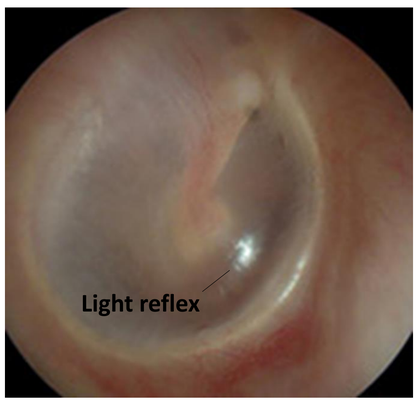


Figure 1

Formation of Cholesteatoma



Cholesteatomas primarily form in the middle ear space which is behind the eardrum and near the base of the brain (Illustration by Clancy, 2018).



Normal Eardrum
A normal eardrum is translucent and exhibits a light reflex in the bottom right quadrant.

Ear Infection
An ear infection is characterized by fluid behind the ear drum, signs of inflammation (e.g., redness) and the absence of the light reflex.

Retracted Eardrum
Unresolved ear infections can lead to retraction of the eardrum into the middle ear space.

Attic Cholesteatoma
Contact between eardrum retraction pockets and the middle ear wall leads to formation of a cyst-like cholesteatoma that grows into the middle ear attic, mastoid cavity, and potentially into the base of the skull.

Otoscopy images credited to Katherine Kavanagh, MD

Auditory Brainstem Response

Auditory Brainstem Response (ABR) is utilized clinically to objectively assess auditory nerve function. As part of the ABR protocol, electrodes are placed on the scalp and short bursts of sound are presented to stimulate the auditory nerve and brainstem. The responses (i.e., waveforms) that are generated are graphed as shown below in Fig. 2. Due to cholesteatoma blocking the middle ear, an alternative sound stimulation mode called bone conduction must be utilized to assess inner ear function.

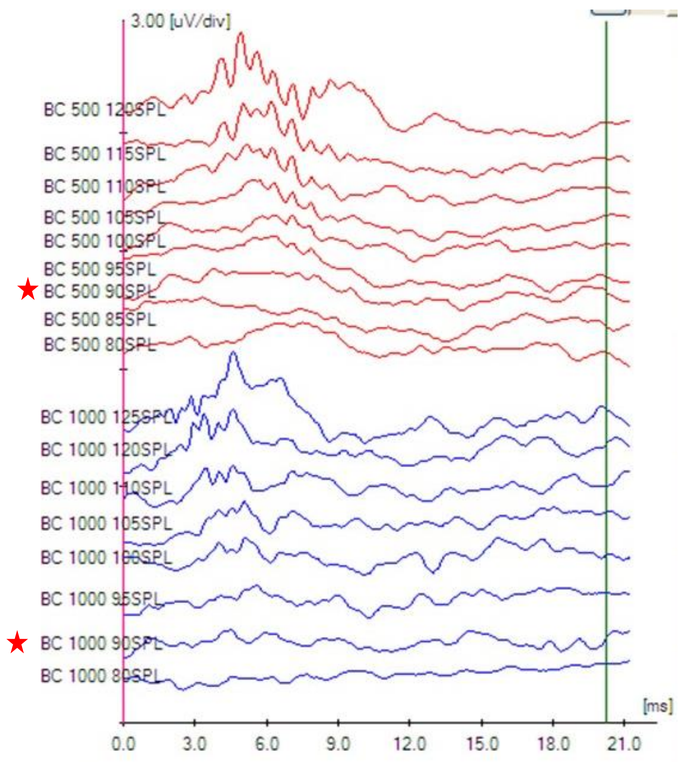


Figure 2

Figure 2. Representative bone-conduction ABR waveforms recorded from one gerbil (red and blue lines) are graphed with time (milliseconds; ms) on the x-axis and response magnitude on the y-axis in microvolts (uV). Each waveform is labeled with the sound frequency (Hertz; Hz) and sound intensity (decibels in peak sound pressure level; dB pSPL). Higher sound pressure levels are shown at the top of each group of waveforms while lower sound pressure levels are at the bottom of each group of waveforms. Inferring hearing sensitivity from the ABR involves identifying the lowest dB SPL level at which the multi-peak waveform is observed (*see red stars).

Comparison of Hearing Sensitivity via Bone-Conduction

Gerbils were chosen as the animal model for this study due to the similarity between human and gerbil middle ear anatomy as well as hearing sensitivity. Table 1 illustrates the similar bone-conduction hearing sensitivity between normal-hearing human ears and a normal-hearing gerbil for 500, 1000, and 2000 Hz sound stimuli.

Table I. Comparative hearing sensitivity for bone-conduction stimulation for 500, 1000, & 2000 Hz.

Frequency (Hz)	Human #1 (dB pSPL)	Human #2 (dB pSPL)	Gerbil (dB pSPL)
500	90	85	90
1000	75	75	90
2000	80	70	85
3000	90	70	TBD
4000	90	65	TBD
6000	105	80	TBD
8000	110	90	TBD

Conclusion

These preliminary data suggest that bone-conduction auditory brainstem response testing may be a valid technique to assess hearing sensitivity at the level of the inner ear in a gerbil model of cholesteatoma.

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