Spectroscopic middle ear disease diagnosis

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Technology Overview:

Spectroscopic disease diagnosis has been successfully applied to many organ systems. Recently, LBRC initiated a new research direction, middle ear disease diagnosis. For easy clinical acceptance, multi-wavelength fluorescence otoscope was developed based on otoscope. Raman spectroscopy was used to investigate the chemical composition of otitis medium and cholesteatoma. Label-free real-time spectroscopy could provide surgical margin information.

Biomedical application potential:

The most common middle ear disease is otitis media, which refers to a continuum of inflammatory conditions of the middle ear, including acute infection. It is the second most common illness diagnosed in U.S. children, with over 8 million cases each year. Over 20 million antibiotic prescriptions per year in the U.S. are for otitis media cases [1,2]. However, successful diagnosis of otitis media is estimated at only 51% for U.S. pediatricians, with over-diagnosis occurring 26% of the time [2,3]. The resulting excess antibiotic therapy has made otitis media a primary factor in increased antibiotic resistance [4]. The endogenous NIR Raman spectrum from the middle ear may provide sufficient information for diagnosis. The clinical instrument will collect Raman spectra from human patients' otitis media. This project will address fundamental questions such as molecular makeup of otitis media, and biochemical changes during infection.

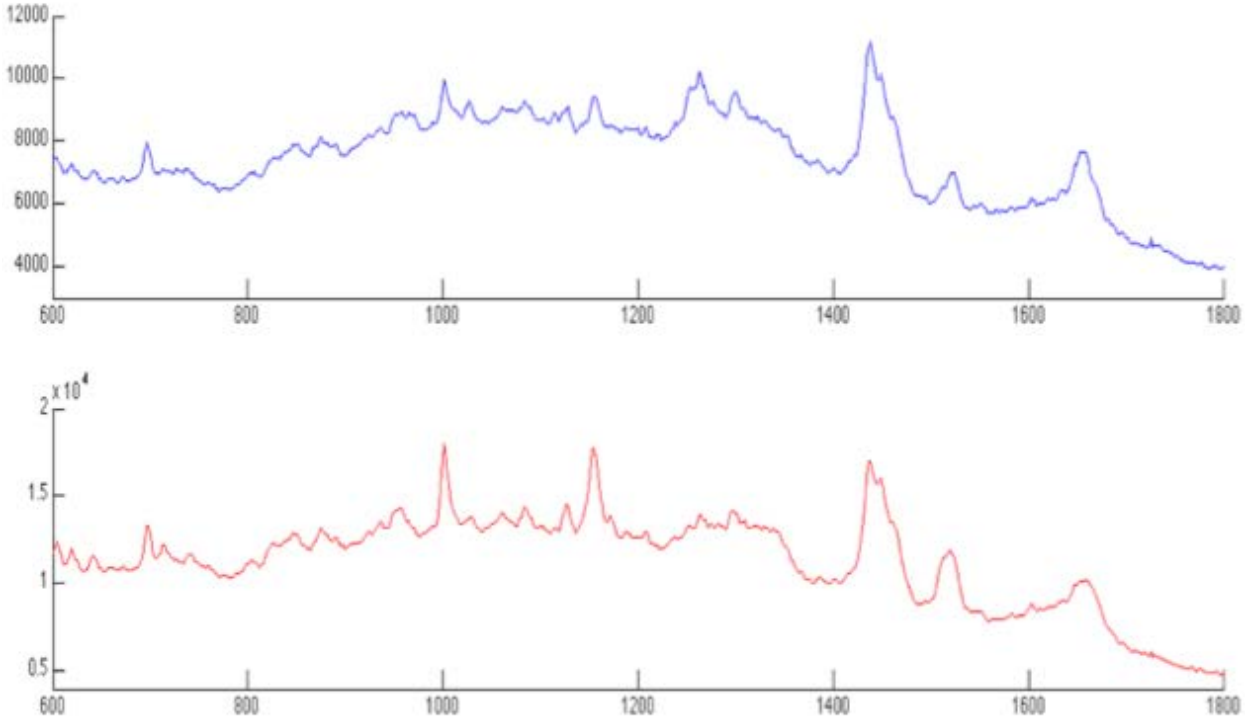
Despite its widespread prevalence, middle ear pathology, especially the development of proliferative lesions, remains largely unexplored and poorly understood [5,6]. Diagnostic evaluation is still predicated upon a high index of clinical suspicion on otoscopic examination of gross morphologic features. We report the first technique that has the potential to non-invasively identify two key lesions, namely cholesteatoma and myringosclerosis, by providing real-time information of differentially expressed molecules. In addition to revealing signatures consistent with the known pathobiology of these lesions, our observations provide the first evidence of the presence of carbonate- and silicate-substitutions in the calcium phosphate

plaques found in myringosclerosis. Collectively, these results demonstrate the potential of Raman spectroscopy to not only provide new understanding of the etiology of these conditions by defining objective molecular markers but also aid in margin assessment to improve surgical outcome.

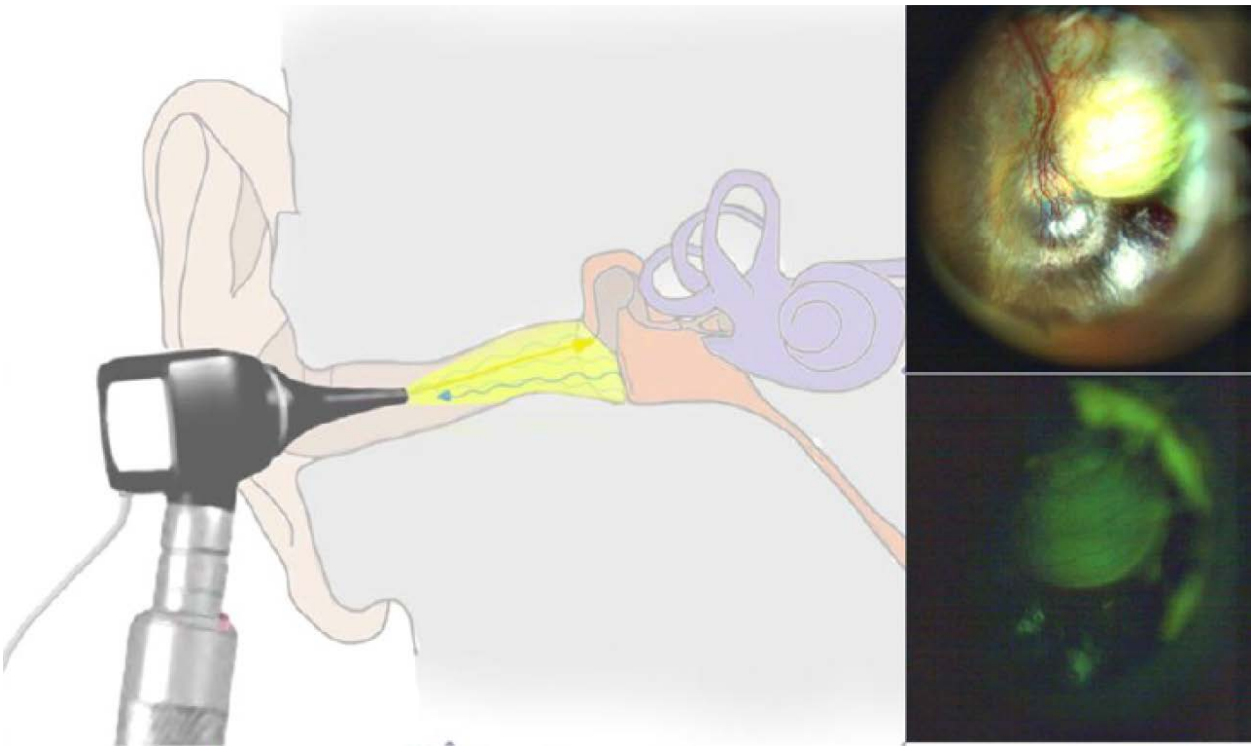
Ongoing project:

Raman spectroscopic investigation of otitis medium

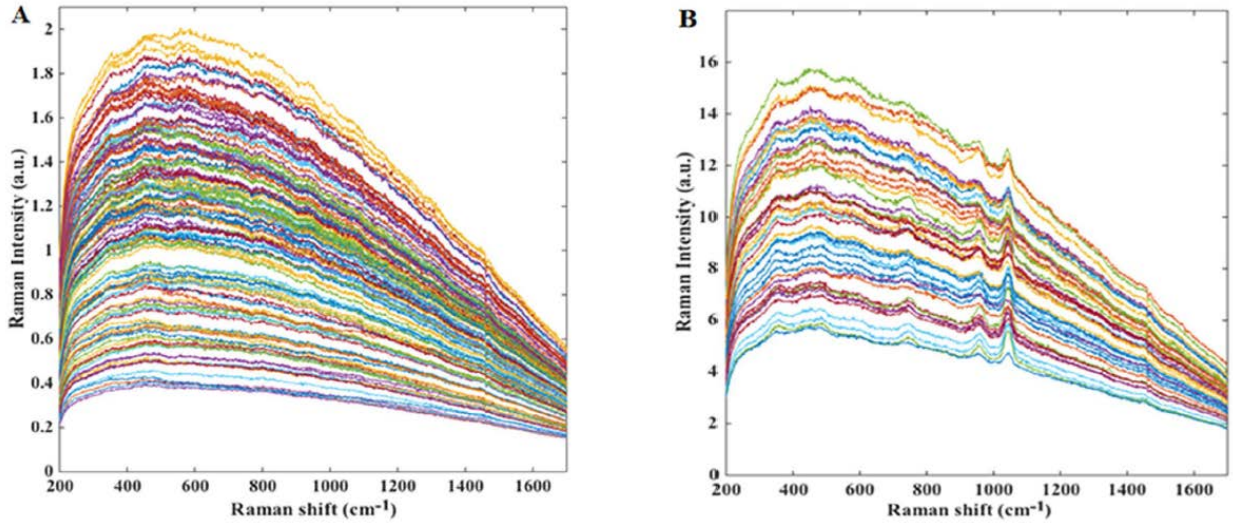
Developing surgical guidance tool for cholesteatoma



Representative Raman Spectra of serous (top) and mucoid (bottom) fluids.



Fluorescence differentiates cholesteatoma on otoscopy exam



(A) cholesteatoma lesion sites, (B) myringosclerosis sites that exhibit mineralization on histological evaluation

Background Publications

1. Soni, A. STATISTICAL BRIEF #434: The Five Most Costly Children's Conditions, 2011: Estimates for U.S. Civilian Noninstitutionalized Children, Ages 0-17. (Agency for Healthcare Research and Quality, 2014).
2. Long, S., Pickering, L. & Prober, C. Principles and practice of pediatric infectious diseases. (Churchill Livingstone, 2003).
3. Pichichero, M. & Poole, M. Assessing Diagnostic Accuracy and Tympanocentesis Skills in the Management of Otitis Media. Arch. Pediatr. Adolesc. Med. 155, 1137–1142 (2001).
4. Steinbach, W. J., Sectish, T. C., Benjamin, D. K., Chang, K. W. & Messner, A. H. Pediatric Residents' Clinical Diagnostic Accuracy of Otitis Media. Pediatrics 109, 993–998 (2002).
5. Pelton, S. I. & Leibovitz, E. Recent advances in otitis media. Pediatr. Infect. Dis. J. 28, S133-137 (2009).
6. Gupta, A. & Agarwal, S. R. A study of prevalence of cholesteatoma in complications of suppurative otitis media. Indian J. Otolaryngol. Head Neck Surg. 50, 140–146 (1998).

Center Publication

1. Valdez TA, Pandey R, Spegazzini N, Longo K, Roehm C, Dasari RR, Barman I. Multiwavelength fluorescence otoscope for video-rate chemical imaging of middle ear pathology. Anal Chem. 2014; 86(20):10454-60.
2. Valdez TA, Spegazzini N, Pandey R, Longo K, Grindle C, Peterson D, Barman I. Multi-color reflectance imaging of middle ear pathology in vivo. Anal Bioanal Chem. 2015; 407(12):3277-83.
3. Pandey R, Paidi SK, Kang JW, Spegazzini N, Dasari RR, Valdez TA, Barman I. Discerning the differential molecular pathology of proliferative middle ear lesions using Raman spectroscopy. Sci Rep. 2015; 5:13305.