**SP6 Middle ear diseases:** Tulio A. Valdez, M.D., MSc, University of Connecticut, Connecticut Children's Medical Center

**Funding Source and Period:** SPARK Technology Commercialization Fund (Indefinite), Connecticut Innovations Bioscience Pipeline (1 year), (Valdez, PI), **Associated With**: TRD1.1, TRD3.1

**Significance:** Dr. Valdez is an associate professor of Otolaryngology at the University of Connecticut School of Medicine. Since 1999, when he was a visiting scientist at LBRC, he has investigated different spectroscopic modalities for the diagnosis of head and neck conditions ranging from cancer to infectious processes. Two specific publications show his early work with spectroscopy for detection of premalignant conditions [1,2]. Most recently he has incorporated spectroscopic imaging and computer vision to address diagnosis and surveillance of middle ear conditions. As a service collaborator with LBRC, he adapted LBRC technologies to implement a multi-wavelength otoscope using reflectance and fluorescence images and various computer vision algorithms to achieve identification and segmentation of middle ear and tympanic membrane structures [3–5].

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 [6]. Over 20 million antibiotic prescriptions per year in the U.S. are for otitis media cases [8,11]. However, successful diagnosis of otitis media is estimated at only 51% for U.S. pediatricians, with over-diagnosis occurring 26% of the time [12-14]. The resulting excess antibiotic therapy has made otitis media a primary factor in increased antibiotic resistance [10,15-17]. On the other hand, failure to diagnose otitis media can lead to long-term hearing impairment, a delay in language acquisition, or formation of destructive skin growths in the middle ear (cholesteatoma) which require surgical excision [18-21].

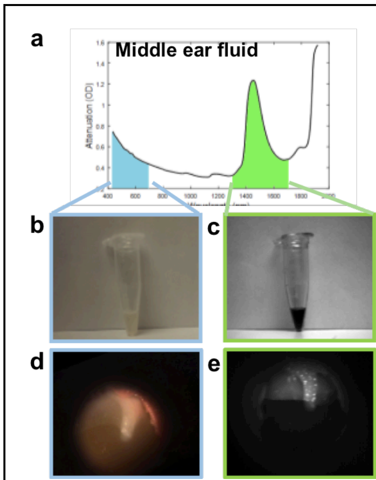


Fig. 1: The attenuation of light through a sample of middle ear fluid shows strong absorption in the SWIR (a). The absorption causes the fluid to appear black in a SWIR image (c), whereas it is translucent with visible imaging or by eye (b).A model filled with fluid shows the improvement in contrast that results using SWIR otoscopy (e) compared with visible otoscopy (d).

**Approach:** Shortwave infrared (SWIR, 1-2 micrometer) from TRD1.1 and NIR Raman spectroscopy from TRD3.1 will be used for better diagnosis of middle ear disease. Adapting LBRC technology, Dr. Valdez implement an otoscope sensitive to SWIR wavelengths of light for middle ear disease diagnostics. With a first prototype, Dr. Valdez carried out a proof of concept IRB-approved study and showed that in healthy adult human ears, deeper tissue penetration of SWIR light enables improved visualization of middle ear structures through the tympanic membrane compared to conventional visible light otoscopy [6]. In addition, Dr. Valdez has investigated the potential for detection of middle ear fluid, which has significant implications for diagnosing otitis media. Middle ear fluid shows strong light absorption between 1400-1550 nm, enabling straightforward fluid detection in a model using the SWIR otoscope (Fig. 1). As an alternative approach, the endogenous NIR Raman spectrum from the middle ear may provide sufficient information for diagnosis. To address this need, LBRC transferred an already-established multimodal spectroscopy clinical instrument to Connecticut. This instrument will collect Raman spectra from human patients' otitis media. (Fig. 2) This service project will address fundamental questions such as molecular make up of otitis media, and biochemical changes during infection.

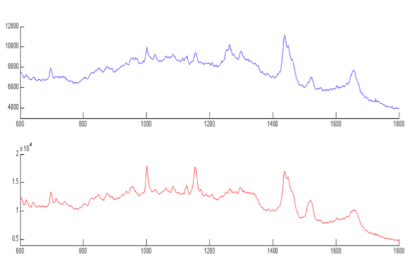

Fig. 2. Representative Raman Spectra of serous (top) and mucoid (bottom) fluids.

Two protocols-one for the SWIR otoscope, and one for the Raman instrument- have been approved by the Connecticut Children's Medical Center and Massachusetts Institute of Technology Institutional Review Boards and we are currently enrolling patients. Our goal is to establish the sensitivity and specificity of the SWIR otoscope and NIR Raman spectroscopy for detection of middle ear fluid and to compare to the current diagnostic standard, pneumatic otoscopy.

**Center Offering:** LBRC has provided instrumentation and technological knowledge for characterizing middle ear tissue and fluid to obtain a fundamental understanding of their spectroscopic properties. With LBRC advices, Dr. Valdez is developing a SWIR otoscope and develop clinical data analysis algorithm. LBRC also installed a multimodal spectroscopy (MMS) instrument in Dr. Valdez's laboratory. Since 2014 December, collected spectroscopy data has been analyzed using existing algorithms in LBRC guided by LBRC researchers.

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