Middle ear ossicles mineralization in the osteogenesis imperfecta murine model

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Background: Osteogenesis Imperfecta (OI) is a group of inherited genetic disorders characterized by collagen defects that affect roughly 25,000 people annually. People with OI have a greater risk of bone fractures, impaired bone growth, and other body impairments such as hearing loss. The hearing loss typically worsens with age, and can be conductive, sensorineural or mixed. To date, there is no treatment to cure or ameliorate hearing loss in OI. To identify potential mechanisms for the hearing loss in conductive hearing loss, this study determines differences in concentrations of biologically essential elements in the middle ear ossicles of a mouse model for OI the osteogenesis imperfecta murine (*oim/oim*) model of OI, and their wild type (WT) mice using X-ray fluorescence microscopy (XFM). Elements included calcium, phosphorus, sulfur, zinc, copper, and iron.

Methods: The middle ear ossicles (malleus, incus, and stapes) originated from 14 weeks old adult mice. After euthanizing the animals, we harvested both temporal bones containing the middle ears and cochleae. After the bullae were removed, they were instantly frozen in liquid nitrogen and subsequently transferred into a -80 degrees Celsius freezer. For imaging, we mounted the three middle ear ossicles on Ultralene® XRF Pre-Cut Window Film, 4 μm. At beamline 8-BM at the Advanced Photon Source (APS), the samples were scanned at 10 keV photon energy. The samples were scanned initially at a step size of 20 μm for a low-resolution overview. From those initial scans, we selected regions of interest to be scanned at 25 μm spatial resolution. With MAPS, software available through Argonne National Laboratories, the XFM scans were analyzed, and the concentration for each element of interest was determined.

Results: The results of our study show that the *oim/oim* mouse had higher iron and calcium and lower phosphorus concentrations than WT mice. The other elements investigated were similar in concentration in the *oim/oim* and wild-type mice.

Conclusions: The increased calcium and iron content in bone may contribute to hearing loss in people with OI by increasing the bone tissue stiffness and therefore affecting the biomechanics of the hearing. Treatment of the hearing loss in OI would need to reduce their bone porosity but also aim to decrease the bone tissue mineralization by regulating the calcium uptake.