

## Smaller and Deformed Ossicles in *Oim/Oim* Mouse Model of Osteogenesis Imperfecta

Category: Middle and External Ear

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### Background

Progressive hearing loss affects 70% of the people with Osteogenesis Imperfecta (OI), a genetic disorder generating mutations in collagen type I of connective tissues. Hearing loss in OI has early onset and is either conductive, sensorineural, or mixed. There is no cure for OI, and treatments for its hearing loss rely on conventional treatments for the general population. To date it is still unknown the mechanisms of hearing loss in OI. In this study, we examine the morphometric analysis of middle ear ossicles in the *oim/oim* mouse model of OI, suffering from hearing loss.

### Methods

The ears of 14-week-old *oim* (n = 6) and wild type (WT) (n = 6) mice were imaged using synchrotron microtomography. Volumetric-morphometric analysis was conducted for the auditory ossicles. For each ossicle we determined volume, thickness and intracortical bone porosity density. Additional parameters calculated for the malleus included head volume (MhV), body volume (MbV), lamina's enclosed area, and length of the manubrium (Mm). For the incus, we measured functional length (IfL), and area of the disk. For the stapes we assessed total height (Sh), footplate-height (SfH), crura and head height (SchH), footplate's 3D surface area (SfA), and smallest and biggest head-heights. The lever arm ratio and an estimation of the area convergence ratio were also calculated. Finally, presence of fractures in the ossicles were quantified.

### Results

The *oim* mice ossicles are significantly ( $p < 0.005$ ) smaller (total volume of the ossicles WT =  $0.18 \pm 0.005 \text{ mm}^3$ , *oim* =  $0.17 \pm 0.012 \text{ mm}^3$ ) than WT counterparts, with a smaller malleus (malleus volume WT =  $0.13 \pm 0.003 \text{ mm}^3$ , *oim* =  $0.11 \pm 0.009 \text{ mm}^3$ ) with a smaller head (MhV WT =  $0.018 \pm 0.0009 \text{ mm}^3$ , *oim* =  $0.015 \pm 0.0009 \text{ mm}^3$ ) and body volume (MbV WT =  $0.11 \pm 0.003 \text{ mm}^3$ , *oim* =  $0.098 \pm 0.008 \text{ mm}^3$ ), smaller footplate-height (SfH WT =  $0.148 \pm 0.004 \text{ mm}$ , *oim* =  $0.133 \pm 0.007 \text{ mm}$ ) and 3D surface area (SfA WT =  $0.176 \pm 0.011 \text{ mm}^2$ , *oim* =  $0.163 \pm 0.005 \text{ mm}^2$ ), and larger SchH:SfH ratio (WT =  $3.34 \pm 0.08$ , *oim* =  $3.72 \pm 0.27$ ). Besides, half of the *oim* incudes were fractured at the facet for the malleus. WT ossicles had no fractures.

### Conclusions

Our results report for the first time on a volumetric-morphometric analysis of the ossicles in OI and indicate a series of morphological differences between the auditory ossicles of WT and *oim* mice that may affect the biomechanics of the middle ear in *oim* mice further contributing to their hearing loss. This knowledge will aid in the understanding of hearing loss in OI and in clinical care of the same.