Altered otic capsule morphology of the *oim* mouse model of osteogenesis imperfecta

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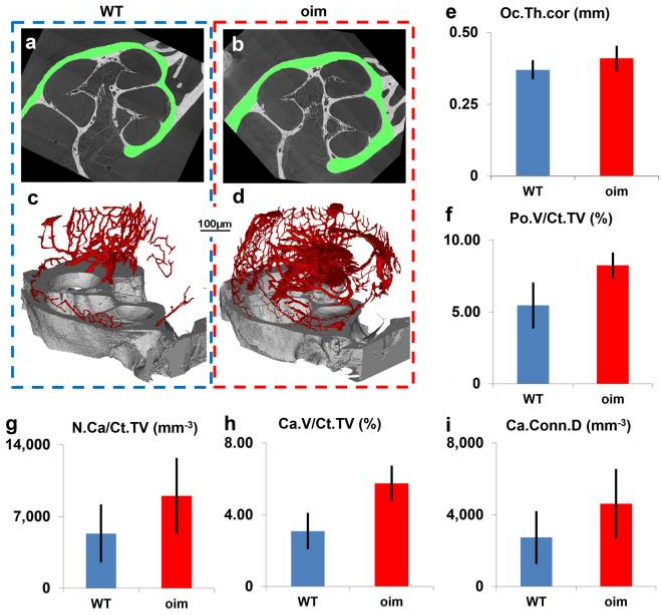
Osteogenesis imperfecta (OI) is a genetic disorder caused by mutations in the encoding of type I collagen. Skeletal fragility, deformities, and functional disabilities, including hearing loss, are typical symptoms of OI. Hearing loss in OI is progressive and in 11-31% of cases occurs in children below 10 years old [1-3]. There is no cure or treatment for OI hearing loss, and very little is known about the properties of the OI inner ear or the mechanisms leading to hearing loss. In this study we investigate the morphology of the otic capsule and the cochlear spiral duct in the *oim* mouse model of OI, which also suffers hearing loss [4]. High-resolution images of 8 week old *oim* and WT inner ears (N=6/group) were acquired using synchrotron microtomography at sub-micron resolution. Morphological indexes were evaluated on the coronal and sagittal planes at their intersection with the cochlear modiolus and on two transverse planes crossing the middle and apical turn of the cochlea. Otic capsule thickness was measured on the aforementioned planes and otic capsule length was measured in the coronal plane. At the tissue level, cortical bone porosity, canals and lacunae were measured [5]. The total volume of the duct and of the helicotrema, and the external spiral length were quantified on 3D renderings of the fluid scalae. Duct and helicotrema surface area and perimeter were measured on the coronal and sagittal planes, turn pitches on the coronal plane, and maximum axes on the transverse planes. The morphology of the *oim* inner ear is mainly preserved in the 8 week old mouse, but increased coronal cortical thickness and intracortical canal density, volume and connectivity affect the *oim* otic capsule (Figure 1). These results portray a state of compromised bone quality in the *oim* otic capsule which may contribute to hearing loss by making the bone tissue more susceptible to microfractures and/or by varying the hydrodynamics inside the cochlear duct. Further studies are also needed to examine the growth and development of *oim* ear bones in relation to osteoprotegerin distribution and hearing loss.

1 Pedersen, Scand Audiol, 13:2, 1984
2 Pillion et al., Genet Res Int, 2011
3 Ting et al., Clin Otolaryngol, 37:3, 2012
4 Chen et al., Clin Genet, 71:5, 2007
5 Miller et al., ORS Annual Meeting, 2017

Figure 1. (**a**, **b**) Synchrotron x-ray microtomographic slice of WT and *oim* representative otic capsule showing the difference in coronal cortical thickness. The region of interest considered for the calculation of the mean Oc.Th.cor is reported in green. (**c**, **d**) Surface render of the canal network (red) respectively within the WT and *oim* cochlear otic capsule (gray). (**e, i**) Bar graphs comparing WT and *oim* otic capsule morphological indexes (mean ± SD; $p<0.05$): thickness in the coronal plane (Oc.Th.cor), porosity (Po.V/Ct.TV), canal number density (N.Ca/Ct.TV), canal volume density (Ca.V/Ct.TV), and canal connectivity density (Ca.Conn.D).



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