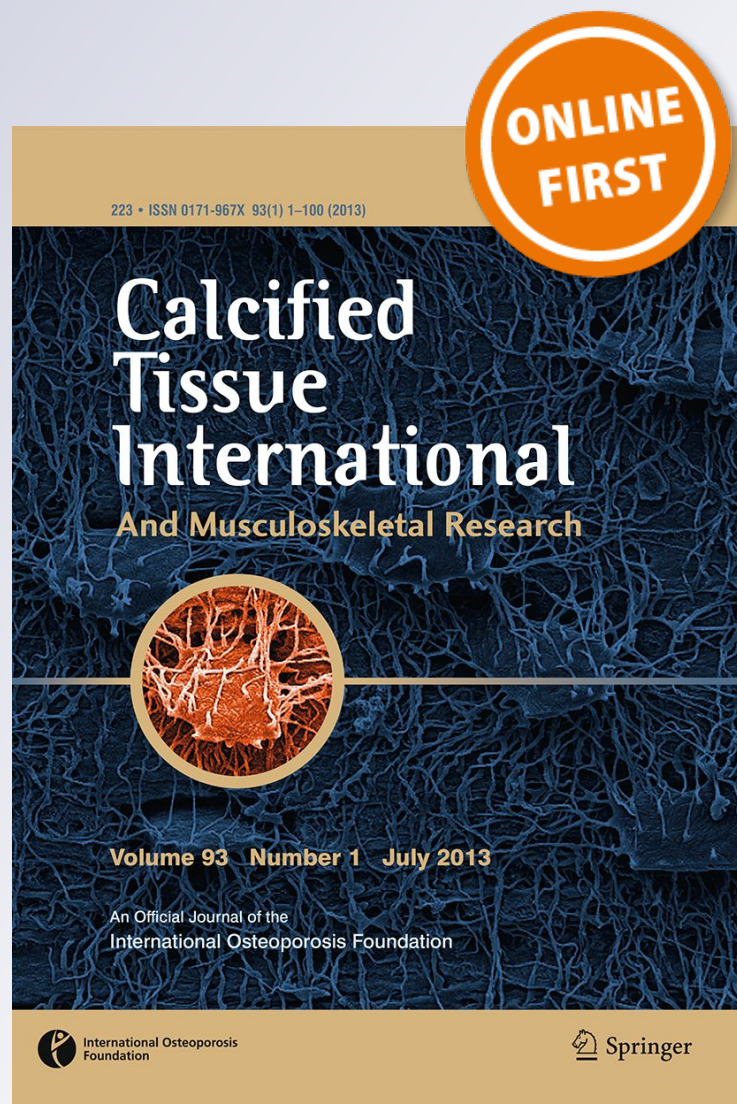


# Abstracts of the ECTS Congress 2018

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## Abstracts of the ECTS Congress 2018

### ECTS 2018

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Bone biopsy analysis revealed, in patients, fibrous tissue, increase of osteoclasts, vessels and osteocyte lacunae. In patient sera high levels of ICTP, VEGF-A, IL-6 and Sclerostin were observed. Patient's osteoclast precursors showed a twofold increased ability to differentiate into osteoclasts, with more nuclei per cell. About 75% of GSD osteoclasts displayed a more motile phenotype. A twofold increased ability to resorb bone was observed in GSD osteoclast cultures. Transcriptome analysis revealed an enrichment of PI3 kinase, EGF receptor and beta-arrestin pathways. To investigate the involvement of systemic factors in GSD, Healthy Donor (HD)-PBMC were treated with GSD sera and showed increased osteoclastogenesis compared to control sera-treated cells (Osteoclast number/field, HD:  $17.24 \pm 2.38$ ; GSD:  $26.27 \pm 2.43$ .  $p < 0.02$ ). Bone Marrow MSC isolated from a patient revealed a defect of osteogenic differentiation, as shown by reduced ALP activity and expression compared to HD-MSC. Affected osteoblasts displayed reduced ability to form mineralized nodules. Transcriptome analysis revealed in GSD osteoblasts a modulation of pathways involved in bone morphogenesis and ossification and an increase of osteoclastogenic potential. Moreover, mature HD-osteoblasts treated with GSD sera showed decreased expression of *ALP* and *COL1a2* and increased *RANKL/OPG* ratio.

These results suggest that in GSD the skeletal alterations are related to bone cell autonomous defects and systemic factors, opening the way for the identification of new therapeutic approaches.

**Keywords:** Gorham-Stout; Osteoclast; BM-MSC

### Oral Posters 3—Basic

#### P042

3D bone microstructure of the mandibular condyle correlates with masseter muscle mass in adult mice

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**Background:** Masticatory muscle activity is required for temporomandibular joint homeostasis. As we previously demonstrated in adult mice, the masseter muscle atrophy induced by botulinum toxin type A (BoNTA) produces bone loss in the mandibular condyle when assessed with bone histomorphometry after 14 days. However, covariation between skeletal muscle features and bone quality in the masticatory apparatus is still poorly understood. Therefore, we hypothesized that the 3D bone microstructure of the mandibular condyle correlates with the masseter muscle mass.

**Methods:** As approved by the ethics committee, adult BALB/c mice were randomly assigned to a *control group* without intervention ( $n = 10$ ), and a *BoNTA group* ( $n = 8$ ) that received one BoNTA injection in the right masseter and saline solution in the left masseter (intra-individual control). After 14 days, all mice were euthanized, and masseter muscles and mandibles were obtained. The mandibles were scanned with high-resolution X-ray Microtomography and bone morphometric parameters from each mandibular condyle were quantified.

**Results:** BoNTA intervention significantly reduced masseter mass ( $-43\%$ ;  $p < 0.001$ ). In the mandibular condyle of the BoNTA-injected side, bone volume fraction ( $-11.3\%$ ;  $p < 0.001$ ), and trabecular thickness ( $-21.4\%$ ;  $p < 0.001$ ) were significantly reduced. In contrast, trabecular separation was significantly increased ( $7.7\%$ ;  $p < 0.05$ ) if compared with both sides of the *control group*. Interestingly, there was a positive correlation between masseter mass and either bone volume fraction ( $r = 0.742$ ;  $p < 0.001$ ) or trabecular thickness ( $r = 0.711$ ;  $p < 0.001$ ), and a negative correlation with trabecular separation ( $r = -0.496$ ;  $p = 0.001$ ).

**Conclusions:** These results support the hypothesis that the 3D bone microstructure is significantly correlated with masseter muscle mass in our model. Moreover, bone quality of the mouse mandibular condyle markedly reduces after masseter muscle atrophy induced by BoNTA intervention.

**Keywords:** mandibular condyle, masseter muscle, X-ray Microtomography

#### P044

High-resolution 3D X-ray imaging of the osteocyte lacunar network in the *Chihuahua* zebrafish model of osteogenesis imperfecta to assess cellular mechanisms associated with bone fragility

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The *Chihuahua* (*Chi+*) zebrafish has been proposed as model system for the study of classical dominant osteogenesis imperfecta (OI). Previous assessment of bone quality in *Chi+* showed a multi-scale phenotype similar to human OI, i.e. skeletal deformities and fractures associated with altered collagen composition and mineralization, leading to impaired local mechanical properties. A better understanding of the cellular mechanisms behind increased bone fragility in *Chi+* is needed to identify potential drug targets and to improve treatment strategies of OI. This study aims to quantify the osteocyte-lacunar network as indicator for bone turnover in *Chi+* and wild type (WT) zebrafish utilizing 3D X-ray microscopy (XRM).

Vertebrae of adult WT and *Chi+* zebrafish were dissected and scanned with high-resolution 3D XRM at 0.75  $\mu\text{m}$  resolution. Osteocyte-lacunar properties were quantified in the distal, central and proximal regions of each vertebral body and pooled for quantification. 3D parameters included lacunar porosity (Lc.V/BV), lacunar number density (N.Lc/TV), and mean lacunar volume (Lc.V/N.Lc).

Data gained from one vertebral body per group indicate a less pronounced osteocyte-lacunar network and altered lacunar morphology in *Chi+* vs. WT. The resulting 3D analysis of the XRM data showed lower lacunar porosity ( $0.12 \pm 0.05$  vs.  $0.35 \pm 0.09\%$ ), lower lacunar number density ( $20,337 \pm 4223$  voids/ $\text{mm}^3$  vs.  $51,651 \pm 12,521$  voids/ $\text{mm}^3$ ), and lower lacunar volume ( $40 \pm 12$  vs.  $73 \pm 98$   $\mu\text{m}^3$ ) for *Chi+* vs. WT ( $p \leq 0.05$  for all parameters).

Quantification of 3D osteocyte-lacunar properties in *Chi+* supports our previous 2D histological findings indicating a bone formation defect due to altered osteoblast activity, and weakened capability for bone tissue maintenance and repair due to an osteocyte network with reduced mechanosensitivity. High-resolution 3D imaging of the osteocyte-lacunar characteristics in *Chi+* provides new insights into bone quality in zebrafish and moreover bares the potential to elucidate the pathology of human OI, fostering the design of new therapies.

**Keywords:** Osteogenesis imperfecta, zebrafish, osteocyte network, X-ray microscopy



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