

## MEETING REPORT

# Advances in bone imaging/diagnostics: ECTS 2012

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Trabecular bone score (TBS) is a relatively new technique to extract textural information from regular dual-energy X-ray absorptiometry (DXA) images. On the basis of regular DXA images, a special software analyzes the spatial variability of the DXA signal within the vertebrae. The TBS is a measure that correlates with trabecular microstructure and as such may provide information on bone fragility independent of bone mineral density (BMD). One oral presentation and four posters added to the body of evidence that this techniques provide information on bone fragility independent of areal BMD. Lamy *et al.*<sup>1</sup> from Lausanne, Switzerland, presented data showing independent cross-sectional associations of BMD and TBS with osteoporotic fractures. Similar independent associations were reported by Vasic *et al.*<sup>2</sup> from Belgrad, Serbia, for vertebral grade 2/3 and major osteoporotic fractures, and for vertebral grade 2/3 and clinical osteoporotic fractures by Krieg *et al.*<sup>3</sup> from Lausanne. Folkestad *et al.*<sup>4</sup> from Odense, Denmark, reported lower TBS values in patients with osteogenesis imperfect type I, but the decrease was not as pronounced as for areal BMD of the spine. The pooled relative risk of TBS for major osteoporotic fractures as based on studies involving 32 000 women was reported to be 1.79 (1.37–2.37; Hans *et al.*<sup>5</sup> from Lausanne). All of the above studies were published with co-authorship of researchers associated with the company Medimaps producing the software.

Two of the studies on TBS also included fracture assessment by vertebral fracture analysis (VFA) using DXA, along with another study specifically dedicated to VFA. In this latter study, Diacinti *et al.*<sup>6</sup> from Rome reported excellent agreement of VFA and radiography with an almost perfect  $\kappa$ -scope of 0.984. These studies document that VFA has become a viable low-dose alternative to radiography for the assessment of vertebral fracture status.

Digital X-ray radiogrammetry (DXR) is a technique that originated in Scandinavia, and most of the studies have been performed here. Consequently, it was not surprising to see new data presented in Stockholm. DXR is based on measurements of cortical thickness of the metacarpals, converted into BMD units. Arvidsson *et al.*<sup>7</sup> presented Swedish reference data obtained on 1440 women aged 20–79 years, which showed age-associated increases in BMD up to age 43 and a fairly

linear decline thereafter. On the basis of register data on hip fracture incidence in Sweden, Wilczek *et al.*<sup>8</sup> reported that among 5420 women and 2842 men measured with DXR, both men and women with hip fracture had significantly lower BMD at the time of measurement (that is, before the fracture) compared with non-fractured controls, after adjustment for age. These are encouraging results documenting the value of diagnostic techniques that are exclusively based on cortical bone.

Klaushofer and colleagues<sup>9</sup> from Vienna have a long track record in the analysis of mineral in bone in different disease and treatment settings. This year they presented data (Pemmer *et al.*<sup>9</sup>) on the distribution of trace elements Zn, Pb and Sr in cortical and trabecular bone. Data were obtained by synchrotron radiation based micro X-ray fluorescence (XRF) and quantitative backscatter electron imaging (qBEI). XRF permits to obtain elemental maps with  $10 \times 15 \mu\text{m}^2$  pixel size. The qBEI images were used to associate these maps with histologically identified regions of interest. Zn and Pb concentrations were highest in the cement lines. Unlike Zn, Sr and Pb, concentrations are high in areas high in Ca concentration, and the authors postulate that this is an indication that Sr and Pb are replacing deposited Ca after the end of the mineralization process. Using qBEI Roschger *et al.*<sup>10</sup> also presented data showing very high mineralization in a case of sclerosing osteosarcoma with a peak tissue mineral density (bone mineralization density distribution) of 27–28% weight compared with a normal peak value of 22.5%. The mechanism how such a high level of mineralization is achieved remains to be investigated. Scanning acoustic microscopy is a powerful method to image bone micro and ultrastructure down to a lateral resolution of about  $1 \mu\text{m}$ . Compared with nanoindentation, this offers higher resolution and non-destructiveness. Determination of elasticity can be achieved by combination with a densitometric method. Fix *et al.*<sup>11</sup> from Potsdam, in collaboration with the Vienna group, showed results for a combination of scanning acoustic microscopy (SAM) with qBEI, pointing to partial volume effects if SAM of insufficient spatial resolution is used.

The mineral crystal orientation within the lamellar structure of bone can be visualized by polarized light microscopy, but

small and wide angle X-ray scattering methods obtained from synchrotron light sources provide additional information about size and orientation of collagen and crystals. The methods were presented by Beraudi *et al.*<sup>12</sup> for a team of Italian and Swiss Researchers.

BoneTag and OsteoSense are two fluorescent markers used in molecular imaging of skeletal tissue. The ability to attach to mineralized surfaces makes them also suitable for quantitative *in vitro* assays of mineralization in cell cultures instead of more time consuming Alizarin red S staining as reported by Moester *et al.*<sup>13</sup> from Leiden.

The power of fluorescent-labeling approaches was demonstrated in a lecture by Rowe<sup>14</sup> from Farmington, Connecticut, USA. Using the application example of fracture repair, he showed<sup>14</sup> how multiplexed green fluorescent protein reporter mice, which yield color signals specific to subsequent differentiation stages, can be created. The impact of donor cells on callus formation fracture healing can be differentiated by color coding host versus donor cells. Rowe also presented<sup>15</sup> how traditional dynamic histomorphometry analyses could be facilitated and performed faster by semi-automated image processing of multiple fluorescent labels characterizing fluorescent mineralization and endogenous enzymatic signals.

Longitudinal micro-CT are established to determine changes in bone microstructure. Schulte *et al.*<sup>16</sup> from Zürich, Switzerland, showed that by careful co-registration of micro-CT images, the distribution of resorption spaces and areas of bone formation can be depicted. As the method is totally non-destructive, this also enables to temporally disentangle the sequence of resorption and formation at a given location, something that so far can only be calculated indirectly based on dynamic histomorphometric modeling. Schulte *et al.*<sup>16</sup> applied the method in a model of loading of tail vertebrae of mice. She showed differences between bisphosphonate and parathyroid hormone in their ability to activate formation at previously quiescent bone sites.

## Conflict of Interest

C-C Glüer is a consultant for Medi-Maps.

## References

- Lamy O, Krieg MA, Metzger M, Aubry-Rozier B, Stoll D, Hans D. Bone mineral density (BMD), micro-architecture estimation (TBS) and vertebral fracture assessment (VFA) extracted from a single DXA device in combination with clinical risk factors improve significantly the identification of women at high risk of fracture. *Bone* 2012;**50** (Suppl 1):S29.
- Vasic J, Gojkovica F, Eleza J, Culafic Vojinovic V, Hans D. Spine micro-architecture estimation (TBS) discriminates major osteoporotic fracture from controls equally well than site matched BMD and independently: The Eastern Europe TBS Study. *Bone* 2012;**50** (Suppl 1):S148.
- Krieg MA, Lamy O, Aubry-Rozier B, Stoll D, Krieg C, Berthoud M *et al.* The micro-architecture estimation by TBS discriminate women with and without osteoporotic fracture independently of age, BMI and BMD: The osteo-mobile vaud cohort study. *Bone* 2012;**50** (Suppl 1):S150.
- Folkstad L, Hald JD, Hansen S, Gram J, Langdahl BL, Abrahamson B *et al.* Reduced trabecular bone score in patients with OI type 1 compared with healthy controls. *Bone* 2012;**50** (Suppl 1):S170.
- Hans D, Winzenrieth R, Aubry-Rozier B, Stoll D, Lamy O, Krieg MA. Can the trabecular bone score (TBS) be considered as a major clinical risk factor (CRF) of osteoporotic fractures? A meta-like analysis. *Bone* 2012;**50** (Suppl 1):S151.
- Diacinti D, Del Fiaccio R, Pisani D, Diacinti II D, Todde F, Romagnoli E *et al.* Performance of vertebral fracture assessment (vfa) using the ge idxa (dual-energy x-ray absorptiometry) scanner compared to conventional radiography. *Bone* 2012;**50** (Suppl 1):S147.
- Arvidsson B, Bodin L, Rask E, Schwarcz E, Möller M. Reference data for bone mineral density in swedish women, using digital x-ray radiometry. *Bone* 2012;**50** (Suppl 1):S146–S147.
- Wilczek M, Kälvesten J, Algulin J, Beiki O, Brismar T. Predicting hip fracture risk with hand or wrist radiographs using digital X-ray radiogrammetry. *Bone* 2012;**50** (Suppl 1):S150–S151.
- Pemmer B, Roschger A, Hofstaetter J, Wobraschek P, Simon R, Roschger P *et al.* Distribution of trace elements ZN, PB and SR in bone packets and cement lines of cortical and trabecular human bone. *Bone* 2012;**50** (Suppl 1):S124.
- Roschger P, Hofstaetter JG, Roschger A, Dominkus M, Puchner S, Sulzbacher I *et al.* High mineralization of tumor bone matrix in a case of sclerosing osteosarcoma. *Bone* 2012;**50** (Suppl 1):S130.
- Fix D, Puchegger S, Pilz-Allen C, Roschger P, Blouin S, Fratzi P *et al.* Functional mapping of bone on the micrometer-scale by scanning acoustic microscopy. *Bone* 2012;**50** (Suppl 1):S125–S126.
- Beraudi A, Siliqi D, Baruffaldi F, Bunk O, Ladisa M, Stea S *et al.* Scanning small and wide angle scattering analysis compared to circularly polarized light analysis of healthy and pathologic human bone sections. *Bone* 2012;**50** (Suppl 1):S166–S167.
- Moester MC, van Beusekom MM, Mol IM, Löwik CM, de Rooij KE. Validation of an easy new method to quantify *in vitro* mineralization using Bonetag or Osteosense. *Bone* 2012;**50** (Suppl 1):S79–S80.
- Rowe DW. GFP reporters as tools for investigating bone cell biology and regenerative medicine. *Bone* 2012;**50** (Suppl 1):S18.
- Rowe DW. Automated, observer independent dynamic and cellular bone histomorphometry. *Bone* 2012;**50**:MTP09.
- Schulte FA, Weigt C, Ruffoni D, Lambers FM, Levchuk A, Webster DJ *et al.* Parathyroid hormone but not bisphosphonate therapy interferes with the local mechanoregulatory mechanism in trabecular bone. *Bone* 2012;**50** (Suppl 1):S40.