

College of Radiologists, a trustee of the National Osteoporosis Society (NOS) & chairman of the NOS Bone Density Forum & of the Osteoporosis Group of the European Society of Skeletal Radiologists (ESSR). She was awarded the Founders' gold medal of the International Skeletal Society (ISS) in 2007, Clinician of the Year of the International Society for Clinical Densitometry (ISCD) in 2009 and elected an honorary member of the ESSR in 2012. She is author of 234 peer reviewed publications, 27 invited reviews and 34 chapters & has had collaborative research grants in excess of £5.5M over the past 15 years, & this year was awarded, with computer scientist colleague Professor Tim Cootes, £660K over 3 years from the UK National Innovation Challenge Fund (NICF) to automate identification of vertebral fractures in radiology PACS.

#### ABNORMAL BONE QUALITY AND MICRO ARCHITECTURE IN AIS

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Adolescent Idiopathic Scoliosis (AIS) is a complex three-dimensional (3D) spinal deformity of unknown etiology. It mostly occurs in girls between 10 and 16 years old with a prevalence of 2 to 3% worldwide. AIS could be a disabling condition associated with significant morbidities. It is important to elucidate the pathophysiology and etiology of AIS so that effective prophylactic and therapeutic measures could be devised.

The etiology of AIS is believed to be multi-factorial and around one-third of AIS girls demonstrated low bone mass. Dual-energy X-ray Absorptiometry (DXA) has been used in previous studies showing the association between AIS and osteopenia the degree of which was correlated with curve severity. Low bone mass has been reported to be present as a systemic phenomenon at the hip, spine and other peripheral sites including the distal tibia, radius and os calcis in a significant percentage of AIS patients. Furthermore, osteopenia could persist longitudinally into adulthood in AIS.

Although DXA has generated important information on the profile that characterized AIS, it has the limitation of being a projectional integrated areal-BMD (aBMD) and thus cannot differentiate between cortical and trabecular bone. Our group has further reported lower volumetric BMD with peripheral quantitative computed tomography (pQCT) study and noted reduced bone volume fraction and trabecular bone thickness with low osteocyte and osteoblast density in a pilot histomorphometric study in AIS. Quantitative Ultrasound (QUS) study also demonstrated significantly lower Broadband Ultrasound Attenuation (BUA) and Stiffness Index (SI) at the non-dominant os calcis in AIS girls, suggesting the possibility of altered bone micro-architecture in AIS. Recently, our group has also shown that SI is a significant and independent prognostic factor for curve progression in AIS after adjusting for age, puberty and curve severity. It is logical to hypothesize that low BMD, abnormal cortical and trabecular bone geometry and micro-architecture could play an important role in the etiopathogenesis of AIS.

In contrast to QUS which can only provide indirect assessment of bone mineral densities and bone quality, the high-resolution peripheral quantitative computed tomography (HR-pQCT) can offer non-invasive measurement of bone structural and mechanical indices including bone geometry, volumetric BMD (vBMD) and bone micro-architecture at the trabecular and cortical compartment separately, without being confounded by bone size. This presentation will give an overview and summary of the evolution of our serial studies on the bone density, bone micro-architectural parameters as well as cortical and trabecular bone quality and bone strength indices in AIS patients versus normal matched controls.

#### Brief CV

**Research Area(s):** Adolescent Idiopathic Scoliosis, Paediatric Orthopaedics

**Technical Expertise:** DXA, HR-pQCT, MRI

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#### INFLUENCE OF ANTHROPOMETRIC PARAMETERS ON ASSESSMENT OF PEDIATRIC BONE MINERAL DENSITY AND BONE MINERAL CONTENT

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The goal of this study was to assess the implication of including relevant anthropometric variables in the creation of reference curves for areal bone mineral density (aBMD) and bone mineral content (BMC) in pediatrics.

Analysis of the dual-energy X-ray absorptiometry (DXA) data collected as part of the Bone Mineral Density in Childhood Study1, including 2012 boys and girls, 5–22 y old, with a total of 10,525 visits, resulting in aBMD and BMC observations at the lumbar spine, hip (neck and total), forearm and whole body (total body and total body less head). Multivariate statistics were used to rank order the influence of the independent variables age, gender, race (black/non-black), height, weight, percent body fat (%fat) and sexual maturity. Two different models were created for each aBMD and BMC parameter, the practical model containing age, gender, race, height and weight as well as the full model, adding %fat. We compared the number of subjects that fell below 2 standard deviations in our models with those below the same limit of the currently standard LMS model2, which is based on age, sex and race, and of the height adjusted Z-scores3.

Between 50% and 82% of subjects identified as below normal (<−2 SD) based on the LMS model were not classified as being below normal in our practical model. Using the full model, misclassification increased for all aBMD and BMC parameters, ranging from 49% to 92%. Height-adjusted Z-scores reduced the misclassifications to 33–60% in comparison to the practical model and to 41–73% in comparison to the full model. For both the practical and the full model, misclassifications in comparison to the LMS model were worse for BMC than for BMD at all sites with the exception of the femoral neck. Considering that BMC is more heavily influenced by bone size than BMD, inclusion of body height and weight in the model reclassifies small, underweight subjects away from the lower tail of the distribution, which is not done by the LMS model, as this model takes care of body size only through the surrogate of age.

The traditional comparison of pediatric BMD and BMC data against age-, sex- and race-matched controls can be refined if anthropometric parameters are taken into account.

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#### Brief CV

**Research Area(s):** Characterizing Bone Growth through maturation. Micro-pixel edge detection. Finding objects smaller than instrument resolution. Quantitative Bone Analysis. CT. DXA. Image Processing Technique.

**Technical Expertise:** Quantitative bone analysis from instrumentation development to image analysis to population characterization. Software streamlining and optimization.

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#### PATIENT TRANSLATIONAL MOTION CORRECTION FOR REDUCTION OF ARTIFACTS IN A FAN-BEAM CT SCANNER

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In computed tomography (CT) systems, many different artifacts may be present in the reconstructed image. For our laboratory prototype CT system, a fan-beam/cone-beam focal high-resolution peripheral quantitative computed tomography (fHRpQCT) scanner, careful calibration of all geometric system parameters are of utmost importance. However, patient-based motion, leading to image artifacts, is hard to avoid.

An algorithm for correction of translational motion was developed and implemented. In this method, the integral mass and center of mass at each projection angle was seen to follow a sinusoidal or sinusoidal-like curve. Fits were used on the motion-encoded sinograms to determine both of these curves and, consequently, the amount and direction of motion that occurred. Each projection was individually adjusted to compensate for this motion by widening or narrowing the projection based on the ratio of the actual and calculated ideal projection integrals and shifting the projection to match the actual centroid to the calculated ideal location.

A custom imaging phantom with an outer diameter of approximately 16 mm was used to test the motion-correction algorithm in both simulated and experimental cases. A baseline of the error measured, taken as a fraction, was established as 0.16 for motion-free images measured on the scanner. Various motion patterns were tested (Fig. 1). These included the distance of motion, the angle at which the motion occurred, and the ratio of the sinograms that was corrupted by motion. Experimental testing showed a maximum error increase of 2.7% from the baseline error for the motion-corrected images (Fig. 2) at 4 mm motion.

The overall optimization provided acceptable results for the reconstructed image and good-quality projections for use in the motion-correction algorithm. The motion-correction algorithm implemented in this project helps minimize the amount of error due to translational motion and provides a foundation for future corrections of more complex motions.

#### Brief CV

**Research Area(s):** quantitative assessment of bone, dual-energy X-ray absorptiometry, quantitative computed tomography

**Technical Expertise:** physics of X-ray-based imaging

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Dr. Hangartner is a native of Switzerland. He received his doctorate in experimental physics at the Swiss Federal Institute of Technology in Zurich in 1978. After having spent several years at the University of Alberta in Edmonton, Canada, he went to Wright State University in Dayton, Ohio, in 1986, and he is now a Distinguished Professor of Biomedical Engineering, Medicine & Physics as well as the Director of the BioMedical Imaging Laboratory and the Chair of the Department of Biomedical, Industrial & Human Factors Engineering of Wright State University.

Dr. Hangartner's research interests center around the non-invasive, quantitative evaluation of bone. He was involved in the early development of peripheral quantitative computed tomography, and he contributed to the field with investigations into beam-hardening and scatter effects on the quantitative evaluation of bone. More recently, he developed patented methods to analyze the geometry and density of cortical bone at a high level of accuracy. Another research area focuses on the quality assurance and control of dual X-ray absorptiometry devices. He has developed special algorithms that, together with a dedicated phantom, promise to better correct for differences between scanners.

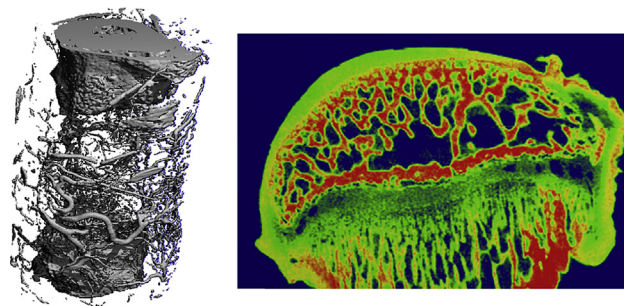
#### CONTRAST-ENHANCED MICROCT IMAGING OF VASCULAR AND CARTILAGINOUS TISSUES

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Advanced imaging methods play an increasingly important role in rigorous preclinical studies of tissue structure/function changes associated with degenerative diseases and regenerative medicine therapeutic strategies. Microcomputed tomography (micro-CT) imaging offers excellent resolution for quantifying 3D tissue morphology and composition but has typically been restricted to analysis of x-ray attenuating materials or tissues such as bone. Micro-CT analysis has therefore primarily been applied as a valuable evaluation tool for osteoporosis and bone repair studies. Unfortunately, soft tissues such as blood vessels and cartilage alone are not sufficiently radiodense relative to surrounding tissues to allow micro-CT analysis. However, vascular ingrowth into scaffolds or regions of tissue injury may be imaged nondestructively following perfusion of a radiodense contrast agent. Subsequent morphological analysis can provide quantification of 3D vascular volume, vessel thickness and density, and vascular network connectivity. Micro-CT imaging in combination with an appropriate contrast agent thus overcomes some of the shortcomings of other vascular assessment techniques by providing high resolution, efficient, volumetric, and quantitative analysis. Contrast-enhanced micro-CT imaging of cartilaginous tissues has also been recently established as a method to assess cartilage regeneration following injury or prevention of degeneration during osteoarthritis. In addition to providing quantitative analysis of articular cartilage morphology, the spatial equilibration of ionic contrast agents provides a nondestructive indicator of proteoglycan content within the cartilage. Furthermore, standard micro-CT analysis can be used to quantify changes in subchondral bone thickness and osteophyte development. Contrast-enhanced micro-CT imaging is therefore a highly sensitive and versatile tool for quantifying the effects of potential disease modifying therapies on multiple aspects of degenerative joint diseases.



#### Brief CV

Dr. Robert E. Guldberg holds the Parker H. Petit Chair in Bioengineering and Bioscience. He is a Professor in the Georgia Institute of Technology's Woodruff School of Mechanical Engineering and Georgia Tech/Emory Department of Biomedical Engineering. Dr. Guldberg received all of his degrees from the University of Michigan in mechanical engineering and bioengineering. His research interests focus on musculoskeletal growth and development, regeneration of limb function following traumatic injury, and degenerative diseases such as skeletal fragility and osteoarthritis. In 2009, he was appointed Executive Director of the Petit Institute for Bioengineering and Bioscience (IBB). Under his leadership, the Petit Institute has expanded significantly to support the research of over 150 faculty from a broad range of science, engineering, and clinical disciplines, 17 interdisciplinary research centers, and two graduate programs in bioengineering and bioinformatics. Dr. Guldberg also co-directs two research centers, the GT/Emory Center for Regenerative Engineering and Medicine (REM) and the GT/CHOA Center for Pediatric Innovation (CPI).