

the mechanisms and consequences of bone fragility *in vitro* in specimens and *in vivo* in laboratory animals.

Now, for this 20th IBDW, we have assembled senior scientists and clinicians, along with post-doctoral students and trainees, to observe and deliver an amazing array of presentations covering traditional and more novel developments and applications of CT, MRI and ultrasound imaging and quantification. We address not only morphological imaging but also functional, cellular and molecular imaging. We explore not only technical developments related to imaging the osseous tissues but also to imaging and quantifying muscular, cartilaginous, vascular and hematopoietic tissues across a range of disorders.

In summary, the past four decades have witnessed tremendous progress in the development and application of quantitative bone and soft tissue imaging techniques. These currently provide a vast array of exquisite research and clinical tools to examine and explore the depths and boundaries of human and animal tissues in health and disease. Over this time interval, The International Bone Density Workshop series, and its leaders, participants and sponsors have been instrumental, indeed pivotal, in promoting and fostering the development, advancement and maturation of these most exciting research arenas.

Table. International bone density workshops – presidents, locations and years.

	Presidents	Conference Locations	Year
1	Harry K. Genant	San Francisco, California, USA	1979
2	Peter Rueggsegger	Zuoz, Switzerland	1981
3	Thomas R. Overton & Thomas N. Hangartner	Banff, Canada	1982
4	Anne-Marie Laval-Jeantet	Fontevraud, France	1984
5	Frederick S. Kaplan	Bretton Woods, New Hampshire, USA	1985
6	Judith E. Adams	Buxton, England	1987
7	Bruce Ettinger	Rancho Mirage, California, USA	1989
8	Dieter Felsenberg & Willi Kalender	Bad Reichenhall, Germany	1991
9	Dianna D. Cody & Bradford J. Richmond	Traverse City, Michigan, USA	1992
10	Sergio Ortolani & Maria Luisa Bianchi	Venice, Italy	1994
11	Kenneth G. Faulkner & Michael R. McClung	Gleneden Beach, Oregon, USA	1995
12	David Reid & Peter Tothill	Crieff, Scotland	1997
13	Charles R. Wilson	Delavan, USA	1998
14	Claus Glueer	Warnemuende, Germany	2000
15	Sharmila Majumdar & John Shepherd	Monterey, California, USA	2002
16	Didier Hans & Pascal Laugier	Annecy, France	2004
17	Akira Itabashi, Masako Ito & Masao Fukunaga	Kyoto, Japan	2006
18	Giuseppe Guglielmi	Pugnochiuso, Italy	2008
19	Paul D. Miller	Breckenridge, Colorado, USA	2012
20	Ling Qin & James F. Griffith	Hong Kong	2014

#### Brief CV

Harry K. Genant, MD, is Professor Emeritus of the University of California San Francisco, and Emeritus Member of the Board of Directors of Synarc, Inc. He received his medical degree from Northwestern University in Chicago, Illinois and completed his internship on the Osler Service at Johns Hopkins University in Baltimore, Maryland. He received residency training in Medicine and in Radiology at the University of Chicago, and was Chief Resident and Assistant Professor in Radiology. In 1974 he assumed a faculty position at the University of California, San Francisco, as Chief of Musculoskeletal Radiology. He remained at UCSF for over 30 years, achieving the rank of Professor of Radiology, Medicine, Epidemiology and Orthopaedic Surgery. He founded the Osteoporosis and Arthritis Research Group (OARG) in the Department of Radiology, UCSF, and served as its Executive Director. This group, once numbering over 130 physicians, scientists and research associates, was recognized as a leading source of research on the development and

assessment of noninvasive and quantitative imaging methods for osteoporosis, arthritis and orthopaedics. In 1998 he co-founded Synarc, Inc, a global, contract research organization (CRO) specializing in management of quantitative imaging and biomarkers in large, multicenter, multinational, pharmaceutical drug trials. He served as a Member of the Board of Directors from 1998 to 2013, and is currently a Senior Consultant for Synarc Imaging. Dr. Genant has been editor or co-editor of more than 40 books and author or co-author of more than 300 chapters or invited articles, over 600 articles in peer-reviewed scientific and medical journals, and over 1500 abstracts presented at national and international scientific and professional gatherings. He is Associate Editor of Bone and on the editorial boards of Osteoporosis International and the Journal of Clinical Densitometry.

Among the numerous awards and honors Dr. Genant has received are honorary lifetime memberships for the American Academy of Orthopaedic Surgeons and for the International Society for the Study of the Lumbar Spine. He is an honorary member of the Italian Radiologic Society, the Chinese Osteoporosis Society, the Chilean Society of Osteology, the Hungarian Society of Osteology, and the European Society of Skeletal Radiology. He is a Fellow of the American College of Radiology and an Honorary Fellow of the Royal College of Radiologists, United Kingdom. He was named The Outstanding Physician of the Year in 1998 and the recipient of The Paul D. Miller ISCD Service Award in 2013, by the International Society for Clinical Densitometry. He was designated The Annual Orator in 2004, by the Radiologic Society of North America, and The Louis Avioli Annual Lecturer in 2012, by the American Society of Bone and Mineral Disease. He was nominated and elected by the American College of Rheumatology as an ACR Master in 2012, and was named the Olof Johnell Science Awardee at the ECCEO/IOF Congress in 2013.

Dr. Genant has served as President of the Association of University Radiologists, President of the International Skeletal Society, First President and Founder of the International Bone Density Workshop series, Scientific Chair of the First through Sixth International Congresses on Osteoporosis in China, Co-Chair of the Second International Conference on Osteoporosis in Japan, Chair of the WHO Task Force on Osteoporosis, Chair of the International Steering Committee for Artificial Gravity for the joint US, German and Russia Space Programs, Member of the Radiologic Devices Panel of the US Food and Drug Agency, Member of the Board of Directors of the International Osteoporosis Foundation and Co-Chairman of the IOF Global Initiative on Vertebral Fracture Assessment and Co-Chairman of the IOF Bone Quality Working Group.

#### PRECLINICAL BONE AND CARTILAGE MRI

Sharmila Majumdar

University of California San Francisco, USA



Second only to cardiovascular disease in producing long term disability[1], osteoarthritis (OA) is a chronic degenerative disease in which the salient feature is the progressive loss of articular cartilage. Traditionally, OA has been diagnosed via radiographic examination, which relies on the assessment of secondary indicators of disease such as the presence or absence of osteophytes and the width of the joint space for diagnosis [2,3]. However, this approach is limited in that it is effective only at later stages of disease progression because soft tissue quality can only be inferred from relative bone appearance and health using planar X-ray imaging techniques [4]. Moreover, in OA the early stages of cartilage degeneration are often marked by the loss of specific biologic components of the cartilage matrix [5–8]: changes that are invisible in conventional radiographs.

Magnetic resonance imaging (MRI) has been used to assess cartilage morphology directly and has shown promise for the detection of soft tissue changes 4, 9–12. In particular, T2 and T1ρ relaxation times have proven to be valuable in the assessment of cartilage biochemistry, in particular hydration, proteoglycan and collagen content, and collagen orientation [9–15]. T2 tissue relaxation time has been found to be inversely correlated with both cartilage volume and thickness, and focal areas of increased T2

levels have been found to correspond to cartilage lesions upon arthroscopic evaluation [14–17]. Lesions found in T2-weighted images and T2 maps have also been correlated with degradations of cartilage matrix (i.e., fibrillation, clefts [14,15]).  $T1\rho$  describes longitudinal relaxation in the rotating frame, and has been associated with proteoglycan loss, which is thought to precede the development of symptomatic.

Assessment of bone quality in OA using MR and micro-computed tomography ( $\mu$ CT) in bone samples has also revealed much information about bone density and micro-architecture.

Although the disruptive and degradative events accompanying the advent of disease progression in OA are known, the mechanisms and order in which these events occur is still an active area of research. Preclinical studies designed to address this need employ several animal models, which exhibit disease phenotypes similar to those observed in humans. These studies will be reviewed in this talk, and future directions will be identified.

#### Brief CV

**Research Areas:** Osteoporosis, Osteoarthritis

**Technical Expertise:** Imaging

**Email:** [sharmila.majumdar@ucsf.edu](mailto:sharmila.majumdar@ucsf.edu)

#### DEVELOPMENTS IN PRECLINICAL AND CLINICAL IMAGING

Bruno J. Koller, Nicolas Vilayphiou

SCANCO Medical AG, Brüttisellen, Switzerland



The XtremeCT (Scanco Medical AG, Brüttisellen, Switzerland) developed in 2004 was the first scanner to propose *in vivo* assessment of trabecular microarchitecture at the ultradistal radius and tibia. At that time we proposed a 2.8 min scan over a 9.02 mm region, with 82  $\mu$ m voxel size, for a radiation dose lower than 3  $\mu$ Sv [Laib et al – Bone 1999].

This was the chance to pursue at the *in vivo* and organic level all the bone research done at the tissue level with restricted region of interest as per histomorphometry. Various studies exploited this new opportunity to better understand the mechanisms of bone loss in osteoporosis or the actions of drugs affecting bone metabolism.

During the past decade, applications focused on bone research are being developed as cortical bone analysis, finite element analyses or 3D registration. But bone is not the only field that can take advantage of the XtremeCT. Research in rheumatoid arthritis also finds interest into bone erosions, or joint space width in 3D that can be obtained from high resolution joint imaging [SPECTRA]. With the interest in sarcopenia growing in the community, we are currently validating a method to assess muscle volume to fully exploit the images obtained with XtremeCT, even on the low density range [Erlandson et al – ASBMR 2012]. Vascular calcification may also be assessed, in addition to bone micro-architecture changes in patients suffering chronic kidney disease, or diabetes [Patsch].

Movement artifacts are known to affect XtremeCT scans, notably at the radius. They impact the reproducibility of the measurements and reduce the number of valid scans in longitudinal studies on bone fragility or osteoporosis treatment efficacy [Pialat et al – Bone 2011].

This motivated the design of a new HR-pQCT scanner (XtremeCT II) to address the movement artifacts issue. Hardware improvements allow for scan time shortening with no cost on image quality, with two different scan protocols over a 10 mm range. The basic protocol was specified to be compatible with XtremeCT: 1.5 min scan, 82  $\mu$ m voxel size and 3  $\mu$ Sv dose. The second protocol has better resolution and is still acceptable for patient scans: 61  $\mu$ m voxel size, 2 min scan time and 5  $\mu$ Sv dose.

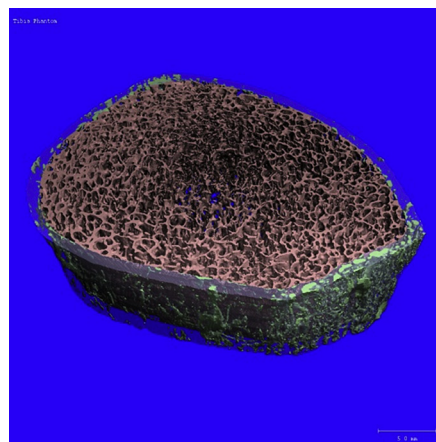
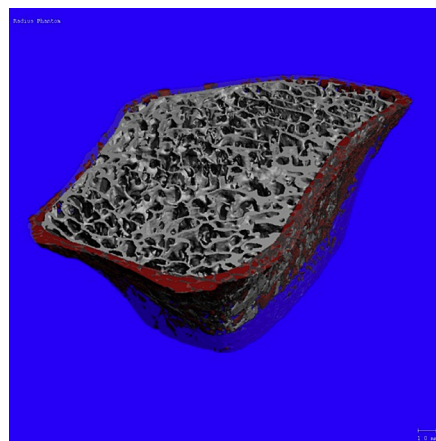
A set of 20 cadaver bone phantoms (EBS, UCSF) was scanned to compare results across the different scan protocols, between XtremeCT II, XtremeCT and  $\mu$ CT 100. We obtained excellent correlations between all datasets, and

good agreements were met between XtremeCT II both at 82 and 61  $\mu$ m when compared to XtremeCT. We also found that the accuracy of bone micro-architecture measurements improved as the voxel size decreased, with respect to  $\mu$ CT 100 results.

Reduced scan time should lead to significant improvements regarding movement artifacts on *in vivo* scans. Also a new forearm cast will help to limit patient mobility.

XtremeCT II is also able to scan at 30  $\mu$ m voxel size, which may find use in *ex vivo* studies or preclinical research involving relatively large animals such as rabbits.

XtremeCT II does not only improve the research in osteoporosis, but is more flexible hence widening the horizon of its applications.



#### Brief CV

**Research Area(s):** MicroCT, Bone, Materials

**Technical Expertise:** Image Processing

**Email:** [bkoller@scanco.ch](mailto:bkoller@scanco.ch)

**Website:** [www.scanco.ch](http://www.scanco.ch)