IMAGING VASCULATURE OF BONE

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For decades scientists have tried to measure bone blood flow but this is fraught with difficulty for several reasons. Any attempt to penetrate the bone cortex will invariably disrupt blood flow measurement; as opposed to say the heart or the brain, most bones are supplied by many small arteries, and blood flow often varies tremendously from one bone area to another. Traditionally microspheres or radionuclide techniques have been used to measure blood flow. Nowadays, however, reliable assessment of bone vascularity is possible with dynamic contrast enhanced MRI imaging and PET imaging techniques. Dynamic contrast-enhanced MR imaging is the most widely applied technique used to measure bone perfusion. The terms blood flow and tissue perfusion represent different physiological processes. Bone blood flow is flow within blood vessels while perfusion is much more encompassing and biologically relevant term reflecting not just vascular flow but also capillary capacitance, capillary permeability and interstitial diffusion. Dynamic contrast-enhanced MRI imaging measures bone perfusion rather than bone blood flow. Good tissue perfusion is essential to fracture healing including healing of trabecular microfracture. The most metabolically active areas of bone are those which are best perfused whilst trabecular rich areas of bone typically represent areas of good perfusion. The principal factor driving bone marrow perfusion seems to the marrow red cell mass. This is understandable since red marrow is many times more metabolically active than fatty marrow. Marrow perfusion decreases with increasing age and is especially decreased in osteoporotic bone in line with an increase in marrow fat content. It is understandable that are quite osteoporotic fractures slow to heal.

In the future, more advanced MR imaging techniques (such as blood oxygenation level dependent [BOLD] imaging or intravoxal incoherent motion [IVIM]) may well allow assessment of bone perfusion without having to administer to intravenous contrast agent.

Brief CV

Research Area(s): Marrow changes in osteoporosis
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Professor James F Griffith MB, BCh, BAO, MRCP, FRCR, HKFAM (radiology), MD, studied medicine in University College Cork Ireland, practiced clinical medicine in the UK and underwent radiological training in the West Midlands UK. His current clinical practice comprises all aspects of musculoskeletal imaging. He has published almost 300 peer-reviewed papers with particular research interests being glenoid bone loss in should dislocation and the imaging of marrow fat and bone vascularity with a view to the early detect of osteoporosis.
Some representative papers are:

Griffith JF, Yeung DK, Ma HT et al. Bone marrow fat content in the elderly: a reversal of sex difference seen in younger subjects. J Magn Reson Imaging. 2012;36(1):225—30.
Griffith JF, Wang YX, Zhou H et al. Reduced bone perfusion in osteoporosis: likely causes in an ovariectomy rat model. Radiology. 2010;254(3):739—46.
Griffith JF, Yeung DK, Chow SK et al. Reproducibility of MR perfusion and (1)H spectroscopy of bone marrow. J Magn Reson Imaging. 2009 ;29(6):1438—42.
Griffith JF, Yeung DK et al A study of bone marrow and subcutaneous fatty acid composition in subjects of varying bone mineral density. Bone. 2009;44(6):1092—6.
Griffith JF, Yeung DK, Tsang PH et al. Compromised bone marrow perfusion in osteoporosis. J Bone Miner Res. 2008;23(7):1068—75.
Griffith JF, Yeung DK, Antonio GE et al. Vertebral marrow fat content and diffusion and perfusion indexes in women with varying bone density: MR evaluation. Radiology. 2006;241(3):831—8.

Yeung DK, Griffith JF, Antonio GE et al Osteoporosis is associated with increased marrow fat content and decreased marrow fat unsaturation: a proton MR spectroscopy study. J Magn Reson Imaging. 2005 ;22(2):279—85.

HR-QCT ASSESSMENT OF BONE BEYOND BONE MINERAL DENSITY

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Amongst techniques providing more comprehensive information on bone fragility compared to Dual X-ray Absorptiometry (DXA) Quantitative Computed Tomography (QCT) is the strongest and most versatile approach. It has potential for assessment of bone microstructure and bone material properties, two factors considered most relevant as predictors of bone fragility beyond bone mineral density (BMD). In order to exploit its potential for accurate 3-D assessment of these factors, accurate delineation of bone tissue from marrow, fat or muscle tissue is essential. High Resolution QCT (HR-QCT) approaches have been developed over the past years with substantial progress in the pursuit of these goals.

In this contribution I will focus on HR-QCT of the spine and the proximal femur, the two most relevant sites for assessment of bone fragility. By using higher collimation (<0.5 mm), higher photon flux (radiation exposure 2—3 mSv) and high resolution reconstruction kernels one can reconstruct images with in-plane resolution of 150—200 μm. Special software (e.g. Structural Insight at our institution) permits refined assessment of the trabecular network, e.g. by estimation of apparent trabecular separation and bone volume fraction. Spatial deconvolution techniques generate estimates of cortical thickness and tissue mineral density (TMD) with strong improvement in accuracy. Moreover, the status of marrow fat can be estimated providing a basis for correction of BMD and TMD.

Interestingly, the software also improves structural assessment on regular QCT images, documenting substantial improvement over standard QCT results. The improved spatial depiction also provides a superior basis for finite element modeling. I will present validation results and document the merits of HR-QCT in the assessment of treatment effects, e.g. by differentiating bone anabolic from anti-resorptive effects.

In conclusion, HR-QCT has potential for substantially improved assessment of bone fragility and treatment effects.

Brief CV

Research Area(s): Preclinical and clinical imaging of bone metabolism, bone fragility, and bone metastases
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Dr. Claus-C. Glüer is a Professor of Medical Physics at the Department of Radiology and Neuroradiology, University Hospital Schleswig-Holstein in Kiel, Christian-Albrechts-Universität zu Kiel, Germany. His research is aimed at the development of innovative parametric imaging techniques and their quantitative evaluation. Since 1987 when he started his postdoc in the *Osteoporosis Research Group* of Prof. Harry K. Genant at the University of California, San Francisco, Dr Glüer has focused his research on osteoporosis and other bone disorders. He has contributed specifically to the development of bone densitometry, quantitative ultrasound and high resolution computed tomography approaches. He has coordinated several multicentre studies including *OPUS*, a European project on epidemiology and optimised diagnostic assessment of osteoporosis.

Dr. Glüer also has a strong research interest in multimodal methods for molecular imaging with applications in oncology, inflammation, and skeletal

research. He co-founded the *Molecular Imaging North Competence Center* (*MOIN CC*) at the *Christian-Albrechts-Universität zu Kiel*, a preclinical imaging lab. At *MOIN CC*, multi modal imaging studies combining micro computed tomography, high-field magnetic resonance imaging, high resolution ultrasound, fluorescence and bioluminescence imaging can be carried out to study morphological, functional, cellular, and molecular processes in health and disease and to assess therapeutic effects.

Dr. Glüer is the current president of the German Society for Osteology (DGO), past president of the German Academy of Bone & Joint Sciences (DAdorW) and President of the European Calcified Tissue Society. He has published more than 175 original papers, 20 books and book chapters, and holds 3 patents.

OPPORTUNISTIC BONE DENSITY SCREENING BY DUAL-USE OF CT SCANS

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Central DXA of the lumbar spine and proximal femur is the preferred method for bone mineral density (BMD) testing. Despite the fracture risk statistics, osteoporosis testing with dual energy X-ray absorptiometry (DXA) remains underused. However, BMD can also be assessed with other radiologic imaging tools, such as quantitative computed tomography (QCT) that may be available when access to DXA is restricted.

For patients undergoing screening CT colonography (CTC), a potential opportunity exists for concurrent BMD screening by QCT without the need for any additional imaging, radiation exposure, or patient time. In addition, there are a number of indications for CT imaging for which there is a large overlap between the need for a CT scan and a patient having risk factors for osteoporosis. Use may also be made of these CT images for BMD measurement by QCT. Such dual-use of CT images could increase screening rates or, alternatively, preclude the need for DXA screening in some individuals.

Previous studies combining standard CT imaging and QCT have generally focused on BMD measurement at the lumbar spine. QCT provides a volumetric BMD measure of the trabecular vertebral bone in isolation. This can have an advantage of superior sensitivity due to the higher turnover rate of trabecular bone, but QCT T-scores are somewhat lower than DXA T-scores for the same age and the established WHO classification of osteoporosis by DXA T-score is not appropriate. In contrast, at the proximal femur, QCT 3D data may be used to derive a projectional 2D image of the proximal femur and this image may be analyzed using standard DXA ROIs to determine DXA-equivalent "CTXA" aBMD values in g/cm^2. Using this method, the WHO T-score classifications may be applied and the aBMD measures may be included in FRAX calculations.

The workflow associated with such dual-use of CT scans may be improved by the use of phantomless or "asynchronous" calibration methods, so that the BMD measurement does not need to be planned in advance of the CT scan. In addition, using such methods, it is possible to make use of archived CT scans retrospectively. Finally, the use of IV contrast-enhanced CT images for QCT is usually contraindicated and a measurement bias has been shown at the spine. However, some recent studies suggest that for measurements made at the hip, the measurement difference due to contrast enhancement may not be clinically significant, further widening the utility of CT scans for BMD measurement.

Brief CV
Research Area(s): osteoarthritis, osteoporosis, rheumatoid arthritis, medical imaging analysis, machine vision
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Mindways Medical Ltd, Manchester, UK	2011 — Present
VP, Business Development	
Optasia Medical Ltd, Manchester, UK	2006 — 2011
Chief Technical Officer	
Image Metrics Ltd, Manchester, UK	2000 — 2006
Technical Services Director & CEO,	
Medical Division	
University of Manchester, Manchester, UK	1995 — 2000
Research Associate, Dept. Imaging	
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Education
University College (UCL), University of London, UK
1991 — 1994 PhD, Medical Image Acquisition and Analysis
Birmingham University, Birmingham, UK
1990 — 1991 MSc, Applied Radiation Physics (1991 Ratcliffe Prize)
1985 — 1988 BSc (Hons), Physics
Publications
Over 40 original articles, proceedings articles and conference abstracts.
Filed patents
Computer Program Products and Methods for Detection and Tracking of Rheumatoid Arthritis. U.S. Patent Application 60/880601, January 16th 2008. Methods of and System for Detection and Tracking of Osteoporosis. U.S. Patent Application 61/057369, November 2nd 2009.

ADVANCED vQCT AND HR-pQCT IN SCIENCE AND CLINICAL TRIALS

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QCT is increasingly used for the analysis of clinical studies and of epidemiology data. To date a number of different software options exist for the analysis of QCT images. As a consequence, a multitude of parameters related to bone mineral density, bone geometry and related to bone strength can be obtained in various volumes of interest in the spine and proximal femur. Many of them are highly correlated and appropriate analysis strategies will be discussed. In addition a number of different algorithms such as global or local adaptive thresholds using different criteria to segment the cortex are in use to quantify parameters such as cortical BMD, BMC or thickness. Strengths and weaknesses of the different approaches will be discussed by comparing effects on accuracy errors of one-time measurements and on accuracy errors of changes during longitudinal measurements. In contrast to QCT, hr-pQCT measurements of the radius and tibia are more standardized as only the XtremeCT scanner is available for hr-pQCT measurements in humans. But also for this scanner different algorithms to assess the cortex exist and a newer version, which allows for faster scan times and slightly higher spatial resolution has been introduced recently.

The lecture will review recent use of QCT using whole body CT scanners and of hr-pQCT to predict or discriminate hip fracture and to monitor age related changes or treatment efficacy in recent clinical trials in osteoporosis. It will include a brief introduction to advanced QCT methodology. Learning objectives are to understand what is measured by QCT, what are the advantages of QCT and hr-pQCT (in particular compared to DXA) and what potential pitfalls exist in the interpretation of QCT and hr-pQCT parameters.

Brief CV
Research Area(s): Musculoskeletal Imaging and Image Processing
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