

approach to investigating bone quality across the lifespan". Natural Sciences and Engineering Research Council of Canada (NSERC) "Non-invasive detection and monitoring of bone strength in osteoporosis". Natural Sciences and Engineering Research Council of Canada (NSERC)

"Image-based finite element prediction of bone micro-structural mechanical parameters".

Pure North S'Energy Foundation (PNSF) "A randomized double-blind study investigating dose-dependent longitudinal effects of vitamin D supplementation on bone health".

HR-PQCT IN CLINICAL RHEUMATOID ARTHRITIS

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HR-pQCT has been used to define cortical and trabecular bone changes at different anatomical sites involved in the disease processes of rheumatoid arthritis (RA), which include the distal radius, the proximal interphalangeal joints and the metacarpophalangeal joints. Three HR-pQCT studies have shown that RA is associated with a significant reduction in cortical and trabecular volumetric bone mineral density (vBMD), microstructure and biomechanical indices at the distal radius compared to controls. Inflammation-associated increased bone resorptive activity produces greater deficits in cortical than trabecular bone, and the changes were more pronounced than those revealed by areal BMD (aBMD), independent of body weight, hormonal level and aBMD. Changes in density and microstructure in RA patients correlated with disease activity, disease severity and serum levels of proinflammatory cytokines.

HR-pQCT is also useful for defining the anatomical sites prone to develop bone erosions as well as to quantify the size of such erosions. Bone erosions of >2 mm width in cortical break have been identified as highly specific for inflammatory joint diseases. The pathogenesis of these lesions is unclear, but mechanical forces might be considered as the potential triggers. Furthermore, HR-pQCT has been helpful in validating the capability of other imaging techniques, such as MRI and ultrasonography, in detecting bone erosions. HR-pQCT has been shown to be particularly useful in monitoring the dynamics of individual bone erosions and their responsiveness to treatment. Repair processes of existing bone erosions have been studied in a longitudinal manner and were identified in patients with RA treated with cytokine-blocking agents such as the TNF inhibitors as well as the IL-6-receptor blocker tocilizumab.

Aside from bone erosions, HR-pQCT is also useful for visualizing early nonerosive cortical bone changes in patients with RA. Areas of the periarticular bone where the cortical lining is thin and porous (cortical fenestration) have been defined by HR-pQCT. In patients with RA-specific autoantibodies against citrullinated proteins, such lesions have also been identified before they develop inflammatory disease, suggesting that bone is altered by autoimmunity in patients with RA before inflammation emerges, and creates new concepts in understanding the pathogenesis of RA.

Brief CV

Research Area(s): Gluco-corticoid and inflammation induced osteoporosis

Premature atherosclerosis in rheumatic diseases

Technical Expertise: HR-pQCT for assessment of bone loss in rheumatic diseases

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MOLECULAR IMAGING TECHNOLOGIES FOR OSTEOARTHRITIS/RHEUMATOID ARTHRITIS STUDIES

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Arthritis, including rheumatoid arthritis and osteoarthritis, is a common disease affecting millions of people worldwide. Murine models of arthritis are an important tool for both the preclinical study of arthritis pathogenesis and the testing the efficacy of anti-arthritis drugs, which have significantly advanced our understanding of arthritis. However, they are limited by a lack of longitudinal translational outcome measures of disease progression or interventional therapy. This issue presents 3 problems for prototypical preclinical investigations of drug effects on inflammation and tissue damages: 1) most cross-sectional studies in mice with "established arthritis" do not include an objective assessment of disease severity prior to treatment, and neither rates of change nor healing responses can be assessed; 2) the commonly used end points (i.e., histology and ex vivo molecular analyses) require the death of the mice, thus markedly increasing the number of animals needed to assess efficacy at multiple time points; 3) although the incidence and severity of arthritis vary among genetically identical littermates, there are no established scoring criteria to stratify different groups of mice based on disease activity in an intervention study. To overcome these problems, our group recently developed several imaging techniques based on their clinically used protocols. These techniques include contrast-enhanced magnetic resonance imaging, near-infrared lymphatic imaging, and Power Doppler ultrasound, which allow us to assess disease activity and progression in vivo in arthritic mice longitudinally. We used these in vivo imaging techniques in TNF transgenic mice, a mouse model of rheumatoid arthritis, and a Meniscal Ligamentous Injury-induced mouse model of osteoarthritis to study the association between synovial lymphatic draining function and the development and progression of joint lesions in these mice, as well as the in responses to a lymphatic based therapy. In this presentation, I will present our work using these imaging techniques. I will also introduce recently developed near-infrared dye based molecular imaging in preclinical arthritis study. Thus, molecular imaging technologies will greatly enhance the utility of murine models of arthritis in biological research.

Brief CV

Research Area(s): Inflammatory bone diseases

Technical Expertise: bone cell biology, in vivo imaging

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Positions and employment

1985–1987	Resident, General Hospital, Gastroenterology, Beijing, China
1987–1989	Visiting Research Scholar, Penn State University, Surgery, Hershey, PA
1995–1996	Postdoctoral Fellow, Department of Surgery, Penn State University, Hershey, PA
1996–1999	Postdoctoral Fellow, Department of Pathology, University of Texas Health Science Ctr., San Antonio, TX
1999–2004	Research Assistant Professor, Department of Pathology, University of Rochester, NY
2004–2008	Assistant Professor (tenure-track), Department of Pathology, University of Rochester, NY
2008–2011	Associate Professor (tenure-track), Department of Pathology, University of Rochester, NY
2011–2014	Associate Professor with tenure, Department of Pathology, University of Rochester, NY
2014	Professor with tenure, Department of Pathology, University of Rochester, NY