Imaging osteoporosis

Andy Kin On Wong describes the importance of a multidisciplinary approach to the pioneering Canadian Multicentre Osteoporosis Bone Quality Study, and the future of bone research

Could you begin by providing an overview of the key aims and objectives of your work?

My research largely involves using advanced imaging technologies to capture details about bone, muscle and fat to develop useful medical outcomes that can help doctors make decisions about the care of their patients. I work with engineers to refine tools to extract information out of medical images, analyse the data with appropriate statistical models and then interpret the results. As an interdisciplinary scientist, I enjoy playing multiple roles, bridging a number of fields to target a question that often demands various scientific perspectives. It is also interesting how dynamic our field has become – we have seen the focus on bone emerge from 2D to 3D, then to its interaction with muscle. Now fat is slowly trickling into the picture. It really provides room for collaboration and innovation.

What makes the Canadian Multicentre Osteoporosis Bone Quality Study (CaMos BQS) a landmark investigation?

Over the last decade, higher and lower resolution CT scanners have been specifically developed for imaging the arms and legs, and we have reached a point where everyone is wondering where the technology will go next. Many academic institutions are acquiring these machines – which are much cheaper to run, confer lower radiation and require less space to store than full-body scanners. The question though is: do the bone quality measurements obtained from these machines help us better predict whose bones are going to fracture? The CaMos BQS addresses this question, which many have been waiting a long time to answer.

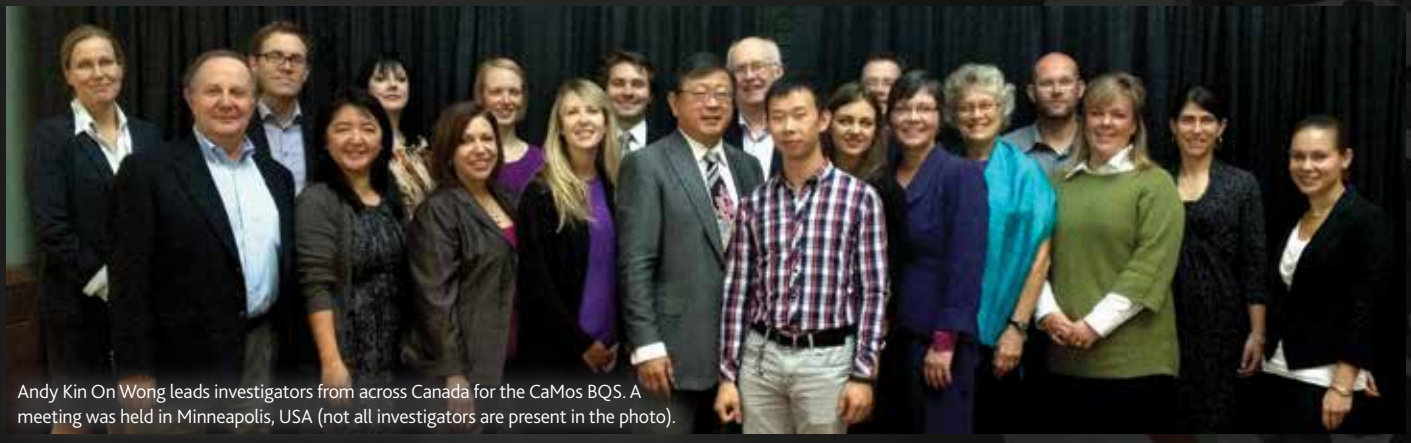
You are working with over 20 investigators across Canada. What are the challenges of leading a multicentre project?

It helps to have engineers to design more specialised software for specific tasks, medical physicists to guide quality assurance efforts, and epidemiologists and biostatisticians to ensure the study is designed correctly and that data are analysed using the right statistical models. The diversity and critical feedback from our co-investigators gives the study integrity and improves its design and execution. The greatest challenge is making sure messages are clearly communicated and understood to ensure procedures are streamlined and CT scanners cross-calibrated.

Moreover, each site has local feasibility challenges that need to be dealt with on a case-by-case basis. It helps to have study coordinators involved early in the planning phase, as they are the ones most familiar with the barriers and enablers to the study, such as transportation and participants' work schedules.

Could you explain Dr Jonathan D Adachi's, Director of the Centre for Appendicular MRI Studies (CAMRIS), role as your mentor and within the study?

I met Dr Adachi almost six years ago through the Alliance for Better Bone Health. He recognised potential in me and allowed me to lead smaller studies on knee osteoarthritis, which enabled multi-institutional collaborations. I then gained more experience in MRI and CT analyses of bone. When the idea of CaMos BQS started brewing, Dr Adachi believed I was well placed to lead and guide its direction. At the time we applied for the operating grant to fund the study, I was a PhD candidate under Dr Adachi, who is the Principal Investigator. However, he has let me sit in the driver's seat to execute the study from beginning to end. No young investigator could have a better experience. Dr Adachi continues to mentor me in my position as Director of the CaMos BQS.



Andy Kin On Wong leads investigators from across Canada for the CaMos BQS. A meeting was held in Minneapolis, USA (not all investigators are present in the photo).

Scanning for fractures

A large multicentre Canadian study is elucidating the potential benefits of recent technological advancements in the prediction of osteoporosis-associated fractures and the subsequent monitoring of bone quality

OSTEOPOROSIS IS A disease of the bones that increases in prevalence with age. Defining osteoporosis is difficult, but it is generally indicated by a reduction in bone mineral density, causing weak bones and, subsequently, an increased risk of fracture. Whilst fractures may seem medically benign, they are often more complicated for older adults. Indeed, up to 40 per cent of people who break a hip bone die within a year.

The global cost of treating fragility fractures (occurring due to osteoporosis as opposed to trauma) runs into billions of pounds. In this context, researchers and medical professionals are attempting to develop better tools and treatments to deal with this huge medical and social burden. One of the more recent advances has been the development of new CT scanners, which are capable of providing a more detailed 'snapshot' of bone and muscle quality in at-risk patients.

TESTING THE TECHNOLOGY

The new equipment looks promising, but since it is still relatively untested for direct clinical application, its true benefits remain elusive. The Canadian Multicentre Osteoporosis Bone Quality Study (CaMos BQS) was established to elucidate the advantages of these imaging devices and hence quantify their potential for tackling osteoporosis. Current medical practice for osteoporosis employs flat-bed scanners which produce 2D images of the hip and spine. While this approach has been medically justified up until now, it has pitfalls. The scanner itself is expensive and large, and although capable of predicting a reasonable portion of fractures, the limited technology is unable to correctly identify a large proportion of patients who, despite having an acceptable bone density, eventually develop fragility fractures.

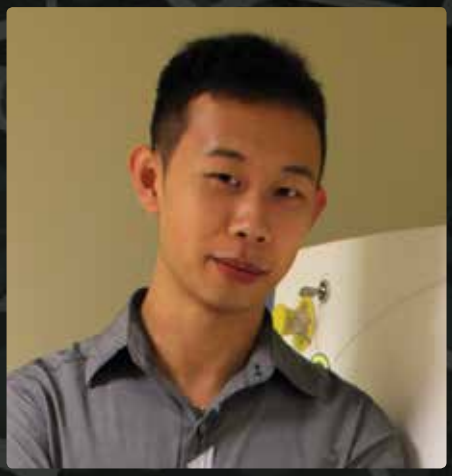
The new CT scanners, on the other hand, not only counteract these drawbacks, they may also offer an improvement on the status quo, as CaMos BQS Director Andy Kin On Wong explains: "We believe the 3rd dimension in structural information, previously lacking from flat-bed scanners, could make up the fracture cases we are currently unable to predict". The CT scanners are similarly superior in their ergonomics and design, in that they produce notably less radiation, are more compact and may be run at a reasonable cost. The scanning process is also less intrusive for the patient because it focuses on the arms and legs as opposed to the entire body. Moreover, the radiation that is produced is concentrated on areas of the body away from vital organs.

Despite these advantages, however, the ability of the technology to complement the current standard of care to improve management of osteoporosis remains unknown. In the CaMos BQS, Wong and colleagues are testing two variations of the new CT scanners: a high resolution and low resolution version. The higher resolution scanner is specialised to take detailed 3D images of patients' wrist and ankle bones; the lower resolution variant provides both bone and muscle measures at a considerably lower cost. By comparing the two, the team is aiming to evaluate which, if either, should be widely adopted in medical practices, and how much better predictions of who will develop a fragility fracture can be: "Although these scanners are not routinely used clinically, results of this study may give evidence for their utility in the clinic and increase availability worldwide," points out Wong.

Prior to the CaMos BQS, the team conducted smaller pilot studies to establish the reliability of the bone structure outcomes and feasibility of executing this large multicentre investigation. Initial results have been encouraging. The new scanners seem to be reliable, providing both valid and repeatable measurements. The extended study now encompasses around 1,400 women over 60 years of age from six major municipalities in Canada who will undergo high and low resolution CT and flat-bed scans, as the standard of care. These women will be followed over five years, and any incident fractures will be recorded. At the end of the five years, the group will have a robust and informative dataset which can assess the efficacy of the new CT scanners as a tool for predicting fractures. If found useful, this technology can then be employed in medical settings to further improve fracture risk quantification in patients, allowing doctors to assess the necessity of interventions that reduce patients' likelihood of suffering fractures in the future.

THE WIDER BENEFITS

The CaMos BQS is just one component of a wider network of studies. The study has a sister project called the CaMos Muscle Quality Study (MQS), with a similar framework looking at muscle quality in older adults using the lower resolution CT. Both of these studies sit within the parent project, CaMos, which has collected bone density and fractures data from over 9,000 Canadians since 1993. As Wong highlights, the benefit of this network is clear: "Because of the long history of data the CaMos study has collected, the CaMos BQS and MQS have the opportunity to fall back on 16 years of existing data on fractures".



What have been your key achievements to date, and what are your hopes for the future?

Through conference presentations, invited lectureships and internships at multiple institutions, I have made connections with a number of research teams and collaborators, and this has enabled me to become internationally recognised for my work in bone and muscle. I have demonstrated that muscle can interact with bone on many levels, but my recent assessment of fat in muscle is proving to be more groundbreaking. I believe that over the next few years osteoporosis research will involve fat quantification and researchers will assess its clinical role in frailty and fractures. With this idea in development, I hope to work with more endocrinologists and nutritionists to better understand how metabolic status can translate into altered fracture risks mediated through fat redistribution in tissues. As a pharmacologist, I also hope to examine potential mechanisms for combating pathways leading to compromised musculoskeletal integrity and to identify potentially efficacious drugs by working with pharmaceutical companies.

THE CANADIAN MULTICENTRE OSTEOPOROSIS BONE QUALITY STUDY (CAMOS BQS)

OBJECTIVES

- To determine the ability of bone structure to complement bone density in order to diagnose osteoporosis
- To compare two peripheral quantitative computed tomography scanners' ability to compute bone structure and predict fractures
- To create a national repository of bone structure data to serve as a normative sample

KEY COLLABORATORS

Dr Jonathan D Adachi, Alliance for Better Bone Health Chair in Rheumatology • **Dr Alexandra Papaioannou**, Eli Lilly Chair in Osteoporosis • **Dr Steven Boyd**, engineer in advanced mechanical assessment of bone • **Dr David Goltzman**, Director of CaMos • **Drs Christopher Gordon** and the late **Colin E Webber**, medical physicists for the CaMos BQS

Other collaborators: **Angela M W Cheung**, **Karen Beattie**, **Jerilynn Prior**, **Heather McKay**, **Heather MacDonald**, **Maureen Ashe**, **David Hanley**, **Kyle Nishiyama**, **Lauren Burt**, **Wojciech Olszynski**, **Saija Kontulainen**, **Shawn Davison**, **Andrew Frank**, **Chantal Kawalilak**, **Lora Giangregorio**, **George Ioannidis**, **Robert Josse**, **Norma MacIntyre**, **Tassos Anastassiades**, **Karen Rees-Milton**, **Famida Jiwa**, **Marta Erlandson**, **Leigh Gabel**

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ANDY KIN ON WONG has a background in pharmacology and expertise in musculoskeletal CT and MRI imaging. His training in epidemiology enabled him to design and direct a national study such as the CaMos BQS. He was mentored by two Research Chairs in bone health and was a graduate of the BioPharm programme at McMaster University in Canada.

Furthermore, the BQS employs the same study coordinators involved in the larger parent project. These coordinators have already established relationships with the volunteer participants; consequently, participant completion rates are high and follow-up data collection effective, two areas which often pose problems for long-term cohort studies. Moreover, both the BQS and Wong have benefited measurably from the supervision and mentorship of Dr Jonathan D Adachi, Director of the Centre for Appendicular MRI Studies (CAMRIS) and Principal Investigator. His recognition of the young researcher's potential has allowed Wong to develop rapidly – resulting in his leadership of the multicentre BQS at an impressively young age.

The BQS continues to yield important results, allowing Wong and colleagues to turn their attentions to other key areas of research, such as fat content in both bone and muscle tissue. "We believe fat may be interfering with how bone and muscle communicate to maintain their strength," elucidates Wong. In an early pilot study, the researchers observed an increased likelihood of fragility fractures in individuals with fattier muscle. It is believed that weakened muscular strength on nearby bones subsequently reduced the strength of those bones, and this may be responsible for their fragility. In addition, fat cells may be directly replacing areas where bone and muscle used to be. Thus, the CaMos MQS seeks to understand the mechanisms linking fat content in muscle to bone fragility. Indeed, current literature suggests that diet and metabolic status, elements that can dictate fat distribution, may be contributory risk factors to osteoporosis development.

> The group will have a robust and informative dataset which can assess the efficacy of the new CT scanners as a tool for predicting fractures

A NOTABLE VICTORY

These multicentre projects are vital to improving our understanding of osteoporosis, its causes and management. By creating well-designed and rigorous studies, researchers will have the necessary data to elucidate the intricate relationships among bone, muscle and fat tissues, with the ultimate goal of improving predictions of osteoporosis-mediated fragility fractures in older adults.

Furthermore, clinicians will be tooled with new CT scanners, as well as the essential knowledge that these can be relied upon for precise quantification of bone structure. As a consequence, at-risk patients can be identified earlier on, and medical or behavioural interventions can be implemented to reduce the risk of fractures. Certainly, decreasing the incidence of fragility fractures in the population would be a notable victory against the social, financial and medical burdens associated with this often underestimated condition.

Top left: low-resolution CT scanner (pQCT) providing bone and muscle structural information. **Top right**: high-resolution CT scanner (XtremeCT) providing specialised 3D bone information. **Bottom left to right**: pQCT scan of calf muscle, pQCT scan of wrist bone and 3D XtremeCT scan of wrist bone.