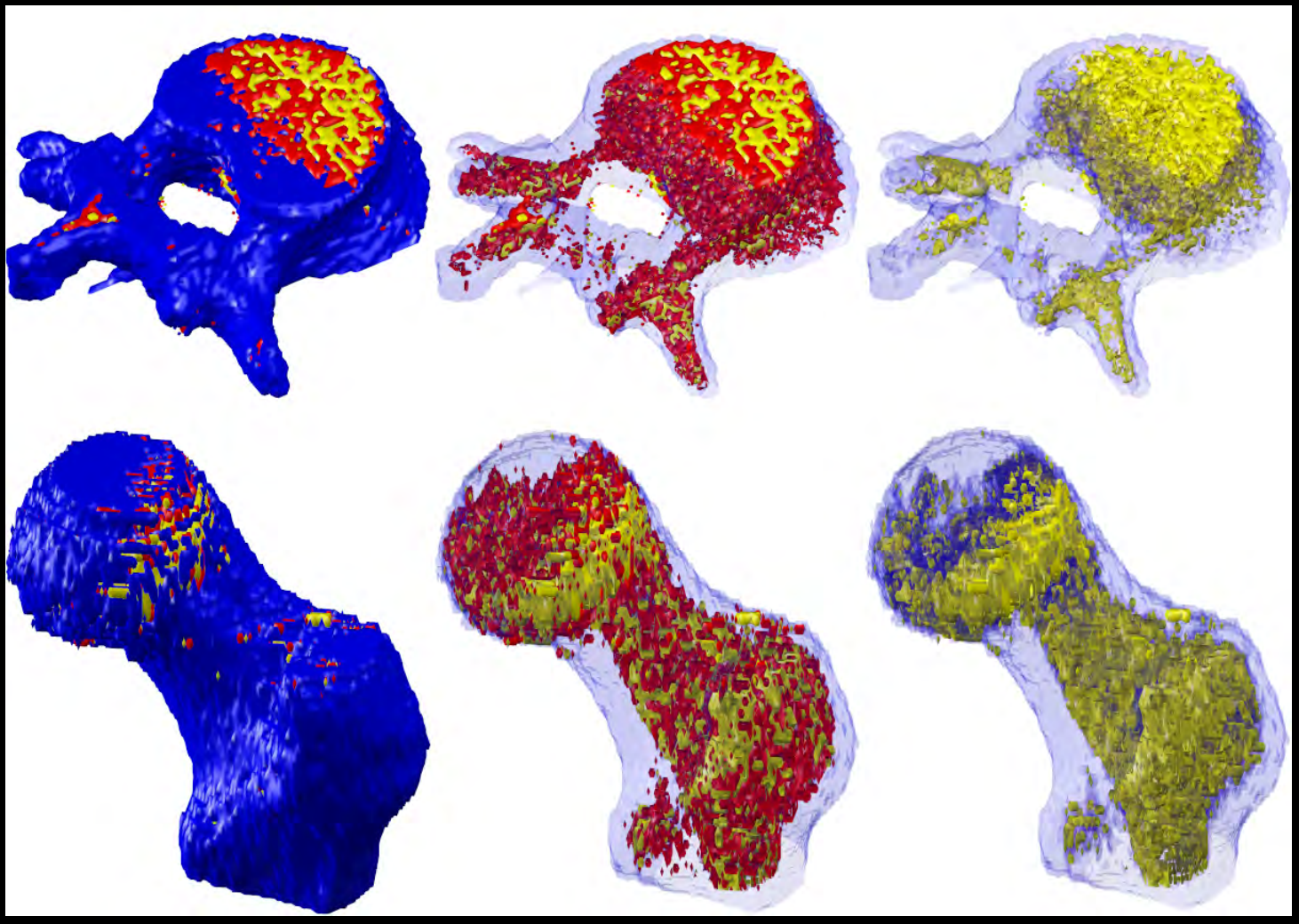
Issue 6, November 2021

ANZBMS Newsletter

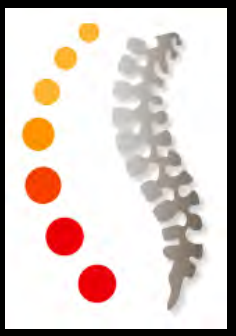


Comment from the outgoing ANZBMS President

Affiliate society - IFMRS

Member achievements

Cover image: Example of 3D visualization of CT images with different levels of transparency using Tissue Compass at the L1 (upper panels) and left hip (lower panels) level. Colours blue, red and yellow represent bone, haematopoietic bone marrow, and marrow adipose tissue, respectively. Courtesy of Mahdi Imani, Gustavo Duque, and colleagues. *(See Pg.8)*



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Welcome to ANZBMS newsletter

Welcome to the November Issue!

With the upcoming ESA-SRB-ANZBMS meeting just around the corner, it has come to that time when there is a changing of the guard, as Natalie Sims reflects on the past 2 years as she passes the presidency over to Mark Forward (Pg. 3).

Continuing our theme of highlighting ANZBMS affiliate societies, in this issue we have an informative piece about the International Federation of Musculoskeletal Research Societies (IFMRS) by Federico Moscogiuri, CEO of IFMRS.

This edition we highlight a range of ANZBMS member articles about:

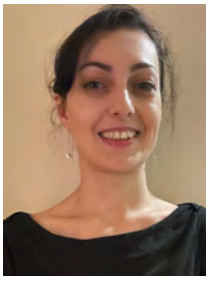
- Bone architecture following parathyroidectomey in patients with hyperparathyroidism (Pg. 7)
- Semiautomatic software for quantifying musculoskeletal tissues (Pg. 8)
- Osteoblastic glucocorticoid signalling during obesity (Pg. 9)
- Normative data for pQCT bone parameters in Australian men (Pg. 10)
- Cross-sectional study associating circulating osteoprogenitors with BMD and lean mass (Pg. 11)
- Ten year follow up on osteopenic women that received 1 or 2 doses of zoledronate (Pg. 11)

Have news to share? Want to provide us with feedback? Contact us at newsletter@anzbms.org.au

Happy reading!

Newsletter Editorial Board

ANZBMS Newsletter Editorial Board



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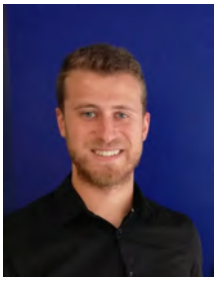


James Smith

Natalie Wee

Emma West

President's comment

Thank you from outgoing ANZBMS President, Prof Natalie A Sims

Our Annual Scientific Meeting and AGM this month marks the end of my 2 years as President of ANZBMS. What a strange 2 years it has been. Even though COVID19 has made it impossible to meet in person with ANZBMS Council, affiliates, or ANZBMS members (apart from my own laboratory and close collaborators), our society has achieved so much – you can read about all of these in the AGM papers, and our annual report which will be published after that. Here are some additional reflections as I leave the post of President.

We who make up ANZBMS are a diverse group at multiple levels. We have people primarily employed in research, in teaching, in clinical practice, and some people who are active in all three types of activities. Just as some people talk about bone as a multiscale organ, the diversity of ANZBMS also exists at multiple scales. For example, within the field of research, we have people with interest in exercise physiology, in bioarchaeology, in cell biology, in regenerative medicine, in epidemiology, in clinical trials, in genetics, in cancer biology, and in bioinformatics (just to name a few specialties). Within clinical practice we have endocrinologists, geriatricians, general practitioners, densitometrists, physiotherapists, rheumatologists and orthopedic surgeons (again, just to name a few – there are others!). Despite this diversity we have a common interest in skeletal biology and a desire to improve skeletal health.

Members of our Council and Committees all act in a voluntary capacity to make the work of ANZBMS happen, and I'm very grateful for all that has been done this year. There are very many people involved in making the activities of ANZBMS happen, including conferences, Coffee Catchups, clinical guidelines, submissions to government, newsletters, training and mentoring programmes, and grants and awards. It has been inspiring to see the hard work that many members contribute to help our society grow and change to carry out its mission. Please have a look at the lists of Council Members and Committee Members on the ANZBMS website, and take a moment to thank these individuals when you see them online at the Annual Scientific Meeting. Perhaps you may like to think about how you could become involved too!

I am grateful for the opportunity to serve the ANZBMS as President, and very thankful to all those who have contributed to the work of the society over these past two very challenging years. I end by asking you to remain involved in the society. We continue to face challenging times in both research and practice – funding is needed for our field to grow and thrive, new support from government is required for patients to receive the best treatment, and for those in clinical practice to have clear guidelines for how to provide that treatment and support. I hope that our Annual Scientific Meeting this year will provide you with the opportunities to talk with each other about what new things we can do to improve research and patient care throughout Australia and New Zealand, and that we will all be able to reflect and celebrate, in person, next year on the Gold Coast about what ANZBMS achieves in the next 12 months during Mark Forwood's first year as President.

Prof. Natalie Sims

Outgoing ANZBMS President

Affiliate Society: IFMRS

More than the sum of our parts

I always say that good things happen when you get people around a table. Throughout my years of working for various organizations, including several coalitions and alliances with a very broad and varied membership, I have only become more convinced of this fact. Most if not all of us are not simply fixated on the job at hand – we see the need to make change happen at a bigger scale, and we understand that we have a role in doing that, even if in a small way. Some of us also understand that to make change happen at scale, and achieve deep, lasting impact, we need to work together, and make common cause with those who share our aims and concerns.

That's what the International Federation of Musculoskeletal Research Societies (IFMRS) is, at heart, all about.

The IFMRS began life in 2013, out of a need shared by various organizations mainly active in the field of bone and mineral research – including the ANZBMS - to increase overall funding for research in this area. From the very beginning, however, the IFMRS was envisaged as having a much broader role than simply research funding, to include the development of a global awareness of musculoskeletal research, and the provision of opportunities for training, networking and development, through a collaborative approach. And this vision is reaffirmed today in our Purpose statement, underpinned by a set of shared Values.

Our new, 3-year Strategic Plan comprises three pillars: Network, Knowledge and Influence, each with an overarching aim and a set of focus areas. These three separate but mutually reinforcing core areas of work really capture what the IFMRS is all about: creating a space and opportunities for sharing and developing knowledge by building a diverse and genuinely inclusive global community, capable of speaking with one voice. Although our focus is research, we know that the purpose of research is ultimately to improve care and outcomes for people, and for wider society. Which is why we're also partnering with other organizations, particularly the Global Alliance for Musculoskeletal Health,to advance the cause of musculoskeletal health in the broadest sense. Their recent landmark report sets out a comprehensive strategic framework which has research & innovation as one of its pillars, and which we will play a key part in taking forward.

A big part of what we do, however, is aimed at being of direct service to individual researchers and scientists, including early career researchers. Our online learning platform for young investigators,HubLE, and our musculoskeletal data platform, the MSK Knowledge Portal, are two channels designed to facilitate the capture, interrogation and sharing of knowledge, and together make up our International Knowledge Hub. We have also published a series of online workshops from our virtual H Fleisch series earlier this year.

It's fair to say that we've grown a lot in recent years, and none more so than the last two years. Today, the IFMRS has 21 member organizations and 7 affiliate members, between them covering all continents and nearly all parts of the musculoskeletal research spectrum of activity, representing roughly 20,000 worldwide. From Australia and New Zealand alone, we have as members, in addition to the ANZBMS, ANZORS, ANZSSFR and MEPSA. We also have members from as far afield as Argentina, South Korea and Egypt. One of our greatest strengths lies precisely in our diversity.

Affiliate Society: IFMRS

So where do you, and your member societies, come in?

Firstly, we'd like as many people as possible to visit our two online platforms, HubLE and the MSK KP- use them, explore, share, make suggestions and give us your feedback. These are resources that are there to help all of you in your work, your studies and your careers, and we want you to help us make them as useful as possible to you. Also please check out our growing Virtual Library of digital resources.

And of course be sure to follow us on Twitter: @IFMRSGlobal

Finally, ANZBMS is leading by example by inviting me to write this article. As a federation, we rely on our member organizations to help us raise awareness of what we do, and how together we're working to improve musculoskeletal research in the broadest sense. Thanks, ANZBMS!

When we get together, good things happen. That's when we cease to be a collection of individuals, or societies, and something new emerges:we become more than the sum of our parts.Looking towards the future, it is clear that collaboration is the key, be it in the lab, in clinical practice or in the strategic planning underpinning the IFMRS. To quote Charles Darwin, "It is the long history of humankind (and animal kind too) that those who learned to collaborate and improvise most effectively have prevailed".

Federico Moscogiuri,

CEO, IFMRS

Meet our newest ANZBMS members

Associate Professor Dawn Coates

Affiliation: Sir John Walsh Research Institute, Faculty of Dentistry, University of Otago, Dunedin, New Zealand.

Research category: Basic research and clinical translational dental research

Research interests: I am a cellular and molecular biologist with a focus on osteogenesis and angiogenesis. I lead DEnTReneg (Dental Engineering and Tissue Regeneration) and have a focus on 3D-bioprinting and production of enriched scaffolds for bone regeneration, proteomics of stem cells, stem cell regeneration, silver nanoparticles, novel antimicrobials and new grafting materials.

What you hope to gain from joining ANZBMS? It is my pleasure to join the ANZBMS as a council member effective mid-November 2021. The ANZBMS is a cross-platform organisation and I have much to learn from specialists in this field. I look forward to meeting ANZBMS members in the future.

Connect with Dawn on ResearchGate

Member achievements

Dr Alexander Rodriguez

Monash University

2021 ASBMR Young Investigator award

Dr Ahmed Al Saedi

University of Melbourne

2021 ASBMR Fund for Research and Education Research and Collaborative Grants

Dr Jiao Jiao Li

University of Technology Sydney

Falling Walls Lab Australia 2021

2021 NHMRC Grant Recipients

Congratulations to the following ANZBMS members for receiving NHMRC Grants.

Prof Peter Croucher

Garvan Institute of Medical Research

Leadership 3: "*The Dormant Cancer Cell Life Cycle*"

Prof Allison Pettit

University of Queensland

Ideas Grant: "*Increasing hematopoietic stem cell niches post transplantation through enhancing bone marrow macrophage resilience and regeneration mechanisms*"

Dr Melissa Cantley

University of Adelaide

Ideas Grant: "*Development of a novel glucose lowering medication targeting mTORC1 in osteoblasts*"

Member publications

Ruderman I, Rajapakse CS, Xu W, Tang S, Robertson PL, Toussaint ND. Changes in bone microarchitecture following parathyroidectomy in patients with secondary hyperparathyroidism. Bone Rep. 2021 Aug 24;15:101120. doi: 10.1016/j.bonr.2021.101120.

What is the background of this study?

Chronic kidney disease – mineral and bone disorder (CKD-MBD) is almost ubiquitous in people with advanced chronic kidney disease (CKD). Development of secondary hyperparathyroidism (SHPT) as part of this disorder leads to effects on bone, involving both trabecular and cortical compartments. Parathyroidectomy, as management for severe SHPT, results in biochemical improvement in mineral metabolism, but whether there are improvements in bone microarchitecture as evaluated by high-resolution imaging modalities is not known. Magnetic resonance imaging (MRI) provides in-depth 3D assessment of bone microarchitecture, as well as determination of mechanical bone strength determined by finite element analysis (FEA), and we conducted a single-centre longitudinal study to evaluate changes in bone microarchitecture with MRI in patients with SHPT undergoing parathyroidectomy.

What did you find and what message you want readers to take away from your paper?

We determined that patients with severe SHPT requiring parathyroidectomy had persistent changes in bone microarchitecture, at least 12 months following surgery. We reported that in 15 patients (13 on dialysis, 1 kidney transplant recipient and 1 with CKD), MRI parameters at follow up were consistent with loss in trabecular and cortical bone thickness when compared to baseline pre-parathyroidectomy. Dialysis patients who underwent a kidney transplant in the follow-up period (n=7) had reduction in trabecular thickness, whereas those who continued on dialysis (n=6) had reduction in cortical thickness and mechanical bone strength on FEA.

What is an application of your finding?

High resolution MRI can be performed at the distal tibia to determine bone microarchitecture and assess trabecular and cortical parameters, as well as bone mechanical competence using FEA. Patients with SHPT undergoing a parathyroidectomy still have persisting evidence of ongoing decline in trabecular and corticalthickness despite surgical management.

Did you face any challenges during the study?

The predominant challenges of our study were (i) small sample size (reduced number of patients undergoing parathyroidectomy in an era where cinacalcet is available), (ii) number of dialysis patients transplanted over the 12-month follow-up period (which complicated bone findings given immunosuppression in this cohort), and (iii) cost of MRI scans.

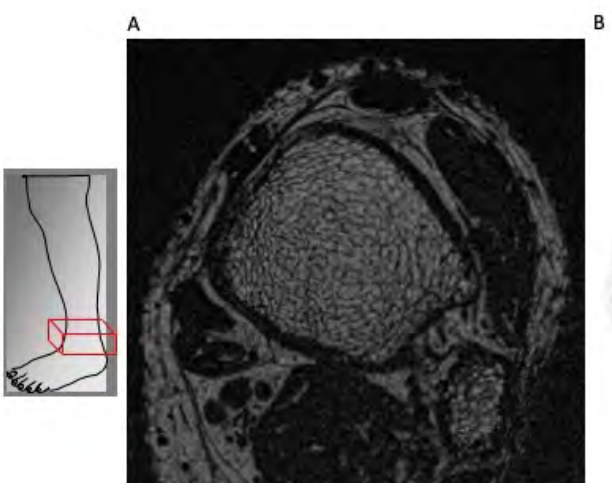


Figure: a. Anatomic site of MRI image of distal tibia and fibula**; b.** High-resolution MRI image through distal tibia showing trabecular and

Member publications

Imani M, Bani Hassan E, Vogrin S, Ch'Ng ASTN, Lane NE, Cauley JA, Duque G. Validation of a Semiautomatic Image Analysis Software for the Quantification of Musculoskeletal Tissues. Calcif Tissue Int. 2021. doi: 10.1007/s00223-021-00914-4.

What is the background of the study?

Musculoskeletal conditions such as osteoporosis and sarcopenia affect a large section of the population worldwide. Already available assessment methods for these conditions provide limited accuracy, especially for fracture prediction or muscle mass quantification. These limitations call for novel imaging techniques for diagnosis and prognosis of these diseases and their adverse outcomes.

What did you find and what message do you want readers to take away?

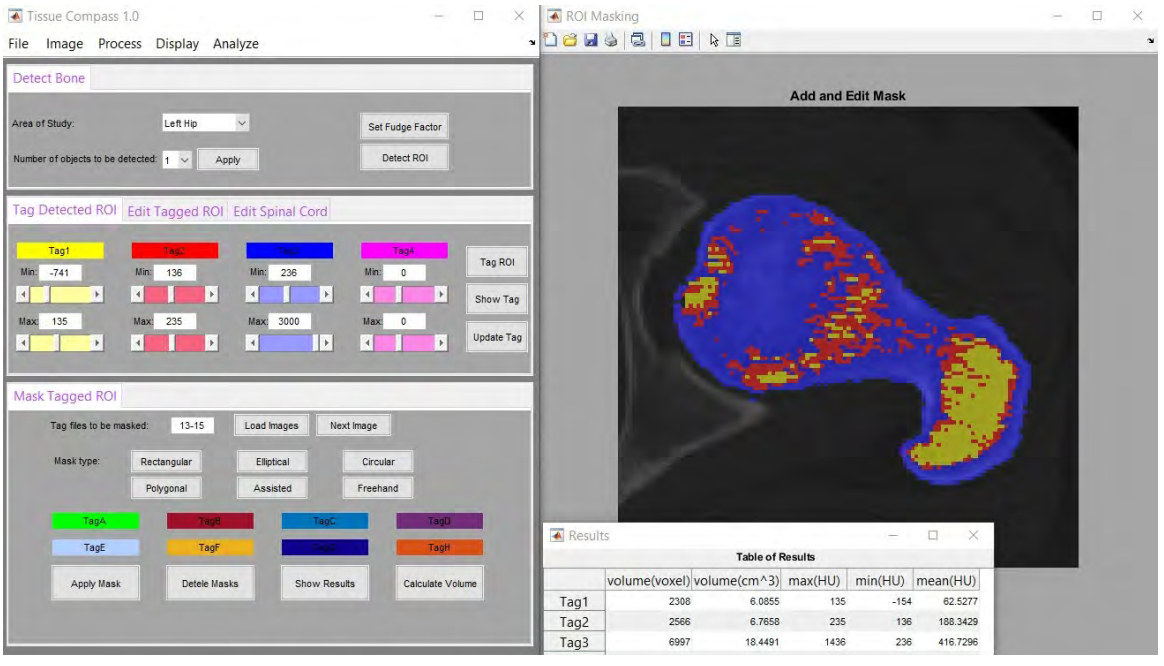
In this study, we developed semi- automatic techniques to segment and quantify muscle, intermuscular adipose tissue, bone, and marrow adipose tissue in computed tomography images of proximal hip and abdomen. This publication shows the possibility of developing novel techniques for the assessment and diagnosis of musculoskeletal conditions that go beyond bone density or lean mass while exploring other components of these conditions, such as tissue volumes and fat infiltration.

What is an application of your finding?

Using the developed software (Tissue Compass), users can analyse medical images faster and easier than already available conventional methods. Tissue Compass is currently at the research stage, and free access could be obtained via the AIMSS webpage (www.aimss.org.au). We expect that a future version can be used in clinical settings for diagnosis and prognosis purposes.

Did you face any challenges during the study?

The software's development and validation were highly dependent on analysed ground truth images. These images had to be manually analysed, which was a challenging part of this project.



Member publications

Kim S, Henneicke H, Cavanagh L, Macfarlane E, Thai L, Foong D, Gasparini S, Fong-Yee C, Swarbrick M, Seibel M, Zhou H. Osteoblastic glucocorticoid signaling exacerbates high-fat-diet-induced bone loss and obesity. Bone Res 2021. doi: 10.1038/s41413-021-00159-9.

What is the background of the study?

Chronic high- fat diet (HFD) consumption not only promotes obesity and insulin resistance, but also causes bone loss. We found that in mice, HFD feeding activated glucocorticoid signalling locally in bone, independently of circulating corticosterone concentrations. We therefore examined whether skeletal glucocorticoid signalling was necessary for HFD- induced bone loss, using transgenic mice lacking glucocorticoid signalling in osteoblasts and osteocytes (HSD2OB/OCY-tg mice).

What did you find and what message do you want readers to take away?

In WT mice, HFD induced significant bone loss which was due to deterioration of the osteocyte lacunocanalicular network (LCN), enhanced sclerostin expression and, consequently, reduced bone formation.In contrast, mice with disrupted glucocorticoid signalling in bone were protected from the deleterious effects of HFD feeding. In fact, HFD increased skeletal Wnt signalling and osteoblast activity, resulting in significantly increased bone formation (twice the rate seen in chow-fed mice). As bone formation is an energy-intensive process, skeletal glucose uptake was increased 4.5- fold in HFD- fed HSD2OB/OCY- tg mice compared to chow-fed mice.

Looking further afield, we realised that skeletal glucose metabolism contributes substantially to systemic energy homeostasis. While HFD-fed WT mice developed insulin resistance, glucose intolerance, dyslipidaemia and obesity, these features were all markedly attenuated in HFD- fed mice in which glucocorticoid signalling had been abrogated in osteoblasts and osteocytes. As both WT and HSD2OB/OCY-tg mice had identical caloric intake, our results indicate that glucocorticoid action in osteoblasts and osteocytes contributes in a major way to the negative effects of excess dietary energy intake on systemic fuel metabolism. Conversely, disruption of osteoblastic glucocorticoid signalling allows these cells to utelise excess energy form HFDs, thus attenuating insulin resistance, weight gain and, at the same time, bone loss.

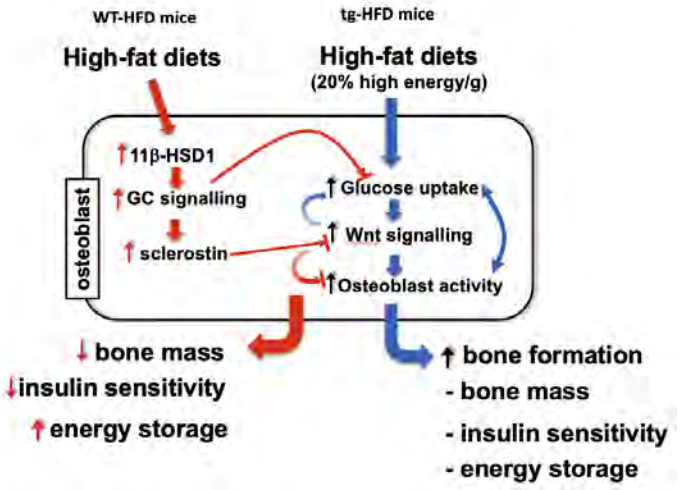
What is an application of your finding?

1) Osteoblasts and osteocytes are potential targets for the pharmacological inhibition of glucocorticoid action, e.g. via 11β-HSD1 inhibitors.

2) Bone is a major energy user in the body and activation of osteoblasts and bone formation has the potential to significantly increase energy consumption, with clear flow-on effects on systemic fuel metabolism, obesity and peripheral insulin sensitivity

Did you face any challenges during the study?

The interactions between bone and systemic fuel metabolism are complex and sometimes rather hard to untangle. It took as us a while to get most of the pieces of the puzzle together. Further research along these lines may eventually open new avenues to better understand, prevent and treat obesity and diabetes in humans.



Member publications

Anderson KB, Tembo MC, Sui SX, Hyde NK, Rufus PG, Pasco JA,Kotowicz MA, Holloway-Kew KL. Normative data for peripheral quantitative computed tomography (pQCT) bone parameters in Australian men. Bone Reports 2021;15:101107. doi: 10.1016/j.bonr.2021.101107.

What is the background of the study?

With an ageing population, the significant burden of fragility fractures on individuals, the community and the healthcare system is increasing. Current methods for assessing bone strength and quality such as bone mineral density (BMD) alone or in combination with clinical risk factors provide an indication of individual fracture risk, but are unable to discriminate well on a population level. This is particularly true when considering comorbid conditions such as type 2 diabetes mellitus or medication exposures such as glucocorticoids that alter the relationship between BMD and fracture risk. An alternative technique, pQCT, may be able to improve fracture discrimination. In this study we aimed to develop normative data for pQCT measures at the radius and tibia based on a population-based sample that can be used clinically for comparative purposes

What did you find and what message do you want readers to take away?

We measured pQCT in 508 men, aged 33-96 years, as part of the Geelong Osteoporosis Study (GOS). The GOS is a cohort study with participants randomly selected from the electoral roll, and not selected on the basis of disease. We found variation by age in a number of pQCT values, including bone area, bone density and cortical bone thickness at both the radius and tibia, suggesting that these measures may capture age-related declines in bone health.

What is an application of your finding?

As our participants were not selected on the basis of disease, our data can provide an Australian reference point for other investigators as well as for clinical use. We hope that as the accessibility of the pQCT device in clinics across Australia improves, our data may play an integral role in these areas.

Did you face any challenges during the study?

There are always some challenges when it comes to undertaking an epidemiological study such as this. For example, recruiting and retaining a cohort of men in a health study is very important but can be challenging. In the GOS, we have been successful at engaging our returning men with the study, even when unforeseen circumstances such as the COVID-19 pandemic added extra barriers to participation. We also had some machine malfunctions that set us back many weeks during data collection. The pQCT device is made in Germany, and there's only one technician in Australia, so when we had an inevitable breakdown of the device, it took a long time to diagnose our issue and get our amazing technician out to fix the problem.

A GOS participant undergoing pQCT scanning during the 15-year follow-up

Member publications

Feehan J, Smith C, Tripodi N, Degabrielle E, Al Saedi A, Vogrin S, Duque G, Levinger I. Higher Levels of Circulating Osteoprogenitor Cells Are Associated With Higher Bone Mineral Density and Lean Mass in Older Adults: A Cross-Sectional Study. J Bone Miner Res Plus 2021. doi: 10.1002/jbm4.10561.

What is the background of the study?
Circulating osteoprogenitor (COP) cells are a relatively newly described population of cells in the peripheral blood, with some capacity for mineralization. There has been some preliminary evidence tying their number to states of bone pathology, but no direct investigation into their relationships with bone mineral density (BMD) and body composition, or their capacity to identify those with osteoporosis. We hypothesized that if they have some role in the maintenance of bone mass, they may have potential as a biomarker for osteoporosis.

What did you find and what message do you want readers to take away?

The study found that COP cells were strongly associated with femoral neck, and total body BMD, as well as some relationship with appendicular lean mass. They were also a high performing biomarker for osteoporosis of both the femoral neck and total body, with more than 80% sensitivity and specificity. While these findings must be validated in larger studies, they provide important proof of concept to inform future research and development.

What is an application of your finding?
Our study could pave the way to a screening blood test for osteoporosis, which could aid early detection and intervention in osteoporosis. The associations with bone and muscle mass may also hint at therapeutic applications for the cells, however further research is required to develop this.

Did you face any challenges during the study?
Running clinical studies in the time of COVID-19 has been difficult, particularly with a metropolitan Melbourne hospital as a primary study site. We were fortunate to have an excellent team who took rapid action to ensure the study could be completed, in a way that ensured the safety of the participants and staff.

Grey A, Bolland MJ, Horne A, Mihov B, Gamble G, Reid IR. Bone Mineral Density and Bone Turnover 10 Years After a Single 5 mg Dose or Two 5-Yearly Lower Doses of Zoledronate in Osteopenic Older Women: An Open-Label Extension of a Randomized Controlled Trial. J Bone Miner Res. 2021 Sep 29. doi: 10.1002/jbmr.4453.

What is the background of the study?
Intravenous zoledronate reduces fracture risk (5mg at 18mo intervals) and prevents bone loss (doses of 1-5mg for 3 to >5y), but the duration of action of a single 5mg dose and the effects of lower doses beyond 5 years are unknown.

What did you find and what message do you want readers to take away?
Both a single baseline 5mg dose of zoledronate and 5-yearly doses of 1mg and 2.5mg zoledronate prevented bone loss at hip and spine for 8-10 years in older postmenopausal women. Clinical trials to evaluate the effects on fracture risk of these very infrequent and lower doses of zoledronate are justified.

What is an application of your finding?
Clinical trials to evaluate the effects on fracture risk of very infrequent and lower doses of zoledronate are justified.

Did you face any challenges during the study?
Conducting clinical studies of 10 years duration presents logistical and organisational challenges, including maintaining participant retention.

Member publications

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Calendar of Events and Webinars

AUSTRALIAN & NEW ZEALAND

ESA-SRB-ANZBMS Annual Scientific Meeting
21 - 24 November 2021
Melbourne
More information here

Australasian Paediatric Endocrine Group - Annual Scientific Meeting
22-23 November 2021 (Virtual)
More information here

Australasian Biomechanics Conference
6-7 December 2021 (Virtual)
More information here

INTERNATIONAL

10th International Conference on Children's Bone Health
Abstracts due: 15 February 2022
More information here

ASBMR Webinar Series
Monthly webinars
More information here

ECTS 2022
7-10th May 2022 (Helsinki, Finland)
Abstract submission closes 11th Jan 2022
More information here

ECTS Webinar Series
More information here

IO - ASBMR Rare Bone Disease TeleECHO
Delivered virtually the first Thursday of each month 1500 EST
More information here

OI Foundation Osteogenesis Imperfecta TeleECHO clinic series
Delivered virtually the second Wednesday of each month 15:00 hours EST
More information here