



University of Sheffield



The Mellanby Centre

The University of Sheffield's Medical School has a strong track record in basic, translational and clinical musculoskeletal research (<https://www.sheffield.ac.uk/mellanby>). The recent era began with the establishment of the Department of Chemical Pathology in 1974 by Professor Jack Martin and continued as the Department of Human Metabolism and Clinical Biochemistry under the leadership of Professor Graham Russell for 25 years to 2001. Its standing in musculoskeletal research is best illustrated in an independent assessment by Evidence Ltd, which ranked the University of Sheffield top in the UK (www.evidence.co.uk). Internationally, we are the second most highly cited institution for osteoporosis from 1990 to 2019 (<https://pubmed.ncbi.nlm.nih.gov/32935223>)

The Medical School is unique in the UK and one of only a limited number of institutes worldwide, where clinical research interests in musculoskeletal research span skeletal diseases of childhood through to the elderly person, and cover both benign and malignant bone disease, disease of the joint and spine, including osteoarthritis, intervertebral disc degeneration. Our clinical research for example, is in the metabolic bone diseases such as osteoporosis, childhood bone diseases (including osteogenesis imperfecta and osteopetrosis) in the tumour-induced bone diseases such as multiple myeloma and metastatic bone disease (breast and prostate bone metastases), the related topic of tumour microenvironment and in osteoarthritis, rheumatoid arthritis and conditions of the spine.

The Mellanby Centre for Musculoskeletal Research is a key component of the Arthritis Research/Medical Research Council Centre for Musculoskeletal Ageing (CIMA, <http://www.cimauk.org/>) and the Paget's Disease Centre of Excellence.

Our clinical research is underpinned by a world-class programme of basic biomedical research, which has been further strengthened by continued investment. This includes the newly refurbished Henry Wellcome Laboratories in the Medical School and two 'core' laboratories. one for 'musculoskeletal biochemistry' and the other for bone analysis called skelet.AL, each of which are supported by full time technicians. These laboratories contain the latest automated immunoassay analysers and 'state of the art' high resolution microCT imaging equipment and the equipment and expertise for undertaking quantitative dynamic bone histomorphometry. For clinical research, we have the NIHR funded Clinical Research Facility, which has state of the art bone imaging such as high resolution peripheral computed tomography. Few institutes in the UK or Europe have such well-established core facilities. The University has recognised our pre-eminence in this field and has created the Mellanby Centre for Musculoskeletal Research. The Centre is being directed by Professor Richard Eastell.

The Centre will undertake to:

- Establish a focus for musculoskeletal research at the University of Sheffield called the 'Mellanby Centre for Musculoskeletal Research' (MCMR)
- Foster the development of inter-disciplinary research across the University of Sheffield
- Develop collaborative research programmes and grant applications within the MCMR
- Position the MCMR to apply for externally funded Centre status
- Develop our links with the pharmaceutical and biotechnology industry
- Widen the profile of musculoskeletal research at the University of Sheffield

Professor Richard Eastell MD, FRCP, FRCPath, FMedSci

Professor of Bone Metabolism, Division of Clinical Medicine, University of Sheffield; NIHR Senior Investigator; Director, Mellanby Centre for Musculoskeletal Research

Understanding the causes of bone diseases and improving their treatment



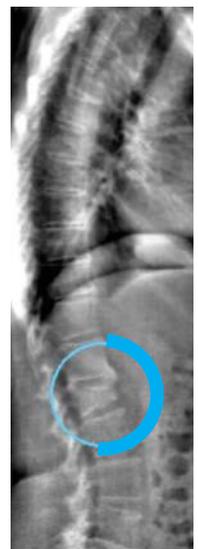
Professor Eastell graduated in Medicine from Edinburgh University in 1977 and trained as an endocrinologist in Edinburgh, London (Northwick Park Hospital) and the USA (Mayo Clinic) before coming to work in Sheffield in 1989. Currently the head of the Academic Unit of Bone Metabolism, he was awarded funding from the National Institute for Health Research (NIHR) in April 2008 to set up the Sheffield Biomedical Research Unit (BRU) in Bone Diseases and has since been appointed as an NIHR Senior Investigator. Professor

His work has been recognised by the Philippe Bordier Award (2012) (European Calcified Tissue Society), Frederic C Bartter Award 2014 and William F Neuman Award 2023 (American Society for Bone and Mineral Research), Kohn and Linda Edwards Awards from the Royal Osteoporosis Society (2004, 2018), the Clinical Endocrinology Trust Award from the European Society for Endocrinology (2020) and the Dent Lecturer from the Bone Research Society (2021). He has authored or co-authored over 300 papers on osteoporosis and related topics and is also Senior Editor for the journal Bone and a member of the editorial board of Osteoporosis International. Richard is Past President of the European Calcified

Tissue Society and Bone Research Society and Past Chairman of the National Osteoporosis Society.

Well known for his work on biochemical markers of bone turnover and the definition of osteoporotic vertebral fractures, Richard's research interests are also wide ranging. He leads an active group that conducts research into all aspects of osteoporosis, funded by the NIHR, MRC and Versus Arthritis and in collaboration with important international research groups, such as the Universities of Kiel (Germany) and California, San Francisco (USA) and the Mayo Clinic (USA). The main foci of Richard's current research include anabolic treatments for osteoporosis, novel tests for bone turnover markers and biomechanics of hip and spine fracture.

Vertebral fracture in the lumbar spine resulting from osteoporosis.



Professor Janet Brown MB BS, MSc, MD, FRCP

*Professor of Translational Medical Oncology, Division of Clinical Medicine,
University of Sheffield*

Understanding the impact of cancer on the skeleton and optimisation of prevention and treatment strategies



As a clinician scientist, Janet's research is both lab-based and clinically-based and is focused on the effects of cancer on the skeleton, including the development, prevention and treatment of bone metastasis and the skeletal impact of cancer treatments. Her laboratory group is focused on proteomics, genomics and other approaches to develop biomarkers to predict risk of bone metastasis and response to treatment, in the context of understanding the biological mechanisms by which bone metastasis develops, especially in breast cancer.

Her clinical practice includes breast, prostate and renal cancers, all of which are associated with bone metastasis and she runs a range of clinical trials (Phase I, II and III), as national Chief Investigator or as local

Principal Investigator, focusing especially on bone-targeted agents and their combination with other novel therapies. Within the Mellanby Centre, she has special expertise in the assessments of bone endpoints in clinical studies of new anti-cancer agents and the measurement and interpretation of bone turnover markers, with several ongoing collaborations with other UK centres.

Janet has published around 100 papers in peer-reviewed journal and 200 abstracts. Her research is funded by Cancer Research UK, NIHR, Yorkshire Cancer Research, Weston Park Cancer Charity, Breast Cancer Now and Prostate Cancer UK.

Dr Paul Arundel

Consultant in Paediatric Metabolic Bone Disease, Sheffield Children's NHS Foundation Trust

Improving care and outcomes for children and families affected by rare bone diseases



Dr Paul Arundel has been the lead consultant for the service for children with bone disease at Sheffield Children's Hospital since 2011. His work encompasses the delivery and improvement of care to children and young people with a wide range of rare bone diseases through collaboration and multidisciplinary team working. He enjoys close links with co-located colleagues in orthopaedics, spinal surgery, neurosurgery, genetics and radiology as well as with partners in the Mellanby Centre for Bone Research.

Clinical activity and research interests extend to a wide range of skeletal disorders in childhood. Sheffield is one of four centres in England commissioned to provide care for children with complex childhood osteogenesis imperfecta and one of three paediatric centres able to prescribe asfotase alfa (recombinant alkaline phosphatase) to children with severe, childhood-onset hypophosphatasia. Alongside "general" clinics for children with known or suspected bone disease, he runs paediatric clinics dedicated to achondroplasia and other skeletal dysplasias, and to disorders of mineralisation.

He is local principal investigator for a number of

commercially-sponsored clinical trials and open-label extension drug studies in children with achondroplasia, including one of a small molecule CNP agonist, and another of a small molecule specific tyrosine kinase inhibitor. He was previously involved in the early phase trials of asfotase alfa that led to its licensing and adoption into NHS practice, a clinical trial of denosumab in childhood osteogenesis imperfecta, and both placebo-controlled and dose-ranging studies of risedronate. He is a local investigator for commercially-sponsored natural history and registry studies of children with achondroplasia, X-linked hypophosphataemic rickets and hypophosphatasia.

He is a member and former secretary of the British Paediatric and Adolescent Bone Group, a network which includes most of the clinicians and researchers from across the UK and Ireland with an interest in children's bone disease and health. He works with patient groups including the Brittle Bone Society. He currently serves as chair of the Highly Specialised Technology Evaluation Committee of the National Institute of Health and Care Excellence, having served as a committee member since 2018.

Dr Meena Balasubramanian MBBS, DCH, FRCPCH, MD

Senior Clinical Lecturer, Division of Clinical Medicine, University of Sheffield; Honorary Consultant Clinical Geneticist, Sheffield Children's NHS Foundation Trust

Understanding genetic aetiology and phenotypic variability in bone fragility and translational biology of bone disease



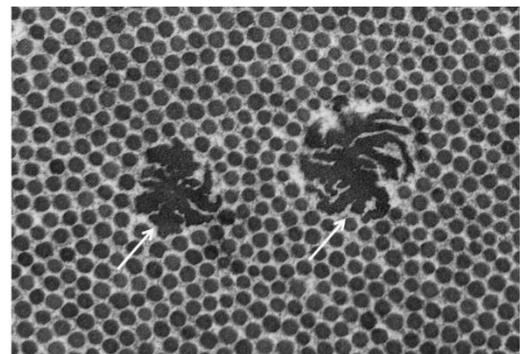
Dr Balasubramanian completed her Paediatric training before undertaking specialist training in Clinical Genetics in Southampton and Sheffield. Her MD is on atypical presentation of Osteogenesis Imperfecta (OI) obtained from the University of Sheffield in 2012, where Meena is now a Senior Clinical Lecturer in Musculoskeletal Genetics. She has been a Consultant in Clinical Genetics at Sheffield Children's Hospital since 2012 and provides genetics input to the national OI service, seeing patients referred across UK. She has led several projects focused on genetics of OI and is pursuing research projects focussed on identifying novel genetic causes in OI and exploring newer targets for therapy for OI. Meena has been the Clinical Director for Research at Sheffield Children's Hospital since 2023 and oversees a diverse portfolio of clinical research.

Meena is the Founding Director of and Rare Disease lead for South Yorkshire Children and Young People's Health Research (SCYPHeR), a collaboration between University of Sheffield, Sheffield Children's Hospital and Sheffield Hallam University. SCYPHeR aims to empower the next generation of child health researchers and create a more collaborative approach to research in the region.

Meena's research interests include in-depth phenotyping of rare bone diseases through skin and bone tissue analyses combined with detailed clinical phenotyping and molecular genotyping. Advances in genomic medicine has led to increased use of next generation sequencing to identify new candidate genes and explore their phenotypic associations. Meena is the Bone fragility lead for the Genomic Clinical Interpretation Partnership (GeCIP), which is part of the 100,000 Genomes project initiative to establish genetic causes of rare as diseases in UK. She works across faculties in Sheffield, including projects with INSIGNEO on digital disease phenotyping as well identifying new targets for treating bone fragility in industry. She

has close links with clinicians in other regional metabolic and genetic centres and patient support groups including Brittle Bone Society. Several of Meena's research outputs have led to changes in diagnostic and clinical practice in rare bone diseases and neurodevelopmental disorders.

Meena's other areas of specialism include Genetics in autism & Paediatric Dysmorphology. She has published over 40 first and senior-author publications in these areas and text books including a recent molecular medicine series on OI. In total, Meena has published 128 original peer reviewed articles and has an h-index of 28.



Electron microscopy image from skin biopsy of a patient with OI demonstrating collagen flowers

Dr Pinaki Bhattacharya

Lecturer in Solid Biomechanics, Division of Clinical Medicine, University of Sheffield and the Insigneo Institute for in silico Medicine

Understanding mechanisms of bone disease progression across space and time scales



Dr Pinaki Bhattacharya lectures in the Department of Mechanical Engineering at the University of Sheffield. He is also a member of the Insigneo Institute for in silico Medicine – a unique collaboration between the Sheffield Teaching Hospitals NHS Foundation Trust and the University of Sheffield. Pinaki obtained his PhD in biomechanics (2012) from Purdue University (West Lafayette, USA) and undertook post-doctoral research in biomechanics at KU Leuven (Leuven, Belgium) and the University of Sheffield (UK). Earlier, he studied and worked in India, obtaining his first degree in engineering from IIT Kharagpur, followed by industry and academic experiences in computer-aided engineering.

Presently, Pinaki is interested in developing mechanistic theories that explain the progression of

bone diseases such as osteoporosis. These "multiscale theories" integrate disease characteristics (and its determinants) from regions of space and time that are vastly different in scale, such as microscopic changes in bone morphology occurring over months and whole body movements occurring over a few minutes of walking. Pinaki is equally interested in developing clinical tools that leverage these theories in medical practice: be it to predict the risk of disease in a patient-specific manner, or to determine the efficacy of an intervention, or to design novel multifactorial interventions tailored to a group of patients. As such, this research is central to the mission of the Insigneo Institute, that is to produce a transformational impact on healthcare. Pinaki's work on the complexity of bone disease progression is supported by the EPSRC and EU H2020 programme.

Professor Nick Bishop MB, ChB, MRCP, MD, FRCPCH

Professor of Paediatric Bone Disease, Division of Clinical Medicine, University of Sheffield; Director of the Children's Clinical Research Facility

Understanding the causes of bone fragility in children and improving treatment for children with disabling bone diseases



The UK's only Professor of Paediatric Bone Disease. Trained in Manchester (clinical), Cambridge (MRC and Wellcome Fellowships) and Montreal (visiting Professor at McGill). Appointed to Chair in Sheffield in 1998. Clinical research group focused on treatment of childhood bone fragility and rare bone diseases; basic science group on early life events and skeletal development, as well as pathophysiology of childhood bone diseases.

Nick's main interest is in the causes and treatment of bone fragility in children. His work has shown that in mild osteogenesis imperfecta (OI), oral bisphosphonate therapy can reduce fracture risk by as much as 50%; he is now working with European partners, funded by Horizon Europe

as part of the drug repurposing Consortium REMEDI4ALL, to assess the potential of losartan to inhibit the TGF-beta signalling pathway in osteogenesis imperfecta. He is global chief investigator for two pharma-sponsored studies in children and young adults with OI, and remains an Associate Director of the Experimental Arthritis Treatment Centre for Children. He continues to collaborate with colleagues in Southampton and Oxford to try and understand the effects of early life interventions with vitamin D.

He was awarded Honorary Fellowship of the Royal College of Paediatrics and Child Health for his contributions to Science and Research in Paediatrics during his time as Vice President for Science and Research there.

Professor Ashley Blom MBChB, MD, PhD

Vice President and Head of the Faculty of Medicine, Dentistry and Health

Optimising joint replacement



Professor Ashley Blom joined the University of Sheffield as the new Vice-President and Head of the Faculty of Health in 2023 from Bristol where he was the Head of the Bristol Medical School. Ashley is an Orthopaedic surgeon whose research covers a broad range of basic science and applied methodologies primarily focussing on arthroplasty. He is part of the team that holds the contract to analyse the National Joint Registry, the largest arthroplasty database in the world. Ashley is an NIHR Senior Investigator, Fellow of the Academy of Medical Sciences and past President of the European Orthopaedic Research Society.

Research Interests

Arthroplasty, particularly hip and knee replacement.

Research Group Members

Ashley collaborates with a diverse group of clinicians and methodologists nationally and internationally.

Teaching Interests

Musculoskeletal conditions.

Professional activities

Arthroplasty surgeon at Sheffield Teaching Hospitals.

Dr Andy Chantry MB ChB, MRCP

Consultant Haematologist, Sheffield Teaching Hospitals NHS Foundation Trust; Honorary Senior Lecturer, University of Sheffield

The use of bone anabolic agents in myeloma bone disease



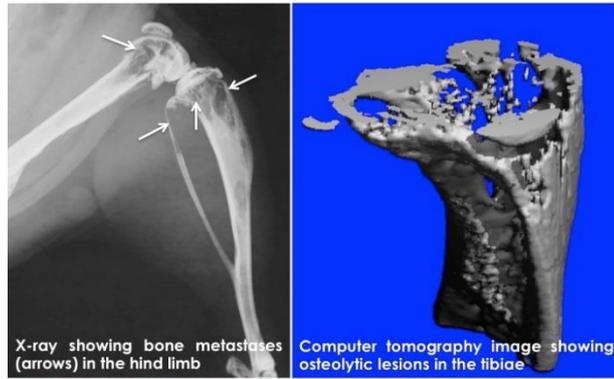
Dr Andy Chantry is an Honorary Senior Lecturer in the Division of Clinical Medicine, University of Sheffield and leads the Sheffield Myeloma Research Team (SMaRT). He is also a Consultant Haematologist in the Department of Haematology, Sheffield Teaching Hospitals NHS Foundation Trust. Nationally, he is an executive member of the United Kingdom Myeloma Research Alliance (UKMRA), through which all significant UK Myeloma Clinical Trials are designed and developed. He is also an executive member of the United Kingdom Myeloma Forum, the national body for Haematologists with a special interest in myeloma leading clinical and research led developments in the UK. He is a member of the UKMF National Guidelines Group with a special interest in myeloma bone disease. Locally, he is an executive member of the local Cancer Clinical Trial Executive Committee and a member of the Sheffield Experimental Cancer Medicine Centre. He is an executive member of the Mellanby Centre for Bone Oncology and a member of Insigneo, the Centre for *in Silico* Medical Research.

His principal research interests are anabolic strategies in the treatment of myeloma bone disease and novel strategies to target myeloma tumour. Anabolic targets include components of the Wnt signalling pathway and the TGF- β signalling pathway in combination with both standard anti-resorptive strategies (zoledronic acid) and novel bisphosphonates. Novel anti tumour strategies include targeting the quiescent myeloma cells that remain after chemotherapy has been administered and patients enter plateau phases during which time it is hypothesized that quiescent myeloma cells reside in protective niches within the bone marrow micro-environment. His research team are modelling this putative niche, attempting to disrupt the niche and the array of adhesion molecules thought to bind quiescent myeloma cells to other cellular components of the niche and thus target the previously protected myeloma cells using conventional and novel chemotherapies and also including adapted viral therapy. Since appointment in 2012, he has been awarded over £2million in research grants notably from Bloodwise (formerly Leukaemia and Lymphoma Research).

Professor Philippe Clezardin BSc, MSc, PhD, DSc

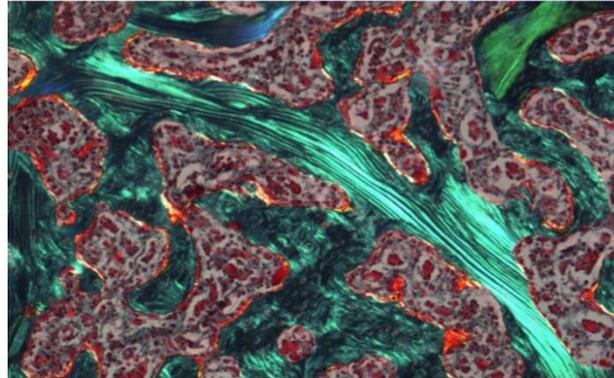
Honorary Professor, Division of Clinical Medicine, University of Sheffield

Understanding molecular mechanisms governing breast cancer cell colonization in the bone marrow and development of novel biomarkers for the identification of patients who are at risk of developing bone metastases



X-ray showing bone metastases (arrows) in the hind limb

Computer tomography image showing osteolytic lesions in the tibiae



Osteoblastic bone metastasis (mineralized bone is stained green, osteoid lining the bone surface is stained orange and tumour cells in the bone marrow are stained red) (courtesy of JP Roux, INSERM, Lyon, France).

Professor Philippe CLEZARDIN graduated with a PhD in Biochemistry from the University of Lyon, France, in 1983. He completed a postdoctoral training at the Medical Research Council / Scottish National Blood Transfusion Center in Edinburgh (1984-1986). Philippe was then appointed as Research Scientist at INSERM (National Institute for Health and Medical Research) in 1987. He undertook a sabbatical (1990) as visiting scientist at the Ottawa General Hospital (Ottawa, Canada). On returning in Lyon in 1991, he obtained his DSc from the University of Lyon and became Senior Research Scientist at INSERM. He is now Research Director at INSERM and, since 2011, head of the INSERM Research Unit UMR_S1033 entitled: "Pathophysiology, Diagnosis and Treatments of Bone Diseases" (<http://www.lyos.fr>) in Lyon, France. Before that he was head of the INSERM Research Unit UMR_S664 entitled: "Mechanisms and Treatments of Bone Metastases" (2005-2010) and Director of the Federative Research Institute "IFR62" entitled: "Cancer, Nutrition and Metabolism" (14 laboratories, circa: 500 people; 2007-2010).

For the past twenty years, Philippe's main research interest is in the characterisation of molecular mechanisms that drive bone metastasis formation in breast cancer, with the goal of developing new biomarkers and anticancer therapies. He has authored 135 publications with over 6000 citations, and contributed to about 15 chapters in textbooks on cancer research (Web of Science June 2016, *h-index*: 45). Philippe is Associate Editor of BoneKEy Reports (Nature Publishing Group) and a member of the editorial board of the Journal of Bone Oncology (Elsevier). Philippe is Past President of the Cancer and Bone Society. He has been engaged, as academic partner or coordinator, in several European projects within the framework of FP6, FP7 and H2020 research programmes [MetaBre (2004-2007), PROMET (2006-2010), BONE-NET (2011-2014), miROMeS (2016-2017)]. In this respect, he received a European Star Award (Paris, France, 2015) for the coordination of Marie Curie ITN project BONE-NET.

Mr Ashley Cole FRCS (Tr & Orth), DM

Consultant Orthopaedic Spine Surgeon, Sheffield Children's & Northern General Hospitals, Sheffield



Mr Ashley Cole is a Consultant Orthopaedic Spine Surgeon working at Sheffield Children's and Northern General Hospitals, Sheffield from 2003. Since 2005 the Sheffield Spinal Centre has trained many Spinal Fellows in adult and paediatric spinal surgery, equipping them with the skills they need to be Spinal Consultants.

Whilst on the British Association of Spine Surgeons (BASS) Executive between 2010 and launch in 2012, Ashley co-developed the British Spine Registry (BSR) with Mr Lee Breakwell which collects patient reported outcome and experience measures on patients having spinal surgery in the UK. In July 2024, there are over 300,000 patients on the BSR. He became the first Chair of a British Orthopaedic Association group developing the newer Orthopaedic Registries (TORUS) and has re-joined the BASS Executive as BSR Lead (2023-2027).

Since 2005, he has been the Spinal Chair of the Orthopaedic Expert Working Group advising the NHS on spinal coding, healthcare resource groups and tariff. After being a member of the last NHS Spinal

Taskforce in 2010/11, he became Chair of the Spinal Services Clinical Reference Group advising NHS England on commissioning specialised spinal surgery and spinal cord injuries. During this role between 2012 and 2019, a national service specification for specialised spinal surgery was introduced and Regional Spinal Networks were developed. Ashley was President of the British Scoliosis Society from 2021-2023.

Since 2019 Ashley has returned to clinical research in spinal surgery and is currently Chief Investigator of the NIHR HTA funded Bracing Adolescent Idiopathic Scoliosis (BASIS) study, a multi-centre RCT comparing full-time versus night-time bracing. He is also a co-applicant on the NIHR HTA funded PRAISE trial (Pain Relief After Instrumented Spinal surgery) evaluating the effectiveness of erector spinae block, intra-thecal opiates and usual care in instrumented lumbar spine fusion and the FORENSIC trial (FusiOn verSus bEst coNServative Care) evaluating the clinical and cost-effectiveness of lumbar fusion surgery for patients with persistent, severe low back pain. He is leading new research looking at the data in the British Spine Registry.

Emeritus Professor Robert Coleman MBBS, MD, FRCP, FRCPE

Professor of Medical Oncology, University of Sheffield

Development of new strategies for the prevention and treatment of
cancer induced bone disease



Professor Robert (Rob) Coleman is Emeritus Professor of Medical Oncology in the Division of Clinical Medicine at the University of Sheffield. He graduated in medicine from King's College Hospital Medical School in 1978 and trained in London and Edinburgh before moving to Sheffield in 1991, where he was instrumental in developing clinical cancer research in the city and establishing an internationally respected bone oncology research team in Sheffield.

Since the mid-1980s his main research interest has been in cancer induced bone disease especially, but not exclusively, with relevance to breast cancer. His research in this area has included a range of clinical aspects of care, the development of bone targeted agents in oncology, evaluation of bone markers in oncology to aid drug development and provide both prognostic and predictive information in the management of metastatic bone disease, and the assessment of adverse effects of cancer treatments on bone health and evaluation of various treatment strategies.

Professor Coleman was Director of the Cancer Clinical Trials Centre for many years and has held multiple leadership roles within the University and the National Institute for Health Research (NIHR) Cancer Research Network. He has published over 460 peer-reviewed manuscripts and numerous book chapters. He is a past-president of the Cancer and Bone Society and the founding editor of "Journal of Bone Oncology", the only journal specifically devoted to this area of medical research and clinical practice.

In 2017 Rob retired from clinical practice and his formal appointment within the University of Sheffield. He continues as an advisor and mentor and remains research active in an emeritus position. This involves lecturing at a range of international meetings, developing medical education programmes for independent medical education providers, advising a range of pharmaceutical companies on phase II/III drug development, and sitting on both academic and pharma-led trial steering committees.

Professor Enrico Dall'Ara PhD

Professor of Musculoskeletal Biomechanics, Division of Clinical Medicine, University of Sheffield

Characterisation of biological tissues with experimental, imaging and computational tools

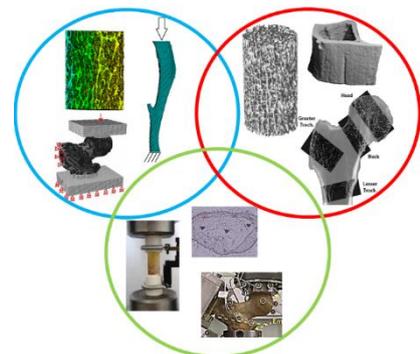


Professor Enrico Dall'Ara holds a Mechanical Engineering degree from the University of Bologna and a PhD in Biomechanics from the Vienna University of Technology. Just after his PhD (2012) he was awarded an Intra-European Marie Curie postdoctoral Fellowship to join the Insigneo Institute at the University of Sheffield and in 2015 he started his independent academic career at the Division of Clinical Medicine. In 2024 he became Professor of Musculoskeletal Biomechanics.

Enrico is Research Director of Insigneo (Computational Modelling research theme) and directs the Skeletal analysis laboratories, working on novel imaging and computational models for preclinical and clinical applications in musculoskeletal research. He is current the President of the European Society of Biomechanics (2024-2026).

His main research interests are bone mechanics, developments of validation and calibration studies for *in silico* models at different dimensional scales, and predictive models of bone adaptation. He has

published more than 110 papers, contributed to more than 180 abstracts at international conferences and secured more than £4m apportioned research income mainly from UKRI and EU. In particular, in 2024 he was selected for an EU ERC Consolidator award that has been funded by EPSRC EU Guarantee scheme to work on the "Virtual Mouse and Human Twins for optimising Treatments for Osteoporosis (VHMTs-OP)" project.



Ms Sarah Davis MPhys

Health Economics Lead, University of Sheffield

Cost-effectiveness modelling, technology appraisal and clinical guideline development



Sarah graduated with a Masters in Physics from the University of Oxford in 2003. Her work in the field of osteoporosis began in 2004 when she took up a graduate placement position as an Operational Researcher at the University of Sheffield. Here she used the Sheffield Osteoporosis model, developed by Professor Matt Stevenson, to conduct a cost-effectiveness analysis to inform national guidance on treatments for osteoporosis in postmenopausal women on behalf of the National Institute for Health and Care Excellence (NICE). She also collaborated with Professor Kanis and Professor Stevenson on a National Institute for Health Research (NIHR) Health Technology Assessment (HTA) funded report on the treatment of glucocorticoid-induced osteoporosis.

She is currently a Senior Research Fellow in Health Economics at the Sheffield Centre for Health and Related Research (SCHARR) where she is a member of the SCHARR Technology Assessment Group (SCHARR-TAG). In 2015, she was the project lead for SCHARR-TAG on the NICE Technology Appraisal of bisphosphonates to prevent fragility fracture. One of

the aims of this appraisal was to provide a link between fracture risk assessment using online tools such as QFracture and FRAX, and thresholds for cost-effective treatment. For this appraisal, she developed a new Sheffield Osteoporosis model for estimating the cost-effectiveness of bisphosphonates at varying levels of fracture risk whilst taking into account the variety of different risk factor combinations that may result in a particular risk score. She used a flexible discrete event simulation methodology which facilitates the simulation of a diverse population with varying patient characteristics and allows for an individual's characteristics and clinical history to influence their pathway through the model. This model was later adapted in 2018 for the NICE technology appraisal of non-bisphosphonates. She also acted as project lead for SCHARR-TAG on a NICE appraisal of abaloparatide in 2024. Sarah has an ongoing research portfolio of osteoporosis related work funded by the NIHR, industry partners and charities and has collaborated with researchers across several UK universities, including Bristol, Keele, Nottingham, and Manchester.

Professor Paul Dimitri BSc, MBChB, FRCPCH, PhD

*Professor of Child Health and Consultant in Paediatric Endocrinology;
Director of Research & Innovation, Sheffield Children's NHS
Foundation Trust*

Investigating the impact of body composition on skeletal growth and developing novel skeletal imaging



Professor Paul Dimitri is an Honorary Professor of Child Health and a Consultant in Paediatric Endocrinology at Sheffield Children's Hospital. He is also Director of Research and Innovation at Sheffield Children's Hospital and Division Lead for the Division of Child Health, Genetics, Non-malignant Haematology and Reproductive Health and Child Health at the NIHR Yorkshire and Humber Clinical Research Network. Paul studied Medicine at the University of St Andrew's, Scotland where he received a medal in pathology and the University of Manchester where he received a Distinction in Paediatrics. He moved to Sheffield in 1998 where he trained in Paediatrics and Paediatric Endocrinology. In 2010 he was Awarded a PhD in Medicine from the University of Sheffield for his work on the relationship between obesity and skeletal health in children, and received his Fellowship of the Royal College of Paediatrics and Child Health. He was subsequently appointed as a Consultant in Paediatric Endocrinology in 2010 and an Honorary Professor of Child Health in 2014.

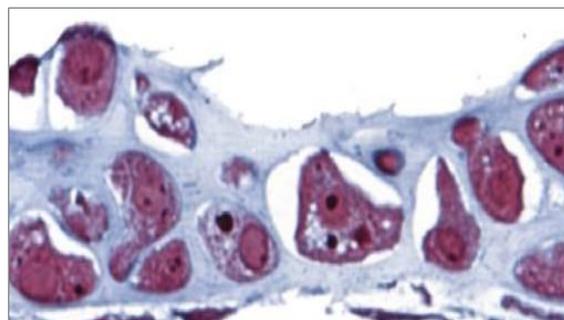
Paul's research focus is on the impact of obesity on skeletal development and the development of novel skeletal imaging modalities. He has been invited to give lectures both nationally and internationally and has published in key peer-reviewed journals in his field of research.

He was awarded the Michael Blacow Memorial Prize by the RCPCH for his work relating to the impact of childhood obesity on skeletal health, and has received two research prizes from the British Society of Paediatric Endocrinology and Diabetes to support his work. Paul has led on an initiative to establish a National Paediatric Health Technology Network for Children in England (TITCH – Technology Innovation Transforming Child Health), dedicated to the development of technology and digital solutions to improve the health of children and young people and to enable greater independence. He is also the Director of SIIRCH (The South Yorkshire Institute for Innovation and Research in Child Health) designed to support cross-disciplinary collaborative research to improve child health and the lives of children. He has recently led on the development of the National Institute of Children's Sports and Exercise Medicine (NICSEM). NICSEM is the first dedicated Institute for children's sport and exercise medicine in the UK and provides access to highly specialised clinical services relating to physical activity and sports in children and young people. NICSEM also supports the development of world class research that will deliver long-term systematic change to benefit the health of the children and young people.

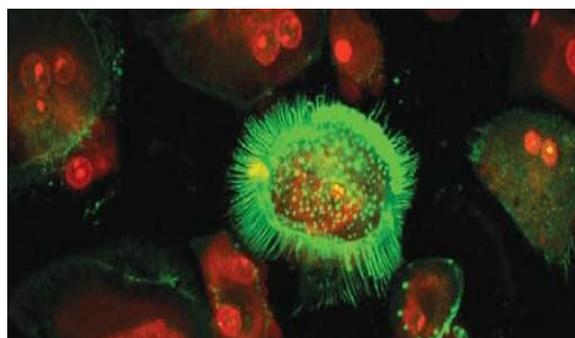
Professor Alison Gartland BSc, PhD

Professor of Bone and Cancer Biology, Division of Clinical Medicine, University of Sheffield

Understanding the basic cellular and molecular mechanisms of musculo-skeletal diseases



Cross-section through a primary chondrocyte culture *in vitro*



P2X7R-induced ethidium bromide uptake (red) in human osteoclasts *in vitro*



TRAP stained human osteoclasts (red) resorbing the surface of ivory (blue-purple)

Professor Alison Gartland studied for her PhD at The University of Liverpool, completed Post-Doctoral Researcher positions at IGMM, CNRS France and University of Massachusetts Medical School, USA. She is a Professor of Bone and Cancer Cell Biology at The University of Sheffield with expertise in purinergic signalling, bone and cancer cell biology, *in vitro* and *in-vivo* murine models of MSK disorders, including in the setting of cancer. Her principal research area focus is on developing fundamental understanding of the

basic cellular, molecular and genetic mechanisms responsible for musculoskeletal disease and cancer.

Professor Gartland has over 40 publications in leading journals in the field of bone and cancer and has also authored several book chapters on human bone cell culture technique. Current projects include looking at the mechanisms of breast cancer metastasis to bone, effect of metal ions on bone cell function, and P2 receptors in bone health and disease.

Dr Alanna Green PhD, FHEA, BBiomedSci (Hons)

Principal Investigator, Division of Clinical Medicine, University of Sheffield

New therapeutic approaches to treat incurable cancers in bone



Dr Alanna (Leni) Green is a Research Fellow and Head of the Cancer and Bone Laboratory at The University of Sheffield, UK. Leni completed her PhD in 2016 at the St Vincent's Institute of Medical Research, The University of Melbourne, Australia, where she discovered retinoic acid receptors regulate bone biology and in turn blood cell production. She also identified a new subpopulation of bone lining cells that form a niche for B-lymphopoiesis. In her first postdoctoral position at The University of Sheffield, she developed advanced preclinical models of myeloma and showed a bone anabolic can heal myeloma bone disease. This was followed a second postdoctoral position as a Project Leader in Sheffield with Prof Thomas Helleday, leading a programme of work on new cancer drugs targeting one-carbon metabolism enzyme, MTHFD2.

Dr Green's group now focuses on bone control of cancer processes. Her team are developing novel

therapeutic strategies for targeting cancer dormancy to eradicate disease in myeloma and cancers in bone.

Leni has been recognised as one of the best young researchers in the bone field, receiving over 20 awards for her research including the AIMM-ASBMR John Haddad Young Investigator Award and election to the ECTS Academy. She has 18 peer-reviewed publications (10 as first author, 1 senior author and 4 corresponding author) in top journals including JBMR, Bone, Blood, Nature Cancer and Nature Metabolism. She has given 7 invited talks and 25 conference presentations. Leni is on the Bone Research Society Committee, an Editor for the International Federation of Musculoskeletal Research Society's initiative HubLE, in the National Cancer Research Institute (NCRI) Bone Metastasis Working Group and regularly reviews papers and grants. Leni's work is currently funded by Blood Cancer UK and Sheffield Hospitals Charity.

Professor Paul Hatton BSc, PhD.

Professor of Biomedical Engineering, University of Sheffield; Head of Oral Biomaterials Research Group; Co-Director Sheffield Medical Innovation Centre

The development of medical devices and regenerative therapies for the repair of skeletal tissues



Professor Paul Hatton graduated with a BSc in Applied Biology from Lanchester Polytechnic in Coventry in 1985, and completed a PhD in the Department of Biomedical Sciences at Sheffield City Polytechnic in 1989. He spent three years as a postdoctoral researcher in the Department of Biomedical Sciences at the University of Sheffield before taking up a lectureship in the School of Clinical Dentistry in 1992. Paul was awarded a personal chair in 2003, and was President of the UK Society for Biomaterials from 2004 to 2007 before election to the European Council of the Tissue Engineering & Regenerative Medicine International Society (TERMIS) until 2012. He is currently the Director of Research at the School of Clinical Dentistry.

His principal research expertise is in medical devices and regenerative medicine for the repair of musculoskeletal tissues. He also has a longstanding interest in the application of electron microscopy to the study of musculoskeletal tissue-material interaction.

His interdisciplinary research group works on innovative and emerging technologies ranging from nanostructured materials through to regenerative therapies that have the potential to improve the repair of human musculoskeletal tissues and functional structures. In addition to his pioneering research, Paul is very active in undergraduate and postgraduate education, and is well known for his passionate support of academic-industrial collaboration and knowledge exchange. He was until early 2016 the Co-Director of the Sheffield Healthcare Gateway.

Professor Hatton's recent and current research is supported by the European Commission (EC), industry, Innovate UK, and the Engineering and Physical Sciences Research Council (EPSRC). He is the Sheffield lead for our participation in the EPSRC Centre for Innovative Manufacturing of Medical Devices (MeDe Innovation), a national programme led by the University of Leeds and involving Newcastle, Bradford and Nottingham universities.

Professor Ingunn Holen BSc, MSc, PhD

Professor of Bone Oncology, Leader of Laboratory Research Team, Clinical Oncology, Division of Clinical Medicine, University of Sheffield

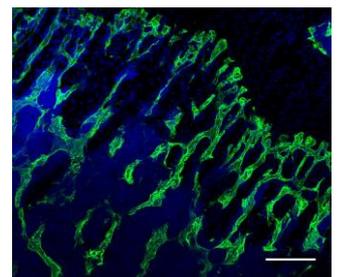
Bone metastases in breast and prostate cancer – molecular mechanisms and effect of therapies



Professor Ingunn Holen completed her PhD at the University of Oslo and the Norwegian Radium Hospital, Oslo, Norway in 1995, before joining the University of Sheffield as a Research Associate in the Department of Human Metabolism and Clinical Biochemistry. Ingunn is Professor of Bone Oncology and leads the Section of Cancer Biology and Therapeutics in the Division of Clinical Medicine. She has more than 25 years' research experience in advanced breast cancer, in particular in the context of translational studies of bone metastasis and therapeutics where she has been involved in a number of clinical trials. She has published 130+ scientific papers with more than 10,000 citations and is a frequent speaker at international scientific conferences. Ingunn is a Trustee of Breast Cancer Now, has chaired the BCN Scientific Advisory Board and served on the NIHR Doctoral Research Fellowship panel. She is the current Chair of the British Association of Cancer Research and is a member of a number of international grant and research institute review committees, editorial boards of scientific journals and conference organising committees.

Ingunn's research is focused on metastatic breast cancer. Her main interest is elucidating the molecular mechanisms involved in tumour cell-bone cell interactions, and how these can be targeted by anti-cancer therapies. This work also includes investigating the role of the microenvironment in regulation of tumour cell dormancy and in driving bone metastasis. Ingunn has several collaborative projects both with other researchers in the medical school, nationally and internationally. She works closely with the clinical staff on translational research projects, transferring the results from our laboratory projects into clinical feasibility studies.

Ingunn's research is funded by a number of local and national charities, including Weston Park Hospital Cancer Charity, Yorkshire Cancer Research. Industry, the EU, MRC, CRUK, Breast Cancer Now and the NC3R



Endomucin expressing (in green) microvasculature in the mouse tibia

Dr David Hughes BMedSci, MB ChB, PhD, FRCPath

Consultant Histopathologist and Deputy Medical Director, Sheffield Teaching Hospitals NHS Foundation Trust; Honorary Senior Lecturer, University of Sheffield

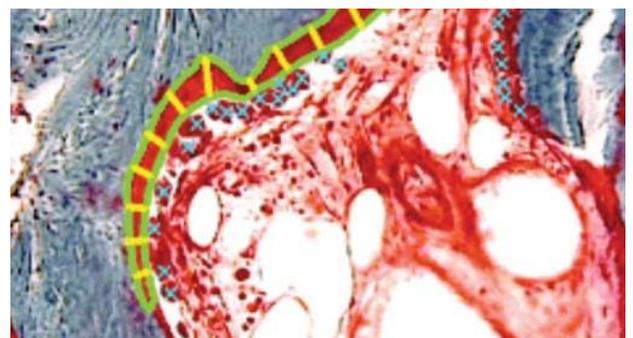
Applying the insights of morphology to understanding bone disease



Dr Hughes obtained a BMedSci at the University of Sheffield in 1985 and went on to complete a PhD in 1988 and to graduate in Medicine in 1989 at the same University. He then worked as a Clinical Lecturer in Pathology at the University of Edinburgh between 1990 and 1995. During this period he also undertook a sabbatical (1994-95) as Visiting Assistant Professor at the University of Texas Health Science Center, San Antonio. Dr Hughes then worked as a Clinical Lecturer in Pathology at the University of Sheffield between 1995 and 1998. Since then, David has worked as an NHS Consultant Histopathologist at Chesterfield Royal Hospital (1998-2003), the Royal Orthopaedic Hospital, Birmingham (2003-5) and Sheffield Teaching Hospitals from 2005 onwards.

David's initial research was the investigation of the role of cytokines in bone metabolism and through his PhD, he developed an interest in understanding the mechanism of action of bisphosphonates. This interest was carried forward during his sabbatical in San Antonio, establishing the pro-apoptotic effect of bisphosphonates on osteoclasts and during his clinical lectureship in Sheffield he contributed to the work of the team of Dr (now Professor) Mike Rogers in demonstrating the role of the mevalonate pathway in bisphosphonate action. More

recently, David has worked collaboratively, using his skills in tissue interpretation to contribute to a variety of projects such as describing the phenotype of IL-1 receptor antagonist knockout mice and tissue engineering using conditionally-immortalised chondrocyte progenitors. David contributes histology support and advice to a number of Mellanby Centre projects. He is also the reference pathologist for the national VORTEX and Axitinib-STs sarcoma clinical trials.



Histomorphometric analysis of bone

Dr Michelle Lawson BSc, PhD, FHEA

School Director of Postgraduate Research, Senior Lecturer in Cancer and Bone Biology, Division of Clinical Medicine, University of Sheffield

The use of novel-bone targeted therapies to treat multiple myeloma



Dr Michelle (Shelly) Lawson is Senior Lecturer in Cancer and Bone Biology in the School of Medicine and Population Health, where she leads the Sheffield Myeloma Research Team. Shelly graduated from the University of Sheffield with a BSc (Hons) in Molecular Biology in 1997 before completing a PhD at the University of Bristol focused on the use of cytokines as DNA vaccine adjuvants. In 2001 she began her career in bone biology at the University of Oxford using various biomaterials for bone scaffolding and developed a novel technique to measure the bone binding affinities of bisphosphonates. In 2005 Shelly moved back to the University of Sheffield to assess the effects of bisphosphonates in preclinical models of multiple myeloma, where she later became a Research Fellow and Lecturer. Over the last 15 years Shelly has developed and established several preclinical murine models of myeloma to study therapeutic intervention in the early, mid, and late stages of the disease. This has led to an increased understanding of the role of the bone marrow microenvironment and how it influences tumour growth. Her main research interests are on improving the treatment of myeloma-induced bone disease and developing novel therapeutics to target dormant cancer cells. Her current research focusses on understanding the role of osteocytes and their network in cancer-induced bone disease, assessing patient samples (bone marrow trephines from an observational Bone Recovery After Treatment Study - BRATS) and therapeutic intervention in preclinical models. Recently Shelly gained access to rare synchrotron beam time and is currently assessing a large dataset of high-resolution bone images. The eventual aim of her research is to develop novel bone modulating agents to repair bone damage.

Dr Lawson's original research articles include those in journals such as Nature Communications and the Journal of Bone and Mineral Research. Her research expertise in myeloma-induced bone disease, as well as establishing and utilising preclinical models of myeloma, has led to the publication of several original research and review articles. Because of her established expertise, she frequently collaborates with both academic institutes (University of Oxford, University of Leeds, University of Birmingham, and Queens University Belfast) and industry partners (Oxford Biomedica, Theolytics in Oxford, Shin Poong Pharmaceuticals in Seoul, and Bold Therapeutics in Canada).

Dr Lawson is also the Postgraduate Research (PGR) Director in the School of Medicine and Population Health and is developing a school PGR strategy to deliver on the University of Sheffield's vision of enhancing the PGR experience.

Nationally Dr Lawson is a member of the UK Myeloma Society (UKMS) executive committee, a member of the UK NC3Rs student panel committee, and until recently was the Treasurer of the Bone Research Society (BRS). She is a current member of the BRS and the Cancer and Bone Society. For the UKMS, Dr Lawson has organised their annual Scientific Forum. For the BRS, Dr Lawson has previously organised their "Basic course in bone and cartilage biology and disease" held at the University of Sheffield (2017, 2019 and 2022).

For further details please visit:

<https://www.sheffield.ac.uk/smph/people/clinical-medicine/michelle-lawson>

Professor Christine Le Maitre PhD, FHEA

*Professor of Musculoskeletal Cell Biology and Tissue Regeneration,
Division of Clinical Medicine, University of Sheffield*

Musculoskeletal Cell Biology and Tissue Regeneration



Professor Christine Le Maitre is a Professor of Musculoskeletal Cell Biology and Tissue Regeneration in the Division of Clinical Medicine in the Medical School, University of Sheffield where she co-leads the Joint and Disc Research Group in the Bone and Joint theme, she is also a Principal Investigator at the Insigneo Institute for *in silico* Medicine, at the University of Sheffield. Professor Le Maitre is also a member of the Integrated Musculo-Skeletal Biomechanics research group, with a particular interest in mechanobiology within musculoskeletal health and disease. She is also a member of the Society of Back Pain Research, AO spine, the British Orthopedic Research Society, Orthopaedic Research UK, the Orthopaedic Research Society and the associated spine section, Tissue Cell Engineering Society, Tissue, Engineering and Regenerative Medicine International Society and is current Chair lady for the UK based Charity DISCs.

Professor Le Maitre's research investigates the cellular pathogenesis of musculoskeletal conditions. Including intervertebral disc degeneration and its links to low back pain; osteoarthritis; and bone physiology; working in close collaboration with relevant clinical partners and collaborators nationally and internationally. With a particular interest in the interaction of cells, biomechanics and matrix biology. Professor Le Maitre's research has provided key insights to the normal physiology of musculoskeletal conditions and identified dysregulated cellular mechanisms during pathogenesis of intervertebral disc degeneration and osteoarthritis. Including the roles of inflammatory cytokines, cellular senescence and altered mechano-transduction pathways. With a passion for developing alternative disease models, which utilise human 3D cell and tissue cultures within physiologically relevant environments. These systems are utilised to understand normal physiology and pathogenesis and test new therapeutic strategies.

Such as 3D culture systems to maintain the phenotype of isolated chondrocytes, nucleus pulposus cells, annulus fibrosus cells, osteoblasts and osteocytes, or drive stem cell differentiation enabling cell and mechanobiology to be investigated using primary human cell sources. Professor Le Maitre has developed several complex tissue culture systems enabling maintenance of cell/matrix interactions from osteochondral and IVD tissue explants to whole organ culture systems. Current PhD students under her supervision are also developing 3D printed models of cortical and trabecular bone and bone infection models. The improved understanding in pathogenesis of musculoskeletal conditions have led to strategies for next generation therapies involving stem cells, biomaterials and gene therapy approaches to inhibit disease processes and support regeneration. Investigating a range of potential cell sources to promote regeneration including bone marrow and adipose stromal cells; and induced pluripotent stem cells (iPSCs). Her work has investigated these cell strategies either alone or in combination with smart biomaterials which can restore the biomechanical environment, whilst inhibiting catabolic signalling processes and supporting stem cell differentiation. She has also investigated the potential of gene therapy approaches to modulate abnormal cytokine signalling to inhibit cellular pathogenesis, providing the correct tissue niche to support repair and regeneration. Her work on next generation therapies has led to patent generation, industry collaborations and potential commercialisation opportunities.

Professor Le Maitre's research to date has led to >110 publications with >10,000 citations and a current H index of 49 and i10 index 90 (September 2024), with over £23.4 million in research grant income and £10 million in doctoral training grant income to date and is involved in a number of large consortia projects, including iPSPINE and Disc4all

Dr Xinshan (Shannon) Li

Senior Lecturer, Mechanical Engineering, University of Sheffield

Continuum modelling of the musculoskeletal system



Dr Xinshan (Shannon) Li obtained her PhD in Bioengineering from the Auckland Bioengineering Institute in 2011. Her thesis focused on the biomechanics of pelvic floor muscles during childbirth. Xinshan joined the Department of Computer Science at the University of Sheffield in 2011, working on cell-based modelling for skin inflammation in collaboration with P&G. In 2013, Xinshan joined the Department of Mechanical Engineering as a lecturer.

Xinshan's main research interest is in continuum modelling of the musculoskeletal system. She has extensive experience in creating computer models of bones and skeletal muscles based on medical images (CT, MRI

scans). These models are used in a wide range of applications from investigating children's bone mechanics, to predicting the risk of fracture in elderly, and obstetrics & gynaecology.

Research Interests:

- Biomechanics of paediatric bone in the application of child abuse
- Risk of fracture prediction in adults using finite element approach
- Biomechanics of the female pelvic floor muscles and the cervix

Professor Eugene McCloskey MD, FRCPI

Professor in Adult Bone disease, Division of Clinical Medicine, University of Sheffield; Director of Versus Arthritis Centre for Integrated research in Musculoskeletal Ageing

Characterising the risk factors for bone diseases and integrating them into management tools



Professor Eugene McCloskey graduated in Medicine from Trinity College, Dublin in 1983. He is currently Professor in Adult Bone Diseases in the Division of Clinical Medicine at the University of Sheffield. In addition to clinical work as an Honorary Consultant Physician in metabolic bone disease at the Northern General Hospital, Sheffield, he is also the current Director of the Versus Arthritis Centre for Integrated research in Musculoskeletal Ageing (CIMA). He has published over 500 peer-reviewed publications, book chapters and reviews and is an acknowledged authority in the fields of vertebral fracture definition, osteoporosis epidemiology, fracture risk and bone health in cancer.

He contributed to the development of the FRAX tool for fracture risk assessment and the subsequent guideline from the National Osteoporosis Guideline Group. He is on a number of editorial boards and is a member of committees within organisations including the International Osteoporosis Foundation (Board and current Chair of

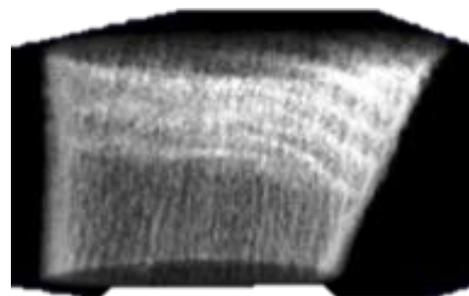
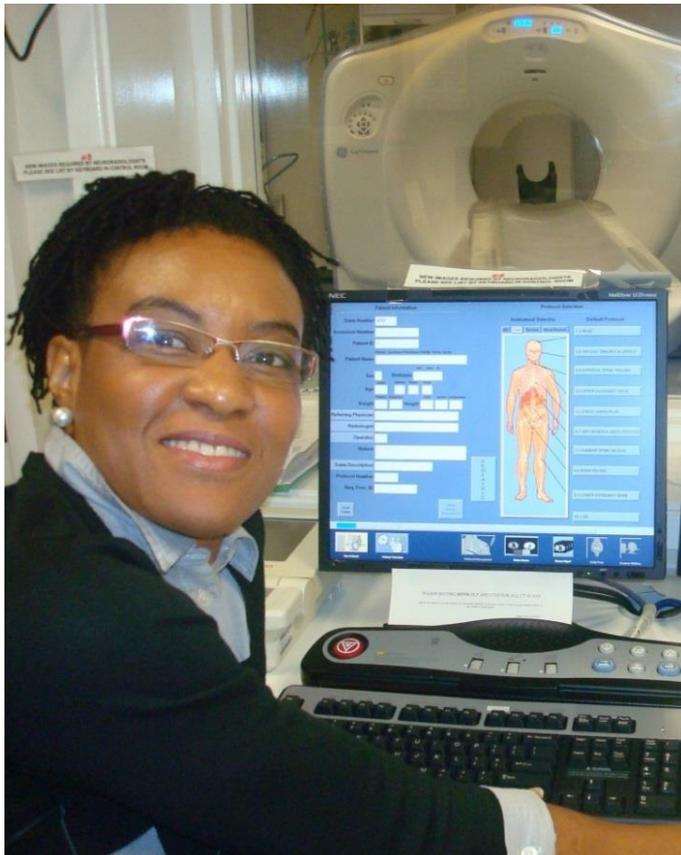
the Committee of Scientific Advisors). Eugene has been principal and co-investigator in a number of MRC, ARUK and/or pharmaceutical-funded osteoporosis studies. He has been involved with writing national and international guidelines in osteoporosis and cancer-related bone disease as well as contributing to Health Technology Assessments.

He has important long-standing collaborations with national and international research groups and is a member of the MRC Musculoskeletal Network. In addition to continuing development of the FRAX tool, his current research foci include novel risk factor models for fracture, sarcopenia, and potential interactions between physical and pharmacological therapies for the treatment of musculoskeletal frailty. His research papers have been in the top 1% of all citations in his field over the past 10 years.

Professor Amaka C Offiah, BSc, MBBS, MRCP, FRCR, PhD

Professor of Paediatric Musculoskeletal Imaging, Division of Clinical Medicine, University of Sheffield

The optimisation of current and development of novel methods of imaging the paediatric musculoskeletal system



High resolution peripheral quantitative computed tomography (HRpQCT) scan of the wrist in a child with osteogenesis imperfecta, showing the characteristic "zebra-lines" of pamidronate therapy

Professor Amaka C Offiah graduated as a doctor from Ahmadu Bello University, Zaria, Nigeria, trained as a radiologist in Sheffield and obtained a PhD while at Great Ormond Street Hospital for Children and the Institute of Child Health, UCL, London. Amaka then returned to Sheffield in as a HEFCE-funded Clinical Senior Lecturer. She is currently Professor in Paediatric Musculoskeletal Imaging in the Faculty of Medicine and Honorary Consultant Paediatric Radiologist at Sheffield Children's Hospital.

Amaka's main research interest lies in the imaging of suspected child abuse and skeletal dysplasias and in methods of determining which children have fragile bones prone to fracture and which do not, including optimizing current and development of novel methods of distinguishing

brittle from normal bones, understanding the mechanisms of injury in infants and young children and improving the detection and dating of the subtle fractures seen in abuse. Other areas of research relate to developing artificial intelligence tools for the detection of accidental, inflicted and vertebral fractures.

Amaka is the first ethnic minority and first female Managing Editor of the journal "Pediatric Radiology" (the only international paediatric radiology journal), Convener of the Skeletal Dysplasia Group for Teaching and Research, Chairperson of the European Society of Pediatric Radiology Child Abuse Taskforce and initiated and leads the International Guidelines for Imaging in Suspected Physical Abuse (IGISPA) consensus group.

Professor Penny Ottewell BSc, PhD

Professor of Bone Oncology, University of Sheffield

Molecular mechanisms that drive breast cancer metastasis to bone and identification of therapeutic interventions



Professor Penelope (Penny) Ottewell completed her PhD at The University of Liverpool, before joining the University of Sheffield as a Research Associate. Whilst being based in Sheffield Penny has carried out international collaborative work spending time at INSERM (University of Lyon), France and at TUFTS Medical School in Boston, USA. She has been awarded a total of 13 national and international prizes for her research including the International Bone and Mineral Society Gregory Mundy Research Fellowship. In 2022 Penny was awarded her personal chair as Professor of Cancer Biology in the Department of Oncology and Metabolism.

Penny's work is focussed in the field of cancer metastasis where her team specialise in generating clinically relevant models for cancers that metastasise to bone including breast, prostate and lung. Penny's team utilise these models to identify mechanisms that drive bone metastasis and improve efficacy of treatments for

metastatic bone disease. Projects being undertaken in Penny's team include: Generating new gene-based therapies to target dormant tumour cells in bone; improving efficacy of immunotherapies in the bone environment and overcoming resistance to Ra-223 in breast and prostate cancer bone metastasis. Her work in this field is currently funded by AstraZeneca, MRC, Breast Cancer Now and Yorkshire Cancer Research. Penny works on the editorial board for multiple peer reviewed journals, sits on the NCRI Bone metastasis strategy working group and is also a member of the grant review committees for Breast Cancer Now (UK) and The National Science Centre (Poland). Penny also serves on the Cancer and Bone Society executive committee and has previously been chair of the ECMC JING steering committee, a been a member of the Cancer and Bone Society Executive Committee and the Executive Committee of the British Association for Cancer Research.

Emeritus Professor Graham Russell PhD, DM, FRCP, FRCPath, FMedSci, FRS

*Professor of Musculoskeletal Pharmacology, and Botnar Research Centre,
University of Oxford; Mellanby Centre for Musculoskeletal Research, University of
Sheffield*

Understanding the causes of bone and joint diseases and the pharmacology
of drugs to improve their treatment



Graham's life-time research interests have included bone cell biology, cytokines, pathogenic mechanisms in bone and joint diseases such as arthritis, myeloma, bone metastases, and osteoporosis, and the evaluation of new therapeutic agents and their modes of action.

In the 1960s he was involved in the original discovery of the biological effects of bisphosphonates which became and still are the major medicines used worldwide for the treatment of disorders of enhanced bone resorption. Throughout his career he has played

a central role in studying their pharmacological and clinical effects. During the 1990s, Michael Rogers and others within his group in Sheffield elucidated the molecular mechanisms of action of bisphosphonates, and showed that nitrogen-containing bisphosphonates act as inhibitors of mevalonate metabolism resulting in inhibition of protein prenylation. His current research focuses on further understanding their structure activity relationships, the design of novel compounds, eg for drug delivery to bone, and on their potential non-skeletal benefits on life span and ageing.

Dr Syazrah Salam MBChB, PhD, FRCP

Consultant, Sheffield Teaching Hospitals NHS Trust; Honorary Senior Clinical Lecturer, Division of Clinical Medicine, University of Sheffield

Chronic kidney disease-mineral bone disorder and bone fragility in renal osteodystrophy



Syazrah graduated from the University of Sheffield in 2004. She is a consultant in metabolic bone and nephrology at Sheffield Teaching Hospitals NHS Foundation Trust. She was awarded a Kidney Research UK Clinical Research Training Fellowship during her nephrology training. She was awarded her PhD from the University of Sheffield in 2020. Her PhD focussed on assessing non-invasive tests (bone turnover markers and high resolution bone imaging) as an alternative to bone biopsy in diagnosing renal osteodystrophy (ROD) in advanced chronic kidney disease (CKD). Her research in CKD mineral bone disorder also includes vascular calcification.

Fracture risk is high in patients with advanced CKD but the pathophysiology is complex and not fully understood. This is Syazrah's current research focus and she has been awarded the European Calcified Tissue Society Clinical Research Fellowship in 2022 to study bone quality in ROD. She was also a steering committee member of the European Renal Osteodystrophy Initiative (part of the European Renal Association) between 2016 and 2023; and remains an active member of the initiative. She was awarded the Royal College of Physicians Turner-Warwick Lecture in 2020.

Dr Marian Schini MD, PhD, FHEA

Senior Clinical Research Fellow, Division of Clinical Medicine, University of Sheffield

Osteoporosis and calcium metabolism disorders



Marian completed her training in Endocrinology in 2014. She has been working as a clinical research fellow for the University of Sheffield since 2015, with an interest in osteoporosis and calcium metabolism disorders. She was funded by CIMA to undertake a PhD, focusing on the prevalence and natural history of normocalcaemic hyperparathyroidism and hypoparathyroidism. After completing her PhD in 2020, she was appointed as a consultant at the Metabolic Bone Centre at Sheffield Teaching Hospitals, still maintaining her role as a Fellow with the University of Sheffield, to pursue her research interest in bone metabolism further.

Due to her growing interest in calcium, she was asked to participate in the expert group preparing the international guidelines on primary hyperparathyroidism.

Marian won several awards, including a young investigator award for ASBMR, the most prestigious bone society in the world. This award was for a project on zoledronate and kidney function, which changed clinical practice locally and allowed more patients to gain access to treatment to prevent fractures.

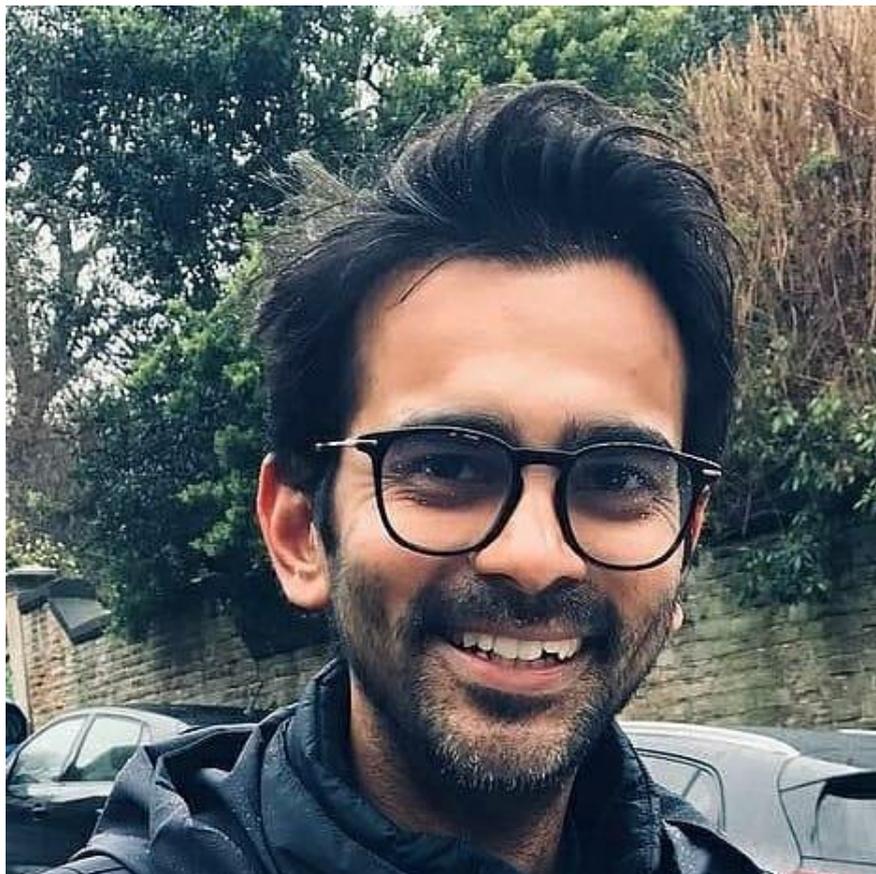
Marian is a Fellow of the Higher Education Academy (FHEA), and has been an active member in several scientific groups, taking part in regular meetings, discussion, and publications in high-impact journals; the FNIH-ASBMR-SABRE international project, which aims to advance bone mineral density (BMD) as a regulatory endpoint in clinical trials, the FRAX international group, The Bone and Calcium Specialized Endocrine Network, the Steering Group for the Hypoparathyroidism Real World Data Register and the ASBMR Professional Practice Committee.

Marian's current research interests mainly involve her work around the SABRE Project, understanding the overshoot effect observed after treatment with denosumab, which can lead to a decrease in BMD and vertebral fractures, and exploring whether a similar mechanism is involved in patients treatment with romosozumab. Marian also has an interest in bone turnover markers (BTMs), recently completed a study called POSE (PINP and Osteoporosis in Sheffield Evaluation) for which she was awarded grant funding and led a review covering topics from basic biology to clinical applications published in a high-impact journal. She is active in teaching around BTMs in the Mellanby Centre Training Course.

Dr Karan M Shah BTech, MSc, PhD

*Research Associate in Bone Oncology, Division of Clinical Medicine,
University of Sheffield*

Molecular mechanisms that drive pre-metastatic niche formation and organotropism in cancer



Dr Karan Shah completed his PhD at The University of Sheffield, UK in 2014, with a research focus on understanding the role of metal debris on bone cells in the context of hip prostheses. Subsequently, he joined the Department of Oncology and Metabolism as a Research Associate to continue his research on the effects of metals on bone cell physiology. In 2014, he was awarded the William H. Harris Award for 'outstanding work in orthopaedic research related to the hip' by Orthopaedic Research Society.

In 2016, Karan took a post with Prof. Alison Gartland and investigated the role of lysyl oxidase and purinergic signalling on breast cancer metastasis to bone. It is during this post, that he developed a strong interest in understanding how primary tumour facilitates pre-

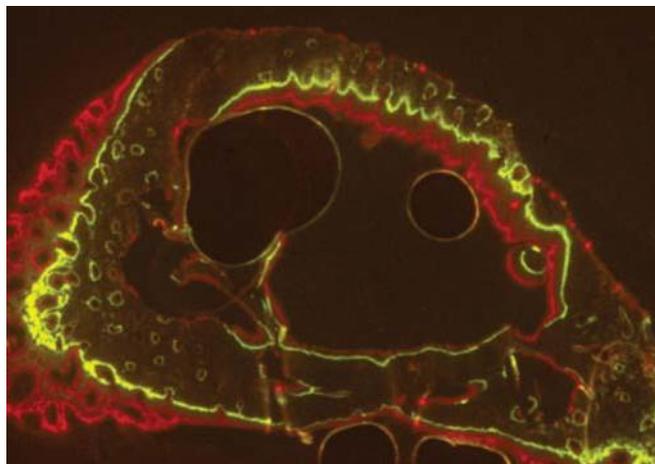
metastatic niche formation in specific distant organs.

His current research aims to understand how primary tumour facilitates pre-metastatic niche formation in specific distant organs. To that end, he is exploring the role of extracellular vesicles (EV) in metastasis and organotropism in osteosarcoma – a primary bone cancer. Specifically, he is interested in the mechanisms that regulate EV release from tumour cells, and the effects these EVs have on the cells of the distant metastatic sites. He is also interested in the molecular mechanisms that govern pathogenesis of osteoarthritis and works closely with Prof Mark Wilkinson to understand single-cell regulatory dynamics of knee OA. Karan specialises in working with primary bone cells and pre-clinical models of primary bone cancers and metastases

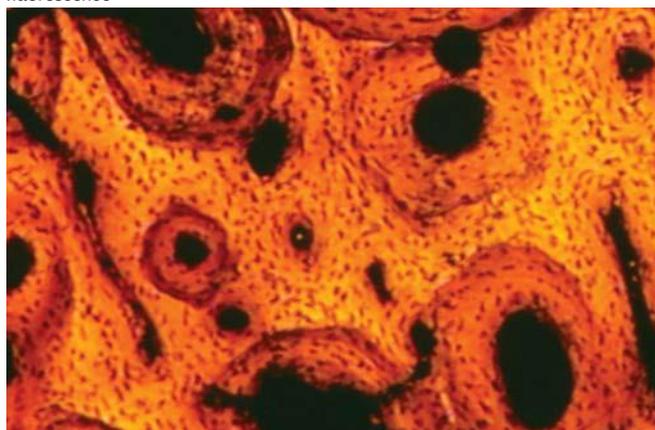
Professor Tim Skerry BVet.Med, PhD, Cert.SAO, FRCVS

Professor of Orthopaedic Biology, Division of Clinical Medicine, University of Sheffield

Adaptive responses in bone and drug discovery



Section showing new bone formation shown by incorporation of fluorescence



Fossil tibia of an iguanodon (c. 150M year)

Bone Biology

Professor Tim Skerry's interest for many years has been the mechanism by which bone responds to exercise. Much of that work has been focused on use of subtractive techniques to determine potential targets for interventions, but more recently the work has grown towards more translational studies.

In a project funded by the EPSRC, Dr Corinne Niger has been using RNA-seq methods to compare transcriptomes of skull and fibial osteocytes from the same individuals in a range of species. This work is to determine how the skull is able to resist the systemic influences that lead to bone loss in the rest of the skeleton as a result of the menopause or weightlessness.

Jasmine Samvelyan is a Student funded by the MRC/ARUK Centre for Integrated research into Musculoskeletal Ageing (CIMA), and is investigating the interactions of gut derived hormones and mechanical influences on bone, in order to understand how to optimise timing of meals and exercise in humans.

Drug Discovery

Together with Dr Gareth Richards, Tim has developed an interest in signalling of a small family of cell surface receptors that interact with accessory proteins to modulate their activity. The calcitonin receptor and calcitonin like-receptor have altered selectivity for different hormones depending upon interactions with so-called receptor activity modifying proteins (RAMPs). Other receptors have their responses to hormone stimulation altered by RAMP interactions. Together Tim and Gareth work on understanding the physiology of those receptors and their signalling, and in a translational programme funded by the Wellcome Trust (awarded to Tim, Gareth, Professor Joe Harrity and Drs Matt Tozer and Karl Gibson) on development of small molecule drugs to target specific receptor RAMP combinations for therapeutic purposes, focusing initially on applications in cancer. Tim and Gareth also have developed a monoclonal antibody against one of those accessory proteins (RAMP3), which is in the process of commercial development through a licensing deal with University spinout company Medella Therapeutics.

Dr Tatiane Vilaca PhD

Research Associate, Division of Clinical Medicine, University of Sheffield

Diabetes and Bone



Dr Tatiane Vilaca is a Postdoctoral Research Associate at the University of Sheffield. She trained as an Endocrinologist in Brazil and completed her PhD at the University of Sheffield in 2020, having studied bone health in diabetes. She investigated several aspects of bone health in this disease, including microarchitecture using high-resolution peripheral quantitative computed tomography, the effects of neuropathy and other potential mechanisms associated with bone fragility in diabetes, such as the role of AGEs.

She has a particular interest in the effects of chronic diseases and medications on bone and the underlying mechanisms. She has several publications on the impact of chronic diseases on the risk of fractures. She has also investigated the endocrine mechanisms associated with favourable bone structure in obesity.

Tatiane has vast experience in systematic reviews; she has led three systematic reviews and taken part in a few others. These projects resulted from several

collaborations within the University of Sheffield (e.g., ScHARR) and international groups from the USA and Denmark.

Currently, Tatiane is involved in a family mapping project in hypophosphatasia, the FAME study, in collaboration with the Sheffield Children's Hospital. The aim is to characterise musculoskeletal features, mineral metabolism and the impact on quality of life in individuals with HPP, a rare bone disease. She is also involved in clinical trials investigating treatments for HPP and osteogenesis imperfecta.

Finally, she is involved in the FNIH-ASBMR-SABRE Project (Study to Advance BMD as a Regulatory Endpoint). This multidisciplinary international initiative aims to change the regulation on the requirements for osteoporosis drug approval from decreases in clinical fractures to treatment-related changes in BMD, which would encourage the development of new drugs.

Professor Jennifer Walsh PhD^{PhD, FRCP, FHEA}

Professor of Clinical Education, University of Sheffield; Honorary Consultant Physician, Sheffield Teaching Hospitals NHS Foundation Trust

Bone microarchitecture and endocrine interactions



Professor Jennifer Walsh graduated with the University of Sheffield in 1997. She trained in Endocrinology, and was awarded her PhD on Peak Bone Mass in 2008, funded by an ARUK Clinical Research Fellowship.

She has a translational clinical research programme; current projects include high-resolution pQCT imaging for bone microarchitecture, the interactions of fat and bone, vitamin D physiology, phenotyping of hypophosphatasia, and clinical trials of teriparatide and losartan in osteogenesis imperfecta.

She has published on peak bone mass, skeletal effects of hormonal contraception, obesity and bone and bisphosphonate treatment for osteoporosis.

She has had prizes and commendations from the European Calcified Tissue Society, American Society for Bone and

Mineral Research and Late Effects of Cancer annual conferences.

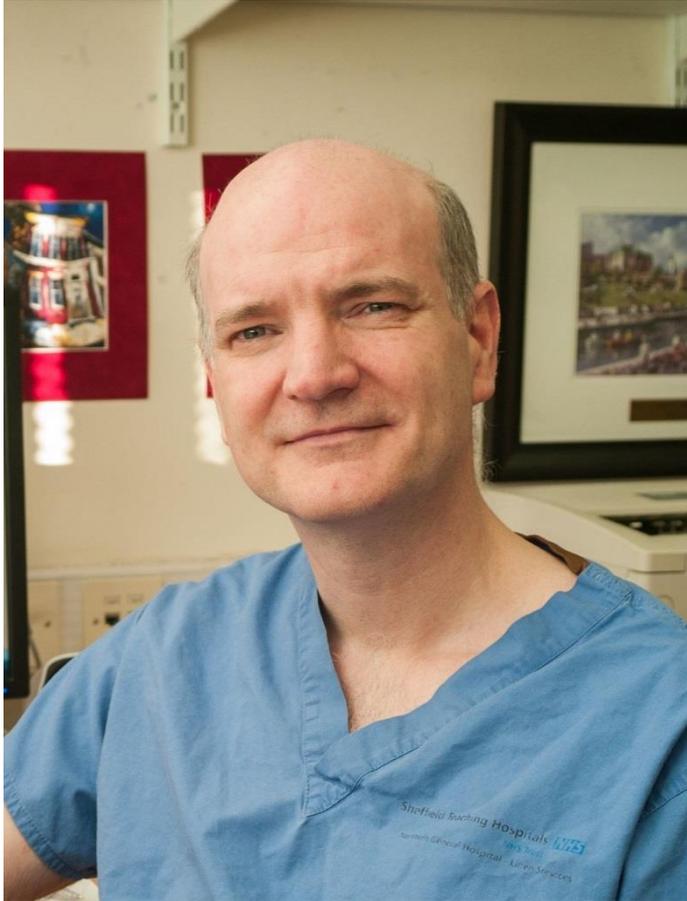
She has held grant funding from the Department of Health, National Institute for Health Research, Cancer Research UK, National Osteoporosis Society and local charities.

Her clinical interests are in young adult bone disease and late effects of cancer. She is a member of the Brittle Bone Society Medical Board and the UK Rare Disease Clinical Network for bone. She completed the RCP/UCL Postgraduate Diploma in Medical Education in 2012 and was awarded Senior Fellowship of the Higher Education Academy in 2024. She is Programme Director of the Sheffield MBChB.

Professor Mark Wilkinson MB ChB, PhD, FRCS (Orth)

Professor of Orthopaedics, University of Sheffield; Honorary Consultant Orthopaedic Surgeon, Sheffield Teaching Hospitals NHS Foundation Trust

Understanding the causes of musculoskeletal diseases associated with joint replacement and developing new approaches to their treatment



X-ray of hip joint prosthesis

Professor Mark Wilkinson graduated in Medicine from the University of Sheffield in 1991 and trained as an orthopaedic surgeon in North Trent and Wrightington. As a specialist registrar in orthopaedics, Mark received Clinical Research Fellowship awards from the Arthritis Research Campaign and The Royal College of Surgeons of England. In 2001 he completed his PhD in the Academic Unit of Bone Metabolism, University of Sheffield. Following a period in clinical practice he returned to the University of Sheffield after receiving a 5-year Clinical Senior Lectureship Award from HEFCE/UKCRC in 2007. He was awarded the chair in orthopaedics in 2012. Mark is also an honorary consultant in Orthopaedics at the Northern General Hospital, Sheffield, with a specialist interest in hip and knee arthroplasty.

Mark's research interests include genetic and metabolic aspects of joint diseases and host responses to prosthetic materials. He was a member of the arcOGEN consortium that identified many of the known risk alleles for osteoarthritis. He conducted the first genome-wide association studies of developmental dysplasia of the hip, and of osteolysis and heterotopic ossification after hip replacement, identifying several novel risk alleles. He published the first studies in humans to show that bisphosphonates may suppress bone loss after hip

replacement, and the first studies to show the systemic effects of metal exposure after hip resurfacing. His work also includes the identification of novel techniques for quantitation of bone mass and architecture, and exploration of the molecular mechanisms that underpin the development of osteoarthritis.

Mark has received several awards, including young investigator awards from the Orthopaedic Research Society, USA (2002) and the National Osteoporosis Society (2000), The British Orthopaedic Association Robert Jones Gold Medal and Association Prize (2003), The British Hip Society McKee Prize (2001, and 2008) and the William Harris Award from the Orthopaedic Research Society (2007). He has co-authored more than 90 papers. Mark is the chair of the South Yorkshire and North Derbyshire Musculoskeletal Biobank, chair of the National Joint Registry Research Committee, and a member of its steering committee. He is a member of the Board of Directors of the Orthopaedic Research Society (United States), and an editorial board member for the Journal of Orthopaedic Research. His sources of research funding include HEFCE, Arthritis Research UK, Orthopaedic Research UK, the Cavendish Foundation, and industry.

Dr Caroline Wilson PhD, MRCP

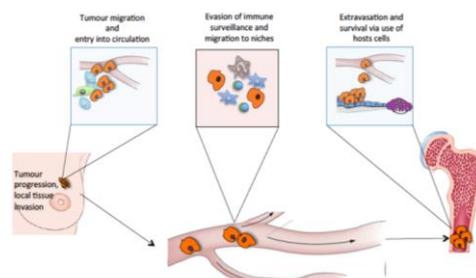
*Medical Oncology Consultant and Honorary Clinical Senior Lecturer,
University of Sheffield*

Breast cancer and bone metastasis



Caroline graduated with distinction from Sheffield Medical School in 2002 and subsequently completed her junior doctor training in Sheffield, Australia and New Zealand. She began her higher specialist training in Medical Oncology in 2007 and in 2011 she took time out of her clinical training to carry out her PhD in Sheffield Medical School, focusing on the influence of hormones on breast cancer in the bone microenvironment.

After completing her PhD she was appointed as a consultant at Weston Park Cancer Hospital where she specializes in the treatment of breast cancer. Her research time is funded by Weston Park Cancer Charity, and focuses on new therapies and therapeutic combinations for breast cancer and breast cancer bone metastases including immune-therapy. She has been primary author and co-author on multiple papers on breast cancer, bisphosphonates and bone metastases published in journals including the Lancet Oncology, Annals of Oncology, Clinical Cancer Research, JAMA oncology. She is also a reviewer for several journals.



Bone Densitometry and Imaging Suite

The Bone Densitometry and Imaging Suite is based within the NIHR Clinical Research Facility (CRF) at the Northern General Hospital. The Mellanby Centre for Musculoskeletal Research employs dedicated and highly experienced scanning technicians to perform a wide range of bone densitometry techniques using specialised imaging equipment. The Bone Densitometry and Imaging Service is managed by Dr Margaret Paggiosi.

The Bone Densitometry and Imaging Suite is equipped with a dual energy x-ray absorptiometry (DXA) densitometer (Discovery A, Hologic Inc.) for the measurement of bone mineral density (BMD) in the whole body, hip, spine and wrist. Body composition (including android and gynoid fat) can also be determined when performing DXA of the whole body.



The Discovery A dual energy x-ray absorptiometry (DXA) densitometer (Hologic Inc)

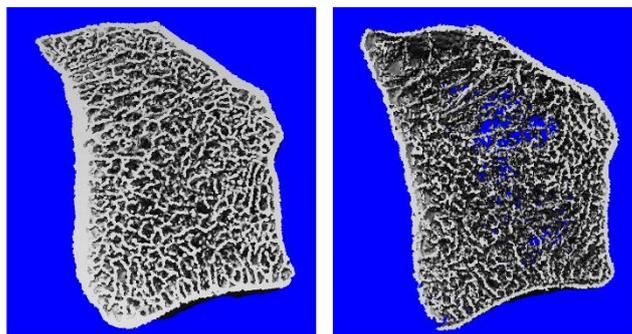
Funding from the NIHR was used to purchase a high resolution peripheral quantitative computed tomography (HR-pQCT) device; the XtremeCT (Scanco Medical AG). This is also housed in the Bone Densitometry and Imaging Suite.



The XtremeCT device (Scanco Medical AG)

The XtremeCT, which acquires high resolution (to 82 μm) 3D images using a very low dose of ionising radiation (3 microSv per scan), is used to study the densitometric, geometric, microarchitectural and biomechanical properties of bone. Primarily, *in vivo* examinations of the wrist and lower leg are performed but cadaveric (*ex vivo*) studies can also be

conducted. A number of image analysis approaches are available including finite element analysis which reveals information about the biomechanical properties of bone.



High resolution peripheral quantitative computed tomography (HR-pQCT) of the radius. Images show healthy bone (left) and osteoporotic bone (right)

Researchers based at the Metabolic Bone Centre, Northern General Hospital have studied the effects of growth, ageing, treatment and disease on the densitometric, microarchitectural and biomechanical properties of bone. We are currently performing a detailed evaluation into the fracture healing process.

In-depth imaging studies of the spine, for the identification of osteoporotic vertebral fractures, can also be performed. The presence of vertebral fractures is a strong independent risk factor for future fracture and is, therefore, an important indicator of patients most likely to benefit from treatment for osteoporosis. Our studies are based on both vertebral fracture assessment (VFA) by DXA and spinal radiography. A combination of VFA and bone density measurements offers a low radiation assessment of an individual's risk of fracture.



An osteoporotic vertebral fracture

Accurate identification of osteoporotic vertebral fractures still remains challenging. Researchers based at the Metabolic Bone Centre have been at the forefront of work in this area for over a decade. This has led to the development, evaluation and clinical implementation of the algorithm-based qualitative (ABQ) approach. Furthermore, researchers from Sheffield have advised the International Society for Clinical Densitometry (ISCD) on the development of guidelines for the application of VFA in clinical practice. Our current research focusses on the development of an automated approach to vertebral fracture identification. Our work has been funded by ARC, MRC and the National Osteoporosis Society.

The Bone Densitometry and Imaging Service provides imaging resources for both clinical trials and investigator-led projects.

For more information visit our website: www.mellanbycentre.org
Or contact Dr Margaret Paggiosi: m.a.paggiosi@sheffield.ac.uk



Cancer Clinical Trials Centre, Weston Park Hospital

Weston Park Hospital has a purpose built clinical research facility, the Cancer Clinical Trials Centre (CCTC) that is funded jointly by the Weston Park Hospital Cancer Appeal, NIHR and the University of Sheffield. The CCTC provides dedicated facilities for the assessment and treatment of patients, office space for staff with fully networked computer systems, a laboratory and certain specialist activities such as bone densitometry. Integration between University and NHS staff is excellent.

The Cancer Clinical Trials Centre hosts the North Trent Cancer Research Network (NTRN) that provides infrastructure for the conduct of clinical trials in Sheffield and across the North Trent Network of associated Foundation Trust hospitals. It also provides the research infrastructure for the Experimental Cancer Medicine Centre (ECMC), a joint translational research venture between clinical oncology and several of the laboratory based academic units within the medical school. In 2015, the Weston Park Hospital Clinical Research Unit opened and replaced our previous treatment facility. This day unit is designed for the delivery of a wide range of research treatments in a safe and comfortable environment.

The CCTC has a well-established track record in clinical research across a broad range of cancer sites and clinical situations. The emphasis is on drug development and improvements in delivery of radiotherapy but there are also research interests in bone oncology, biomarker development, rehabilitation, late effects of cancer treatment and tumour imaging.

Since 2001, more than 10% of all patients with cancer have been entered into a nationally approved clinical trial or well designed research study, with a little over half of these patients taking part in randomised controlled trials. The burden of clinical trial related follow-up is ever increasing and utilises a significant amount of both specific research funds and NHS resources. More than 80% of our overall research activity and 95% of therapeutic trial recruitment is into NIHR approved trials.

In partnership with the Academic Unit of Clinical Oncology, the CCTC has more than £10 million in active research grants. Academic and NHS consultant staff have a high publication output with more than 50 manuscripts a year published in high quality peer reviewed journals. Many of the senior medical staff are members of National Cancer Research Institute (NCRI) Clinical Study Groups and have experience of being a Chief Investigator, and/or membership of Data Monitoring and Safety Boards, Trial Steering Committees and Trial Management Groups.

Head of Unit: *Professor Rob Coleman*

Academic Directorate Lead and NIHR Cancer Lead: *Jon Wadsley*

Senior Research Nurse Lead: *Alison Clarke*

Senior Manager: *Wendy Wilson*

Informatics: *Janet Horsman*

Data Management Lead: *Lucy Birch*

Contact: 0114 2265008



Sheffield CR-UK/DoH Experimental Cancer Medicine Centre

Director - Dr Sarah Danson, Tel: 0114 226 5235

The Sheffield Experimental Cancer Medicine Centre (ECMC) provides early phase clinical trials to the patients of South Yorkshire (population 1.8 million) and beyond. Sheffield ECMC is funded jointly by Cancer Research UK and the Department of Health and has supported work covering a range of priority areas, from innovative treatments to biomarkers to in-house translational research, whilst delivering high quality early phase trials.

Sheffield has an international reputation for bone oncology research, both clinical and translational, and has been key to the registration of bisphosphonates and RANK ligand inhibitors in cancer. Sheffield ECMC has built on this area of strength. Our translational research includes novel combinations with radium-223; prevention of metastasis by bone-targeted agents; biomarker development; relationships between metastasis development and reproductive hormones; patient selection and prediction of treatment benefit; delineation of novel mechanisms of bone metastasis; and treatments for cancer-related bone pain. Sheffield ECMC has led research in the development of novel biomarkers of bone metastases, and has linked with national and international studies in breast, prostate, renal and lung cancer. Sheffield ECMC has developed early phase studies using data from our own discoveries. The Trojan horse study (Brown/Danson) uses macrophage-targeted therapy in prostate cancer. This approach (Lewis/Muthana) is also being assessed in breast cancer and myeloma.

In recent years, the bone oncology team of Professor Coleman (clinical) and Professor Holen (translational) has been expanded with the appointments of Professor Brown (breast and prostate cancer), Dr Chantry (myeloma), Dr Wilson (breast cancer), Professor Heymann (primary bone tumours) and Professor Clezardin (patient selection and novel mechanisms). These appointments demonstrate the commitment of the University and Sheffield ECMC to remain at the forefront of bone oncology research and significantly strengthen international collaborations, for example with INSERM in France.

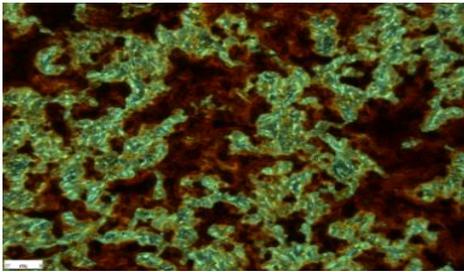
Radiotherapy research is a further area of strength of Sheffield ECMC. Sheffield leads several early phase clinical trials of improved radiotherapy delivery for non-small cell lung cancer (Hatton) and is a world-leader in inhaled gas MRI, which provides clinically relevant functional information for lung cancer radiotherapy (Wild/Hatton). With regards to chemotherapeutic trials, some are Sheffield-led, such as HSV1716 in mesothelioma (Woll) and olaparib in small cell lung cancer (Woll).

Sheffield ECMC is proud of its work in rare tumours, which require more effective collaboration than needed in trials of more common tumours. Sheffield ECMC has led on clinical trials in Kaposi's sarcoma and angiosarcoma (Woll/Young), thyroid cancer (Wadsley) and gestational trophoblastic disease (Coleman/Winter). Recently, we achieved a Bloodwise Trials Acceleration Programme award to support early phase trials in haematological malignancies.

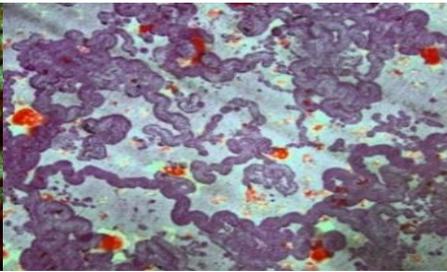
Sheffield ECMC has a robust governance infrastructure. At the core are an ECMC Executive and the Clinical Trials Executive, which assesses scientific credibility and prioritises trials. Sheffield has a long history of patient input in all areas of cancer research, with active patient membership on the ECMC Executive and the Clinical Trials Executive. Trial ideas are presented to our local consumer research group, which provides invaluable insight and feedback.

South Yorkshire & North Derbyshire Musculoskeletal Biobank

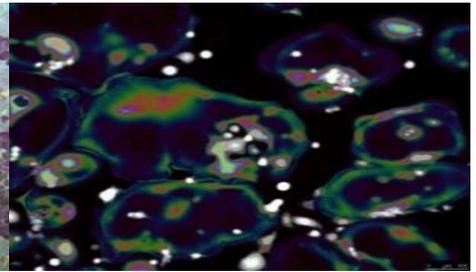
The Academic Unit of Bone Metabolism within the University of Sheffield Mellanby Centre for Musculoskeletal Research manages the South Yorkshire and North Derbyshire Musculoskeletal Biobank. Our research interests span musculoskeletal disorders of childhood through to the elderly person, and cover both benign and malignant diseases. Our clinical research covers osteoporosis, osteoarthritis and prosthesis-related bone loss, childhood bone diseases, tumour-induced bone diseases such as multiple myeloma, and metastatic bone disease.



Mineralisation by human osteoblasts



Resorption trails by human osteoclasts on dentine surface

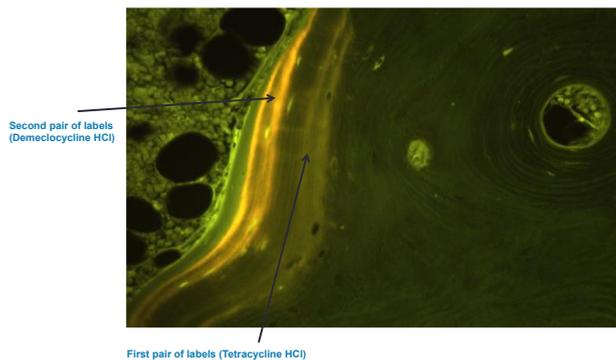


Fluorescence image of calcein loaded human osteoclasts for visualisation of metal uptake

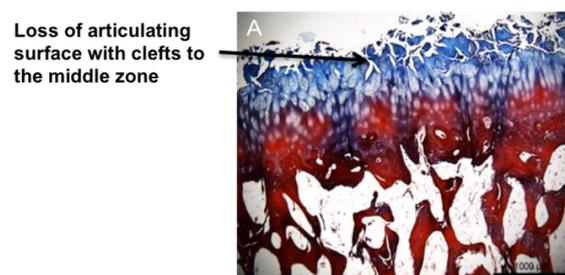
The aim of the biobank is to make use of these clinical and tissue resources to address research questions relevant to musculoskeletal disease. The biobank holds tissue samples obtained from donors and completed, ethically approved projects with appropriate consent for biobank storage and use for future research projects. Samples are stored in the Sheffield Biorepository, which is an HTA licensed facility. The biobank operates under the guidance of a steering committee to assure compliance with current best ethical practice.

All applications for use of tissue through the SYNDMB are submitted in collaboration with a member of the Academic Unit of Bone Metabolism and reviewed by the SYNDMB Steering Committee, which includes representatives from the Biorepository, STH Research Office, Lay members of the public and clinicians from the Metabolic Bone Centre and Orthopaedics.

Fluorescent quadruple labelling of trabecular bone



Osteoarthritic cartilage



Contact : Joanna Chowdry - j.e.chowdry@sheffield.ac.uk

Bone Biochemistry Laboratory

The Bone Biochemistry Laboratory is based at the Medical School. The Mellanby Centre for Musculoskeletal Research employs dedicated and highly experienced laboratory technicians to perform measurements of bone turnover markers and other biochemical tests. The laboratory uses several automated immunoassay analysers. The Bone biochemistry service is managed by Fatma Gossiel.

The Laboratory is equipped with a Vitros 250 and Vitros Eci analysers (Ortho-Clinical Diagnostics), a Cobas E411 analyser (Roche Diagnostics) and an IDS-iSYS analyser (Immuno Diagnostic Systems). This equipment enables the staff to perform high throughput measurements of the bone resorption markers: C-terminal crosslinking telopeptides of type I collagen (CTX) and N-terminal crosslinking telopeptides of type I collagen (NTX) and the bone formation markers: procollagen type I N-propeptide (PINP), bone alkaline phosphatase (bone ALP) and osteocalcin (OC).

Automated immunoassay analysers

The IDS-iSYS Multi-Disciplined automated immunoassay analyser uses of chemiluminescence and spectrophotometric methodologies. It measures levels of CTX, intact PINP, OC, bone ALP and hormones including parathyroid hormone (PTH), IGF-1, 25 OH D and 1,25- (OH)₂ vitamin D in human serum and plasma samples.



The IDS-iSYS analyser



The Bone Biochemistry Laboratory

The Cobas e411 uses electrochemiluminescence methodology to measure levels of CTX, total PINP, OC, PTH and 25-(OH) vitamin D in serum and plasma samples.



The Cobas e411 analyser

The laboratory staff also perform biochemical measurements using manual enzyme-linked immunosorbent assay (ELISA) format. These include: sclerostin, DKK1, α and β -CTX, Fetuin-A, periostin, FGF-23 and vitamin D binding protein.

Researchers at the Academic Unit of Bone Metabolism, University of Sheffield have studied the effects of growth, age, gender, treatment and diseases on bone turnover markers and other related biochemical tests. Levels of bone turnover markers are assessed in clinical trials and other investigator lead studies. We perform detailed investigations into the effects of anabolic and catabolic agents on bone turnover markers and other biochemical tests, in osteoporosis. Our studies are based on using bone turnover markers for treatment monitoring and to assess bone quality. Researchers have been at the forefront of work in this area for over 20 years.

The Bone Biochemistry Laboratory performs measurements and provides advice about the most appropriate bone turnover markers to use, sample collection and storage. We collaborate and provide an assay service to other University departments, external institutions and industry. For further information, visit our website: www.mellanbycentre.org

Or contact Fatma Gossiel: f.gossiel@sheffield.ac.uk

skelet.AL

Skeletal Analysis Laboratories



Innovative, customized solutions for analysis of the skeleton

<http://skeletal.group.shef.ac.uk/>

Who we are:

Part of the Mellanby Centre for Musculoskeletal Research, skelet.AL has a diversified expertise in imaging, histology and bone biology. Established in 2003 (formerly the Bone Analysis Lab), it provides state of the art bone analysis services to members of the University of Sheffield Faculty of Health, as well as the Musculoskeletal research and industry communities more generally.

Our approach:

Flexible:

- You can choose to simply use our equipment and perform your own analysis.
- Receive training or ask us to perform the experiments on your behalf.
- Receive advice on the design of experiments or interpretation of the data.

Versatile:

- From *in-vivo* experiments and sample preparation to data analysis and writing of the reports.

Cutting edge:

- Always developing new expertise and technologies.
- Always adapting existing technologies to new applications.

Friendly:

- We welcome all queries, and do our best to provide the answers you seek.

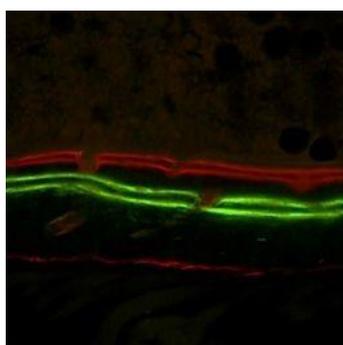
Our services:

We offer a wide range of services for bone analysis:

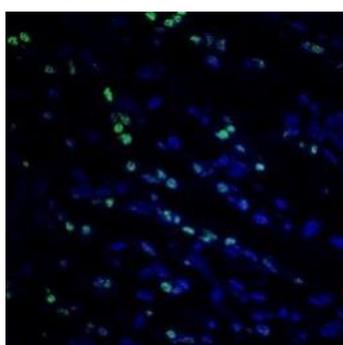
- *In-vivo* and *ex-vivo* Micro-CT.
- Histology and histomorphometry.
- Immunohistochemistry and image analysis.
- Biomechanical testing.

For more information, visit our website: <http://skeletal.group.shef.ac.uk/>

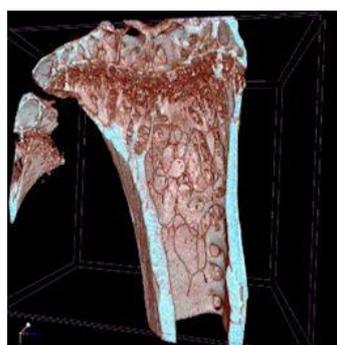
Contact: Prof. Enrico Dall'Ara e.dallara@sheffield.ac.uk



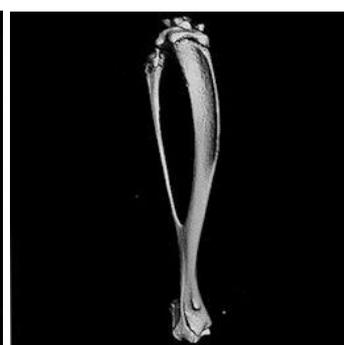
Dynamic istonmorphometry



Immunofluorescence_
Osterix on mouse



Ex vivo micro-CT of mouse
proximal tibia bone section



In vivo-CT of mouse
whole tibia