

Positions and employment	
1996–98	Assistant Professor, Departments of Pediatric Dentistry and Medicine, UTHSCSA, San Antonio, TX
1998–06	Associate Professor (tenured, 2003), Oral Biology, Dentistry, Univ. of Missouri-Kansas City, MO
2000–07	Director of Transgenic Core Facility, School of Dentistry, Univ. of Missouri-Kansas City, MO
2006–07	Professor, Oral Biology, Dentistry, University of Missouri-Kansas City, MO
2007	Professor with tenure, Biomedical Sciences, Texas A&M Baylor College of Dentistry, Dallas, TX
2013	Vice Chair for research

Selected Peer-reviewed Publications (Selected from over 140 peer-reviewed publications)

- Feng JQ., L.M. Ward, S. Liu, Y. Lu, B. Yuan, X. Yu, F. Rauch, Y. Xie, S.I. Davis, S. Zhang, H. Rios, M.K. Drezner, L.F. Bonewald, L.D. Quarles and K.E. White, (2006) Loss of DMP1 Causes Rickets and Osteomalacia and Identifies a Role for Osteocytes in Mineral Metabolism *Nature Genetics* 38:1310–5
- B. Jiang, Z. Cao, Y. LU, C.B. Janik, S. Lauziere, Y. Xie, A. Poliard, C Qin, L.M. Ward, and Feng JQ. (2010) DMP1 C-terminal Mutant Mice Recapture the Human ARHR Tooth Phenotype *J Bone Mineral Res* 25:2155–2164, PMID: 20499360
- JQ. Feng, Feng-Jin Guo, Bai-Chuan Jiang, Sally Frenkel, Yan Zhang, David Wang, Wei Tang, Y., Xie, Chuan-ju Liu, (2010) Granulin epithelin precursor: a bone morphogenic protein 2-inducible growth factor that activates Erk1/2 signaling and JunB transcription factor in chondrogenesis *Faseb Journal* 24:1879–92, PMID: 20124436
- Han XL, Liu M, Voisey A, Ren YS, Kurimoto P, Gao T, Tefera L, Dechow P, Ke HZ, and Feng JQ. (2011) Postnatal Effect of Overexpressed DKK1 on Mandibular Molar Formation. *J Dent Res* 90:1312–7, PMID: 21917600
- Ma D, Zhang R, Sun Y, Rios HF, Haruyama N, Han X, Kulkarni AB, Qin C, Feng JQ. (2011) A novel role of periostin in postnatal tooth formation and mineralization. *J Biol Chem* 286:4302–9, PMID: PMC3039381
- Zhang R, Lu Y, Ye L, Yuan B, Yu S, Qin C, Xie Y, Drezner MK, Bonewald LF, Feng JQ. (2011) Unique roles of phosphorus in endochondral bone formation and osteocyte maturation. *J Bone Mineral Res* 26:1047–56, PMID: 21542006
- Yongbo Lu, Baozhi Yuan, Chunlin Qin, Yixia Xie, Sarah L. Dallas, Marc D. McKee, Marc L. Drezner, Lynda F. Bonewald, and Feng JQ. (2011) The Biological Function of DMP1 in Osteocyte Maturation is Mediated by its 57 kDa C-terminal Fragment *J Bone Mineral Res* 26: 331–340, PMID: 20734454
- Z. Cao, H. Zhang, X. Zhou, X. Han, Y. Ren, T. Gao, Yin Xiao, B. de Crombrughe, M.J. Somerman, and Feng JQ. (2012) Genetic Evidence for the Vital Function of Osterix in Cementogenesis *J Bone Miner Res* 27:1080–92, PMID: 22246569
- Feng JQ, Clinkenbeard EL, Yuan B, White KE, Drezner MK 2013 Osteocyte regulation of phosphate homeostasis and bone mineralization underlies the pathophysiology of the heritable disorders of rickets and osteomalacia. *Bone* 2013; 54(2):213–221
- Shuxian Lin, Qi Zhang, Zhengguo Cao, Yongbo Lu, Hua Zhang, Kevin Yan, Ying Liu, Marc D. McKee, Chunlin Qin, Zhi Chen, and JQ. Feng Constitutive nuclear expression of dentin matrix protein 1 fails to rescue the Dmp1-null phenotype *J Biol Chem* 2014 Jun 10. pii: jbc.M113.543330. [Epub ahead of print]

MICRO-TOMOGRAPHY BONE IMAGING CHALLENGES: HIGH RESOLUTION (OSTEOCYTE LACUNAE), HIGH DENSITY (METAL IMPLANTS)

Phil Salmon
Bruker-microCT, Belgium



Bone and osteoporosis research has played a role in driving the development of microCT systems with high resolution and throughput for analysis of preclinical and clinical bone samples. Bone research continues to create requirements that test the frontiers of performance of micro/nanoCT technology. It does so in two different directions.

First, in the direction of submicron nano-CT imaging: interest is growing into the role of osteocytes within the bone matrix. MicroCT can measure in 3D the size, shape and distribution of osteocyte lacunae, providing information about the history of lacunar formation and remodeling – a four dimensional time-stamp of the activity of the osteoblasts-osteocytes in growing and remodeling bone. Osteocyte lacunae have a diameter range of 5–9 microns, meaning that microCT voxel sizes of near or below a micron are ideal for accurate measurement of osteocyte lacunar morphology. Good image signal to noise ratio is also essential to resolve the lacunae from noise dots.

Second, in the direction of imaging of metal orthopedic implants which pose a particular difficulty for microCT due to strong Z⁴-proportional X-ray absorption and consequent extreme beam hardening in metals. It is not the imaging of metals per se that is the problem, but more the imaging of much lower density materials surrounding the metal – and in this context bone itself becomes a “very low density material”. This is a different technical challenge for microCT requiring innovations in camera and source technology and reconstruction software.

A new nanoCT instrument, the SkyScan2211, represents a step toward solving both the above requirements, with two X-ray cameras optimized respectively for both the above imaging challenges. The first is an 11 megapixel CCD, precisely coupled without geometric distortion to a scintillator optimized for submicron resolution. The second camera is a flat panel detector with special radiation-hardened electronics, optimized for large and high-density objects, and a thicker scintillator for detection of high energy X-rays. An X-ray source is fitted which again meets both the submicron and the large object-high density challenges. While allowing a submicron emission spot size for submicron resolutions, it also has a high top voltage of 190 kV, significantly extending the possibilities for imaging metal objects such as orthopedic implants. This instrument thus provides a multi-scale solution from submicron imaging up to imaging of large metal-containing objects. It represents a new technical resource extending the frontier of imaging possibilities for bone and orthopedic research.

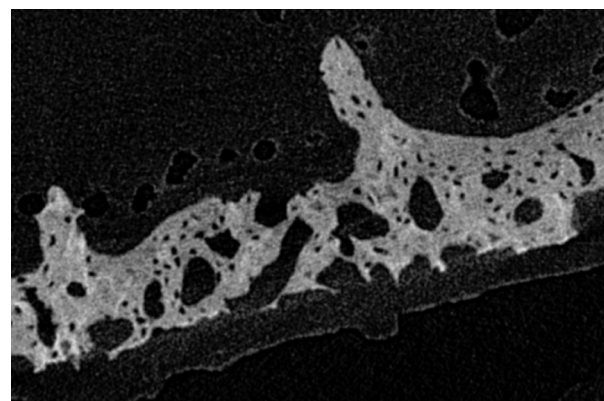


Fig. 1. Submicron pixel resolution allows visualisation and analysis of osteocyte lacunae as well as mineralisation heterogeneity.

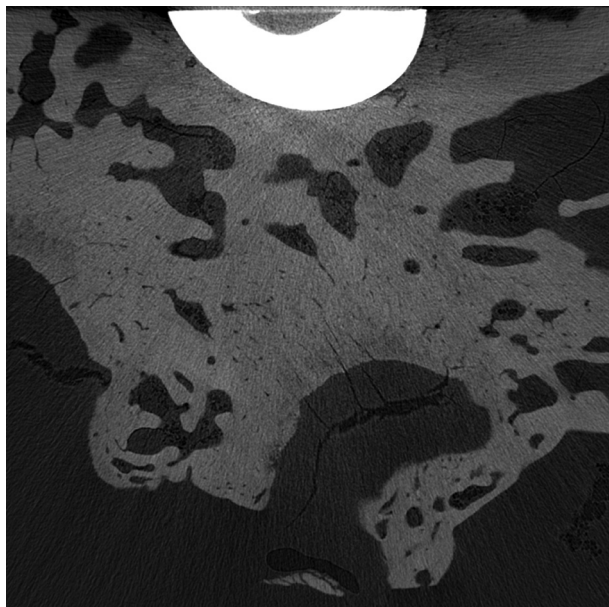


Fig. 2. Imaging of bone close to a metal implant tests the ability of microCT hardware and software to overcome artefacts associated with extreme beam hardening in metals.

Brief CV

Research Area(s): Bone biology, microCT imaging, quantitative 3D image analysis, 3D visualisation software, tomographic reconstruction methods, in-vivo small animal imaging, general microCT application support in many fields.

Technical Expertise: MicroCT imaging and 3D image analysis and quantification (morphometry and microdensitometry), bone and dental biology; bone histomorphometry (e.g. OsteoMeasure system) including dynamic fluorescent double-labelling, radiation biology and biophysics (alpha radionuclide semiconductor detectors, solid state track detectors, nuclear contamination monitoring, radionuclide dosimetry and biokinetics); marine biology, oceanography.

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CALCIUM-DEPENDENT ACTOMYOSIN CONTRACTILITY IN OSTEOCYTES UNDER MECHANICAL LOADING

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Intracellular Ca^{+2} ($[\text{Ca}^{+2}]_i$) oscillations, mediated by mechanosensitive Ca^{+2} channels and the ER Ca^{+2} store, have been observed in osteocytes in response to mechanical loading *in vitro* and *ex vivo* in our laboratory. While many distant downstream gene expression pathways of $[\text{Ca}^{+2}]_i$ signaling have been studied, the immediate, temporally-regulated effects of these numerous $[\text{Ca}^{+2}]_i$ oscillations in osteocytes have not been elucidated. A recent study in the gene expression of primary osteocytes has suggested high levels of muscle contraction-related proteins. A hallmark of muscle is its $[\text{Ca}^{+2}]_i$ -dependent actomyosin contractility. We hypothesized that

osteocytes utilize $[\text{Ca}^{+2}]_i$ oscillations to activate pulsing, muscle-like contractile mechanical behavior. In this study, we used a quasi-3D imaging technique to simultaneously measure the contractile behavior of the actin networks and $[\text{Ca}^{+2}]_i$ in single osteocytes.

$[\text{Ca}^{+2}]_i$ spikes were induced using fluid flow, ATP, or ionomycin in MLO-Y4 osteocytes. Contraction in the actin networks was measured immediately upon onset of $[\text{Ca}^{+2}]_i$ influx in all groups, indicated by a decrease in the strain value. Microtubule networks did not display a similar contractile response. Longer imaging of actin contractions displayed reversible, phasic contractions in the actin networks over a period of ~ 180 s.

As non-muscle and smooth muscle myosin II isoforms are regulated by myosin light chain kinase (MLCK) and skeletal and cardiac myosin II isoforms by troponins, we sought to determine the myosin responsible for the observed contraction. Under ATP stimulation, MLCK inhibition by ML-7 drastically altered the kinetics of contraction, but skeletal and non-muscle myosin II inhibition by blebbistatin had no effect. This pointed towards a smooth muscle myosin mediated contraction. Furthermore, we verified the presence of smooth muscle myosin heavy chain (SMMHC) in primary osteocytes and MLO-Y4 osteocytes.

Here, we demonstrate a novel osteocyte mechano- and transduction behavior where $[\text{Ca}^{+2}]_i$ oscillations activate dynamic actomyosin contractions. Future studies will verify this mechanism in *ex vivo* osteocytes, as well as investigate downstream behaviors of contractility in osteocytes, such as contractility-mediated vesicle exocytosis.

Brief CV

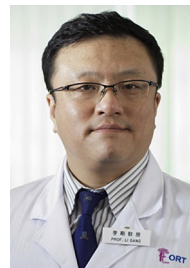
Dr. Guo received his M.S. in 1990 and Ph.D. in 1994 in Medical Engineering and Medical Physics from Harvard University-MIT. In 1994–1996, Professor Guo did his postdoctoral fellowship in the Orthopaedic Research Laboratories at the University of Michigan at Ann Arbor with Professor Steven A. Goldstein in orthopaedic bioengineering. In 1996 he joined the Department of Mechanical Engineering and then Department of Biomedical Engineering at Columbia University. He directs the Bone Bioengineering Laboratory in the Department of Biomedical Engineering at Columbia focusing his research interests in micromechanics of bone tissue, computational biomechanics, and mechanobiology of bone. His past honors include Young Investigator Recognition Award from the Orthopaedic Research Society, National Research Service Award from the US National Institutes of Health (NIH), a CAREER award from the US National Foundation of Science (NSF), Funds for Talented Professionals (Joint Research Fund for Overseas Chinese Young Scholars) from the National Natural Science Foundation of China. He was elected as a fellow to the American Institute for Medical and Biological Engineering. He was one of the founders and served as co-Editor-in-Chief of Cellular and Molecular Bioengineering (CMBE), an international journal of US Biomedical Engineering Society (BMES). He served as President of International Chinese Musculoskeletal Research Society, the Society for Physical Regulation in Biology and Medicine, Member of Board of Directors of Orthopaedic Research Society, and Member of Board of Directors of American Institute for Medical and Biological Engineering.

Technical Expertise: Bone Mechanics, Imaging and Finite Element Analyses of Human Bone Microstructure, Mechanobiology of Bone, Mechanotransduction, and Cell Mechanics.

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TRACING STEM CELLS USING IN VIVO IMAGING TECHNIQUES IN BONE REPAIR AND CANCER RESEARCH

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Regenerative medicine with the use of stem cells is the therapeutic alternative for many disease states. Questions remain regarding the viability