BIOGRAPHICAL SKETCH

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NAME: Ryan K. Roeder

eRA COMMONS USER NAME (credential, e.g., agency login): rroeder

POSITION TITLE: Professor, University of Notre Dame

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Purdue University	B.S.	05/1994	Materials Engineering
Purdue University	Ph.D.	05/1999	Materials Engineering
Indiana University Medical Center		06/2001	Biomaterials and Bone Biomechanics

A. Personal Statement

My research interests broadly span biomaterials, including nanoparticles for targeted contrast agents and drug delivery and scaffolds for regenerating tissues, as well biomechanics, including the mechanobiology and micromechanics of musculoskeletal tissues. My research group is thus intentionally diverse, including students from a variety of different backgrounds, which enhances their training experience. I have trained 3 postdocs, and 18 doctoral students over the last 18 years; 50% of these trainees have gone on to faculty, postdoctoral, and research positions at universities, research hospitals, and private research institutes and the other 50% have gone on to industry positions after leaving my lab. I have served as Project Director on a number of large projects funded by the NIH, NSF, CDMRP PRMRP, as well as industrial sponsors and private foundations. I have a number of national and international collaborations, which have resulted in productive scientific exchange and new research directions. My lab has extensive expertise in nanoparticle design, synthesis, surface functionalization and characterization; *in vitro* and *in vivo* models for targeted delivery; and various X-ray computed tomography (CT) imaging techniques (contrast-enhanced, dual-energy, photon-counting). In particular, we recently developed and demonstrated capabilities for multi-contrast imaging with photon-counting spectral computed tomography, which will be utilized for the proposed project. Expertise relevant to the proposed project is highlighted by the following four peer-reviewed publications:

1. T.A. Finamore, T.E. Curtis, J.V. Tedesco, K. Grandfield and R.K. Roeder, "Nondestructive, Longitudinal Measurement of Collagen Scaffold Degradation Using Computed Tomography and Gold Nanoparticles," *Nanoscale*, **11**, 4345-4354 (2019). doi:10.1039/c9nr00313d
2. T.E. Curtis and R.K. Roeder, "Quantification of Multiple Mixed Contrast and Tissue Compositions using Photon-Counting Spectral Computed Tomography," *J. Med. Imaging*, **6** [1] 013501 (2019). doi:10.1117/1.JMI.6.1.013501
3. L.C. Cole, T.L. McGinnity, L.E. Irimata, T. Vargo-Gogola and R.K. Roeder, "Effects of Bisphosphonate Ligands and PEGylation on Targeted Delivery of Gold Nanoparticles for Contrast-Enhanced Radiographic Detection of Breast Microcalcifications," *Acta Biomaterialia*, **82**, 122-132 (2018). doi:10.1016/j.actbio.2018.10.014
4. T.E. Curtis and R.K. Roeder, "Effects of calibration methods on quantitative material decomposition in photon-counting spectral computed tomography using a maximum *a posteriori* estimator," *Med. Phys.,* **44** [10] 5187-5197 (2017). doi:10.1002/mp.12457

B. Positions and Honors

Professional Employment

1999-2001 Postdoctoral Fellow, Department of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN
2001-2007 Assistant Professor, Department of Aerospace and Mechanical Engineering

2007-2016 Associate Professor, Dept. of Aerospace & Mechanical Eng., Bioengineering Graduate Program
2016-present Professor, Dept. of Aerospace & Mechanical Engineering, Bioengineering Graduate Program, University of Notre Dame, Notre Dame, IN

Professional Memberships

Orthopaedic Research Society (ORS), Society for Biomaterials (SFB), The American Ceramic Society (ACerS), The Materials Research Society (MRS), The Minerals, Metals, and Materials Society (TMS)

Professional Activities (selected, last three years)

2020-Present Editorial Board, *Biosensors*
2019 Session Organizer, Seeing More Clearly: Nanoparticle Imaging Probes in Biomedicine, *Society for Biomaterials Annual Meeting*, Seattle, WA
2018-Present Board of Directors, HAPPE Spine, LLC
2018-Present Mentor, Society for Biomaterials Faculty Mentoring Program
2018 Scientific Committee, *MARS Spectral CT Workshop*, Christchurch, NZ
2018 Session Organizer, Translation of Nanoparticle Contrast Agents for Clinical X-ray Imaging Modalities, *Society for Biomaterials Annual Meeting*, Atlanta, GA
2016-Present Project Development Team, Indiana Clinical and Translational Sciences Institute, Notre Dame
2016 Abstract Reviewer, *10th World Biomaterials Congress (WBC)*, Montreal, Canada
2016 Abstract Reviewer, *2016 Annual Meeting of the Orthopaedic Research Society*, Orlando, FL
2014-2019 Executive Committee, Program Co-Leader, Harper Cancer Research Institute, Notre Dame
2014-2018 Editorial Board, *Adv. Health Care Technol.*
2013-Present Founder and President, Spinesmith LLC
2011-Present Editorial Board, *PLoS ONE*
2011-Present Editorial Board, *J. Mech. Behav. Biomed. Mater.*
2009-Present Advisory Committee, Purdue University, School of Materials Engineering

Peer Review: AAAS, ACS, NIH, NSF, numerous journals, including *Acta Biomaterialia, ACS Nano, Adv. Healthcare Mater., Biomaterials, Chem. Mater., Chem. Rev., J. Biomed. Mater. Res., J. Mech. Behav. Biomed. Mater., Langmuir, Nano Lett., Nanomedicine, Nanoscale, Nat. Commun.*

Honors and Awards (selected)

2013 Rev. Edmund P. Joyce, C.S.C., Award for Excellence in Undergraduate Teaching, Univ. of Notre Dame
2012 Outstanding Materials Engineer Award, School of Materials Engineering, Purdue University
2008 Top Reviewer, *Journal of the Mechanical Behavior of Biomedical Materials*
2007 Early Career Faculty Fellow Award, The Minerals, Metals, and Materials Society (TMS)

C. Contributions to Science

1. **Photon-counting computed tomography (PCCT)**. PCCT enables multi-energy image acquisition for high quantitative molecular imaging at high spatial resolution. As such, PCCT could be transformational for clinical diagnostic imaging. Therefore, this contribution is motivated by a need to develop preclinical PCCT systems, capabilities and applications as a foundation for clinical translation. My lab was the first site in North America equipped with commercially-available preclinical PCCT system (MARS Bioimaging) in 2015. We have developed calibration methods and non-proprietary software for precise and accurate material decomposition, which has been demonstrated in experimental studies characterizing the accuracy of multi-material (contrast and tissue) identification and quantification in PCCT. We further demonstrated, for the first time, that PCCT enabled quantitative molecular imaging of multiple spatially coincident contrast agent and tissue compositions, which is not possible with current clinical molecular imaging modalities (PET and MRI). Finally, I conceived and developed a "spectral library" of nanoparticle contrast agents that can function as a radiopharmacy for PCCT, analogous to radionuclides in nuclear imaging.

   a. T.E. Curtis and R.K. Roeder, "Quantification of Mixed Contrast and Tissue Compositions using Photon-Counting Spectral Computed Tomography," *J. Med. Imaging*, **6** [1] 013501 (2019). doi:10.1117/1.JMI.6.1.013501
   b. T.E. Curtis and R.K. Roeder, "Effects of calibration methods on quantitative material decomposition in photon-counting spectral computed tomography using a maximum *a posteriori* estimator," *Med. Phys.,* **44** [10] 5187-5197 (2017). doi:10.1002/mp.12457

c. R.K. Roeder, T.E. Curtis, P.D. Nallathamby, L.E. Irimata, T.L. McGinnity, L.E. Cole, T. Vargo-Gogola and K.D. Cowden Dahl, "Nanoparticle Imaging Probes for Molecular Imaging with Computed Tomography and Application to Cancer Imaging," *Proc. SPIE*, **10132**, 101320X (2017). doi:10.1117/12.2255688
d. T.L. McGinnity, O. Dominguez, T.E. Curtis, P.D. Nallathamby, A.J. Hoffman and R.K. Roeder, "Hafnia (HfO_2) nanoparticles as an X-ray contrast agent and mid-infrared biosensor," *Nanoscale*, **8**, 13627-13637 (2016). doi:10.1039/c6nr03217f

2. **Nanoparticle imaging probes for CT**. This contribution is motivated by opportunities to transform CT into a molecular imaging modality. CT is the most widely used clinical diagnostic imaging modality but is currently limited to anatomic imaging, requiring adjunct modalities for molecular imaging. Therefore, my lab is striving to enable molecular imaging capabilities with CT and PCCT using nanoparticle contrast agents and this contribution has quickly become the main theme in my lab over the last 8 years. We developed bisphosphonate functionalized gold nanoparticles (BP-Au NPs) for targeted delivery to breast microcalcifications, which are the most common abnormality associated with breast cancer. We also developed new murine models which allowed us to demonstrate the ability of BP-Au NPs to enhance sensitivity and specificity for the detection of breast microcalcifications by CT in both normal and "dense" mammary tissue. Importantly, the accuracy of mammography is known to be decreased by up to three-fold among premenopausal women with elevated breast tissue density. Therefore, our results suggest that a targeted nanoparticle contrast agent could be used to improve screening within this high risk subpopulation. We are also investigating new nanoparticle imaging probes designed for leveraging the capabilities of PCCT, enabling multi-modal imaging, immunotargeting specific cell populations, and monitoring drug delivery.

a. L.E. Cole, T. Vargo-Gogola and R.K. Roeder, "Contrast-enhanced X-ray detection of breast microcalcifications in a murine model using targeted gold nanoparticles," *ACS Nano*, **8** [7] 7486-7496 (2014). doi:10.1021/nn5027802
b. L.E. Cole, T. Vargo-Gogola and R.K. Roeder, "Contrast-enhanced X-ray detection of microcalcifications in radiographically dense mammary tissue using targeted gold nanoparticles," *ACS Nano*, **9** [9] 8923-8932 (2015). doi:10.1021/acsnano.5b02749
c. P.D. Nallathamby, J. Hopf, L.E. Irimata, T.L. McGinnity and R.K. Roeder, "Preparation of fluorescent Au-SiO_2 core-shell nanoparticles and nanorods with tunable silica shell thickness and surface modification for immunotargeting," *J. Mater. Chem. B*, **4**, 5418-5428 (2016). doi:10.1039/c6tb01659f
d. T.A. Finamore, T.E. Curtis, J.V. Tedesco, K. Grandfield and R.K. Roeder, "Nondestructive, Longitudinal Measurement of Collagen Scaffold Degradation Using Computed Tomography and Gold Nanoparticles," *Nanoscale*, **11**, 4345-4354 (2019). doi:10.1039/c9nr00313d

3. **Non-destructive detection of microdamage in bone using contrast-enhanced micro-computed tomography.** This contribution was motivated by a lack of clinical means to non-invasively assess bone quality in patients at risk for fatigue or fragility fractures, and a lack of scientific means to non-destructively measure microdamage accumulation in bone tissue. In 2000, a panel at the European Society of Biomechanics identified these problems to be critically important but with little feasibility of a solution. My group demonstrated non-destructive, 3-D detection of the presence, spatial location, and accumulation of fatigue microdamage *in vitro* for the first time using contrast-enhanced micro-CT with a precipitated barium sulfate stain developed in my lab. We have demonstrated our new methods in cortical and trabecular bone specimens, whole rodent bones and whole human teeth in numerous publications. Importantly, we validated the new methods against gold-standard histological measurements and have used these methods to perform the first studies to ever simultaneously and nondestructively measure the effects of mineralization, porosity and microdamage on cortical bone fracture susceptibility.

a. H. Leng, X. Wang, R.D. Ross, G.L. Niebur and R.K. Roeder, "Micro-computed tomography of fatigue microdamage in cortical bone using a barium sulfate contrast agent," *J. Mech. Behav. Biomed. Mater.*, **1** [1] 68-75 (2008). doi:10.1016/j.jmbbm.2007.06.002
b. M.D. Landrigan, J. Li, T.L. Turnbull, D.B. Burr, G.L. Niebur and R.K. Roeder, "Contrast-Enhanced Micro-Computed Tomography of Fatigue Microdamage Accumulation in Human Cortical Bone," *Bone*, **48** [3] 443-450 (2011). doi:10.1016/j.bone.2010.10.160
c. T.L. Turnbull, J.A. Gargac, G.L. Niebur and R.K. Roeder, "Detection of fatigue microdamage in whole rat femora using contrast-enhanced micro-CT," *J. Biomechanics*, **44** [13] 2395-2400 (2011). doi:10.1016/j.jbiomech.2011.06.032

d. T.L. Turnbull, A.P. Baumann and R.K. Roeder, "Fatigue microcracks that initiate fracture are located near elevated intracortical porosity but not elevated mineralization," *J. Biomechanics*, **47** [12] 3135-3142 (2014). doi:10.1016/j.jbiomech.2014.06.022

4. **Bioactive hydroxyapatite (HA) reinforced polyetheretherketone (PEEK) composites and scaffolds**. This contribution was motivated by a clinical need for improved osteointegration in interbody spinal fusion implants composed of PEEK. Despite many favorable characteristics, PEEK is bioinert requiring augmentation with autograft or growth factors in order to achieve a bony fusion. Therefore, my lab developed novel bioactive HA whisker reinforced PEEK composites and scaffolds tailored to mimic the mechanical properties of human bone tissue. We further demonstrated the ability to manufacture PEEK implants with tailored levels and placement of bioactive reinforcements and porosity, opening new opportunities for implant design which may translate into new treatment options for improved osteointegration. This contribution has led to patent applications, both awarded and under continuing examination, and the launch of a start-up company which has raised $2M in venture capital funding to translate this technology to the clinic.

   a. G.L. Converse, W. Yue and R.K. Roeder, "Processing and tensile properties of hydroxyapatite-whisker-reinforced polyetheretherketone," *Biomaterials*, **28** [6] 927-935 (2007). doi:10.1016/j.biomaterials.2006.10.031
   b. G.L. Converse, T.L. Conrad and R.K. Roeder, "Mechanical properties of hydroxyapatite whisker reinforced polyetherketoneketone composite scaffolds," *J. Mech. Behav. Biomed. Mater.*, **2** [6] 627-635 (2009). doi:10.1016/j.jmbbm.2009.07.002
   c. G.L. Converse, T.L. Conrad, C.H. Merrill and R.K. Roeder, "Hydroxyapatite whisker reinforced polyetherketoneketone bone ingrowth scaffolds," *Acta Biomaterialia*, **6** [3] 856-863 (2010). doi:10.1016/j.actbio.2009.08.004
   d. R.K. Roeder, "Bioactive Polyaryletherketone Composites"; pp. 203-227 in the PEEK Biomaterials Handbook, 2nd Edition. Edited by S.M. Kurtz. Elsevier, Inc., Amsterdam, 2019. doi:10.1016/B978-0-12-812524-3.00012-0

5. **Structural and mechanical anisotropy in human cortical bone tissue.** This contribution was motivated by limited understanding of the key structural factors governing anisotropy in cortical bone. My lab was able to reconcile prior conflicting reports by showing that the elastic anisotropy of human femoral cortical bone varies systematically, exhibiting transverse isotropy near the mid-diaphysis and orthotropy in the distal and proximal portions of the diaphysis. We simultaneously developed a specimen-specific, multiscale micromechanical model to accurately predict elastic anisotropy in cortical bone. Through a combination of experimental measurements and computational modeling, we identified that the predominate transverse isotropy of cortical bone is primarily governed by the orientation distribution of apatite crystals in the collagen matrix, while more subtle variations in orthotropy are primarily governed by intracortical porosity. Therefore, we provided new insights into structure-function relationships in cortical bone tissue. Our experimental data and micromechanical models are now frequently cited in a subsequent proliferation of studies in this area.

   a. A.A. Espinoza Orías, J.M. Deuerling, M.D. Landrigan, J.E. Renaud and R.K. Roeder, "Anatomic variation in the elastic anisotropy of cortical bone tissue in the human femur," *J. Mech. Behav. Biomed. Mater.*, **2** [3] 255-263 (2009). doi:10.1016/j.jmbbm.2008.08.005
   b. J.M. Deuerling, W. Yue, A.A. Espinoza Orías and R.K. Roeder, "Specimen-specific multiscale model for the anisotropic elastic constants of human cortical bone," *J. Biomechanics*, **42** [13] 2061-2067 (2009). doi:10.1016/j.jbiomech.2009.06.002
   c. D.J. Rudy, J.M. Deuerling, A.A. Espinoza Orías and R.K. Roeder, "Anatomic variation in the elastic inhomogeneity and anisotropy of human femoral cortical bone tissue is consistent across multiple donors," *J. Biomechanics*, **44** [9] 1817-1820 (2011). doi:10.1016/j.jbiomech.2011.04.009
   d. A.P. Baumann, J.M. Deuerling, D.J. Rudy, G.L. Niebur and R.K. Roeder, "The relative influence of apatite crystal orientations and intracortical porosity on the elastic anisotropy of human cortical bone," *J. Biomechanics*, **45** [16] 2743-2749 (2012). doi:10.1016/j.jbiomech.2012.09.011

D. Research Support

Ongoing Research Support

1. Improvements in Breast Cancer Screening by Molecular Imaging — PI
   Kelly Cares Foundation and St. Joseph Regional Medical Center — 1/1/2016-12/31/2020

The goals of this project are to develop a new translational model to enable imaging of biological tumors from animal models within a human anatomic breast tissue-equivalent phantom using clinical imaging instrumentation and to use this model to evaluate novel methods for breast cancer detection.

2. Indiana Clinical and Translational Science Institute co-I (A. Shekhar *et al*., PIs)
   NIH NCATS UL1TR002529 5/18/2018-5/17/2023
   The overall goal of this project is to accelerate clinical and translational research by the three research universities (Indiana, Purdue and Notre Dame), with partner health care systems, local foundations and corporate partners. The Indiana CTSI provides resources and services to conduct the highest-quality clinical and translational research, offers education and training programs to build a robust translational workforce, engages our community as a partner at all levels, and is an exemplary member of the national CTSA network.

3. Spatial Correlation of Osteocyte Gene Response to Local Mechanical Strain in Bone… co-I (G. Niebur, PI)
   NIH NIAMS R21 AR075937 4/1/2020-3/31/2022
   The goal of the proposed research project is to detect altered gene expression in bone cells in response to local mechanical loads in order to determine the levels and types of load that induce drive bone physiology.

Completed Research Support (last three years)

1. Selective targeting and destruction of trastuzumab resistant breast cancer cells co-PI (C. Osipo, co-PI)
   Loyola University Medical Center Collaborative Grant 9/1/2015-12/31/2019
   The goal of this project is to target and kill HER2+/Jagged-1+ breast cancer cells to prevent or reverse resistance to anti-HER2 therapy using nanoparticles conjugated with trastuzumab and anti-Jagged-1.

2. Predictive computational model for the combined effects of intracortical porosity, fatigue microdamage, and mineralization on fracture susceptibility in cortical bone PI
   Merck, Sharp and Dohme Corporation 10/1/2015-12/31/2018
   The goal of this project is to develop and validate a predictive specimen-specific computational model for the combined effects of intracortical porosity, fatigue microdamage, and mineralization on the fracture susceptibility of cortical bone.

3. Cytocompatibility of Hafnia Nanoparticles for Biomedical Applications co-I (M. Epple, PI)
   German Ministry of Education and Research (BMBF), Deutscher Akademischer Austausch Dienst (DAAD), PPP: Project Related Exchange with the USA 1/1/2016-12/31/2018
   The goal of this project is to facilitate the exchange of German researchers to the United States investigating the cytocompatibility of hafnia NPs of varying size and surface treatment.

4. Holographic Assembly of Reconfigurable Nanoscale Plasmonic and Photonic Elements co-I (Bohn, PI)
   DARPA-14-56-A2P-PA-055, Atoms to Product (A2P) TA1 4/1/2015-8/30/2018
   The overall goal of this project is to develop and assemble reconfigurable lattices of dielectric and/or metallic nanoparticles within polymer matrices. Dr. Roeder's contribution is focused on nanoparticle synthesis and assembly in anisotropic structures.

5. *In Vivo* Imaging of Ovarian Cancer Stem Cells using Targeted Imaging Probes… co-PI (Cowden Dahl, co-PI)
   Walther Cancer Foundation, Advancing Basic Cancer Research (ABC) Grant 7/1/2015-6/30/2018
   The goal of this project is to target, identify and quantify ovarian cancer stem cells within a heterogeneous environment using spectral CT and nanoparticle probes with surface ligands targeting CD133.

6. A Spectral Library of Nanoparticle Contrast Agents for Spectral (Color) X-ray Imaging PI
   NSF DMR-1309587 1/1/2014-12/31/2017
   The goal of this project is to develop a spectral library of nanoparticle contrast agents to fully leverage the capabilities of spectral (color) X-ray imaging.

7. Acquisition of a Preclinical Spectral Micro-CT System PI
   University of Notre Dame Equipment Renewal and Restoration Program 4/1/2016-6/31/2017
   The goal of this project is to acquire a preclinical photon-counting spectral micro-CT system for the Notre Dame Integrated Imaging Facility.

8. Cytocompatibility of Hafnia Nanoparticles for Biomedical Applications PI
   University of Notre Dame Global Collaboration Initiative 7/1/2016-6/30/2017
   The goal of this project is to facilitate the exchange of members of Dr. Roeder's lab to the University of Duisburg-Essen in Germany investigating the cytocompatibility of hafnia NPs.