BIOGRAPHICAL SKETCH

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NAME: Ryan K. Roeder

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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 17 Ph.D. students and 3 postdocs over the last 12 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 active collaborations with investigators at the University of Canterbury and MARS Bioimaging (Christchurch, New Zealand), the University of Duisburg-Essen (Germany), the Indiana University School of Medicine (IUSM), and the Loyola University Medical Center, which have resulted in productive scientific exchange and new research directions.

A recent focus of my lab has been on targeted nanoparticle contrast agents and computed tomography (CT). Since 2010, my lab has published more than 30 papers focused on these topics. These publications demonstrate expertise in nanoparticle synthesis, surface functionalization, and characterization; *in vitro* and *in vivo* models for targeted delivery, especially in cancer; and various CT imaging techniques (contrast-enhanced, dual-energy, spectral). The following four peer-reviewed publications highlight my experience and qualifications in this area of research:

1. 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
2. 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
3. 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
4. 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 Press release.

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, University of Notre Dame, Notre Dame, IN

2007-2016 Associate Professor, Department of Aerospace and Mechanical Engineering, Bioengineering Graduate Program, University of Notre Dame, Notre Dame, IN

2016-present Professor, Department of Aerospace and 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)

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
2015 Special Session Co-organizer (jointly with JSME), Bone Tissue Engineering, Summer Biomechanics, Bioengineering and Biotransport Conference (SB^3C), Snowbird, UT
2015 Co-organizer, *2nd International PEEK Meeting*, Washington, DC
2014-Present Executive Committee, Program Co-Leader, Harper Cancer Research Institute, Notre Dame
2014-Present Editorial Board, *Adv. Health Care Technol.*
2011-Present Editorial Board, *PLoS ONE*
2011-Present Editorial Board, *J. Mech. Behav. Biomed. Mater.*

Peer Review: AAAS, ACS, NIH, NSF, > 25 journals, including *Acta Biomaterialia, ACS Biomater. Sci. Eng., Adv. Healthcare Mater., Biomaterials, Bioconjugate Chem., Chem. Rev., J. Biomed. Mater. Res., J. Mater. Sci. Mater. Med., J. Mech. Behav. Biomed. Mater., Langmuir, Nanoscale.*

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. **Targeted nanoparticle X-ray contrast agents**. Computed tomography is the most widely used clinical diagnostic imaging modality but is limited by sensitivity and soft tissue contrast. Therefore, my lab is striving to enable molecular imaging capabilities with CT using targeted nanoparticle contrast agents. This contribution has quickly become the main theme in my lab over the last 6 years. We developed and investigated bisphosphonate functionalized gold nanoparticles (BP-Au NPs) for achieving targeted delivery to bone and 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 X-ray imaging 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 contrast agents (e.g. HfO_2) for leveraging the capabilities of spectral (multienergy) computed tomography.

   a. 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

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 Press release.
c. L.E. Cole, R.D. Ross, J.M.R. Tilley, T. Vargo-Gogola and R.K. Roeder, "Gold nanoparticles as contrast agents in X-ray imaging and computed tomography," *Nanomedicine*, **10** [2] 321-341 (2015). doi:10.2217/nnm.14.171
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. **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

3. **Bioactive hydroxyapatite (HA) reinforced polyetheretherketone (PEEK) composites and scaffolds**. This contribution was motivated by a clinical need for improved osteointegration of current spinal 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 patents applications, both awarded and under continuing examination, and the launch of a start-up company to translate this intellectual property.

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. R.K. Roeder, G.L. Converse and S.M. Smith, "Porous Composite Biomaterials and Related Methods," International Patent Application Serial No. PCT/US08/55391, U.S. Patent Application No. 20080206297, August 28, 2008. Under continuing examination.
c. 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
d. 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

4. **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. Moreover, 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

Complete Lists of Publications

https://ame.nd.edu/research/faculty-research-labs/rroeder/publications
https://scholar.google.com/citations?user=ube4zJkAAAAJ&hl=en
http://www.researcherid.com/rid/A-9398-2008

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 — 1/1/2016-12/31/2017
   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. 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.

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 — 1/1/2016-12/31/2017
   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. 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 of varying size and surface treatment.

5. *In Vivo* Imaging of Ovarian Cancer Stem Cells using Targeted Imaging Probes for Spectral CT — co-PI (Cowden Dahl, co-PI)

Walther Cancer Foundation, Advancing Basic Cancer Research (ABC) Grant 7/1/2015-6/30/2017
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. Holographic Assembly of Reconfigurable Nanoscale Plasmonic and Photonic Elements co-I (Bohn, PI)
DARPA-14-56-A2P-PA-055, Atoms to Product (A2P) TA1 4/1/2015-3/31/2018
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.

7. 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.

8. Development of a Rabbit Model for 'Atypical' Fractures in Cortical Bone During Long-Term Bisphosphonate Therapy co-PI (M. Allen, co-PI)
Indiana CTSI, CTR Pilot Grant (supported by NIH RR025761) 10/1/2014-9/30/2016
The goal of this project is to develop a preclinical animal model of atypical femoral fractures.

9. 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 10/1/2015-6/31/2017
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.

10. Selective targeting and destruction of trastuzumab resistant breast cancer cells co-PI (C. Osipo, co-PI)
Loyola University Medical Center Collaborative Grant 9/1/2015-8/31/2017
The goal of this project is to specifically target and kill HER2+/Jagged-1+ breast cancer cells to prevent or reverse resistance to anti-HER2 therapy using HER2-targeted nanoparticles conjugated with trastuzumab and anti-Jagged-1.

Completed Research Support (last three years)

1. Improved delivery and clearance of targeted nanoparticles for contrast-enhanced X-ray detection of breast microcalcifications co-PI (T. Vargo-Gogola, co-PI)
Walther Cancer Foundation, Walther Seeding Research in Cancer (SRC) Grant 7/1/2014-6/30/2015
The goal of this project was to prepare and evaluate the performance of BP-PEG-Au NPs using established murine model for microcalcifications in radiographically dense mammary tissue.

2. Which Characteristics of Intracortical Porosity Compromise Fracture Resistance? PI
Merck, Sharp and Dohme Corporation 11/1/2013-12/31/2014
The goal of this project was to identify the characteristics of intracortical porosity which compromise the fracture resistance of bone.

3. Contrast-Enhanced X-Ray Detection of Breast Microcalcifications in a Murine Model of Radiographically Dense Mammary Tissue co-PI (T. Vargo-Gogola, co-PI)
St. Joseph's Regional Medical Center, Seeding Research in Cancer (SRC) Grant 5/1/2013-4/30/2014
The goal of this project was to develop a novel mouse model to enable *in vivo* investigation of targeted labeling and radiographic imaging of breast microcalcifications.