BIOGRAPHICAL SKETCH

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NAME: John Beyer Brunski

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

POSITION TITLE: Senior Research Engineer

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
University of Pennsylvania, Philadelphia, PA	B.S.	05/1970	Metallurgy & Mat. Sci.
Stanford University, Stanford, CA	M.S.	06/1972	Materials Sci. & Eng.
University of Pennsylvania, Philadelphia, PA	Ph.D.	05/1977	Metallurgy & Mat. Sci.

A. Personal Statement

My research over the last 40 years has centered on implants in bone (both oral/maxillofacial and orthopedic), with an emphasis on biomechanics of the dental implant-bone interface. At the translational level, I've worked with clinicians (e.g., Dr. Kenji Higuchi) and dental implant companies (e.g., Nobel Biocare) to develop methods to predict and measure *in vivo* loading of oral and maxillofacial implants in humans, and to assess implant stability. That work has helped give clinicians better methods for estimating the expected loadings on implants and, in turn, the stress-strain limits of peri-implant bone. At the basic science level, I have worked with biological scientists (Dr. Helms at Stanford and Dr. Nanci at University of Montreal) to understand cell and molecular determinants of tissue response to stresses and strains at bone-implant interfaces. This latter research on interfacial "mechanobiology" has helped define key biomechanical factors regulating bone healing around implants and an improved mechanistic understanding of how implants function biomechanically.

B. Positions and Honors

Positions

1977 - 1983 Assistant Professor of Biomedical Engineering, Rensselaer Polytechnic Institute, Troy, NY
1983 - 1994 Associate Professor of Biomedical Engineering, Rensselaer Polytechnic Institute, Troy, NY
1994 - 2009 Professor of Biomedical Engineering, Rensselaer Polytechnic Institute, Troy, NY
2009 – Senior Research Engineer, Division of Plastic & Reconstructive Surgery, Dept. of Surgery, School of Medicine, Stanford University, Stanford, CA

Federal Government Public Advisory Committees

2000 – 2004 Ad hoc Member, ZRG1 SSS-M (03), on Bioengineering Research Grants/Partnerships; plus ZRG1 SSS-M (02 and 01) Musculoskeletal & Dental Sciences Special Emphasis Panel
2004 - 2005 Ad hoc Member, NIDCR Special Grants review Committee
2004 – 2008 Ad hoc Member, ZRG1 MOSS-G (01), now (MTE) "Musculoskeletal Tissue Engineering"
2009 - 2012 Member, MTE "Musculoskeletal Tissue Engineering" study section
2018, June Small Business Review Meeting (ZRG1 MOSS-D10), June 28, 2018

Honors and Awards

1995 *Boeing Outstanding Educator Award*: member of a Rensselaer faculty team receiving a $50,000 prize for "a significant difference" in undergraduate teaching in engineering, manufacturing, computing, etc.
2000 *NEEDS Premier Courseware 2000 Award*: part of a Rensselaer team supported by NSF's "Project Links", for web-based materials linking mathematical topics to applications in engineering and science

2001 *American Society of Mechanical Engineers (ASME) Curriculum Innovation Award*, given to the "Project Links" team
2001 *Isaiah Lew Memorial Research Award*, American Academy of Implant Dentistry Research Foundation
2006 First *William R. Laney Visiting Professor*, Division of Prosthodontics, Mayo Clinic, Rochester, MN
2006 *Jerome M. and Dorothy Schweitzer Research Award*, Greater NY Academy of Prosthodontics
2011 Fellow, International Academy for Oral and Facial Rehabilitation (IAOFR)

C. Contributions to Science

1. Brunski JB, Moccia, AF Jr., Pollack SR, Korostoff E, and Trachtenberg D, "The Influence of Functional Use of Endosseous Dental Implants on the Tissue-Implant Interface, Part I: Histological Aspects*," J. Dent. Res. 58*(10): 1953-1969 (1979)
My first paper in the dental implant field (supported by NIDR), this publication started to explain the origin of "fibrous tissue encapsulation" of dental implants; the work pointed out that this fibrous tissue was likely triggered by excessive instability ("micromotion") related to early loading of the implant after implantation. Prior to this work, many clinicians believed – with little evidence -- that fibrous tissue around dental implants acted as a kind of "pseudo-periodontal ligament". This publication argued that this idea of a pseudo-periodontal ligament was not supported by the evidence. This paper also started a discussion – which continues to the present -- about the basic science behind immediate vs. delayed loading of implants, and referenced the 10-year monograph of P-I Brånemark in Sweden, which employed titanium implants having a direct bone-implant anchorage that was termed "osseointegration". I was recently invited to write a paper that provided an historical backdrop surrounding this 1979 paper as well as the rest of my work: Brunski JB "Where are we coming from?", an invited paper in a supplement of *Int J Prosthodontics* entitled "On Implant Prosthodontics: One Narrative, Twelve Voices", *Int J Prosthodontics 31*, Suppl 2018, pp. S15 – S22.

2. Brunski JB, "Biomechanical Factors Affecting the Bone-Dental Implant Interface," *Clin. Materials 10*:153-201 (1992)
This early publication was a review that recast the dental implant problem as a *design problem in bioengineering*. That is, with NIH support, this review defined the need to have a better basic science understanding of the inter-relationships among biomechanical factors in this multidisciplinary problem, e.g., implant loading, timing of loading, prosthetic design, implant geometry, bone properties, and, importantly, the mechanobiological reactions of bone to interfacial stresses and strains. This paper emphasized that informed design of an implant can only be done on the basis of a solid foundation of basic science, including clinical, engineering and biological science. I was the sole author, but the perspective was based on the basic design process that any engineer would apply in looking at a multi-disciplinary problem such as the use of oral implants. This approach spawned a number of papers from my lab relating to measuring bite forces on implants, developing models for predicting implant loading, and using new instruments to measure implant stability. A few example publications were: (A) Skalak R, Brunski JB and Mendelson M, "A Method for Calculating the Distribution of Vertical Forces Among Variable-Stiffness Abutments Supporting a Dental Prosthesis," *1993 Bioengineering Conference, BED-Vol. 24*, (Eds. N.A. Langrana, M.H. Friedman and E.S. Grood) ASME, NY, pp. 347-350; (B) Elias JJ and Brunski JB, "Finite Element Analysis of Load Distribution Among Dental Implants," *1991 Advances in Bioengineering*, BED-Vol. 20 (R. Vanderby, Ed.) ASME, NY, pp. 155-158 (1991); and (C) Elias JJ, Brunski JB, and Scarton HA, "A dynamic modal testing technique for non-invasive assessment of bone-dental implant interfaces" *Int. J. Oral Maxillofac Implants 11*:728-734 (1996).

3. Hoshaw SJ, Brunski JB, and Cochran GVB, "Mechanical Loading of Brånemark Fixtures Affects Interfacial Bone Modeling and Remodeling," *Int. J. Oral Maxillofacial Implants 9*:347-359, 1994.
This paper represented a start at testing one of the numerous (and often confounding) hypotheses about load-related bone remodeling with or without the presence of implants. A doctoral student of mine (Hoshaw) and my orthopaedic colleague (Cochran) took to heart a maxim offered by Noam Chomsky, who wrote: "It is a merit of a theory to be proven false," i.e., a "good" theory (hypothesis) is one that can actually be tested. We set out to test one aspect of the then well-known "Mechanostat" hypothesis of Harold Frost, whose legacy in bone mechanobiology can be tracked in numerous articles and books over the last 5 decades, sampled in these two: Roberts WE et al.

Semin Orthod 2006;12: 216-237; and Martin RB, Burr DB and Skarkey NA *Skeletal Tissue Mechanics*, Springer, 1998. In brief, Frost's "Mechanostat" theory – outlined on pp. 260-262 in Martin et al. above, and in Frost HM. "Bone 'mass' and the "mechanostat": a proposal. *Anat Rec* 1987;219:19 -- asserted that strain magnitudes in bone ("mechanical usage") were involved in turning on (or off) bone *modeling* (on periosteal and endosteal surfaces) as well as *remodeling* ("internal" remodeling). We set up an experiment with Brånemark implants installed in dog tibiae as a way to test this theory with unloaded implants vs. loaded implants. We observed an increase in both modeling and remodeling at loaded interfaces, which was consistent with an understanding of microdamage formation and repair near implants. This work was the first in North America to use Brånemark implants in an animal study. While the authors would be the first to acknowledge some of the work's shortcomings, it helped introduce mechanobiological thinking into the study of oral implants. The study's awareness of osteonal-based remodeling in dogs has also been useful as background to questions that we are currently proposing herein, e.g., What factors go into evaluating an animal model in dental implant research?

4. Leucht P, Kim JB, Wazen R, Nanci A, Brunski J, Helms JA. "Effect of mechanical stimuli on skeletal regeneration around implants". *Bone* 2007 Apr;40(4):919-930.
   This paper was the first to emerge from a tri-institutional NIH grant involving my old university, RPI, plus Drs. Jill Helms at Stanford and Antonio Nanci at Univ. of Montreal. (I retired from RPI in 2009 and moved the NIH project to Stanford.) I reached out to these researchers in 1998 to join me in exploring the dental implant problem from a multidisciplinary perspective involving bioengineering, molecular biology, and calcified tissue science. Post-docs Leucht, Kim, and Wazen (and later Mouraret, see 5 below) helped develop a completely new mouse model that permitted control of implant micromotion during healing. Our analyses involved immunohistochemistry, decalcified and undecalcified histomorphometry, plus in vivo and computational mechanical analyses. This work ushered in a whole new phase of work for us that allowed a much more in-depth molecular and mechanical look at tissue response and "mechanobiology". We began to define tolerable strain magnitudes for osseointegration during early implant motion in a healing site. The noted paper spawned several more papers, e.g.: (A) Leucht P, Kim JB, Currey J, Brunski J, Helms JA. (2007) FAK-mediated mechanotransduction in skeletal regeneration. *PLoS ONE* 2007 Apr 25;2:e390; (B) Colnot C, Romero D, Huang S, Rahman J, Currey J, Nanci A, Brunski JB and Helms JA (2007) "Molecular analysis of healing at a bone-implant interface" *J. Dent. Res. 86*(9):862-867; (C) Wazen RM, Currey, JA, Spilker, RL, Guo, H, Brunski, JB, Helms JA, Nanci A "Micromotion-induced strain fields influence early stages of regeneration at bone-implant interfaces", Acta Biomaterialia 9(5):6663-6674 (2013); and (D) Cha JY, Pereira MD, Smith AA, Houschyar KS, Yin X, Mouraret S, Brunski JB, and Helms JA "Multiscale analyses of bone/mini-implant interfaces", *J Dent Res* 2015 Vol. 94(3) 482-490 [Jan 27. pii: 0022034514566029, Epub ahead of print] PMID: 25628271

5. Mouraret S, Hunter DJ, Bardet C, Brunski JB, Bouchard P, Helms JA. "A pre-clinical murine model of oral implant osseointegration." Bone 2014 Jan;58:177-84. doi: 10.1016/j.bone.2013.07.021. Epub 2013 Jul 23, PMID: 23886841
   This paper represented our move from studying implant-tissue mechanobiology in long bones of mice to studying this topic in mouse maxillae. This was a challenge from the point of view of miniaturizing implants and biomechanical testing methods even further than in the mouse tibial models. But we believed it was necessary to use an intraoral model in maxillofacial bone. So with the aid of talented surgical and biological experts (Mouraret, Bardet, Bouchard, and Helms) and engineering input (Hunter and Brunski), we were successful in launching this model. This model has shown us that we can achieve osseointegration under the proper mechanobiological conditions – namely sufficient minimization of implant micromotion similar to what we had determined in our long-bone testing. Moreover, we also found that when the implant stability was not sufficient, fibrous tissue formation ensued, e.g., (A) Yin X, Li J, Chen T, Mouraret S, Dhamdhere G, Brunski JB, Zou S, and Helms JA "Rescuing failed oral implants via Wnt activation", *J Clin Periodontol* 2016; 43: 180–192. PMID: 26718012. So with this work we continued to test ideas about mechanobiology in a relevant intraoral model. Recently we also tested whether it makes sense for clinicians to try to enhance implant primary stability by "condensing" bone using osteotomes. For example, in (B) Wang L, Wu Y, Perez KC, Hyman S, Brunski JB, Tulu U, Bao C, Salmon B, Helms JA. "Effects of

Condensation on Peri-implant Bone Density and Remodeling." *J Dent Res.* 2017 Apr;96(4):413-420. doi: 10.1177/0022034516683932. Epub 2017 Jan 3. PMID: 28048963 we found that while condensing bone at an implant site may appear to be a reasonable idea, actually the condensed bone – even while having a higher BV/TV than uncondensed bone of the site -- does not possess a modulus related to the higher BV/TV because the trabecular is damaged from surgery and compaction. In another type of study in the mouse model we looked at the different regenerative potential of bone in a healed molar extraction site vs. more cortical bone in an edentulous site in mouse maxillae – see (C) Li J, Yin X, Huang L, Mouraret S, Brunski JB, Salmon B, Helms JA. "Relationship between bone quality, implant osseointegration and Wnt signaling." *J Dent Res.* 2017 Jul;96(7):822-831. doi: 10.1177/0022034517700131. Epub 2017 Mar 22.2017. Overall, it is this expertise in small animal models that sets the stage for similar work in a rat model – which is a model that we have also begun to use: (D) Chen CH, Pei X, Tulu US, Aghvami M, Chen CT, Gaudillière D, Arioka M, Maghazeh Moghim M, Bahat O, Kolinski M, Crosby TR, Felderhoff A, Brunski JB, Helms JA. "A Comparative Assessment of Implant Site Viability in Humans and Rats." *J Dent Res.* 2018 Apr;97(4):451-459. PMID:29202640

D. Additional Information: Research Support and/or Scholastic Performance

<u>ACTIVE</u>

<u>Federal:</u>

5R01 EB000504-10 Brunski (contact PI in 2016-2017) 7/1/14 – 4/30/19

"Mechanobiology at Healing Bone-Implant Interfaces"
This study hypothesizes that biomechanical factors, including principal strain, influence bone healing around implants.

Role: Co-PI on a multiple-PI project (PI is Dr. J.A. Helms, Stanford, Co-PI is A. Nanci, Univ. of Montreal)