BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Billi, Fabrizio	Associate Professor Dept. of Orthopaedic Surgery
eRA COMMONS USER NAME	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Univ. di Roma "La Sapienza" – Rome, Italy	M.S. equiv.	07/1995	Chemical Engineering
Univ. di Roma "La Sapienza" – Rome, Italy	Ph.D.	05/2000	Materials Engineering - Biomaterials and Biomechanics

A. Personal Statement

I have a broad background in material science, with specific training and expertise in biomaterial characterization, degradation and tissue integration, tribology and biomechanics, and non-destructive testing. As a research scientist at the Joint Research Center of the European Commission, Institute for Advanced Materials, I worked on the application of acoustic emission to composite materials for aerospace components, ceramic materials for adiabatic engines, oxides for high temperature applications, engine wear, and hip wear simulators. I also have a Level III Certification in Acoustic Emission Technology.

My research in the Department of Orthopaedic Surgery at UCLA, and in The Harry McKellop, PhD Research Center for Orthopaedic Biology, Biomaterials, Biomechanics, Tribology, and Wearable Technologies I am directing, includes collaboration with materials engineers, tribologists, biologists, and clinicians. I have developed a strong understanding of the problematic related to natural and artificial joints, including cell and bone biology, and immunology. It is my intention to bring/integrate sensor monitoring into the clinical setting in order to help surgeons formulate more precise diagnosis and patients live a longer productive life. In the past, the program has been supported by funding from a number of industry sponsored and foundation grants. Recently, NIH/ NIAMS has awarded us an R43 grant to study the application of acoustic emission to monitor artificial knee prosthesis, and an R21 grant to monitor soft joint tissue joint degradation. The combination of my background knowledge, my hands-on expertise and my ability to manage research projects will serve well in the successful performance of the proposed studies. The team behind this proposed study is strong and has demonstrated successful interaction and cooperation.

B. Positions and Honors **Positions and Employment**

01/01/1994 – 07/01/1995	Research Assistant – Dept. Chemical Engineering, Università di Roma "*La Sapienza*", Italy
12/01/1995 – 12/15/1996	Researcher, Joint Research Center of the European Commission, Institute for Advanced Materials
01/15/1997 – 10/31/2001	Researcher, Joint Research Center of the European Commission, Institute for Health and Consumer Protection
11//01/2001 - 03/31/2002	Adjunct Assistant Professor, Dept. Materials Engineering, Università di Roma *"La Sapienza"*, Italy
06/01/2002 - 4/30/2005	Visiting Assistant Researcher, Dept. of Orthopaedic Surgery, Orthopaedic Hospital & UCLA
05/01/2005 – 6/30/2006	Postdoctoral Fellow, Dept. of Orthopaedic Surgery, Orthopaedic Hospital & UCLA
07/01/2006 – 06/30/2012	Assistant Professor, Dept. of Orthopaedic Surgery, Orthopaedic Hospital & UCLA /Director, Biomaterials and Particle Analysis Laboratory, Orthopaedic Hospital; Director of Electron Microscopy Core Facility at Orthopaedic Hospital.
07/01/2012 – present	Associate Professor, Dept. of Orthopaedic Surgery, OIC & UCLA / Director, The *H.A. McKellop, Ph.D*. Research Center for Orthopaedic Biology, Biomaterials, Biomechanics, Tribology, and Orthopaedic Wearable Technologies (OrB3iT)

Other Experience and Professional Membership

Professional Society Memberships

2006-	Member - Society for Biomaterials (SFB)
2002-	Member - European Society for Biomaterials (ESB)
2006-	Member - Orthopaedic Research Society (ORS)
2007-	Member - Materials Research Society (MRS)

2008- Member - American Association for the Advancement of Science (AAAS)
2005- Member - American Society of Metals (ASM)
2007- Member - American Chemical Society (ACS)
2010 Member – ASTM International

2008- Editorial Board **-** Journal of Applied Biomaterials and Biomechanics
2011- Editorial Board - Orthopedic and Muscular System
2016- Editorial Board - Journal for Orthopedics and Rheumatology
2016- Editorial Board - Journal of Orthopedic Research & Therapy

Honors

1996 Italian Educational Ministry Doctorate Fellowship (4-year support)
1998 Marie Curie Fellowship - European Commission (3-year support)
2002 Elinor Barry Fellowship - Orthopaedic Hospital / UCLA (3-year support)
2008 June Marshall Award – Exemplary Achievement in Orthopaedic Research
2011 Lloyd Taylor Award, Western Orthopedic Association
2011 John Charnley Award, The Hip Society
2012 The Stein-Oppenheimer Award, UCLA
2013 Invited chair of Session 28 "Bone Failure Mechanisms and Assessment", International Meeting of the Orthopaedic Research Society, San Antonio, TX - January 26-29
2015 Panel Grant Reviewer - National Academy of Science - U.S.-Egypt Science and Technology Joint Fund
2016 Panel Grant Reviewer - National Academy of Science - U.S.-Egypt Science and Technology Joint Fund

C. Contribution to Science

a. My early publications directly related to the study the behavior of ceramic and composites materials via non-destructive testing. These publications demonstrated that acoustic emission could be successfully employed to predict crack formation and failure in these materials. Application of acoustic emission to composite materials, demonstrated how the technology could be successfully employed to distinguish failure of matrix and reinforcement and laid the ground to extend its use in monitoring health status of composite parts in aeronautics, automotive, and construction industries. Furthermore, the publications relative to zirconia partially stabilized with yttria documented how acoustic emission was able to detect crystal phase changes due to the application of external loads even at level of stresses well below those that were taught to be necessary to induce such a transformation. These allowed to perfect zirconia sinterization that eventually led to applications in the orthopaedic field. Following these studies I extended the use of acoustic emission to natural composites, more specifically bone, and in monitoring mechanical failure and wear in dental and orthopaedic implants.

1. **F.Billi,** C.Caneva, C.Santulli
   Acoustic emission Monitoring of Zirconia Partially Stabilized with Yttria during 4-point Bending Tests – Fracture Mechanics, 34,5, 33-42 (1997*)*
2. **F.Billi,** L.Paracchini, C. Santulli
   Acoustic Emission Real Time Monitoring of Compression Strength in Healthy and Damaged Tibial Bone - Biomateriali, 12, 3/4, 11-19 (1999*)*
3. **F.Billi**, C. Santulli
   Wavelet Time-Scale Analysis to Study the Attenuation of Acoustic Emission Body Waves in Acrylic Bone Cement And Natural Bone - Biomateriali, 14, 2, 12-22 (2001)
4. M.Valente, **F.Billi**
   Micromechanical Modification Induced by Cyclic Thermal Stress on Metal Matrix Composites for Automotive Applications Monitored with Acoustic Emission and Thermographic Analysis. Composite: Part B, 32/6, 529-533 (2001) - doi:10.1016/S1359-8368(01)00024-5
5. **F.Billi,** C.Santulli
   Evaluation of the bone–implant interface strength using acoustic emission - Biomateriali, 14, 4, 36-48 (2001)
6. C. Santulli; **F. Billi**
   Normal and off-axis compression tests of biocompatible titanium dental implants monitored by acoustic emission - Journal of Materials Science Letters **21**(9): 727-730; May 2002 – doi: 10.1023/A:1015793223749

b. In addition to the contributions described above I developed two wear simulators one for fretting studies in orthopedics and one for testing artificial intervertebral spine disc. The studies that followed showed how fretting wear was contributing substantially to the overall wear produced by artificial knees. The spine wear simulator was among the very first spine simulator developed in the field. The publications showed the severe wear that artificial disc were subjected during normal activity. Furthermore, the publication served as a guide to developed current ASTM standard.
    1. **F Billi**, E Ebramzadeh, SN Sangiorgio, S Mattes, W Schmoelz, L Dorr
    Simulation of fretting wear at orthopaedic implant interfaces - Journal of Biomechanical Engineering 127 (3), 357-363, 2005 - doi:10.1115/1.1894121
    2. JL Lee, **F Billi**, SN Sangiorgio, W McGarry, DJ Krueger, PT Miller
    Wear of an experimental metal-on-metal artificial disc for the lumbar spine - Spine 33 (6), 597-606, 2008 - doi: 10.1097/BRS.0b013e318166aaa4

3. Following the studies on wear and tribology, with a team of collaborators, I developed protocols to isolate wear debris generated by artificial joints. The publications showed characteristics nanometer-sized debris that could not be previously identified. These protocols were recognized with The John Charnley Award from The Hip Society.
    1. **Billi F**, Benya P, Kavanaugh A, Adams J, Ebramzadeh E, McKellop H.
    The John Charnley Award: an accurate and sensitive method to separate, display, and characterize wear debris. - Clin Orthop Relat Res. 2012 Feb;470(2):329-38. doi: 10.1007/s11999-011-2057-x.
    2. **F.Billi**
    Wear Debris Isolation and Characterization - Tribology and Bearing Surfaces in Total Joint Tribology and Bearing Surfaces in Total Joint Replacement, 2011: ISBN: 978-81-7895-525-4 R.M.Streicher editor
    3. Zhang D, Page JR, Kavanaugh AE, **Billi F.**
    A new method for shape and texture classification of orthopedic wear nanoparticles - J Appl Biomater Funct Mater. 2013 Sep 27;10 (2):141-8. doi: 10.5301/JABFM.2012.9680.
    4. A. Kavanaugh, P.Benya, **F.Billi**
    A Method to isolate and characterize metal debris from synovial fluid and periprosthetic tissue – In "Metal-On-Metal Total Hip Replacement Devices", Kurtz et al. Editors, ASTM - STP1560 August 2012 - ISBN 978-0-8031-7546-4
    5. RA Pedowitz, **F Billi**, A Kavanaugh, A Colbert, S Liu, FH Savoie, Z You
    Micro-particles from Arthroscopic Tools May Induce a Pathologic Cascade Mediated by Synoviocytes - Arthroscopy 29 (6), e10, 2013 - DOI: 10.1016/j.arthro.2013.03.027

4. More recently I have been involved in the characterization of the efficacy of antimicrobial implant coatings.
    1. Bernthal NM, Stavrakis AI, **Billi F**, et al. *A mouse model of post-arthroplasty Staphylococcus aureus joint infection to evaluate in vivo the efficacy of antimicrobial implant coatings.* PLoS One. 2010 Sep 7;5(9):e12580. doi: 10.1371/journal.pone.0012580.
    2. Pribaz JR, Bernthal NM, **Billi F**, et al. *Mouse model of chronic post-arthroplasty infection: noninvasive in vivo bioluminescence imaging to monitor bacterial burden for long-term study.* J Orthop Res. 2012 Mar;30(3):335-40. doi: 10.1002/jor.21519. Epub 2011 Aug 11.
    3. Niska JA, Shahbazian JH, Ramos RI, Pribaz JR, **Billi F**, et al. *Daptomycin and tigecycline have broader effective dose ranges than vancomycin as prophylaxis against a Staphylococcus aureus surgical implant infection in mice.* Antimicrob Agents Chemother. 2012 May;56(5):2590-7. doi:10.1128/AAC.06291-11
    4. Stavrakis AI, Niska JA, Loftin AH, **Billi F**, Bernthal NM.*Understanding infection: a primer on animal models of periprosthetic joint infection*. ScientificWorldJournal. 2013 Sep 22;2013:925906. doi: 10.1155/2013/925906. eCollection 2013.
    5. Stavrakis AI, Niska JA, Shahbazian JH, Loftin AH, Ramos RI, **Billi F**, Francis KP, Otto M, Bernthal NM, Uslan DZ, Miller LS. *Combination prophylactic therapy with rifampin increases efficacy against an experimental Staphylococcus epidermidis subcutaneous implant-related infection*. Antimicrob Agents Chemother. 2014 Apr;58(4):2377-86. doi: 10.1128/AAC.01943-13.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/fabrizio.billi.2/bibliography/46818141/public/?sort=date&direction=ascending

D. Research support <u>Ongoing Research Support</u>

1. PI Initiated Industry Sponsored Grant 09/10/2015 – 09/01/2016
   A Comparative Investigation of Acetabular Cup Removal Systems in an *in vitro* Hemi-Pelvis Model.
   The goal of this study is to establish a biomechanics in vitro model able to evaluate and compare the performance of acetabular cup removing tools. *Clinical Relevance*: Conservation of bone stock during revision surgery is a primary goal to improve the outcome of the procedure and induce better fixation and stability of the revised acetabular component. An additional goal during explantation is risk reduction for intra-operative iatrogenic acetabular fracture associated with implant removal.

2. 1R21AR069287-01 03/10/2016 – 02/28/2018
   Real-time monitoring of knee injuries.
   The goal of this study is to determine the feasibility of developing a novel non-invasive and sensitive joint health diagnostic device capable of detecting the integrity of soft-tissue. Role: PI

3. PI Initiated Industry Sponsored Grant 07/15/2016 – 07/14/2018
   An In-vitro 3D Model for Osteogenesis, Mineralization, and Bone Resorption/Osteoclastogenesis.
   The goal of this study is to evaluate the effects of pulsed electro magnetic fields (PEMF) on the development of bone in a new, unique 3D *in vitro* culture model of bone formation. The 3D bone-like tissue provides an environment closely similar to the *in vivo* situation which will allow screening and optimization of PEMF protocols with cells and matrix in a near native state. Importantly, the model will evaluate multiple stages of bone formation for responsiveness to PEMF and will use classical measures of bone quality for outcome determination rather than short-term surrogates of a few osteoblast “markers”.

<u>Completed Research Support</u>

1. 1R43AR067048-01A1 05/01/2015 – 10/31/2015
   Rapid Detection of Common Failure Modes for Knee Prosthetics
   Scope of this Phase I SBIR grant is to develop a proof of concept detection device based on acoustic emission technology and ultrasounds naturally emitted from joint during daily dynamic activity. Role: PI

2. Industry Sponsored Research - Wear Simulation Study on Hip Artificial Joints 7/1/2014 – 9/30/2015
   The aim of the study is to characterized the wear and wear damage produced on a new artificial hip implant design. Complete morphological classification of wear particles helps to screen materials and designs employed in artificial joints. Furthermore, complete morphological characterization is a mandatory requirement from FDA for any new implant approval.
   Role: PI

3. Industry Sponsored Research - Metal Particles from Arthroscopic Surgical Tools. 8/1/2014 – 6/30/2015
   Objective of this PI initiated research is to characterize the morphology of metal particles produced during arthroscopic procedure in the Shoulder and quantify their effect on chondrocyte viability. Role: PI

4 . Industry Sponsored Research - Wear debris, metal-on-metal, hip prostheses 10/01/2009 - 2/28/2010
   Goal of this grant is to fully characterize metal wear debris from new hip implant employing advance new metal alloy. Role: PI

5. Industry Sponsored Research - Wear debris, metal-on-metal, hip resurfacing 11/15/2009 – 3/31/2010
   Goal of this grant is to fully characterize metal wear debris from new hip resurfacing implant. Role: PI

6 . Orthopaedic Hospital Foundation 01/11/2009 – 10/31/2010
   Morphological characterization of wear debris from artificial hip joints in synovial fluid
   Goal is to develop a protocol to isolate and characterize wear particles from aspirated synovial fluid and monitor the wear progression in patients. A sensitive, efficient isolation and characterization is particular important in order to better evaluate the needs for a revision surgery. The isolation is particularly challenging for the characteristic of synovial fluid and especially for metal particles where currently available protocols will provoke irreversible corrosion of the wear particles. Role: PI

7. 1 R21 AR056885-01A1 Adams (PI) 08/01/2009 – 07/31/2011
Orthopaedic Wear Debris, Vitamin D, and Innate Immunity
The goal of this study is to examine the problem of human joint compromise by testing the dual hypothesis that Toll-like pattern recognition receptors mediate inflammatory responses to polyethylene wear debris particles, and that such responses are impaired by vitamin D deficiency. Role: Co-Investigator

8 . Orthopaedic Hospital Foundation 01/11/2010 – 10/31/2011
Morphological characterization of wear debris from artificial hip joints in synovial fluid and correlation to metal ion levels in blood and urine.
Goal is to develop a protocol to isolate and characterize wear particles from aspirated synovial fluid and monitor the wear progression in patients. Role: PI

9. Industry Sponsored Research - Isolation and characterization of UHMWPE debris from hip and knee prostheses. 04/01/2011 – 3/31/2012
Goal of this grant is to fully characterize UHMWPE wear debris from new hip and knee implants. Role: PI

Industry Sponsored Research - 10/01/2011 – 05/30/2012
UHMWPE Particles characterization from ankle wear simulator tests. Role: PI

10. Industry Sponsored Research - 05/01/2011 – 11/30/2012
A new protocol to evaluate wear from analysis of a new polymer cup wear debris. Role: PI

11. Stein/Oppenheimer Endowment Award, UCLA 06/01/2012 – 09/30/2014
Identification of specific TCR-cognate antigens responsible for T-cell mediated pseudotumors in a subset of patients with Metal-on-Metal Hip Replacements Role: PI

12. Industry Sponsored Research - UHMWPE Particles characterization from ankle wear simulator tests. 11/01/2012 – 05/31/2013
Role: PI

13. Industry Sponsored Research - Metal wear particle characterization from TMJ implants. 08/01/2012 – 12/31/2013
Goal of this grant is to fully characterize wear and metal wear debris from new temporomandibular implant. Role: PI

14. Industry Sponsored Research - 03/01/2013 – 02/28/2014
Evaluation of metal ion content from a new fracture stabilization implant design: rabbit model. Role: PI

15. Industry Sponsored Research - 4/30/2012 – 5/15/2013
UHMWPE Particles characterization from hip wear simulator tests. Role: PI