Published in final edited form as:
IEEE Trans Biomed Eng. 2011 October ; 58(10): 2991–2994. doi:10.1109/TBME.2011.2160722.

Establishing Multiscale Models for Simulating Whole Limb Estimates of Electric Fields for Osseointegrated Implants

Brad M. Isaacson,
Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. at Walter Reed Army Medical Center, Washington DC, 20307 USA (610-772-7252; fax: 202-782-4365)

Jeroen G. Stinstra,
Scientific Computing and Imagining Institute, University of Utah, Salt Lake City, UT 84112 USA. He is now with Numira Biosciences, Salt Lake City, UT 84108 USA

Roy D. Bloebaum,
Department of Veterans Affairs, Salt Lake City, UT 84148 USA and the Departments of Orthopaedics, Bioengineering and Biology, University of Utah, Salt Lake City, UT 84112 USA

COL Paul F. Pasquina, and
Colonel in the United States Department of the Army and serves as the Chief of the Integrated Department of Orthopaedics & Rehabilitation at Walter Reed Army Medical Center, Washington DC, 20307 USA

Rob S. MacLeod[IEEE Member]
Scientific Computing and Imagining Institute, University of Utah, Salt Lake City, UT 84112 USA, the Nora Eccles Harrison Cardiovascular Research and Training Institute, Salt Lake City, UT 84112 USA and the Departments of Bioengineering and Internal Medicine, University of Utah, Salt Lake City, UT 84112 USA

Brad M. Isaacson: bmisaacson@gmail.com; Jeroen G. Stinstra: jstinstra@numirabio.com; Roy D. Bloebaum: roy.bloebaum@hsc.utah.edu; COL Paul F. Pasquina: paul.pasquina@us.army.mil; Rob S. MacLeod: macleod@cvrti.utah.edu

Abstract

Although the survival rates of warfighters in recent conflicts are among the highest in military history, those who have sustained proximal limb amputations, may pose additional rehabilitation concerns. In some of these cases, traditional prosthetic limbs may not provide adequate function for returning to an active lifestyle. Osseointegration has emerged as a potential prosthetic alternative for those with limited residual limb length. Using this technology, direct skeletal attachment occurs between a transcutaneous osseointegrated implant (TOI) and the host bone, thereby eliminating the need for a socket. While reports from the first 100 patients with a TOI have been promising, some rehabilitation regimens require 12–18 months of restricted weight bearing to prevent overloading at the bone implant-interface. Electrically induced osseointegration has been proposed as an option for expediting periprosthetic fixation and preliminary studies have demonstrated the feasibility of adapting the TOI into a functional cathode. To assure safe and effective electrical fields that are conducive for osseoinduction and osseointegration, we have developed multiscale modeling approaches to simulate the expected electric metrics at the bone-implant interface. We have used computed tomography scans and volume segmentation tools to create anatomically accurate models that clearly distinguish tissue parameters and serve as the basis for finite element analysis. This translational computational biological process has supported

Disclaimer: The views expressed in this article are those of the authors and do not reflect the official policy of the Department of Army, Department of Defense, or U.S. Government.

biomedical electrode design, implant placement, and experiments to date have demonstrated the clinical feasibility of electrically induced osseointegration.

Index Terms

electrical stimulation; osseointegration; skeletal attachment; finite element analysis; biomedical electrodes

I. Introduction

Advancements in body armor and evacuation strategies in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) has resulted in a 92% service member survival rate, higher than any other major military conflict [1, 2] (Table 1). Between September 2001 and September 2010, approximately 1,400 warfighters sustained amputations in OIF and OEF, 1,050 of which were major limb loss. More recently, statistics from Afghanistan report approximately 38% (65/171) of warfighters treated at Landstuhl in 2010 incurred multiple limb loss, a 10% increase from the previous year (21/75) [3].

Most if not all members of the military who have experienced orthopaedic trauma during their deployments to Iraq and Afghanistan were physically fit at the time of their injury. All are highly motivated and possess a strong desire to return to an active life, including continued military duty when possible. For those with combat-related limb loss, conventional prosthetic limbs may offer a means to regain functional independence. However, military personnel with high proximal amputations, hip disarticulations or shoulder disarticulations may reject or not qualify for this prosthetic technology given their limited residual limb volume for prostheses attachment. For this patient population, transcutaneous osseointegrated implants (TOI) may improve function by allowing direct skeletal attachment between an implant and the host bone [5], thus alleviating the need for a soft tissue socket all together. The advantage of TOI is that the mechanism for attachment is more physiologic than a standard socket fixture and this technique avoids problems with stress shielding and osteopenia [6, 7].

While osseointegrated implants have improved the mobility and quality of life for the 100+ European patients who have received them thus far [8], a 12–18 month rehabilitation process designed to prevent overloading at the bone–implant construct [9] may restrict activity levels, and subsequently, the likelihood for TOI acceptance. To enhance skeletal fixation of the implant, accelerate rehabilitation regimens, and strengthen the residual limb bone, we have proposed utilizing the periprosthetic implant as a functional cathode and applying controlled electric current to the bone-implant interface [6, 7].

Electrical stimulation has been successfully used as a therapeutic alternative for healing atrophic bony non-unions, with 100,000 cases reported as of 1990 [10]. However, to our knowledge only three studies to date, all from our laboratory, have evaluated the potential for electrically induced TOI [6, 7, 11]. The mechanism of electrical stimulation based ossification has been associated with electrochemical reactions that alter pH and oxygen content around a bony defect [10]. However, despite the promise of this technique, clinical use of electrical stimulation for increased osseointegration rehabilitation still requires extensive optimization, evaluation, and testing. To this end, we have developed a complete system for multiscale modeling to ensure that localized electric fields and current densities remain safe and in an effective range for accelerating periprosthetic attachment within the residual limb.

Our previous reports have demonstrated the design principles for predicting electrically induced osseointegration in amputees with limited residual limb length [6, 7]. In short, computed tomography (CT) scans of residual limbs from combat-wounded service members were imported into Seg3D, a volume segmentation and processing tool, to develop anatomically accurate hierarchical models. The resulting models preserved tissue geometry, i.e., the spatial position of hard and soft tissues within the residual limb, and thus provided an anatomically realistic and patient specific basis for finite element analysis (FEA) [6, 7]. SCIRun, a comprehensive simulation environment for bioelectric field problems provided the tools for FEA, including modules to represent physiologic tissue conductivities, biomedical electrodes, and boundary conditions for simulating osseointegration. Preliminary studies using this streamlined computational approach demonstrated the ability to predict virtual electric fields and current densities within service members' residual limbs.

In this report we describe the technical details of the computational approach for estimating the electric fields in the human residual limbs that have not appeared in previous publications. We emphasize the multiscale approach to these simulations beginning with geometric models of the entire residual limb and then predict bioelectric fields at the interface between the implant and surrounding bone.

II. Materials & Methods

In order to estimate the electrical fields and current densities in the tissues which arise when performing electrically induced TOI, multiscale models from service member residual limbs were generated using CT scans in accordance with Walter Reed Army Medical Center Institutional Review Board approval. This imaging modality was used to define the patient specific anatomy within the residual limb and served as the basis for an electrical model of the limb. Anatomical images were translated into a passive electrical model of the limb by identifying separate tissue types using Seg3D [12], a software package which boasts both manual and automatic segmentation filters for biomedical applications. CT files were imported from their original DICOM format and a median filter was applied to reduce noise in the images while preserving the edges in the volumetric image. Tissue types consisting of bone, bone marrow, adipose tissue and musculature were identified in a semi-automated procedure in which a selected contrast range was extracted and thresholded (Fig 1).

Segmentations were manually inspected to ensure all tissues were anatomically correct and formed a continuous volume. Seed points were set within each tissue boundary and the volume was filtered using a confidence connected filter to find all of the tissue connected to the seed points within a prescribed range of gray values from the CTs. All layers except for the skin were extracted in this fashion. Because the skin layer was poorly visible in the CT scan, the dilate-erode feature in Seg3D was used to ensure a homogenous skin layer that was 2mm in thickness [13]. Finally, the individual segmentations were combined into one label map in which each voxel was assigned to a single tissue type. This label map was exported and formed the basis for the creation of polygonal geometric models.

Discrete geometric models consisting of 1.8 million hexahedral elements were created to solve the necessary bioelectric field equations based on the realistic anatomies. Electrically induced osseointegration was simulated between two electrical bands placed on the exterior of the residual limb (both serving as anodes), and the TOI, which served as the orthopaedic implant/cathode (Fig 2). In order to estimate the electrical field within the narrow region surrounding the implant, it was assumed that each tissue type was a homogeneous, linear volume conductor. Similarly, the cathode/anodes were modeled as perfect surface conductors since their conductivity greatly exceed the neighboring tissues.

The potential inside the model was solved by assuming that the outer boundaries were isolated and a zero Neumann condition existed at these boundaries. For the surfaces that were covered by electrodes, a Dirichlet boundary condition was utilized. As the internal electrode resistance was assumed to be negligible each location with the surface electrode was assumed to have the same potential. Although a small potential difference would be expected as no current would flow to the electrode otherwise, this potential difference would be small in comparison to the much larger potential differences observed in the tissue, due to the large mismatch in conductances (several orders of magnitude). At the boundaries between tissue types, the potential and current density component perpendicular to the surface were preserved over the boundary. With all the boundaries having a Neumann or Dirichlet boundary condition, the potential could be uniquely solved using Laplace’s equation for each homogeneous volume conductor. The electric field was calculated by computing the negative gradient of the potential field and the local current density was obtained by applying Ohm’s law.

Numerical approximations were performed using the FEA software package SCIRun [14]. Using a high resolution map of tissue types and surface models of electrodes, a lower resolution computation grid was defined. This grid was based on the hexahedral elements that were subdivided into five tetrahedrons each. In order to ensure enough computation accuracy the volume directly surrounding the electrodes and the implants was refined by dicing the tetrahedral elements in four smaller elements. Tissue conductivities were assigned based on peer-reviewed literature estimations [6, 7].

In order to insert the electrodes into the model, the outer boundary of the mesh was computed and the electrode models were projected onto this outside mesh. All nodes inside this mesh were assigned a dirichlet boundary condition that matched the potential of the electrode. The model was subsequently solved by computing the stiffness matrix using the finite element method and solving the resulting matrix equation using the conjugate gradient method. The goal of the simulations was to identify through manual iteration external electrode locations and potentials that would result in uniform electric fields and current densities at the bone-implant interface that did not exceed 10 V/cm and 2 mA/cm^2 respectively. This criteria was established to prevent joule heating effects and to reduce the chance of tissue necrosis within the residual limb from thermal effects when using electrically induced TOI [15].

III. Results

Using tissue level parameters to simulate whole limb estimates was an effective tool for predicting periprosthetic electric fields and current densities within the residual limbs of injured service members (Fig 3). The uniqueness of this multiscale modeling approach has been that CT-based reconstructions preserved tissue orientation and geometry, while providing accurate three dimensional representations for FEA. This stepwise progression will likely improve the potential for successful clinical application of TOI in the future.

Investigations conducted to date by our team have indicated that electric fields may be maintained between 1.30–3.10 V/cm using service member-derived reconstructions [6], a threshold which should theoretically induce osteoblast migration and accelerate TOI rehabilitation regimens. However, current densities from these same data sets have at times exceeded the 2 mA/cm^2 recommendation when ectopic bone growth, commonly known as heterotopic ossification (HO) exists within the residual limb. HO formation has been reported to occur in approximately 63% of blast-related injuries [16] has bioelectric implications since the abnormal bone growth may exist at the point of current injection from the externally applied anodes [6]. Spearman’s rho correlation coefficients in a previous study demonstrated that the potential difference in the electrical system was significantly correlated, and directly proportional to the volume of HO (p=0.024, r=0.670), as higher ectopic bone volumes required increased voltages due to the resistivity of mature lamellar bone [6].

Electrically induced osseointegration has been demonstrated in humans [6, 7] and experimentally validated in an *in vivo* animal study [11] using the multiscale modeling process described herein as an initial measure. Preliminary work has demonstrated that electrical stimulation may alleviate problems with poor implant fit and fill [11] and with additional experimental refinement, may directly demonstrate the link between mutiscale modeling assumptions and periprosthetic skeletal attachment. However, before electrical stimulation can be used as a therapeutic aid, model refinements which account for tissue orientation and fiber direction will be necessary to increase model accuracy.

IV. Conclusion

While osseointegration have not been used as a prosthetic limb alternative in the United States to date, multiscale modeling has demonstrated the ability to theoretically expedite skeletal attachment of a TOI and in future may accelerate rehabilitation regimens. The advantage of this technique is that realistic approximations of periprosthetic electric fields and current densities may be computed using tissue parameters for whole limb estimates. Preliminary data has demonstrated the need for patient specific models. The potential for electrically induced TOI for assisting with poor implant fit and fill at the bone-implant interface has also been supported, but will require additional investigations.

Acknowledgments

This material is based upon work supported by the Veterans Affairs Office of Research and Development, Rehabilitation R&D Service, DVA SLC Health Care System, Salt Lake City, UT; the Albert & Margaret Hofmann Chair and the Department of Orthopaedics, University of Utah School of Medicine, Salt Lake City, UT; the Technology Commercialization Office, University of Utah, Salt Lake City, UT; the Department of the US Army under Award Number W81XWH-06-2-0073 to the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Fort Detrick, MD. Technical support for the simulations was provided by the Center for Integrative Biomedical Computing of Scientific Computing and Imaging Institute and was made possible in part by software from the NIH/NCRR Center for Integrative Biomedical Computing, P41-RR12553-07.

B.M. Isaacson and R. D. Bloebaum thank Gwenevere Shaw for support with manuscript preparation.

References

1. Gajewski D, Granville R. The United States Armed Forces Amputee Patient Care Program. J Am Acad Orthop Surg. 2006; 14(10 Spec No):S183–187. [PubMed: 17003196]
2. Isaacson BM, Weeks SR, Pasquina PF, Webster JB, Beck JP, Bloebaum RD. The Road to Recovery and Rehabilitation for Injured Service Members with Limb Loss: A Focus on Iraq and Afghanistan. US Army Med Dep J. 2010 Jul-Sept.:31–36. [PubMed: 21181652]
3. Brown, D. The Washington Post. March 4. 2011 Amputations and genital injuries incerase sharply among soldiers in Afghanistan.
4. Fischer, H. US Military Casualty Statistics: Operation New Dawn, Operation Iraqi Freedom, and Operation Enduring Freedom. September 28. 2010
5. Albrektsson T, Albrektsson B. Osseointegration of bone implants. A review of an alternative mode of fixation. Acta Orthop Scand. 1987 Oct; 58(5):567–577. [PubMed: 3321881]
6. Isaacson BM, Stinstra JG, MacLeod RS, Pasquina PF, Bloebaum RD. Developing a quantitative measurement system for assessing heterotopic ossification and monitoring the bioelectric metrics from electrically induced osseointegration in the residual limb of service members. Ann Biomed Eng. 2010 Sep; 38(9):2968–2978. [PubMed: 20458630]

7. Isaacson BM, Stinstra JG, MacLeod RS, Webster JB, Beck JP, Bloebaum RD. Bioelectric analyses of an osseointegrated intelligent implant design system for amputees. J Vis Exp. 2009; 29:1–6. [PubMed: 19609251]
8. Hagberg K, Branemark R. One hundred patients treated with osseointegrated transfemoral amputation prostheses--rehabilitation perspective. J Rehabil Res Dev. 2009; 46(3):331–344. [PubMed: 19675986]
9. Isaacson BM, Vance RE, Rosenbaum Chou TG, Bloebaum RD, Bachus KN, Webster JB. The Effectiveness of Resonance Frequency in Predicting Orthopedic Implant Strength and Stability in an In Vitro Osseointegration Model. J Rehabil Res Dev. 2009; 46(9):1109–1120. [PubMed: 20437317]
10. Isaacson BM, Bloebaum RD. Bone Bioelectricity: What Have We Learned in the Past 160 Years? J Biomed Mater Res A. 2010; 95(4):1270–1279. [PubMed: 20878899]
11. Isaacson B, Brunker L, Brown A, Beck J, Burns G, Bloebaum R. An evaluation of electrical stimulation for improving periprosthetic attachment. J Biomed Mater Res B. 2010; 97B(1):190–200.
12. Seg3D. Volumetric Image Segmentation and Visualization. Scientific Computing and Imaging Institute (SCI); http://www.seg3d.org
13. Tortora, GJ.; Nielsen, MT. Structure of the Skin. In: Roesch, B.; Trost, K.; Wojcik, L.; Muriello, L.; Raccuia, L., editors. Principles of Human Anatomy. Hoboken, NJ: John Wiley & Sons, Inc; 2009. p. 117
14. SCIRun. Scientific Computing and Imaging Institute (SCI); www.scirun.org
15. Soong HK, Parkinson WC, Bafna S, Sulik GL, Huang SC. Movements of cultured corneal epithelial cells and stromal fibroblasts in electric fields. Invest Ophthalmol Vis Sci. 1990 Nov; 31(11):2278–2282. [PubMed: 2242993]
16. Potter BK, Forsberg JA, Davis TA, Evans KN, Hawksworth JS, Tadaki D, et al. Heterotopic ossification following combat-related trauma. J Bone Joint Surg Am. 2010 Dec; 92(Suppl 2):74–89. [PubMed: 21123594]

NIH-PA Author Manuscript
NIH-PA Author Manuscript

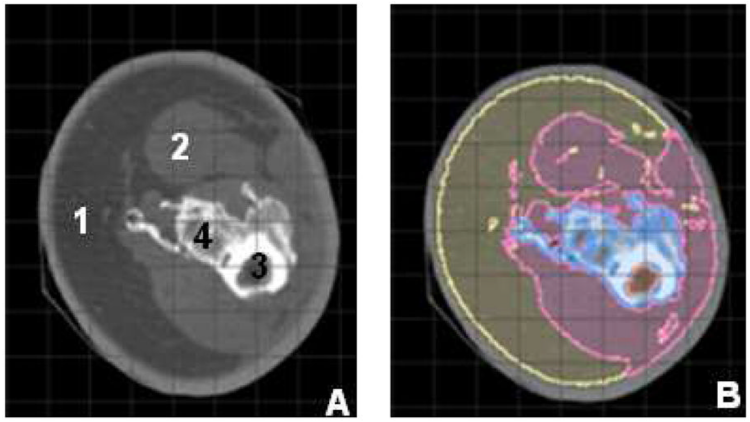

Fig 1.

An axial CT scan demonstrating 4 distinct tissues within a residual limb (A). This cross section image in Panel A and segmentation in Panel B clearly identify the adipose tissue (yellow) (1), musculature (pink) (2), bone marrow (orange) (3), and cortical bone (blue) (4). Seg3d was used to threshold the tissues and ensure accurate reconstructions (B).

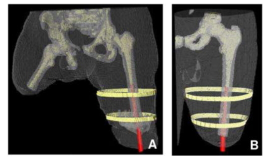

Fig 2.

Two service member reconstructions demonstrating the finite element mesh used for bioelectric analysis (A & B). Two externally applied electrical bands (anodes, yellow) were placed on the exterior of the residual limb and an intramedullary implant (cathode, red) was inserted into the medullary canal. Electric fields were generated between the anodes and cathode.

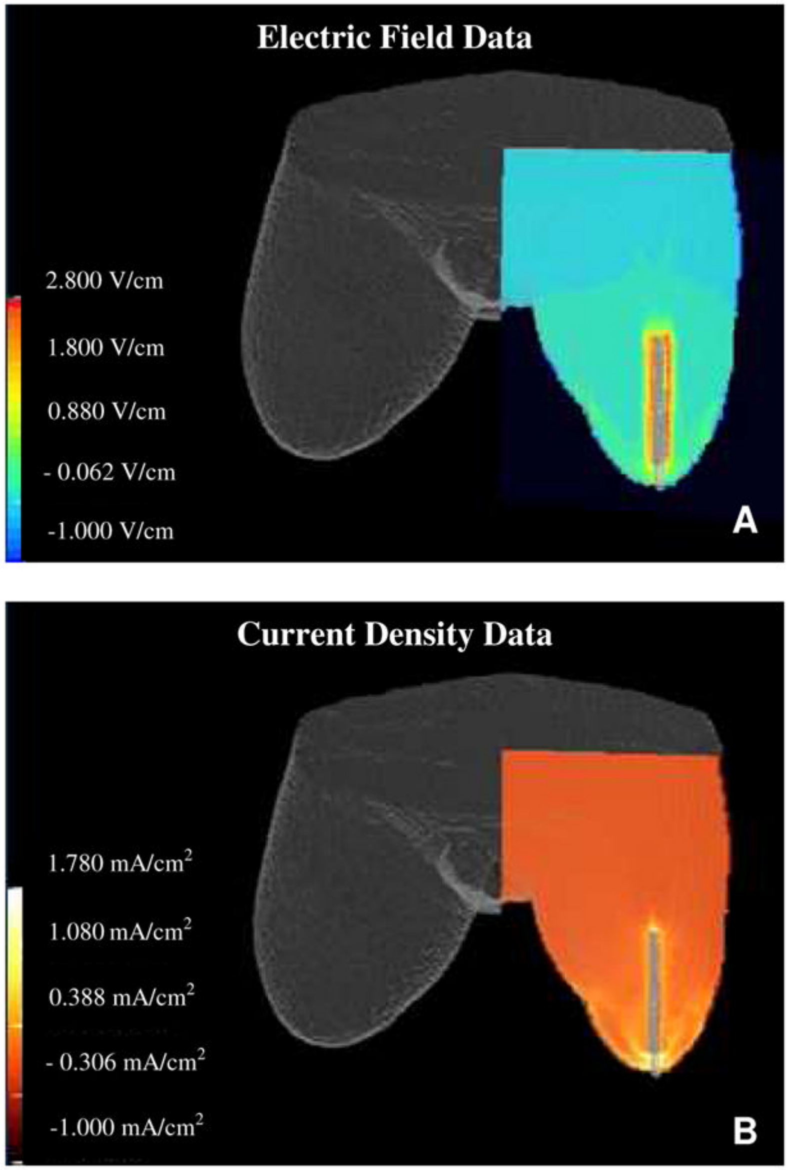

Fig 3.
FEA demonstrating the electric fields (A) and current densities (B) within the residual limb of a service member who may at some point advocate for osseointegration technology.

Table 1

Service member battle field statistics [4]. OIF and OEF statistics are given for September 2001 to September 2010. Note the change in A:D ratio given the advancements in evacuation strategies and improved medical care.

Military Conflicts	Deaths (D)	Wounded (W)	Amputations (A)	A:D Ratio
OIF	4,408	49,390	1,158	1:3.8
OEF	1,261	13,851	249	1:5.1
Vietnam War	58,220	153,303	5,283	1:11.0
Korean War	36,574	103,284	1,477	1:24.8
World War II	405,399	670,846	7,489	1:54.1
World War I	116,516	204,022	2,610	1:44.6