INTRODUCTION: The frequency of heterotopic ossification (HO) from improvised explosive devices (IEDs) in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) has been reported as high as 63% in the wounded service members [1]. Because HO has a maturation rate upwards of 18 months in 53% problems arise with poor prosthetic fit and discomfort for those requiring assistive ambulatory devices [4]. Improper docking of a soft tissue socket may cause skin breakdown [2] and limit the mobility for amputees who wish to return to active duty or the civilian community [5].

To help alleviate problems associated with socket prostheses, our team has developed an external electrical stimulation device which utilizes the exposed exoprosthesis attachment as a functional cathode [8]. In order to demonstrate the effectiveness of electrical stimulation in patients with limb loss and osseointegrated implants, safety and efficacy must be confirmed. However, wide variations in residual limb anatomy and HO may be estimated with finite element analysis (FEA) to determine the bioelectric effects at the distal residual limb for amputees who may advocate for osseointegration. Therefore, the goals of this study were (1) to demonstrate that safe and effective electric stimulation of osseointegrated implants is possible even in patients with significant HO, (2) to show that patient specific modeling and simulation is necessary to determine the relevant metrics for such stimulation, (3) to develop a quantitative method for determining the volume of HO, and (4) to characterize the prevalence, the extent, and the structure of HO in returning service members.

DESIGN AND METHODS:

Study Population
11 male service members with retrospective CT scans were included in the IRB approved study. Subjects were on average 28.2 ± 5.0 years of age at the time of injury, and 85.5 ± 11.3 kg and 181.2 ± 4.4 cm prior to injury. While age was routinely recorded for each subject, weight and height were reported in only 10/11 and 6/11 of the patient’s medical records. The study population consisted of above knee amputations with an average limb length of 26.7 ± 6.1 cm, as measured from the apex of the greater trochanter to most distal bone in the residual limb. Ten (91%) of the included warfighters sustained limb deficiencies as a result of combat related injuries (9/11 OIF, 1/11 OEF) while 1 subject sustained limb loss from a non-military conflict. The injury mechanism most frequently reported was IEDs which resulted in 82% of traumatic amputations, while 2 cases were the direct result of an RPG (9%) and motor vehicle accident (9%) respectively.

Image Reconstructions
The tissue boundaries of the internal organs, bone, bone marrow and adipose tissue were generated by thresholding the CT files interactively (Seg3d, Scientific Computing and Imaging Institute, University of Utah, UT). The musculature was obtained by manually setting seed points inside the tissue and using a confidence connected filter to find all the tissue connected to the seed points. Because the skin was impossible to discern reliably from CT images, an estimate of the skin layer was generated by dilating the outermost tissue to produce a 2mm layer of homogeneous thickness (the average thickness of human skin) to surround the full model (Figure 1). Axial cross sections of CT scans were manually inspected and the entire volume of HO was collected using customized software which multiplied voxel height and width by the slice thickness (Analyze 9.0, Mayo Clinic, OH) (Figure 2).

Finite Element Analysis
A 10cm percutaneous osseointegrated implant was set to the endosteal wall of the distal residual limb. External electrodes, which consisted of two continuous bands, each 1.6cm in thickness, were placed equidistant from the implant site and positioned 2cm from the most proximal and distal ends of the Utah Ribeck osseointegrated implant on the residual limb (Figure 3). This experimental setup has previously demonstrated homogenous fields at the bone-implant construct [6].

Electric Metric Criterion
Evaluations were assessed manually following each simulation. Electric fields (EF) were restricted between 1-10 V/cm to prevent joule heating effects, while current densities (CD) could not exceed 1.8 mA/cm² to prevent localized tissue necrosis (Figure 4).

RESULTS: Investigation of FEA demonstrated lower current density magnitudes when the volumes of HO increased. For each potential selected in subjects 2,3 and 11, each with high volumes of HO, current density remained below the 1.8 mA/cm² threshold. In each of these cases, a dense aggregation of HO was located at the band placement site and resulted in more resistive medium at the point of current injection. This trend was consistent throughout the study and results of a Spearman’s rho correlation coefficient, assessing the relationship between the volume of HO and optimal potential, were statistically significant (p=0.024, r=0.670). Therefore, effective use of electrical stimulation in this patient population would require altering the voltage in the system or modifying the band placements slightly to avoid resistive HO medium.

When the volume of HO was compared to subject’s demographical information, only age was statistically significant (p=0.041, r=0.622). This inverse relationship demonstrated that the volume of HO decreased with increasing age of the service members.

Histological analyses were also performed on retrieved HO specimens in a separate University of Utah IRB approved study to determine the morphology of HO; since speculation exists in the peer-reviewed literature regarding whether HO is lamellar or woven bone. SEM images collected from a patient with HO in the pericarticular region of the hip demonstrated a stark comparison in bone mineralization compared to a healthy sample femur and clearly demonstrate that HO is lamellar bone (Figure 5).

DISCUSSION: Ectopic bone formation presents a difficult challenge for rehabilitation and post-amputation quality of life. Therefore, electrically induced osseointegration is a unique alternative to traditional prosthetic technology and may stimulate positive bone remodeling. In the service member sample population, the frequency of HO occurred in 73% of the cases (9/11) and was variable in severity and location. The formation of HO resulted in “serpentine” structures which connected to the skeleton and “small islands” in the neighboring soft tissue. To help categorize the HO in a non-subjective manner, thresholding software provided volumetric measurements which assisted in determining the severity in the residual limb of service members. To the authors knowledge this is the first study to quantify the volume of HO without using subjective grading systems and includes the first SEM images of HO.

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