ARTICLE IN PRESS
JID: JJBE [m5G;June 9, 2018;14:7]

Medical Engineering and Physics 000 (2018) 1–8

Contents lists available at ScienceDirect

Medical Engineering and Physics

journal homepage: www.elsevier.com/locate/medengphy

Improved osseointegration with as-built electron beam melted textured implants and improved peri–implant bone volume with whole body vibration

David S. Ruppert [a,*], Ola L.A. Harrysson [a,c], Denis J. Marcellin-Little [a,c,d,1], Laurence E. Dahners [b], Paul S. Weinhold [a,b]

[a] Department of Biomedical Engineering, UNC-NCSU, United States
[b] Department of Orthopaedics School of Medicine, University of North Carolina, Chapel Hill, North Carolina, United States
[c] Department of Industrial and Systems Engineering, North Carolina State University, Raleigh, North Carolina, United States
[d] Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina, United States

ARTICLE INFO

Article history:
Received 5 October 2017
Accepted 28 May 2018
Available online xxx

Keywords:
Additive manufactured implants
Textured implant
Electron beam melting
Bone-implant interface
Osseointegration of Transcutaneous Prostheses
Whole Body Vibration

ABSTRACT

Transcutaneous osseointegrated prostheses provide stable connections to the skeleton while eliminating skin lesions experienced with socket prosthetics. Additive manufacturing can create custom textured implants capable of interfacing with amputees' residual bones. Our objective was to compare osseointegration of textured surface implants made by electron beam melting (EBM), an additive manufacturing process, to machine threaded implants. Whole body vibration was investigated to accelerate osseointegration. Two cohorts of Sprague-Dawley rats received bilateral, titanium implants (EBM vs. threaded) in their tibiae. One cohort comprising five groups vibrated at 45 Hz: 0.0 (control), 0.15, 0.3, 0.6 or 1.2 g was followed for six weeks. Osseointegration was evaluated through torsional testing and bone volume fraction (BV/TV). A second cohort, divided into two groups (control and 0.6 g), was followed for 24 days and evaluated for resonant frequency, bone-implant contact (BIC) and fluorochrome labeling. The EBM textured implants exhibited significantly improved mechanical stability independent of vibration, highlighting the benefits of using EBM to produce custom textured surfaces. Bone formation on and around the EBM textured implants increased compared to machined implants, as seen by BIC and fluorescence. No difference in torque, BIC or fluorescence among vibration levels was detected. BV/TV significantly increased at 0.6 g compared to control for both implant types.

1. Introduction

In 2005, approximately 1 in 190 Americans were amputees. That ratio is expected to double by 2050 [1]. Transcutaneous osseointegrated implants hold the potential to overcome several shortcomings of traditional socket prostheses. An optimal fit is difficult to achieve with socket-type prostheses, often resulting in undesirable stresses on tissues most frequently resulting in painful lesions, bursae, inflammatory edema, soft-tissue calcification or neuromas [2,3]. Socket prosthetic devices also lack stability due to their inefficient connection to the body. Osseointegration allows for a direct structural and functional connection between living bone tissue and the surface of a load carrying implant [4]. This direct osseointegration interface in amputated limbs allows for a more stable connection enabling greater control of the prosthesis and heightened osseoperception (sensory feedback from the environment) while eliminating problems associated with socket devices such as pain and skin irritation and improving overall quality of life [5]. Transcutaneous osseointegration faces several challenges. Osseointegrated implants need to be adapted to patients' specific anatomy. The commonly used Brånemark osseointegrated implants, however, are threaded rods that do not always match the anatomy of the femur in which they are inserted. To avoid fibrous ingrowth into the implant that could result from excessive loading and micromotion, a controlled and gradual rehabilitation period lasting 12 months is required [6,7].

Osseointegration of a metal implant requires some motion at the bone-implant interface for proper healing [8], but excessive

Abbreviations: AM, Additive manufacturing; LMHF, Low magnitude high frequency; SD, standard deviation; BV/TV, medullary bone volume to total volume; BIC, % bone-implant-contact; Ti6Al4V, grade 5 titanium; EBM, electron beam melting; WBV, whole body vibration.

* Corresponding author.
E-mail address: dsrupper@ncsu.edu (D.S. Ruppert).

[1] Current address: Department of Veterinary Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis, CA 95616, USA.

https://doi.org/10.1016/j.medengphy.2018.05.003
1350-4533/© 2018 Published by Elsevier Ltd on behalf of IPEM.

micromotion can lead to the development of a fibrous tissue interface rather than a bone interface. Fibrous interfaces are not mechanically stable in the long term. Another challenge facing transdermal osseointegrated implants is that the transcutaneous interface is prone to infection. More than 48% of patients with transcutaneous osseointegrated implants experienced an infection within three years of implantation. Infection at the skin interface can lead to bone infection. In turn, bone infection may result in implant loosening and removal of the osseointegrated implants [9,10]. Threaded Brånemark implants are the type of implant that is predominantly used in clinical cases [11]. These implants are straight and cylindrical by design, limiting their adaptability to the patients' residual bones. Transdermal implants with a curved and non-cylindrical shape would have a more precise endosteal fit. While conventional manufacturing methods (forging or casting) are used to fabricate curved and non-cylindrical implants for arthroplasty, these methods cannot be realistically used to make the patient-specific transdermal osseointegrated implants.

Additive manufacturing (AM) methods can be used to make non-cylindrical implants matching patients' specific anatomy. Patient specific implants have been shown to decrease initial implant micromotion compared to conventional components under physiologic loading in cadaver studies of cementless femoral total hip components [12]. In cadaver studies of total knee replacement, patient specific implants have been shown to better recreate natural knee kinematics under simulated loading compared to conventional components [13]. Beyond producing patient specific geometries an additional benefit of AM methods is the ability to produce custom surface textures for bone ingrowth or ongrowth at the same time as the manufacturing of the bulk implant.

The focus of this study is the as-built surface texture of titanium alloy implants manufactured by electron beam melting (EBM), an AM method, and how the osseointegration of these surfaces compare to acid-etched threaded implants. The as-built surface texture of EBM titanium alloy implants display greater roughness (arithmetic roughness = 20–50 µm) than conventional bead blasted, acid etched, or plasma sprayed wrought titanium alloy (Ti6Al4V) surfaces [14,15]. However, past studies have observed a clear positive relation between surface roughness and implant anchorage strength [14]. Titanium alloy implants made by chemical texturing methods display similar roughness (18 µm) to as-built EBM implants and have demonstrated greater osseointegration than titanium fiber mesh coated implants that possess porosity [16]. An *in vivo* goat study of osseointegration in the femoral condyle has shown equivalent bone-implant contact area of as-built EBM titanium surface implants to porous EBM implants and plasma sprayed titanium implants at 6 weeks of healing [17]. Furthermore, *in vitro* studies have demonstrated increased osteoblast vitality and proliferation as well as increased blood coagulation activation on as-built EBM titanium surfaces [15,18] as compared to machined titanium surfaces. Overall, these findings suggest the under-appreciated potential of the as-built EBM titanium surface as a useful surface for osseointegration.

Low-Magnitude High-Frequency (LMHF) vibration has been shown to enhance bone mass and could prevent bone loss in a residual limb or accelerate bone ingrowth into a prosthesis to shorten the rehabilitation period [19]. LMHF vibration differs from low-intensity pulsed ultrasound (LIPUS), which has also been investigated for stimulating bone healing, in that the frequency of mechanical stimulation is much lower and it is believed the cellular mechanisms responsible for the induced effects differ. A previous animal study identified improved mechanical stability of osseointegrated implants using LMHF vibration [20]. The study investigated the effects of LMHF vibration on implant push-out which is indicative of the 'property of surrounding bone' [21]. The study didn't investigate torsional stability which represents the 'interface mechanics', a critical aspect of osseointegrated prostheses stability [21]. No dose-response study has determined the optimum amplitude of vibration for stimulating bone ongrowth or whether ongrowth is negatively impacted by higher vibration levels.

The goal of this project was to evaluate osseointegation of implants of two designs with each undergoing identical acid etching. It was hypothesized that an EBM titanium implants with an as-built surface texture would yield greater bone ongrowth and torsional stability compared to a threaded implant. A parallel objective in this study was to identify if the mechanical stability of an osseointegrated implant can be improved dependent on the magnitude of LMHF vibration. Our hypothesis was that bone ongrowth and torsional stability would improve through a range of increasing LMHF vibration but would be impaired at higher vibration levels (>1 g).

2. Materials and methods

2.1. Phase 1 animals

Animal work was approved by the University of North Carolina at Chapel Hill Institutional Animal Care and Use Committee and performed in accordance with ARRIVE guidelines. Female retired breeder Sprague-Dawley rats (Charles River Laboratories, Wilmington, MA) with a mean age of 24 weeks were used. Rats were caged in pairs and given ad libitum access to food and water with a 12-h light/dark cycle (7 a.m. to 7 p.m.) throughout the study.

A power analysis assuming a significance level of 0.05 and power of 0.80 for comparing 5 groups was completed to compute minimum sample sizes. Sample sizes were calculated for each main outcome measure for expected mean differences and standard deviations (SD) between groups relative to the control: 25% improvement in the fraction of medullary bone volume to total volume (BV/TV) (n = 10/group) with SD = 15% [22], 40% improvement in max torque ($n = 15$/group) with SD = 30% [23], 50% improvement in % bone-implant-contact (BIC) (n = 6/group) with SD = 25% [22]. Therefore, 80 rats were used for the five treatment groups ($n = 16$/group).

2.2. Implants

Implants were made of grade 5 titanium (Ti6Al4V). Titanium rods were threaded to M2-0.4 by machining (Allied Titanium, Inc., Lewes, DE). 2-mm diameter titanium rods were produced using electron beam melting (EBM) (Arcam A2, Arcam, Mölndal, Sweden) using a powder size ranging from 45 to 105 µm. A 1.39 mm flat-to-flat hex was machined on the last 2.86 mm of the 10-mm-long implants for insertion and torque-out testing (Fig. 1).

Implants were ultrasonically cleaned in a 1% Alconox 10 gm/L solution at 65 °C for 15 min. The implants were rinsed twice with 65 °C deionized water for ten minutes under ultrasonic agitation. All implants were textured by acid etching—removing the titanium oxide layer and producing a micro-roughness with a stable, biocompatible titanium-hydride layer for promoting bone ongrowth [24,25]—in a 48% sulfuric acid (H_2SO_4) bath at 60 °C and were agitated with a stir bar for 30 min [26]. The implants were rinsed in deionized water, dehydrated in a 70% ethanol solution, and allowed to air dry before packaging for sterilization by autoclave. The surface topography was optically evaluated using a Hirox KH-7700 microscope (Hirox-USA, Inc., River Edge, NJ). Surface roughness (Ra) was obtained through linear regression of the resulting spatial map.

Please cite this article as: D.S. Ruppert et al., Improved osseointegration with as-built electron beam melted textured implants and improved peri–implant bone volume with whole body vibration, Medical Engineering and Physics (2018), https://doi.org/10.1016/j.medengphy.2018.05.003