In Vitro Corrosion Analysis in Low-Intensity, Pulsed Ultrasound

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Abstract

Clinical investigations have demonstrated a reduced time to union in certain fractures whose management is augmented with low-intensity ultrasound. It is hypothesized that ultrasound augmentation is attributable to mechanical stimulations at the cellular level. Additionally, mechanical stimulation of various magnitudes affects the corrosion rate of metals. Therefore, the effect of ultrasound on the corrosion properties of orthopedic implant materials warrants evaluation prior to recommending ultrasound as an adjunctive treatment for fractures in the presence of internal fixation devices.

The purpose of this study was to determine whether low-intensity ultrasound adversely affects the corrosion properties of 316L stainless steel, a commonly used metal in surgical implants. An electrochemical cell was used to expose 316L stainless steel specimens to a corrosion environment. Experimental specimens were subjected to low-intensity ultrasound at the clinically applied intensity. Polarization curves were used to extract average corrosion current density in the passive region, primary passive potentials, and transpassive potentials.

Analysis revealed no significant differences between the experimental and control corrosion current density, primary passive potentials, or transpassive potentials. Based on this in vitro analysis, we demonstrated no significant difference in corrosion rate between controls and exposed samples. We conclude that low-intensity ultrasound has no adverse effect on the corrosion properties of stainless steel implant materials.

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Low-intensity, pulsed ultrasound has been advocated as a therapeutic and diagnostic modality in orthopedic surgery.[1-8] The transmission of acoustic sound waves through biologic tissues has been applied in the form of continuous or pulsed ultrasound in order to stimulate fracture healing. Numerous clinical and basic science investigations have supported the use of low-intensity, pulsed ultrasound as a fracture healing adjuvant.[1,2,4,7,9-15] These trials have established an ideal and clinically accepted ultrasound signal consisting of 200μs bursts of 1.5MHz waves repeating at 1.0kHz and delivering an intensity of 30mW/cm^2. This signal has the ability to produce micromechanical stimulation while remaining safe and non-destructive to living tissue.[12-15]

At low intensity, pulsed ultrasound is considered nonthermal.[16] However, ultrasound application has the potential to increase the molecular activity in the region of fracture fixation implants. Orthopedic fracture fixation implants are primarily produced with surgical-grade stainless steel or titanium. These metals exhibit corrosion resistance by the formation of thin passive films.[17-21] Passive film formation, or passivation, is the accumulation of a thin film of corrosion oxidation products on a metal surface exposed to a corrosion environment.[19,22-24] We hypothesize that the delicate passive film that provides corrosion resistance to most fracture fixation implants is susceptible to disruption in the presence of low-intensity, pulsed ultrasound.

A thorough review of the English-language literature failed to reveal any investigation that analyzed the effects of low-intensity, pulsed ultrasound on the corrosion properties, specifically the passivation properties, of surgical-grade implant materials. The purpose of this study is to determine what effect, if any, low-intensity pulsed ultrasound has on the corrosion properties of 316L stainless steel in an in vitro corrosive environment.

Materials and Methods

The analysis of corrosion in metals commonly employs an electrochemical cell.[23] A metal sample is exposed to a corrosion environment similar to body fluid, such as lactated Ringer's solution.[17,18,25,26] An electrical potential is then applied to the sample which induces corrosion at the exposed metal surface. The generated current, or corrosion, is measured in terms of a potentiodynamic polarization curve (Figure 1).[17,23,27,28] The electric potential is adjusted incrementally so that the metal progresses from a state of active corrosion through passivation, or passive film forma-

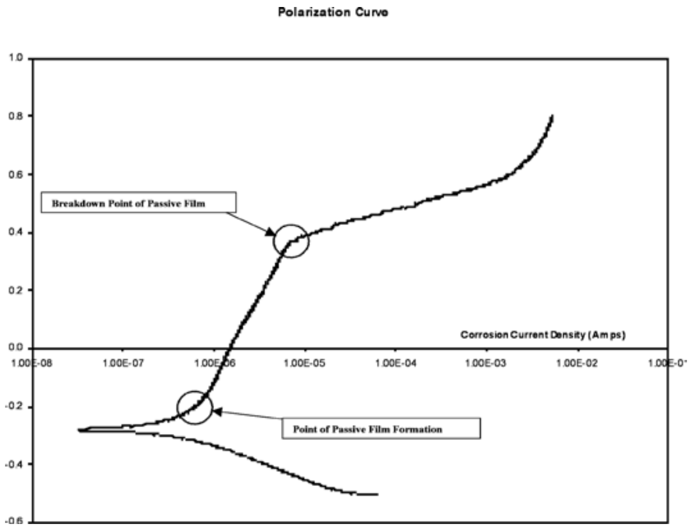

Figure 1. The electrical potential is applied to the sample in order to transition each sample from a state of active corrosion through passivation and onto passive film breakdown or the reinstitution of active corrosion. This potentiodynamic sweep generates a polarization curve as represented in the figure.

tion, onto film breakdown and back into an active state of corrosion. The current density produced as a result of the applied potential and corrosion is recorded throughout the potentiodynamic sweep and a polarization curve is generated (Figure 1).[23]

In order to evaluate the effect of low-intensity, pulsed ultrasound on the corrosion properties of a standard surgical grade fracture fixation implant material, samples of 316L stainless steel were exposed to a corrosion environment and advanced through a potentiodynamic sweep while exposed to an ultrasound signal. The potentiodynamic sweep used in this study polarized samples from -0.5 to +0.8 volts relative to a saturated calomel electrode at a scan rate of 10 mV/sec. The metal samples were certified 316L homogenous austenitic stainless steel dowels, milled according to American Society for Testing and Materials (ASTM) specifications, and cut from the same round bar stock (KG Specialty Steel, Seoul, Korea). Each measured 4.0 cm in length and 0.64 cm in diameter (Figure 2). Standard Lactated Ringer's solution at ambient room temperature in a climate-controlled lab was used to create the corrosive environment. The ultrasound source (Exogen Inc, Piscataway, NJ) was a modification of a clinically used device specially suited for experimentation. It consisted of an array of ultrasound transducers imbedded in a polystyrene plate coupled to polystyrene fluid wells. Each transducer supplied a 30mW/cm^2 pulsed ultrasound signal identical to that available in the clinical device. The signal was tested and confirmed prior to and after all experimental trials with a manufacturer-supplied testing instrument.

Ten labeled dowel samples of 316L stainless steel measuring 0.64 cm in diameter were prepared by wet grinding with a 240 grit paper followed by a wet polish with 600 grit paper in accordance with ASTM standards.[28] The samples were then rinsed thoroughly with purified water. In order to control the surface area exposed to the corrosion environment, the sides of the sample rods were masked with plastic heat-shrink tubing. This left the end exposed, giving a controlled, total surface area exposure of 0.32 cm^2. An experimental fluid well was coupled tightly to the ultrasound transducer using a standard coupling gel provided by the ultrasound manufacturer. The well contained 10 mL of standard Lactated Ringer's solution produced for clinical use (Figure 3). The chemical content and pH of the solution was controlled by the buffers within the solution.

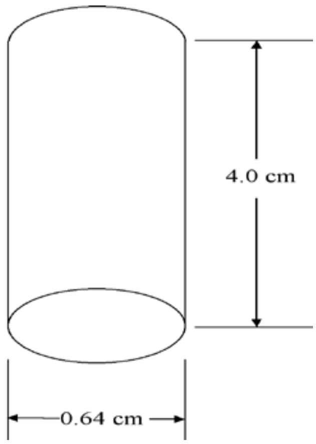

Figure 2. The figure demonstrates the geometric specifications of the test samples of 316 stainless steel.

Five 316L stainless samples were used as the ultrasound exposed group, and 5 unexposed 316L stainless samples were used as the control group. All identical samples were cut from the same rod and were uniform. Each trial was conducted in an identical manner with the exception of ultrasound application for the ultrasound exposed group. For each control trial, the metal sample was suspended in the Lactated Ringer's solution in the experimental well. The ultrasound transducer was not activated. The potentiodynamic equipment was connected to the cell, and the system was allowed to electrically stabilize for approximately 30 seconds. The sample was then polarized by applying a sliding voltage potential from -0.5 to +0.8 volts in order to obtain a potentiodynamic sweep. The potential was adjusted (10mV/sec) in order to transition each sample from a state of active corrosion through passivation and onto passive film breakdown or the reinstitution of active

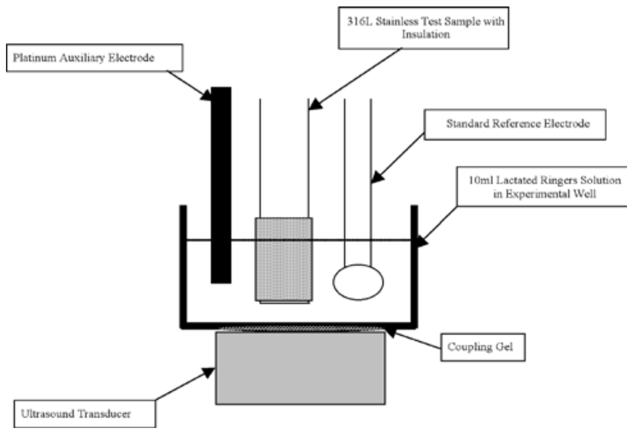

Figure 3. The electrochemical cell is demonstrated with the ultrasound transducer coupled to the test well. The stainless steel sample is immersed in the corrosion environment, with the reference electrode also immersed in the Lactated Ringer's bath. As the electric potential is adjusted, the generated current, or corrosion, is measured in terms of a potentiodynamic polarization curve via the reference electrode.

Table. Results of a Potentiodynamic Sweep in Ultrasound-Exposed and Control Samples

Outcome	Mean (Standard Deviation)	*P* value
Breakdown Potential	volts x 10	
Ultrasound-Exposed	3.66 (0.47)	0.94
Control	3.65 (0.41)	
Primary Passivation Potential	volts x 10^2	
Ultrasound-Exposed	18.51 (2.63)	0.65
Control	19.07 (1.77)	
Corrosion Current Density	amps $x10^6$	
Ultrasound-Exposed	10.1 (9.54)	0.88
Control	10.4 (8.96)	

corrosion. The voltage potential was then reversed in order to cycle each specimen back through the potentiodynamic sweep. Total time for the sweep was 240 seconds. For the ultrasound exposed group, the trials were identical with the exception that a 30mW/cm^2 ultrasound signal was applied through the coupling gel to the corrosion environment throughout the potentiodynamic sweep of 240 seconds. After data collection for all 10 samples, each sample was prepared again and polished to a 600 grit finish. Heat-shrink tubing was reapplied, and the electrochemical corrosion testing was repeated for each sample. This process was repeated a third time for each sample, so that 3 separate trials were obtained from each sample.

Each trial for each sample was plotted using an Excel spreadsheet (Microsoft, Redmond, WA) and the graphs were analyzed manually by 1 investigator. Measurements recorded included primary passivation potential (point of conversion from active corrosion to passive film formation), breakdown potential (point of passive film breakdown), and corrosion current density at each of these points. These 2 corrosion current densities were averaged for each trial to obtain the average corrosion current density in the passive region. The analysis focused on determining if there was a significant difference between the control and ultrasound groups with respect to breakdown potential, primary passive potential, and corrosion current density. Breakdown potential was investigated in order to determine if ultrasound exposure affected the potential at which a passive film deteriorated. The primary passive potential was analyzed to determine whether ultrasound affected the voltage at which passivation occurred. Current density, which directly correlates to corrosion rate, was analyzed to evaluate the influence of low-intensity, pulsed ultrasound on the corrosion rate of 316L stainless steel in the passive region.[19,23] Each outcome was tested for normality prior to the analysis using the Shapiro-Wilks statistic, and normalizing transformations were tried, if necessary. Each variable was analyzed separately using a mixed-effects repeated-measures design. Exposure (ultrasound versus control) was modeled as a fixed effect; sample (within exposure group) and trial were modeled as random effects, since the samples and trials that were used in the study represent only a random sample of a large set of potential samples and trials. Following the analysis, a post-hoc power analysis was carried out. All statistical analyses were carried out using SAS/STAT software (SAS Institute, Inc., Cary, NC).

Results

Empirical mean values and standard deviations of each outcome based on 15 observations per group, along with the *P* values for testing the equality of means of exposure groups were calculated. Statistical analysis showed that there were no significant differences between the means of the ultrasound-exposed group and the control group. ($P > .05$). Corrosion current density values were log-transformed to achieve normality. Breakdown potential data approximated a normal distribution. The results of primarily passive potential were essentially the same when several transformations (including logarithmic and square root) were analyzed, although there was no transformation which successfully normalized the data. Post-hoc power analyses showed that power was at most 0.05 for each analysis (Table).

We had hypothesized that microscopic stresses generated by low-intensity, pulsed ultrasound might disrupt passivation, and thereby alter the corrosion properties of implant metals. We analyzed current density and voltage potentials within and adjacent to the passive region of the polarization curve for 316L stainless steel. We analyzed passivation breakdown potentials to determine if low-intensity, pulsed ultrasound affected the potential at which the passive film deteriorated. The mean breakdown potential was 0.3652 V for the control samples and 0.3661 V for the exposed samples indicating no significant difference in the breakdown potential of the ultrasound-exposed group versus the control group ($P = .937$; see Table). We next examined the primary passivation potential in order to determine whether ultrasound affected the voltage at which passivation occurred. For the control group, the mean passivation potential was -0.1907 V. For the ultrasound-exposed group the mean passivation potential was -0.1851 V. No significant difference in passivation potential existed between the ultrasound-exposed and control group ($P = .651$; see Table). Current density is directly proportional to corrosion rate. Therefore, current density was evaluated in the passive region to determine whether low-intensity, pulsed ultrasound influenced the corrosion rate of 316L stainless steel in the passive region.[19,23] The mean current density for the ultrasound-exposed group was 1.010 x 10^{-5} amps and 1.039 x 10^{-5} amps for the control group. ($P = .882$; see Table).

Discussion

Ultrasound application has been advocated as a therapeutic and diagnostic modality in many disciplines of medicine.[1-8] Ultrasound modalities in clinical practice range from surgical ultrasound (5 to 300 W/cm^2) to diagnostic ultrasound (1 to 50 mW/cm^2).[16,29] Specifically in orthopedic surgery, the application of ultrasound has been found to stimulate fracture healing.[7] In 1952, Corradi and Cozzolino[9,10] demonstrated that fractures exposed to ultrasound energy resulted in bone callus in a rabbit distal radius fracture model. Dyson and Brookes[11] reported more aggressive fracture healing when comparing ultrasound exposure to no therapy in a rat fibula fracture model. Many additional animal studies have supported these results.[12-15] In the clinical environment, low-intensity, pulsed ultrasound has been employed in a variety of fractures and treatment modalities. Heckman and collegues[2] published a randomized, prospective, double-blinded clinical trail evaluating ultrasound augmentation in nonoperatively treated tibial fractures. They reported a significant decrease in clinical and radiographic time to healing in the group augmented with 30mW/cm^2 ultrasound. They also reported no complications related to the use of this low-intensity ultrasound.[2] Other authors have reported similar encouraging findings in distal radius fractures, scaphoid fractures, Jones fractures, and distraction osteogenesis.[4,30-32] Nolte and colleagues[33] found a significant improvement in the healing of established nonunions when treated with low-intensity ultrasound.

How Ultrasound Could Corrode Stainless Steel

Clinically available ultrasound transducers developed for fracture healing augmentation have a signal intensity of 30mW/cm^2. At this low intensity, ultrasound is considered nonthermal.[16] However, even at small magnitudes, ultrasound has the potential to increase the molecular activity and the local microstresses environment in the body.[7] A potential effect of increased molecular activity and microstress in the region of fracture fixation devices is the breakdown of passive films that provide corrosion resistance to implants.

Stainless steel demonstrates corrosion resistance by passivation.[20,21,23] Passivation is the formation of a very thin film of corrosion oxidation products that accumulate on a metal surface exposed to a corrosion environment.[19,22-24] This process, which occurs in vivo, provides corrosion resistance to most orthopedic implant materials.[17-19,21,38] However, this passive film is extremely fragile and can easily be damaged by mechanical, electrical, or other local environment disturbances.[21,23,38,39] Damage to the film, termed breakdown, will lead to accelerated corrosion and/or pit formation in a metal implant.[20,38,39]

In fractures stabilized with internal fixation and treated with adjuvant low-intensity, pulsed ultrasound, the same mechanical stresses that accentuate the healing process may be detrimental to metallic implants and fragile passive films. A study by Bundy and colleagues[18] revealed that a static stress applied to 316L stainless steel, a commonly used implant metal, will increase its rate of corrosion in vitro and increase the release of corrosion degradation products. These adverse effects were due to the ability of the applied stress to disrupt the passive film.[18] Although the stresses created by low-intensity ultrasound are significantly smaller than those in the above static loading analysis, it is conceivable that ultrasound-induced microstresses could disrupt the fragile passive layer on surgical implants. Such a disruption may accelerate the corrosion rate of fracture fixation devices.

How Ultrasound May Speed Fracture Healing

There are a number of ideas and theories to explain how ultrasound may accelerate healing. Several investigators have shown that intracellular processes can be influenced by ultrasound stimulation, including vitamin metabolism, bone generation, and callus formation.[3,6,10,15,34] Studies have also demonstrated that ultrasound can increase gene expression as well as increase blood flow.[1] Sun and colleagues[35] reported that stimulating cell cultures with low-intensity ultrasound increased prostaglandin synthesis and upregulated osteoblasts. It is likely that the application of ultrasound actually produces multiple effects which combine to positively influence all stages of fracture healing.[1] Underlying these positive effects is the mechanical ability of pulsed ultrasound to create nonthermal, microscopic mechanical stimuli on cells.[3,6,7,36,37] Effects such as acoustic streaming and microstreaming can activate cells and potentially increase protein synthesis as well as growth factors.[3,6,14] Mechanical stretch, pressure, and other stresses can activate endothelial cells and upregulate intracellular signaling.[3] These effects are thought to be responsible for the favorable responses of certain fractures to ultrasound stimulation.

The Potential Deleterious Effects of Corrosion Products in Vivo: An increase in corrosion products in vivo has been reported to have deleterious effects on local and systemic tissues. Metal sensitivity can lead to local inflammation, foreign body reactions, and tissue necrosis.[40,41] Corrosion products have been cited as a possible cause of deficiency in white blood cell migration and a weakened immune response.[42] Chronically high levels of products such as aluminum and cobalt can be directly toxic, and some ions of chromium, aluminum, titanium, and cobalt are potential carcinogens.[42-44]

Potential for Acceleration of Corrosion: Acceleration of corrosion rates coupled with cyclic loading in a fracture healing scenario can accentuate corrosion fatigue and stress-corrosion cracking.[18] This is certainly true in the fracture nonunion scenario for which low-intensity, pulsed ultrasound devices have been advocated. In this scenario, a fixation device is exposed to a mechanical environment in which fatigue failure of implants is not uncommon.

No reported cases of catastrophic implant failure have been reported in relation to the application of low-intensity, pulsed ultrasound. However, the potential disruption of passive films and an associated acceleration of corrosion in fracture fixation devices warranted investigation.

Conclusions

Based on this in vitro analysis, we demonstrated no significant difference in passive film breakdown potential, passivation potential, or passive region corrosion current density between controls and ultrasound-exposed samples. We concluded from this data that low-intensity, pulsed ultrasound has no adverse effect on the in vitro corrosion properties of 316L stainless steel.

Avenues for future study include the comparison of the effect of low-intensity, pulsed ultrasound on additional fracture fixation materials such as titanium. Additionally, studies are warranted to evaluate the effect of this ultrasound on the corrosion properties of implant materials under fatigue loading conditions.

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This paper will be judged for the Resident Writer's Award.