Magnetic Resonance Imaging of Osteoconductive Calcium Polyphosphate Drug Delivery Devices

Joshua M. Bray, Steven D. Beyea.
Institute for Biodiagnostics (Atlantic), National Research Council;
Department of Physics, Dalhousie University, Halifax, NS, Canada.

Introduction: Osteomyelitis is an infection by the *S. Aureus* bacteria that occurs in open bone fractures, delaying healing and bone regeneration. Because of the localized nature of this infection, systemic methods of drug administration (oral or intravenous) fail to achieve sustained inhibitory concentrations without toxic damage to other tissues. The accepted alternative involves implantation of drug-saturated polymethylmethacrylate (PMMA) beads into the fracture, which provide localized delivery but require surgery for removal.

Resorbable bioceramic materials offer a solution to this problem because they are designed to completely biodegrade over time. The degradation process is associated with chemical and physical changes to the ceramic microstructure that occur as fluid is absorbed from the environment (in the body). Conversely, changes to the microstructure produce changes in the fluid transport parameters of the material. Because of this dynamic interplay between structure and transport, the study of bioceramic degradation requires a method that is non-invasive and permits in situ measurements. Magnetic resonance imaging (MRI) meets both these requirement, and also offers sensitivity to several parameters that can yield information about diffusive fluid motion and the microstructure within the bioceramic[1].

Calcium Polyphosphate (CPP) is a promising candidate material for drug-delivery. Implanted into bone tissue, it is known to degrade to calcium orthophosphate, which is non toxic and can be metabolized by the body. Not only is CPP biocompatible and resorbable, but it also exhibits osteoconductivity[2]. The aim of this experiment was to non-invasively observe the ingress of fluid into a CPP disk using MRI – an important first step that will eventually lead to characterizing changes in the microstructure and drug elution as a function of biodegradation.

Methods: Amorphous CPP was produced using a melt procedure, as described by Pilliar[3]. Powdered CPP was mixed with fluid to produce a paste, which was then molded into disks. These were then gelled for 5 hours in a humid environment, and then dried for 24 hours. After drying, the disks were pulverized, and the resulting powder was compacted in a metal die at 113 MPa for 5 minutes. Finally, the compacted disks were subjected to another gelling/drying cycle.

In preparation for imaging, a finished disk was placed in a glass Wilmad NMR spectroscopy test tube on top of a spacer. Measurements were performed on a high-field MRI system using a Constant-Time Imaging sequence.

Results / Discussion: MR profiles of the bioceramic were measured. CPP materials fit snugly into the tube, resulting in one-dimensional transport of fluid. A time-series of 1-D profiles of fluid density along the axis of the disk clearly show penetration of the fluid, swelling of the sample, and internal degradation of the material over time.

Conclusions: A method was developed for high-resolution MR microscopy of Calcium Polyphosphate bioceramic. Using this method, the temporal and spatial evolution of fluid density in the bioceramic was observed. Future experiments will include direct observation of the progressive changes in drug transport behavior as a result of microstructural degradation.

References:

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