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Degradation and drug release in calcium polyphosphate bioceramics: An MRI-based characterization

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ABSTRACT

Degradable, bioceramic bone implants made of calcium polyphosphate (CPP) hold potential for controlled release of therapeutic agents in the treatment of localized bone disease. Magnetic resonance imaging techniques for non-invasively mapping fluid distribution, T_1 and T_2 relaxation times and the apparent diffusion coefficient were performed in conjunction with a drug elution protocol to resolve free and bound water components within the material microstructure in two CPP formulations (G1 and G2). The T_2 maps provided the most accurate estimates of free and bound water, and showed that G1 disks contained a detectable free water component at all times, with drug release dominated by a Fickian diffusion mechanism. Drug release from G2 disks was characterized by a combined diffusional/structural relaxation mechanism, which may be related to the gradual infiltration of a free water component associated with swelling and/or chemical degradation.

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1. Introduction

With the increasing use of biomaterials for tissue regeneration and controlled drug release, there is a greater need for characterization techniques that can assist with the optimization of these materials. In particular, biodegradable implant materials represent highly dynamic systems that require a non-invasive approach to fully understanding the fundamental mechanisms of degradation and drug release. Magnetic resonance imaging (MRI), in addition to being a non-invasive tool, offers a range of image contrast mechanisms that are sensitive to the mobility characteristics of sorbed water, and provide an endogenous probe of the chemical and physical microstructure. MRI is therefore a powerful technique for characterizing degradable biomaterials and for understanding their function, as well as potentially speeding their development as effective therapeutic options [1,2].

The present authors have developed an MRI protocol for studying microstructural changes in degradable calcium polyphosphate (CPP) bioceramics. CPP is a form of condensed phosphate, which is sometimes referred to as an "inorganic polymer" [3,4]. The combination of ceramic and polymeric characteristics in CPP make it a potential alternative to other biopolymers, with manipulation of drug release possible through the physico-chemical reactions to water (i.e. chain scission, gelling/swelling, and bulk erosion [3,5,6]). Because of these characteristics, implantable devices made from amorphous CPP have been explored for controlled-rate drug release in localized therapy [7–9], specifically for the delivery of antibiotics in the treatment of chronic, localized bone infections (osteomyelitis) [7,8,10–12]. Furthermore, biodegradable materials such as CPP have the attractive quality that no surgery is required to remove the device, which is beneficial because it reduces both patient discomfort and the risk of reinfection during surgery [13–15].

In a material such as CPP, the goals of controlled-rate release and biodegradation are related, because drug is eluted from the device through fluid absorbed from the environment (i.e. the body), and the fluid transport is, in turn, governed by the physical and chemical microstructure of the implant material. As such, a mechanistic understanding of the relationship between microstructural transformation and drug release behavior is crucial, and must be obtained in a way that does not disrupt the dynamics of the system [16]. Previous research into the structure/elution characteristics of CPP drug delivery bioceramics has been carried out using techniques limited to the study of "dry" materials (e.g. scanning electron microscopy) and to bulk methods averaged over the entire material (e.g. drug elution aliquots). What is lacking is an understanding of how the fabrication parameters influence the microstructure, how local degradation occurs and, ultimately, how this affects rates of release.

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