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New magnetic-resonance-imaging-visible poly(ε-caprolactone)-based polyester for biomedical applications

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ABSTRACT

A great deal of effort has been made since the 1990s to enlarge the field of magnetic resonance imaging. Better tissue contrast, more biocompatible contrast agents and the absence of any radiation for the patient are some of the many advantages of using magnetic resonance imaging (MRI) rather than X-ray technology. But implantable medical devices cannot be visualized by conventional MRI and a tool therefore needs to be developed to rectify this. The synthesis of a new MRI-visible degradable polymer is described by grafting an MR contrast agent (DTPA-Gd) to a non-water-soluble, biocompatible and degradable poly(ε-caprolactone) (PCL). The substitution degree, calculated by ^{1}H nuclear magnetic resonance and inductively coupled plasma-mass spectrometry, is close to 0.5% and proves to be sufficient to provide a strong and clear T1 contrast enhancement. This new MRI-visible polymer was coated onto a commercial mesh for tissue reinforcement using an airbrush system and enabled in vitro MR visualization of the mesh for at least 1 year. A stability study of the DTPA-Gd-PCL chelate in phosphate-buffered saline showed that a very low amount of gadolinium was released into the medium over 52 weeks, guaranteeing the safety of the device. This study shows that this new MRI-visible polymer has great potential for the MR visualization of implantable medical devices and therefore the post-operative management of patients.

1. Introduction

Polymeric biomaterials are being increasingly used for biomedical applications as implantable devices or drug delivery systems [1–3]. As these biomaterials offer a great variety of structures, and therefore possess a broad range of properties, they can be used in a host of applications. One of the most important applications in the biomedical field is the use of these polymers for medical devices, especially prostheses. Such materials can be used for permanent or temporary applications, depending on their structure [4–6]. Unfortunately, all these polymeric materials are transparent to X-rays and are invisible using magnetic resonance imaging (MRI). This inability to visualize implanted material restricts any evaluation of tissue integration and post-operative fixation, and any determination of fate in the body [7].

A radio-opaque poly(ε-caprolactone) (PCL)-based aliphatic polyester has been developed in our laboratory in which a covalent link has been formed between a radio-contrast dye (typically iodine) and the polymeric backbone [8].

MRI is a non-ionizing technique that is widely used in clinical practice, mainly because of its non-invasive nature, its capability to produce high-definition images and its ability to depict pathological tissues [9–12]. Image contrast is often enhanced by using contrast agents [13,14] and this approach may be used to visualize polymeric material. In a recent report, Kramer et al. have reported the synthesis of surgical textile implant loaded with iron oxide nanoparticles during the polyvinylidene fluoride threads extrusion [15]. The resulting material was visualized by MRI using the positive-contrast inversion recovery with on-resonant water suppression sequence [16]. Positive contrast may also be gained using conventional MRI sequences if paramagnetic agents, such as gadolinium salts Gd(III), are used [17]. Unfortunately, gadolinium salts are toxic and must be chelated [18]. Of all gadolinium chelates, diethylenetriaminepentaacetic acid (DTPA) is the most frequently used in medical imaging [19].

Several methods have been reported in the literature to design macromolecular DTPA-Gd complexes. Applications of these new contrast agents in blood pool imaging are focused on the

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