OPTIMIZING COMPOSITION OF PDTEC/PI$_2$DTEC TISSUE SCAFFOLDS FOR X-RAY IMAGING USING COMBINATORIAL FABRICATION METHODS*

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Abstract

Previous studies on poly(desaminotyrosyl-tyrosine ethyl ester carbonate) (pDTEc) indicated that it is biocompatible, degradable and possesses good mechanical properties, which make it a candidate material for tissue scaffolds. Yet, pDTEc is radiolucent making X-ray imaging difficult. The ability to image radiopaque medical implants *in vivo* with X-ray radiography enables clinicians to non-invasively monitor wound healing and regeneration *in situ.* In addition, the internal microstructure of radiopaque implants can be observed *in vitro* with X-ray microcomputed tomography (μCT) without undergoing physical sectioning and histology. A radio-opaque analog of pDTEc, pI$_2$DTEc, has been made by iodinating the desaminotyrosine ring. However, molecular changes within the polymer structure often affect physicochemical properties and influence performance. Therefore, blending pDTEc with a minimum amount of pI$_2$DTEc should yield a material that retains many of the desirable properties of pDTEc but is also radio-opaque like pI$_2$DTEc. Continuous variable composition gradient scaffold libraries of pDTEc and pI$_2$DTEc were fabricated to determine the optimal blending composition in an efficient, combinatorial approach. The rod-shaped polymer libraries with pI$_2$DTEc content ranging from 17.5 % to 95.4 % (mass fraction) were then analyzed by three X-ray imaging techniques: X-ray microradiography, μCT and dental X-ray radiography. In X-ray microradiographs (540 mAs), the entire range of compositions was visible while higher fractions of pI$_2$DTEc yielded images with higher contrast. For μCT, at least 50 % pI$_2$DTEc (mass fraction) was required for optimal imaging and quantitative analysis of scaffold structural parameters such as degrees of anisotropy, porosity, wall thickness, and pore size. When the mass fraction of pI$_2$DTEc was lower than 50 %, μCT images of scaffolds can still be obtained. However the signal to noise ratio is low making quantitative image analysis difficult. Furthermore, when dental X ray (2 mAs) was applied, good X-ray contrast could only be obtained for the most pI$_2$DTEc-rich compositions. *In vitro* MC3T3-E1 cell culture with pDTEc and pI$_2$DTEc, either in 2-D films or 3-D scaffolds, indicated similar biocompatibility when compared to other FDA approved degradable polymers, although pI$_2$DTEc showed less cell proliferation than pDTEc. These results demonstrate the efficiency of using pI$_2$DTEc as an X-ray contrast agent as well as the feasibility of a novel, combinatorial approach for determining the optimal composition of polymer blending systems.