Assessment of Poly(diol citrate) Composites of Micro/Nano Hydroxyapatite

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Statement of Purpose: Biodegradable devices [1] are a well recognized alternative to metallic devices in the internal fixation of certain fractures and osteotomies. Concerning biocompatibility, poly(L-lactide) implants (PLLA) [2-3] are generally considered to be inert, but in some cases, they lead to unwanted foreign body responses. A strategy to improve the osteointegration capacity of polymers has been to blend them with hydroxyapatite (HA). We have recently described the preparation and characterization of poly (diol citrate)-HA composites [4]. Their mechanical properties and degradation rates can be controlled with the synthesis conditions of poly(diol citrate) and percentage of the HA component. In particular, poly (1, 8-octanediol-co-citrate) (POC) has faster degradation rate (a few months to 1 year) than PLLA and good biocompatibility with soft tissue. They also are inexpensive and easy to synthesize, an additional advantage for clinical use. The objective of this study was to characterize the mechanical properties and biocompatibility of POC-micro and nano HA composites.

Methods: Hydroxyapatite nanocrystals (medical grade, 100 nm) and hydroxyapatite ceramic powder (medical grade, 20-50 μm) were purchased from Berkeley Advanced Biomaterials, Inc. 1, 8-octanediol (98%) and citric acid (99.5%) were purchased from Sigma-Aldrich (St. Louis, MO, USA). To prepare POC-HA composites, POC pre-polymer was mixed with various amounts of HA particles to obtain 40%, 50%, 60% and 65 wt.% HA components by weight [4]. The right and left knee of 7 New Zealand white rabbits (Covance, Kalamazoo) were used to assess biocompatibility. A bone defect with a 2.7 mm (diameter) x 4.0 mm (depth) was created in both medial femoral condyles. POC-HA non-porous plugs containing relatively low (40 wt.%) or high (~60 wt.% for nano HA or 65wt% for micro HA), were inserted into the left and right defects, respectively via press fit. After 6 weeks, the implant and surrounding tissue were harvested and evaluated by histology and histomorphology. Gross examination was documented with a digital camera. Hemotoxylin and eosin (HE), Masson-Goldner Trichrome (MT) and von Kossa (VK) stains were used to characterize biocompatibility. Sections were evaluated via standard light microcopy.

Results/Discussion: POC-HA composites with an HA percent of up to 65 wt% could be fabricated using micro particles. However, nanoparticles only allowed the fabrication of composites with 60 wt% HA. The bending (Eb) and compression (Ec) moduli of nano HA composites were higher than those of micro HA composites (at 60 wt.% of HA, Eb=322±19 and Ec= 328±20 for nano HA composite, and Eb=24±1 and Ec=25±2 for micro HA composite, all values in MPa). At the tissue-implant interface, there was no evidence of a significant fibrous capsule formation or inflammation (Fig.1). To the contrary, bone formation was evident adjacent to the implants. The bone surrounding the implant was active as osteoids with layers of osteoblasts were observed. Far from the implant, the bone histology was normal. Cells were observed to migrate into the POC-nanoHA composites at a higher frequency than with the POC-micro HA composites.

Conclusions: Mechanical properties of the composites with nano HA are in the range of those reported for PLLA-HA composites. All the composites demonstrated very good biocompatibility although the nano HA composites seemed to have a higher osteostimulatory response at tissue-implant interface. The composites described herein are easy to fabricate, required to catalyst and integrated with bone tissue. Future research will evaluate the long-term tissue responses during degradation of implant.

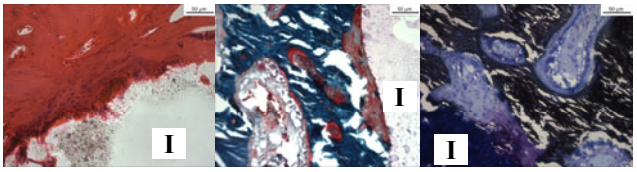

Figure 1 Histological stains of POC-HA (40% nanoHA) composites that were implanted in the medial femoral bone for 6 weeks: a) HE; b) Masson Goldner; c) von Kossa (I: implant)

References:

1. Böstman OM. J Bone Joint Surg [Am]. 1991; 73-A:148-153.
2. Nordström P. Clin Orthop. 2001; 382:247-257.
3. Bergsma JE. Biomaterials. 1995; 16:25-31.
4. Qiu H. Biomaterials. 2006; 27:5845-5854.