Synthetic Bone Grafts: A Surface Mineralized Approach
By Jacqueline Harding, Chemical and Biological Engineering Department, Colorado School of Mines, Golden, CO

Bone is a dynamic system continuously undergoing remodeling with 10% of the skeleton regenerated annually in adults. The existing bone is utilized as a growth template for remodeling and repair alike. As such, in the event of a critical defect in the tissue, natural processes are unable to repair the damaged site. As shown in Figure 1, the use of grafts of natural and synthetic origin are used as regenerative templates in the repair of damaged tissue.

Figure 1. Scheme for the repair of bone injury with synthetic bone grafts.

Synthetic Alternatives to Harvested Bone Grafts

Natural grafts sourced from the patient as autografts or harvested from organ donors as allografts are the most successful graft options currently available. The use of natural graft materials possesses the inherent advantage of fully formed bone matrix resulting in an ideal scaffold for promoting graft integration. Despite the success, natural grafts are not without limitations. The donor site of autografts is subjected to long term complications and the amount of graft tissue available is limited. While the supply of allograft materials is considerably less restricted, the risk of disease transmission and immunogenic responses associated with all donor tissues is a persistent concern.
The use of synthetic grafts is highly desirable because they are deemed safe, available in an unlimited supply, easily stored and tailorable in size and shape based on the intended application. A critical challenge to the development of synthetic grafts is tuning the material to support the regeneration of bone matrix. In contrast to natural grafts, synthetic bone grafts are saddled with the burden of generating functional bone matrix in its entirety. The success of synthetic bone grafts are rated based upon the materials capacity to integrate with surrounding bone tissue and the mechanical stability at defect sites during the healing process.\(^2\)

Bone is formed as a result of an inorganic mineral calcium phosphate (CaP) polymorph nucleating on the surface of a collagen template. As an attempt to mimic the composition of bone, many synthetic bone substitutes are formulated to contain various CaP polymorphs. Remarkably all CaP polymorphs — synthetic and bioavailable alike — are found to exhibit exceptional biocompatibility and promote an osteoconductive (cell adhesion and growth on surface) response when in contact with cells. The osteoconductivity of graft surfaces is known to be variable depending on the surface topology and composition of the material.\(^3\) Current preparation methods of synthetic bone substitutes rely on the dispersion of the mineral phase throughout the polymeric matrix. As a dispersion, it is difficult to maintain the homogeneity of the particles throughout the material matrix and control the surface properties of the graft.

**Biomimetic Surface Mineralization of Synthetic Bone Grafts**

A promising alternative to dispersion preparation of CaP materials for improving the physicochemical properties of bone substitutes is to mimic the mineralization process of natural bone tissue. This approach will not only facilitate the ordered deposition of a mineral phase of the material surface, it will also contribute to the tuning of the deposited mineral phase to mimic the CaP composition of the surrounding tissue on an application-specific basis.

The most widely explored method for surface mineralization of polymeric materials is the immersion in ionic solutions of simulated body fluid. After immersions spanning weeks to months, the resulting mineral phase deposited on the surface is characterized as
biomimetic apatite. A significant drawback to this approach is the slow rate of crystal formation and a lack of control over the resulting mineral composition and morphology. Mineralization of scaffolds has shifted towards the surface modification with carboxyl functional groups on the polymeric surface of the material to provide nucleation sites mimicking those found in natural collagen scaffolds. Resulting CaP phases nucleated onto the template surface are frequently granular particles lacking surface homogeneity and control over the chemical composition of the mineral phase, in comparison to the smooth plate like appearance of bone mineral.

Although highly desirable, current technology in the preparation of synthetic bone substitutes remains limited by the lack of systematic method for the predictable synthesis of CaP polymorphs with control over the chemical composition and particle morphology in the presence of polymeric templates. A possible synthetic route will closely follow the mineralization mechanisms of bone as a multistep reaction involving the maturation of CaP polymorphs from unstable precursor phases to stable apatite phases. Synthetic control over the resulting chemical compositions and surface morphologies of the deposited mineral phase will allow for the application specific tuning of synthetic grafts in future biomaterials.

References