

Addition of shape-fitting poly(lactic acid) mechanical supports and immunomodulatory amniotic membrane to enhance mineralized collagen scaffolds for craniofacial bone repair

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Craniofacial (CMF) defects are a unique type of bone loss in which the defect size is too great for the body to naturally repair and surgical intervention is required. This type of bone defect presents unique challenges. CMF defects are usually irregular in size and shape, ill-fitting bone replacements can be rejected by the body, and chronic inflammation can cause the replacement to fail. Current methods of repair involve the use of autografts which involve using bone from one's own body and can lead to bone morbidity, or allografts, which use donor bone that varies widely in success rates. Our lab has recently developed a mineralized collagen-glycosaminoglycan scaffold to promote

mesenchymal stem cell osteogenic differentiation and CMF bone regeneration in the absence of traditional pro-osteogenic signals [1]. However, these porous scaffolds do not have sufficient mechanical properties for load-bearing applications, such as with CMF defect repair. In addition, these scaffolds do not resist chronic inflammation. We explored further modifications to the composition of the collagen

scaffold, incorporating the amniotic membrane derived from placentas, to alter mesenchymal stem cell response to inflammatory challenge. We have previously shown the benefit of incorporating this membrane into non-mineralized collagen scaffolds [2], leading to exploration of the development of mineralized collagen-poly(lactic acid) composites with immunomodulatory properties for CMF repair.

Here, we describe combining mineralized collagen with a shape-fitting 3D printed poly(lactic acid) (PLA) frame, and alternatively, combining it with the amniotic membrane. We demonstrate that the addition of PLA increases mechanical strength of the mineralized collagen, as well as provides it with a shape-fitting behavior to allow conformal fitting. The addition of PLA does not impact the bioactivity and bone regeneration capabilities of the mineralized collagen. In addition to this, we demonstrate that the amniotic membrane can be integrated with mineralized collagen and increases its mechanical properties, as well as affect the pore size of the scaffold. Changes in mechanical properties due to PLA fiber diameter and measurement of pore size will be examined.

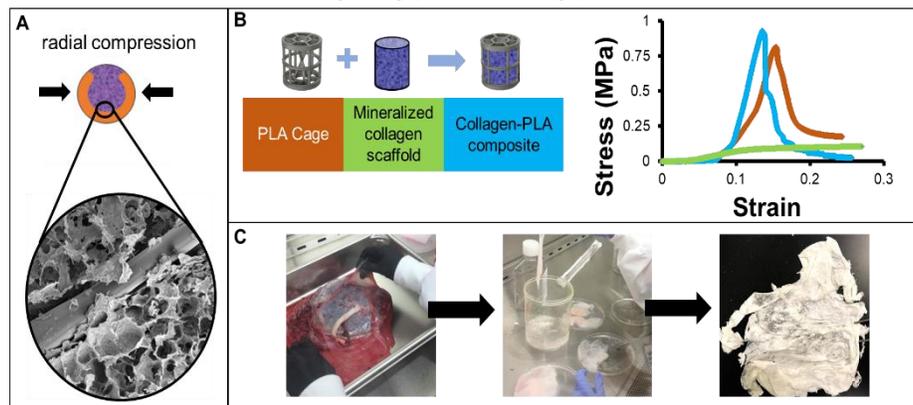


Figure 1: (A) SEM image demonstrating incorporation of PLA fiber into mineralized collagen and radial compressibility of shape-fitting design. (B) Representative image of increased compressive strength of mineralized collagen on the addition of a PLA reinforcing frame. (C) Isolation of the amniotic membrane from placentas. The membrane is removed from the placenta, decellularized, then lyophilized. The lyophilized membrane is then incorporated into mineralized collagen scaffolds.

References

- [1] Ren X, Bischoff D, Weisgerber DW (2015) Osteogenesis on nanoparticulate mineralized collagen scaffolds via autogenous activation of the canonical BMP receptor signaling pathway. *Biomaterials* 50, 107-114.
- [2] Hortensius RA, Ebens JH, Harley BAC (2016) Immunomodulatory effects of amniotic membrane matrix incorporated into collagen scaffolds. *Journal of Biomedical Materials Research* 104, 1332-1342.