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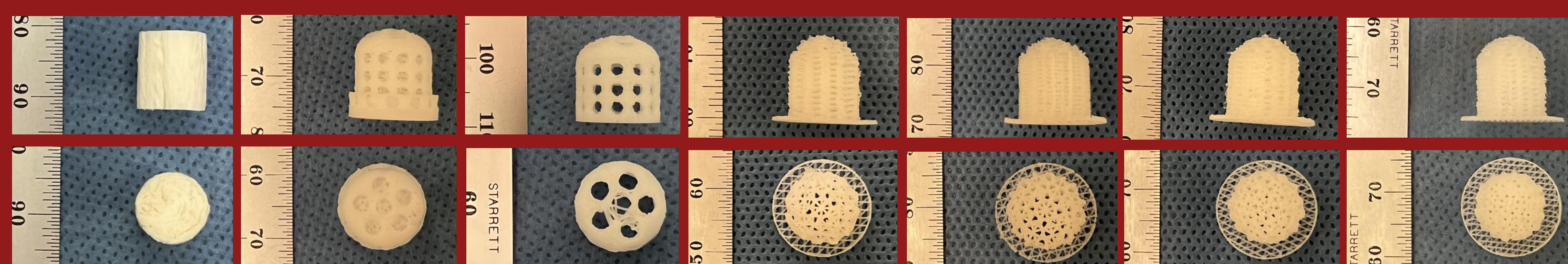
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Introduction

Creating the nipple is the last surgical step of breast reconstruction. However, autologous tissue techniques are limited due to scar contracture and significant loss of neo-nipple projection. Poly-4-Hydroxybutyrate (P4HB) is a biodegradable polymer with a long track record of clinical use as a surgical mesh and we have previously shown long-term maintenance of nipple projection using 3D-printed P4HB nipple scaffolds filled with processed cartilage in nude rats. Here we aim to modify the interior reticular structure of the 3D-printed P4HB cylindrical scaffold to better mimic the biomechanical properties of the native nipple while maintaining the nipple projection in an immunocompetent rodent model.

Methods

Nipple scaffolds were 3D-P4HB printed (diameter: 1.0cm, height: 1.0cm) with different internal 3D latticework of P4HB filaments (infill density (ID): 20, 25 and 30%; printing filament diameter (FD): 0.15 and 0.2mm). All the nipple scaffolds were subcutaneously implanted in Sprague-Dawley rats using a CV flap technique. P4HB scaffolds with porous external shell, P4HB scaffolds without the internal latticework (empty) and Cook Biodesign® Nipple Cylinder were implanted as controls.



Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7
Cook Biodesign® Nipple Cylinder	ID: 25% FD: 0.2mm External shell	ID: 0% (empty) FD: 0.2mm External shell	ID: 20% FD: 0.2mm No Shell	ID: 20% FD: 0.15mm No Shell	ID: 25% FD: 0.2mm No Shell	ID: 30% FD: 0.2mm No Shell

Fig. 3D-printed P4HB nipple scaffolds (Pre-implantation)



Fig. Nipple projection reservation after nipple reconstruction (provided by Dr. Jason Spector)



Fig. CV flap technique for nipple reconstruction (post-op Day 0)

Results

The diameter and projection of reconstructed nipples with 3D-P4HB scaffolds were well maintained over 3 months (>90%, $p>0.05$) and the stiffness of the reconstructed nipples slowly declined as the P4HB polymer was gradually replaced by the host tissue. In contrast, the Cook Biodesign® nipple lost 25% and 50% projection at 1- and 3-month respectively ($p<0.05$).

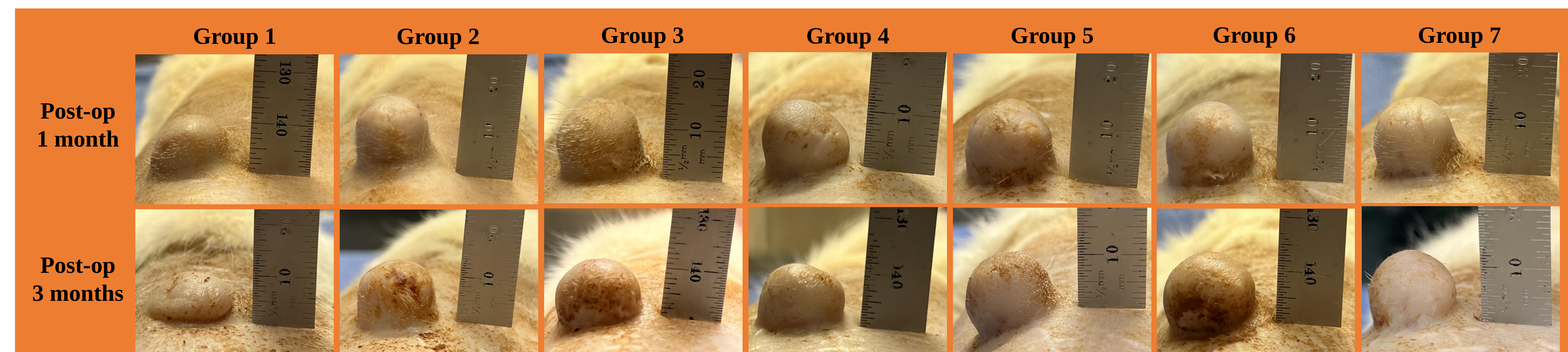


Fig. Diameter and projection reservation of reconstructed nipples after 1 and 3 months

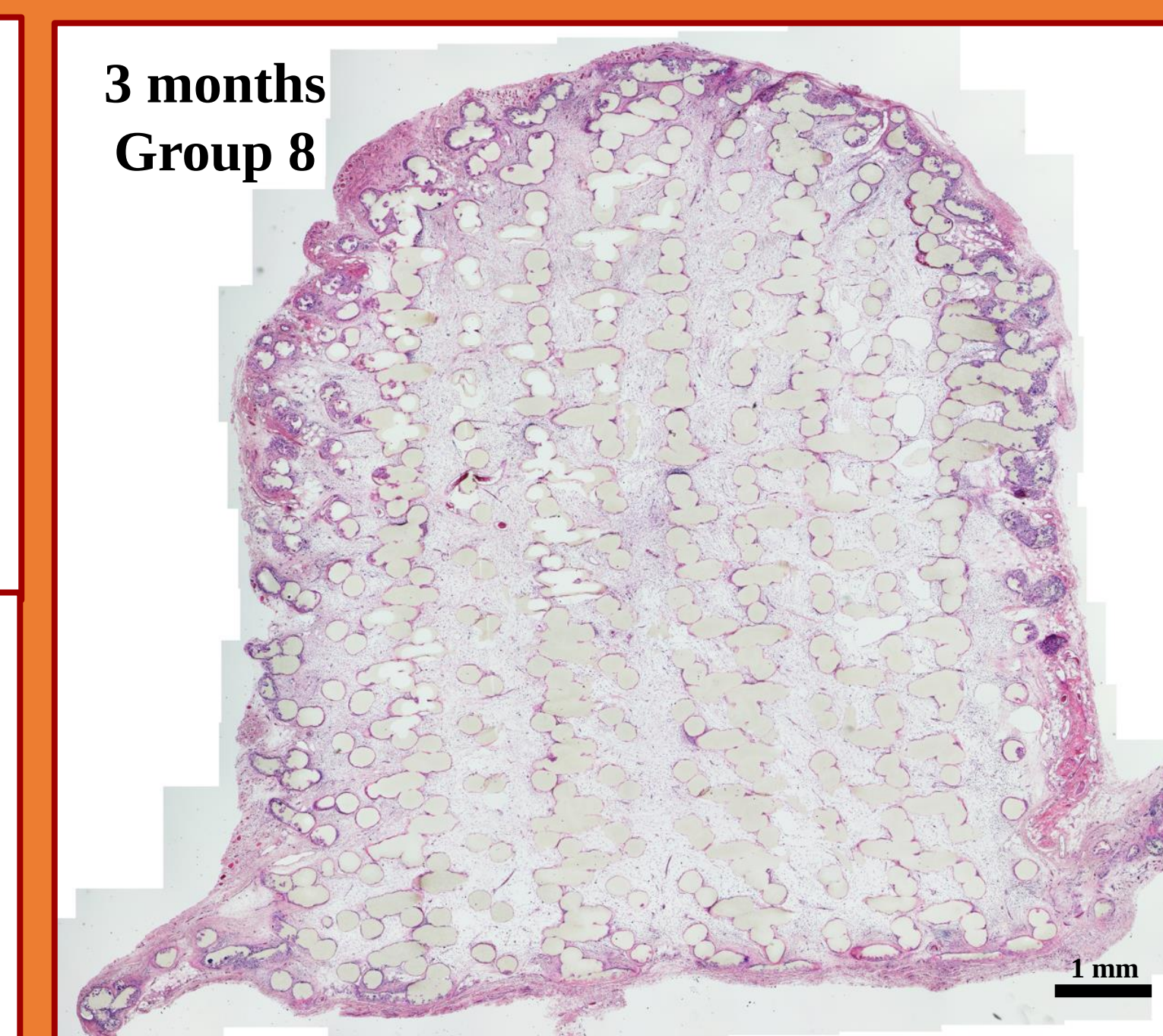
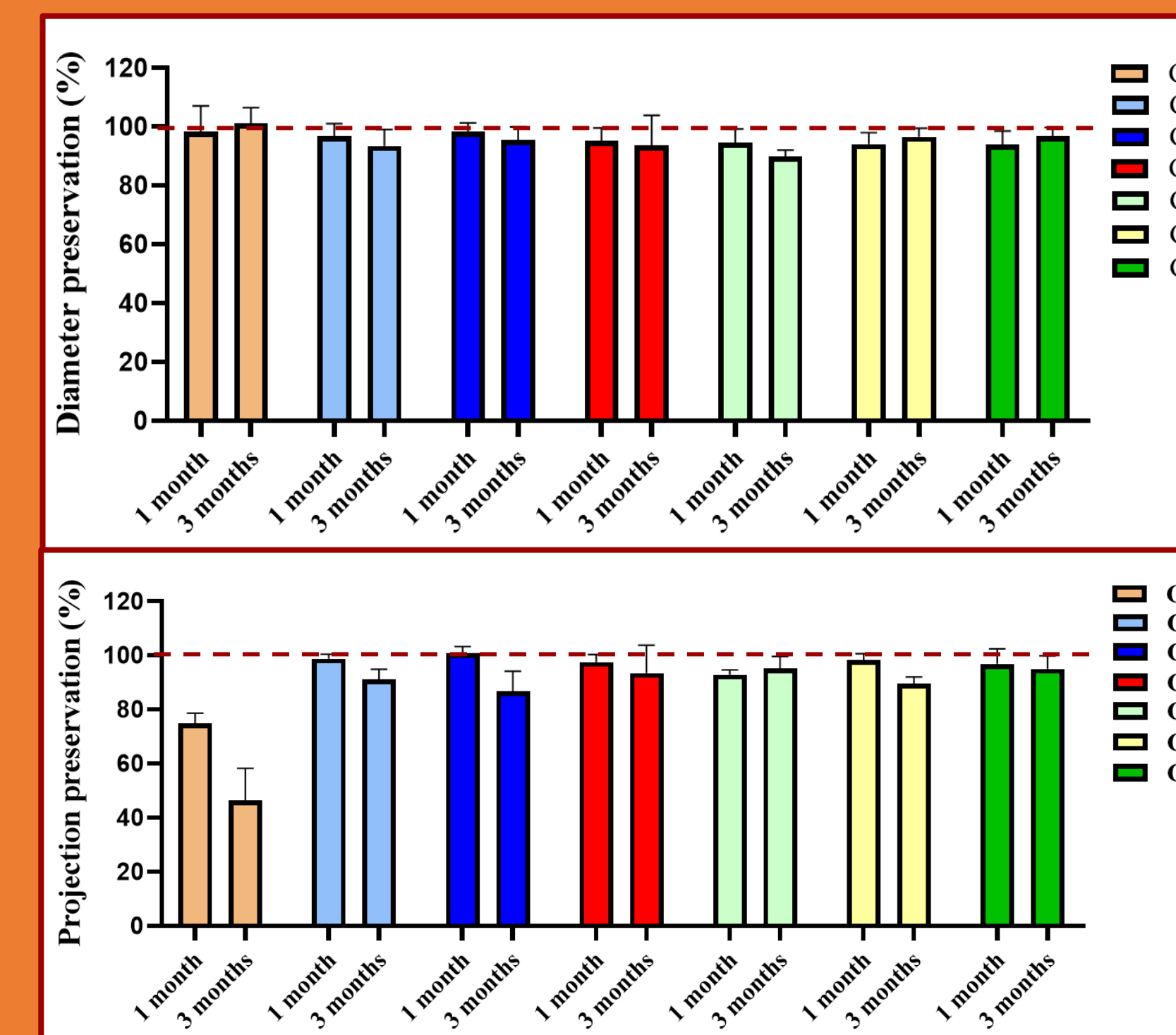


Fig. Representative H&E image of a neo-nipple

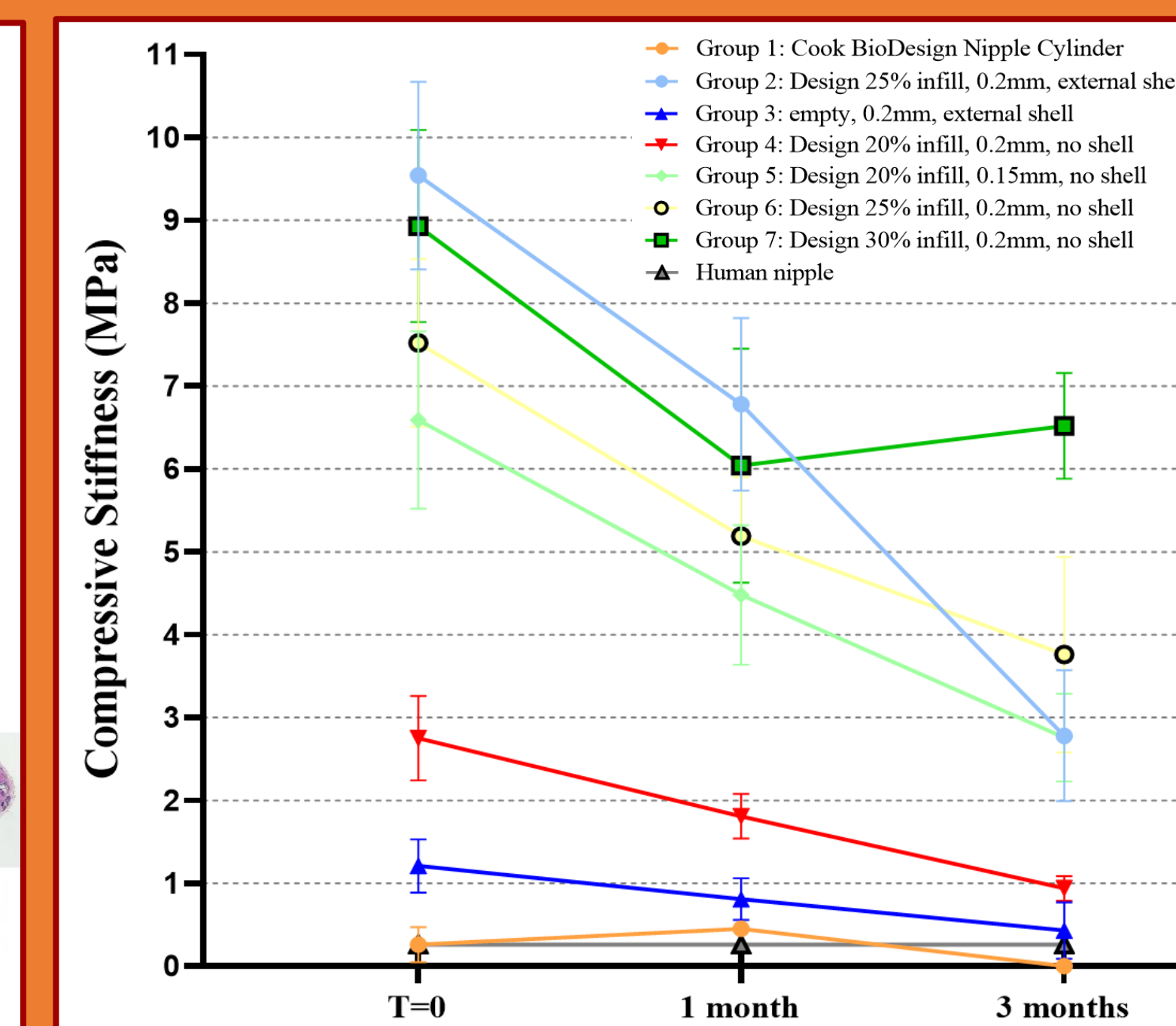


Fig. Biomechanical testing of neo-nipples

Conclusions

We have successfully engineered neo-nipples that maintain projection over time, while simultaneously allowing for tissue ingrowth that is biomechanically similar to that of native nipples. Long-term observation will be warranted to verify the translatability of this novel 3D-P4HB nipple scaffold.