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RESPONSE OF SCAFFOLD MATERIALS DESIGNED FOR TREATMENT OF STRESS URINARY INCONTINENCE (SUI) AND PELVIC ORGAN PROLAPSE (POP) TO DISTENSION

Hypothesis / aims of study

Polypropylene mesh (PPL) is commonly used for stress incontinence and prolapse surgery, however serious complications associated with these meshes are currently under investigation by regulators. Mesh erosion through tissues may occur as a result of a mismatch between the mechanical properties of this mesh and the host tissues, while more elastic polyurethane polymer materials have shown promise recently for hernia repair (1). We hypothesize that materials with a greater degree of elasticity can be produced by using polyurethanes, which will also allow cell penetration and proliferation. Our aim therefore is to develop techniques to electrospin polyurethane scaffolds and compare these with poly-L-lactic acid (PLA) scaffolds, which have already demonstrated an ability to support cell growth *in vitro* and are biocompatible following implantation in rat models (2). To test this hypothesis, electrospun materials along with commercial PPL underwent mechanical testing before and after 7 days of cyclical distension. Cell viability and total collagen production of cells cultured on these scaffolds was assessed following 14 days *in vitro.*

Study design, materials and methods

Poly-L-lactic acid (PLA), polyurethanes (PUZ1 and PUZ3) and composites of the two (PUZ1/PLA), were electrospun to form monofilament, microfibrous scaffolds. All materials were subjected to mechanical testing (Bose electroforce tensiometer) before and after 7 days of static conditions or dynamic distension using a bioreactor and compared to commercial PPL mesh and healthy paravaginal tissues (3). Adipose derived stem cells (ADSC) were selected as an appropriate cell source and were isolated from human subcutaneous fat, donated by patients giving informed consent under a research tissue bank license under the Human Tissue Authority. ADSC were cultured on each scaffold, with cell viability and total collagen production assessed (AlamarBlue and Sirius red assay respectively) up to 14 days *in vitro*.

Results

Following 14 days of culture, all electrospun scaffolds demonstrated a dense surface matrix coverage on scanning electron microscopy assessment. DAPI staining shows cells growing throughout all tested scaffolds (Figure 1).

All scaffolds supported an increase in cell viability from day 7 to day 14, however the greatest increase was seen in those scaffolds containing PLA (either alone or as a copolymer with PUZ1). Furthermore, cells cultured on scaffolds of either PLA or PUZ1/PLA showed a significant four-fold increase in total collagen expression compared to that seen on Z1 or Z3 alone after 14 days of culture (Figure 2).

Figure 3 demonstrates that PPL had the greatest ultimate tensile strength (UTS) before and after seven days of cyclical dynamic distension, whereas PLA had the lowest UTS of all tested materials, despite this being in the range for healthy tissue. Polyurethane Z1 had the lowest Young's modulus, followed by polyurethane Z3 and these values remained relatively static following cyclical distension. PLA however demonstrated a significant increase in Young's modulus following distension along with PPL. The copolymers of PUZ1 and PLA failed following cyclical distension and therefore results are censored in this analysis.

Interpretation of results

PPL was the strongest material tested and became much stiffer after dynamic loading, however PPL, PLA and co-polymers of polyurethane and PLA all deformed irreversibly following 7 days of dynamic distension. Only polyurethane scaffolds successfully withstood dynamic distension. However, scaffolds containing PLA resulted in greater cell viability and total collagen production as compared to polyurethanes alone.

Concluding message

Polypropylene mesh plastically deforms following cyclical distension and polyurethanes possess more appropriate mechanical properties than polypropylene. Despite this however, cells do not seem to proliferate well on polyurethane scaffolds. Methods of fabrication can be investigated to combine polyurethanes and PLA in order to increase cell proliferation without impacting upon mechanical appropriateness.

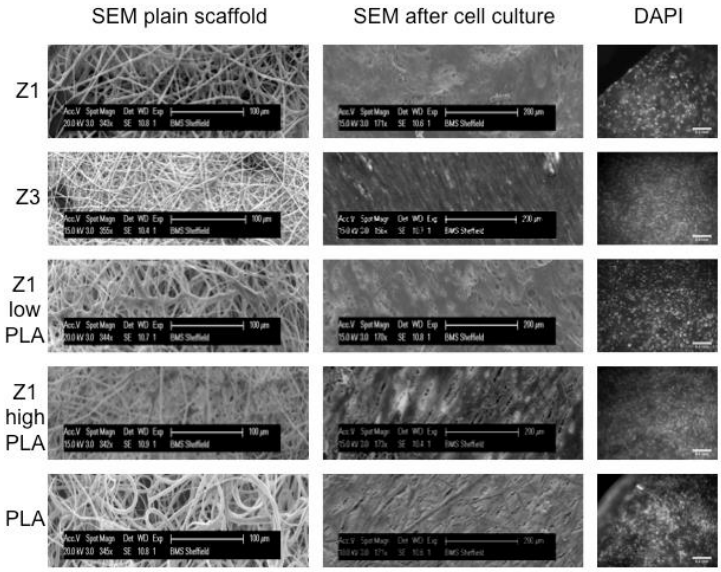

Figure 1. Scanning electron microscopy before and after culture and DAPI staining of cell nuclei

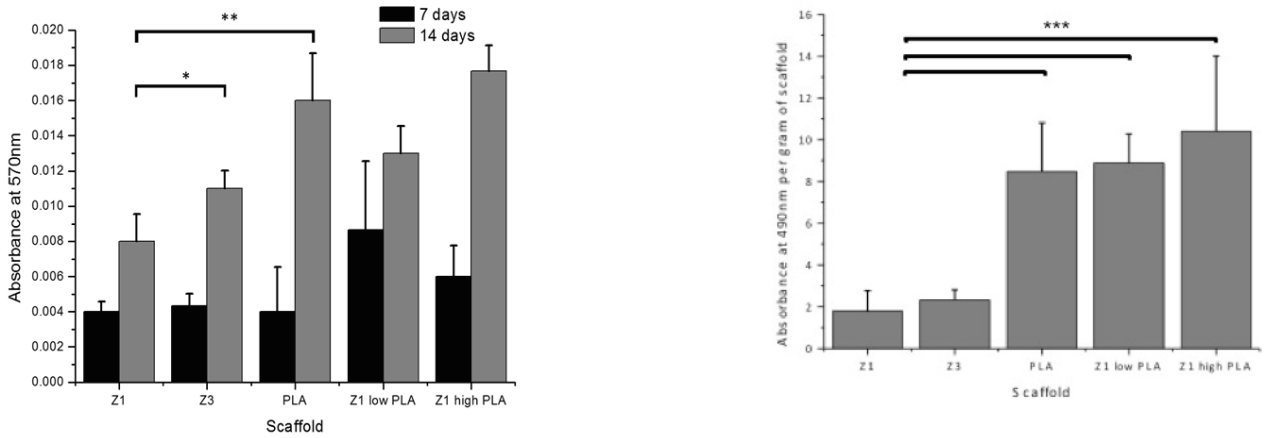

Figure 2. Viability of cells cultured on scaffolds (left) and total collagen production (right)

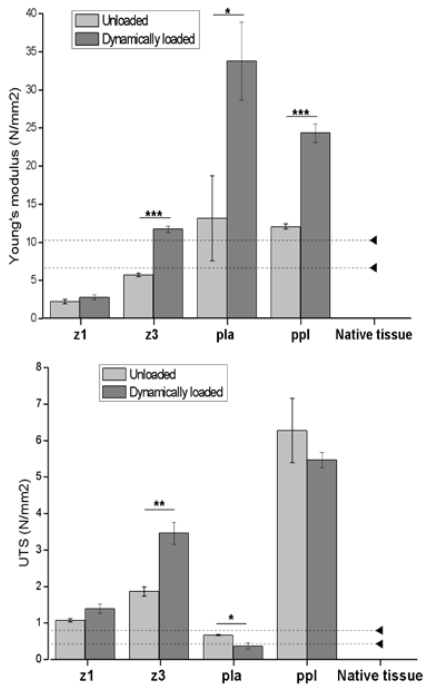

Figure 3. Ultimate tensile strength (top) and Young's modulus (bottom) of scaffolds following 7 days in static conditions versus dynamic distension.

References
1. Takanari, K., Y. Hong, R. Hashizume, et al., Abdominal wall reconstruction by a regionally distinct biocomposite of extracellular matrix digest and a biodegradable elastomer. J Tissue Eng Regen Med 2013
2. Roman Regueros, S., M. Albersen, S. Manodoro, et al., Acute in vivo response to an alternative implant for urogynecology. Biomed Res Int 2014;2014:853610
3. Lei, L., Y. Song, and R. Chen, Biomechanical properties of prolapsed vaginal tissue in pre- and postmenopausal women. Int Urogynecol J Pelvic Floor Dysfunct 2007;18:603-7

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