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THE IN VIVO RESPONSE TO IMPLANTABLE ENGINEERED REPAIR MATERIALS DESIGNED FOR PELVIC FLOOR RECONSTRUCTION

Hypothesis / aims of study

Pelvic organ prolapse (POP) and stress urinary incontinence (SUI) are common conditions that can cause significant physical, psychological and social debility for patients. Polypropylene mesh (PPL) is currently used to reinforce the surgical repair of POP and to augment sphincteric weakness and urethral hypermobility in SUI surgery. However, severe complications including erosion and infection have been demonstrated to occur in 10% of patients undergoing POP repair (1) and to a lesser extent, those undergoing mesh sling surgery for SUI. Current evidence suggests that these complications occur due to a mechanical mismatch between the rigid polymer mesh and paravaginal tissues, excessive fibrosis of the implant and a degree of chronic inflammation (2). We have therefore developed a range of degradable polymer scaffolds produced through electrospinning that demonstrate suitable mechanical properties *in vitro* and also support cell integration and growth (3). We hypothesise that these novel materials will provide a more appropriate degree of support for POP or SUI surgery and will be biocompatible, allowing tissue remodelling to occur as the material degrades. To test this hypothesis, these materials were implanted and compared to PPL in a rabbit model over a three month period to assess the host response to materials, degree of cellular proliferation and mechanical properties of the repair.

Study design, materials and methods

Synthetic, sterile electrospun scaffolds of poly-L-lactic acid (PLA) and polyurethane Z3A1 (PU) were tested in addition to commercial polyvinylidine fluoride (PVDF) and PPL meshes. Full thickness abdominal wall defects were created in New Zealand white rabbits, which were repaired using non-absorbable sutures. An onlay of repair material was then implanted prior to skin closure (Figure 1). Animals were sacrificed following 1 and 3 months of implantation. Materials and tissue were explanted, including appropriate control groups (Sham repair (suture repair only) and healthy tissue)).

Mechanical properties of samples were assessed using a ramp tensile test (Bose tensiometer) and compared to values of healthy fascia. Samples underwent histology (Haematoxylin and Eosin) to assess cell infiltration and immunohistochemistry. Appropriate antibodies used included CD31 (endothelial cells), Ram-11 (macrophages), T-lymphocytes, CD206 (M1 macrophage response), HLA-DR (M2 macrophage response and collagen III.

Results

Figure 2 demonstrates that after 30 days of implantation, use of all repair materials resulted in a greater ultimate tensile strength (UTS) of samples, PLA was the weakest, whereas PPL was the strongest. PLA had the lowest Young's modulus, followed by PU, PVDF and PPL.

By 90 days, the UTS of PLA had significantly increased, while the mechanical properties of PU remained unchanged.

PLA demonstrated the greatest host cell infiltration at both 30 and 90 days, with the material itself undergoing obvious degradation over 3 months. This material was replaced by extensive matrix components, which resembled muscle tissue. With PU, cells populated the surface of these scaffolds and there was some cellular penetration of the material by 90 days. In contrast, host cells surrounded the individual fibres of PVDF and PPL.

With respect to new tissue formation, PLA stained the greatest for CD31, HLA-DR and collagen III after both 30 and 90 days, whereas PPL and PVDF demonstrated a greater staining for Ram-11 and CD206 (Figure 3).

Interpretation of results

Tissues repaired by PLA become stronger despite the material itself undergoing degradation and becoming replaced with cells and collagen. The macrophage response to PLA was an M2 response, which is indicative of constructive remodelling. PPL and PVDF however demonstrated evidence of an ongoing M1 inflammatory response. The mechanical properties of PU would make this material ideal for implantation due to its suitable strength and elasticity, however, at 90 days, cells do not infiltrate this material well.

Concluding message

We have demonstrated that polypropylene mesh remains strong and rigid following implantation. However, use of this material in these animal experiments showed a poor host response, which may explain the chronic inflammation seen with this non-degradable material clinically.

PLA in contrast shows evidence of constructive remodelling as the material degrades and does not lead to a sustained inflammatory response becoming well integrated into the host tissues. This material may therefore offer a potential alternative to PPL for reconstruction of the pelvic floor. PU was mid-way between the two-offering reasonable strength and elasticity but relatively poor tissue integration.

Figures

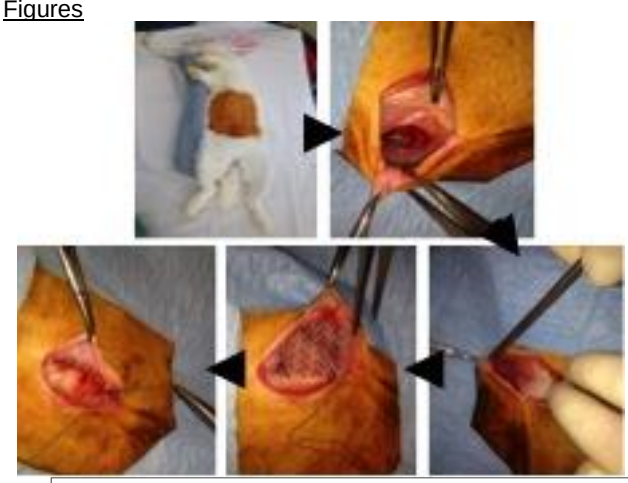

Figure 1. Schematic of implantation steps

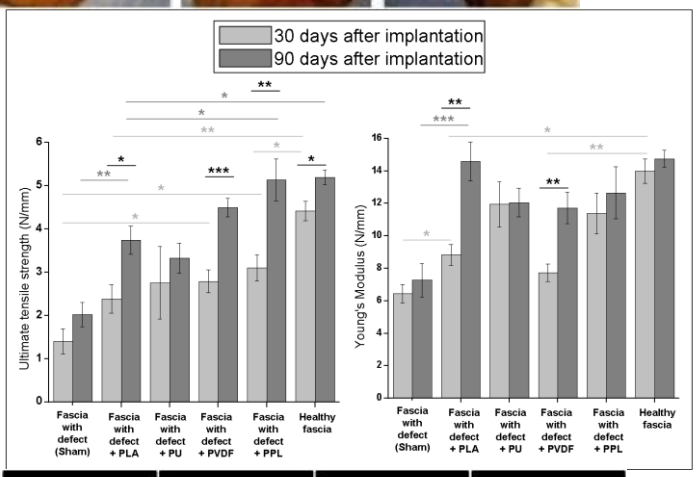

Figure 2. Biomechanical properties of explanted samples

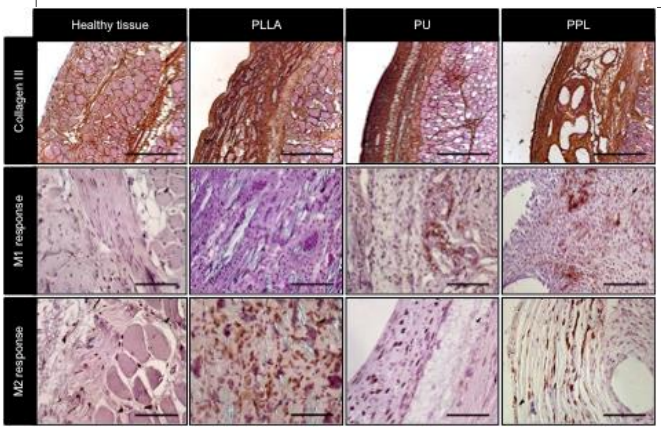

Figure 3. Immunohistochemistry of tested samples

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Disclosures

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