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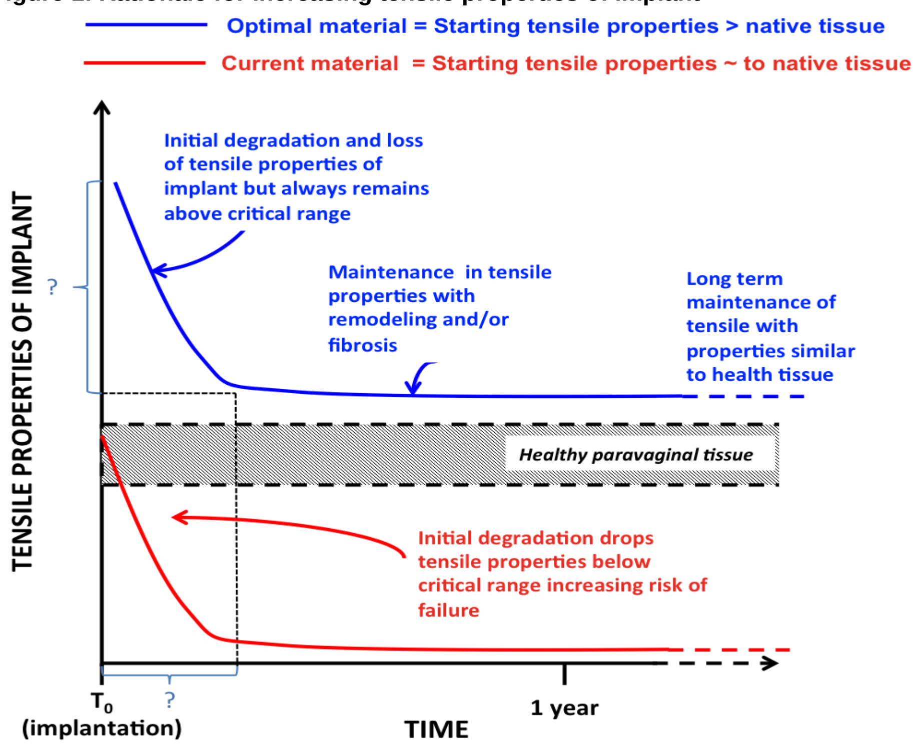
DESIGNING A NOVEL TISSUE INDUCTIVE BIO-ABSORBABLE IMPLANT FOR PELVIC FLOOR REPAIR: AN ASSESSMENT OF TENSILE AND SURGICAL HANDLING PROPERTIES VERSUS POLYPROPYLENE MESH AND PORCINE SMALL INTESTINE SUBMUCOSA

<u>Hypothesis / aims of study</u>

Polypropylene mesh is associated with serious complications when used in pelvic floor reconstructive surgery and is becoming unavailable for use in North America highlighting the growing need for an alternative repair material. Previously we have shown that a scaffold composed of polylactic acid, an FDA approved biodegradable polymer, is a suitable substrate for the attachment and growth of fibroblasts and induces a favourable host response, including collagen ingrowth, at 7 days when implanted in rats (1). However the material is weaker than desired in terms of tensile properties (see figure 1). The aims of this study were to (1) improve upon the strength of the scaffold (2) perform an evaluation of handling properties in comparison to a biological implant (porcine small intestine submucosa, SIS) and polypropylene mesh (PPL).

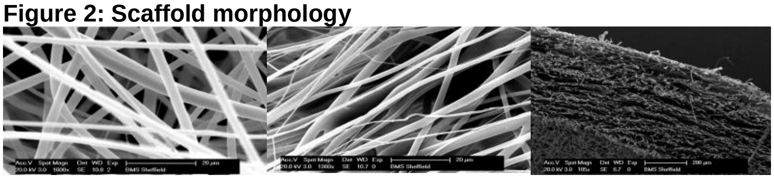
Figure 1: Rationale for increasing tensile properties of implant



<u>Study design, materials and methods</u>

3 designs of implant were assembled by lamination of sheets of electrospun PLA scaffolds to 0.5mm thickness composed of (1) 4 layers of randomly orientated fibre scaffolds (2) 4 layers of aligned fibre scaffolds (3) Composite: 2 layers of randomly oriented (outer) and 2 layers of aligned scaffolds (inner). Fibre orientation was checked using electron microscopy (figure 2). Layers were adhered using heat annealing in a dry oven at 60^{o}. Uniaxial tensiometry was performed on the 3 implant designs with an of assessment suture retention strength, tear resistance and ball burst strength in comparison to porcine small intestine submucosa (4 ply) and polypropylene mesh. All implants were tested after ten minutes of wetting in saline ensuring all layers were moistened.

Figure 2: Scaffold morphology



(a) random fibre scaffold (b) aligned fibre scaffold (c) Crosssection 4-ply scaffold

Results
The results of tensile and surgical property testing are summarised in Figure 3.

Figure 3:Tensile and surgical handling properties of implants (n=9+/-SEM)

Test	**4-ply random**	**4-ply aligned**	**4-ply composite**	**SIS**	**PPL**	**Native tissue**
Ultimate tensile strength Mpa(sem)	1.9 (0.1)	4.8 (0.5)	5.7 (0.6)	12.5 (0.6)	5.6 (0.5)	0.42-0.79
Elastic modulus Mpa(sem)	13.3 (1.6)	92.6 (9.5)	52.9 (14.2)	15.8 (3.5)	5.4(0.3)	6.65-10.26
Tear resistance Mpa(sem)	0.9 (0.10)	0.2 (0.03)	0.41 (0.03)	1.89 (0.19)	0.56 (0.18)	-
Suture retention strength Mpa(sem)	1.45(0.14)	0.66(0.10)	0.93 (0.10)	1.29 (0.38)	3.45 (0.66)	-

Interpretation of results
Introducing aligned fibres significantly increases both the strength and elastic modulus of implants. A composite material composed of both aligned and random fibres achieved the optimal strength (equivalent to PPL and greater than the normal range of healthy paravaginal tissue) whilst avoiding excessive stiffness of aligned implants. In terms of resistance to tearing and suture retention strength a random fibre orientation implant was optimal, followed by the composite implant.

Concluding message
We have designed a novel 4-ply implant with improved strength. Taking the results of tensile properties and surgical handling properties into account, a composite implant may provide the optimal balance, This material can potentially be preseeded with autologous cells or stem cells before implantation or alternatively fabricated with bioactive factors (eg oestrogen, heparin) to increase tissue in growth and neovascularisation. Further in vivo studies will determine how much tensile properties decrease after implantation and at what rate as well as the nature of the long term response (remodelling and/or fibrosis) before a first-in-woman clinical study.

References

1. Roman S, Osman N, Mangera A, Bullock AJ, Chapple C, MacNeil S. In vivo assessment of the acute host response against a novel tissue engineered to treat stress urinary incontinence and pelvic organ prolapse. Poster 109. European Association of Urology Annual meeting Milan March 2013

Disclosures

Funding: Robert Luff Foundation Rosetrees Trust **Clinical Trial:** No **Subjects:** NONE