Rational engineering and design 3D printed meshes with biofunctional assessment for Pelvic Reconstructive Surgery: A pre-clinical assessment

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Background

Pelvic organ prolapse (POP) is a debilitating urogynaecological condition caused by the descent of the pelvic organs, namely, the uterus, bladder or bowel, affecting more than 50% of women at the post-menopausal stage for whom surgical reconstruction is the only treatment option. In clinics, non-degradable monolayer-knitted meshes such as polypropylene (PP) meshes have widespread applications for treating POP.

However, given the adverse events including mesh erosion and pain, non-degradable meshes have been banned from their clinical applications restoring bladder/bowel functions by the regulatory authorities in several countries namely Australia, New Zealand, USA and UK.

Aim

- Mesh-related adverse events are associated with the in vivo deformation of meshes represented by pore collapsing that leads to tissue-degenerative foreign body reactions, thereby chronic inflammation.
- We developed degradable surgical implants using the state-of-the-art 3D printing process called melt electrowriting (MEW) printing.
- We investigated the impact of distinct mesh geometries and porosities to attribute compatible mechanical tensile strength leading to tissue regenerative cellular events, thereby, inducing favourable foreign body response.

Method

- Develop rational design of degradable meshes using 3D Printing
- Investigate biophysical interaction in vitro and foreign body response in vivo
- 3D Printing parameters were optimised at melting temperature 100°C, voltage (V): 5 KV, nozzle to workspace: ~10 mm, extrusion pressure (P): 8 KPa and printing speed at 10 mm/s.

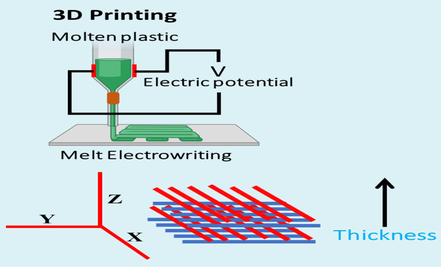


Figure 1. Melt electrowriting (MEW) printing for the generation of customisable MEW degradable mesh.

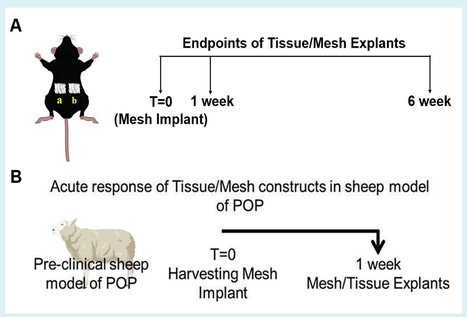


Figure 2. Experimental timeline of preclinical **A)** mouse and **B)** sheep models of vaginal POP to assess the foreign body response at 1 and 6 weeks.

Results

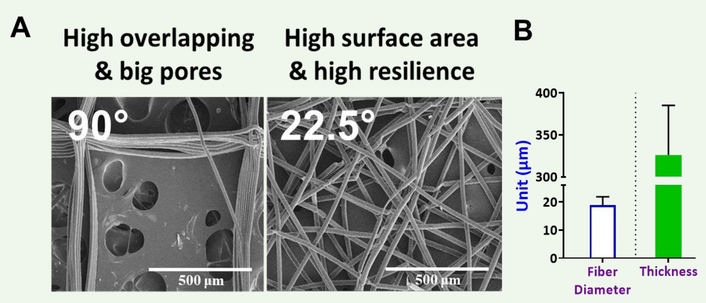


Figure 3. A) Fabrication of MEW meshes with an array of geometries and biophysical characterization of hierarchical MEW meshes showing SEM images of mesh morphologies with fibre deposition, open pores, and MEW surface at 90° and 22.5° and **B)** MEW fibre diameter and thickness of 50 layers. Data are mean ± SD for n = 10 meshes/group.

- Lower angular meshes have mechanical resilience sustaining structural integrity under tensile stretch.

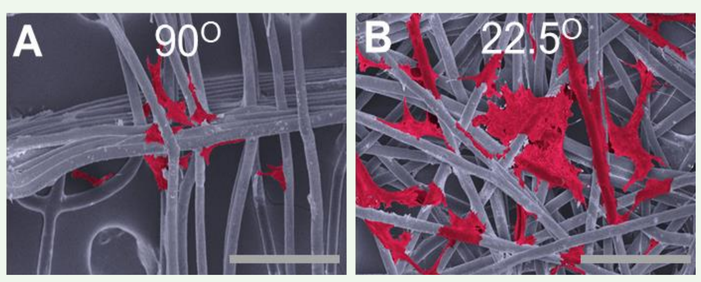
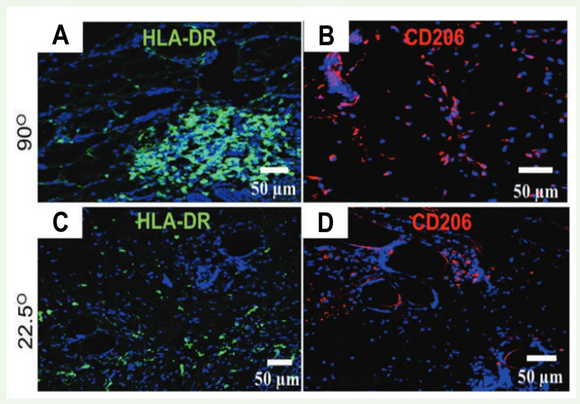


Figure 5. SEM image of vaginal fibroblast attachment (cell cytoskeleton; red colour, white scale bars are 500 µm), on 90° and 22.5° MEW meshes.



- 22.5° angular meshes showed the greatest recruitment of anti-inflammatory CD206+ macrophages at 1 week followed by immune suppression at 6 weeks in vivo leading to better tissue integration.

Mechanical strength & tissue response in vitro & in vivo

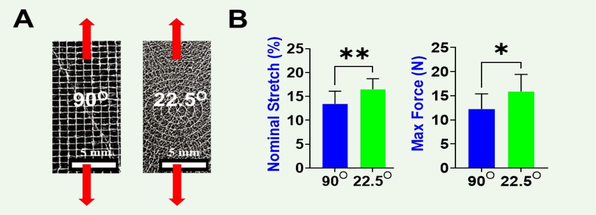


Figure 4. A) Biophysical characterization of hierarchical MEW meshes showing mesh architecture/gross morphologies at 90° and 22.5°. **B)** Mechanical characterization of MEW meshes under tensile loading showing nominal stress and maximum force at rupture. Data are mean ± SD, n= 10 samples/group. Statistical analysis are parametric T-test (*p<0.05; **p<0.001).

- **Morphologic study by electron microscopy reveals the fibre diameter to be 18.86 ± 2.16 µm.**

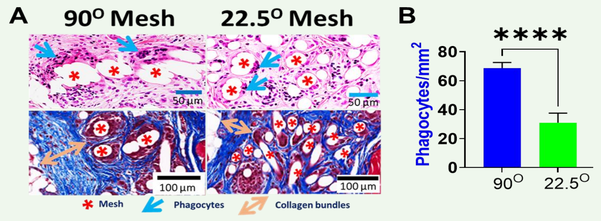


Figure 6. Preclinical assessment of the acute response of MEW meshes in a preclinical mouse model with vaginal POP after 1 week **A)** acute tissue response showing the presence of phagocytes (blue arrows) and neo-collagen deposition (blue color) around 90° and 22.5° meshes fibres (red asterisks) and **B)** quantification of phagocytes. Data are mean ± SD, n= 10 samples/group. Statistical analysis are parametric T-test (****p<0.0001).

Figure 7. Preclinical assessment of the acute response of MEW meshes in a preclinical sheep model with vaginal POP after 1-week, acute tissue response **A, C)** showing HLA-DR expression for pro-inflammatory M1 macrophages (in green) and **B, D)** showing CD206 expression of anti-inflammatory M2 macrophages (in red) around 90° and 22.5° meshes.

Conclusion

- We have developed a guideline for functional mesh-fabrication for POP application to improve the design and fabrication of next-generation vaginal implants for pelvic reconstructive surgery.
- The pattern and geometry of the layered MEW implants influence the foreign body response.
- 22.5° angular meshes have mechanical resilience, show better vaginal fibroblast attachment in vitro and improved tissue integration in preclinical mouse and ovine models compared to 90° meshes.

References

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