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Research paper

Porcine extracellular matrix scaffolds in reconstructive urology: An *ex vivo* comparative study of their biomechanical properties

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ABSTRACT

Functional reconstruction of the human urinary bladder has been attempted by replacing defective bladder tissue with tissue-engineered xenogenic extracellular matrix (ECM) scaffolds. However, experimental studies that demonstrate the effects of implanted ECMs on important biomechanical properties such as total bladder capacity (TBC) and compliance (C) are lacking. In the current study, the effects of ECM scaffold surface area (SA) on TBC and C was assessed, *ex vivo*, in an ovine model ($n = 5$). TBC and C were measured at pressures (P) of 5, 10, 15 and 20 mm Hg prior to performing a 3 × 3 cm (9 cm^2) partial cystectomy defect. Equal-sized 3 × 3 cm (9 cm^2) and larger 6 × 6 cm (36 cm^2) urinary bladder matrix (UBM) scaffolds of porcine origin replaced the 3 × 3 cm cystectomy defect, and TBC and C were re-recorded for comparative analysis. The results showed that TBC decreased by 39.6%±0.005% (122.9 ml ± 15 ml, $p < 0.05$) and C by 38.9% ± 0.51%, ($\Delta P = 0$–5 mm Hg, $p < 0.05$) in ovine bladders reconstructed with 3 × 3 cm UBM scaffolds compared to their native values. It was also found that TBC increased by 25.6 ± 0.64% (64.2 ml ± 8.8 ml, $p > 0.05$) and C by 24.5 ± 0.43% ($\Delta P = 0$–5 mm Hg, $p > 0.05$) in the 6 × 6 cm UBM scaffold group compared to the 3 × 3 cm UBM scaffold group; however, these values were not statistically significant. The present work demonstrates that a fourfold increase in ECM scaffold SA relative to its intended defect does not lead to a significant improvement in TBC and C values.

1. Introduction

The urinary bladder can be affected by multiple pathological processes in which autogenous donor gastrointestinal tissue may be applicable for treatment purposes. However, the presence of mucus-secreting epithelium is associated with long-term complications such as recurrent calculus formation, resistant urinary tract infections and metabolic abnormalities (Flood et al., 1995). These persistent and debilitating complications have led researchers to seek an alternative donor material that may be more suitable for reconstructive purposes. Synthetic materials such as

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tetrafluoroethylene (Teflon®), silicone, polyvinyl sponge, vicryl matrices and collagen matrices have been used in experimental and clinical settings (Bono and De Gresti, 1966; Rohrmann et al., 1996). Unfortunately, these materials have failed on account of structural, functional and biocompatibility problems, and gastrointestinal tissue has remained the gold standard since tissue transplants were first introduced in 1917 (Davis et al., 2010; Neuhof, 1917).

More recently, tissue-engineered extracellular matrices (ECMs) have shown early promise as suitable biomaterials for urological reconstructive purposes (Badylak, 2004). ECMs are decellularised 'off-the-shelf' biological scaffolds usually derived from xenogenic sources (Shaikh et al., 2010). Urinary bladder matrix (UBM) is an ECM of porcine origin and it possesses a number of noteworthy clinical advantages over autogenous gastrointestinal tissue as a potential replacement scaffold. After implantation, UBM induces a host derived tissue remodelling response while undergoing simultaneous degradation and excretion processes. Furthermore, as UBM is completely inert due to its acellular nature, post-operative inflammatory reactions are uncommon and are usually avoided (Gilbert et al., 2007).

Potential disadvantages of ECMs in a urological setting are their comparatively poor distensibility and viscoelasticity. Implantation of a biomechanically limited ECM scaffold into highly viscoelastic bladder tissue may lead to poor functional outcomes, as important biomechanical parameters such as total bladder capacity (TBC) and compliance (C) are adversely affected (Zhang et al., 2006). An increase in ECM scaffold surface area (SA) relative to its intended defect may prevent such complications, as this principle is highly effective when bladder augmentation is performed with autogenous tissue. Large increases in TBC and C can be achieved by applying large segments of autogenous gastrointestinal tissue to poorly compliant, contracted reservoirs (Rink and Mitchell, 1990). As there are no published studies investigating the effects of tissue-engineered ECM scaffolds on these important biomechanical properties, specific objectives in the current study were to assess, *ex vivo*, the effects of implanted ECMs on TBC and C. We also aimed to determine whether an increase in ECM scaffold SA can lead to improved TBC and C values.

2. Materials and methods

2.1. Overview of experimental design

The urinary bladders of seven female lambs were sourced from an abattoir (Gaelic Meats, Patrickswell, Limerick, Ireland) immediately after euthanasia. Porcine UBM was received from the McGowan Institute of Regenerative Medicine, University of Pittsburgh, and all other materials were obtained from CABER (Centre for Applied Biomedical Engineering Research, Limerick, Ireland) unless indicated. Two bladders were used for comparative biomechanical tensile testing purposes and the remaining five bladders were used to assess, *ex vivo*, the effect of implanted UBM scaffolds on TBC and C. The primary endpoint of the study was to compare TBC and C of native bladder tissue with those of urinary bladders reconstructed with UBM scaffolds.

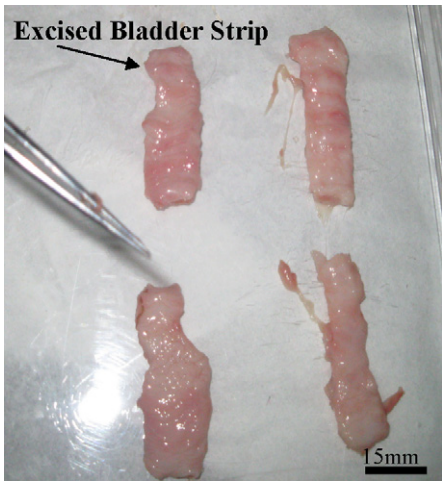

Fig. 1 – Excised circumferential ovine bladder strips. The distal and proximal ends of each strip were clamped in a custom-fabricated tensile tester with a distance of 25 mm between both grips and an incremental load (N) was applied.

Our secondary endpoint assessed whether implanting ECM scaffolds with an SA greater than their intended defect improved TBC and C.

2.2. Biomechanical testing

Longitudinal strips ($n = 6$) of bladder tissue were prepared for tensile testing purposes by performing two parallel circumferential incisions, 15 mm apart, around each empty bladder (Fig. 1). All strips of prepared bladder tissue were matched for length width and thickness (60 mm × 15 mm × 4 mm) and maintained in tissue transport medium (Dulbecco's modified medium, Invitrogen, Ireland). Strips of 4-ply UBM (60 mm × 10 mm × 0.24 mm) were prepared for comparative analysis ($n = 6$). Tensile testing was performed by clamping each prepared specimen into a custom fabricated tensile tester with a 50 N load cell (Mecmesin®, Newton House, Spring Copse Business Park, Slinfold, West Sussex, United Kingdom). The bladder tissue and UBM scaffolds were clamped at a distance of 25 mm and 40 mm respectively between both grips. An incremental extension rate of 1 mm/s was applied to each clamped tensile specimen and the magnitude of the load (N) was measured in newtons.

2.3. Measurement of native bladder compliance

The urinary bladder and both ureters of five female lambs, all 7 months old, were removed intact by blunt and fine dissection techniques and transported on ice in tissue transport medium (Dulbecco's modified medium, Invitrogen, Ireland) to the laboratory immediately after euthanasia (Fig. 2). Each urinary bladder was individually connected to a custom-built 'pressure/volume' rig after all intravesical contents were emptied and both ureters were ligated (Fig. 3). Oxygen was then fed into a fluid-filled container at a constant rate via an air line. Constant infusion of oxygen resulted in an increase in hydrostatic pressure within the vessel