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The effects of stent interaction on porcine urinary bladder matrix employed as stent-graft materials

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ABSTRACT

Deployment of stent-grafts, derived from synthetic biomaterials, is an established minimally invasive approach for effectively treating abdominal aortic aneurysms (AAAs). However, a notable disadvantage associated with this surgical technique is migration of the deployed stent-graft due to poor biocompatibility and inadequate integration in vivo. Recently, tissue-engineered extracellular matrices (ECMs) have shown early promise as integrating stabilisation collars in this setting due to their ability to induce a constructive tissue remodelling response after in vivo implantation. In the present study the effects of stent loading on an ECM's mechanical properties were investigated by characterising the compression and loading effects of endovascular stents on porcine urinary bladder matrix (UBM) scaffolds. Results demonstrated that the maximum stress was induced when the stent force was 8-times higher than a standard commercially available stent-graft and this represented about 20% of the failure strength of the UBM material. In addition, the influence of stent shape was also investigated. Findings demonstrated that the stress induced was higher for circular stents at low forces and a higher stress was induced on square stents when increased force was applied. Our findings demonstrate that porcine UBM possesses sufficient mechanical strength to withstand the compression and loading effects of commercially available stent-grafts in the setting of endovascular aneurysm repair.

1. Introduction

Over the last number of decades, researchers have investigated the effectiveness of stents and stent-grafts for the treatment of cardiovascular disease, with particular emphasis on optimising stent design and graft materials (Lally et al., 2005; Lally et al., 2004). Notably, the concept of applying cardiovascular stent-grafts in combination with tissue-engineered extracellular matrix (ECM) scaffolds has only recently evolved. ECMs are biodegradable decellularised biomaterials that induce a constructive tissue remodelling and regenerative response after in vivo implantation (Badylak et al., 2011, 2012; He and Callanan, 2012; Turner and Badylak, 2012).

Small intestinal submucosa (SIS) and urinary bladder matrix (UBM) are 2 porcine derived ECMs that have demonstrated potential for tissue regeneration in stented environments (Hoppo et al., 2012; Ishii et al., 2005; Nakata et al., 2003; Niyyati et al., 2005; Schoder et al., 2004; Yamada et al., 2001; Yavuz et al., 2006). Studies investigating SIS 'stent-grafts' have demonstrated incorporation of the stent-graft into aortic tissue after deployment (Noishiki et al., 2001; Schoder et al., 2004; Yamada et al., 2001; Yavuz et al., 2006). Over time the ECM was replaced by a dense neointima with partial re-endothelisation of the aortic wall. SIS has also demonstrated early promise for the prevention of endoleaks in endovascular aneurysm repair (EVAR) and in grafting peripheral vessels (Noishiki et al., 2001; Schoder et al., 2004; Ishii et al., 2005; Nakata et al., 2003; Niyyati et al., 2005). More recently, UBM has demonstrated an advantage over SIS in the setting of stent-graft environments (Hoppo et al., 2012) as it retains an intact basement membrane and may therefore have the potential for greater re-endothelialisation of host vessels (Brown et al., 2006). In addition in recent in vitro studies UBM has demonstrated potential as a stent graft collar, highlighting that it may reduce the frequency of migration and endoleaks (Callanan et al., in press; Davis et al., 2013a).

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Although the biological features of ECMs in stent-graft environments are well characterised; there is a paucity of data on their mechanical properties. In particular, the effects of stent loading on an ECM biomaterial is poorly characterised with regard to alterations to the scaffold's mechanical properties and disruption to its architecture. In the present study, the main objectives were to investigate and characterise compression and loading effects of endovascular stents on porcine UBM scaffolds.

2. Methods

2.1. Preparation of ECM material

2.1.1. Preparation of porcine urinary bladder matrix (UBM)

Preparation of UBM has previously been described (Callanan et al., 2012; Davis et al., 2011). Briefly, porcine urinary bladders were harvested from pigs (110–130 kg). The bladders were rinsed repetitively in distilled water (dH20) and the specimens were divided along one side to form a sheet. The tunica serosa, tunica muscularis externa, tunica submucosa and the muscularis mucosa were manually removed by manual delamination while preserving an intact basement membrane and lamina propria. The decellularisation process was completed by soaking the matrix in buffered saline (pH 7.4) to promote cell lysis and placing it in peracetic acid/4% ethanol for 2 h on a shaking device. The success of the decellularisation technique was confirmed by histological staining with haematoxylin and eosin (H&E) and with 4, 6-diamidino-2-phenylindole (DAPI) staining.

2.1.2. Manufacture of multi-layered urinary bladder matrix (UBM)

The manufacturing process for multi-layered UBM has been previously described (Callanan et al., 2012). In brief, prepared specimens of single-ply UBM were compressed between constructed 'mesh plates' lined with gauze and covered with a vacuum film. Compressed UBM was then connected indirectly to a vacuum pump via two condensation cylinders. Moisture was extracted from UBM into the cylinders via the vacuum pump and 2 multilayered UBM scaffolds were constructed with this preparation technique. Vacuum extraction of moisture occurred at a negative pressure of −28InHg (−711 mmHg) over durations of 8–10 h. After undergoing compression and moisture extraction protocols, multilayered lyophilised UBM scaffolds were sterilised by exposure to ethylene oxide (ETO) for 24 h. In the present study, 10 multilayered (4-layered) devices were manufactured from 40 sheets of decellularised UBM.

2.2. UBM stent interaction testing

2.2.1. Radial force testing of a commercial stent graft stent-ring

The stent radial force was evaluated from a commercial stent-graft (Medtronic®). An individual 'stent-ring' was removed from the stent-graft and it was placed into a compression test device. The compression test device was constructed to evaluate radial force from stent devices by applying equally distributed radial compression during the testing protocol. The test involved loading and unloading of the stent device to evaluate its mechanical properties. A total of 3 tests were carried out on each stent-ring ($n=3$).

2.2.2. Experimentally modelling tissue compliance

Analysis of stent anchorage to the ECM collar on the arterial wall was performed with a stent ring (Medtronic®). The stent was deployed into freshly isolated porcine aorta for a period of 24 h. Analysis was conducted at 37 °C in

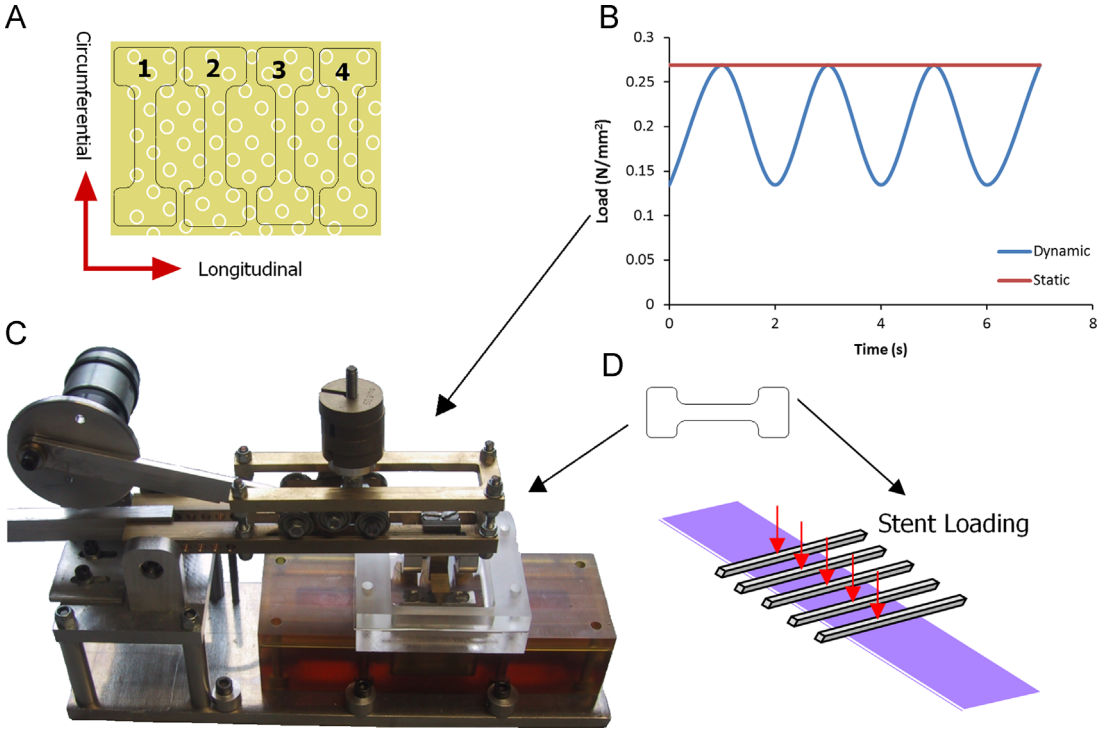

Fig. 1. (A) The sample cutting arrangement from the UBM sheets, with sample 1 – a control, sample 2 – a static loaded stent, sample 3 – a control and sample 4 – a oscillating loading stent, (B) the loading regime applied (load C – 8 ×) to static and dynamically loaded specimens, (C) the experimental test rig used on the UBM samples under oscillating load conditions, and (D) the stent loading configuration on the dog-bone UBM samples.

Table 1
Loading regime developed by the Medtronic® stent-graft during experimental testing. Loading regimes applied during experimental and numerical testing correspond to A, B, and C which represent 2 ×, 6 × and 8 × respectively of the loaded developed by the Medtronic®.

Medtronic stent (force/area)	Load regime	Equivalent max load	Experimental static load (force/area, N/mm^2)	Experimental dynamic load, (force/area, N/mm^2)
X=0.033–0.043 N/mm^2 (0.033–0.043 MN/m^2)	A	≈2 ×	0.073	0.033–0.073
	B	≈6 ×	0.196	0.098–0.196
	C	≈8 ×	0.269	0.1345–0.269