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Mechanical strength vs. degradation of a biologically-derived surgical mesh over time in a rodent full thickness abdominal wall defect

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ABSTRACT

The use of synthetic surgical mesh materials has been shown to decrease the incidence of hernia recurrence, but can be associated with undesirable effects such as infection, chronic discomfort, and adhesion to viscera. Surgical meshes composed of extracellular matrix (i.e., biologically-derived mesh) are an alternative to synthetic meshes and can reduce some of these undesirable effects but are less frequently used due to greater cost and perceived inadequate strength as the mesh material degrades and is replaced by host tissue. The present study assessed the temporal association between mechanical properties and degradation of biologic mesh composed of urinary bladder matrix (UBM) in a rodent model of full thickness abdominal wall defect. Mesh degradation was evaluated for non-chemically crosslinked scaffolds with the use of ^{14}C-radiolabeled UBM. UBM biologic mesh was 50% degraded by 26 days and was completely degraded by 90 days. The mechanical properties of the UBM biologic mesh showed a rapid initial decrease in strength and modulus that was not proportionately associated with its degradation as measured by ^{14}C. The loss of strength and modulus was followed by a gradual increase in these values that was associated with the deposition of new, host derived connective tissue. The strength and modulus values were comparable to or greater than those of the native abdominal wall at all time points.

1. Introduction

Approximately 920,000 hernia repair procedures are conducted every year in the United States alone, of which an estimated 360,000 are ventral hernia repairs [1]. Use of surgical mesh to augment the repair is associated with a decreased incidence of recurrence compared to primary repair [2–4]. A variety of surgical mesh materials are approved or allowed for ventral hernia repair, however the most commonly used surgical meshes are composed of synthetic, non-degradable materials such as polypropylene and expanded polytetrafluorethylene [5]. Surgical mesh devices composed of naturally occurring materials (i.e., biologically-derived surgical mesh), such as those composed of extracellular matrix (ECM) derived from a variety of tissues including dermis, small intestine or urinary bladder are also used for augmentation of hernia repair [6]. These bioscaffolds provide an alternative to synthetic mesh but are less frequently used due to higher cost [7,8], lower mechanical strength when compared to polypropylene and concern for the risk of recurrent hernia during the postoperative period in which the mesh is degraded and replaced by host tissue. However, clinical trials suggest that biologically-derived surgical meshes are more resistant to infection and have equivalent hernia recurrence rates when compared to synthetic mesh [9].

Although ECM biologically-derived surgical meshes are stronger than the native abdominal wall at the time of implantation [6,10], there have been few quantitative studies to determine the temporal changes in their mechanical strength following implantation and even fewer studies that correlate bioscaffold degradation/remodeling with changes in mechanical strength [11–13]. The objective of the present study was to determine via qualitative and quantitative

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methods the degradation over time of chemically crosslinked and non-crosslinked ECM surgical meshes composed of urinary bladder matrix (UBM), and correlate mesh degradation with the temporal changes in mechanical properties when used to repair a full thickness abdominal wall defect in a rat model.

2. Materials and methods

2.1. Experimental overview

All procedures involving ^{14}C were approved by the University of Pittsburgh Radiation Safety Committee and all animal procedures were approved by the Institutional Animal Care and Use Committee and complied with the National Institutes of Health guidelines for the Care and Use of Laboratory Animals.

Bilateral ventrolateral full thickness abdominal wall defects measuring 1.5 × 1.5 cm in size were created in female Sprague Dawley rats. The defects were repaired with an inlay graft of a 6-layer sheet of urinary bladder matrix (UBM). The devices used were: a commercially available 6-layer UBM device (MatriStem®, ACell Inc, Columbia MD), a chemically crosslinked version of the MatriStem® scaffold, chemically crosslinked and non-crosslinked 6-layer UBM devices produced in the laboratory (UBM and XL-UBM), and a 6-layer ^{14}C-proline labeled-UBM device (^{14}C-UBM). The mechanical properties were compared against those of the native abdominal wall muscle.

The grafts were explanted at 7, 14, 21, 90 and 180 days following surgery. The mechanical properties of the explanted graft materials were assessed by uniaxial tensile testing (N = 6 per time point). Histomorphologic evaluation was performed for qualitative assessment of scaffold degradation and remodeling (N = 6 per time point). Quantitative assessment of scaffold degradation was assessed for the ^{14}C-proline labeled UBM explants (N = 2 per time point). The explanted radioactive grafts were snap frozen in liquid nitrogen and the residual ^{14}C was determined by accelerator mass spectrometry (AMS).

2.2. Preparation of ^{14}C labeled porcine tissue

The method for producing ^{14}C-labeled porcine tissue has been previously described [14–16]. Beginning at three weeks of age, piglets were given weekly intravenous injections (ear vein) of 10–30 μCi (dependent on weight) of ^{14}C-labeled proline (Amersham Life Science, Piscataway, NJ) until reaching 200 lbs. at approximately 5–6 months of age. The animals were sacrificed and tissues collected for the subsequent preparation of biologically-derived surgical mesh materials. In general, these tissues showed greater than 10^3 increase in ^{14}C content over non-labeled tissue [14].

2.3. Preparation of UBM

UBM was prepared from ^{14}C-labeled and non-radiolabeled porcine bladders as previously described [17,18]. The tunica serosa, tunica muscularis and tunica submucosa were mechanically removed, leaving the basement membrane and tunica lamina propria intact (termed UBM). The UBM was decellularized and disinfected with a 0.1% peracetic acid/4% ethanol solution with mechanical shaking and then rinsed several times in phosphate buffered saline and deionized water. Six sheets of the resulting acellular matrix were laminated in a vacuum press maintaining the luminal-abluminal orientation of each layer. Crosslinked versions of these scaffolds (XL-UBM) were obtained by incubating the multilaminate devices in 10 mM N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (Sigma Aldrich, St Louis MO) in 90% acetone/10% deionized water (v/v) for 24 h. For comparison, commercially available 6-layer UBM devices (MatriStem® Surgical Matrix PSMX, ACell Inc., Columbia MD) and a chemically cross-linked version of these MatriStem® devices (XL-MatriStem®) were also implanted. The preparation of the laboratory devices and the commercial devices was conducted by identical methods.

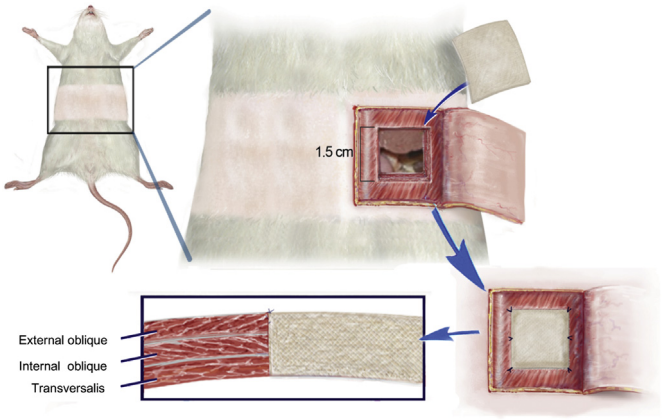

Fig. 1. Defect creation and repair. Full thickness abdominal wall defect of 1.5 × 1.5 cms repaired with inlay implantation of a 6-layered device of porcine urinary bladder matrix. The device was held in place with six sutures.

All devices were cut into 1.5 × 1.5 cm squares and individually packaged. Commercial devices were terminally sterilized by the manufacturer with electron beam irradiation and were cut and repackaged under sterile conditions. Laboratory made devices were sterilized by ethylene oxide, after packaging (16 h cycle at 50 °C in a Series 3plus EOGas Sterilizer, Anderson Sterilizers, Inc., Haw River, NC).

2.4. Surgical procedure

One hundred and thirty female, 6–8 week old Sprague Dawley rats were used in this study. Each animal had bilateral ventrolateral full thickness abdominal wall defects created that measured 1.5 × 1.5 cm in size. This defect size matched the dimensions of the devices that were implanted (Fig. 1) [19,20]. Devices were created from these five different materials: UBM, XL-UBM, MatriStem®, XL-MatriStem® and ^{14}C-UBM. The devices were hydrated for 30 min in sterile saline solution and then implanted as an inlay graft, then sutured in place with 4-0 prolene (Ethicon, Somerville, NJ) suture. Subgroups of the animals were sacrificed at 5 different time points: 7,14,21,90 and 180 days. Fifty percent of the non-radiolabeled devices were used for uniaxial tensile testing (N = 6 devices) and the remaining 50% used for histomorphologic analysis (N = 6 devices). ^{14}C –labeled devices were used for AMS analysis (N = 2 devices).

2.5. Uniaxial tensile testing

Determination of uniaxial mechanical strength was performed following ASTM standard D882-12 [21]. All testing was performed on the Instron 3340 series mechanical testing system (MTS® Eden Prairie, MN), fitted with a 100 N load cell, and 100 kN vice grips. A layer of 200 grit sand paper was placed between the grips and the samples to prevent the sample from slipping within the grips. The explanted tissue was defined by the 1.5 × 1.5 cm^2 area of tissue delineated by the implantation sutures and the grips were placed outside of the device boundaries in the native abdominal wall