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REPAIR OF ABDOMINAL MUSCLE DEFECTS WITH IMPLANTS COMPOSED OF XENOGENIC FETAL COLLAGEN
LONG TERM (15 MONTH) IN VIVO EVALUATION OF IMPLANT RECONSTITUTION AND REMODELING

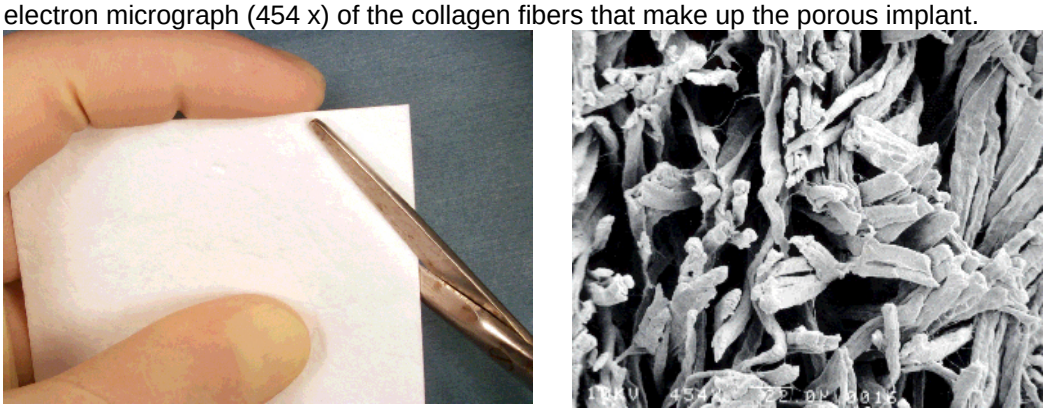
Hypothesis / aims of study

Surgeries for pelvic reconstruction and urinary incontinence increasingly use autologous, allogenic, or synthetic grafts to provide adequate and durable repairs. Autologous grafts may lead to increased morbidity and operative time due to harvesting and may not be available in the dimensions necessary for operative repair. Episodic shortages of cadaveric grafts have limited their use. A potentially serious complication when using synthetic materials is graft erosion. Xenografts may address these issues in that they are readily available and their mechanical properties (stiffness) are comparable to the contacting tissues. Host incorporation and subsequent remodeling of autologous and allogenic collagen implants remains an ideal to which xenogenic collagen implants can be compared.

We report on an in vivo response to a novel, porous xenogenic implant, Cytrix Soft Tissue Repair Matrix (TEI Biosciences, Boston MA, USA) (Figure 1). This collagen biomembrane is derived from fetal bovine dermis that is dissected of over- and underlying tissues and chemically processed to remove cells, lipids, and carbohydrates as well to inactivate any potentially contaminating viruses. The World Health Organization recognizes fetal bovine tissues as having no detectable infectivity for transmissible spongiform encephalopathies. While destructive to most tissue constituents, the processing preserves the fetal collagen makeup of the dermis in a native, non-denatured state. Unlike other xenogenic collagen implant processing methodologies, this collagen implant is not chemically crosslinked.

We evaluated the acute and chronic inflammatory response to Cytrix in a rat abdominal incisional hernia repair model. Specific attention was paid to the reconstitution and remodeling of the implant with host cells and blood vessels.

Figure 1: (left) Low magnification photo of Cytrix Soft Tissue Repair Matrix. (right) Scanning electron micrograph (454 x) of the collagen fibers that make up the porous implant.



Study design, materials and methods

Male Sprague-Dawley rats (~275 g) were anesthetized and abdomens shaved and swabbed with Betadine. A midline incision was made through the skin to expose the abdomen. A 2 cm incision was made through the midline taking care not to harm underlying organs. Cytrix was trimmed such that the material extended approximately 1.5 cm beyond the wound on all sides. The implant was sutured to the underlying musculature along the perimeter of the wound with 4-0 Prolene. The skin was closed with stainless steel clips. Fifteen animals underwent the procedure with five animals being euthenized at 3 weeks, 9 months, and 15 months (n=5 animals/time point).

Following euthanasia, the implant and underlying musculature were removed, photographed, and fixed in 10% formalin. Histological sections were made in the transverse plane through

the implant and adjacent muscle. The sections were processed with Masson's connective tissue trichrome stain.
Endpoints included herniation through the muscle defect, surgical adhesions, the character of the foreign body response, evidence of implant reconstitution with host cells, evidence of remodeling of the implanted collagen fibers, and new tissue development.

Results

Endpoint	Result
Herniation	At 3 weeks, the incised muscle underneath the implant had contracted to form an oval defect in the abdominal wall approximately 2 cm x 1cm. There were no herniations through the defect in any animal at any time point.
Surgical adhesions	There were no surgical adhesions to the implant in any animal at any time point.
Foreign body response	There was no evidence of accumulating inflammatory cells, (including foreign body giant cells) at the perimeter of the implant and no evidence of fibrous encapsulation in any animal at any time point.
Implant reconstitution and remodeling	Acute (3 week) explants showed no gross evidence of remodeling. Histological examination revealed the implant had been infiltrated with host fibroblasts and blood vessels. A new tissue layer had formed on the surface of the implant.
New tissue development	New connective tissue developed at the site of the soft tissue defect. The implant served as a scaffold upon and within which new tissue developed. By 15 months the implant had been replaced by reparative tissue with a distinctly new fibrous collagen structure.

Interpretation of results

Similar to autograft or allograft tissues, the porous, fibrous Cytrix implant was populated by host fibroblasts and a supporting vasculature following implantation. Subsequently, the collagen fibers of the implant were incrementally remodelled and replaced by the host over a period of 15 months into collagen that repaired the muscle defect. The rate of remodelling was such that the implant did not weaken enough at any point to permit herniation.

Concluding message

The Cytrix xenogenic collagen implant can be handled, placed, and sutured much like an autologous or allogenic fascia graft. This in vivo study demonstrated that this xenogenic implant can elicit a biological response similar to autologous or allogenic implants. Although long-term follow up is needed, initial clinical experience with Cytrix has shown encouraging results, and appears to be a promising graft option for pelvic reconstructive surgery.