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Comparative Analysis of Histopathologic Effects of Synthetic Meshes Based on Material, Weight, and Pore Size in Mice

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Background. **While synthetic prosthetics have essentially become mandatory for hernia repair, mesh-induced chronic inflammation and scarring can lead to chronic pain and limited mobility. Mesh propensity to induce such adverse effects is likely related to the prosthetic's material, weight, and/or pore size. We aimed to compare histopathologic responses to various synthetic meshes after short- and long-term implantations in mice.**

Material and Methods. **Samples of macroporous polyester (Parietex [PX]), heavyweight microporous polypropylene (Trelex[TX]), midweight microporous polypropylene (ProLite[PL]), lightweight macroporous polypropylene (Ultrapro[UP]), and expanded polytetrafluoroethylene (DualMesh[DM]) were implanted subcutaneously in mice. Four and 12 wk post-implantation, meshes were assessed for inflammation, foreign body reaction (FBR), and fibrosis.**

Results. **All meshes induced varying levels of inflammatory responses. PX induced the greatest inflammatory response and marked FBR. DM induced moderate FBR and a strong fibrotic response with mesh encapsulation at 12 wk. UP and PL had the lowest FBR, however, UP induced a significant chronic inflammatory response. Although inflammation decreased slightly for TX, marked FBR was present throughout the study. Of the three polypropylene meshes, fibrosis was greatest for TX and slightly reduced for PL and UP. For UP and PL, there was limited fibrosis within each mesh pore.**

Conclusion. **Polyester mesh induced the greatest FBR and lasting chronic inflammatory response. Likewise, marked fibrosis and encapsulation was seen surrounding ePTFE. Heavier polypropylene meshes displayed greater early and persistent fibrosis; the reduced-weight polypropylene meshes were associated with the least amount of fibrosis. Mesh pore size was inversely proportional to bridging fibrosis. Moreover, reduced-weight polypropylene meshes demonstrated the smallest FBR throughout the study. Overall, we demonstrated that macroporous, reduced-weight polypropylene mesh exhibited the highest degree of biocompatibility at sites of mesh implantation.**

Key Words: **synthetic; mesh; porosity; weight; mouse; hernia; *in vivo*.**

INTRODUCTION

Hernia repair is one of the most prevalent procedures performed by general surgeons in the world [1–3]. Many, if not most, herniorrhaphies require the use of a prosthetic reinforcement to reduce the incidence of hernia recurrence [4–9]. The identification of a prosthetic mesh that is pliable, resistant to mechanical stress, relatively inert, and well-tolerated by patients, however, continues to be a challenge. While synthetic meshes have been utilized for over half a century, little has changed in their design since Usher *et al.* popularized the use of polypropylene in the late 1950s [6, 7]. Although heavyweight meshes are still in use, it has been suggested that those meshes have been over-engineered [10]. The use of such meshes may result in undesirable sequelae, including chronic inflammation and excessive fibrosis, with resulting loss of mesh pliability and increased stiffness at the site of the implantation [10–12].

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One of the proposed recent mesh improvements has been development of lighter weight meshes with modifications in pore size and filament caliber. By limiting the amount of implanted foreign material, it is believed that successful hernia repair can be achieved while reducing the inflammatory and fibrotic responses within and surrounding the implanted mesh. However, it remains unclear which characteristic(s) of a given mesh is most defining of its biocompatibility. In this study, we aimed to determine how mesh material, weight, and pore size contribute to the biocompatibility of the implanted prosthetic. We hypothesized that as the mesh weight declined and pore size increased, a graded reduction in local tissue inflammation, host foreign body response, and fibrosis would occur.

MATERIALS AND METHODS

Surgical Meshes

Five different synthetic surgical meshes were studied. Trelex (TX; Boston Scientific Corp., Natick, MA) is composed of heavyweight microporous polypropylene; ProLite (PL; Atrium Medical Corp., Hudson, NH) is a midweight microporous polypropylene mesh; Ultrapro (UP; Ethicon Inc., Somerville, NJ) is a lightweight macroporous polypropylene and poliglecaprone 25 mesh; Parietex (PX; Covidien, Norwalk, CT) is a three-dimensional macroporous polyester; Dualmesh (DM; W. L. Gore and Assoc Inc., Flagstaff, AZ), is composed of expanded polytetrafluoroethylene (ePTFE) (Table 1). With the exception of the poliglecaprone 25 component of Ultrapro, the polypropylene or polyester components/meshes are permanent. Multiple 5-mm circular samples were cut from each mesh using a sterilized metal punch. The mesh samples were re-sterilized using a Sterrad 200 hydrogen peroxide gas plasma sterilizer (Advanced Sterilization Products, Irvine, CA).

Animals

Thirty 6–10 wk-old adult C57BL/6J mice (The Jackson Laboratory, Bar Harbor, ME), weighing approximately 25–30 g were used. All experiments were performed in accordance with protocols approved by the University of Connecticut Health Center Animal Care Committee. The animals were housed within the Center for Laboratory Animal Care at the University of Connecticut Health Center throughout the study. They were maintained on a regular 12/12 light/dark cycle at 74 ± 2°F with food and water available *ad libitum*.

Surgical Implantation

Prior to midline skin incision, the abdominal hair of each mouse was removed with Nair (Church and Dwight Co Inc., Princeton, NJ) followed by thorough rinsing with water. Povidone-iodine was used for skin disinfection. A 1-cm skin incision was made in the middle third of the abdomen. Bilateral subcutaneous pockets were developed by blunt dissection and a 5-mm piece of mesh was placed in each of the bilateral subcutaneous spaces. Each mouse received two identical pieces of mesh, one in each of the bilateral subcutaneous pockets. Finally, the skin was closed with a running 5-0 plain gut suture.

A sham surgery group was also included. Sham surgeries were performed in a similar fashion; subcutaneous pockets were developed by blunt dissection, however no mesh was implanted. All mice received subcutaneous injections of buprenorphine (0.1 mg/kg) for postoperative analgesia.

Explantation and Histologic Evaluation

All mice were euthanized at 4 and 12 wk post-implantation. Following euthanasia, the abdomen was resected *in toto*, with cut specimens including skin, mesh, and abdominal wall. Each specimen was fixed in formalin, processed, embedded in paraffin, and sectioned. The sections were stained with hematoxylin and eosin (H&E) and Gomori's one-step Trichrome for histologic evaluation.

The slides were viewed and assessed by a blinded experienced histopathologist (DLK) using a modified histologic scale (Table 2) [13–15]. Histologic parameters included inflammatory response, foreign body reaction, fibrotic response, collagen organization, and neovascularization. After an initial review of all slides to gain a baseline measure of histologic parameters, each sample was re-evaluated and scored against each other to obtain a semiquantitative measure of tissue responses to the implanted mesh. For inflammatory response, the degree of infiltration of chronic inflammatory cells, principally lymphocytes and macrophages, surrounding mesh fibers was noted. Foreign body reaction was determined by the relative quantity of foreign body giant cells (FBGCs) surrounding each mesh fiber or within bundles of mesh fibers. Fibrotic change was a function of relative abundance of new collagen deposition at sites of mesh implantation, while collagen organization was determined by factors such as connective tissue density (loose *versus* dense) and arrangement of collagen bundles (parallel *versus* haphazard pattern). Neovascularization was a reflection of the number of new blood vessels per high power field.

RESULTS

Each mesh type induced varying levels of inflammation at both the 4- and 12-wk time points. There was limited, if any, acute inflammation seen throughout the study as evidenced by lack of neutrophils

TABLE 1

Synthetic Mesh Characteristics

Mesh product	Material	Weight–density (g/m^2)	Pore size (mm)
Trelex	Polypropylene	Heavyweight–95	Microporous–0.6
ProLite	Polypropylene	Midweight–85	Microporous–0.8
Ultrapro	Polypropylene with poliglecaprone	Lightweight–28	Macroporous–2.0-4.0
Parietex	Polyester	Midweight–78	Macroporous–1.8 × 1.5
Dualmesh	Expanded polytetrafluoroethylene (ePTFE)	(Solid laminar sheet)	2-Aided: micro- and macroporous*

*Pore size measurements not available.