

# "The Histological Pattern of Xenograft Remodelling in Vaginal Paravaginal Repair with SurgiSIS® Overlay Graft".

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## BACKGROUND

Pelvic connective tissue is not structurally suited to chronic passive loadbearing. Normal pelvic support depends on a complex inter-dependence of two main factors:

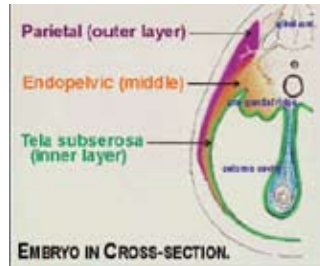
- Levator plate acts as a dynamic backstop, which absorbs most of Valsalva pressure wave.
- Pelvic viscera are stabilized over levator plate by an embryologic mesentery, which attaches these organs to the pelvic skeleton.

Symptomatic prolapse = failure of both components, usually from childbirth trauma

- Pelvic floor muscle damage is important, but is not presently treatable.
- Hence, strategies for prolapse repair depend almost entirely on improving the strength and function of the endopelvic connective.

### Embryologically, there are THREE different types of endopelvic fascia

- **Parietal fascia** (A true collagenous aponeurosis, derived from dermatomes).
- **Endopelvic fascia** (A smooth muscle and fibrovascular mesentery, derived from urogenital ridge).
- **Tela subserosa** (A thin collagenous basement membrane underlying celomic mesothelium).



Cystocele and rectocele = An avulsion of the endopelvic mesentery from its normal anchor points on the parietal fascia of obturator internus muscle.

- **"Traditional colporrhaphy"** = plication of the endopelvic fascia overlying the bulge (ie, a palliative operation, without curative potential).
- **"Paravaginal repairs"** = re-attachment the endopelvic fascial hammock onto the parietal fascia (and thence to the pelvic girdle).

Paravaginal repair is curative, but durability is limited by suture line tension and secondary collagen degeneration of avulsed hammock. Hernia principles point to the value of mesh, both to create a 'tension-free' repair, and to re-strengthen adjacent connective tissue.

The **'benefit: morbidity ratio'** of mesh usage is governed by two sets of bio-engineering principles, depending on surgical objective:

- If used to build a new **"Suspensory Strut"**, the tensile strength of the implanted biomaterial is the primary consideration.
- If used as a **"Bridging Graft"** to rebuild the central bed of a vaginal hammock, emphasis should be placed on good flexibility and low morbidity, rather than on tensile strength.

From a biochemical perspective, biomaterials can be classified into two types, depending on their interaction with the Host Immune Response:

- Materials which evoke a **foreign body inflammatory reaction**, with subsequent encapsulation of the implant. Materials in this class may be either synthetic (eg, polypropylene) or biological (eg, grafts prepared with cross-linked collagen, such as Pelvicol).
- Minimally altered biological grafts which act as a scaffold for **host cell re-population, and subsequent remodeling** into a permanent new layer of Host Tissue. (eg, SurgiSIS®).

The composition of this new tissue layer depends on the source of the re-populating Host Cells. Hence:

- A sheet of SurgiSIS® biomesh placed within the vesico-vaginal space at colpopexy would be expected to remodel into a fibrovascular tissue with high smooth muscle content.
- A sheet of SurgiSIS® biomesh sewn onto the obturator fascia during a paravaginal repair would be expected to remodel into a much stronger, more highly collagenized tissue.

Any strategy that increases the tensile strength of the healed surgical wound may profoundly improve repair durability.

## MATERIAL AND METHODS

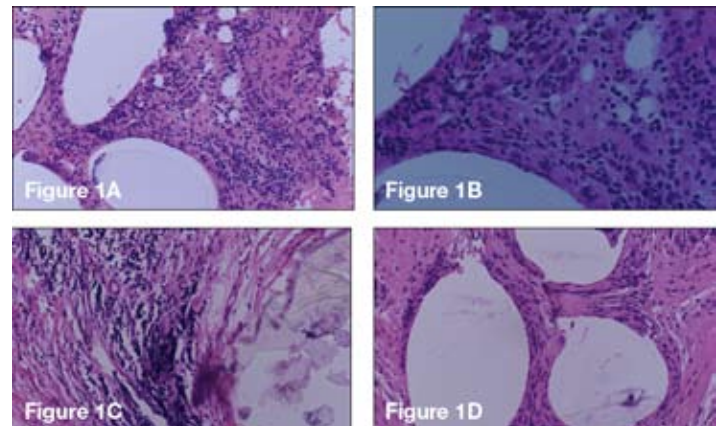
**Study Material** = 10 vaginal biopsies, from women who had had a prior VPVR using SurgiSIS® remodeling biomesh.

**Histological parameters** were:

- The collagen: smooth muscle content of the healed repair (an index of graft re-population by parietal fibroblasts from obturator fascia).
- The degree of inflammation and scarring (an index of any xenograft evoked foreign body reaction).
- Whether porcine antigens were still being expressed within the matrix (an index of whether the xenograft truly acted as a temporary extracellular matrix, lasting only until re-population and remodeling was complete).

## RESULTS

**Figure 1. By > 6 months after implantation, synthetic mesh or suture typical evokes severe inflammatory scarring.**



**Figure 1A** A low power view, showing three strands of implanted alloplastic mesh surrounded by cystic spaces. There is an intense inflammatory cell infiltrate (at centre), and some neovascularization (to the right) (200x).

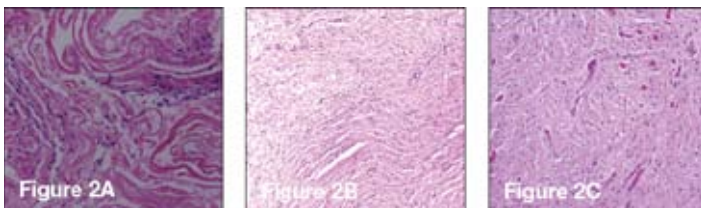
**Figure 1B** A higher magnification of the central field from Fig 1A, showing numerous plasma cells and multinucleated FB giant cells, both of which are commonly seen in the chronic inflammation surrounding synthetic mesh and/or suture (400x).

**Figure 1C** A photograph illustrating the intense lymphocyte infiltration that is another common aspect of the chronic inflammation surrounding implanted alloplastic material (200x).

**Figure 1D** An image typifying the late histological appearances of implanted synthetic mesh and/or suture. The photograph shows three cystic spaces containing leached-out synthetic implant material, surrounded by a dense fibrous capsule. The implanted alloplastic material is no longer the subject of an intense Host Immune Response, and scar tissue within the fibrous capsule has matured.

to the point of marked avascularity. The extreme density of this scar indicates a lack of other components crucial to normal connective tissue function, such as a GAG layer (needed to provide normal tissue turgor, lubricating properties and cell migration lanes). In short, the histological pattern shown here reflects inflammatory encapsulation of an implanted alloplastic mesh - a process that is entirely distinct from Host remodeling of an implanted 'new generation' biomesh (see Fig 2C). From a biomechanical perspective, a dense FB scar reaction like this has good tensile strength, and is reasonably well suited for the re-building of a "suspensory strut" within non-mobile tissue (eg, placing a TVT-type tape); however, this type of tissue response would not be ideal if the implant had been used as a "bridging graft", to repair a torn fascial hammock within the anterior or posterior vaginal walls (eg, when used as a bolster for cystocele or rectocele repair). When such dense FB scar reactions are found in close proximity to motile hollow organs like bladder and rectum, the poor tissue turgor and lack of lubricating properties create a heightened propensity to mesh exposure or viscus erosion (200x).

**Figure 2. By < 8 months after implantation, minimally altered SurgiSIS® biomesh has re-populated with Host Cells, and remodeled.**



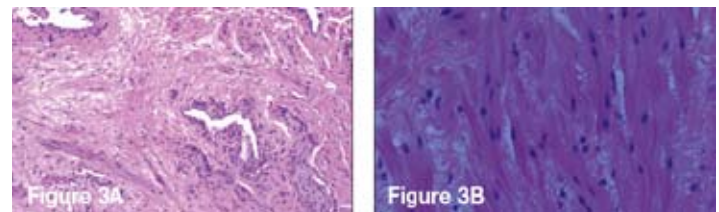
**The remodeling properties of SurgiSIS® grafts.**

**Figure 2A** Shortly after implantation (10 wks), some SurgiSIS® can still be identified as dense strands of relatively acellular collagenous tissue. The SurgiSIS® is beginning to repopulate with a mix of cell types, including neutrophils (indicating a continued but limited inflammatory response) and connective tissue fibroblasts (200x).

**Figure 2B** A biopsy taken eight months after implantation of an SurgiSIS® bridging graft at the time of vaginal paravaginal repair. The implanted SurgiSIS® has been completely replaced by moderately dense collagen bundles, oriented into the pattern of parallel arrays that characterize strong physiological connective tissue (such as true ligaments and aponeuroses). No inflammation or residual porcine elements can be identified (100x).

**Figure 2C** Eight months after implantation, an area of SurgiSIS® implantation has been completely replaced by fibrous connective tissue. This image specifically highlights the presence of a healthy vascular supply within this remodeled fibrous connective tissue. Again, no inflammation or residual SurgiSIS® can be identified. These appearances are in stark contrast to the dense, avascular, inflammatory scar that typically surrounds an implanted alloplastic mesh. From a biomechanical perspective, this remodeled SurgiSIS® would also be expected to exhibit good tensile strength, albeit perhaps not quite as strong as that of the scar tissue depicted in Fig 1D. However, the less compact organization of this fibrous tissue response suggests the presence of the GAG and proteoglycan molecules that are essential to normal connective function. As such, this tissue is highly suitable for use as a "bridging graft", to repair a torn fascial hammock within the anterior or posterior vaginal walls. The good tissue turgor and lubricating properties of such tissue would be protective against exposure or erosion, even when placed in direct juxtaposition to a hollow viscus (100x).

**Figure 3. A "collision zone" was seen between two different directions of cell re-population.**



**Figure 3A** A low-power image of a remodeled SurgiSIS® implant, 8 months post operation. This image shows a "collision zone" between an area of structurally normal, highly collagenized fibrous connective tissue (upper left) and a field of structurally normal smooth muscle bundles (lower right). The existence of such a "collision zone" supports the study hypothesis. Namely, that tissue within upper left half of the photograph derived from extensive repopulation by fibroblasts from the parietal fasciae of the pelvic sidewall (thus remodeling into a connective tissue), while tissue within lower right half of the photograph probably regenerated from extensive repopulation by smooth muscle cells from the vesico-vaginal space (thus remodeling into a much looser fibrovascular tissue with considerable smooth muscle content) (100x).

**Figure 3B** A high-power image from an area of constructive tissue remodeling of an SurgiSIS® xenograft, harvested 8 months after implantation. This photograph shows numerous large, elongated cells with plump nuclei. Cellular characteristics are consistent with smooth muscle cells. These cells are surrounded by loose fibrous connective tissue. Architecturally, the presumptive smooth muscle cells have aligned in parallel fashion, probably in response to exposure to mechanical stress during the remodeling process (400x).

**IMPLICATIONS**

**Normal pelvic support depends on a complex interplay of pelvic floor muscles and fascia:**

- **Damage to the levator plate is untreatable.**
- **Hence, reconstructive surgeons have to rely unduly on maneuver to bolster the endopelvic fascial supports.**

**Placing an SurgiSIS® xenograft against the parietal fascia simplifies the operation of VPVR, and also results in a very collagenous healed wound.**

**Results of this study support the view that, when mesh is to be used as a bridging graft in prolapse repair, emphasis should be placed on morbidity and tissue flexibility rather than attaining maximal tensile strength.**

