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Mesh-tissue integration of synthetic and biologic meshes in wall surgery: brief state of art

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Abstract. **Many studies show that surgical hernia repair with the use of prosthetic meshes can result in pain, hernia recurrence, contraction and mesh rupture. Numerous experimental studies have been conducted to understand the effect of mesh stiffness, pore size and mesh patterns on mesh biocompatibility.**

The purpose of this mini review is to present an overview of the contracture, adhesion, tissue regrowth and histological response characteristics of permanent and absorbable mesh. Indeed, the mechanics of mesh-human tissue interaction is poorly understood in the literature. It has been shown that early integration of biological meshes is critical for sustained hernia repair.

One of the emerging experimental approaches is to combine cell-based regenerative medicine with mesh materials. Studies in preclinical models show that the use of synthetic and biological meshes with autologous cell implantation improves the biocompatibility of biomaterials, promoting key tissue regeneration processes such as adhesion and vascularisation.

Key Words:
Prosthetic mesh, Hernia, Prolene, tissue ingrowth; regenerative medicine.

Introduction

The abdominal muscles are the muscles located at the level of the abdomen. These muscles can be divided into two categories: the muscles of the anterolateral abdominal wall and the muscles of the posterior abdominal wall[1,2].

To the first category belong the rectus abdominis muscle, the external oblique muscle, the internal oblique muscle, the transverse muscle of the abdomen and the pyramidal muscle[2]; these muscles are responsible for important functions, such as protecting the internal abdominal organs, contributing to posture or regulating intra-abdominal pressure. In the case of an injury or deformity that or a deformity that causes tissue weakening or damage, the supporting structures of the organ may fail[2]. A common occurrence due to such events is a hernia, in which an organ pushes through a tissue or muscle that usually holds it in place[2]. The most common type of hernia is the inguinal hernia, in which the intestine pushes through the inguinal canal[2]. Other types include incisional, femoral and hiatal hernias[2]. These gaps can be closed using prosthetic mesh, which provides flexible support and disperses tension from the hernia site[2]. Recently, with advances in medical diagnostics, several complications associated with surgical mesh have been identified[3]. Some of the main problems reported are mesh contraction and failure, which cause tissue tension, pain, infection and hernia recurrence[3]. Other common problems with mesh include mesh erosion, where the surgical mesh wears through nearby soft tissue, and organ perforation, where the mesh cuts through a hollow organ such as the bladder or bowel[3].

Complications arising from the use of prosthetic mesh during abdominal wall repair surgery have led to a significant increase in research through testing and development of new, commercially available mesh[4]. Indeed, extensive experimental studies in animal models have been conducted to understand some of the effects of prosthetic mesh including: the phenomenon of

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mesh stiffness, the correlation of mesh with pore size and mesh patterns on mesh biocompatibility[5-7]. However, to date, very few studies have analysed the mechanics of meshes implanted in the human body, where tissue properties are very different from those in animal models[6,7]. Moreover, no study has so far modelled the mechanical interaction between the prosthetic mesh and the human tissue. As the mesh does not act independently and intrinsically but is an integral part of a biological process with surrounding tissues and interacts in tension, a comprehensive understanding of mesh-tissue interactions is therefore required[6-8].

The purpose of this mini-review was to review the literature on the effects of cellular coating in the integration of human tissues with synthetic and biological meshes. In particular, an attempt was made to define the role of the host's inflammatory and fibrotic response to the absorbable barrier mesh.

Biological Response of the Meshes

The field of hernia wall surgery continues to evolve rapidly. The development and implementation of new technical approaches and new biomaterials have led to improved results. However, complication and failure rates remain quite common[3,4]. It is still not entirely clear, which is the ideal material for hernia repair, nor the best anatomical plan for prosthesis implantation. Furthermore, various strategies are being experimented with to optimise the surface properties of the mesh to reduce unwanted reactions between tissue and mesh[9,10]. While the ability of mesh coating has already been demonstrated, for the first time, researchers have explored the effects of mesh coating on tissue integration of coated meshes placed with one of the two commonly used implantation techniques: onlay and underlay[9,10].

The three most commonly used canonical positions of the mesh in the anatomical plane are: "onlay'', in which the mesh is positioned anterior to the anterior rectus sheath; ''sublay'', between the rectus muscle and the posterior rectus sheath; and ''underlay'', intra-abdominally against the peritoneal cavity[11,12]. Some authors, compared tissue integration between the onlay (ON) and underlay (UN) positions by means of a biomechanical test that was termed a *t*-test[13-14]. The data demonstrated superior tissue growth for both uncoated and biologically implanted synthetic meshes in the ON position compared to the UN position[13,14]. Subsequently, combining the results with the recently reported efficacy of onlay repairs and the known morbidity of large skin flaps required for onlay mesh placement, the use of the onlay technique may need to be reconsidered[13,14]. Early integration of biological mesh has proven to be of critical importance for hernia repair over time[15].

Biological grafts that do not integrate in the early post-implantation period are known to be associated with more frequent seroma formation and network resorption/rupture[15-17]. In the study conducted, the cell coating influenced the regrowth strength of the biological mesh, especially in the short term[18]. The prostheses used in this study represent three categories of mesh: synthetic non-resorbable, synthetic resorbable (TIGR) and biological non-crosslinked (Strattice)[18]. The Parietex mesh is a commonly used prosthesis with a long track record of clinical effectiveness[19]. As an alternative to permanent synthetic materials, a new type of resorbable materials has been developed[20]. Although clinical data are still evolving, resorbable materials are gaining popularity. TIGR is has been said to behave similarly to traditional polypropylene mesh in the first year after implantation, but is subsequently resorbed and replaced by well remodelled quasi-native connective tissue in 3 years[20,21]. Finally, the wide use of biological meshes prompted us to include the most commonly used porcine dermal matrix, Strattice[22,23]. In addition to superior clinical results, studies have shown a lower immunogenicity of the non-cross-linked Strattice mesh compared to its cross-linked counterparts[22-24]. The polypropylene mesh was not considered in this study, as difficulties have previously been demonstrated with coating fibroblasts with polypropylene materials[23]. The incorporation of the mesh has been evaluated in various modalities by other researchers[24]. The current methodology of analysis, including the processing of explants and the analysis devices themselves, varies widely, thus limiting our ability to compare and contrast absolute data[24]. Although several authors have reported the use of the T-peel test to study mesh regrowth, it is currently known that this is the first study on tissue integration of cell-coated mesh[24]. Furthermore, to define collagen deposition after mesh implantation, several methods must be used. From a histopathological point of view, it is of fundamental importance to be able to quantify and qualify the kinetics of collagen deposition during the process of mesh integration to the surrounding tissues[24].

Modeling of Prosthetic Mesh and Human Tissue Interaction

Recent advances in tissue engineering combined with progress in regenerative medicine highlight the advantages of combining cells with implanted materials to accelerate prosthesis integration and tissue repair[21-23]. Preclinical studies tend to show that coating the mesh with cells brings advantages in terms of tissue integration and attenuates the immune response against foreign materials[24,25]. Preclinical investigations have also shown that coating the mesh with cells prevented the formation of adhesions[24,25]. More recently, a clinical case confirmed that lining a prosthesis with the patient's own cells improved fascial healing and could be a feasible strategy for challenging elective surgeries, such as incisional hernia with a herniated port size greater than 10 cm, wound infection or surgery on obese patients [25]. Cell seeding could also be imagined for the preparation, as other authors have shown, of '3D network-like cellular scaffolds' to repair and 'fill in' large defects not only in classic hernia repair, but also for pelvic floor reinforcement after abdominoperineal resection, or during rectal prolapse reduction surgery[25].

A fibrin-filled microfragment (SVF) is prepared and shown to be a suitable lining for hernia mesh. In this animal model, the quality of the mesh integration is assessed[26]; the fiber density of the newly formed peri-prosthetic tissue defined by means of a scale (a, 1-very loose; 2-very loose; 3-dense; 4-very dense) The intensity of the immune response was analysed by counting the foreign body giant cells (no statistical difference was observed between the control and SVF-coated group, but only between day 10 and day 21 for the staining of the control and SVF-coated group of the SVF-coated group at day 21 (the scale bar represents 50 μm, the black star indicates the network cross-section, the black arrows indicate the foreign body giant cells and the blue triangles the vessels) [26]. The following was also performed positive anti-human mitochondrial immunostaining was detected by the brown colour between the network filaments, and the level of angiogenesis in the initial phase of healing was seen to correlate with the degree of tissue inflammatory reaction. After the initial growth of blood vessels activated by proangiogenic factors released by inflammatory cells, tissue healing is characterised by a proliferative and a remodeling phase[26].

These phases are associated with a decrease in the level of wound vascularisation, until it returns to the normal level. In fact, the preclinical rat study using an onlay model, presented by authors Wolf et al., showed that the post-surgical vascular response peaks between 7 and 35 days, a reaction that is attenuated by using an ECM-based coating[26]. To date, among the emerging trends in stem cell therapies, SVF cells are being evaluated in numerous preclinical and clinical studies. In this study, we developed a workflow that allows liposuction products to be processed to obtain SVF cells without the need for enzymatic protocols. SVFs can be embedded in a temporary support, such as fibrin gel, and be used as a biological mesh lining ready for transplantation, without the need for further cell processing[26]. The first attempt to repair hernia defects using SVF-coated mesh, presented in this publication, revealed that cellular grafts were well tolerated by patients. In fact, they reduced vascular growth in the short term[26,27].

Conclusions

The integration of the prosthesis during wall surgery depends on several factors. Some studies show that the different integration with the surrounding tissues depends on the position of the prosthesis in the anatomical space in the context of the abdominal wall. In fact, some authors have shown that a prosthesis housed in the intraperitoneal space has a greater capacity for integration than the onlay position. In contrast, lining with MSCs (rat mesenchymal stem cells) seems to be a viable option for the biological network, with improvements in both collagen deposition and growth, especially when implanted in the onlay position. Indeed, some authors argue that the cellular coating of the surgical mesh could be an interesting addition to future mesh modulations to maximise surgical results.

Furthermore, the use of minimally manipulated cells from autologous biological tissues has experienced tremendous growth in the field of regenerative medicine.

The use of stem cells has been extensively studied in numerous preclinical and clinical studies. Some authors show how the use of stem cells embedded in a fibrin gel can be used as a coating for a biological prosthesis. This procedure has been tolerated in the animal sample, however, studies are still needed to confirm that the use of these cells helps stabilise angiogenesis processes and improves the integration of the prosthesis.

Conflict of Interest
The authors declare that they have no conflict of interest.

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Ethical Approval
All procedures performed in studies were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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Authors' Contribution
All the authors have made substantial contributions to the conception and design of the study, data acquisition, or data analysis and interpretation, drafting of the article or critically revising it for important intellectual content, final approval of the version to be submitted.

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