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# Evaluation of a new composite prosthesis for the repair of abdominal wall defects

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**Abstract** The degree of integration of biomaterials used in the repair of abdominal wall defects seems to depend upon the structure of the prosthesis. The present investigation evaluates the behaviour in terms of adhesion formation and integration of a new composite prosthesis that could be employed in this clinical application. Full-thickness abdominal wall defects (7 × 5 cm) were created in 16 anaesthetized New Zealand white rabbits and the prosthesis were placed in direct contact with the visceral peritoneum during the experiment. The defects were repaired with a composite prosthesis or pure polypropylene mesh to establish two study groups ($n$ = 8 each). The composite device was constituted by a polypropylene mesh physically attached to a poly(ether)urethane–polydimethylsiloxane laminar sheet. Animals were sacrificed 7, 14, 21 and 30 days after implant and prosthesis/surrounding tissue specimens subjected to light and electron microscopy. Firm adhesions were detected in the polypropylene implants, while they were not present in the composite implants. The excellent behaviour of the composite prosthesis shown in this study warrants further investigation on its use for the repair of abdominal wall defects when a prosthetic device needs to be placed in contact with the intestinal loops.

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## Introduction

Hernia repair represents one of the most frequent surgical procedures performed each year in the United States. Worldwide, over 20 million abdominal repair procedures are performed every year [1]. More than 90% of these operations involve the use of mesh prosthesis and are performed on an outpatient basis. Through patient follow-up, the tension-free repair proposed by Lichtenstein et al. [2] has been demonstrated to achieve a significant reduction in the hernia recurrence rate and both early and late post-operative pain. In a recent review, Macintyre [3] concluded that conventional herniorrhaphy is a technique of the past and that prosthetic repair is the procedure of choice for inguinal hernias. Recently, an experimental observation has clearly demonstrated the high incidence of recurrence when the parietal defect is sutured after drawing its edges together [4].

One of the biomaterials most widely used in the repair of abdominal wall defect is polypropylene (PP) in the form of a macroporous prosthesis. In contrast with other laminar biomaterials of microporous structure, such as expanded polytetrafluoroethylene (ePTFE), PP achieves total integration with newly formed surrounding tissue and it affords a high degree of resistance to rupture at the interface between the mesh and the surrounding tissue at the repair site [5]. Besides, PP is well tolerated by the recipient organism. However, the major disadvantage of the use of a macroporous material over that of ePTFE is that it induces

a high incidence of adhesion formation and erosion of the intestinal loops which may lead to the formation of fistulas, when placed in direct contact with the viscera of the peritoneal cavity [6, 7]. This is generally the case in the repair of large, often multi-operated incisional hernias or when a laparoscopic reparatory technique is used.

Recent studies concerning the behaviour of different biomaterials at the interface with the visceral peritoneum demonstrated that the structure and porosity of the biomaterial play an essential role in inducing adhesions. Best results was obtained using a laminar prosthesis type, which promotes generation of a linear, perfectly organized neo-peritoneum. In opposite, when a reticular mesh is used as the prosthesis, peritoneal regeneration is irregular and non-homogeneous and it invariably induces the formation of adhesions [5, 8, 9].

Therefore it was speculated that the combination of a macroporous biomaterial with a laminar one in the form of a composite prosthesis might serve to achieve an optimum behaviour at the visceral peritoneum, avoiding complications and allowing rapid host tissue incorporation. Based on the scar tissue formation process induced by biomaterials of different structure, a composite prosthesis constituted by a PP mesh physically attached with a poly(ether)urethane–polydimethylsiloxane (PEtU–PDMS) laminar sheet was designed. This type of elastomeric formulation combines the excellent biocompatibility and physical–mechanical properties of PEtUs with the low toxicity and long-term biostability of PDMS. Such a composite device would have anti-adhesive properties due to the PEtU–PDMS visceral surface and optimal mechanical strength due to the PP mesh. The present investigation was designed to evaluate the capability of the new composite prosthesis to reduce adhesion events, that represent the major problem when PP mesh are employed in surgical hernia repair.

## Materials and methods

### Prosthetic material preparation

A PEtU–PDMS laminar sheet was attached to the PP mesh (Repol Angimesh 9®, Angiologica, Pavia, Italy) in a physical way without chemical adhesives.

The PEtU–PDMS layer was realized by spray-phase inversion technique as previously described from Okoshi et al. [10] using a solution of PEtU–PDMS containing 10% of PDMS. The polymer concentration solution was 3% (w/v) in a blend of tetrahydrofuran/dioxane THF/DX 1:1 and this solution was brought near to the precipitation point by adding 17% of non-solvent (distilled water).

The smooth surface of Angimesh, that is usually put in contact with subcutaneous tissue, was coated, while the rough one, that contacts the skin, was left free.

A particular instrument was ideated to attach the PEtU–PDMS material to the mesh: a vertical press composed by Teflon® plates was lodged in a hot air oven that allows to keep a constant temperature during the attachment procedure. The mesh covered with the PEtU–PDMS layer was placed inside the oven previously warmed at 120 °C and pressed up to 800 μm thickness. The coated mesh was kept pressed for 2 h, after this period the mesh was slightly cooled at room temperature and finally cut in rectangular specimens (7 × 5 cm). The composite prosthesis was placed into heat-sealable bags and sterilized by low-temperature hydrogen peroxide gas plasma sterilization. Plasma sterilization of heat sensitive material, as PEtU–PDMS, appears as an attractive substitute for ethylene oxide processing which leaves adsorbed toxic residues [11]. In fact plasma sterilization method did not affect either the PEtU–PDMS material physical structure or the adhesion between the two prosthesis components.

### Physical characteristics of PEtU–PDMS composite mesh

Superficial morphology of the composite mesh was characterized by a Jeol 5600 scanning electron microscope (Jeol Italia, Milano, Italy) after gold–palladium metallization (Sputter coater S150B, Edwards, Irvine, CA).

The water contact angles of the PEtU–PDMS composite device layer were measured by putting a droplet of deionized water on the polymer surface using the Data-Physics OCA15Plus contact angle apparatus (FKV S.r.l., Bergamo, Italy). With each specimen, the measurement was repeated at different sites, and average values were obtained for the contact angles.

### Experimental animals

Sixteen male New Zealand white rabbits weighting 2,500–3,000 g were studied. All the animals were caged under constant light and temperature conditions in accordance with the guidelines from *Dipartimento Alimenti, Nutrizione e Sanità Pubblica Veterinaria – Ministero della Salute* which approved this study.

### Surgical technique

Anaesthesia was induced with a mixture of 0.3 ml/kg Ketamine and 0.33 ml/kg Domitor injected intramuscularly. Some rabbits required an additional intraperitoneal dose of anaesthetic.

Using sterile surgical technique, a full-thickness $7 \times 5$ cm defect involving all the wall layers with the exception of the skin was created in the abdominal wall of the animals [8, 9].

The prosthetic material implants were used to close the defects and were placed in direct contact with intestine and subcutaneous tissue. The implant was sutured to the edges of the defect using continuous polypropylene 6/0 suture that was interrupted only at the corners. A post surgical antibiotic treatment was carried out for 5 days.

Two study groups ($n = 8$ each) were established as follows: PP mesh physically attached with a PEtU–PDMS laminar sheet as sample and bare PP mesh as control.

Two rabbits for each groups were sacrificed at 7, 14, 21 and 30 days post-implant to evaluate the integration of the prosthesis within recipient tissue and the formation of a neoperitoneum.

### Macroscopical analysis

The animals were macroscopically checked for signs of infection and rejection and to estimate the degree of adhesion formation between the prosthesis and the abdominal viscera. The adhesion was graded on the basis of consistency according to the scoring system in Table 1.

### Histological evaluation and SEM analysis

Specimens were taken from the following interfaces: prosthesis-visceral peritoneum and prosthesis-subcutaneous tissue. The specimens were processed for light microscopy (LM) and scanning electron microscopy (SEM).

Specimens for LM were fixed in 10% formaldehyde, embedded in paraffin and cut into 5 μm sections. After haematoxylin–eosin staining the sections were examined using a Zeiss Axiophot 2 microscope (Carl Zeiss, Oberkochen, Germany).

Specimens for SEM were fixed in 3% glutaraldehyde, placed in sodium cacodylate buffer pH 7.2 and dehydrated in a graded acetone series. Critical point was reached in a CPD 030 (Balzers, Milano, Italy). Once metallized with gold–palladium, specimens were examined under scanning electron microscope.

**Table 1** Scoring system for estimating the adhesion degree in the samples

| Degree | Adhesion classification |
|---|---|
| 0 | None |
| 1 | Loose, easy dissection |
| 2 | Firm, dissection by forceps |
| 3 | Integration between prosthesis and peritoneum, impossible separation |

## Results

### Physical characteristics of PEtU–PDMS composite mesh

SEM analysis of the composite device demonstrated that the PEtU–PDMS layer consist of an even and smooth surface (Fig. 1). In this in vivo study this side of the composite device was put in contact with subcutaneous tissue. Moreover, SEM observation showed on the other side the typical PP weaving interpenetrated with the PEtU–PDMS material (Fig. 2a and b).

To investigate the wettability of the PEtU–PDMS, water contact angle measurements were carried out: the PEtU–PDMS layer exhibited contact angles of $65 \pm 3$ degrees. This value suggests a relative hydrophilicity of the composite material, in which the content of PDMS, polymer known for his hydrophobic property, is only 10%.

### Macroscopical analysis

There was no post-implant mortality. Both types of prosthetic material were well tolerated by the recipient animal, with no episodes of rejection or infection. No animal developed signs of subcutaneous seroma. Only in the odd case there were signs of residual seroma between the PEtU–PDMS sheet and the PP mesh. No fluid leakage through the prosthesis was observed.

The results concerning adhesions of both sample and control devices are shown in Table 2.

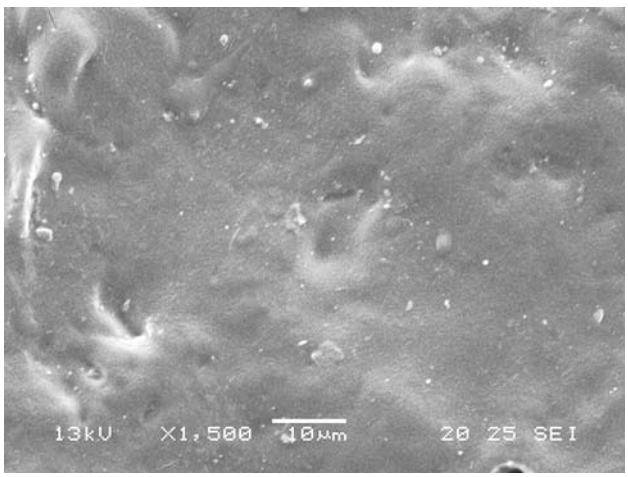


**Fig. 1** SEM image of PEtU–PDMS layer of the composite device at high magnification (1,500×) in which the smooth and even surface can be noted

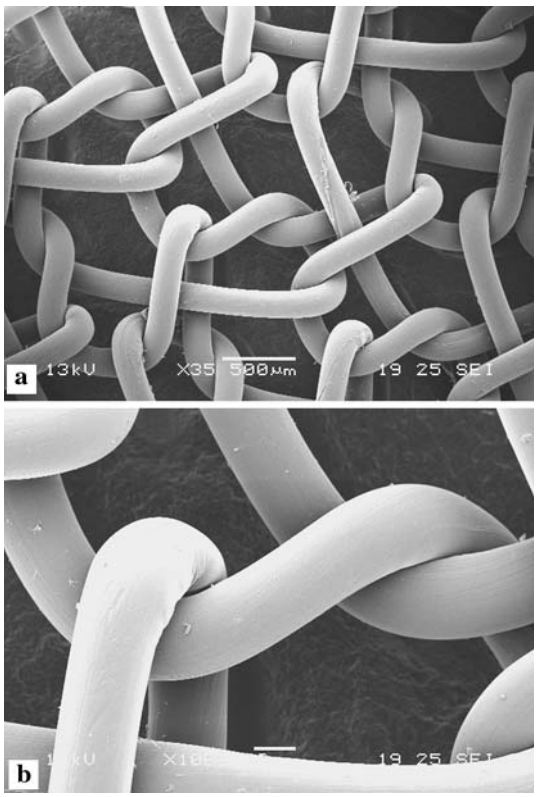


**Fig. 2** SEM images of PP layer of the composite device, in which the underlying PEtU–PDMS layer can be observed at different magnifications 35× (**a**) and 100× (**b**)

No adhesions were noted between the composite mesh and the intestinal viscera, at each time-point as shown in Fig. 3. Therefore the adhesion degree was 0 according to Table 1.

Adhesions within surrounding tissue were observed in the case of the bare PP meshes at all time points: after 7 days of implant the adhesion degree scored 1 and 2. After 14 and 21 days the score was 2 and 3 respectively, and after 30 days was 3 (Fig. 4). In all the control specimens the adhesions affected both the areas of suture and the prosthesis itself.

Histological evaluation and SEM analysis

The histological analysis concerning the composite mesh at 14 days after the implant showed a narrow presence of blood cells (polymorphonuclear leukocytes and macrophages), some fibroblasts and neo-formed capillary vessels; at 21 days there was a marked presence of fibroblasts and collagen fibers. After 30 days of implant this fibrillar tissue was replaced by a reparative tissue constituted by a neoformed mesothelium with a slightly inflammatory reaction and abundance of newly formed blood vessels (Fig. 5a and b).

At all time points the PP mesh surrounding tissue showed a chronical inflammatory reaction with presence of macrophages, foreign body giant cells (FBGCs), fibroblasts, collagen, microcalcification, and a lack of vascularization.

SEM analysis of the composite devices confirmed the presence of a well-organized newly formed tissue with high vascularization and covered on the inner prosthetic surface by a layer of typical polygonal mesothelial cells (Fig. 6a and b).

## Discussion

The behaviour of some biomaterials at the peritoneal level compromises their clinical use at this site. In the case of large incisional hernias often requiring multiple interventions, there is no available peritoneal plane and the biomaterial has to be placed in direct contact with the visceral peritoneum [12, 13]. This also occurs when a laparoscopic procedure is used for reparative surgery. It is therefore necessary to select carefully the most appropriate biomaterial to avoid post-implant complications including the appearance of adhesions formation, intestinal fistulas or even migration of the biomaterial to hollow organs [14, 15].

The origin of adhesions between the organs and the parietal peritoneum has yet to be determined. These for-

**Table 2** Score of adhesion formation at 7, 14, 21 and 30 days of implant

| Adhesion degree | Time-points (days) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 7 | | 14 | | 21 | | 30 | |
| | *S* | *C* | *S* | *C* | *S* | *C* | *S* | *C* |
| 0 | 2 | 0 | 2 | 0 | 2 | 0 | 2 | 0 |
| 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 0 |
| 3 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 2 |

S = sample, composite mesh; C = control, bare PP mesh

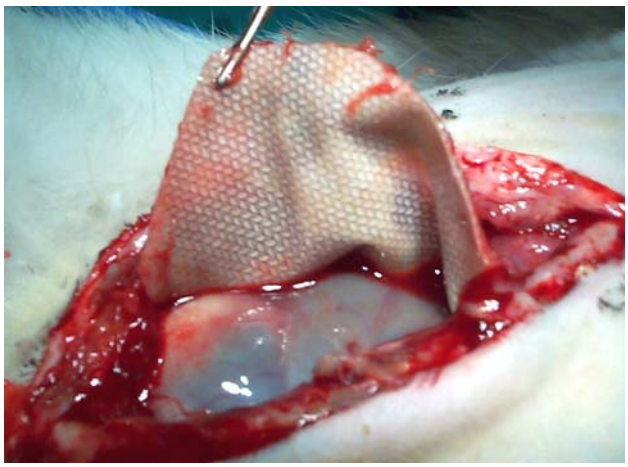

**Fig. 3** Composite mesh free of adhesion 30 days after implant: the lack of complications, such as infection, rejection or exudates, was observed

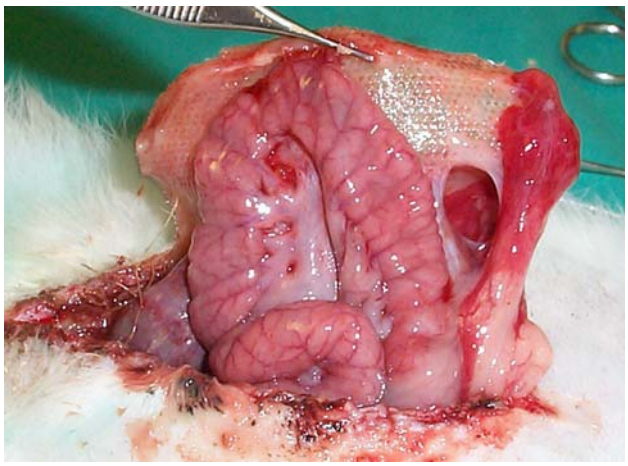

**Fig. 4** General view of the adhesions between the pure PP mesh and the organs of the abdominal cavity 30 days after implant

mations also appear after biomaterial implantation to repair abdominal wall defect, mainly when macroporous biomaterials, such as PP mesh, are utilized. This fact has been observed by several authors in animal models, such as the Sprague-Dawley rat and the New Zealand white rabbit [16]. Moreover in human it is well known that intraperitoneal positioning of conventional parietal mesh provides efficient reconstruction, but it causes visceral adhesion formation in 80–100% of the cases [17].

The adhesion formation depends on material surface geometry and affects the correctly organized neo-peritoneum regeneration. In previous in vitro studies in which mesothelial cells were seeded onto various biomaterials, it has been established that mesothelialization occurs early when the prosthesis is of laminar type. In contrast, when the biomaterial has the structure of a reticular mesh, mesothelial deposition takes place in an irregular manner, with cells settling on the prosthetic filaments, achieving an uneven cover [18]. The early formation of a mesothelium covering a laminar prosthesis probably explains the lack of adhesion formation observed following implantation. Besides, it is likely that the delay in mesothelialization associated with the mesh-type implant gives rise to the frequent adhesions that occur at the prosthesis–visceral peritoneum interface.

Accordingly, the PEtU–PDMS material was processed to obtain a smooth and thin laminar sheet. In particular, a PEtU–PDMS material containing a slight percentage of PDMS was chosen in order to combine the excellent biosatibility and hemocompatibility of silicone with the elastomeric characteristics of the PEtU. Moreover, in order to improve mechanical strength and resistance, the laminar sheet was physically attached to a PP mesh realizing the particular composite device employed in this in vivo study.

The observations concerning the composite prosthesis at all time-points showed no incidence of adherence with peritoneal visceri, no infection in the tissue surrounding the implant and a poor seroma/foreign body reaction.

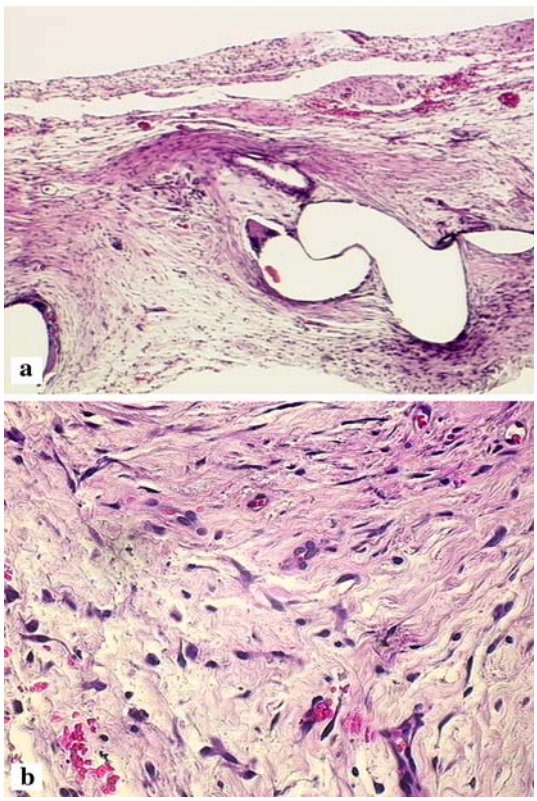


**Fig. 5** Neoperitoneum formed on composite mesh 30 days after implant. At this time a well-organized mesothelial cell layer could be seen on the inner surface of the biomaterial (**a**) light microscopy 70×; (**b**) light microscopy 200×

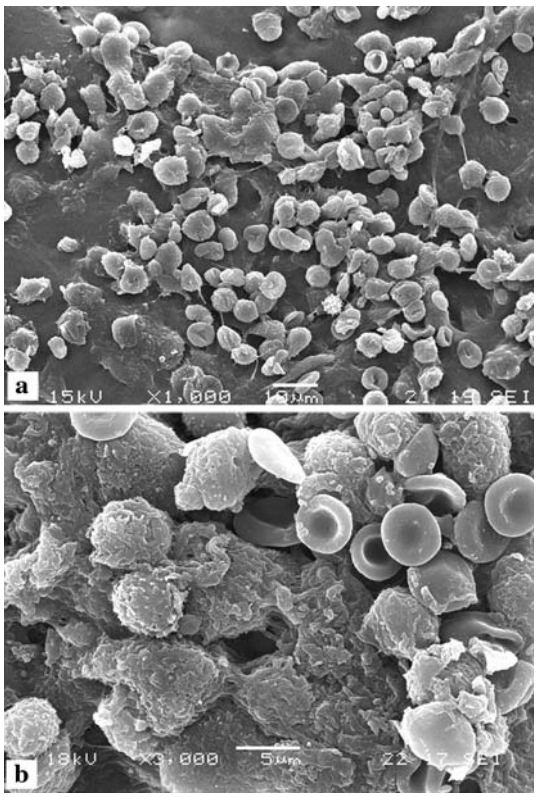


**Fig. 6** Scanning image of composite mesh 30 days after implant showing a mesothelial layer (**a**) scanning electron microscopy 1,000× (scale bar 10 μm) in which the presence of microvilli on cell surface is evident; (**b**) scanning electron microscopy 3,000× (scale bar 5 μm)

The present findings demonstrate that the laminar composite prosthesis is an ideal device for application in direct contact with visceral peritoneum, due to its PEtU–PDMS visceral surface that allows to avoid adhesion formation and induces a well-organized neoperitoneum generation. In contrast, the bare PP mesh gives rise to an uneven peritoneum with an irregular mesothelium, which is prone to develop adhesions. Therefore it may be concluded that the chemical composition of PEtU–PDMS laminar sheet positively influences the behaviour at the peritoneal interface.

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