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In vivo evaluation of a new composite mesh (10% polypropylene/90% poly-L-lactic acid) for hernia repair

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Abstract The increasing use of mesh insertion for groin hernia repair is dashed by a worrying prevalence of chronic pain frequently related as a reaction to the biomaterial implantation. Thus, new biocompatible prosthesis, designed as a composite material associating polypropylene (PP) and long-term absorbable material, are now under development. In the present study, the typical commercially available Prolene® mesh has been compared to two new meshes designed with 3-fold less PP, either alone (light PP) or associated with poly-L-lactic acid (PP-PLA) accounting for 90% of the mesh weight. These PP-mesh variants were implanted in an extraperitoneal position within the abdominal wall of 90 rats. Mesh adhesion and size were determined at autopsy 2, 4 and 8 weeks after implantation (10 animals per group) and morphometric parameters of the host tissues by light microscopy. Prolene® and light PP-meshes presented intra-corporeal shrinkage and tissue adhesion, both more pronounced with light-PP, whilst PP-PLA meshes were not affected in spite of a strongest fibrosis. In contrast to Prolene® and even more with light PP meshes, inflammation and cell-mediated immune responses were reduced without occurrence of angiogenesis or oedema. All these findings advocate together for a better tolerance of this new composite biomaterial, more likely due to a low macrophage response that appeared statistically correlated to the absence of mesh shrinkage and to a decreased adhesion to the tissue. On the basis of these experimental observations, it could be expected that the better tolerance of this composite biomaterial may avoid both long-term pain and recurrence when used as plug in groin hernia repair.

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1 Introduction

Inguinal hernia repair is the most common surgical procedure performed in the western countries. But evidence from several earlier studies reveals that primary repair had a high recurrence rate of 10–15% [1]. This failure in hernia repair by conventional surgical techniques remains a major concern for general surgeons over the last decades and sustains research and development of prosthetic biomaterials to reinforce the closure of the muscular defect. Indeed, besides the 3-layered suture called ''Shouldice'' procedure, which serves as the basic gold standard for comparison with all other new techniques [2], exists the opportunity of prosthetic repair by performing a tension-free hernioplasty, called the ''Lichtenstein'' procedure [3]. The introduction of this tension-free technique in the so-called ''open'' procedures for groin hernia repair (to differentiate them from the ''laparoscopic transabdominal pre-peritoneal'' hernioplasties) is assessed to reduce recurrences [4]. Another progress seems result from the use of per-fix plugs [5]. In this latter procedure the prosthetic material does not bridge the groin defect but plug the internal ring to avoid inguinal herniation.

The convenient prosthesis for this simpler procedure must comply with several requirements, i.e. be strong enough to compensate intra-abdominal pressure, have flexural rigidity for simple handling, serve as a framework for the ingrowth of connective tissue that first reinforces and then substitutes the foreign material and must be consequently slowly resorbable [6]. There is an adequacy between the rate of fibrosis induced by the biomaterial and the success of the hernia repair [6–8]. But the ideal prosthesis remains to be developed. As a matter of fact a chronic pain persisting after ending of healing with its train of paresthesias, neuritis, testicular atrophy, strain and reduced activity constitutes the major complication of all hernia-repair procedures [9–11] including plug application [12]. It has been thought in the past to be rare but prospective studies give now the clear indication of a huge prevalence of either severe (6%) or mild (43%) chronic pain [11].

The strategy to avoid this serious long-term complication might be either to reduce the amount of foreign prosthetic materials or to use resorbable biocompatible products. As a matter of evidence, absorbable materials such as polyglactin or polyglycolic acid are not strong enough and/or are too quickly degraded to maintain a prolonged tensile strength able to counteract efficiently the abdominal pressure [13–15]. The use of current absorbable meshes cannot avoid recurrence of the inguinal hernia. Reducing the amount of non-resorbable material in the prosthesis may be the alternative. This strategy seems to be effective, as a 36% reduction of polypropylene (PP) amount did not affect tensile strength of the meshes in vivo [16]. It seems however that exists a limit in reducing PP amount, as observed by Klosterhalfen et al. [16] testing the properties of a 75%-PP reduced mesh. We must also consider another parameter consisting in mesh shrinking. Shrinkage was more or less observed with all kind of non-resorbable materials in vivo [17–19] and seems linked to the ubiquitous inflammatory response to a foreign body [8, 20]. Thus, it can be hypothesized that reducing the amount of non-resorbable materials should decrease the rate of shrinkage.

Find a good compromise between material tightness and stiffness has to be addressed by amending mesh composition. This objective should be achieved by using a composite prosthetic material designed with resorbable component balancing a low amount of permanent material. This kind of composite mesh, knitted with both resorbable and non-resorbable materials and named Vypro® (Ethicon, a Johnson & Johnson company, Somerville, NJ) is currently under evaluation [21, 22]. It is designed with equal proportions of polypropylene and polyglactin. Our concern is to demonstrate that it is possible to use safely composite materials designed with less permanent component. We consequently investigate the experimental in vivo properties of a composite mesh designed with hugely less polypropylene (only 10% of the total) and poly-L-lactic acid (PLA), an absorbable biopolymer of constitutive lactate amino acid [15], which is widely applied as a scaffold for tissue engineering allowing successful bone [23], vessels [24], nerves [25] and muscle [26] guided regeneration in vivo.

2 Materials and methods

2.1 Mesh specifications

Three prosthetic materials were used in this study. Indeed, the polypropylene/poly-L-lactic acid mesh (PP-PLA), manufactured by Cousin Biotech (Wervicq-Sud, France) was compared with two polypropylene meshes of different designs. The first was the commercially available basic mesh Prolene® (Ethicon, Cornelia, GA, USA); the second was a newly constructed PP-mesh (Cousin Biotech) designed with reduced amount of PP (light-PP). Specifications of each kind of mesh are summarized in Table 1. All meshes are knitted with pure woven polypropylene monofilaments giving different size of pores (0.5–2.5 mm) as shown in Fig. 1. The quantity of PP is the same in both light-PP and PP-PLA meshes and corresponds to only 37.5% of the Prolene® mesh amount. The newly constructed PP-PLA mesh was obtained by an additional coating of the thin PP-layer with absorbable PLA, which accounts in total for 90% of the mesh weight. The PP-PLA mesh is bi-layered with a thin layer of mixed composition by an additional stratum of PLA on the PP-monofilaments, reducing drastically the size of the pores (Fig. 1, Table 1), and a thick layer of only PLA.

Table 1 Characteristics of the meshes

Type of mesh	Prolene®	Light-PP	PP-PLA
Percentage of polypropylene	100	100	10
Percentage of poly-L-lactic acid	0	0	90
Type of PP-filament	Mono	Mono	Mono
Weight (gm^{-2})	80	30	310
Proportion of the pores	80	87	74
Mean pore size (mm)	0.5	2.5	0.5
Thickness (mm)	0.4	0.25	0.8–1.0

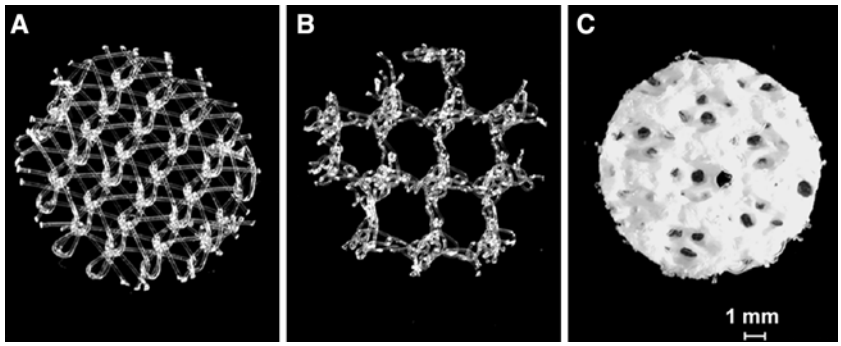

Fig. 1 Macroscopic aspects of polypropylene mesh variants investigated in the present study. (**A**) Commercially available Prolene® from Ethicon (**B**) light polypropylene mesh manufactured by Cousin Biotech with 3-fold less non-absorbable material, which is knitted more closer with larger stitches, and (**C**) composite mesh manufactured by Cousin Biotech with the same amount of polypropylene than B, accounting for 10% of the total weight, and poly-L-lactic acid for the remaining 90%. A knitting of polypropylene monofilaments as in B covered with poly-L-lactic acid constitutes the visible part of this bi-layered mesh, the pure poly-L-lactic acid layer remaining hidden behind

2.2 Experimental animals

Ninety male Wistar rats (Janvier, le Genest-St-Isle, France) weighing 250–300 g were housed under conditions of cycled light and constant temperature (22 ± 2 °C) with unrestricted access to a balanced pellet diet and water. Animal experiments were performed according to french laws for animal use and care and to the directives of the European Community Council (number 86/609/EEC of November 24, 1986). The animals were randomly divided into three groups (n = 30). Each of these test-groups received one of the meshes Prolene®, light-PP or PP-PLA.

2.3 Surgical procedure

The rats were anaesthetized with 2% isoflurane anaesthetic gas (Aerrane®; Baxter, Maurepas, France) in oxygen. The abdominal skin was shaved and disinfected with a povidone-iodine solution. A midline incision of 3-cm in length was performed on the linea alba up to the peritoneum. Then the rectus muscles were dissected from the peritoneum on both sides of the incision to generate two extra peritoneal spaces in which were inserted two 1-cm in diameter circular pieces of a sterile mesh. These pieces of mesh were fixed on the inner face of the fascia of the rectus muscle by three stitches of Prolene® 5/0 (Ethicon). For the bi-layered PP-PLA meshes, the thin PP-layer was always in contact with the muscle. The laparotomy was closed at length by a bi-layered continuous Polysorb® 3/0 (Tyco Healthcare, Plaisir, France) suture. No antibiotic treatment was given before or during the experiments. There was no postoperative mortality or wound infection.

2.4 Observation periods

Ten animals from each group (Prolene®, Light-PP and PP-PLA) of 30 animals were randomly sacrificed in sequence at day 14, 28 and 56, corresponding to 2, 4 and 8 weeks after mesh insertion, for retrieval and evaluation of the behavior of the meshes and of the surrounding tissues. Animals were examined throughout the whole period of 8 weeks, daily for the first postoperative week and then three times a week until sacrifice.

2.5 Sampling and macroscopic examination of the meshes

Implanted pieces of the meshes were removed under gas anesthesia. Prosthesis was excised with its surrounding muscles and peritoneum on the both sides after a midline incision. Euthanasia was performed under anesthesia immediately after mesh sampling by direct injection of potassium chloride solution into the heart through the diaphragm. One of the mesh specimens was used for the evaluation of adherence and its size was measured after dissection. The other was fixed in formalin for histological examination.

The presence of any seroma, hematoma, infection or adhesion of the mesh to the external side of the peritoneum was carefully checked at gross examination before sampling. One of the removed mesh specimen was further dissected to separate the mesh from the muscular layer assessing in this way the strength of mesh adhesion to the abdominal wall. This strength was scored on a 0 to 3 scale (0: no sticking; 1: filmy adhesion with easy mesh disjointing; 2: mild adhesion with a possible removal of the mesh; 3: strong adhesion

requiring a sharp scalpel dissection for removal) determining the adhesion index of the mesh. Then, the retrieved pieces of mesh were examined using a binocular magnifying glass to assess a possible intracorporal shrinkage. Their maximal diameters were determined and measured with a calliper.

2.6 Morphological study

Mesh specimens were investigated by light microscopy. They were fixed with 10% formalin and embedded in paraffin. Serial sections of 3 μm were stained with hematoxylin–eosine (H&E). Light microscopy was performed at a 20-fold magnification, looking at the mesh interface with tissue on three different H&E-stained slices of the same paraffin-embedded block and taking micrographs from 10 distinct areas of the same slice.

2.7 Morphometry

The morphometric evaluation consisted in a semi-quantitative analysis of both inflammation and healthy tissue behavior. The density of neutrophils reflects infection, of lymphocytes the cell-immune response and of macrophages plus foreign body giant cells the grade of the inflammation. Cell densities were scored in each slide of the 10 distinct fields of the three H&E-slices in a semi-quantitative way from 0 to 3 (0: no cell; 1: few cells; 2: medium; 3: numerous cells). All the slides were randomly read and scored by the same anatomo-pathologist without knowledge of prosthesis design.

The evaluation of the behavior of surrounding healthy tissue was performed through the determination of the occurrence of fibrosis, oedema, neoangiogenesis and fat accumulation. The extent of fibrosis was scored taking in account both the density of fibroblasts and the amount of collagen fibers. These two parameters were scored together on a 0 to 3 scale (0: nothing, 1: few fibroblasts and collagen deposit, 2: moderate number of fibroblast and collagen fibers and 3: huge rate of both collagen and fibroblasts). Neo angiogenesis as fat and oedema reactions were scored in the same way from nothing to a huge amount of new vessels, fat deposits or a high rate of tissue infiltration.

2.8 Statistics

Mean and standard error of the mean were calculated. Statistical analysis was carried out using the Statistical Package for Social Sciences 6.1 (SPSS, Inc., Chicago, IL, USA). Mean values were compared using the independent Wilcoxon test. The correlations between some of the investigated parameters were determined using a parametric Pearson test, as variances were not significantly different, with an Instat 2.00® Macintosh software (GraphPad Software, San Diego, CA, USA). A value of $p < 0.05$ was considered as statistically significant. These correlation studies were carried out to verify the hypothesis supported by some publications [8, 18, 27] that mesh shrinkage and/or adhesion were linked to some morphometric parameters such as the intensity of the macrophage reaction or of fibrosis reaction.

3 Results

3.1 Macroscopic examination of the meshes

No reaction to foreign material (i.e. serum or hematic suffusion, abscess or inflammation of the peritoneum in close contact with the prosthetic material) was seen at mesh retrieval for the three periods of examination in the three experimental groups. An obvious folding of the light-PP meshes was reported in most of the cases using this prosthesis.

All kinds of meshes were tightly stuck to the inner fascia of the rectus muscle. But meshes of the PP-PLA group were significantly less adhesive than those of the pure PP groups, 2 and 4 weeks postimplantation (Fig. 2A). Adhesiveness of the PP-PLA meshes increased with time, reaching those of both Prolene® and light-PP meshes 8 weeks after implantation. It is noteworthy that the adhesion score of the light-PP meshes remained the highest for the two first periods of observation. This can be the result of mesh folding.

Size of the PP-PLA meshes remained unchanged throughout the experiment (Fig. 2B) when the Prolene® meshes have already shrunk by 6% their original diameter 8 weeks after implantation ($p < 0.05$ versus PP-PLA group) that tallied with at least a 10% surface loss. The strongest shrinkage, however, occurred for the light-PP meshes that reduced continuously in size up to 20% of their original diameter at the end of the experiment ($p < 0.001$ versus PP-PLA group), which was consistent with a 40% reduction of the original surface. As a matter of fact the addition of PLA on the light-PP mesh prevents efficiently the occurrence of shrinkage.

3.2 Morphometry

The results of the morphometric evaluation of inflammation and of surrounding tissue behavior in the

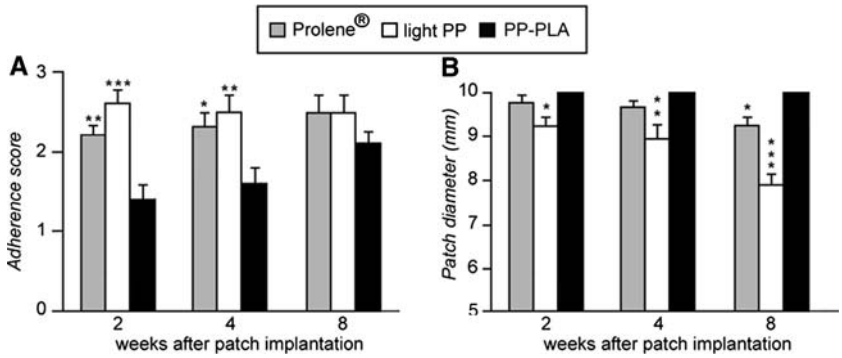

Fig. 2 Meshes behavior with time reflected by two macroscopic parameters determined at the autopsy: (**A**) adhesion was scored according to a 0 to 3 scale (see Sect. 2) and (**B**) size of the mesh reflected by its bigger diameter measured after retrieval. Results are means ± SEM of 10 animals for each implantation interval. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

presence of prosthesis were summarized in Table 2. No neutrophils were seen in any of the mesh types whatever the time of retrieval (data not shown), corroborating the absence of infection at gross examination. A slow decrease in lymphocyte infiltration was observed over time for all groups, without preferential infiltration for one particular kind of PP-mesh, suggesting that cell-mediated immune response is not modulated by the amount of PP. But, with adjunct of PLA, the presence of lymphocyte was slightly, but significantly reduced throughout the experiment, arguing for a lowered immune response.

At the opposite, the macrophage infiltration remained less important with PP-PLA meshes over the whole experiment when compared with the both kinds of PP-meshes (Table 2). This finding suggests that addition of PLA material seems to reduce inflammation in spite of its degradable feature. The amount of infiltrating foreign body giant cells reflects also the inflammatory response around the mesh [28]. This morphometric parameter was significantly enhanced throughout the investigation only for light-PP meshes. In this situation the addition of PLA on the thin PP-layer of the light-PP mesh reverses the foreign body giant cell infiltration. It must be emphasized however that the amounts of foreign body giant cells became only similar to those found in the Prolene® group.

The first morphometric parameter that reflects the behavior of the healthy tissue surrounding the prosthesis deals with fibrosis (Table 2). Collagen fiber deposits and fibroblasts were preeminent for PP-PLA meshes over the whole investigated period. For both Prolene® and light-PP groups, 8 weeks were necessary to reach a same level of fibrosis. This suggests that the PP-PLA mesh can provide an earlier support for an abdominal wall defect. Neo angiogenesis was slightly enhanced when using light PP by comparison with Prolene® and PP-PLA meshes. The addition of PLA material seems also to affect this parameter. Oedema remained reduced, but slightly higher when using the Prolene® meshes. This result comforts the other data of the morphometric evaluation of inflammation. Fibrin deposits and fibrinoid necrosis did not accompany oedema, confirming a relatively reduced inflammatory response to prosthesis implantation. Fat deposits increased over the experiment in all cases, but slightly more with Prolene® meshes.

3.3 Correlation studies

To assess the compliance of the investigated prosthesis with clinical application, we have also tried to establish the existence of a possible correlation between some morphometric parameters and mesh shrinkage and/or adhesion. The salient results of this analysis are plotted at the level of the Fig. 3. We tested as a first hypothesis that the mesh shrinkage depends on the intensity of the macrophage reaction. Correlation study revealed that the magnitude of mesh shrinkage was dependant on macrophage amount. It exists an inverse correlation between the size of the meshes and the intensity of the macrophage reaction that is particularly obvious 8 weeks after mesh implantation (Fig. 3A) with a regression coefficient value $r = -0.854$ ($r^2 = 0.73$, which is significant). Correlations are less significant at 4 weeks ($r = -0.68$, with $r^2 = 0.46$) and not significant at 2 weeks ($r = -0.66$, with $r^2 = 0.43$).

The second tested hypothesis was that the magnitude of mesh shrinkage was dependant on fibrosis reaction. But, in our hands, there was no correlation between these two parameters over the experiment, even 8 weeks after implantation (Fig. 3B) as the regression coefficient reached a maximum of $r = 0.30$ ($r^2 = 0.09$ which is not significant).

Table 2 Morphometric index evolution as a function of time postmesh implantation

Morphometric index	Weeks of implantation	Prolene®	Light-PP	PP-PLA
Lymphocyte	2	1.73 ± 0.20	2.06 ± 0.08	1.61 ± 0.13**
	4	1.43 ± 0.08*	1.71 ± 0.09	1.43 ± 0.08*
	8	1.28 ± 0.09	1.35 ± 0.07	1.20 ± 0.05*
Macrophage	2	2.58 ± 0.12	2.77 ± 0.10	1.16 ± 0.08***
	4	2.49 ± 0.11	2.58 ± 0.15	1.08 ± 0.08***
	8	2.40 ± 0.08*	2.75 ± 0.12	1.15 ± 0.08***
Foreign body giant cell	2	1.37 ± 0.23**	2.30 ± 0.25	1.16 ± 0.08***
	4	1.36 ± 0.12*	2.09 ± 0.29	1.21 ± 0.10**
	8	1.21 ± 0.20**	2.04 ± 0.21	1.41 ± 0.08**
Connective tissue fibroblast	2	1.79 ± 0.20	1.85 ± 0.16	2.70 ± 0.10***
	4	2.04 ± 0.18	2.04 ± 0.11	2.53 ± 0.10**
	8	1.97 ± 0.06	2.05 ± 0.13	2.24 ± 0.13†
Angiogenesis	2	1.67 ± 0.10*	1.95 ± 0.08	1.57 ± 0.11**
	4	1.49 ± 0.11*	1.75 ± 0.07	1.51 ± 0.11*
	8	1.19 ± 0.08*	1.57 ± 0.16	1.47 ± 0.11
Oedema	2	1.97 ± 0.15***	1.16 ± 0.08	1.16 ± 0.08
	4	1.13 ± 0.08	1.06 ± 0.04	1.10 ± 0.08
	8	1.10 ± 0.08	1.00 ± 0.00	1.10 ± 0.08
Fat tissue	2	1.17 ± 0.10	1.32 ± 0.10	1.03 ± 0.03**
	4	1.73 ± 0.20*	1.30 ± 0.10	1.71 ± 0.19*
	8	2.61 ± 0.08**	1.85 ± 0.24	1.84 ± 0.14

Results of morphometric evaluation of immune cell stimulation (trough lymphocyte index), of inflammation (through macrophage and foreign body giant cell indexes) and of surrounding tissue behavior in the presence of prosthesis (connective, vascular, oedema and fat indexes) at the interface between meshes and recipient abdominal wall. Indexes are expressed on a 0 to 3 scale (specifications given for each of them in the Sect. 2). Data are given as mean ± SEM of 10 animals. Morphometric changes were scored in 10 separated fields of three different slices originating from the same animal and averaged to a single value

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ towards light-PP values. †$p < 0.05$ towards Prolene® values

Then we tested another hypothesis in which the adhesion of the mesh to the surrounding tissues is linked either to the amount of macrophages or to the intensity of the fibrosis reaction. Correlation studies revealed a direct linear correlation between the adhesion and the macrophage indexes 2 weeks after mesh implantation (Fig. 3C) with $r = 0.76$ (significant with a $r^2 = 0.58$). But correlation disappeared at 4 weeks ($r = 0.64$, with $r^2 = 0.41$, not significant) and 8 weeks after mesh implantation ($r = 0.38$, with $r^2 = 0.14$). Correlation studies did not corroborate the hypothesis that the magnitude of mesh adhesion to surrounding tissues was dependant on fibrosis reaction. Indeed, no correlation was found even 2 weeks after mesh implantation (Fig. 3D).

4 Discussion

As a matter of evidence, the increasing use of different types of reinforcement meshes in groin hernia repair is not only a trendy effect. Indeed, the history of hernia surgery reveals a slow evolution from the Bassini 2-layered suture to the Lichtenstein and then the plug procedures (6) both relying on the application of biocompatible prosthesis. The use of biomaterials circumvents the risk of recurrence in consequence of a constitutive muscle deficiency, often encountered in elderly, or of the necessity to apply a very high tensile strength on the stitches for closing a large abdominal wall defect. In such a situation the use of the plug procedure appears obviously as one of the most convenient strategy. What should be simpler than close a hole by a plug? Thus, there is currently an increasing use of plugs for groin hernia repair [5]. It remains however a persistent problem resulting from the significant prevalence of long-term pain linked to prosthesis biocompatibility [6, 10–12].

The search for an ideal biomaterial for hernia repair started during the past fifties with Usher's application of polypropylene Marlex® meshes [29], followed in the seventies by the studies of Rives on Dacron®, a polymer obtained by condensation of ethylene glycol plus terephthalic acid [30]. Stoppa et al. [31] and Arnaud et al. [32] assessed the interest of Mersilene, another polyester mesh. Neglected during a short period, polypropylene reappeared during the sixties at first as a suture material [5], and then as a mesh that was increasingly used and constitutes nowadays, under the trademark of Prolene®, the ''gold standard'' for hernia repair [33]. Since recent prospective studies gave clear evidence of

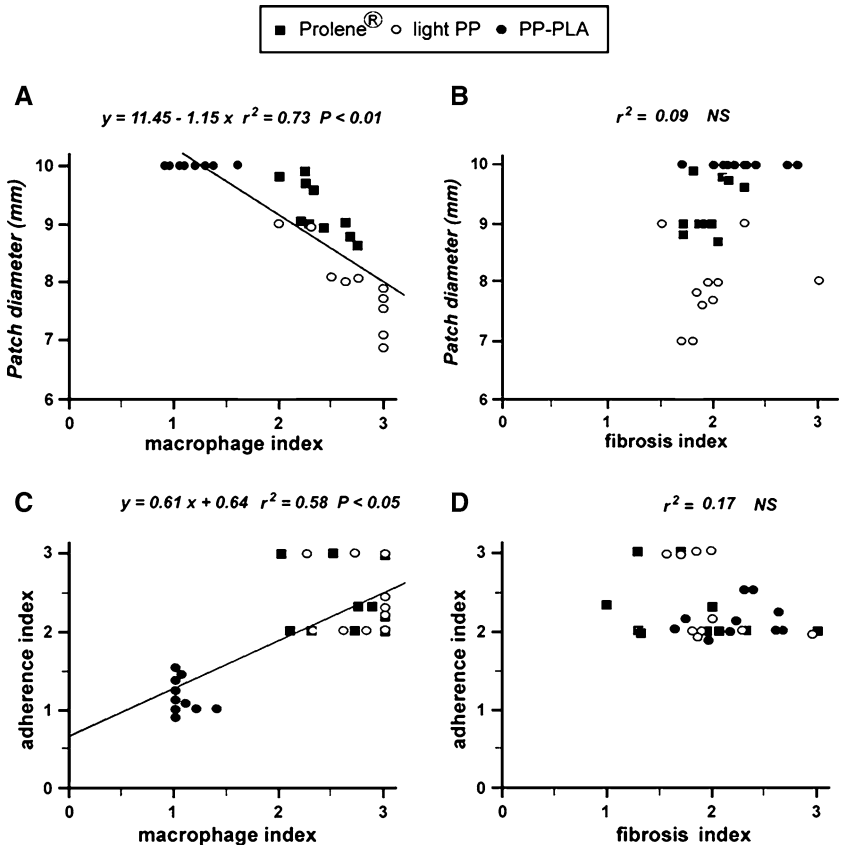

Fig. 3 Interactions between meshes and surrounding behaviors. Size of the mesh was expressed by its bigger diameter measured after retrieval. Adhesion, macrophage and fibrosis were scored according to a 0 to 3 scale (see Materials and Methods). Correlations between the parameters were made using a parametric Pearson test. Representative results of correlations between macrophages and mesh diameters after an 8-week implantation in (**A**) significant with a regression coefficient *r* equal to –0.854. Representative results of the absence of correlation between the magnitude of the fibrosis and mesh diameters after an 8-week implantation in (**B**) not significant with a coefficient *r* equal to 0.30. Representative results of correlations between macrophages and mesh adhesion after a 2-week implantation in (**C**) significant with a coefficient *r* equal to 0.76. Representative results of the absence of correlation between the magnitude of the fibrosis and mesh adhesion after a 2-week implantation in (**D**) not significant with a coefficient *r* equal to 0.41

the prevalence of worrying chronic pain after polypropylene mesh implantation [11], the design of prosthesis with an improved biocompatibility appears as a major concern. Reduction of the amount of polypropylene appears as a necessity, but with an increased risk of recurrence according to the unavoidable shrinkage of this material [5]. Using a less compact material as done in the current study does not seems to be the solution, since shrinkage being consistently increased. Moreover, as observed in the study of Klosterhalfen et al. [16], there was a significant lost in the tensile strength of the material. Some companies developed composite meshes mixing absorbable components, such as polyglactin (Vypro II®, Ethicon), poliglecaprone-25 (Ultrapo®, Ethicon) or poly-L-lactic acid (no current trademark, Cousin Biotech) with standard polypropylene. The present study was designed to investigate some performances of this later composite mesh.

Our results revealed an addition of several positive points when using such a composite. Any of them can be considered by itself as a conclusive data providing a fantastic improvement. But the addition of a complete absence of shrinkage of the meshes, of a higher rate of fibrosis induction than with the sole polypropylene meshes, of a reduced inflammation without angiogenesis or oedema and of a weak activation of the cell-mediated immunity, all these findings advocate together for a better tolerance of this new composite biomaterial. The only negative point consists in a delayed adhesion of the mesh to muscle and peritoneum, as the material needed more than 1 month to reach the adhesiveness of polypropylene. This can be considered as a consequence of a better immune tolerance, as adhesion appears to be directly correlated to the amount of macrophages, the activation and proliferation of which is under the control of inflammation [27]. It can be postulate that it

is fibrosis that restores composite mesh adhesion, in spite of the absence of correlation between adhesion and fibrosis induced by the meshes. The delay in adhesion can be considered as the price to pay for a better tolerance, which in turn may avoid persistent pain accompanying polypropylene meshes. Another major advantage of this composite, which seems also to be linked to the weakness of macrophage reaction, consists in the complete absence of mesh shrinkage, rendering particularly safe its application for groin hernia repair.

Our data regarding the behavior of polypropylene meshes were in agreement with previous findings [7, 16, 19, 28, 34]. Indeed, shrinkage of polypropylene meshes [19], induction of macrophage proliferation and activation [7], foreign body giant cell reaction [28], transient oedema [34] as the occurrence of an intense angiogenesis [7] and of a good integration within the living tissue [7] have been already described. Noteworthy is the fact that all these effects were exhausted in the light polypropylene mesh. It was particularly obvious for foreign body giant cells and for macrophage reaction with a huge correlation with the grade of both shrinkage and mesh adhesion. This can be a result of the structure of these ''light PP'' meshes, which are knitted with bigger stitches, allowing the adhesion of more fibroblasts and macrophages per pore and in turn a greater contraction of the stitches of the mesh induced by these cells [8, 18, 27]. It must be emphasized that all these drawbacks of the ''light PP'' mesh are reversed by the addition of poly-L-lactic acid. This can be a result of the reduction of the size of the pores by PLA coating. It can be hypothesize that the low PLA absorption with time was substituted by fibrotic tissue restoring mesh adhesion and improving its resistance. The design of this new polypropylene/poly-L-lactic acid composite allows reducing polypropylene amount while complying with prosthesis requirements upon demonstration of an adequate tensile strength for clinical use.

Comparison with other existing composite meshes conceived for groin hernia repair is difficult since little information is available on the behavior and the tolerance of these so-called ''lightweight'' meshes [21, 24, 28, 35, 36]. Ethicon Inc develops two kinds of composites, namely Vypro® and Ultrapro® as prosthetic materials for hernia repair. Vypro® and its derivatives (Vypro II® and Vypro II visor®) are built with polypropylene and absorbable polyglactine-910, which is a copolymer of 90% glycolic acid and 10% lactic acid. According to Ethicon website (www.ethicon.com) the Vypro® prostheses are designed with multifilament stitches and equal proportions of polypropylene and polyglactin. But in the study of Junge et al. [21] Vypro II® was assessed to weigh 83 g m^{-2} in total, with 32 g m^{-2} of polypropylene and 51 g m^{-2} of polyglactin, i.e. 40% and 60%, respectively. The amount of non-absorbable polypropylene is consequently similar in our PP-PLA meshes and in the Vypro II® (31 versus 32 g m^{-2}) and there is 5-fold more absorbable material in the PP-PLA than in the Vypro II® meshes (279 versus 51 g.m^{-2}). Nevertheless, behaviors of Vypro II® and PP-PLA meshes were very similar at the end with less inflammation and lower cell immune response in comparison with Prolene® mesh [21, 35]. It should be noted, however, that conversely to PP-PLA mesh, angiogenesis was very intense with absorbable polyglactin [21] and that both inflammatory and fibrotic reaction were initially increased during the two first months after implantation [35]. In fact, polyglactin filaments of the Vypro II® mesh must be totally absorbed prior to inflammation decrease [35]. It seems likely that poly-L-lactic acid is better tolerated than polyglactin, but no conclusive data can be draw out, especially as no investigation has been carried out on the possible shrinkage prevention of the Vypro II® mesh by polyglactin addition or of the Ultrapro II® mesh by poliglecaprone [36].

In conclusion, the current study argues for a better tissue behavior in rats after abdominal wall insertion of a newly designed PP-PLA mesh in comparison with typical heavy or even light polypropylene meshes. Indeed this composite prosthesis, manufactured with 3-fold less polypropylene material than conventional meshes, was responsible for less tissue adherence, intracorporal shrinkage, inflammation, and cell immune response but also for a greater fibrosis reaction than with conventional groin hernia prosthesis. This better tolerance is likely the result of the use of poly-L-lactic acid as the absorbable part of the composite. Embedding of a light polypropylene mesh with poly-L-lactic acid avoids in addition the typical intra-corporeal shrinkage. Further studies on this poly-L-lactic acid composite, including tensile and bursting strength in comparison with other materials must be now carried out to assess its possible superiority over polyglactin and poliglecaprone composites. Animal investigation however just allows a hypothesis on the behavior in the human situation. As a matter of fact, upon confirmation of its advantages, this composite material has to be evaluated in a clinical trial regarding chronic pain as an outcome parameter.

References

1. T. FASHID, T. J. HEIKKINEN, S. WOLLERT, J. OSTERBERG, S. SMEDBERG, H. GRANLUND, S. RAMEL, G. FELLANDER and B. ANDERBERG, *Ann. R. Coll. Surg. Engl.* **82** (2000) 396

2. J. M. HAY, M. J. BOUDET, A. FINGERHUT, J. POUCHER, H. HENNET, E. HABIB, M. VEYRIERES and Y. FLAMANT, *Ann. Surg.* **222** (1995) 719
3. I. L. LICHTENSTEIN, A. G. SHULMAN, P. K. AMID and M. M. MONTLLOR, *Am. J. Surg.* **157** (1989) 188
4. J. E. MCGILLICUDDY, *Arch. Surg.* **133** (1998) 974
5. R. C. READ, *Hernia* **8** (2004) 8
6. H. S. GOLDSTEIN, *Hernia* **3** (1999) 23
7. J. M. BELLON, J. BUJAN, L. CONTRERAS and A. HERNANDO, *Biomaterials* **16** (1995) 381
8. B. KLOSTERHALFEN, K. JUNGE, B. HERMANNS and U. KLINGE, *Br. J. Surg.* **89** (2002) 1043
9. J. KÖNINGER, J. REDECKE and M. BUTTERS, *Langenbeck Arch. Surg.* **389** (2004) 361
10. M. BAY-NIELSEN, F. M. PERKINS, H. KEHLET and DANISH HERNIA DATABASE, *Ann. Surg.* **233** (2001) 1
11. C. A. COURTENEY, K. DUFFY, M. G. SERPELL and P. J. O'DWYER, *Br. J. Surg.* **89** (2002) 1310
12. E. P. PÉLISSIER, D. BLUM, J. M. DAMAS and P. MARRE, *Hernia* **4** (1999) 201
13. J. P. LAMB, T. VITALE and D. L. KAMINSKI, *Surgery* **93** (1983) 643
14. J. TYRELL, H. SIBERMAN, P. CHANDRASOMA, J. NILAND and J. SHULL, *Surg. Gynecol. Obstet.* **168** (1989
15. U. KLINGE, V. SCHUMPELICK and B. KLOSTERHALFEN, *Biomaterials* **22** (2001) 1415
16. B. KLOSTERHALFEN, U. KLINGE and V. SCHUMPELICK, *Biomaterials* **19** (1998) 2235
17. P. K. AMID, *Hernia* **1** (1997) 15
18. A. S. LOWHAM, C. J. FILIPI, R. J. Jr FITZGIBBONS, R. STOPPA, G. E. WANTZ, E. L. FELIX and W. B. CRAFTON, *Ann. Surg.* **225** (1997) 422
19. U. KLINGE, B. KLOSTERHALFEN, M. MULLER, A. P. OTTINGER and V. SCHUMPELICK, *Eur. J. Surg.* **164** (1998) 965
20. B. KLOSTERHALFEN, U. KLINGE, B. HERMANNS and V. SCHUMPELICK, *Chirurg* **71** (2000) 43
21. K. JUNGE, U. KLINGE, R. ROSCH, B. KLOSTERHALFEN and V. SCHUMPELICK, *World J. Surg.* **26** (2002) 1472
22. S. BRINGMAN, T. J. HEIKKINEN, S. WOLLERT, J. OSTERBERG, S. SMEDBERG, H. GRANLUND, S. RAMEL, G. FELLANDER and B. ANDERBERG, *Hernia* **8** (2004) 127
23. M. KELLOMAKI, H. NIIRANEN, K. PUUMANEN, N. ASHAMMAKHI, T. WARIS and P. TORMALA, *Biomaterials* **21** (2000) 2495
24. K. S. FURUKAWA, T. USHIDA, K. TOITA, Y. SAKAI and T. TATEISHI, *Cell Transplant*. **11** (2002) 475
25. G. R. EVANS, K. BRANDT, S. KATZ, P. CHAUVIN, L. OTTO, M. BOGLE, B. WANG, R. K. MESZLENYI, L. LU, A. G. MIKOS and C. W. Jr PATRICK, *Biomaterials* **23** (2002) 841
26. J. R. FUCHS, I. POMERANTSEVA, E. R. OCHOA, J. P. VACANTI and D. O. FAUZA, *J. Pediatr. Surg.* **38** (2003) 1348
27. S. J. LEIBOVICH and R. ROSS, *Am. J. Pathol*. **78** (1975) 71
28. U. KLINGE, B. KLOSTERHALFEN, M. MÜLLER and V. SCHUMPELICK, *Eur. J. Surg.* **165** (1999) 665
29. F. C. USHER, J. OCHSNER and L. L. Jr TUTTLE, *Am. Surg.* **24** (1958) 969
30. J. RIVES, *Int. Surg.* **47** (1967) 360
31. R. STOPPA, J. PETIT and X. HENRY, *Int. Surg.* **60** (1975) 411
32. J. P. ARNAUD, R. ELOY, M. ADLOFF and J. F. GRENIER, *Am. J. Surg.* **3** (1977) 338
33. J. C. MAYAGOITIA, *Hernia* **8** (2004) 64
34. S. DABROWIECKI, K. SVANES, J. LEKVEN and K. GRONG, *Eur. Surg. Res.* **23** (1991) 240
35. R. ROSCH, K. JUNGE, R. QUESTER, U. KLINGE, B. KLOSTERHALFEN and V. SCHUMPELICK, *Eur. Surg. Res.* **35** (2003) 445
36. R. G. HOLZHEIMER, *Eur. J. Med. Res.* **9** (2004) 323