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Adhesion formation of a polyvinylidenfluoride/polypropylene mesh for intra-abdominal placement in a rodent animal model

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Abstract
Background Effective laparoscopic ventral herniorrhaphy mandates the use of an intraperitoneal mesh. Visceral adhesions and shrinkage of prosthetics may complicate repairs. The aim of this study was to compare adhesion formation, mesh shrinkage and tissue ingrowth after intra-abdominal placement of a novel two-component monofilament mesh structure made of polypropylene (PP) and polyvinylidenfluoride (PVDF) with current alternatives.
Materials and methods Forty Sprague-Dawley rats were used in this study. Mesh samples were fixed as intra-abdominal only mesh at the right lateral abdominal wall. The study groups were: PVDF+PP (polypropylene parietally and polyvinylidenfluoride viscerally), PP+Col (polypropylene with a collagenoxidized film), ePTFE (smooth surface viscerally and a textured surface parietally), and PP (a pure polypropylene mesh serving as control). The meshes were explanted after 30 days. Adhesions were scored as a percentage of explanted biomaterials' affected surface area; prosthetic shrinkage was calculated. Foreign-body reaction to mesh materials was measured by investigating the amount of inflammatory infiltrate and fibrotic tissue formation.
Results In terms of adhesion score, the pure PP mesh showed the highest values followed by the ePTFE, PVDF+PP, and PP+Col meshes. Quantitative assessment of adhesion area revealed a significantly higher value of the pure PP mesh sample (62.0 ± 22.1%) compared with the PP+Col (26.8 ± 12.1%) and the PVDF+PP mesh (34.6 ± 8.2%). Percentage of shrinkage showed a significantly higher value of the ePTFE mesh (52.4 ± 13.9%) compared with all other mesh modifications (PP+Col 19.8 ± 13.9%, PVDF+PP 19.9 ± 7.0%, and PP 26.8 ± 9.5%). Inflammatory infiltrate was significantly reduced in the PVDF+PP mesh group compared with all other mesh samples.
Conclusion The use of the novel two-component monofilament mesh structure made of polypropylene and polyvinylidenfluoride was found to be favorable regarding adhesion formation and mesh shrinkage compared to conventional mesh materials used for intra-abdominal placement.

Keywords Mesh · Adhesion · Shrinkage · IPOM

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Options for ventral or incisional hernia repair include open primary sutured repair, open prosthetic mesh repair, and, most recently, laparoscopic repair with intraperitoneal placement of prosthetic mesh [1–3]. The typical laparoscopic incisional hernia repair technique involves the complete reduction of herniated abdominal viscera back into the abdominal cavity and placement of a nonabsorbable prosthetic mesh over the defect [4, 5]. The success of this technique is dependent on three critical properties of the mesh: shrinkage of mesh area as a result of fibrous tissue formation that results in minimizing the critical overlap with the risk of hernia recurrence at the mesh borders, close and sufficient adherence of the mesh to the abdominal wall leading to permanent mesh fixation, and reduction or elimination of the risk of significant intra-abdominal adhesion formation, bowel erosion, and fistula formation. Multiple types of mesh modifications are currently available, and each is a result of a strategy to meet these goals. Each type of mesh has unique properties that affect adhesion formation and tissue ingrowth. Currently available types of mesh include a prosthesis composed of two layers of expanded polytretrafluor-ethylene (ePTFE), a composite mesh of smooth ePTFE for the visceral side and textured polypropylene for the parietal side, and mesh with polypropylene or polyester for the parietal side and an antiadhesive film for the visceral side. However, all of them reveal some disadvantages, and the ideal prosthesis for laparoscopic ventral hernia repair is not yet identified [6, 7].

Polyvinylidenfluoride (PVDF) is a polymer with improved textile and biological properties [8]. In comparison with polyester, PVDF is more resistant to hydrolysis and degradation. Furthermore, ageing does not increase the stiffness, evidently seen in polypropylene. Used for the construction of surgical meshes it was found to have an optimized biocompatibility with a minimized foreign-body reaction, and therefore could be an alternative to the commonly used materials [9]. Due to these suggested advantages we thus tested a two-component monofilament mesh structure constructed with a polypropylene part for the parietal side and PVDF for the visceral side using a rodent animal model.

Material and methods

Mesh materials

Overall four different mesh materials were investigated: PVDF+PP (Dyna-Mesh-IPOM, FEG Textiltechnik, Aachen, Germany, a two component monofilament mesh structure with the PP side placed parietally and the PVDF side viscerally, Fig. 1), PP+Col (Parietene Composite, Sofradim, Trévoux, France, woven polypropylene fibers bonded on the visceral side to a collagenoxidized film), ePTFE (Gore-Tex Dual Mesh, Gore & Associates, Flagstaff, Arizona, USA, ePTFE mesh with a smooth surface for minimal tissue attachment to the visceral side and a textured surface for tissue ingrowth to the parietal side), and PP (FEG Textiltechnik, Aachen, Germany, a pure monofilament polypropylene mesh which served as control).

Animal studies

Forty male Sprague–Dawley rats (250–300 g) were housed under conditions of constant light and temperature and received a complete diet of rat feed and water ad libitum throughout the entire study, which was performed according to the rules of the *Deutsche Tierschutzgesetz* (50.203.2-AC 18, 35/03) and to the NIH guidelines for the use of laboratory animals. The animals were randomly divided into the four groups PVDF+PP, PP+Col, ePTFE, and PP ($n = 10$ in each group).

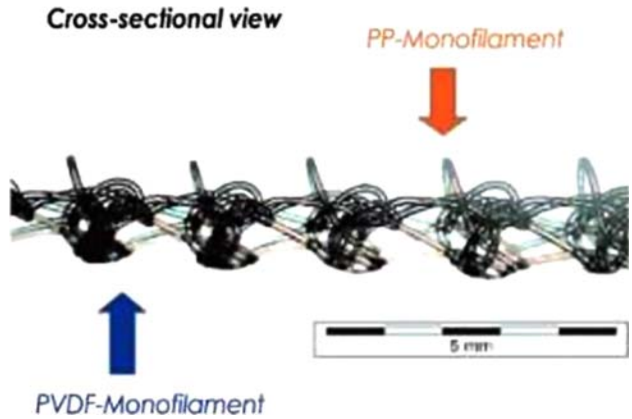

Fig. 1 Cross-sectional view of the PVDF+PP mesh (PP side placed parietally and the PVDF side viscerally)

Surgical procedure

Following anaesthesia the skin was shaved and disinfected with polividone-iodine solution. Laparotomy was performed using a left paramedian incision. Following exploration of the intra-abdominal cavity, mesh samples (2 × 3 cm) were fixed as intra-abdominal only mesh (IPOM) at the right lateral abdominal wall using 5/0 single polypropylene sutures. Laparotomy and skin closure was performed using 4/0 continuous polyglactin sutures. No antibiotic treatment was given before or during the experiments. Throughout the whole observation period all animals were objectively controlled and underwent daily clinical investigation to assess local and systemic complications. Thirty days after mesh implantation all animals from each group ($n = 10$) were sacrificed for morphological observations. The abdomen was opened via a full left paramedian incision for complete exploration. Adhesions were examined and registered.

Assessment of adhesions and shrinkage

Adhesions were assessed qualitatively and quantitatively according to the method described by the Surgical Membrane Study Group [10] using the following parameters: extent of site involvement, type, and tenacity (Tables 1, 2). Furthermore, areas of adhesions compared to the overall remaining mesh area (%) were measured using computer-aided planimetry. Percentage mesh shrinkage was calculated with respect to the initial mesh size during implantation and the remaining mesh size during explantation.

Table 1 Textile characteristics of the PVDF+PP mesh

Test	Unit	
Weight	[g/m^2]	Corresponding to 60*
Thickness	[mm]	0.7
Porosity, 3D	[%]	91
Porosity, 2D	[%]	51
Pore size	[mm]	80% > 1.0
Maximum stability	[N/cm]	62
Physiological elasticity at 32 N/cm	[%]	28
Maximum suture pull-out strength	[N]	36

* Effectively 108 g/m^2 but with a different density, corresponding to a conventional PP mesh of approximately 60 g/m^2 due to the material composition of 88% PVDF (density 1.78 g/cm^3) + 12% PP (density 0.9 g/cm^3)

Table 2 Adhesion score according to the Surgical Membrane Study Group [10]

Adhesion characteristics	Score
Extent of site involvement	
None	0
<25%	1
<50%	2
<75%	3
<100%	4
Type	
None	0
Filmy, transparent, avascular	1
Opaque, translucent, avascular	2
Opaque, capillaries present	3
Opaque, larger vessels present	4
Tenacity	
None	0
Adhesion falls apart	1
Adhesion lysed with traction	2
Adhesion required with sharp dissection	3
Possible total	11

Histological analysis

Tissue specimens were fixed in 10% formaldehyde and embedded in paraffin. Histological investigation was performed on 3 µm sections after haematoxylin and eosin (H&E) staining. All sections were processed at the same time to reduce internal staining variations. The amount of inflammatory and connective tissue formation was analyzed semiquantitatively by measuring the diameters of the inner ring of the granuloma which represents the inflammatory infiltrate and the outer ring of the granuloma as component of the fibrotic tissue reaction. After capturing five granulomas per sample with a digital camera (400×, Olympus C-3030, Hamburg, Germany) separate measurements of four quadrants of the inner and outer ring of the granulomas were performed with the help of a digital image analyzing software (Image-Pro Plus, Media Cybernetics, Silver Spring, MD, USA).

Statistics

Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS®) software. Data were organized according to mesh modification. Analysis of adhesion score, shrinkage, and histological parameters was performed using Kruskal–Wallis and Mann–Whitney-U test. p-values < 0.05 were considered to be significant. All data are presented as mean ± standard deviation if not otherwise mentioned. The Pearson correlation coefficient was calculated as an indicator of the association between the percentage of adhesion area, mesh shrinkage, and histological parameters.

Results

Macroscopic observation, adhesion, and shrinkage

Surgical procedure was well tolerated by all animals and postoperative period proceeded uneventfully. At necropsy, all animals demonstrated some degree of visceral adhesion formation. Representative macroscopic images of all mesh samples are shown in Fig. 2. Whereas the PP+Col and the PVDF+PP mesh showed at most filmy adhesions, which dropped spontaneously or could by lysed with traction, the ePTFE and the pure PP mesh presented with dense adhesions requiring sharp dissection.

Calculating adhesion score according to the Surgical Membrane Study Group [10], the pure PP mesh showed the highest values (median 9, range 5–11) followed by the ePTFE mesh (median 7, range 6–10), the PVDF+PP (median 6.5, range 3–8), and the PP+Col mesh (median 6, range 3–9). Quantitative assessment of adhesion area (Fig. 3) revealed a significantly higher value of the pure PP mesh sample (62.0 ± 22.1%) compared to the PP+Col (26.8 ± 12.1%) and the PVDF+PP mesh (34.6 ± 8.2%). No significant difference was found comparing the PP and the ePTFE mesh samples (52.9 ± 26.1%).

Shrinkage occurred to a lesser or greater degree in all samples investigated (Fig. 4). The calculated percentage of shrinkage in relation to the initial mesh size showed a significantly higher value of the ePTFE mesh (52.4 ± 13.9%) compared to all other mesh modifications (PP+Col 19.8 ± 13.9%, PVDF+PP 19.9 ± 7.0%, PP 26.8 ± 9.5%).

Histological analysis

Microscopic investigation showed typical formation of foreign-body granulomas at the mesh–host tissue interface

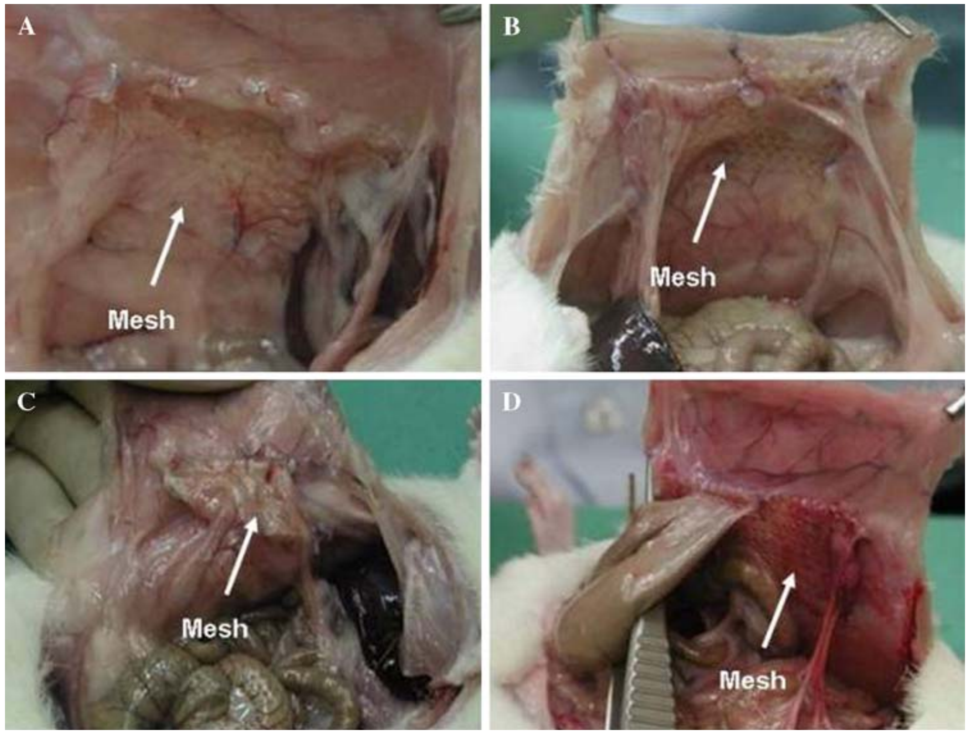

Fig. 2 Macroscopic view of mesh samples and adhesions 30 days following implantation: (**A**) PVDF+PP, (**B**) PP+Col, (**C**) ePTFE. and (**D**) PP

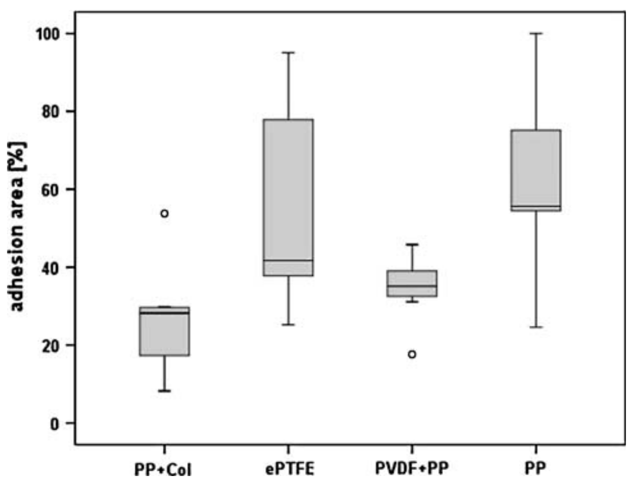

Fig. 3 Percentage of adhesion area in relation to overall mesh area

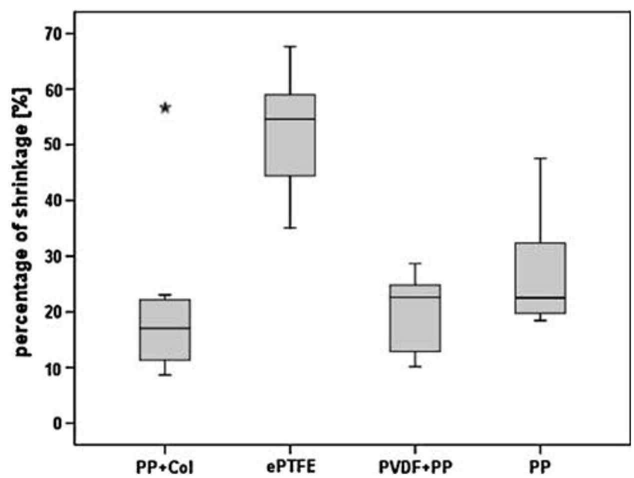

Fig. 4 Percentage of mesh shrinkage (%) in relation to initial mesh size

(Fig. 5). Diameters of the inner ring (Fig. 6A) of the granulomas representing the amount of inflammatory infiltrate (IF) were significantly reduced in the PVDF+PP mesh group (15.0 ± 3.3 μm, $p < 0.01$) compared to the PP+Col (17.5 ± 4.5 μm), the ePTFE (28.3 ± 6.8 μm), and the PP mesh group (20.8 ± 4.8 μm).

Diameters of the outer ring (Fig. 6B) of the granulomas represent the amount of connective tissue infiltrate (CT) and were significantly reduced in the PVDF+PP mesh group (46.1 ± 8.7 μm) compared to the ePTFE (108.1 ± 19.0 μm, $p < 0.01$) and the PP mesh group (56.6 ± 10.5 μm, $p < 0.01$), whereas no difference was found with regard to the PP+Col mesh (44.5 ± 8.1 μm, $p = 0.165$).

Comparing histological (IF, CT) and macroscopic parameters (shrinkage, adhesion) a significant linear correlation was found between amount of shrinkage compared to inflammatory tissue ($r = 0.969$, $p = 0.031$) as well as connective tissue formation ($r = 0.999$, $p < 0.01$).

Discussion

Effective laparoscopic ventral incisional hernia repair mandates the use of an intra-abdominal mesh placement. Optimal laparoscopic prosthesis require a sufficient fibrous

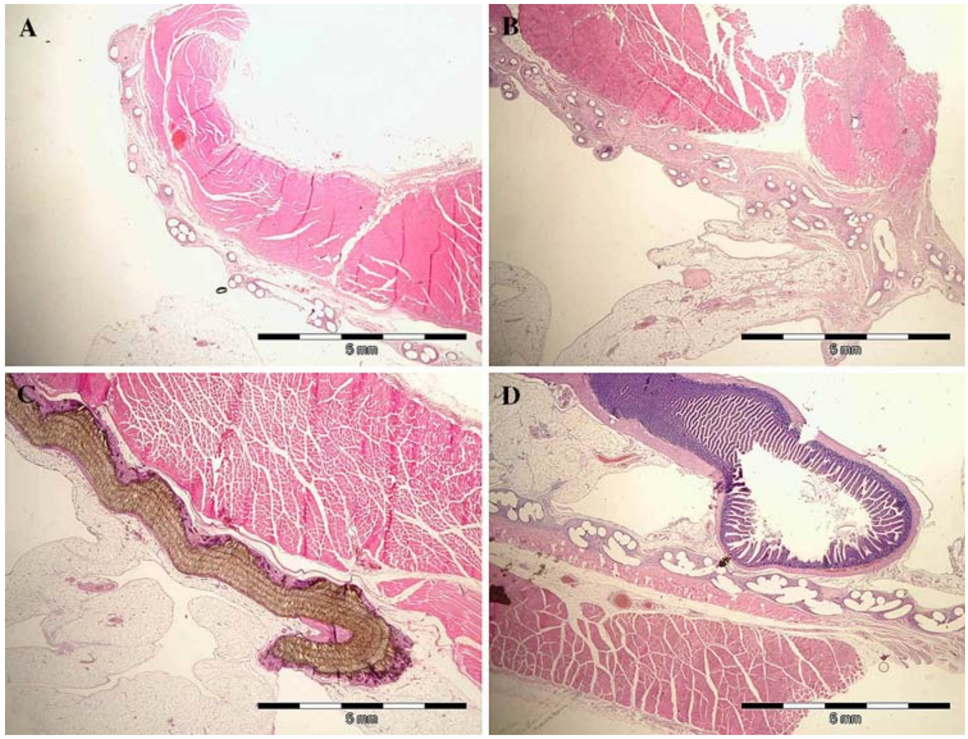

Fig. 5 Histological cross-sectional view of the excised abdominal wall with (**A**) PVDF+PP, (**B**) PP+Col, (**C**) ePTFE, and (**D**) PP mesh integrated

tissue formation at the parietal side and a negligible amount of mesh shrinkage minimizing risk of hernia recurrence at the mesh borders, and dislocation of the prosthesis. Furthermore, because intra-abdominal adhesion formation connecting visceral organs to mesh surface can potentially lead to bowel erosion and fistula formation, it should be eliminated or at least best possibly reduced. Multiple types of mesh modifications are currently available for laparoscopic hernia repair, but all of them exhibit some disadvantages. The optimal mesh for laparoscopic ventral hernia repair has yet to be found [11]. Pure ePTFE meshes, which are probably regarded as the gold-standard intra-abdominal mesh were found to show the least peel strength of mesh from the abdominal wall compared to other materials, and therefore, insufficient tissue integration at the parietal side [12]. Furthermore, adhesions are reported in up to 57% of mesh area [12, 13] and shrinkage was found to be almost half of the original surface area [13]. Comparable to this experimental results, within the clinical situation up to 70% of ePTFE meshes showed insufficient fixation, 80% had intra-abdominal adhesions, as well as a remarkably reduced mobility of the abdominal wall in 18% [14, 15].

To further improve patient outcomes a new prosthesis was constructed. The mesh mainly consists of PVDF, which has been proven to induce the least inflammatory response in comparison to other polymers [9, 16, 17]. To avoid insufficient fixation to the parietal abdominal wall a thin layer of polypropylene threads was added. A rodent animal model was used to analyze the potency of adhesion formation, percentage of shrinkage, and histological parameters indicating amount of foreign-body reaction. The novel two-component monofilament mesh structure with a polypropylene side placed parietally and a polyvinylidenfluoride side viscerally was compared to polypropylene (PP), which was chosen due to its known potency for fibrous tissue integration at the parietal side [7]. Polypropylene meshes (e.g., Prolene) are commonly used prosthetic materials for open ventral hernia repair. They have pores that allow fibroblast ingrowth, improving tissue integration and strength of the repair. However, the advantages of improving tissue strength are lost when the improvement in fibroblast integration is responsible for an increase in adhesion formation. Structure and porosity of the biomaterial play a fundamental role in the formation of adhesions, in their consistency, and especially in the organization of the neoperitoneum formed in between the biomaterial and the visceral peritoneum [18]. Within our study a strong conjunction of the parietal side of the new mesh to the abdominal wall was found, indicating fibrous tissue integration of the polypropylene part.

Polyvinylidenfluoride (PVDF), as a nonabsorbable fluoropolymer consisting of alternating mythelene and difluoromethylene groups, was chosen for the visceral side of the mesh due to its improved biostability, lowered bending stiffness, and the minimized foreign-body response [9, 16, 17], which is supposed to lead to minimized adhesion formation at the visceral side. The moderate foreign-body reaction to PVDF fibers was verified within this animal

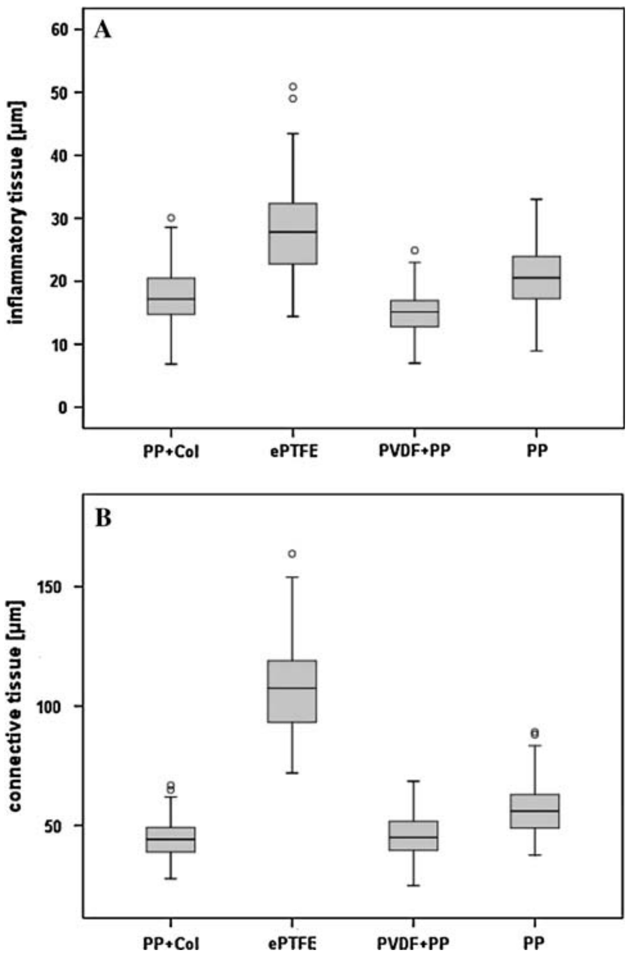

Fig. 6 Amount of (**A**) inflammatory and (**B**) connective tissue formation at the mesh–host tissue interface (µm)

model. Investigating the amount of foreign-body reaction diameters of the inner ring of the granulomas representing the amount of inflammatory infiltrate (IF) were significantly reduced in the PVDF+PP mesh group compared to all other mesh materials. Furthermore diameters of the outer ring of the granulomas representing the amount of connective tissue infiltrate (CT) were significantly reduced in the PVDF+PP mesh group compared to the ePTFE and the PP mesh group. Investigating adhesion formation, the PVDF+PP and the PP+Col mesh showed at most filmy adhesions which dropped spontaneously or could by lysed with traction whereas the ePTFE and the pure PP mesh presented with dense adhesions requiring sharp dissection. In accordance, the adhesion score according to the Surgical Membrane Study Group [10] as well as the quantitative assessment of adhesion area showed the lowest values for the PVDF+PP and PP+Col mesh group. On the one hand this might be explained by the beneficial pore size of PVDF and PP with regard to adhesion formation [19]. On the other hand, inflammatory and cellular responses are known key factors in maintaining adhesion formation. In this regard, PVDF as an alloplastic material is known to reveal a minimal cellular response without onset of an excessive fibrous tissue reaction.

The tendency of mesh materials to shrink over time has been studied in several animal studies. The phenomenon is a well-known clinical observation at reoperation in patients with formerly inserted mesh and is an important item concerning mesh fixation as well as mesh overlap. Animal studies showed significantly greater shrinkage of ePTFE mesh of up to 51% compared with other mesh types [20–22]. One retrospective human study evaluating mesh shrinkage at open reoperation after primary open ventral hernia repair in 77 patients has been published. Fifty-eight percent of small-pore-sized PP mesh, 5% of large-pore-sized PP mesh, and 57% of ePTFE meshes were noted to be "heavily shrunken" at the time of reoperation [23]. Within the presented study shrinkage occurred to a greater or lesser degree in all samples investigated. In accordance with the literature the calculated percentage of shrinkage in relation to the initial mesh size showed a significantly higher value for the ePTFE mesh compared to all other mesh versions. However, most mesh materials undergo some degree of shrinkage after implantation in living tissue. Mesh shrinkage has been related to hernia recurrence and the degree of shrinkage varies between different mesh materials with a tendency towards most shrinkage occurring after ePTFE implantation. The causal factors causing mesh shrinkage are not fully identified, but contraction as a consequence of the physiological wound healing process, pore size, and weight of the mesh may play a crucial role [24].

To summarize, for many years, great effort has been put into the challenge of creating a mesh that completely fulfils the criteria for the ideal laparoscopic mesh, which currently has not been found. However, the tested novel two-component monofilament mesh structure with the PP side placed parietally and the PVDF side viscerally showed beneficial aspects with regard to cellular response, tissue ingrowth, and adhesion formation without the need for a composite construction using an antiadhesive film (i.e., PP+Col). However, animal experiments, particularly rodent animal models, have their natural limitations, and results cannot be extrapolated directly to the situation in humans. In particular, the animals cannot reflect any underlying human disease or comorbidity. Therefore, clinical studies have to be conducted to prove the supposed beneficial aspects of this mesh.

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