IDEAL in Meshes for Prolapse, Urinary Incontinence, and Hernia Repair

Holger Gerullis, Bernd Klosterhalfen, Mihaly Borós, Bernhard Lammers, Christoph Eimer, Evagelos Georgas and Thomas Otto

SURG INNOV published online 20 January 2013
DOI: 10.1177/1553350612472987

Surgical Innovation
XX(X) 1–7

DOI: 10.1177/1553350612472987
http://sri.sagepub.com
SAGE

IDEAL in Meshes for Prolapse, Urinary Incontinence, and Hernia Repair

Holger Gerullis, MD[1,2,3], Bernd Klosterhalfen, PhD[4], Mihaly Borós, PhD[5], Bernhard Lammers, MD[1,3], Christoph Eimer, MD[1,3], Evagelos Georgas, MD[1,3], and Thomas Otto, PhD[1,2,3]

Abstract

Purpose. Mesh surgeries are counted among the most frequently applied surgical procedures. Despite global spread of mesh applying surgeries, there is no current systematic analysis of incidence and possible prevention of adverse events after mesh implantation. *Materials and Methods*. Based on the recommendations of IDEAL an in vitro test system for biocompatibility of surgical meshes has been generated (Innovation). Coating strategies for biocompatibility optimization have been developed (Development). The native and modified alloplastic materials have been tested in an animal model over 2 years (Exploration and Assessment and Long-term study). *Results*. In 3 meshes, implanted in sheep and explanted at 4 different time points (a, 3 months; b, 6 months; c, 12 months; and d, 24 months) over 24 months, thickness of inflammatory tissue (TVT a, 35 µm; b, 32 µm; c, 33 µm; d, 28 µm; UltraPro, a, 25 µm; b, 24 µm; c, 21 µm; d, 22 µm; PVDF a, 20 µm; b, 21 µm; c, 14 µm; d, 15µm), connective tissue (TVT a, 37 µm; b, 36 µm; c, 43 µm; d, 41 µm; UltraPro a, 33 µm; b, 32 µm; c, 40 µm; d, 38 µm; PVDF a, 25 µm; b, 22 µm; c, 22 µm; d, 24 µm), and macrophage infiltration (TVT a, 36%; b, 33%; c, 23%; d, 20%; UltraPro a, 34%; b, 28%; c, 25%; d, 22%; PVDF a, 24%; b, 18%; c, 18%; d, 16%) revealed comparable ranking characteristics at every time point after explantation. The in vivo performance of these meshes in a sheep model was predictable with a previously developed in vitro test system. Coating of meshes with autologous plasma prior to implantation seems to have a positive effect on the meshes biocompatibility. *Conclusion*. We have applied IDEAL criteria on a new innovation for surgical meshes. The results permit the generation of a ranking of currently available meshes with potential to optimize future meshes.

Keywords

mesh, biocompatibility, IDEAL, plasma coating, in vivo, in vitro, predictability

Introduction

In a public health notification issued in 2008, the American Food and Drug Administration (FDA) reported more than 1000 unexpected and severe adverse events, mostly associated with transvaginal placement of surgical mesh to treat pelvic organ prolapse and stress urinary incontinence.[1] In 2011, a second FDA warning has been amended on the basis of 2874 newly identified Medical Device Reports; 1503 associated with pelvic organ prolapse repairs and 1371 associated with stress urinary incontinence repairs.[2] Currently, regulatory changes are considered, including an upgrading in risk classifications for meshes, clinical studies to address the risks and benefits of mesh used to treat pelvic organ prolapse and stress urinary incontinence and expanded postmarket monitoring of device performance.[2] Manufacturers should be urged to initiate and complete postmarketing safety studies, which, in reality, is difficult to assure. Normally, once a product is set on the market, financial support for further investigations decreases and ongoing evaluation with unknown results is often not desired.

When assessing quality standards of surgical meshes, comparability to other meshes should be possible. Despite the existence of several models for assessing different

[1]Lukas Hospital, Neuss, Germany
[2]West German Cancer Center (WTZ), University of Essen, Essen, Germany
[3]German Centre for Assessment and Evaluation of Innovative Techniques in Medicine (DZITM), Neuss, Germany
[4]German Center for Implant-Pathology, Düren, Germany
[5]University of Szeged, Szeged, Hungary

Corresponding Author:
Holger Gerullis, Department of Urology, Lukas Hospital Neuss, Preussenstrasse 84, 41464 Neuss, Germany
Email: holger.gerullis@gmx.net

meshes with regard to their particular biomechanical characteristics, there are currently nearly no standardized tools for comparison among meshes.[3,4] With regard to this weak point, in a previous study, we developed a tissue culture in vitro test system for the evaluation of biocompatibility of alloplastic materials (meshes).[5] On that basis, we established a scoring systems for in vitro biocompatibility features. Without any doubt, in vivo behavior of a particular alloplastic material cannot be reliably extrapolated from in vitro studies, thus appropriate in vivo approaches are required.

Compared with the strict regulations for drug development and market implementation, the process of adopting and improving surgical innovations is still unregulated, unstructured, and variable. In 2009, *The Lancet* dedicated a series to the topic of "Surgical Innovation and Evaluation" and its current status.[6-8] A 5-stage description of the surgical development process has been proposed, the so-called IDEAL model (Innovation, Development, Exploration, Assessment, and Long-term study), which allows to assign every surgical innovation to its particular corresponding step of development. The aim of this study was to translate an in vitro approach into an animal experiment in order to assess the prognostic value of the in vitro test system regarding biocompatibility of different meshes following IDEAL recommendations.

Materials and Methods

In Vitro Test System

In a preliminary study, we randomly investigated 7 different mesh types, currently used in different indications with regard to their adherence performance using an in vitro tissue culture approach.[5] Meshes were incubated with tissue representative for fibroblasts, muscle cells, and endothelial cells originating from 10 different patients. After 6 weeks, the meshes were assessed microscopically and a ranking of their adherence performance was established.

We did not remark interindividual differences concerning the growth and adherence performance after incubation with the different meshes in the investigated 10 patients. The ranking was consistent in all patients. In this test system, polyvinylidene fluoride (PVDF) was the mesh with the best adherence score (Table 1). The test system was feasible and reproducible.

We expanded our in vitro test system to modify the mesh surface and to evaluate a possible effect of plasma coating on adherence performance. This additional approach was also used for internal validation of the previous in vitro test system. Meshes were incubated with 1 mL autologous plasma from the respective patient. Over 12 hours, the meshes had to be dried and were then added to the tissue culture and investigated as previously described.[5]

Table 1. Mesh Ranking From Preliminary In Vitro Study

Ranking[a]	Mesh Type	Adherence Score
1	Polyvinylidene fluoride (PVDF) Dynamesh, FEG Textiltechnik	2.2
2	TFT Motifmesh, ProxyBiomedical	2.0
3	Vitamesh, ProxyBiomedical	1.6
4	UltraPro Hernia System Medium UHSM, Ethicon	1.4
5	Mersilene Band, Johnson & Johnson	1.2
6	Proceed surgical mesh, Ethicon	1.2
7	TVT polypropylene	1.0

[a]Ranking from previous in vitro study.[5]

In Vivo Experiments

The animal experiment was conducted at the Institute for Experimental Surgery of the University of Szeged, Hungary, in accordance with the National Institutes of Health guidelines (Guide for the Care and Use of Laboratory Animals). The experimental protocol was approved by the Animal Welfare Committee at the University of Szeged (license/permission Nr. V01353/2010).

Fourteen female sheep, weighing from 20 to 25 kg and 6 months old, were housed and cared for at Szeged University's farm for experimental animal studies. We included 2 more animals than the needed 12 for safety calculations. All animals had free access to food and water, and were cared for by an educated keeper and routinely inspected by a veterinarian. On the basis of the previously described test system and the resulting ranking, we selected three meshes representing good, intermediate and poor in vitro performance (Table 1). Sheep were operated on in a supine position. The animals were intubated and an aspiration tube was introduced into the stomach. Anesthesia with isoflurane 2% mixed with air and O_2 (50%/50%) was then established. Surgery was performed by using a longitudinal laparotomy. We choose 3 different locations in the sheep to implant the meshes via open surgery. To represent different in vivo surrounding 3 meshes were placed in the following localization: (*a*) interaperitoneally, (*b*) as fascia onlay, and (*c*) as muscle onlay (fascia sublay). The size of the implanted meshes was 3 × 5 cm. Then, 3 plasma-coated versions of the same mesh type were implanted in equivalent localizations on the contralateral site of the torso. The meshes

had to be incubated with autologous plasma at least 12 hours prior to implantation. This procedure was repeated in 14 animals, resulting in 4 animals per mesh type (plus 2 animals with polypropylene TVT [tension-free vaginal tape]/PVDF). Mean operation time was 1.5 hours.

After 3, 6, 12, and 24 months, 3 animals, respectively, underwent surgery for mesh explantation. The meshes were identified and then harvested, and the extent of local reactions was described macroscopically. The animals were sacrificed directly after mesh explantation and harvesting of probes of parenchymatous organs (liver, intestine, kidney, lung, heart). The harvested material was then assessed for foreign body reaction, scar formation, and inflammatory reaction.

Morphological Studies

A single longitudinal section of mesh and adhesive tissue was obtained from each explanted mesh. Tissue samples were fixed in 10% formalin, then sliced into 0.3 × 1 cm pieces and embedded in paraffin. Each 10 to 15 sections of 4 μm thickness were stained with hematoxylin and eosin, as well as periodic-acid Schiff (PAS) plus diastase and Elastica van Gieson (EvG). All mesh specimens were studied by light microscopy. Light microscopy was controlled by immunohistochemistry, which was performed on the material embedded in paraffin using the avidin-biotin complex method with diaminobenzidine as a chromogen. The procedure was repeated twice for every sample.

Antibodies used in this study included polyclonal rabbit anti-human CD3, 1:50 as pan-marker for T-lymphocytes (DAKO, Hamburg, Germany), polyclonal rabbit anti-human CD138, 1:50 as pan-marker for plasma cells (DAKO, Hamburg, Germany), monoclonal mouse anti-porcine CD68, 1:50 (DAKO, Hamburg, Germany) as pan-marker for macrophages, monoclonal anti-human CD15, 1:10 (Becton Dickinson, Heidelberg, Germany) as marker for polymorphonuclear granulocytes, polyclonal rabbit anti-actin protein, 1:200 (DAKO, Hamburg, Germany), and monoclonal anti-CD34 1:200 (BIOMOL, Hamburg, Germany) as markers for fibromyocytes well as monoclonal porcine CD31, 1:10 (DIANOVA, Hamburg, Germany) as marker for endothelial cells. The morphometric evaluation consisted of a quantitative cell analysis of the inflammatory reaction and soft-tissue reaction. The cells were counted each in 5 hematoxylin and eosin slides in 10 fields at a grid of 10 points (100×, area 0.1 mm^2) and in the interface (0-300 mm, 400×, area 625 mm^2). Parameters measured were the inflammatory infiltrate (μm), connective tissue (μm), vessels (PV%), macrophages (%), leukocytes (%), polymorphonuclear granulocytes (%), and fibroblasts (%) as well as TUNEL, Ki67, and HSP 70 expressing cells (%). The influence of the clinical data on the tissue response was tested for significance by performing an analysis of variance with least significant difference modification according to Bonferroni. Statistical significance was assumed at $P < .05$.

Results

After the surgical procedure of implantation we did not see major complications in the animals. Only in one sheep a seroma occurred at day 3 postoperatively, which had to be drained. All animals survived and gained weight during the investigation period. At each explantation time point, we microbiologically excluded zoonoses through vaginal, nasal, oral smear. There were no clinical infections or mesh-related complications during follow-up. We explanted the meshes after 3, 6, 12, and 24 months. When microscopically investigating the different mesh reactions after explantation, main focus was set on parameters measured for inflammatory infiltrate, connective tissue, and macrophages (CD68). The respective quantifications are demonstrated in Tables 2-4. For each explantation time point, we observed the same trend of extent of the investigated parameter (Figure 1). High extent of connective tissue reaction and inflammatory reaction were assumed as indicative for reduced biocompatibility. The ranking originating from the in vitro test system was reproducible, characterizing PVDF as the mesh (among the 3 meshes investigated) with less foreign body reaction, scar formation, and inflammatory reaction at every single time point. Reinforced polypropylene (UltraPro) remained in second and polypropylene (TVT) in third position. This constant ranking was repeated along the entire experiment. In addition, the modified coated version of the 3 meshes revealed the same result at a lower level of the respective reactions (Figure 1). The entire experiment suggested a beneficial effect of plasma coating prior to implantation, which is shown in Figure 2. The extent of improvement remained variable in the different meshes.

Discussion

In vitro models to investigate biocompatibility features of alloplastic materials like meshes have limitations with regard to their predictability for in vivo surroundings. A mesh, per se, is a foreign body that induces a foreign body reaction. This foreign body reaction is triggered by the initial acute phase reaction and the subsequent construction of the implant matrix, mostly conducted by migration of fibroblasts producing glycosaminoglycans and collagen. There is controversy about which implant-induced reactions are desirable and which are not. The development of new meshes should be based on a solid understanding of the mechanisms of foreign body reaction.[9] In our in vivo study, the histologic investigations

Table 2. Inflammatory Infiltration[a]

	3 Months		6 Months		12 Months		24 Months	
Mesh	Native	Coated	Native	Coated	Native	Coated	Native	Coated
UltraPro	25 ± 11	20 ± 8	24 ± 7	19 ± 5	21 ± 10	17 ± 4	22 ± 11	18 ± 6
TVT polypropylene	35 ± 12	33 ± 10	32 ± 8	30 ± 6	33 ± 14	26 ± 9	28 ± 8	28 ± 12
Polyvinylidene fluoride (PVDF)	20 ± 9	16 ± 4	21 ± 9	17 ± 8	14 ± 9	13 ± 6	15 ± 6	12 ± 2

[a]Standard deviations are shown for every single measurement. Thickness of the infiltrate is displayed in micrometers (μm).

Table 3. Connective Tissue Infiltration[a]

	3 Months		6 Months		12 Months		24 Months	
Mesh	Native	Coated	Native	Coated	Native	Coated	Native	Coated
UltraPro	33 ± 18	24 ± 4	32 ± 7	24 ± 11	40 ± 19	33 ± 12	38 ± 13	34 ± 7
TVT (polypropylene)	37 ± 12	30 ± 17	36 ± 8	28 ± 12	43 ± 14	20 ± 19	41 ± 10	24 ± 12
Polyvinylidene fluoride (PVDF)	25 ± 12	19 ± 7	22 ± 9	23 ± 10	22 ± 9	17 ± 9	24 ± 5	19 ± 3

[a]Standard deviations are shown for every single measurement. Thickness of the infiltrate is displayed in micrometers (μm).

Table 4. Macrophages (CD68)[a]

	3 Months		6 Months		12 Months		24 Months	
Mesh	Native	Coated	Native	Coated	Native	Coated	Native	Coated
UltraPro	34 ± 6	34 ± 9	28 ± 11	26 ± 12	25 ± 6	19 ± 4	22 ± 4	18 ± 6
TVT (polypropylene)	36 ± 12	26 ± 11	33 ± 9	19 ± 3	23 ± 4	18 ± 5	20 ± 6	21 ± 7
Polyvinylidene fluoride (PVDF)	24 ± 4	22 ± 8	18 ± 7	16 ± 3	18 ± 8	14 ± 2	16 ± 5	15 ± 1

[a]Standard deviations are shown for every single measurement. Values are percentages of recognizable cells at the implant surface.

for inflammatory infiltrates show a slight reaction associated with PVDF, which increases in reinforced polypropylene (UltraPro) and even more in native polypropylene (TVT). This reduced inflammatory reaction can be considered an expression of good biocompatibility. However, this observed postoperative sign of an inflammatory reaction was noninfectious as counts for cells involved in infectious immune defense as CD3 remained unaltered at low levels.[10] In addition, when investigating connective tissue, the same trend is observable: PVDF exhibits the thinnest layer for connective tissue, followed by reinforced polypropylene (UltraPro) and polypropylene (TVT). We observe a macrophage decrease in all meshes along postoperative follow-up; however, the highest number of macrophages was seen in the TVT meshes and the in vitro ranking was consistent regarding this marker. Macrophages are key mediators, involved in the foreign body immune reaction, suggesting that this reaction has been stronger in polypropylene (TVT) than in the other 2 applied meshes. With regard to the 3 investigated parameters, macrophage invasion, inflammatory tissue, and connective tissue formation, in this study, the previously established in vitro ranking of the 3 investigated meshes was confirmed and repeated along the entire animal experiment after 3, 6, 12, and 24 months respectively. Moreover, when modifying the meshes by preimplant coating with autologous plasma, the ranking remained constant. This supports the assumption that the recently developed tissue culture in vitro test system for meshes is able to predict the in vivo performance of meshes. Practically, the test system helps to distinguish between meshes with good and reduced healing performance. The previously described in vitro test system was sterile, thus no physiological in vivo reaction as foreign body reaction or inflammation could be imitated.[5] This indicates that the adherence ability of a mesh is crucial for subsequent foreign body reactions or inflammatory processes that define the meshes in vivo performance. In addition, as in the in vitro approach, we did not see individual recipient features influencing the meshes perfor-

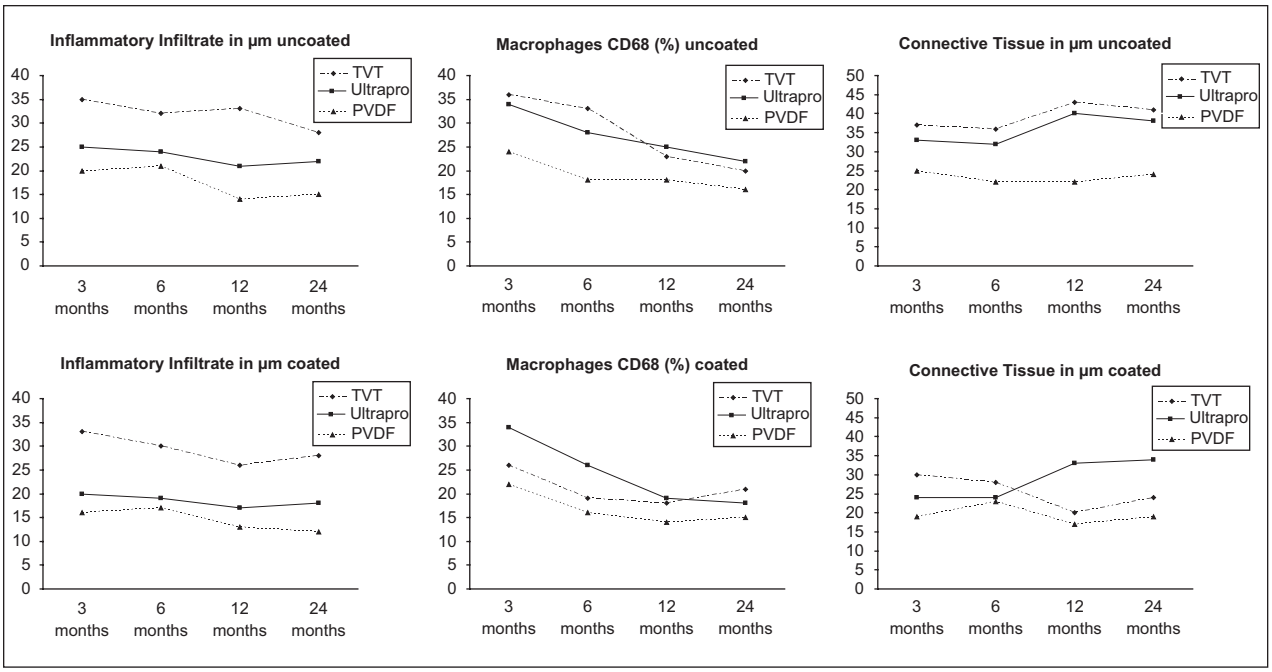

Figure 1. In vivo ranking of polyvinylidene fluoride (PVDF), polypropylene (TVT), and reinforced polypropylene (UltraPro) meshes
High extent of inflammatory reaction, macrophages count, and connective tissue is related to reduced biocompatibility.

mance. Besides quality issues of the material, we assume that the processes that determine the meshes toward a foreign body reaction must have occurred in the early period, before 3 months, after implantation since there was no more trend change during the following explantations. In a recent comparable long-term study in sheep, Zinther et al[11] investigated the shrinkage of intraperitoneal onlay mesh using coated polyester mesh versus covered polypropylene mesh. Besides individual differences of the investigated meshes they describe a peak for shrinkage at 3 months without additional shrinkage in the following 15 months, suggesting an early effect. This is in accordance with our results, which indicate an early process being responsible for the extent of a foreign body reaction and the mid- and long-term performance of an implanted mesh. This trend is independent of the location of the mesh in the body, although its particular extent varies depending on the site of implantation. Although those results have to be confirmed in larger series this could be a novel approach to predict the bio-performance and integration of any available mesh, just using a standardized in vitro experiment.

Several animal studies have been proposed and reported to investigate local reactions after implantation of mesh graft. To the best of our knowledge the present study is the first experimental study conducted in sheep, with a 2-year observation period. Using sheep as animal model has various advantages. Biological behavior of human cells is comparable to cells in the sheep model. Compared with other large-size animals, sheep demonstrate limited growth potential, while the trend to adhesion formation (intra-abdominally) is similar to humans.[12,13] In our study, we did not observe a specific reaction triggered by lymphocytes (B- and T-). Thus, it is very unlikely that the different lymphocyte status of sheep versus human may have had important influence on the in vivo biocompatibility performance. However, to exclude this potential bias, experiments in primates would be necessary, although very unrealistic. Given the advantages mentioned, the sheep model has potential to serve as a template in future experimental mesh studies, in particular when assessing meshes in the abdominal cavity but also other intracorporal locations. Nowadays, data on adequate functional performance and material safety are in the focus of premarket review for mesh devices. Thus, preclinical investigations in terms of bench and/or animal testing are currently used to confirm that engineering specifications are met and that the material chosen for a mesh is biocompatible. Unfortunately, clinical performance data are rarely used to support clearance for meshes for whatever indication.

In the study presented here, we could show the predictive value of a recently developed in vitro cell culture approach for biocompatibility assessment of meshes when translating it to in vivo circumstances. In a second attempt, we investigated coating approaches for meshes to improve their biocompatibility. In preliminary experiments, mesh coating with autologous plasma was shown

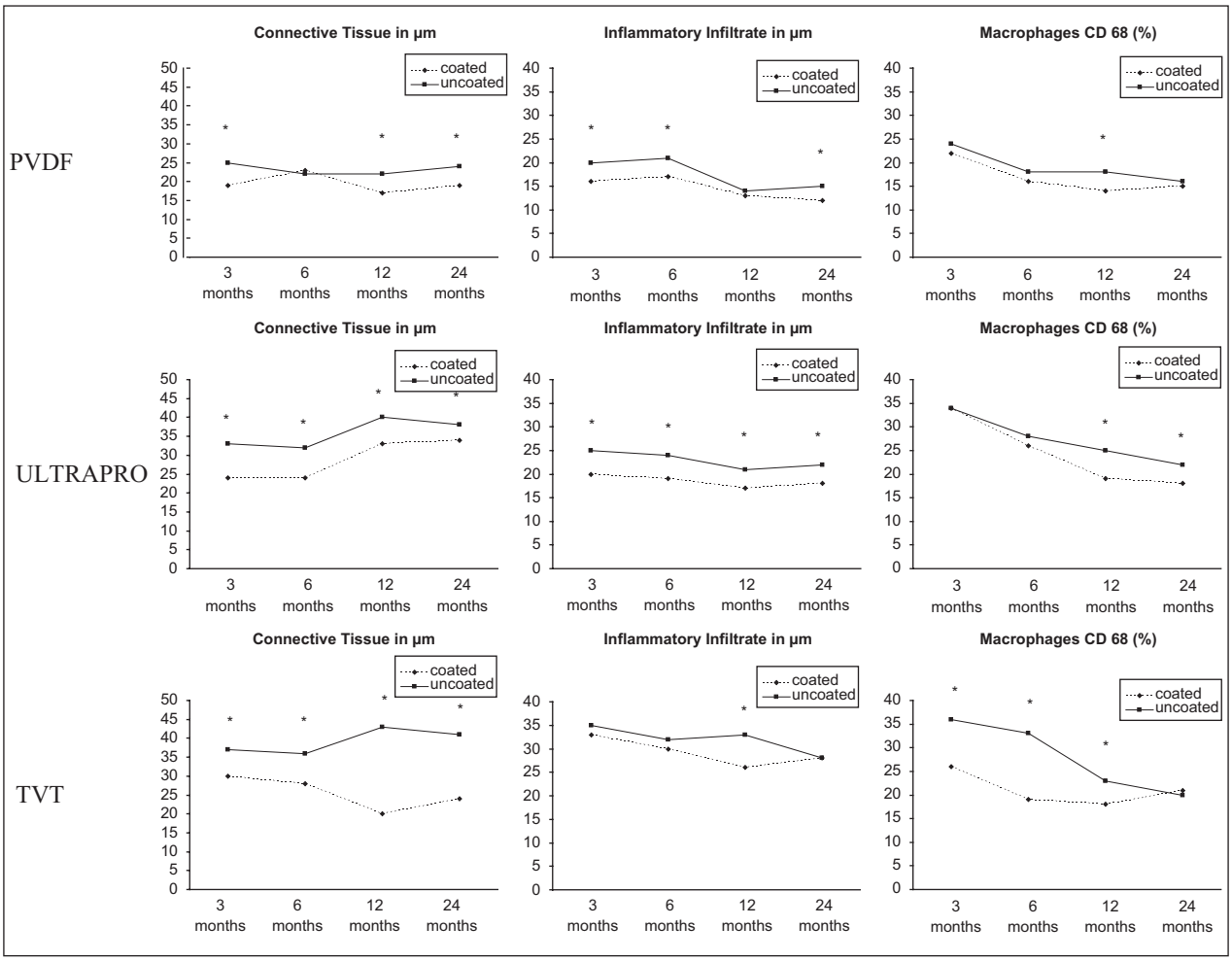

Figure 2. Effect of plasma coating prior to implantation
High extent of inflammatory reaction, macrophages count, and connective tissue is related to reduced biocompatibility. Statistically significant differences in thickness of connective tissue or inflammatory infiltrate and percentage of invading macrophages are indicated by an asterisk (*; corresponding to $P < .05$).

to reduce foreign body reactions in vitro and in vivo.[14] Here, we can show that the influence of plasma coating seems to have a consistent improving effect on the performance of the mesh regarding connective tissue development and inflammatory local reaction at the implant site, thus suggesting an improved biocompatibility. This preclinical in vivo study was initially inspired by the first FDA warning of unexpected and severe adverse events when using mesh devices.[1] We raised the question if the performance of a mesh would be predictable prior to its implantation in order to reduce the probability of unexpected mid- and long-term events as reported and complemented in 2011.[2] Although we did not selectively investigate meshes for the indications reported as pelvic organ prolapse and stress urinary incontinence, our system (in vivo and in vitro) may easily be used with every available mesh. However, in a considerably narrow time frame as reaction to the first FDA warning we developed an in vitro approach, a subsequent animal study and are now translating our results into a clinical trial. This is to conform to the recommendations of IDEAL, and shows how surgical research may be concluded (independent from any result) when strictly driven following standardized recommendations. McCulloch[15] specified the recommendations concerning IDEAL to the field of urology. Although not mentioned in his review, we would add mesh implementing procedures to be an interventional option as topic of current controversy and debate in urology/urogynecology, not only for safety purposes but also for effectiveness considerations.[16-19]

Conclusion

The recently developed in vitro test system for biocompatibility of meshes may predict in vivo performance of the meshes in a sheep model. This effect is independent

of the location of the mesh in the body, although its particular extent varies dependent on the site of implantation. Coating of meshes with autologous plasma prior to implantation seems to have a positive effect on the meshes biocompatibility.

Acknowledgment

Special appreciation is reserved for Dr S. Schauseil for assistance in planning this study and advice on microbiological issues.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article:

Bernhard Lammers has consultancy agreements with Johnson & Johnson and FEG Textiltechnik GmbH (Germany).

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article:

This work was partly supported by the DAAD/DFG (German Research Foundation) ID50753662.

References

1. US Food and Drug Administration. FDA safety communication: Update on serious complications associated with transvaginal placement of surgical mesh for pelvic organ prolapsed. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm262435.htm. Accessed December 26, 2012.
2. US Food and Drug Administration. FDA public health notification: Serious complications associated with transvaginal placement of surgical mesh in repair of pelvic organ prolapse and stress urinary incontinence. http://www.fda.gov/medicaldevices/safety/alertsandnotices/publichealthnotifications/ucm061976.htm. Accessed December 26, 2012.
3. Dietz HP, Vancaillie P, Svehla M, Walsh W, Steensma AB, Vancaillie TG. Mechanical properties of urogynecologic implant materials. *Int Urogynecol J Pelvic Floor Dysfunct*. 2003;14:239-243.
4. Afonso JS, Martins PA, Girao MJ, et al. Mechanical properties of polypropylene mesh used in pelvic floor repair. *Int Urogynecol J Pelvic Floor Dysfunct*. 2008;19:375-380.
5. Gerullis H, Georgas E, Eimer C, et al. Evaluation of biocompatibility of alloplastic materials: development of a tissue culture in vitro test system. *Surg Technol Int*. 2012;21:366-372.
6. Barkun JS, Aronson JK, Feldman LS, et al. Evaluation and stages of surgical innovations. *Lancet*. 2009;374:1089-1096.
7. Ergina PL, Cook JA, Blazeby JM, et al. Challenges in evaluating surgical innovation. *Lancet*. 2009;374:1097-1104.
8. McCulloch P, Altman DG, Campbell WB, et al. No surgical innovation without evaluation: the IDEAL recommendations. *Lancet*. 2009;374:1105-1112.
9. Weyhe D, Belyaev O, Müller C, et al. Improving outcomes in hernia repair by the use of light meshes—a comparison of different implant constructions based on a critical appraisal of the literature. *World J Surg*. 2007;31:234-244.
10. Kaupp HA, Matulewicz TJ, Lattimer GL, Kremen JE, Celani VJ. Graft infection or graft reaction? *Arch Surg*. 1979;114:1419-1422.
11. Zinther NB, Wara P, Friis-Andersen H. Shrinkage of intraperitoneal onlay mesh in sheep: coated polyester mesh versus covered polypropylene mesh. *Hernia*. 2010;14:611-615.
12. Ewoldt JM, Anderson DE, Hardy J, Weisbrode SE. Evaluation of a sheep laparoscopic uterine trauma model and repeat laparoscopy for evaluation of adhesion formation and prevention with sodium carboxymethylcellulose. *Vet Surg*. 2004;33:668-672.
13. Moll HD, Wolfe DF, Schumacher J, Wright JC. Evaluation of sodium carboxymethylcellulose for prevention of adhesions after uterine trauma in ewes. *Am J Vet Res*. 1992;53:1454-1456.
14. Eimer C, Gerullis H, Wishahi M, et al. Improved biocompatibility of meshes used for hernia incontinence and organ prolapse repair by plasma coating—results of in vitro and in vivo studies. *J Urol Suppl*. 2011;185:317.
15. McCulloch P. The IDEAL recommendations and urological innovation. *World J Urol*. 2011;29:331-336.
16. Iglesia CB, Sokol AI, Sokol ER, et al. Vaginal mesh for prolapse: a randomized controlled trial. *Obstet Gynecol*. 2010;116(2 pt 1): 293-303.
17. Sung VW, Rogers RG, Schaffer JI, et al; Society of Gynecologic Surgeons Systematic Review Group. Graft use in transvaginal pelvic organ prolapse repair: a systematic review. *Obstet Gynecol*. 2008;112:1131-1142.
18. Sand PK, Koduri S, Lobel RW, et al. Prospective randomized trial of polyglactin 910 mesh to prevent recurrence of cystoceles and rectoceles. *Am J Obstet Gynecol*. 2001;184:1357-1362.
19. Carey M, Higgs P, Goh J, et al. Vaginal repair with mesh versus colporrhaphy for prolapse: a randomised controlled trial. *BJOG*. 2009;116:1380-1386.