The lightweight and large porous mesh concept for hernia repair

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In modern hernia surgery, there are two competing mesh concepts which often lead to controversial discussions, on the one hand the heavyweight small porous model and on the other, the lightweight large porous hypothesis. The present review illustrates the rationale of both mesh concepts and compares experimental data with the first clinical data available. In summary, the lightweight and large porous mesh philosophy takes into consideration all of the recent data regarding physiology and mechanics of the abdominal wall and inguinal region. Furthermore, the new mesh concept reveals an optimized foreign body reaction based on reduced amounts of mesh material and, in particular, a significantly decreased surface area in contact with the recipient host tissues by the large porous model. Finally, recent data demonstrate that alterations in the extracellular matrix of hernia patients play a crucial role in the development of hernia recurrence. In particular, long-term recurrences months or years after surgery and implantation of mesh can be explained by the extracellular matrix hypothesis. However, if the altered extracellular matrix proves to be the weak area, the decisive question is whether the amount of material as well as mechanical and tensile strength of the surgical mesh are really of significant importance for the development of recurrent hernia. All experimental evidence and first clinical data indicate the superiority of the lightweight and large porous mesh concept with regard to a reduced number of long-term complications and particularly, increased comfort and quality of life after hernia repair.

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Surgical meshes today represent a group of implants used mainly for hernia repair. Modern hernia surgery is no longer imaginable without the application of these special biomaterials, leading to about 1 million implantations each year, worldwide. The net-like alloplastic mesh is used to close the hernial gap and, with extended overlap, to reinforce the abdominal wall.

Since the introduction of surgical meshes for hernia repair in 1959 by Usher [1–3], the main interest of hernia surgeons in the past decades was focused on surgical techniques to optimize hernia repair and the application of the mesh [4–8]. The surgical mesh itself, however, seemed to have little impact on the clinical outcome after hernia repair. The meshes themselves were regarded as biologically inert.

The trend changed in the early and mid 1990s in parallel with increasing numbers of case reports reporting mesh-related complications after heavy mesh-based hernia repair [9–12]. Today, minor local complaints such as seromas, discomfort and decreased abdominal wall mobility are accepted to be frequent and can be observed in about half of the patients. Serious complications such as recurrence, chronic and persisting pain as well as infection, including fistula formation are rare, but sometimes force a surgeon to remove the surgical mesh. Nevertheless, these complications have been the rationale to examine the role of the mesh in hernia repair in detail and to begin to investigate the biocompatibility of different mesh modifications and to challenge old mesh concepts. As a consequence, knowledge

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regarding the biocompatibility of different surgical mesh modifications has dramatically increased in the last 10 years since 1995, based on numerous experimental studies and clinical observations. Two basic problems had to be solved; first, to learn more about the physiology and the mechanics of the abdominal wall to be able to define basic elements of the textile structure and, second, to understand the significance of the mesh construction itself for the integration of the mesh into the recipient tissues after implantation.

As a consequence, today two major mesh concepts are distinguished, the classical concept including so-called heavyweight meshes with small pores and the new concept including lightweight meshes with large pores. Typically, the new mesh generation is characterized by a reduced weight (depending on the specific weight of the basic polymer), a pore size of more than 1 mm, an elasticity of 20–35% (at 16 N/cm) and a physiologic tensile strength of 16 N/cm at minimum.

Textile & mechanical features of heavy- & lightweight meshes

Small and large porous heavy- and lightweight mesh modifications both represent a totally different pathophysiologic view and concept of hernia repair (FIGURE 1, TABLE 1). Heavyweight meshes have been designed to guarantee a maximum mechanical stability, based on the idea of closing the hernial gap with a stiff, nonflexible device inducing maximum scar tissue [13,14]. In this concept the mesh itself and intense scar tissue formation ensure a durable and resistant repair of the hernia. Accordingly, meshes in the heavyweight group are designed with thick polymer fibers, small pores (<1 mm), a high tensile strength and a large surface area (FIGURE 1A).

In contrast, lightweight meshes are designed to mimic the physiology of the abdominal wall and the inguinal region [15,16]. Meshes in this group are produced with small polymer fibers, large pores (>1 mm) and a high flexibility (FIGURE 1B). The tensile strength is adapted to that of local tissues and the surface area in contact with the host tissues is low. A welcome and major side effect of the sensitive mechanical adoption of these meshes to the abdominal wall is a significant reduction of scar tissue formation resulting in a long-term flexible repair [16–18].

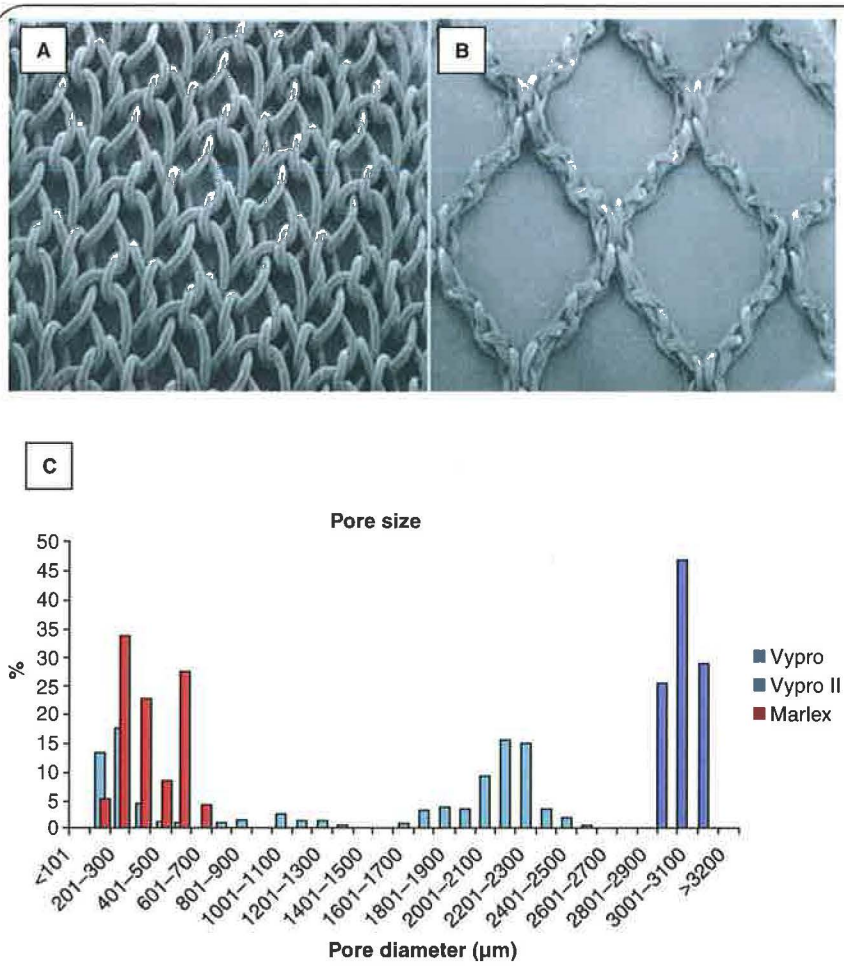

Figure 1. Typical textile structure of the heavyweight small porous mesh Marlex® (A) and the lightweight large porous mesh Vypro® **(B)** in scanning electron microscopy (127x). **(C)** Pore size analysis of Vypro, Vyproll® and Marlex; Vypro exhibits pore sizes between 3 and 5 mm (before absorption of the Vicryl® part), Vyproll between 1 and 2.5 mm (again before absorption of the Vicryl part) and Marlex between 0.2 and 0.7 mm.

Heavyweight meshes with small pores versus lightweight meshes with large pores

The question of what is the ideal mesh for hernia repair, at the very beginning of the development of the lightweight meshes, led to the following specification: the ideal mesh should; restore the abdominal function, be integrated physiologically into the abdominal wall based on a maximum of biocompatibility, be without serious long-term complications such as recurrence, infection or chronic pain and finally, have optimal handling characteristics for an easy, comfortable and safe hernia repair.

The restoration of abdominal wall function

The abdominal wall and the inguinal region, both main areas for hernia development, are complex systems of fascias and muscles. The whole system reveals certain rates of flexibility in different anatomic directions, which could be measured from autopsy specimens (FIGURE 2A). In order to define the physiologic requirements regarding elasticity, it could be shown that the mean distension at a physiologic strain of 16 N, ranges between 11 and 32% [19,20]. Textile analysis of heavyweight meshes revealed an elasticity of only 4–16% at 16 N (FIGURE 3, TABLE 2). Therefore, a restriction

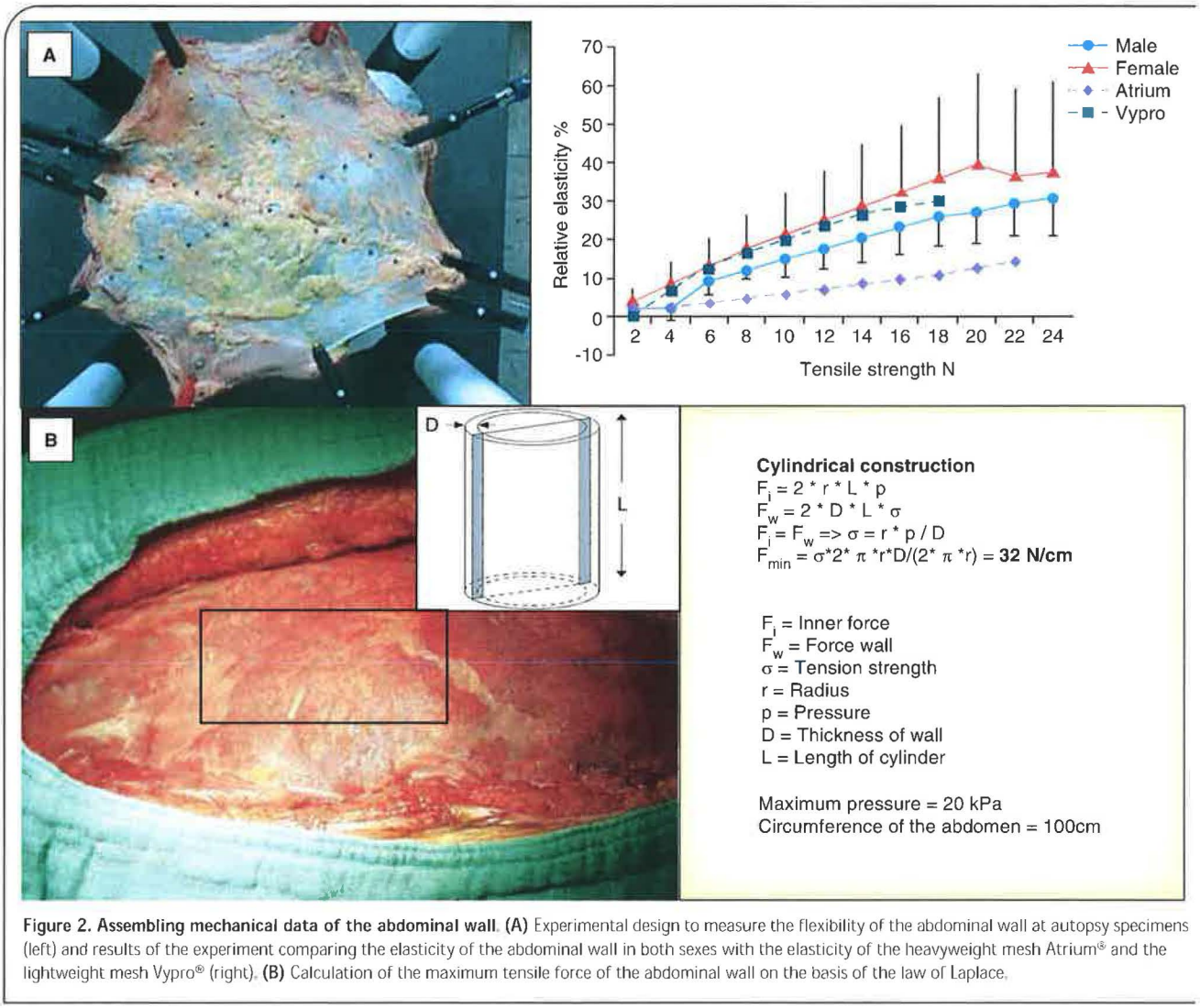

Figure 2. Assembling mechanical data of the abdominal wall. (A) Experimental design to measure the flexibility of the abdominal wall at autopsy specimens (left) and results of the experiment comparing the elasticity of the abdominal wall in both sexes with the elasticity of the heavyweight mesh Atrium® and the lightweight mesh Vypro® (right). **(B)** Calculation of the maximum tensile force of the abdominal wall on the basis of the law of Laplace.

of the abdominal wall is one consequence of the implantation of heavyweight meshes with low elasticity rates [16]. Flexible lightweight mesh constructions with similar elasticity to the abdominal wall demonstrate their superiority with respect to a physiologic abdominal wall repair [21].

After the introduction of the first lightweight mesh (Vypro®) to the German market, one main argument against the mesh appeared to be the significantly lower tensile strength compared with common heavyweight meshes. However, based on the law of Laplace, the tensile strength of surgical meshes for abdominal wall replacement in large hernias (where the mesh has to replace all structures of the abdominal wall and the fascia cannot be closed) is theoretically 32 N/cm at maximum (FIGURE 2B). In abdominal wall augmentation in small hernias (where the fascia can be closed), the tensile strength of the mesh can be reduced to 16 N/cm [19,22,23]. Tensile strengths of more than 100 N/cm of conventional heavyweight meshes are therefore disproportional and not required for an effective fascia closure or augmentation and lead to low flexibility with a subsequent restriction of the abdominal wall and discomfort of the patient (TABLE 2, FIGURE 3) [24,25]. Furthermore, the stiffness of heavyweight and small porous meshes may result in central mesh ruptures [26].

Integration into the abdominal wall: biocompatibility

Modern biomaterials including polymers are physically and chemically inert and stable, nonimmunogenic and nontoxic. However, not all these materials are biologically inert. In contradiction to their physical and chemical stability, the biomaterials trigger a wide variety of adverse responses *in vivo* including inflammation, fibrosis, calcification, thrombosis or infection. The quality of the inflammatory reaction to foreign bodies of a different nature is surprisingly constant, characterized by a rapid accumulation of huge numbers of phagocytic cells, in particular, blood monocytes and tissue-derived macrophages [27,28].

Today, it is not fully clear why inert and nonimmunogenic materials induce this type of inflammation known as a foreign body reaction (FBR). However, the protein absorption theory is

Table 1. A small selection of currently available heavyweight small porous, and lightweight large porous meshes.

Mesh	Producer	Polymer	Fiber
Heavyweight/small pores			
Marlex®	Bard, Inc., USA	PP	Mono
Prolene®	Ethicon, Inc., USA	PP	Mono
Atrium®	Atrium Med. Corp., USA	PP	Mono
Lightweight/Large Pores			
Vypro®	Ethicon GmbH, Germany	PP/PG910	Multi
UltraPro®	Ethicon GmbH, Germany	PP/Monocryl	Mono
TiMesh®	GFE, Germany	PP/Ti	Mono
Others			
DualMesh®	Gore, USA	ePTFE	Foil
Mersilene®	Ethicon, Inc., USA	PET	Multi

Mono: Monofilament; Multi: Multifilament; PET: Polyethylene-terephthalate; PP: Polypropylene.

widely accepted in biomaterial research and illustrates an underlying pathophysiologic process responsible for this typical type of chronic inflammation. The aim of this process is to isolate the foreign body or biomaterial from the host tissues by forming an artificial outside world at the site of implantation. The same mechanism is true in tuberculosis for example, here again the host is not able to remove the inflammatory agent namely *Mycobacterium tuberculosis*. The reaction is typical as well as relatively uniform with the formation of granuloma, which is generally found at the interface of implanted biomaterials as well. Characteristic of these granuloma are multinucleated giant cells that originate from fused macrophages and monocytes seeding on the foreign body–recipient host tissues interface [29].

Implant materials very quickly absorb a layer of host proteins after implantation – in a process lasting a few seconds, which occurs well before an initial cellular response to the biomaterial can be observed. It is generally believed that phagocytes interact with these spontaneously absorbed proteins rather than with the material itself. Immunologic activity from degraded proteins, secondary to their absorption of the biomaterial surface, triggers the activation of the attached phagocytes [27]. Depending on the physicochemical properties of the surface area of the implant and the type of absorbed proteins, the rate of protein degradation should be variable and, therefore generates a typical FBR for each type of implant. In particular, fibrinogen and fibrinogen-derived products beside albumin should play a major pathophysiologic role in the occurrence of FBR [28].

Finally, phagocytes may recognize the degradated proteins of the medical implants and respond by releasing a series of inflammatory and wound-healing responses commonly initiated by fibrin clot formation. The initial inflammatory burst caused by the release of a huge cocktail of potent inflammatory mediators attract other cell types including T-cells, polymorphonuclear and

Table 2. Textile and mechanical data of selected heavyweight (Prolene®) and lightweight (Vypro®, Vyproll® and UltraPro®) meshes.

Mesh	Structure	Polymer	Weight	Suture pull out force		Stamp pressure test	
			(g/m²)	*Longitudinal (N)*	*Vertical(N)*	*Burst pressure P max (mmHg)*	*% Stretching at 16 N/cm tension (%)*
Prolene®	Mono + SP	PP	80–85	116	145	1630	6
Vypro®	Multi + LP	PP§	25*	30	24	360	31
Vypro II®	Multi + LP	PP§	30*	40	31	430	28
UltraPro®	Mono + LP	PP§	28*	42	42	650	25

Note the significantly reduced stretching rate of Prolene® at 16 N/cm and the significantly increased burst pressure of the heavyweight mesh compared with all the lightweight meshes included. (Data provided by Ethicon GmbH, Norderstedt, Germany). *Remaining nonabsorbable part of PP. LP: Large pores; Mono: Monofilament; Multi: Multifilament; PP: Polypropylene; SP: Small pores.

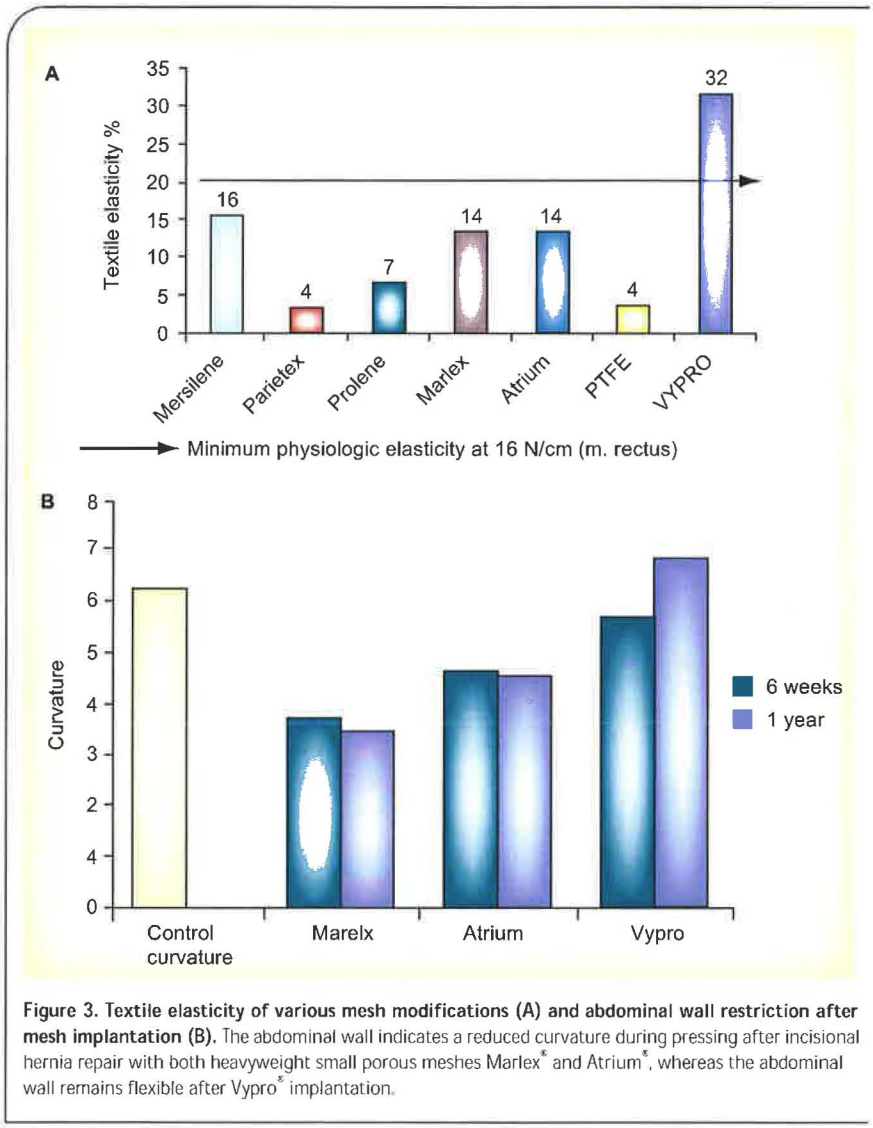

Figure 3. Textile elasticity of various mesh modifications (A) and abdominal wall restriction after mesh implantation (B). The abdominal wall indicates a reduced curvature during pressing after incisional hernia repair with both heavyweight small porous meshes Marlex® and Atrium®, whereas the abdominal wall remains flexible after Vypro® implantation.

eosinophilic granulocytes, plasma cells and fibrocytes [30]. Within a few days this cell cocktail forms the early granuloma with a characteristic stratification of cell layers which can also be identified during maturation recognized by the very typical foreign body giant cells and an outer layer of fibrosis (last stage of inflammation). Moreover, late granuloma is not a static type of chronic inflammation, but represents a chronic wound with an increased cell turnover even years after implantation [31,32]. Monocytes and tissue-derived macrophages at the interface and in contact with the polymer, undergo apoptotic cell death and are replaced by cells at the periphery.

Before the introduction of the lightweight large pore meshes, biocompatibility of meshes has generally been regarded as excellent. The fact that meshes induce a tissue response unfavorable for the outcome of the hernia repair has not been under discussion. Surgical mesh has been regarded as inert and biocompatible.

However, if the foregoing chapters on FBR are correct, surgical meshes should also show the typical inflammatory reaction. In fact, all experimental and clinical studies indicate a typical FBR at the interface of all mesh modifications on the market today [32].

The main polymers for the production of surgical meshes are polypropylene (PP), polyester (polyethylene-terephthalat [PET]) and expanded poly-tetra-fluoroethylene (ePTFE); all of which are nonabsorbable.

Mesh modifications made of PP are frequently used, the majority with small pores. Generally, PP is stable, nondegradable and with an acceptable biocompatibility resulting in a moderate chronic inflammation of the foreign body type with an intense fibrosis. PET histologically reveals an excellent biocompatibility with a decreased FBR compared with PP, however, the long-term stability PET is rather low due to hydrolytically splitting of the polymer. The rate of degradation of PET mesh modifications and its influence on the outcome of hernia repair remains unclear. In contrast to PP and PET, ePTFE again histologically indicates a good biocompatibility. Tissue integration of these patches depends on the microporous modification of one patch surface. Rarely, small particles of ePTFE are detached from the surface (in particular in mesh infection [33]), which may then be found phagocytized in macrophages colonizing the interface.

Due to the disadvantages of PET and ePTFE, today, most of the new mesh modifications are composed of PP. Special mesh modifications are hybrid meshes with an absorbable and nonabsorbable part made of Vicryl® (polyglactine 910) or Monocryl® (polyglecaprone 25). An upcoming new polymer PVDF (polyvinylidenflourid) demonstrates promising results in experimental animal studies [34–38].

However, the FBR depends not only on the polymer, but also the surface area in contact with the host tissues. The surface area again strongly depends on textile properties such as the pore size or the diameter and number of fibers used. The lightweight and large pore size meshes have less surface area than the heavyweight mesh group, consequently, the FBR in the lightweight mesh group is significantly reduced [39]. In addition to this significantly decreased typical chronic inflammatory reaction, the fibrotic reaction around the mesh in total as well as around each single mesh fiber is greatly reduced (FIGURE 4). The fibrotic reaction as a result of the inflammatory response, however, considerably influences the long-term quality of the hernia repair. Today the tissue response to the mesh is understood as a chronic wound persisting over many years at the interface of the

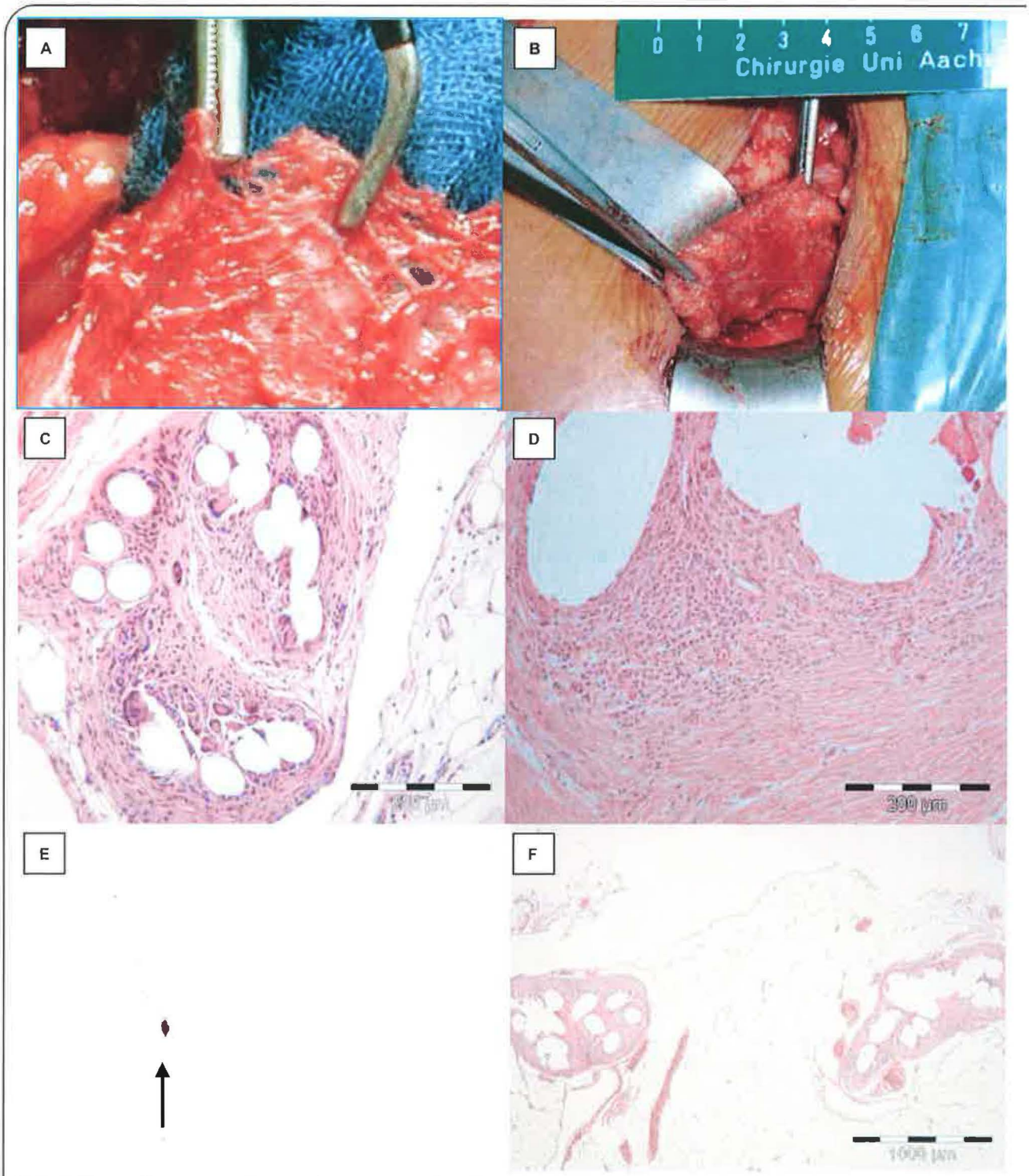

Figure 4. Macroscopical aspect after long-term implantation of a lightweight polypropylene mesh with large pores **(A)** and a heavyweight mesh with small pores **(B)**; note the thin fibrous layer around the lightweight mesh **(A)** all structures of the mesh are still visible. In some cases lightweight meshes with large pores are hardly to identify during relaparatomy, an observation leading to the idiom invisible mesh. In parallel, a specimen of a heavyweight mesh with small pores after long-term implantation **(B)** representing a fibrous mass composed of mesh and recipient tissue due to the increased fibrotic reaction. Typical histological response on lightweight **(C)** and heavyweight **(D)** Polypropylene meshes; note the significantly improved biologic response on the lightweight PP mesh with a significantly decreased chronic inflammation and fibrosis around the polymer fibers (both hematoxylin and eosin, 200×). Comparison of the fibrotic reaction after implantation of mesh modifications with small **(E)** and large pores **(F)**, note that the pores in **(E)** are filled with fibrous tissue skipping from one PP fiber to the next, a phenomenon called bridging; in **(F)** without bridging the mesh pores are filled with fat (both hematoxylin and eosin, 40×).

Table 3. Results of the postretrieval study including 347 explanted mesh specimens [23]; the total number of each mesh was set at 100%; percentage of major complications of each mesh modification leading to explantation of the mesh.

Mesh	Polymer	Features	Fibers	No.	Months	Recurrence (%)	Chronic pain (%)	Infection (%)	Fistula (%)
Mersilene®	PET	LW/SP	Multi	31	28	65	13	26	4
Marlex®	PP	HW/SP	Mono	90	26	57	34	22	8
Prolene®	PP	HW/SP	Mono	90	26	57	40	22	6
Atrium®	PP	HW/SP	Mono	64	20	67	33	17	9
Surgipro®	PP	HW/SP	Multi	17	24	70	35	17	9
Vypro®	PP/PG	LW/LP	Multi	34	15	82	6	12	0
GoreTex®	ePTFE	HW/SP		21	33	57	19	24	0
Total				*347*	*24*	*63*	*30*	*21*	*7*

ePTFE: Expanded poly-tetra-fluoroethylene; HW: Heavyweight; LP: Large pores; LW: Lightweight; Mono: Monofilament; Multi: Multifilament; PET: Polyethylene-terephthalate; PG: Polyglactine; PP: Polypropylene; SP: Small pores.

mesh and recipient tissues. In western countries there is increasing acceptance that the activity of this chronic wound should be diminished to the minimum where possible.

Long-term biocompatibility of surgical mesh: complications

Our knowledge concerning the long-term biocompatibility and tissue response of mesh in humans is still poor, although a few reports exist (FIGURE 5, TABLES 3 & 4). Nearly all of the data regarding the biologic behavior of these implants are obtained from animal experiments.

Postretrieval studies of implants allow the possibility to gain a deeper insight into the local tissue reaction after longer implantation intervals and to get an idea of the main complications of each implant type. Serious complications such as recurrence, chronic and persisting pain as well as infection (including fistula formation), are rare, but sometimes force the surgeon to remove a surgical mesh.

Since 1995 the authors have collected explanted meshes, which failed in hernia repair. Meanwhile, the authors' center has more than 700 explants of different meshes on record and has already analyzed more than 300. The results of the study are quite similar to data published in 2000 as a preliminary report with 121 specimens [32].

Briefly, the data demonstrate that heavyweight small porous meshes have to be explanted due to chronic pain more frequently than lightweight large porous meshes (e.g., 40% Prolene® vs. 6% Vypro). Fistula formation is only observed in the heavyweight mesh group. Recurrences can be observed in all mesh modification independently from the mesh construction. After a mean implantation interval of more than 26 months, 99% of all recurrences occurred at the edges and free margins of the mesh. Over 70% of all specimens explanted after recurrence revealed an altered ratio of collagen Types I and III [23], an observation which supports the hypothesis of ECM alterations as a major pathophysiologic reason of hernia recurrence. Furthermore, the data pool of the retrieval study demonstrates that the reaction of different hosts is highly different and individual. These data reflect that the individual reaction of the patient onto an implanted mesh depends on the genetic background of each host [40].

Table 4. Results of the postretrieval study including 347 explanted mesh specimens [23]; the total number of each mesh was set at 100%; biocompatibility assessment of each mesh modification after long-term implantation.

Mesh	Polymer	Features	Fibers	No.	Months	IF (PV %)	CT (PV %)	Ki67 (%)	Tunel (%)
Marlex®	PP	HW/SP	Mono	90	26	36	41	22	9
Prolene®	PP	HW/SP	Mono	90	26	30	31	19	7
Atrium®	PP	HW/SP	Mono	64	20	26	27	13	7
Surgipro®	PP	HW/SP	Multi	17	24	41	39	25	9
Vypro®	PP/PG	LW/LP	Multi	34	15	16	21	7	3
Total	-	-	-	*295*	*22*	*30*	*32*	*17*	*7*

CT: Connective tissue formation; ePTFE: Expanded poly-tetra-fluoroethylene; HW: Heavyweight; IF: Inflammatory infiltrate; Ki67: Ki67 positive, proliferating cells in the interface mesh/recipient tissues; LP: Large pores; LW: Lightweight; Mono: Monofilament; Multi: Multifilament; PET: Polyethylene-terephthalate; PG: Polyglactine; PP: Polypropylene; SP: Small pores; Tunel: Tunel-positive, apoptotic cells in the interface mesh/recipient tissues.

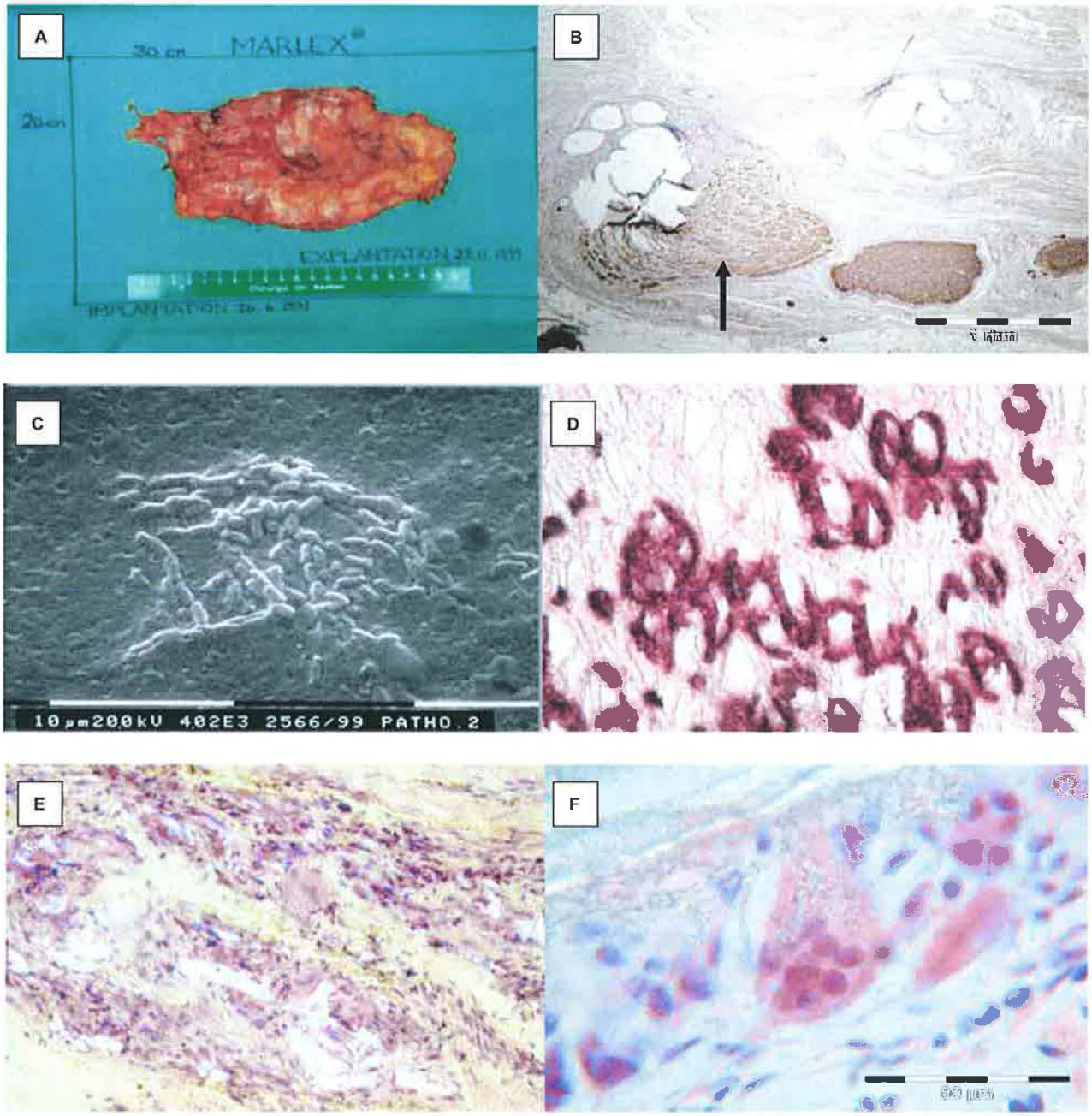

Figure 5. (A) Example of mesh shrinkage after long-term implantation. The mesh surface area was reduced from 20 × 30 cm to 10 × 20 cm after an implantation period of approximately 8 years; it is not the mesh itself undergoing the process of shrinkage, the phenomenon is a result of contracting scar tissues around the mesh. **(B)** Chronic pain in the majority of cases is the result of nerve impairment during implantation, in particular, by clips during fixation or by the mesh itself; in the authors' postretrieval study the involvement of nerve fibers was found in more than 60% of all mesh specimens removed due to chronic pain; in the given example, the mesh traumatically disturbed the nerve, finally forming a post-traumatic neuroma (arrow; S100, 40×). **(C)** Scanning electron micrograph (4020×) indicating a major reason for late mesh infection: persisting bacteria of the staphylococcus family; in the actual example, the mesh was removed 6 years after implantation due to recurrence without signs of infection. **(D)** A frequent observation after long-term implantation in the authors' postretrieval study are calcifications, especially in GoreTex® and heavyweight polypropylene meshes with small pores. **(E)** Long-term stability of polyethylene-terephthalate is still under discussion in hernia surgery, whereas degradation of polyethylene-terephthalate in vascular prosthesis is a well known phenomenon; in the given example the polyethylene-terephthalate mesh Mersilene® has been implanted for approximately 6 years; after explantation the authors only found polyethylene-terephthalate fragments phagocytized by macrophages (hematoxylin and eosin, 400×). **(F)** Expanded poly-tetra-fluoroethylene histologically elicits an excellent tissue response with a minor chronic inflammatory and fibrotic response on the polymer; microporous ePTFE mesh of the newer generation with an improved tissue in-growth after 3 years of implantation and small detached polymer particles phagocytized by macrophages (hematoxylin and eosin, 400×).

Shrinkage

At the beginning, the concept of shrinkage of the mesh was enthusiastically debated. However, there is now a broad acceptance that shrinkage is a common phenomenon after mesh implantation [41–43]. It is not the mesh that shrinks, but the surface reduction is due to a simple retraction of the fibrotic scar tissues around the mesh. Retraction of the scar is a physiologic reaction of maturing scar started by a constant water loss and a subsequent surface-area decrease to an average 60% of the former wound region. It has been assumed that lightweight meshes with a notably decreased fibrotic tissue reaction demonstrate a lesser degree of shrinkage, a hypothesis that still has to be confirmed. Nevertheless, shrinkage is highly important for the repair technique. Sufficient long-term hernia repairs can only be performed with large meshes overlapping the hernia gap by a minimum of 5 cm each side (FIGURE 5A) [44–46].

Fibrotic bridging

Fibrotic bridging is a phenomenon which is, in the authors' opinion, closely associated with the occurrence of shrinkage. Moreover, the incidence of bridging is unrelated to the textile structure of the mesh. Bridging occurs in all mesh modifications with a granuloma size around each mesh fiber exceeding more than half of the pore size of the mesh [47]. Usually, the phenomenon of bridging is observed in all mesh modifications with pore sizes of less than 1 mm. In all of these cases a granuloma of one fiber starts to become confluent with granuloma formations of the adjacent fibers and thus eventually the whole mesh is incorporated into a larger area of granuloma side by side. Granulomas side by side, however, elicit a common outer fibrotic capsule joining each mesh fiber and forming a scar plate covering the whole mesh (FIGURE 4E & 4F). The scar plate again results in the mesh becoming stiff and nonflexible. Conversely, stiff and nonflexible mesh repairs appreciably manipulate the abdominal wall function and quality of life.

Fibrotic bridging is mostly found in heavyweight small pore size meshes. Due to the parallel orientation of the scar formation to the mesh axis, theoretically, shrinkage in meshes with bridging should be more intense – a theory to be proved in the future.

In contrast, lightweight meshes with large pores are constructed in such a way that the granuloma is always notably smaller than half of the pore size. In some of these meshes, the pore size was increased more than six-times compared with the conventional heavyweight meshes, such that bridging is not possible. Lightweight large pore size mesh modifications are characterized by a localized fibrotic reaction around the mesh fibers, with small granulomas allowing the mesh to stay flexible and smooth after implantation.

Recurrence

In approximately 60% of all retrieved surgical meshes, recurrence is the reason why meshes are explanted [32]. Today, clinical studies indicate that recurrence rates of hernia repair based on the use of surgical meshes are significantly decreased compared with suture repair. However, the same clinical studies reveal increasing recurrence rates over time for all types of hernia repair. Essentially, these findings may be interpreted to suggest that today, none of the procedures currently used protects the patients completely from recurrence but the use of surgical mesh decreases their incidence [4,48].

In the postretrieval study the effectiveness of common mesh modifications on the market is comparable concerning recurrence and infection rate. Here, only the rate of recurrences in the Vypro mesh group seems to be higher, as this mesh is mainly used in incisional hernia and, in particular, this lightweight mesh indicates significantly decreased rates of chronic pain (TABLES 3 & 4).

Recurrence following mesh implantation appears after 26 months (mean value, range 3–180 months). The recurrent hernia develops in 99% of all cases at the free edges of the mesh, emphasizing again the importance of a sufficient overlap of mesh and hernia gap. Hernias in the area of the mesh seem to be rare exceptions.

The main reasons for the recurrences are technical faults during the operation (e.g., inadequate fixation in the first 2 weeks after implantation and insufficient overlap), the shrinkage of the mesh after implantation and, finally, alterations of the ECM that are still under investigation in hernia patients. All data from ECM research in these patients indicate an altered collagen metabolism (decreased ratio collagen I/III) in the majority of patients with recurrent hernia [49–55].

The ratio and extent of intermolecular cross-linkage between collagen Type I and III influences the tensile strength and mechanical stability of connective and scar tissues [56,57]. Hernias are therefore more common in patients with collagen disorders such as Marfan's and Ehlers-Danlos syndrome, cutis laxa, osteogenesis imperfecta and hip dislocation in childhood [58,59]. Other factors suggested to influence the collagen I/III ratio and the recurrence rate of hernias are age, sex, smoking and genetic factors [23].

Chronic pain

Chronic pain is an upcoming issue in the field of hernia repair and will probably become the most important topic to be discussed and addressed by the responsible surgeons [11,60–63]. Clinical trials report high percentages of patients with chronic pain after hernia repair, including mesh repair. In contrast to neuropathy-related complaints after intraoperative damage of nerve fibers with pain immediately after surgery, the onset of chronic pain as a consequence of the FBR is typically more than 1 year after hernia repair.

In the postretrieval study, most explants from all the patients with chronic pain in their medical history, indicate nerve fibers and fascicles in the interface of the mesh [23]. Today, immunohistochemical stains allow the detection of even the smallest nerve structures that are mainly found in or around the foreign body granuloma. Due to the nature of the granuloma as a chronic inflammation, it may be speculated that these nerve structures are irritated by the inflammation and cause the sensation of pain. In some cases real traumatic

neuroma can be found at the interface of the mesh–recipient tissues, an indicator of the mechanical destruction of the nerve by the mesh (FIGURE 5B).

In total, all mesh modifications with small pores reveal unacceptably high rates of chronic pain in the retrieval study, in particular, all heavyweight PP meshes (TABLES 3 & 4). Vypro, a lightweight large pore-constructed mesh, demonstrates a dramatically reduced surface area compared with all common mesh modifications on the market. In combination with a favorable foreign body reaction, the small surface area leads to a minimum of nerve irritation and destruction.

Infection

Infection is the third major complication after mesh implantation [12]. Due to the results of the retrieval study, all mesh modifications seem to have similar infection rates. Multifilament mesh constructions as well as microporous ePTFE patches reveal no higher rates of infection as the reason for explantation. Furthermore, scanning electron microscopy studies indicate that colonies of bacteria including biofilm-forming colonies of *Staphylococcus epidermidis* from skin, persisting at the surface of the polymer fibers may be responsible for late infection months or, in rare instances, years after the initial operation (FIGURE 5C).

Fistula & adhesion formation

Fistula and adhesion formation belong to the most serious complications after mesh repair [64,65]. In particular, after intraperitoneal mesh application, adhesions and fistulas are mainly observed in the heavyweight small pore PP mesh group, however, they have also been observed following extraperitoneal mesh implantation [66]. ePTFE appears to have favorable biologic behavior; therefore, GoreTex® mesh modifications have currently been the first choice in all intraperitoneal techniques (IPOM) for incisional hernia repair. However, in the last few years a number of special mesh modifications have been introduced to the market for intraperitoneal hernia repair which seem to have some considerable advantages compared with ePTFE patches. These new mesh modifications mainly work due to different types of films and surface modifications to prevent adhesion of the intestines (e.g., Proceed® or Parietene Composite®) or at least with new antiadhesive polymers like PVDF (DynaMesh® Ipom). Beside enhanced anti-adhesive properties, the generation of new IPOM meshes fulfils all the criteria of modern lightweight meshes with large pores. In particular, the flexibility of the IPOM mesh is of importance in consideration of large defect areas in incisional hernia repair.

Calcification & degradation

Degradation of surgical meshes is rare [23]. Mostly, calcifications are observed after long-term implantation, especially in heavyweight small pore PP meshes as well as in microporous ePTFE (FIGURE 5D). Calcifications are probably due to small porous or even microporous mesh modifications because until now, calcifying depositions have not been observed in large porous constructions. It may be speculated that particularly the small pores disturb local metabolism and substrate exchange leading to a bradytrophic area with increased tendency to calcificate.

Real degradation of the mesh fibers is mainly observed in PET meshes after long-term implantation (FIGURE 5E). Incorporated PET can be degraded hydrolytically, finally resulting in an increased brittleness of the polymer with a loss of the mechanical features. Even ePTFE reveals an increased fragility after long-term implantation. In some explants, small fragments phagocytized by local macrophages were observed (FIGURE 5F).

Handling characteristics

Handling characteristics of lightweight meshes have been improved over the last few years. In particular, the first lightweight large porous mesh, Vypro, seemed to most surgeons to be too soft and smooth for a safe, comfortable and quick hernia repair. Lightweight meshes of the second generation present more stable textile structures or are combined with nonabsorbable polymers to adopt mesh features exactly to the requirements in hernia surgery.

The new generation: lightweight & large porous meshes

Vypro® & Vypro II®

The concept of lightweight large porous meshes for hernia repair was first realized in 1998 with the introduction of Vypro and later Vypro II® by Ethicon, Germany. These meshes represent the first attempt to create a mesh to meet the physiological demands. The amount of remaining material was reduced to approximately 30% of common heavyweight meshes (Vypro 25 g/cm^2 vs. Prolene® 80–85 g/cm^2, TABLE 2) and the pore size was increased by up to 500–600% (Vypro 3–5 mm vs. Prolene® <1 mm, TABLE 2). The nonabsorbable part is composed of multifilament PP combined with an absorbable part made of Vicryl® (PG 910), which is nearly doubled in Vypro II. (Vypro: PP 27g/m^2 and PG 910 27g/m^2; Vypro II: PP 35g/m^2 and PG 910 45g/m^2). The Vicryl® part will be absorbed within the first 6 weeks after implantation and has been added to the nonabsorbable PP to ensure appropriate handling characteristics for the surgeon.

Generally, the construction of Vypro is calculated to augment the abdominal wall and is not designed for complete abdominal wall replacement in large inguinal or incisional hernias. In larger hernias without the possibility to close the fascia Vypro II or another lightweight mesh with a tensile strength of more than 32 N/cm should be used.

First clinical trials confirm the expected superiority of the lightweight large porous mesh concept concerning quality of life after hernia repair [25].

Polypropylene

Most manufactures have added to their range of PP heavyweight small porous mesh modifications, a lightweight large porous adaptation. There are also, numerous monofilament PP meshes on the market, which fulfill all of the criteria for a flexible lightweight mesh with reduced material. An older member

of this group is the Parietene® mesh, a brand new member is the Dynamesh®. In particular, the Dynamesh is matched to the physiologic values with reference to pulling forces and flexibility of the abdominal wall. The textile structure of the warp-knitted mesh generates excellent handling characteristics. All meshes in this group are produced of fibers reduced in diameter and pores of more than 2 mm compared with the heavyweight PP group.

Biocompatibility of the new generation of lightweight PP meshes in experimental studies is acceptable with a significantly decreased FBR and only a minor fibrotic reaction around the PP mesh fibers after long-term implantation in rats (FIGURE 6A). However, clinical trials have yet to confirm the promising preclinical results [43].

TiMesh® light & extra light

TiMesh® light (35 g/m^2) and TiMesh® extra-light (16 g/m^2) represent newer members in the lightweight large porous mesh family. The special feature of these meshes is a surface modification with titanium, which is bound to the PP surface. The basic mesh is a monofilament PP mesh with an average diameter of 67 µm of each single PP fiber and pores of more than 1 mm.

Both mesh modifications were announced as a revolution on the mesh market and have the best biocompatibility possible. Indeed, the titanium-modified meshes exhibit a significantly increased biocompatibility compared with conventional heavyweight small porous meshes [43], however, if the biocompatibility of both titanium meshes is compared with simple lightweight large porous PP meshes without surface modification, the biocompatibility is equal. Basically, titanium modification of the PP surface has no significant effect on FBR in soft tissue contact. This phenomenon has independently been described by the authors' group (Hernia, in press; FIGURE 6B) and by Lehle and colleagues in 2004 [67]. Another important disadvantage of the TiMesh extra-light is a tensile strength of 12 N/cm, a value significantly lower than the calculated minimum of 16 N/cm.

UltraPro®

UltraPro® represents the newest member in the lightweight large porous mesh group. The mesh is constructed of a monofilament lightweight large porous PP mesh with pores of more than 3 mm. An absorbable Monocryl® (polyglecaprone 25) component is added to improve handling characteristics and to optimize implantation and increased tensile strength in the first weeks of the repair.

Monocryl (polyglecaprone 25) is a monofilament derived from a segmented copolymer of ε-caprolactone and glycolide. This complex polymeric system contains soft segments of a random copolymer of ε-caprolactone and glycolide, which provide good handling characteristics and hard segments of polyglycolide that provide high strength. Both hard and soft segments are combined in the same polymeric chain. Evaluating the toxicity potential of Monocryl sutures, no genotoxic, cytotoxic, teratogenic, irritating or allergic effects were found. As suture material it was introduced in 1995 and since then it demonstrated many preferable qualities including a significantly lowered tissue reaction in the early phases of wound healing compared with polyglactine 910 (Vicryl). Monocryl is essentially absorbed without increased cellularity, inflammatory and fibrotic reaction within 84–140 days (FIGURE 6C–F). Interestingly, the supplement of PP with Monocryl leads to significantly decreased FBR compared with simple lightweight large porous PP meshes with identical textile structure; an effect still under investigation. Overall, the Monocryl-PP-composite UltraPro is currently the member of the lightweight large porous mesh family with the lowest FBR and optimized handling. The first clinical studies produced encouraging results to move forward with this mesh concept [68].

Expert opinion

The lightweight large porous mesh concept is one of the most important developments in hernia surgery of the last decade. Mesh modifications of this group represent implants for hernia repair with an optimum of biocompatibility. The new lightweight large porous mesh generation should reveal significant advantages in the field of patient comfort and chronic pain.

More important new data indicate hernias (in general and recurrent hernias in particular) to be a disease of the connective tissues and the ECM. These findings explain why meshes cannot protect the patients completely from recurrence and tell us that we have to learn more about basic pathophysiologic processes of hernia formation. These data will be essential for future mesh modifications and to define populations at risk.

Five-year view

The next 5-year interval in hernia research will give further insight into the advantages or disadvantages of both mesh concepts. Important ongoing clinical studies including multicenter trails will be finished and provide corresponding data.

Furthermore, other nonflat mesh modifications such as plugs or whole systems for hernia repair will be rebuilt with large porous textile structures.

The next generation in hernia meshes will be a bioactive implant. These meshes of the third generation (behind the heavyweight meshes of the first and the lightweight meshes of the second generation) will probably consist of an optimized lightweight large porous mesh construction with chemical and biologic surface and polymer modifications which directly influence hernia development or recurrence. The next 5 years will finish the lightweight mesh period and will introduce a new epoch in hernia and mesh research with the formation of interdisciplinary research groups including basic scientists in biology, polymer chemistry and tissue engineering, as well as pathologists and surgeons. Only these groups will be able to illuminate the complex pathophysiology of hernias and use newest technologies to create the bioactive mesh of tomorrow.

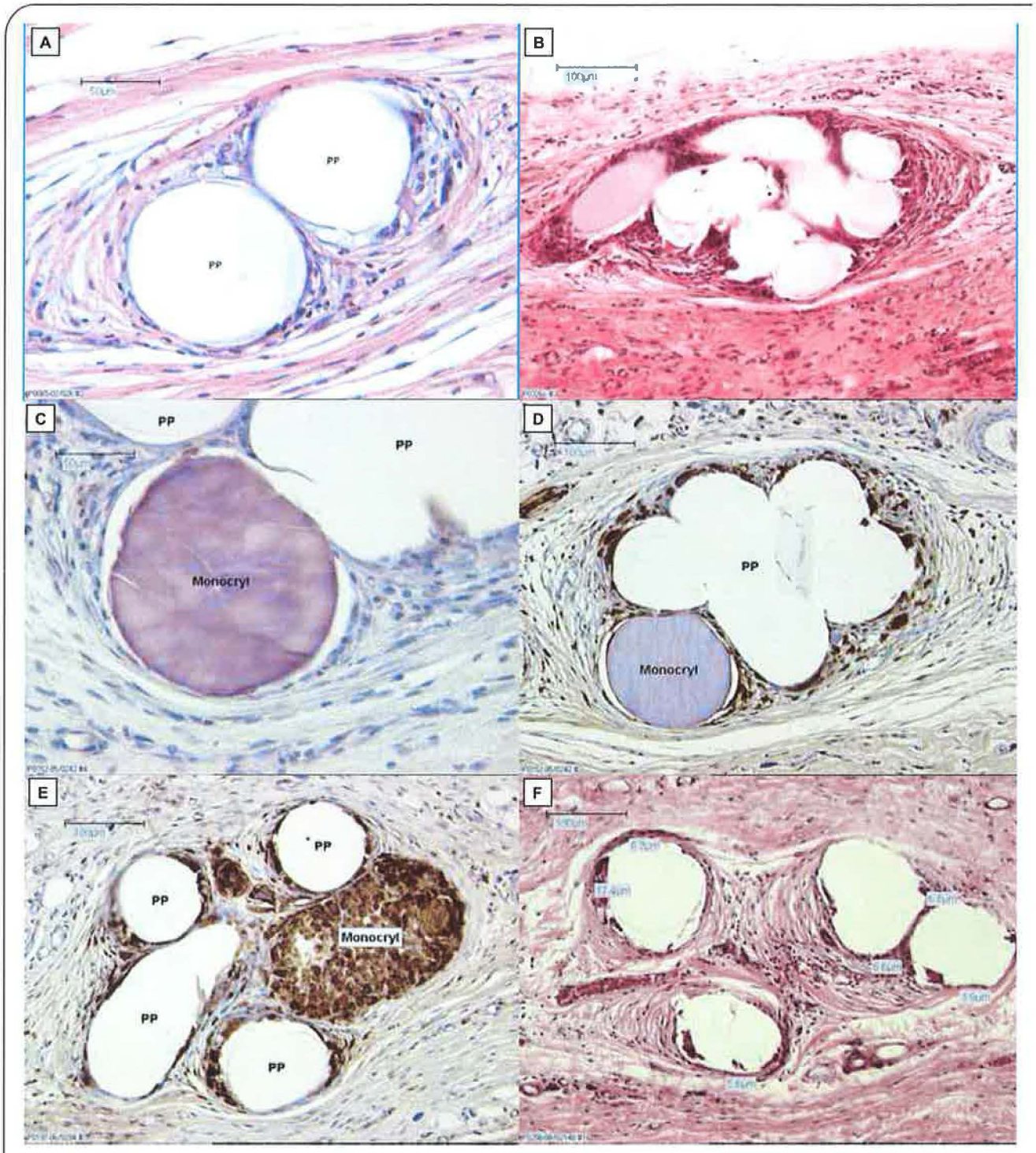

Figure 6. Members of the lightweight and large porous mesh family. (A) Lightweight and large porous PP mesh without surface modification 182 days post implantation in Whiter rats with a minor FBR and fibrotic tissue reaction around the mesh fibers (hematoxylin and eosin, 200×). **(B)** TiMesh® light 182 days after implantation in the same experimental setting; note the still persisting foreign body reaction which is at least equal to that of unmodified polypropylene (hematoxylin and eosin; 100x). **(C)** UltraPro® after 42 days; note the polypropylene and Monocryl® composite (hematoxylin and eosin, 200×). **(D)** Macrophage response on the interface of UltraPro 42 days after implantation with a reduced macrophage response to the Monocryl part (CD68, 100×). **(E)** UltraPro 84 days after implantation; the Monocryl part is absorbed by macrophages, but without increased inflammatory reaction and fibrosis (CD68, 100x). **(F)** UltraPro 182 days after implantation; remaining PP fibers with a remaining granuloma thickness of few µm (hematoxylin and eosin, 100×).

Key issues

- Lightweight large porous meshes indicate newer mesh modifications with main features such as optimized biocompatibility and adoption of the textile structure to physiologic values of the abdominal wall. In particular, mechanical characteristics such as tensile strength and flexibility of mesh and abdominal wall have been the focus of interest during the development of these meshes.
- The textile structure in general is large porous. The large porous construction reveals a significantly improved integration of the mesh into recipient tissues. In lightweight and large porous meshes a significantly decreased foreign body reaction can be observed. The reduced foreign body reaction correlates with decreased rates of connective tissue formation, shrinkage and bridging.
- A postretrieval study of explanted meshes that failed after hernia repair demonstrate that mesh-related complications are rare. However, mesh-related complications might be serious and severe such as fistulas, adhesions, infection and, in particular, chronic pain. Overall, lightweight meshes with large pores seem to have less serious complications, confirmed by the postretrieval study and first clinical studies.
- Recurrence is the most frequently observed complication in hernia surgery. Beside technical faults during operation, alterations of the extracellular matrix play a decisive role in the formation of long-term recurrences. The type of mesh used for the hernia repair plays no or only a minor role in cases of biologic recurrence.
- Future strategies to decrease the rate of biologic recurrences will be the introduction of bioactive meshes.

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