Experimental and clinical examination of abdominal wall closure complications

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PhD thesis
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1. Anatomy and biomechanics of the abdominal wall

The broad muscles of the abdominal wall together with the rectus muscles constitute both anatomically and physiologically a delicately coordinated biomechanical system. A good number of parietal functions such as the protection of internal organs, the equilibration of intrabdominal pressure changes, straining force and respiratory support are all remade possible by this biomechanical system. The musculo-aponeurotic system of the abdominal wall has to resist against several squeezing and expansive forces.

1.1 Changes in biomechanics after laparotomy

The laparotomy basically changes the biomechanics of the abdominal wall, because the ensuing scar does not contain active muscle tissue and strong fascia. The ultimate tensile strength of the postoperative scar reaches only 70% of that of the normal musculo-aponeurotic tissue. Elasticity and blood supply will also worsen considerably, in addition to the denervation caused by the incision which will destroy the parietal function in a much more extensive area behind the cut. Problems in wound healing the site of surgery like haematoma or infection will make scar even poorer in quality and increase the risk of hernia formation. Foreign body reactions due to mesh implants used in hernioplasty add further aberrations of the biomechanical properties, first of all through the increased mass of scar tissue.

1.2. Complications of abdominal wall closure

1.2.1 Factors influencing the result of abdominal wall closure

General factors: lack of essential nutrients, medications, organ failures
Local factors: disturbed blood supply, tension of suture lines, local infection
Surgical technical factors: inappropriate surgical techniques, bad application of a good surgical technique, negligence of the surgeon
Choice of surgical materials: use of inadequate sutures or needles

2. Objectives

- Can we able to decrease surgical site infection by applying surgical threads of different quality and using different surgical abdominal wall closure techniques?
- How many times do we spend more in cases with SSI?
- Are we able to decrease or prevent surgical site infection by the application of triclosan coated suture for abdominal closure after colorectal surgery?
- Does it make sense to implant mesh to reinforce the abdominal wall?
- Which is the best location for mesh implants in the abdominal wall?
- What kind of material is needed for covering the intraabdominal surface of the mesh to prevent adhesion formation?
- What kind of tissue reactions are initiated by mesh implantation?
- What kind of biomechanical changes are caused by the scar formation after hernia repair?
• Does the implanted mesh cause long term changes in the quality of life of the patients?

3. Techniques of abdominal wall closure

The abdominal wall closure is part of all abdominal surgical procedures. Each surgeon has got his own explanation why the actually applied wall closure technique is the most preferable. After the evaluation of several studies from the literature we can state that there is no ideal closure technique. The debate of application of absorbable – non absorbable suture materials nowadays the use of absorbable thread has gained preference. An intriguing question is the suture of the infected wounds, because the thread as a foreign body supports further infection. According to the literature we can state the single layer, running, long term absorbable sutures are more recommendable for abdominal wall closure, because it is much more simple, takes a shorter time and less foreign body is left behind. According to a patient questionnaire the running abdominal wall suture causes less pain in the early postoperative period.

3.1 Clinical trial of the abdominal wall closure options

In 2007 a retrospective evaluation was performed in our department to compare the use of running sutures with interrupted ones for abdominal wall closure. 50 patients had interrupted sutures and the same number of patients had continuous abdominal wall suture in 2005. There were two cases (4%) in the early postoperative period that required resuture because of abdominal wall dehiscence in the interrupted group and there was only 1 (2%) case in the continuous group. After the interrupted suture reconstruction there were 7 (14%) and after the continuous suture technique there were 9 (18%) patients who underwent reconstruction due to incisional hernia in the next two years. Statistically these data are not significant. Our study naturally was not representative but results were similar to those in the literature in that significant differences were not found.

3.2 Clinical trial for abdominal closure

Several international studies support the opinion that foreign bodies left behind together with the local bacterial flora greatly increase SSI rate. In potentially infected circumstances – where the option of contamination is assured – the quality of the applied thread needs more attention. Surgical site infections (SSI) are the third most common hospital-acquired infection and account for 14% to 16% of all such infections. Surgical site infections prolong hospitalization, are expensive and necessitate more dressing materials, a longer antibiotic treatment must be administered and the increased outcome of incisional hernias will make the result of a valuable operation even much worse. The goal of our clinical investigation was to decrease SSI rate to the minimum by choosing the optimal surgical thread.

During the first part of 2009 at the Department of Surgery of The University of Pécs, SSI rates following elective colon and rectal operations were evaluated retrospectively. This rate turned out to be 25% (n=120), which is worse if compared to international data. However, these results gave us a strong impetus to reduce SSI rates and related costs.
3.2.1 Study objective

Colorectal surgery is – according to an earlier study – linked with a SSI rate extremely high. The goal of our study was to evaluate the effect of triclosan (an antiseptic material) in elective colorectal surgery. For planning this study a short pilot study was performed to compare Vicryl Plus® with Vicryl® used for abdominal fascia closure. 50 patients were involved, in 25 patients triclosan coated Vicryl suture (Vicryl Plus®) were used compared to traditional uncoated Vicryl®. After analyzing the data, significant difference was found in favour of the triclosan coated suture (5% vs. 20% - p<0.05).

PDS Plus® a new improvement from Ethicon is a monofil absorbable suture coated with the antiseptic agent triclosan. The new coating is believed to provide protection against colonization developing around the suture. It has been demonstrated through in vitro studies that triclosan forms an inhibiting zone around the suture, and is effective against the most frequent pathogens causing SSI’s (Staph. aureus, epidermidis etc.). This effect on Gram-negative colon cultures has not been investigated before.

The goals of our study on base of the beforementioned retrospective and pilot studies were determined as primary and secondary. The primary goals were to determine whether PDS Plus® is able to reduce the number of SSI’s after colorectal surgery? Is the triclosan coated surgical suture material able to inhibit the growth of colon microorganisms as effectively as it was shown against skin cultures? Can this abdominal closure technique be recommended to surgeons in colorectal surgery too? Secondary goals were to determine whether SSI increases the length of hospital stay? Are there any significant additional costs?

3.2.2 Method

A multicentric, prospective, randomized, internet-based study was initiated. The study involved participation of 7 surgical centers (ClinicalTrials.gov - reg.no: NCT01123616). All of the involved patients underwent elective colon or rectal surgery between the beginning of December 2009 and the end of November 2010.

The inclusion criteria were: patients aged between 18 and 80 years with benign or malignant colon or rectal disease and an elective open surgical procedure were planned involving bowel opening. Patients with systemic disease influencing local surgical site healing, immune-suppression treatment, and inflammatory bowel disease or with unprepared bowel were excluded. For closure of the abdominal fascia, running PDS loop was used. Application of triclosan coated or uncoated PDS was determined by computer randomization. After the operation the following data were entered to the website database: duration and date of the operation, type of intervention, the technique of abdominal closure, presence of SSI, result of microbiology, duration of hospital stay, kind of bandage and number of its changes. 30 days after discharge from hospital a follow up was made by phone and informations such as late complications, outpatient registration due to late SSI, or readmission were collected.

3.2.3 Results

468 patients were suitable for randomization but 83 (18.1%) cases were excluded later. Finally valid results obtained from 385 patients (N=385) were analyzed and compared. In 188 patients the triclosan-
coated suture were applied while in 197 cases uncoated suture material was used. 23 patients (12.23%) from the triclosan coated group and 24 (12.18%) from the uncoated group suffered from surgical site infection, without a statistically significant difference (p=0.982). Out of all cases with SSI, 13 (27.66%) patients were diagnosed only after discharge in the outpatient clinics with the following distribution: 4 patients were in triclosan (17.39%) group and 9 patients in the uncoated (37.50%) group. This difference was found significant (p=0.041).

According to the microbiological results Gram-negative cultures (Pseudomonas aeruginosa, Enterocoli faecium, Escheria coli, Enterococcus sp.) appeared in both groups, but Gram-positive bacteria (2 cases of S. epidermidis) were only found in the uncoated group. From the point of view of BMI in the well-fed, normal and slight overweight group the SSI rate was around 11%. In the undernourished group it ranged at 32.4% (p<0.05).

Expenditures for cases with SSI and for those with normal wound healing were compared. The average amount of dressing material and the average of nursing days were calculated. In normal wound healing cases, the average nursing time were 9 days while for SSI patients it was 15 days (p=0.043). According to our calculation 5.2 dressing units were used for cases with normal wound healing in contrast to 32.7 units used for SSI patients (p<0.001).

![Graph showing surgical site infection rate](image)

**Fig 1** – SSI and late SSI in case of triclosan coated and uncoated thread

### 3.2.4 Discussion

Surgical site infection imposes a severe burden on the health care all over the world by increasing surgical morbidity leading to higher risk of mortality, and none the less increasing health care expenses. Furthermore, although not directly examined in this study, it inevitably influences the patient satisfaction and comfort.

Contrary to literary data there was no significant difference between occurrence of SSI after colon-, and rectum operations. The microbiological results confirm that triclosan inhibits the growth of Gram-positive bacteria. In vitro studies show that triclosan produces a larger inhibition zone among Gram-positive bacteria than among Gram-negative coli and klebsiella strains which appear in great numbers in colon cultures. We had only two cases supporting this finding; however we could not draw the same conclusion as previous studies did. Previous studies suggest that triclosan coated sutures may have a greater advantage in sterile operations, such as orthopaedic, plastic and cardiac surgery as proven in former studies. According to our study triclosan has no real effect against Gram-negative bacteria originating from the colon (12.18% vs. 12.23%).
However the high incidence of late SSI after colorectal operations seems to be interesting information. In this study the appearance of late SSI is a bit lower (17.4% vs. 37.5%), but significantly higher in the uncoated group if compared to the cases who received triclosan coated sutures. This may confirm the inhibiting effect of triclosan against bacterial colonization in the immediate surrounding of the suture material.

The time of hospitalization was significantly longer in cases of SSI. The mean length of hospital stay with normal wound healing was 9 days while in case of SSI it was 15. These extra days caused much more expenses for the Hungarian national health care system. Moreover about 6 times more dressings unites were used when SSI developed and wound discharge was present (p<0.001).

3.2.5 Findings

- The randomised trial could not confirm the excellent result of the former pilot-study.
- It seems that triclosan is not effective against Gram-negative colonic cultures, because does not provide a lower SSI risk if compared to the control group. Results gained from late SSI cases are hopeful, but the low number of cases does not allow to draw further conclusion.
- Before our trial SSI related extra expenses had never been exactly calculated. We stated that in case of SSI the hospitalization charges were twice, the bandages charges were six times higher than without its presence.

4. Prevention and treatment of abdominal wall closure complications

4.1 Prevention of hernia formation

Nowadays genetic and acquired factors of herniogenesis are postulated. The previous ones are examined by means of lineage research according to connective tissue weakness or collagen formation damage (Type I/III rate). The confirmation of the latter one is much more difficult. The truth lies most likely between the two. Hereafter our investigations are focused on established hernias in order to determine those surgical techniques and technical details that could lower the risk of hernia recurrence.

4.2 Treatment options for incisional hernias

If a parietal hernia is present surgery is the choice of solution if the patient is fit enough for operation. The reconstruction can be carried out in the traditional way under tension of suture lines or using tension free techniques with mesh-implant.

According to literary data reconstructions with direct sutures can adequately be made if the size of hernia portal size is under 3-5 cm² and so the pressure load on it is negligible and this is why recurrence rates are not worse than after tension free hernioplasties. Nowadays above this size the mesh implants are required because their long term results are much better. From the surgical point of view the cause of recurrence is the not appropriate surgical technique or the use of too small mesh implant. Optimally, mesh implants have to overlap defect edges at least by 5 cm in all directions. The correct indications of the different reconstruction techniques raise several new questions, the answer to which is absolutely not easy.
4.2.1 Comparison of suture and mesh repairs

Hernia formation is the most common complication after laparotomy (2-11%). It is much more frequent following suture repair and what is more the hernia formation after the reconstruction of the recurrent cases reaches 54%. That is why literature reviews emphasize reduced tension on the hernia portal as the key to a successful hernia repair laying more stress upon the use of mesh implants.

4.2.1.1 Comparison of suture and mesh repairs in inguinal hernias

In case of inguinal hernias several reviews present significantly better results of hernia repair with tension free techniques in comparison with traditional ones.

In our department we observed a 12.5% recurrence rate after the traditional reconstruction of primary inguinal hernia and 33.3% after reconstruction of recurrent cases. We started a multicentric (15 departments) prospective randomised clinical trial to test Lichtenstein’s tension free technique using polypropylene mesh implant (n=1434). As compared to the former high recurrence rate in this study we found only a 2.24% rate as it was recorded by the patients. Moreover the tension free method provided a 3.5 times less early postoperative pain for the patients. Secondary cases were not included in the trial.

An other comparative retrospective clinical trial carried out in our institute has confirmed that long term results of the Lichtenstein procedure are nearly as good as it was found in the previous multicentric study. From a distance of 5 years our analysis still showed 3.4% recurrence rate, which is much closer to the 2.24% rate of the Lichtenstein study than the 12.8% recurrence rate of the suture repair aera. What is more the exploit of questionnaires showed what is known from literature that the tension free repair would give an earlier return to work and daily normal activities. So we found the tension free technique much more cost effective than the traditional suture repair.

Fig 2 – Long term effect of Lichtenstein’s procedure on surgical routine in Hungary

Finally we collected data for the effect of the open tension free surgical technique on the daily surgical routine in Hungary. We found that – according to its far better results – the tension free inguinal repair became widely popular (Fig 2).
4.2.1.2 Comparison of suture and mesh repairs in abdominal wall hernias

According to databases and reviews there is a good evidence that open mesh repair is superior to suture repair in terms of recurrences and an insufficient evidence as to which type of mesh or which mesh position (on- or sublay) should be used. The main goal of this study was to compare the recurrence rate of suture versus mesh repair and sublay versus onlay position of mesh reconstructions for small and large hernias.

4.2.1.2.1 Methods

The main goal of this study was to compare the recurrence rate of suture versus mesh repair and sublay versus onlay position of mesh reconstructions in case of small and large hernias. The study was registered at clinicaltrials.gov. (reg.no: NCT01018524).

All patients with primary umbilical or incisional abdominal hernia were included in the study. The selection criteria were: good patient compliance, signed consent form and normal wound healing conditions. The preoperative exclusion criteria were age under 18 or above 70 years, hernia orifice under 5 cm², planned other gastrointestinal surgery, unstable circulation, uncontrollable diabetic or autoimmune diseases, severe renal or hepatic failure, advanced stage of tumours or currently treated malignancies. Inflammation or turbid content of hernial sac seen on laparotomy and accidental intraoperative bowel lesion resulted exclusion from the study. There were exact instructions for the surgical procedures to be applied; the steps of these are specified in chapter 4.2.1.2.2 of the thesis. Subsequently patient groups were formed and submitted to randomization as shown in Fig 3.

Fig 3 – Flow chart of randomization. In group ‘A’ (small hernias) patients were selected with hernial portals between 5-25 cm², group ‘B’ (large hernias) included cases with hernial portals above 25 cm². In group ‘A’ suture or mesh repair (in sublay position) was performed according to randomization, in Group ‘B’ mesh implantation was obligatory, either in onlay or in sublay by random choice.

Antibiotics were administered before and after the incision for two more days. The size of musculo-aponeurotic defect, type of mesh-fixation and fascial closure, date and duration of operation, postoperative mobilization, time of discharge, recurrence rate, early and chronic postoperative pain (using a
verbal analogue scale) and wound healing complications were all registered. Data were analysed in many ways of statistical analysis.

### 4.2.1.2.3 Results

During the five-year follow-up from 953 randomized cases altogether 219 patients (23%) finished the study earlier than planned. Consequently we were able to draw our conclusions by the evaluation of 734 patients. After randomization, suture repair (subgroup ‘A’/suture) was performed in 184 cases and mesh repair (subgroup ‘A’/mesh) was done in 180 patients. In group ‘B’ mesh implant was applied in 189 cases in sublay (subgroup ‘B’/sublay) and in 181 patients in onlay position (subgroup ‘B’/onlay), respectively.

After the five-year follow-up 50 (27.2%) recurrences were registered following 184 suture repair, and 15 (8.3%) recurrent hernia were recorded out of 180 cases subject to mesh repair in small hernia group. The statistical analysis showed significantly worse recurrence rates after suture repair in comparison to mesh repair (p<0.001). In the large hernia group (group ‘B’) our data showed 38 (20.1%) recurrent cases from 189 sublay mesh reconstructions, and 22 definite recurrences (12.2%) from 181 patients in the onlay mesh repair subgroup. Data analysis showed a significantly higher hernia recurrence rate after sublay mesh repair than in onlay mesh reconstruction (p=0.038) (Fig 4). Considering recurrence free survival time after abdominal wall reconstruction demonstrated that the most part of the hernia recurrences occurred between 6 and 24 month after surgery.

![Fig 4 – Hernia recurrence rate after a five-year-follow-up. The recurrence rate was significantly higher in subgroup ‘A’/suture vs. subgroup ‘A’/mesh (p<0.001), and in subgroup ‘B’/sublay vs. subgroup ‘B’/onlay (p=0.038).](image)

Suture repair provided the worst results at any location in respect of recurrence (23-33%). Comparing the different locations at each group significant differences were only found in the umbilical (p=0.027) and transverse-subcostal (p=0.033) groups among the small hernias. Differences of other locations were not significant (p>0.05).

Fixation of the implanted mesh was also investigated; absorbable-running, absorbable-interrupted, non-absorbable-running and non-absorbable-interrupted sutures were to be chosen. Most of surgeons used non-absorbable-interrupted stitches for fixing the prosthesis. Comparing the running and interrupted suture
techniques in group ‘B’, running sutures provided far better results (p=0.002). In case with small hernias the different fixation types did not show any significant difference.

Analysis of fascial closure in case of group ‘A’ the non-absorbable sutures (both running and interrupted) provides lower rate of recurrence as compared to absorbable threads, but the difference was not significant (p=0.063). In subgroup ‘B'/sublay fascial closure applying running sutures provided nearly a two times lower recurrence rate than the interrupted ones, but this again was not found significant when interrupted and running (p=0.068) and when absorbable and non-absorbable ones (p=0.093) were compared. There was not significant difference noticed in subgroup ‘B'/onlay (interrupted/running – p=0.855, absorbable/non-absorbable – p=0.389).

Among the wound healing disorders perigraft fluid accumulation was observed most frequently (12.6%), and this was more common in group ‘B’, with no differences between its subgroups. A significant difference was found only in group ‘B’ with regard to wound infection (p=0.029) and sterile fat necrosis (p=0.037) where onlay mesh repair was found inferior to sublay mesh plasty.

4.2.1.2.4 Discussion

Incisional hernias represent the most common complications of abdominal surgery. In the last decade the rate of tension-free surgical techniques has considerably increased. According to literary data the results of the different methods of abdominal wall reconstructions show great variety. Until the 1990s, suture repair of incisional hernias was the gold standard technique. Unacceptably high recurrence rates associated with primary suture repair have led to an increased application of prosthetic mesh for the repair of incisional hernias. In our trial suture repair was used only in cases with small wall defects. The suture repair recurrence was 27.2% contrary to the 8.3% rate seen after mesh reconstructions with significantly confirmed (p<0.001) the superiority of tension free repair to suture repair, so mesh implantation is offered recently for hernia reconstruction.

The key of tension free techniques lies in the incorporation of the mesh into the abdominal wall which generates the scar formation. The two routinely used open methods are the onlay and sublay reconstructions. The onlay technique is popular among surgeons because it avoids direct contact with the bowel and technically is not difficult for the surgeons. A good number of studies (more precisely form the Anglo-Saxon area) did not find any difference in recurrence rates between the two reconstruction techniques. On the other hand, there are also studies (German and Scandinavian area) which prove lower recurrence rates following sublay mesh repair. The latter group of studies offer the onlay technique only if the sublay repair can not be carried out.

As opposed to these trials our investigation data show better recurrence rates after onlay reconstruction (12.2%) than in case of putting the mesh into sublay position (20.1%). This difference was statistically found significant (p=0.038). So our study is without parallel in the literature but the size of our database, generated by an independent data recording of a prospective, randomised and multicentric clinical trial must be regarded as representative. From our point of view if we change the well known mechanical approach to a biological approach with aims to minimalize tissue reactions, then maybe we could explain these mechanically strange results.
Differentiation between types of meshes was not the goal of this study. And yet, usefulness of suture material chosen for mesh fixation and fascia closure by the database we have enough data to compare different suture materials and suture techniques. In both branches of group B there was a higher recurrence rate after interrupted suture repair (p=0.002). We postulate that running sutures result in a more outweighed action of power in the levers. The non-absorbable threads and running suture were superior to absorbable and interrupted sutures.

All of the surgical departments participating in our study had a great experience in hernia surgery. Each qualified general surgeon of departments involved was allowed to operate patients within the study which is an important pile of an objective randomized trial. Sublay technique seems to be the most difficult among open abdominal wall reconstructions, but it has a longer learning curve and shows an acceptable outcome in expertise hands. On the other hand incisional hernia surgery is often performed by young surgeons, so those research groups, that only a few number of surgeons or too small number of patients were entered in the study or too strict rules already by start of the trial can make a serious mistake when they draw conclusions, because it can be amounts of miles from the everyday practice.

Several authors published that mesh implants had increased the risk of wound infections and also the positioning of the mesh would make a difference. Most papers demonstrate higher wound infection rates when the mesh was used in onlay position. Although we can not present a relevant difference between mesh and non-mesh repair; yet our data show significantly lower infection rates if the mesh is placed under the muscle. A higher infection risk of onlay repair could be confirmed. The results show a large difference in this respect; however it is statistically not significant. Perigraft fluid accumulation was the most frequent complication in our trial following onlay mesh repair, potentiality subsequent local infection, but it could not be confirmed statistically in this study.

![Number of operative treatment of abdominal wall hernias](image)

Fig 5 – the effect of the clinical trial on the routine surgical practice

4.2.1.2.5 Findings
- From scientific point of view our clinical trial is unique. As to hernia surgery we did not have such a giant multicentric, randomised, prospective clinical trial so far. The effect on the
Hungarian daily routine of hernia repair is more than conclusive (tenfold increase of mesh repairs for incisional hernia as presented by Fig 5).

- Further effect of the study is that the number of the reconstruction of recurrent hernia cases has been dwindled since.
- Knowing the results of other databases and supported by our results we can state mesh implants can be recommended in order to keep low the recurrence rates.
- Former multicentric studies are usually based on the results of expert hernia surgeons. In our trial each general surgeon was allowed to enter his patients which brought our trial closer to the everyday practice.
- The biological attitude to surgical techniques instead of the mechanical one, may explain better results after onlay mesh repairs.

4.3. Prevention of adhesion formation in the abdomen after mesh implantation

Laparoscopic mesh implantation has gained wide acceptance among surgeons and patients. One of the drawbacks of this technique is that the prosthetic material is to be placed intraperitoneally, directly adjacent to the intestines. At the present time, all available prostheses adhere finally to the intestines, with the subsequent complications of intestinal erosion and fistula formation. The largest experience up to now was obtained with polypropylene mesh causing erosions, ileus and fistulas due to immediate contact with the bowels. Quality and construction of the meshes play an important role in the occurrence of complications, then special materials such as PTFE may prevent bowel adhesions. Unfortunately the high costs of such meshes and implants limit further spread and use of laparoscopic hernioplasty.

The aim of our experiments was to study the biological behaviour of intra-abdominally placed widely used macroporous meshes that were covered with different materials on their intra-abdominal side in order to prevent subsequent adhesions.

4.3.1 Method

The investigation was divided into three phases and then after evaluating our experiences a fourth phase was started. The procedure was the same in each phase: four times 12 rabbits were operated on. A midline abdominal skin incision and two symmetric bilateral full-thickness musculo-aponeurotic windows (~3x4 cm) were created in the abdominal wall in each case. During the operation we implanted the mesh so that it got in direct touch with the bowels. The animals from each group were killed randomly at 30, 60, 90, 120 days following primary surgery. The operated abdominal wall was excised in one block and the degree of adhesion formation and its macroscopic appearance were studied. Adhered internal organs were also cut if that was needed. Presence of adhesions, intensity of
adhesion formation, size of its surface, and total score were assessed visually using a modified Diamond scale.

In the first 12 rabbits the right side defect was repaired by using polypropylene mesh (Prolene-Ethicon) covered with either silicone, hyaluronic acid (Opsite foil) or polyurethane, chosen for four rabbits each, in a way that the covered side faced the abdominal cavity. As a control, in all the rabbits, the left side defect was covered by non-coated Prolene mesh alone.

In the second experiment (n=12) the left side defect was covered by a braided multifilamentous polypropylene (Surgipro) mesh of markedly different construction, configuration and with a smaller pore size than Prolene mesh. On the contralateral side in 4 rabbits Surgipro mesh was covered with hyaluronic acid gel, in 4 rabbits Surgipro mesh was covered with polyurethane membrane, and in 4 rabbits the defect was covered with Prolene mesh alone.

In the next 12 rabbits, the incorporation of meshes with reduced amounts of polypropylene was investigated. On the left side uncovered and while on the right side polyurethane-covered mesh was implanted: I. group: a semi absorbable (Vypro-Ethicon), II. group: (Titanium coated Timesh-GfE.), III. group: (Premilene LP-B.Braun).

Inspite of early prosperous experience the use of polyurethane was stopped because some literary data suggested the release of a carcinogenic metabolite (4.4'-methylenedianiline) which were arisen in the course of sterilisation.

The fourth experiment was based on the experiences gained from the first three ones. For this last experiment meshes with reduced polypropylene content such as Premilene LP were coated on one side by silicone sheet to prevent exposure of polypropylene especially at the corners and edges of the mesh. The polypropylene was embedded to a half thick silicone layer under high temperature and pressure circumstances. Applied temperature and pressure measurements for embedding were determined far below why could cause structural changes in the mesh material. In the last 12 rabbits the biological response to such, material-reduced, meshes that were covered by a silicone membrane on their intra-abdominal surface, was evaluated: in all rabbits, in the right side silicone covered Premilene LP was implanted and on the contralateral side silicone embedded Vypro-mesh was implanted.

4.3.2 Results

In the last (fourth) experiment only silicone covered meshes were applied. Results are demonstrated in table I. In 10 rabbits (83.33%) there were no any adhesions found in the intrabdominal cavity and silicone side of neither the silicone embedded Vypro or Premilene LP (mDs grade 0) meshes. In the reoperated group – which was not the elemental part of the study – 11 rabbits were involved. In 10 of them there was absolutely no adhesions (mDs grade 0) on the intrabdominal surface of the silicon
coating 90.9%. Massive adhesion was detected only in one case (1/11 – 9.09%). In this latter case mDs gr 1 adhesions were recorded after the first operation as well.

Table I. – Results of silicone covered mesh repairs in primary and recurrent cases - (PreSi: Silicone embedded Premilene mesh; VySi: Silicone embedded Vypro Mesh. *The animal died on the 6th post operative day because of ileus – (“mDs” in the followings – grade 0, 0%; grade 1, 1-25%; grade 2, 26-50%; and grade 3, > 50% adhesions of implanted surface).

4.3.3 Conclusion
The aim of these series of experiments was to construct a kind of hybrid mesh that generate sufficient fibrosis in the abdominal wall to decrease of hernia recurrence and on the other hand their intra-abdominal surface is expressingly inhibitory to adhesion formation. Moreover, because one material is not capable to act in two opposite directions and in a single location, hybrid meshes should be constructed with different layers or by combination of different materials.

The results of the first three phases of our trial deferred from literary data, but after the elimination of the technical problems (separation of the silicone layer from the mesh) our results became significantly better. Occasional weak adhesions (mDs 0-1) were seen at the edges of the implanted mesh and were closely related to the suture line (4/0 Prolene was used for mesh fixation) and it is well known from
literature that Prolene has an adhesion generating effect. We think that the larger part of these cases is independent from the silicone surface and that makes our results even more respectable in the primary and reoperated (=recurrent) groups as well.

Summarizing our opinion we can state that after the application of silicone covered meshes no adhesions were detected in eleven animals, and only in one case they were negligible amounts of adhesions. Massive intraperitoneal adhesion was detected only is a single case. In the reoperated group the results showed nearly the same (one animal was lost because of adhesions). So we can state that silicone, except weak adhesions in some cases, nearly completely precluded adhesion to the mesh surface.

According to our experience – if we are able to apply a secondary silicone layer on one of the mesh surfaces and fix it properly, a coherent neoperitoneum will be formed on the internal siliconized surface very likely still before the first exploration by the 30th day and does not change even later, as it was observed after 30 and 120 days as well.

4.3.4 Findings
- A standardized animal model was created to investigate the biological behaviour of intraabdominally implanted meshes.
- We succeeded to find a suitable material to cover the inner surface of polypropylene meshes that was able to prevent the adhesion formation successfully within the abdominal cavity.
- Involving chemistry experts we devised the exact technological procedure to create a stable implantable, dual mesh suitable for generating fibrosis in the abdominal wall and prevent it in the abdominal cavity.
- Our mesh prevents intraperitoneal adhesion and is suitable for open and laparoscopic surgical implantation as well as the other dual meshes, but its price is incomparably better.

4.4 A Histopatological study of mesh incorporation
4.4.1. Histological investigations of mesh incorporation according to foreign body content

The investigated specimen stemmed from the third phase of the above mentioned animal models. Our aim was to define the incorporation of the mesh in parietal soft tissue and to ascertain according to foreign body content of the mesh.

All the removed specimens were sent for histology. The tissue samples were fixed in 4% formaldehyde solution and embedded in paraffin. 3 μm thick histological sections were cut, mounted on glass slides, stained with haematoxylin-eosin (HE) or Periodicacid-Schiff (PAS) and evaluated by light microscope.

Macroscopical comparison of the three different meshes applied in the study showed that Premilene® Mesh LP caused the largest adhesions but the result of TiMESH® was nearly the same. The adhesion generating effect of Vypro® II Meshes was significantly lower. Opposite to these findings the morphological evaluation revealed that a foreign body related inflammatory reaction was present in each microscopic section.
So we can state there was no causal relation and effect between the foreign body content and the degree of adhesion formation.

4.4.2 Histological quality control of the newly formed peritoneum

The investigated specimens stemmed from the last phase of the above mentioned animal studies. We tried to investigate the difference between the original and the newly formed peritoneum layers. The silicone layer excellently prevented macroscopic intraperitoneal adhesion formation also confirmed by the HE and PAS strained slides. A thin tissue layer could be identified on the intrabdominal surface of the silicone membrane macroscopically and under the microscope it showed as a well-organised monolayer with developed mesothel cells. We can state the newly formed ‘neoperitoneum’ is totally identical to the original one. So silicone embedded meshes do not cause more severe foreign body reaction in the abdomen than it could be expected.

4.4.3 Immunhistochemical investigation of mesh incorporation

Finally we performed the immunhistochemical and electromicroscopic investigations to recognise long term effects of the incorporated mesh. Ki-67 (for proliferation), VEGF (for angiogenesis) and MNF-116 (for mesothel identification) mouse antibodies were used for immunhistochemical examinations.

The amount of the Ki-67 positive proliferating cells was continuously decreased during the time. So the immune reaction was terminated the mesh is finally incorporated. VEGF positivity confirmed capillary ingrowth to the intraperitoneal surface of the mesh – also visible at macroscopic inspection. MNF-116 cytokeratin marker straining of the specimen showed completely developed mesothelial cells covering the silicone layer already after a few weeks.

4.5 Changes of abdominal wall biomechanics after suture and mesh repair

Any changes in biomechanics can only be measured by biomechanical models. The most simplified definition says that biomechanics comprise the elasticity and the tensile strength of the abdominal wall especially after its reconstruction.

The tensile strength is an important feature of the mesh, which is usually above 32 N/cm, while it is 16 N/cm in average for the human abdominal wall. This is why mesh defect such as the breaking up of the material would cause only seldom in our trials. From point of recurrence the mesh-fascia contact is much more important than the material of the mesh. During the surgery we have to assure a wide contact between them (≥5cm). The requirements of the different mesh elasticity to the different directions follows from the physiology of the abdominal wall muscles.

4.5.1 Tensile strength measurements after direct suture repair

Measurements of tensile strength of the abdominal wall following direct suture were performed in 2008 applying long term absorbable threads. Two variants of different elasticity (70% elongation & 90%
elongation) of a new long term absorbable suture material (poly-4-hydroxybutyrate - MonoMax®) were evaluated in 36 domestic pigs. Polydioxanon (PDS II®) was used for the control group. The absorption time of MonoMax is longer than that of PDS II; 50% of its tensile strength is lost after 8-12 weeks in vivo which is the double of the total absorption time of the PDS II.

Methods: A standard 15 cm long midline incision was made in all animals and the fascia was closed using a continuous suture (loop) technique with suture materials. Animals were randomized into three groups: Group I (n=12): MonoMax 70%, Group II (n=12): MonoMax 90%, Group III (n=12): PDS II. Four-four animals were sacrificed from each group 10 days, 30 days and 90 days after surgery. The sutured part and an equivalent intact part of the abdominal wall were removed in toto and the tensile strength measured using a tensiometer (0–200±0.1 N).

Results: After 30 days the tensile strength was significantly superior in the MonoMax70 group than in the polydioxanon group (p<0.05). The MonoMax90 group provided significantly better results after 90 days than the polydioxanon group (p<0.001).

Discussion: Our data confirmed that the use of the new MonoMax® thread increased the tensile strength of the abdominal wall more than the every day routinely used polydioxanon. After 90 days the strength of the scar is equal or even a bit higher in comparison to the intact fascia. This last result may open a new path in the prevention of incisional hernias, but this can only be stated after randomised multicentric clinical trials.

4.5.2 Investigation of tensile strength after abdominal wall closure using prosthesis

The prosthesis implantation to the abdominal wall increases the thickness of scar tissue. The increased tensile strength of the abdominal wall is unambiguously confirmed by significantly lower recurrence rates. Most recently clinical trials investigate the rigidity and the passive motions of the formed scar and especially how these changes may influence the biomechanical features of the abdominal wall. Our research workgroup set up an animal model as well to detect these changes, but conclusion can not be drawn up to now.

4.6 Assessment of quality of life after hernia surgery

The main goal of clinical reviews is the rate of recurrence after the hernia operations; but the quality of life that we are able to present for the patient is just as important as the recurrence. Long term experiences (2-3 decade) are still lacking with mesh implantations but also shorter term retrospective analysis of questionnaires could give interesting data if we turn back to our patients operated on a few years earlier.

In 2009 we made an assessment of all patients subject to open inguinal hernia repair in 2004 in our department. Besides recurrence the questionnaire asked the different determining factors of quality of life like limitation in normal daily activity and chronic pain. According to the answers the direct and the tension free surgical techniques were compared.

The results were evaluated by the answers of 155 patients. The recurrence rate after mesh repair (M) was 3.4% and 12.8% without mesh implantation (NM). From a five-years distance after the surgery 83% (M) of patients had no complaints at all after mesh repair and this was 89% (NM) of the patients in the tension group. Remarkable chronic pain was present at 1.7% (M) in the mesh repair group and at 7.7% (NM) of the
non-mesh group. In the mesh group usually this pain was few like a twinge to a sudden movement at the side of the mesh which soon disappeared. With regard to postoperative recovery 34% (M) of mesh repair patients were able to return to their daily activities; and while about 21% (M) of these patients had restricted activity even after six weeks. In the tension technique group these were 29% (NM) and 33% (NM) respectively. Significance was not found in these comparisons (p>0.05 – except recurrence rate).

Apart from a lower recurrence rate after Lichtenstein’s reconstruction; we concluded there was no difference between the two groups with regard to chronic pain or return to normal activity. From an other point of view the surgeon does not take a greater risk with mesh implantation.

5. Summary and the new findings
- Are we able to decrease surgical site infection by the application of suture materials of different quality and using different surgical abdominal wall closure techniques? In concordance with the relevant literature we also can state that continuous and absorbable sutures are more preferable for abdominal wall closure because the action of forces is equalized on the different parts of the thread and provide the least foreign body left in the host tissues.
- How many times do we spend more in cases with SSI?
  In Hungary we were the first to specify the exact costs of bandage changes. According to these we found that the costs are highly increased (even 32x) in cases with surgical site infection.
- Are we able to decrease or prevent surgical site infection by the application of triclosan coated suture for abdominal closure after colorectal surgery? After a randomised clinical trial we concluded is that the widely used triclosan is not effective against Gram-negative colon culture, because it does not provide a lower site infection risk compared to the control group.
- Does it make sense to implant mesh to reinforce the abdominal wall?
  Knowing the results of databases supported also by our results we can state that mesh implantation can really be recommended to keep low the recurrence rate.
- Which is the best location for mesh implants in the abdominal wall?
  Contrary to the literature – after one of the largest European multicentric, randomised, prospective clinical trial we proved that the onlay position of the implanted mesh provided better recurrence rates compared to the sublay repair.
- What kind of material is needed for covering the intraabdominal surface of the mesh to prevent adhesion formation?
  The polypropylene surface may cause fatal adhesions in the peritoneal cavity which can be successfully prevented by means of a stabile silicone cover.
- What kind of tissue reactions are initiated by mesh implantation?
The histological study gained from our animal model showed total incorporation of the mesh, the gradual elimination of the tissue reaction to foreign body and finally the restitution of the normal stage (such as neoperitoneum).

- What kind of biomechanical changes are caused by the scar formation after hernia repair? On animal models we were able to demonstrate that scar after adequate suture material may reach the tensile strength of the intact abdominal wall.
- Does the implanted mesh cause long term changes in the quality of life of the patients? According to the long term feedback of the operated patients we can state that in most of the cases the mesh implantation does not cause restrictions in the normal physical activity.
8. Publications

8.1 Original papers in English

8.2. Original papers in Hungarian


8.3. Abstracts


**IF: 25,127**

### 8.4. Oral presentations


18. **J Baracs, I.Takács, S Horváth, OP Horváth, G.Wéber.** Higher recurrence rate at sublay than onlay mesh reconstruction in abdominal hernias (five-years results of a randomized, multicentric clinical trial) Annual Congress of European Society for Surgical Research – May 2009, Nimes, France

19. **J.Baracs, I.Takács, S.Horváth, OP.Horváth, G.Wéber.** Higher recurrence rate at sublay than onlay mesh reconstruction in abdominal hernias (five-years results of a randomized, multicentric clinical trial) 4th Joint Meeting of the American Hernia Society (AHS) and the European Hernia Society (EHS) – Sept. 2009, Berlin, Germany


22. **J.Baracs: Sérvek kezelése – graduális képzés orvostanhallgatók számára – Nov. 2010 Pécs


