

Ethicon Expert Meeting: Meshes for Pelvic Floor Repair

Friday, February 23rd, 2007; Location: Oststr. 1, Norderstedt, Meeting Room "Forum"

External Participants:

Prof. M. Cosson
Prof. B. Klosterhalfen
Prof. J. Deprest
Prof. B. Jaquetin
Dr. Arlt
Dr. D. Miller
Dr. K. Lobodasch

Ethicon:

Bob Roda
Cliff Volpe
Dave Robinson
Axel Arnaud
J. Flatow
O. Berthier
Ed Jacobs

P. Köhler
Aida Astani
K. Spychaj
P. Meier
J. Holste
J. Trzewik
B. Hellhammer



"Agenda-febr Mesh
Meeting.doc"

Agenda:

Highlights from the presentations and related discussion (Please see CD as well):

Introduction and update of project "LIGHTning" (P. Meier)

PM gave a quick overview of the history of the project. Project is now in development phase. Team has achieved discovery work successfully. Ultrapro is the most promising available mesh for pelvic floor repair. Further animal and clinical data has to be collected prior launch of a product to substantiate this.

Plaintiff's Exhibit

PX 210

Experiences with Ultrapro Usage in Hernia surgery (Dr. Arlt, Berlin)

Mesh usage from the general surgeons point of view:

“Sense of foreign body” is higher in heavyweight meshes” (Dr. Arlt); subsequent discussion about evaluation of “foreign body feeling” – is it sufficient to just ask for the patients perception?

Almost no problems like pain, shrinkage or recurrences with modern lightweight meshes in hernia surgery (Dr. Arlt); subsequent discussion about the value of changing Prolene Soft to Ultrapro – is there a real improvement (both are lightweight meshes)?; Difficult to show, because Prolene Soft is not used in hernia surgery in Germany
Also important: large pores (esp. if you place a heavyweight mesh); (Dr. Arlt)

Dr. Arlt about Fixation of mesh: only needed in the first days after surgery (3-5 days), during this time it must be assured that the mesh stays in place; doesn't matter if the material is resorbable or non-resorbable; in some cases, fixation is not needed, since tissue layer fixes the mesh.

On the other hand: If a mesh is not integrated, it is almost impossible to be fixed for a long time
Sutures will cut out, so will not be of help over time if the mesh is not integrated.

Dr. Arlt about shrinkage: In hernia surgery not an issue, if the mesh is large enough to cover the defect sufficiently; on the other hand we must keep in mind that a bigger mesh will automatically lead to more Foreign Body and Tissue reaction.

Prof. Klosterhalfen: Textile structure of the mesh – pores and knitted construction - is more important than the area weight. Terms light-weight and heavy-weight may be misleading.
Optimum pore size: Macrophages reach everything, they immigrate into the nods. Exception: ePTFE, its pores are too small for macrophages to enter.
Same compliance of mesh and tissue = ideal

Prof. Cosson questions if Polypropylene the best material as fractures are observed in pp after time. Polyester better? Known to degrade over time.

Factors related to mesh shrinkage: (K. Spychaj)

What is found in literature?

In pelvic floor surgery, shrinkage seems to be more important than in hernia surgery.

Need for new animal models? We need to develop a model which causes a high shrinkage in general (Dr. Cosson, Dr. Miller, others?).

Discussion about model for pelvic floor: No adequate animal model in this case; might an abdominal wall model be a better solution? – no agreement about that; objection: there is no real fascia in the pelvic floor

Pelvic floor surgeons do not necessarily believe in the theory stating that large pores lead to less shrinkage, they even want some kind of “fibrotic bridging” because they think that the mesh is gaining strength and stability through this phenomenon.

Polypropylene meshes might not be improvable in terms of shrinkage, we may need a completely new material (Dr. Cosson)

Shrinkage:

Physiological maturation of scar (age, gender, genetics dependent)

Shrinkage is not controlled by “softness” of mesh

One approach might be control of fibrosis and neoangiogenesis

Presentation: My vision of an ideal Pelvic Floor implant (Dr. D. Miller)

Discussion after Dr. Miller’s presentation:

Change of priorities: low-weight mesh is already the standard (already adequate); new priority: remain the mesh in place

Vaginal elasticity is very important; vagina must be able to move

It is important to teach the surgeons who are not so experienced (Dr. Lobodasch mentions that his collected data indicates that patients of experienced surgeons have less erosions – learning curve).

Dr. Cosson believes that surgeons don’t dissect the tissue properly.

Critical phase of wound healing seems to be early after the procedure; critical time for erosions: about 3 months

Other Highlights from the discussion:

Connective tissue does not add to strength

In general meshes are too strong in dimension (B. Klosterhalfen, all)

Discussion about “biological material”:

Overall opinion of present surgeons: “there was a trend of biological materials in gynecology in the past, but not anymore, because they are not good enough (resorbable material leads to recurrences); no need for antimicrobial mesh in gynecology; Dr. Miller: some years back I was concerned with infection, but now with mesh experience not worried.

Erosions do not occur because of infections (eroded meshes are incorporated and infected meshes are never incorporated)

Discussion about glue:

Dr. Arlt: more surgeons would use glue if it was less expensive; glues cause less scar formation around nerves, less nerve and bowel damage, less pain

General “brainstorming discussion”:

Need for a general “comfort scale”

Need for a definition for “extrusion” and “erosion”

Need to learn more about special anatomic features in the vaginal region (may be done with cadavers); Vagina consists of muscles and epithelium, there is a lot of movement in interface “epithel/muscle” (completely different from abdominal wall); vagina is a contractile organ, lots of movements occur only during sexual activity

The shape of the implant doesn’t seem to be an issue anymore (it’s adjustable and you can trim it)

Question: Would you prefer a mesh or a foil as an implant? –Difficult to say, but it would be good to have sth. that makes the implant more stable (Problem: vagina is very odd-shaped, so

you cannot use a preformed implant – “you should make the implant stiffer without the disadvantage to make it permanently stiffer”

“If you like to eliminate the arms of the implant you would need some kind of internal fixation”

No need for an antibiotic mesh (“this is not the issue”)

Erosions always occur in the same region; mostly uncomplicated to repair, does not necessarily lead to a recurrence; discussion about a change of the mesh in this region (resorbable material with longer resorption time than Monocryl)

Late erosions: apex the most
Current shape widely physiologic

The following summary of unmet needs generated June 2nd 2006 was again confirmed without any adding:

Unmet clinical needs	Priority (points)
No shrinkage / no long-term contraction Fibrosis reduction Severe contraction → Dyspareunia → sexual function↓ <i>Tension response ↓</i> <i>= ↓ Sexual pain?</i> <i>No folding of mesh</i> <i>No rigidity</i>	10
No vaginal distortion, normal vaginal wall, maintain sexual function, normal sexual function	8
Elasticity simulating physiology	5
No chronic pain Patient comfort <i>Less erosion</i> <i>Less vaginal mesh exposition</i>	4 2
BIO-active, “ long term “ - 90 days <ul style="list-style-type: none"> • growth factors • anti-bacterial • hormonal • angiogenesis 	3
Better handling <i>Implantation process:</i> <i>→ Make it easier</i> <i>→ Correct placement</i> <i>Simple application</i> <i>Even simpler to apply</i>	3

Poor understanding of pathophysiology	3
Durable results <i>Will recurrence rate increase long-term?</i>	2
No foreign body reaction Less inflammatory response No local inflammation Is there an “optimum” foreign body reaction? “No mesh at all is the best”	
Low complications No complications	
Lack of palpable mesh in vagina	
“Smart” incorporation - tissue of adjoining viscera NOT able to in-grow	

For details regarding the human cadaver Wet lab please see Report from E. Jacobs:CR Hamburg 70223 (draft attached)



"CR hamburg 70223
(draft).doc"

Unmet needs for Inserting tools and implants please see pictures on page 6 and 7.

B. Hellhammer, K. Spychaj, P. Meier, 6th March 2007

Unmet needs
Inserter

Less frightening
Nudges

Arm of the mesh
more resistant displacement
with retractable anchor?

Helicoidal needles?
clep out.

Not entering
"No so area"

Avoid the deep anterior
transversator passage.
In-out, severe force

more sophisticated
retrieval device

Quicker, safe way
to place the mesh

Avoid needles by
anchoring?
(with smooth suspension)

better fixation
of the uterine cavity
(shape of the intermediate
part of the mesh)

Essary in the
port of
don't drop?

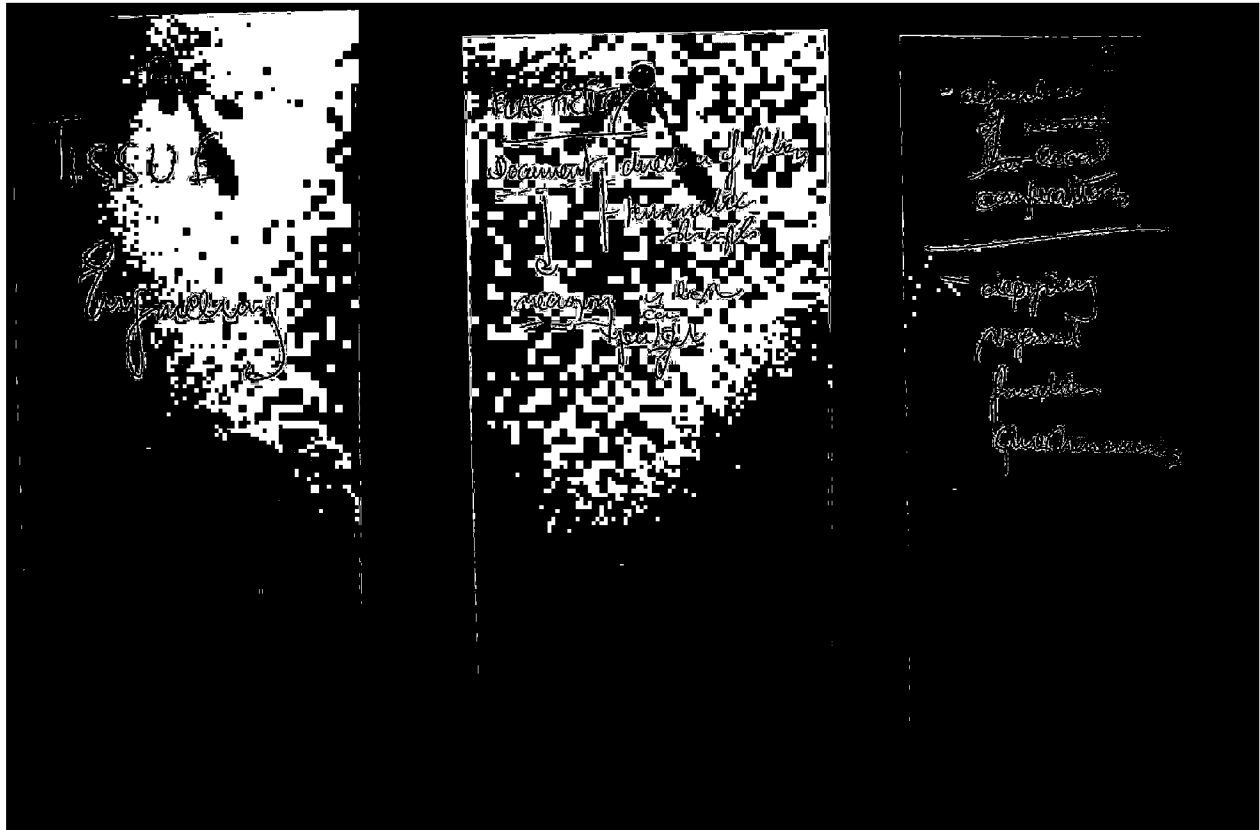
Solution to early
loss to the perineum
transverse cavity.

longer needles
longer needles

better visualization
Control of the mesh
position

Revised apparatus

Coated mesh
Collagen I



OBTAIN
BACKGROUND DATA
MEASURE NORMAL + ANOMALY
VAGINAL COMPLIANCE

Agenda

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Friday, February 23rd 2007

„Forum“ Oststrasse 1, Norderstedt, 9:00 am – 3:30 pm

For all participants arriving Thursday: Dinner will be from 8.00 pm in Hamburg at

*Restaurant **Locks** Marienhof 6, 22399 Hamburg, Tel. 040 / 611 66 00.*

Accommodation is at: Courtyard Hamburg Airport Hotel, Flughafenstrasse 47, Tel: 49 40–531020

Friday February, 23rd, 2007

<u>Time</u>	<u>Target</u>	<u>Name</u>
9.00am - 9.30am	Arrival, Coffee	all
09.30am - 10.00am	Welcome & Update status of project “Ultrapro-Prolift” from Ethicon	R&D and Marketing team;
10.00am - 10.30am	Presentations of participants: • Presentation: Experiences with Ultrapro Usage in Hernia surgery	Dr. med. G. Arlt, Berlin
10.30am – 11.00am	• Factors related to mesh shrinkage: What is found in literature?	Dr. K. Spychaj, Ethicon
11.00 am - 11.15am	Short break if wished	all
11.15 am - 12.30pm	• Presentation of Prototypes • Final Discussion on Ultrapro/Prolift Start a new Project: Next Generation of Pelvic Floor Implants	all
12.30pm - 1.15pm	Lunch	all
1.15 pm - 1.45pm	• Presentation: My vision of an ideal Pelvic Floor implant	Dr. D. Miller, Milwaukee
1.45 pm - 2.30pm	• Presentation Trends and unmet needs in hernia surgery • Biomechanics of meshes	Dr. B. Hellhammer Dr. J. Holste, Ethicon
2.30pm – 2.45pm	Coffee break	
2.45pm – 3.45pm	• Verify unmet needs for ideal Pelvic floor implant generated in previous sessions • Define Characteristics/parameters of an ideal implant/ Inserting means • Define next steps	all, 2 Groups all
	Transfer to Cadaver Lab, Butenfeld 34	
from 4pm	• Human cadaver Wet Lab at University Hospital with “UltraProlift” Prototypes	for those who wish to attend
From 8pm	• Dinner in Hamburg „La Mirabelle“ Bundesstr. 15, Tel. 040 410 75 85	for all who wish to attend

Any Questions or comments: Please contact us: Natascha Nagtegaal (+49 172 9260000) or Peter Meier (+49 172 44 30 697), nnagtega@ethde.jnj.com, pmeier1@ethde.jnj.com