

**Ethicon Expert Meeting
Meshes for Pelvic Floor Repair**

Friday, June 2, 2006; Location: Oststr. 1, Norderstedt, Meeting Room "Forum"

Participants:

Prof. M. Cosson
Prof. B. Klosterhalfen
Prof. J. Deprest
Prof. B. Jaquetin
Dr. V. Lucente
Dr. Vierhout

T. Foltyn
J. Gillespie
Q. Manley
Allison London Brown
O. Berthier
M. Timmer

P. Meier
J. Holste
J. Trzewik
B. Hellhammer

Highlights from the presentations:

Experiences with Vaginal implants (Prof. Cosson)

Complications of pelvic floor surgery using mesh implants:

1. Erosions

May affect vagina, urethra, bladder, rectum

Not considered a big problem in the vagina (3% Vaginal Erosions with Prolift), patient mostly unaware, surgeon cuts out mesh and sutures vaginal wall. More Erosions after Hysterectomy.

There is a need to have a clear definition of erosion, wound dehiscence etc (s.a.)

Clinical experience has demonstrated that uterine preservation and not using a T-incision will help to reduce the risk of erosion.

2. Infection

Monofilament material preferred to multifilament.

Would low density material reduce the infection risk?

Plaintiff's Exhibit

PX 208

3. Contraction

Prof. Cosson offers a classification system. He found a 2,8% symptomatic contraction rate with Prolift.

Clinical symptoms from local palpation through occasional pain and dyspareunia to spontaneous chronic pain.

Chronic pain is not a frequent complication – 1 case observed in 110 Prolift patients – yet it is the complication of most concern to surgeons

Prevention: low lateral tension

Biological response to surgical mesh (Prof. Klosterhalfen)

Huge surface area of meshes (e.g. more than 300 m of suture)

Even after 20 years the tissue is still reacting to the mesh.

Fibrosis is responsible for complications in mesh usage. There is less fibrosis with Vypro compared to PP

Foreign body reaction:

- Fibrinogen and Albumin bind to biomaterial, change and activate the immunologic system
- active process, a “chronic wound”, to be demonstrated by proliferating and dying cells
- combination of material and genetics.

Optimum pore size is material dependent (critical pores size; at least 1-2mm), scar formation a combination of pore size, surface area, polymer.

Large pores: fibrosis on the mesh fiber only

Small pores: interconnection between mesh pores due to fibroses leading to mesh shrinkage.



gray: mesh fibers; **red:** fibrotic tissue

left: large pore size, no interconnection between mesh fibers;

right: small pore size, mesh shrinkage due to fibrotic interconnection between fibers

Benefit of mesh with collagen questionable. Not only the first week of wound healing important.

Early fibrosis in Vypro is reversible.

Bioactive effect needed for 2-3 months, then the scar is mature.

Shrinkage of 20%: Loss of water. Just like scar shrink as well.

Shrinkage of 20% means reduction of mesh area to 64%

Myo-fibrocytes, if many macrophages appear.

Mesh is fixed in tissue within 1-3 days

Observed calcifications in stiff meshes (remaining growth factors, bone formation)

Monocryl causes less inflammatory response compared to Vycril.

Collagen or Titanium on mesh is of no use

Every Individual reacts different to a mesh.

Tension of the mesh changes pore size → change in elasticity

Films or Foils cause more shrinkage than meshes
Meshes can cause Nerve damage due to mechanical irritation (mesh bears on nerve)
There is no inert material

Preclinical models for testing meshes (Prof. Deprest)

He uses 2 animal models: Rat for 2-90 days and Rabbit for 30 days – 2 years
The best results are achieved if meshes are fixed with sutures of identical material
Observations with Pelvicol:
Pelvicol does not integrate in tissue, encapsulation, local degradation (50% of implant), no remodelling, stiff, early and late recurrence (2 y)
It shows little inflammatory response
Xenograft reaction is acellular
Pores versus no pores: better strength with pores
Pro-inflammatory cytokines: less in Pelvicol than in pp
Pelvicol support decreases after 6 months

SIS: bulging after one year (fast remodelling – 90 days)

Clinical experiences with meshes e.g. Vypro (Prof. Jaquetin)

Own results with 106 patients (Vypro 81%, Vypro II 19%, different surgical techniques):
10% recurrence, 9,4% shrinkage (underestimated), 4% rigidity, 17,1% erosions.

Better results achieved in Gynemesh Vypro multicenter study (BHe:

Pelvicol: rejection in 33%, does not recommend its use
TBM: mesh folds and retraction
Concerns: feel edges, arms; own experience with cutting the arm → pain-free
Suggestion: no arms after 2 weeks (all participants agreed), shorter arms.
“could be interesting to use Vypro in prolift”
Erosion is no severe problem, comfort/pain is an issue
Infections can occur 6 months after surgery

Highlights from the discussion:

Connective tissue does not add to strength
In general meshes are too strong in dimension (B. Klosterhalfen, all)
No in-growth in visceral part of mesh
Ligaments stronger (Cosson has data)
center too strong
for recto less than for cysto
Estrogen influence → put estrogen on meshes?!
Blood vessel ingrowth (V. Lucente)
Adhesion barrier is of interest (V. Lucente)
Bioactive: promoting angiogenesis (for 3rd and 4th generation)
Dissection: avoid vessels, no uterine removal
Vaginal pain after implantation of meshes is rare, but feared, since there is no real treatment option (V. Lucente: prefer 20 recurrences or Erosions over 1 pain patient)

Late erosions: apex the most

An acceptance and communication, that erosions will occur in mesh usage for POP-repair could improve the acceptance of meshes.

Devascularisation is one cause for Erosion

Reduce ischemia. Close the vagina? or leave it open?

Pressure inside the vagina (Cosson)

Physiotherapy balloon

Good experience with colporrhaphy + TiMesh extralight (Vierhout)

No deformation of mesh

Coefficient of friction (similar to TVT); friction = holding properties. Friction is important to hold the implant in place for the first hours (friction tests?)

Active role of ProLift = mid of body, beneath the vagina, part of the arms needed for 10 days, no longer (absorbable)

Current shape widely physiologic

Posterior mesh should be longer

TVT + Prolift lowers chance of recurrence

There is a huge need for more research and data in biomechanics of POP and PFR with meshes (Biomechanics model)

Erosion:

Infection, ischemia: technique (surgeon), too superficial, Material

Not a lot to be improved

Shrinkage:

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

More inflammation = more shrinkage ?!

shrinkage is not controlled by “softness” of mesh

One approach might be control of fibrosis and neoangiogenesis

Pronova + Monocryl better than pp + Monocryl?

+ Actives (e.g. plastic surgery to avoid keloid formation, steroids)

Cocktail of steroids (Lucente)

Link Actives to Monocryl or other spacers, absorption 120 d (Klosterhalfen)

Priority: Fibrosis, neoangiogenesis, antibacterial, Collagen test

Ultrapro:

Interesting, confusion, better inflammatory reaction (vaginal outcome?)

Clinical experience

Less shrinkage in animal model (B. Klosterhalfen)

ProLift: excellent, “not ideal” (Jaquetin)

Gynemesh PS: Best material for Sacrocolpopexy

This is the summary of unmet needs:

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	
“Discrete” implant – sections that match needs of physiology	

Different site of PF – Different Implant? (cysto versus recto)	
Cost effective	
Appropriate materials for younger patients	
Thinking outside the mesh for infections <ul style="list-style-type: none"> - managing patient factors , Steroid /smoking/vag. flora - prep of vagina - peri-operative antibiotics - irrigation Role for “local” antibiotics?	
Genetic variability in tissue response Early non-surgical management for “excessive” fibroblast response? Injection of steroids?	

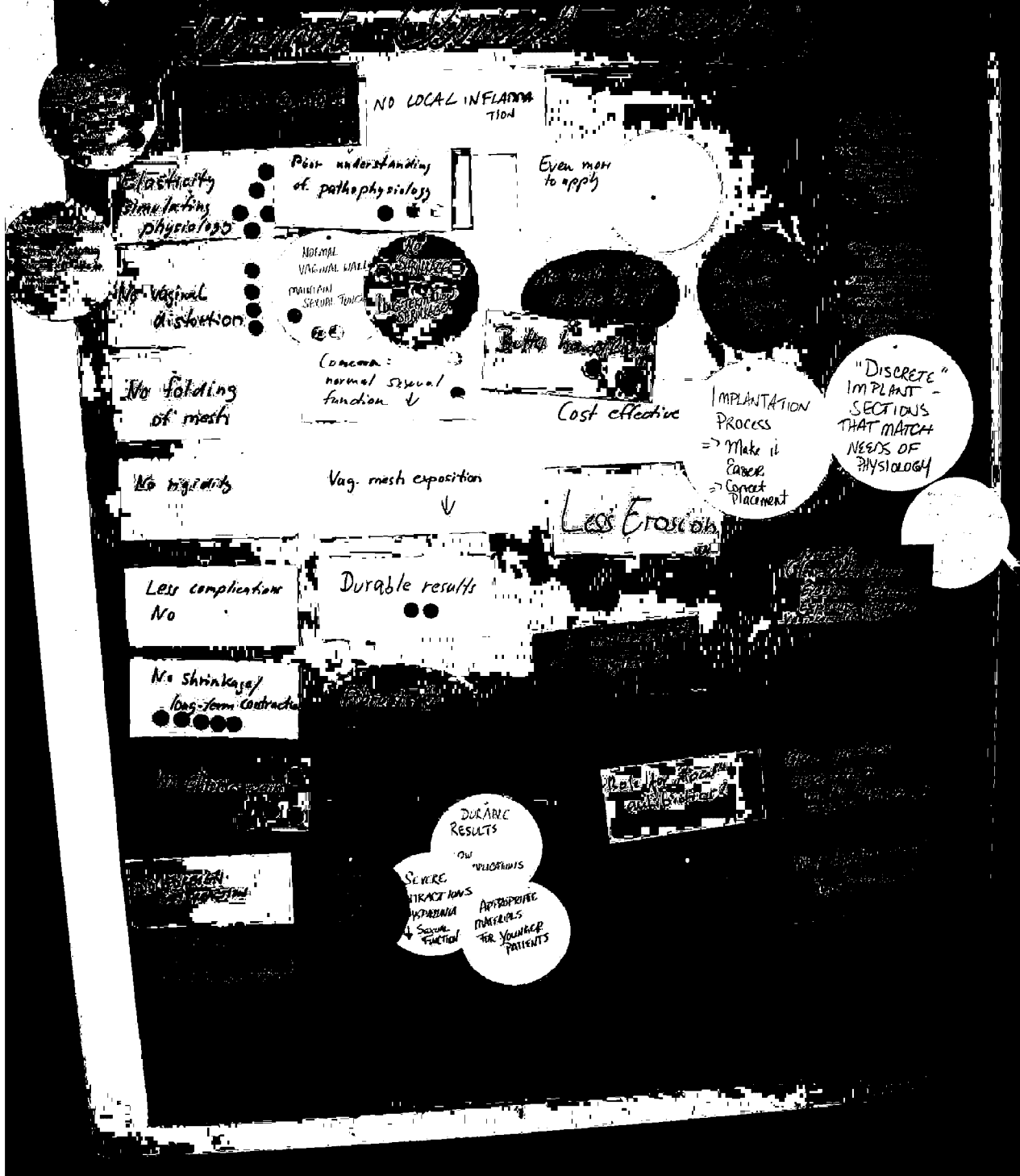
Miscellaneous	Priority
Goals of explant bank	1
Biomechanics model	1
Infection model	1
Model for mesh augmentation in vaginal surgery	1
Education on complication management	
Education for physicians on “shrinkage”, causation and tissue formation	
How to measure “normal” properties of vaginal function? Elasticity, pliability, rigidity, shrinkage	
Extrapolate data on mesh? Hernia versus pelvic floor vs TVT , Best Mesh?	
Strength of mesh? What is needed to support? How much? How little?	
Registry	
Vaginal response during sex cycle	
Why dyspareunia? = Phys. pathology?	
Clear product description multi- versus monofilament	
Need of clear definitions: erosion, exposure, dehiscence, migration, vaginal complications	

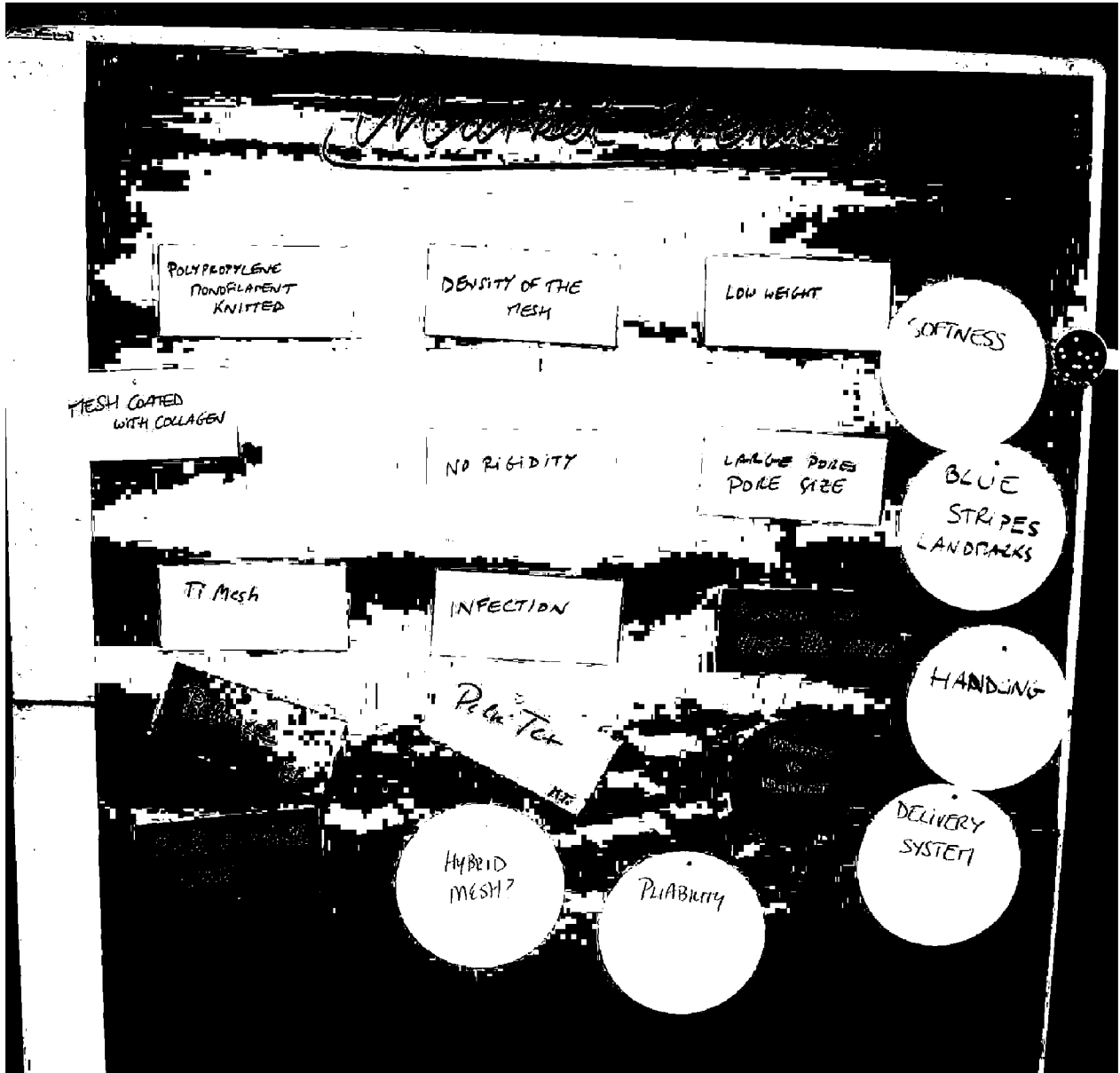
Market trends	
Large Pores; Pore Size	
Low Weight	
Density of the mesh	
Monofilament versus Multifilament	
Infection	
Erosion no longer the issue	

Handling	
Delivery system	
Pliability	
No rigidity	
Softness	
Blue stripes; Landmarks	
Polypropylene monofilament knitted	
Mesh coated with collagen	
Ti Mesh	
Hybrid Mesh ; Partly absorbable hybrid	
Pelvicol	
PelviTex	
Smooth muscle injection	

The usage of Ultrapro in Prolift was fully supported by V. Lucente. M. Cosson and B. Jacquetin like the idea, however would like to have some clinical data before supporting it. Jan Deprest said “Not needed at present, might be confusing, market cannot follow. Maybe later with clinical data” and M. Vierhout was not fully convinced, but is interested in getting some clinical data on usage of UltraPro in pelvic floor repair.

B. Hellhammer, P. Meier, J. Trzewik / June 20, 2006





POLYPROPYLENE
NONWOVEN
KNITTED

DENSITY OF THE
MESH

LOW WEIGHT

SOFTNESS

MESH COATED
WITH COLLAGEN

NO RIGIDITY

LARGE PORE
PORE SIZE

BLUE
STRIPES
LANDMARKS

Ti Mesh

INFECTION

HANDLING

Pliability

HYBRID
MESH?

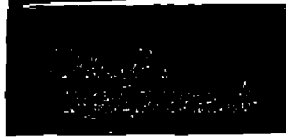
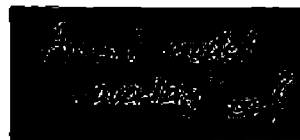
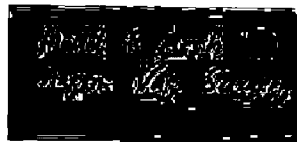
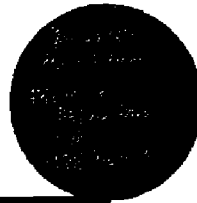
Pliability

DELIVERY
SYSTEM

Miscellaneous

Education
for Physicians
on "Shrinkage"
Caustion &
Tissue Formation

Education
ON
Complication
Management



2010
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