

## POTENTIAL IMPROVEMENT OF PELVIC ORGAN PROLAPSE SURGERY OUTCOME USING A LONG-TERM DEGRADABLE SCAFFOLD WITH OR WITHOUT AUTOLOGOUS MUSCLE FIBER FRAGMENTS – A PILOT STUDY WITH THREE ABDOMINAL MODELS IN RATS.

### Hypothesis / aims of study

To improve long-term outcome of pelvic organ prolapse (POP)-repair, synthetic permanent meshes have been introduced. However, the use of these meshes is controversial and the FDA has issued warnings about the occurrence of frequent and severe complications.

Polycaprolactone (PCL) is a synthetic material which is already approved for some human applications. It has a degradation time of approximately two to four years which could be beneficial in POP repair.

Our aim was to evaluate whether a newly developed electrospun PCL scaffold was sufficiently strong to support increasing tissue loads and whether the scaffold was able to improve tissue regeneration by carrying muscle stem cells in the form of autologous muscle fiber fragments (MFF).

### Study design, materials and methods

We performed an animal study in rats using three different abdominal models that subjected the scaffolds to increasing loads;

- 1) subcutaneous model with limited load, where the PCL scaffold was placed on the existing intact muscle layers of the abdomen,
- 2) partial defect model with moderate load, where the outermost muscle layer of the abdominal wall was removed and the PCL scaffold placed above the defect area,
- 3) full thickness model with high load; all three muscle layers of the abdominal wall were removed and replaced with the PCL scaffold.

The MFF were created by cutting an autologous muscle biopsy into small pieces of approximately 1 mm<sup>3</sup>. The MFF were labeled with PKH26, a fluorescent dye which labels the muscle fibers and the associated stem cells. We used twelve animals in each model; six with and six without MFF. Tissue samples were harvested after eight weeks and subjected to histopathological evaluation, immunohistochemical demonstration of desmin, fluorescence microscopy and uniaxial biomechanical testing.

### Results

#### *Macroscopic evaluation, fluorescence and histopathology*

None of the animals developed hernia. There was a massive in-growth of non-myogenic desmin-negative cells into the PCL scaffold and formation of collagen. A marked foreign body response in the form of numerous giant cells located around the PCL fibers was also observed. No fluorescence-labeled or desmin-positive cells or fibers were observed inside or around the scaffold. The thickness of the PCL scaffold and the ingrowth of cells were comparable among all models and among those with or without MFF.

#### *Biomechanical results*

The following variables were measured and tested for differences between groups; stiffness in the low- and high stiffness zones (N), maximum strength (N), maximum strain (%). The variables were tested for a smaller tissue-strip including only the scaffold and for a larger tissue-strip including the scaffold and the surrounding tissue. Biomechanical testing revealed no significant differences between the three models, and no significant differences between those with or without MFF.

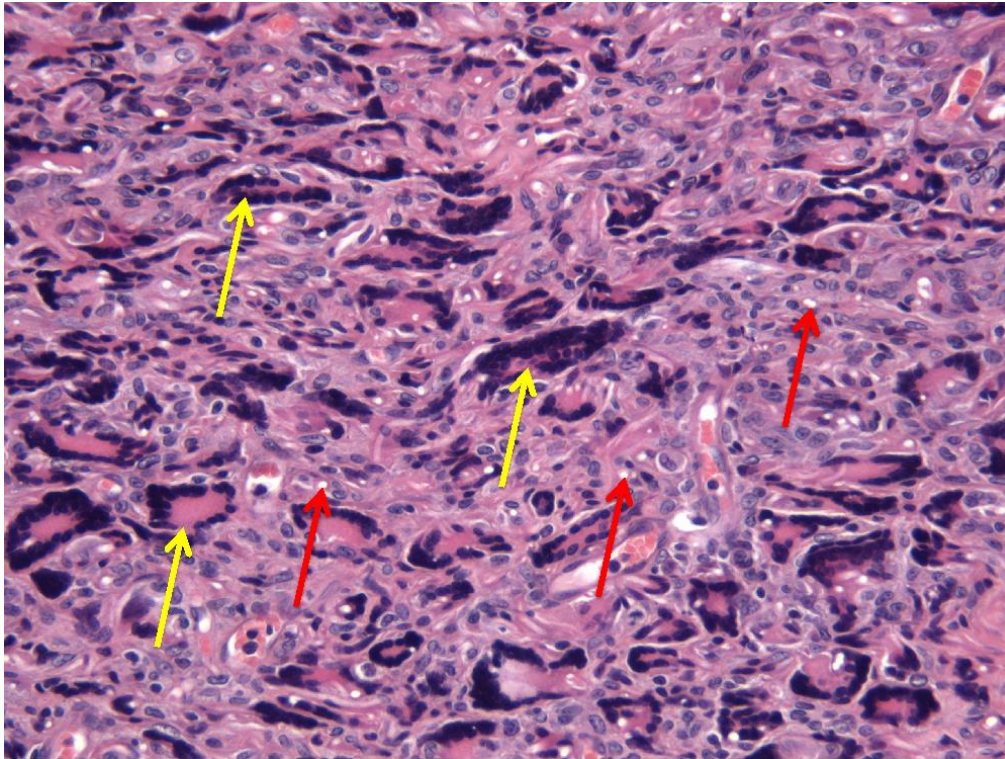


Figure 1. Demonstrating a marked foreign body response with numerous giant cells (examples marked with yellow arrows) located around the PCL fibers (examples marked with red arrows). H&E staining, original magnification x200.

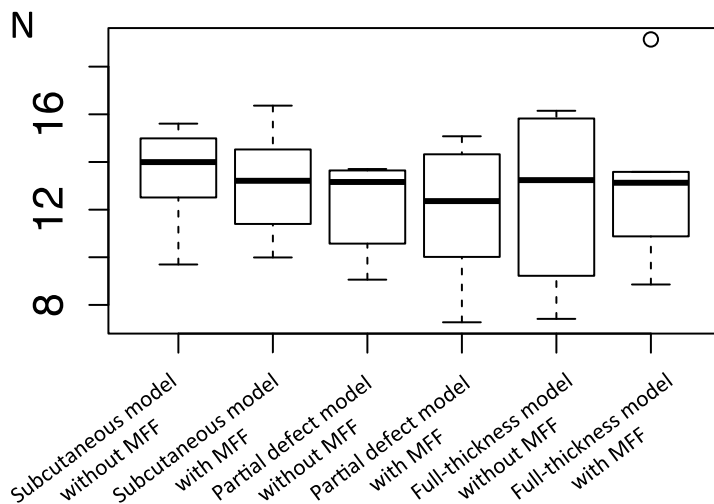


Figure 2. Boxplot visualizing non-significant differences regarding maximum strength (N) for the three models with different loads, with or without MFF.

#### Interpretation of results

After eight weeks, the long-term biodegradable PCL scaffold implanted abdominally in rats developed into a strong neo-tissue with numerous desmin-negative cells, collagen formation and a massive foreign body response. We did not find cells or fibers deriving from the MFF, and it is possible that the significant immune reaction does not allow survival of transplanted cells. We found no significant biomechanical differences between models or groups with or without MFF, and it is therefore unlikely that MFF influence the regenerative response in these settings.

#### Concluding message

PCL allowed formation of a strong neo-tissue after eight weeks, but MFF with associated stem cells did not survive in the models used. To evaluate whether PCL alone has any effect on the outcome in POP surgery, long-term preclinical studies allowing complete degradation of the PCL scaffold are needed.

#### Disclosures

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