

BIOCOMPATIBILITY OF A NEW IMPLANT TYPE FOR PELVIC RECONSTRUCTIVE SURGERY

Hypothesis / aims of study

Due to unacceptable complication rates of currently used synthetic permanent implants for pelvic reconstructive surgery, safer alternatives are demanded. A resorbable implant consisting of MPEG-PLGA (methoxypolyethyleneglycol-poly(lactic-co-glycolic acid)) have been developed. It is chemically and structurally different from the PLGA known as Vicryl®: It is freeze-dried instead of knitted and made more hydrophilic to promote in-growth of cells and improve the repairing process. Figure 1 illustrates the different structures. The aim of the study was to investigate biocompatibility and durability of three MPEG-PLGA implants: plain, enriched with extracellular matrix (ECM, ACell, Inc.) or estrogen (Estradiol, Sigma-Aldrich, Inc.).

Study design, materials and methods

Twenty implants of each preparation, sized 1x2 cm, were implanted subcutaneously on the abdomen of rats, two in each. As control a sham site with blunt dissection and a single stitch of Vicryl suture was used. Explantation was carried out after 3 weeks (15 rats) and after 8 weeks (15 rats). Explants were fixed in 10% buffered formalin, routinely processed for histopathology and stained for hematoxylin and eosin, and Giemsa. Inflammation, vascularization and connective tissue organization were scored semi quantitatively on a scale of 0–4 (none–intense/heavy). At 3 weeks, assessment was done within the implant. At 8 weeks where the implant had disappeared, assessment was done within the remaining granulation tissue at the site. The thickness of the scar tissue was measured at 100x magnification. Each 10 units of measure equal 1.28 mm at this magnification. Two 3-week specimens (both from implants enriched with estrogen) and one 8-week sham specimen were excluded due to errors occurring during histopathological processing. Data are presented as mean and standard error (SE) and analyzed using the non-parametric Kruskal-Wallis analysis of variance test followed by Mann-Whitney U test for pairwise comparisons between groups.

Results

At 3 weeks, all implants had a satisfactory in-growth of cells. The in-growing cells were distributed throughout the implant. Scores of inflammation differed significantly among different implants. Levels were higher in those enriched with ECM than in plain implants (Table 1). Scores of vascularization, connective tissue organization and thickness of the scar tissue did not differ significantly. No traces of the implants remained at 8 weeks. There was no foreign body reaction and no signs of a lingering chronic inflammatory reaction. The possible effects of enrichment of the implant had vanished at 8 weeks (Table 2). No significant differences were found in the thickness of the connective tissue after the implants compared to sham sections.

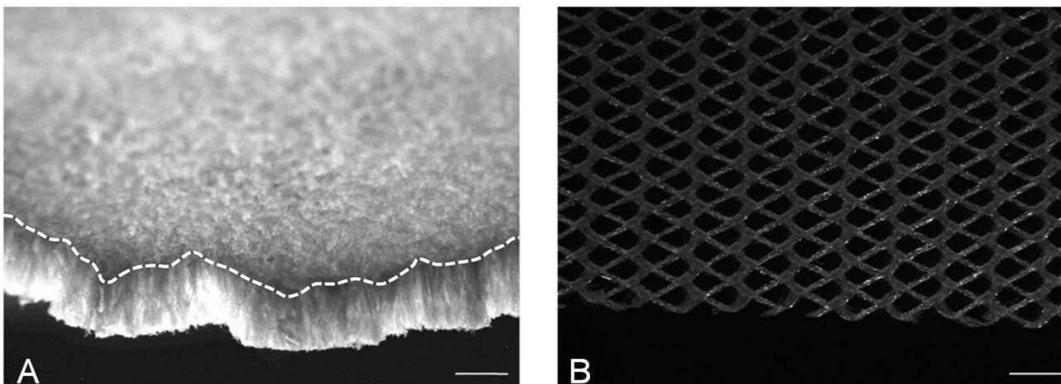
Interpretation of results

The results at 3 weeks indicated a more advanced stage in the healing process in implants enriched with ECM. The initial effects of enrichment with ECM had vanished after 8 weeks. The MPEG-PLGA implants were completely biocompatible, disappearing in 8 weeks and leaving no trace behind. Qualitatively, the tissue response at 8 weeks was the same after implants as after sham surgery. The durability of less than 8 weeks was unexpected and is too short for the use per se in pelvic reconstructive surgery. However, due to the characteristics presented here the implant could have a future role as carrier for stem cells, promoting their growth and not affecting the host tissue.

Concluding message

The MPEG-PLGA in all three preparations had excellent biocompatibility. However, the durability was unexpectedly less than 8 weeks, which makes the implant per se unsuitable for use in pelvic reconstructive surgery, but it could be useful if combined with stem cells.

Figure 1



A: Porous sponge structure of MPEG-PLGA. Dashed line marks edge between the surface and the cross-sectional view of the implant. B: The knitted structure of the Vicryl mesh.

Digital images of dark-field stereomicroscopy at 10x magnification. Scale bar: 1.0 mm.

Table 1

	n	Inflammation	Vascularity	Connective tissue	Thickness
A: Plain implant	10	3.3 (0.15)	1.9 (0.18)	0.7 (0.26)	12.8 (2.3)
B: Implant w/ ECM	10	3.9 (0.10)*	1.5 (0.17)	1.5 (0.27)	11.8 (1.2)
C: Implant w/ estrogen	8	3.8 (0.16)**	1.6 (0.26)	1.3 (0.37)	14.9 (2.0)
A vs. B vs. C		p=0.02	p=0.33	p=0.12	p=0.52

3 week scores for inflammation, vascularity and connective tissue organization, 0–4 (none–intense/heavy). Thickness in absolute measure. Mean (standard error).

*A vs. B: p=0.02, ** A vs. C: p=0.08

Table 2

	n	Inflammation	Vascularity	Connective tissue	Thickness
A: Plain implant	10	1.4 (0.16)	1.5 (0.17)	3.0 (0.0)	8.7 (1.3)
B: Implant w/ ECM	10	1.6 (0.16)	1.6 (0.16)	3.0 (0.0)	9.1 (0.9)
C: Implant w/ estrogen	10	1.4 (0.16)	1.6 (0.22)	3.1 (0.1)	11.1 (2.2)
D: Sham	9	1.0 (0.0)	0.8 (0.20)	3.0 (0.0)	11.6 (2.3)
A vs. B vs. C		p=0.72	p=1.0	p=1.0	p=0.79
A vs. B vs. C vs. D				p=1.0	p=0.87

8 week scores for inflammation, vascularity and connective tissue organization 0–4 (none–intense/heavy). Thickness in absolute measure. Mean (standard error).

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Is this a clinical trial?	No
What were the subjects in the study?	ANIMAL
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	Yes
Name of ethics committee	The Danish Animal Experiments Expectorate