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A LONGITUDINAL MORPHOLOGICAL EVALUATION OF THE HOST RESPONSE TO TWO COLLAGEN BASED AND ONE POLYPROPYLENE IMPLANTS IN A RABBIT MODEL FOR ABDOMINAL WALL HERNIA.

Hypothesis / aims of study

Fascial reconstruction of prolapsed pelvic organs using native tissue can be reinforced with implant materials to prevent or treat recurrence. Biomaterials may overcome the side effects related to the use of non-absorbable implants such as erosion, dyspareunia and infection. Xenografts are increasingly used but little is known about their long term durability. We conducted a long term experimental study comparing the integration of cross-linked porcine dermal collagen (Pelvicol,Bard), collagen matrix derived from small intestinal submucosa (SIS-4L,Cook) and Prolene (Johnson&Johnson) in a rabbit model for abdominal wall hernia repair.

Study design, materials and methods

Four 2.5x2.5cm full thickness abdominal wall defects were created in 45 New Zealand rabbits. In a random fashion the defects were closed with one of the studied materials. Nine rabbits were sacrificed at either 30,60,90,180 or 365 days(d). Explants were fixed, embedded and 5µm sections were stained for morphological evaluation. Representative areas of the implant, as well as the interface between the implant and recipient's native fascia were assessed with a semi-quantitative scale (Badylak,2002) documenting the inflammatory response, neovascularisation (Hematoxylin and Eosin) and the connective tissue deposition (Movat). Immunohistochemistry was performed to document the presence of macrophages (RAM-11; Dako) and collagen deposition.

Results and interpretation of results:

Structural integrity: Prolene implants remained intact the entire observation. SIS-4L implants were not more recognisable from 60d onwards. In the Pelvicol group there were important interindividual differences. Up to 180d the implants remained unchanged but at one year half of the implants were degraded in places; the other half of the implants remaining entirely intact.

Inflammatory response: all materials induced a pronounced inflammatory reaction at 30d, declining over time (Fig.1). At 30d, the infiltrate in collagen materials included mononuclear and polymorphonuclear cells while in the Prolene group the infiltrate was dominated by mononuclear cells. Later on, Prolene was associated with the strongest inflammation, persisting till the end of the experiment. The inflammatory response to collagen materials weakened earlier in time to persist at low levels for SIS. At all times, Prolene and SIS-4L implants had inflammatory cells within the implant. In Pelvicol the infiltrate remained limited to the interface but from 180d onwards, in half of the Pelvicols an infiltrate was seen within the implant without signs of suppurative infection, whereas others did not.

Collagen deposition (Fig.2): Prolene induced an intermediately dense collagen deposition appearing irregularly organised, it's amount showing no significant changes over time. However the nature of the connective tissue went from cellular to more fibrous and organised. Compared to Prolene, the amount of collagen deposited around SIS-4L implants was comparable early on, however the new collagen was more orderly organised. At 365d the area of remodelling appeared as a thin layer of fibrous collagen, macroscopically almost transparent. In Pelvicol, the collagen deposition started off at lower levels to increase slowly over time ending at similar levels as the above after one year. Up to 90 d the connective tissue sandwiched the implant without invading it. From 180 days on there was a progressive connective tissue invasion in half of the implants; the other half remaining intact without any sign of connective tissue invasion.

Neovascularization: Prolene induced the strongest neovascularisation (Fig.3)(4-10 blood vessels/HPF) in in the first 60d. Afterwards the score did not change anymore, but the vessel calibre increased. In the SIS-4L group newly generated blood vessles looked smaller in

calibre. In Pelvicol implants the newly generated blood vessels initially could only be found at the interface, to extend only later on to the centre of the implant

Concluding message:

The host response to Prolene is clearly different from that to collagen based materials, but also between the cross-linked and non-cross-linked materials. Prolene remains intact and induces a strong acute inflammatory response evolving into a persisting chronical inflammation. It gets colonized by a rather disorganised connective tissue. The original SIS-4L collagen matrix is degraded within 60d after inducing a strong acute inflammatory response. The material is rapidly replaced by architecturally well organised collagen, the total amount not increasing over time. Pelvicol remains almost unaffected the first half year, with inflammatory cells not invading the implant and collagen deposition paralleling the implant. At one year half of the Pelvicol implants shows areas of local degradation. Histologically this correlates to an infiltrate by inflammatory cells, and partial replacement with newly formed connective tissue. The other half of the implants remained quasi intact. We have so far no explanation why this would happen in only half of the animals.

References:

Badylak SF et al. Morphologic study of small intestinal submucosa as a body wall repair device. J Surg Research 2002;103:190-202.

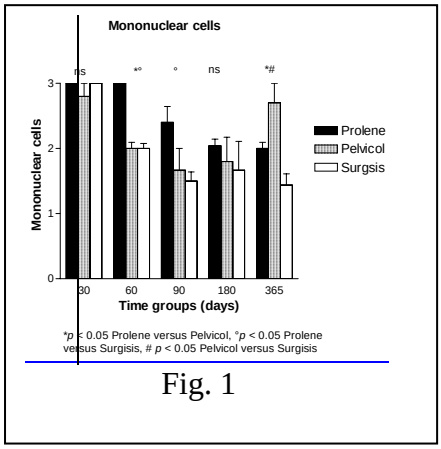

Fig. 1

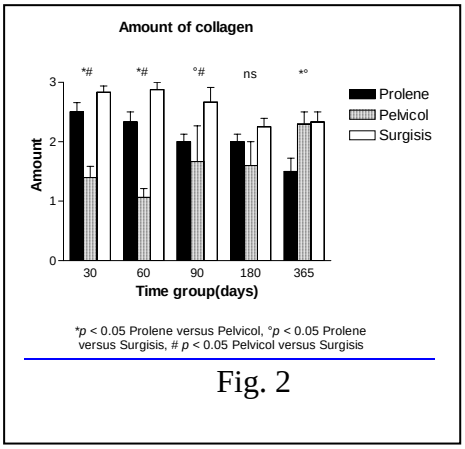

Fig. 2

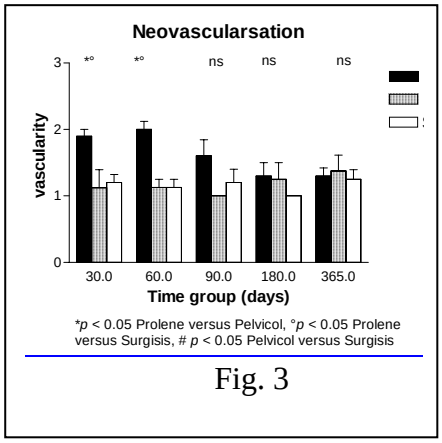

Fig. 3