A New Filtering Approach in Improving Safety and Long Term Effect of Filtering Surgery Utilizing a 3-D Collagen Gag Matrix--An Animal Model

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Purpose:

To devise a means of providing controlled resistance between the anterior chamber and subconjunctival space after trabeculectomy by implantation of a biodegradable, porous matrix.

Material & Method:

The matrices were implanted in the right eyes of 17 rabbits after trabeculectomy, while the left eyes served as surgical controls. Loose sutures were used and the implant provided additional pressure on the scleral flap to reduce overfiltration. Trabeculectomy in the control eyes was performed with tight sutures using standard methodology. Intraocular pressure (IOP) was measured before surgery and on days 3, 7, 14, 21, and 28 post-operatively. Masson-trichrome and alpha smooth muscle actin stains were used for histological study of the filtering blebs.

Result:

Masson's trichrome and alpha-SMA staining

In the unimplanted eyes, immunostaining of alpha-SMA revealed that numerous myofibroblasts aligned parallel to the sclera surface until day 14 after surgery, and the compactly aggregated collagen fibers secreted by myofibroblasts resulted in wound contraction. In contrast, less scattered myofibroblasts were distributed in the implanted areas of the eyes. They adhered randomly to the remaining matrix and the wound area surroundings. As a result, wound contraction seldom occurred in the implanted eyes. During the period of degradation of the implant, the space of the bleb remained functional (Figs_1,2).

On postoperative day 21, wound contraction in the control eyes becomes even more pronounced, due to the aggregation of collagen fibers in the subconjunctival space and the contraction of the myofibroblasts adjacent to the wound. The subconjunctival space was consequently smaller or collapsed. In contrast, the larger subconjunctival space of the implanted eyes was due to the random distribution of collagen fibers and myofibroblasts as well as the degradation of collagen/C-6-S copolymers. Observation on day 28, after surgery showed that in control eyes, the space of the bleb diminished with dense linear collagen filling in the subconjunctival space(Fig. 3). However, in the implanted group, there was a prominent bleb with some collagen dispersed inside the subconjunctival space and no implant remaining (Fig. 4).

IOP

On the first postoperative day, IOP in both groups showed little difference, implying that the tension over the scleral flap was well controlled in both cases. In the control eyes, IOP decreased about 16% immediately after trabeculectomy. In the implanted eyes, IOP decreased about 14% immediately after trabeculectomy. However, the control group maintained the decreased IOP only for the first two weeks, finally reverting back to the pre-operative IOP level. In contrast, for the implanted group, the IOP decreased steadily, finally reaching approximately 55% at day 28 after surgery (Fig 9). The results temporally correlated with morphological observations. The difference on day 7, 14, 21 and 28 is significant. ($P<0.05$)

Discussion

Scar formation is the most common cause of bleb failure. To improve the results of trabeculectomy, the contradictory relationship between safety and long-term efficacy needs to be resolved. A new physiological environment of the bleb should be established, i.e. dynamic drainage of the aqueous from the anterior chamber to the conjunctival space should be preserved. A major complication of scarring is the formation of Tenon's capsule cysts, consisting of compressed collagen lamellae with few cells and no epithelial lining, preventing reabsorption of aqueous humor. The ideal surgical model should control the post-operative IOP stage by stage while normalizing the wound healing without inhibition of fibroblast proliferation to get a normal conjunctiva and functional bleb.Based on the model of wound healing of the conjunctiva in an animal study, wound contraction occurs during the acute inflammatory stage with certain growth pattern of myofibroblasts. With the completion of wound contraction and dense, linear collagen deposition, as experienced in scar formation, the healing process stops. The application of 3-D collagen matrix can lead to a random reorganization of regenerating myofibroblasts, fibroblasts and the secreted extracellular matrix, resulting in less scar formation.To prevent inducing further inflammation of the space between the scleral flap and scleral base and offer effect of controlled drainage, the implant was placed on top of the scleral flap, not in the tunnel. Before wound maturation, the implant sustains its function as a reservior without collapse. After complete degradation of implant, bleb formation was prominent without fibrosis compared with that in the control group. This new approach to normalizing filtering surgical wound healing shows the potential benefits both from the point of physics and of physiology.

Figure 1: The intact implant occupies the subconjunctival space with cells (white arrow) migrating on its surface . The nuclei are stained brown. (Masson Trichrome stain,20X,Day 7)

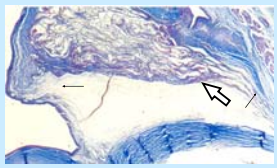

Figure 2: The partially degraded implant (white arrow) floating inside a prominent bleb. There are still cells inside the implant, as opposed to the region where the implant has degraded, in which only collagen remains (black arrow). (Masson Trichrome stain, 20X,Day 14)

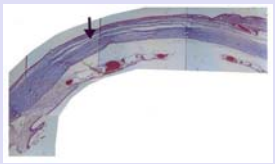

Figure 3: Typical scar tissue shown as compactly arranged collagen fibers distributed in the diminished bleb area of the control group. (Masson Trichrome stain, Day 28).

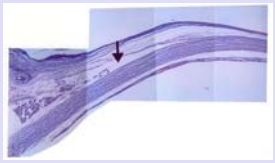

Figure 4: Very little identified collagen randomly distributed in the prominent bleb area of fully degraded matrix. (Masson Trichrome stain, Day 28).

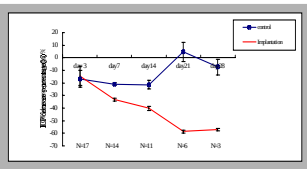

Fig. 5: Course of IOP after implantation of the collagen matrix

Conclusion: Implantation of a biodegradable, porous collagen matrix in the subconjunctival space offers the potential for a new means of avoiding early scar formation and maintaining long-term IOP control by creating a loosely structured filtering bleb.