A confocal study of the prevention of capsular opacification in lens refilling surgery in rabbits and monkeys

TG van Kooten[1,*], SA Koopmans[2], JMM Hooymans[2], HJ Busscher[1], T Terwee[3]

1.BioMedical Engineering, University Medical Center Groningen (UMCG), University of Groningen, A. Deusinglaan 1, 9713 AV Groningen. 2. Ophthalmology, address (1). 3. AMO, Van Swietenlaan 5, 9728 NX, Groningen, The Netherlands

Statement of Purpose: Cataract surgery involves the replacement of the diseased, crystalline lens with a non-accommodating, polymeric intraocular lens (IOL). In order to allow accommodation to occur, it has been proposed to fill the intact capsular bag with a soft, gel-like polymer that is injected into the bag. This approach can also be used to restore accommodation after the onset of presbyopia. The surgical technique involves the creation of a small capsulorhexis through which the lens nucleus and cortex are removed and the refill polymer is injected. As an intact capsular bag is important for a proper accommodation, the treatment must be focussed on the long-term prevention of capsular opacification. The aims of this study are to determine the feasibility of treating the capsular bag during the surgical procedure, and to microscopically assess the effects of the treatment with respect to potential prevention of opacification.

Methods: A prospective implantation / treatment study was performed in 24 New Zealand White rabbits, weighing between 1.6 and 2.2 kg. Pilot experiments were performed in 4 monkeys. The animals underwent lens refilling surgery. A small opening (capsulorhexis) was made in the lens periphery and the lens was removed. Then a 2.7 mm diameter silicone plug was inserted into the capsular bag to prevent leakage during treatment and refilling. Treatment consisted of a 5-minute exposure of the lens epithelium to toxic compounds dissolved in either A.dest or 1.0% (w/v) sodium-hyaluronate in A.dest (h). The A.dest solution was applied through a perfect capsule device (Milvella, Epping, Australia). The sodium-hyaluronate gel was applied directly through the capsulorhexis. Three different solutions were used: A.dest, cycloheximid 25 µg/ml (c) and a combination of cycloheximid 25 µg/ml and actinomycin D 10 µg/ml (ca). Control animals were exposed to the full surgical procedure without treatment. Finally, a two-component silicone polymer (AMO, Groningen, the Netherlands) was injected into the capsular bag (Koopmans 2003). Rabbits were sacrificed at 14 weeks after implantation, monkeys were sacrificed after 17-27 months. Cornea's and complete lenses, with intact capsular bag and implanted silicone lens material, were taken out, fixed, and immunocytochemi-cally stained with DAPI, anti-vimentin antibody and TRITC-Phalloidin. Observations were performed with a LEICA TCS SP2 confocal microscope.

Results/Discussion: Evaluation of the presence of cells on the inner capsular wall with confocal laser scanning microscopy was performed. The nuclei were counted. In Fig. 1 the averages of all counts for a specific treatment are depicted. The large standard errors reflect the high variation in cell densities observed in the case of opacification, as illustrated in Fig.2.

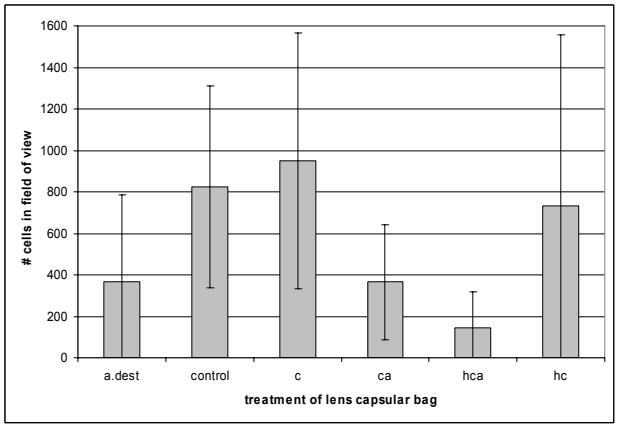

Figure 1. Effect of capsule treatment on presence of cells. See methods for explanation of treatments (h, c, ca and combinations).

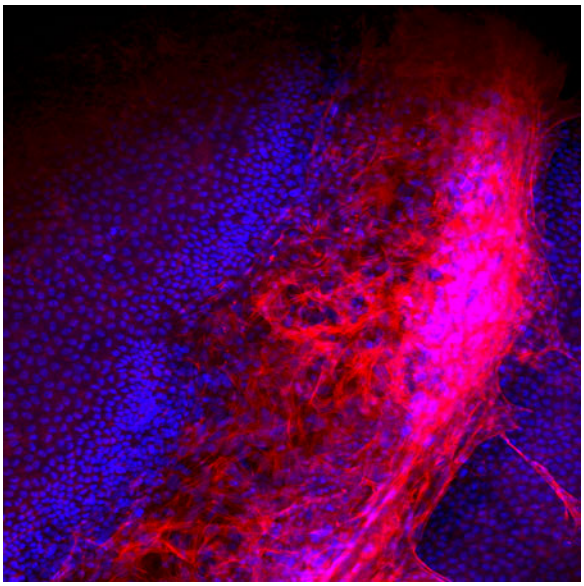

Figure 2. Typical appearance of capsular opcification with blue nuclei and red actin ((750x750) μm^2).

Overall, the application of a combination of cycloheximid and actinomycin D yielded the clearest implanted lenses (ca and hca) in rabbits. In monkeys, a gradual fibrosis occurred despite the treatment resulting in a starting opacification. The use of sodium hyaluronate (h) for delivering the drugs proved to be much safer than the A.dest solutions, as cornea endothelium was damaged in the latter treatment group.

Conclusions: Actinomycin D can be used to prevent capsular opacification in rabbits after implantation of an accommodating silicone lens.

References: Koopmans SA, et al. IOVS 2003;44:250-257.