



# Attenuation of bleb-fibrosis associated with glaucoma filtration surgery by PEI-decorin gene therapy

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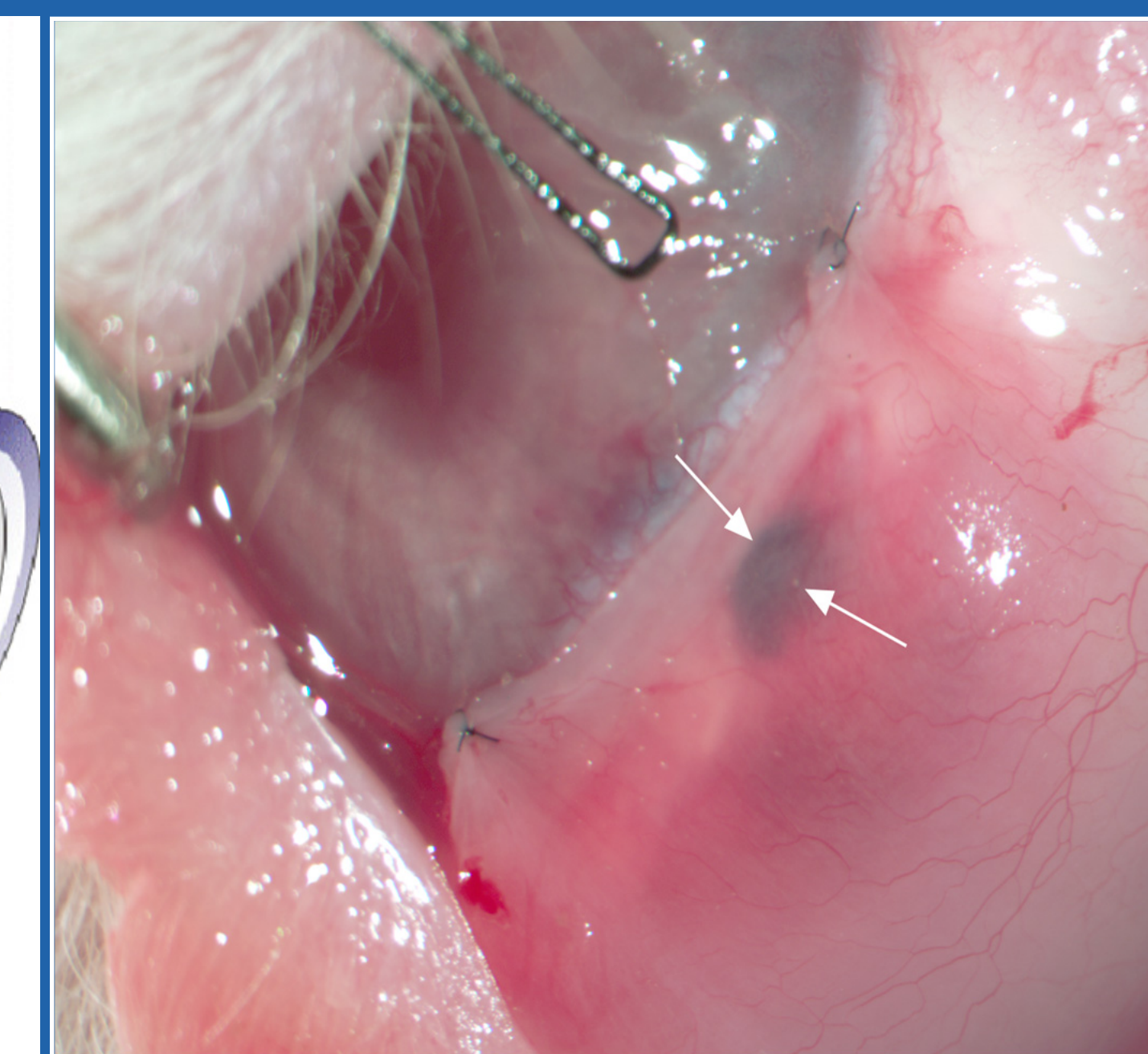
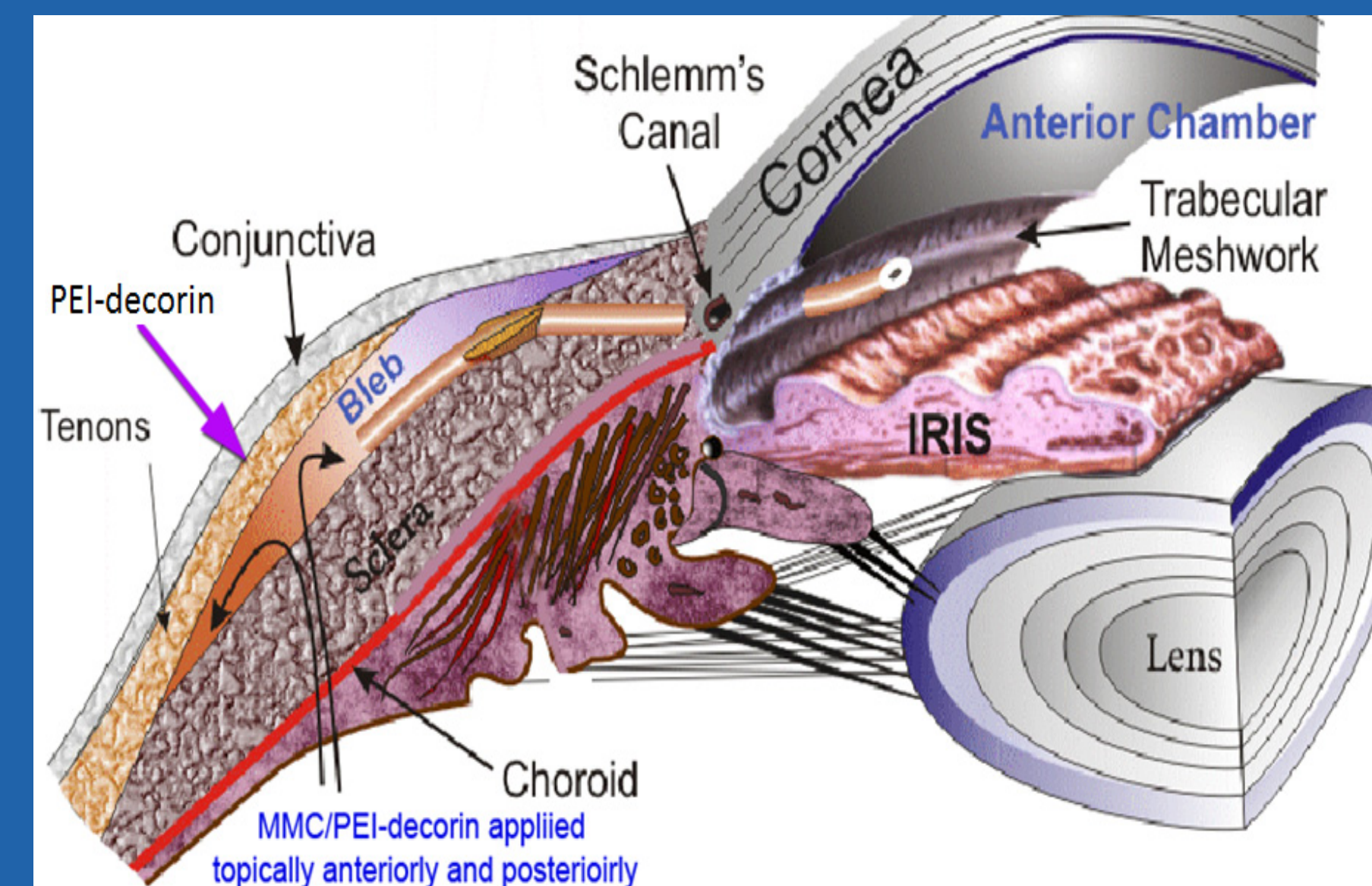


## Rationale

- Glaucoma filtration surgery (GFS) is frequently used to treat glaucoma
- Bleb fibrosis due to excessive wound healing is a major complication and cause for the failure of GFS
- Transforming growth factor beta (TGF $\beta$ ) is a cytokine that plays an important role in wound healing by triggering transformation of keratocytes to fibroblasts and myofibroblasts
- In wound healing there is an excessive amount of TGF $\beta$  activity
- Decorin, a small leucine-rich proteoglycan, is a natural inhibitor of TGF $\beta$

## Hypothesis

We hypothesized that subconjunctival injections of decorin plasmid-PEI nanoconstructs would inhibit TGF $\beta$  activity and attenuate excessive fibrosis while improving the outcome of GFS surgery in rabbit eyes *in vivo*



## Methods

- GFS was performed by creating a 1.5 mm<sup>2</sup> sclerotomy on New Zealand white rabbits
- One group received a sub-conjunctival injection of PEI-decorin nanoparticle plasmid polyplexes 30 minutes before GFS
- Another group received an injection of saline solution
- Biomicroscopy was performed on days 0, 3, 7 and 14
- Bleb height was graded: 0 = flat; 1 = shallow/formed <1mm; 2 = elevated <2mm; 3 = high >2 mm
- Bleb vascularity was graded: 0 = avascular; 1 = normal vascularity; 2 = hyperemic; 3 = very hyperemic
- Intraocular pressure (IOP) was measured using tonopen
- Tissues were collected on day 14 for histological and immunofluorescence analysis

## Results

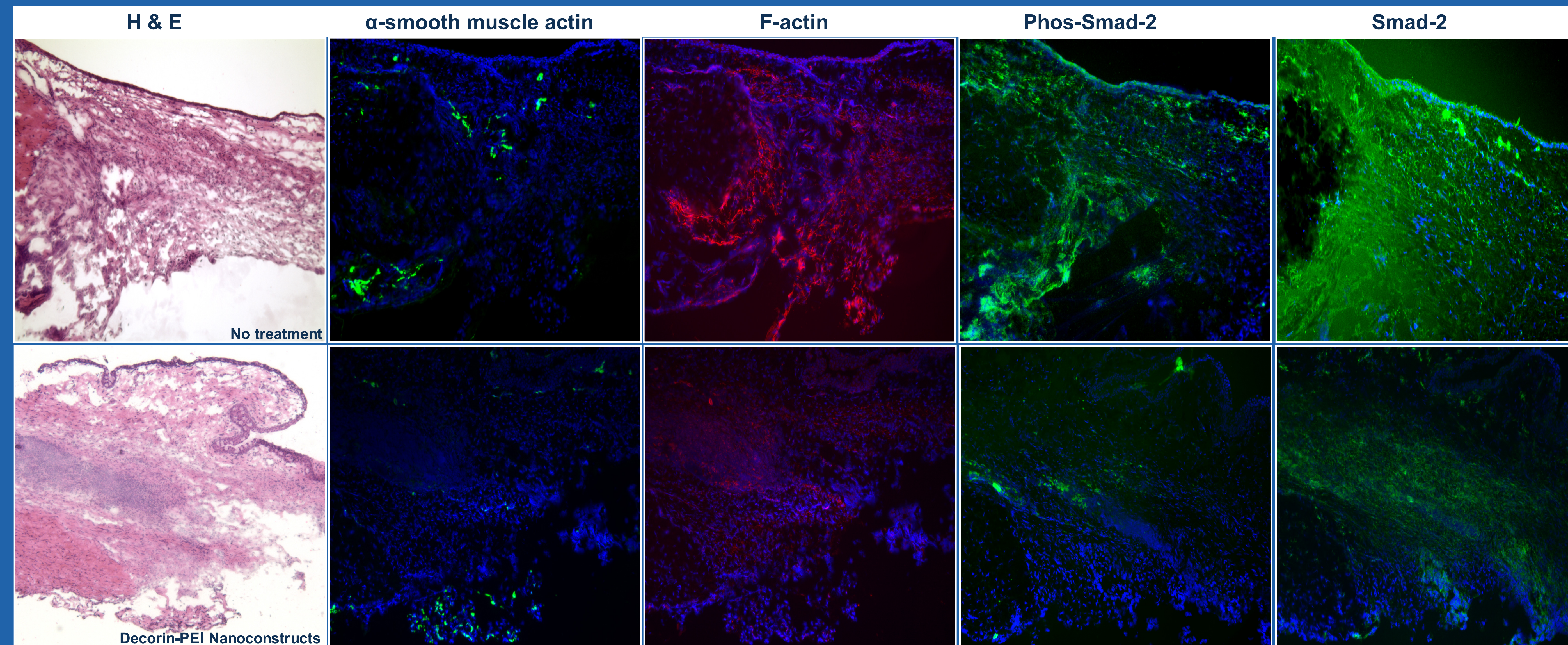
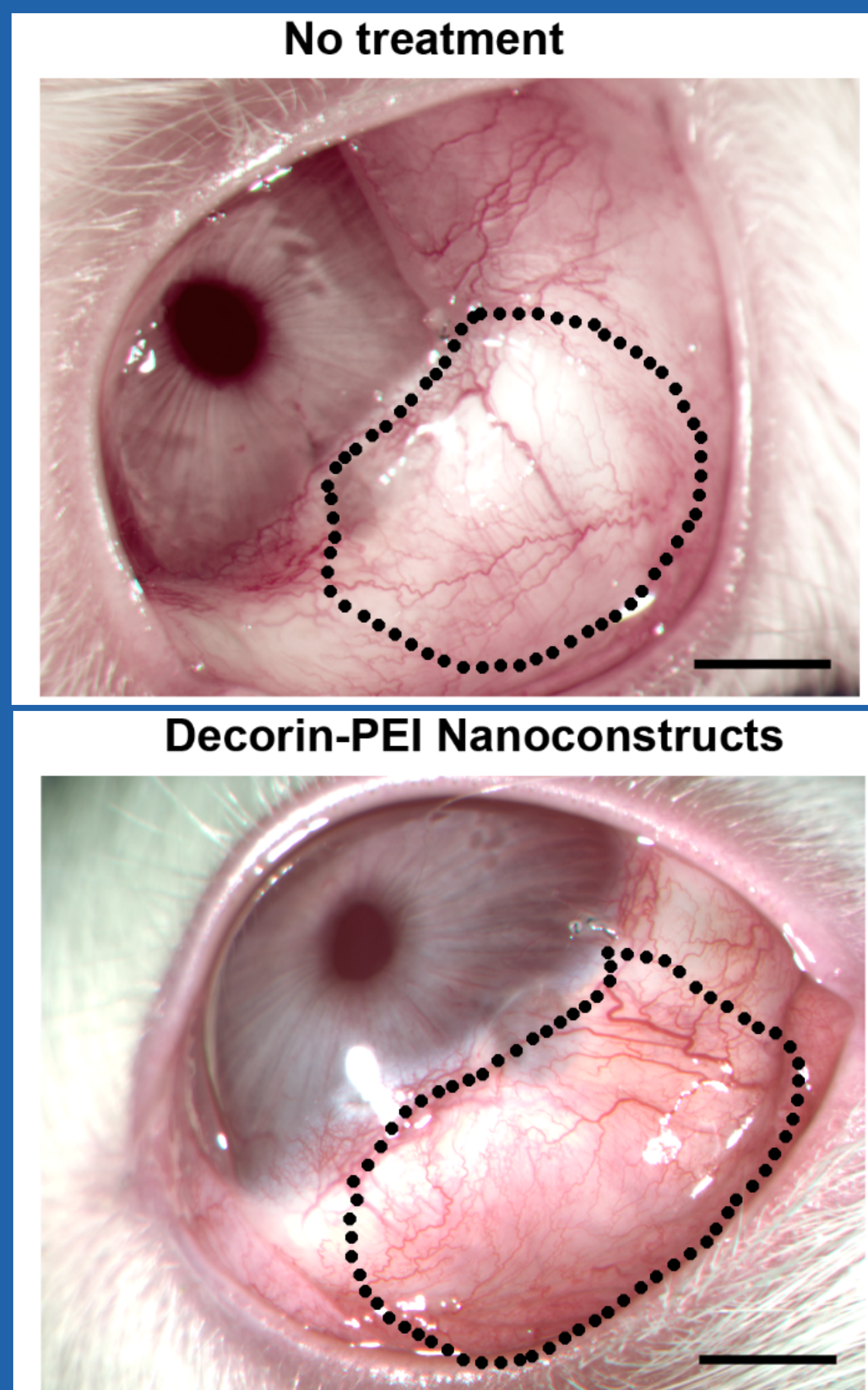


Fig 1: Stereomicroscopic image showing elevated bleb in decorin-PEI Nanoconstructs treated rabbits. Scale bar = 1 mm.

Fig 2: Comparison of non-treated (top) and treated (bottom) tissues with various stains of ocular tissue sections at the site of sclerotomy 14 days after GFS. Decorin-PEI nanoconstructs attenuated postoperative fibrosis as evident by notably less f-actin,  $\alpha$ -smooth muscle actin, and phos-Smad-2 respectively in comparison to non-treated control tissues.

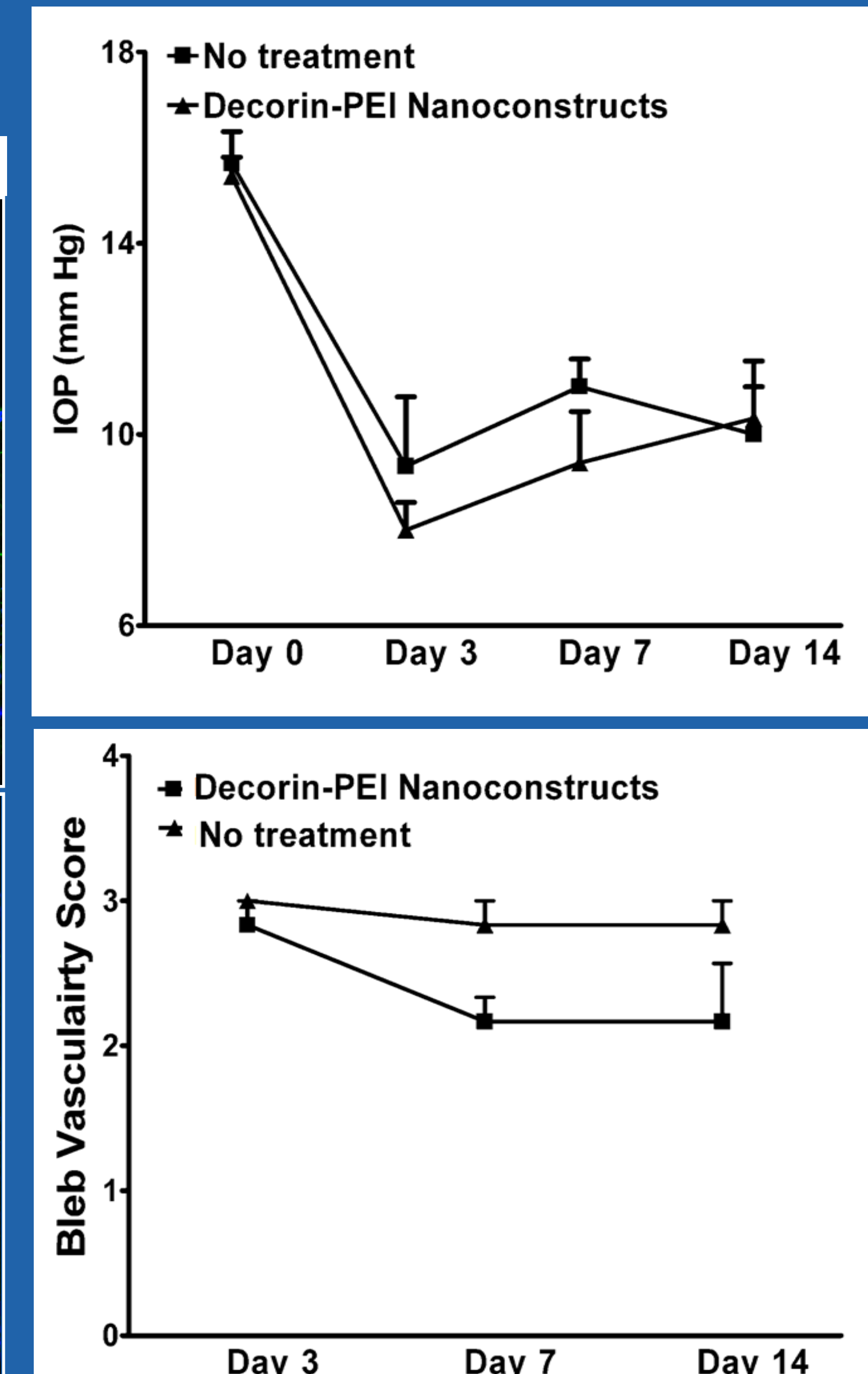


Fig 3: Graphs showing IOP and bleb vascularity at time of GFS and other time points.

## Conclusions

The intraoperative subconjunctival decorin-PEI nanoconstructs significantly decrease postoperative fibrosis and improves the outcome of GFS. This can be seen by the decrease in bleb vascularity and IOP, along with a decrease in fibrosis markers.



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