

## I SLT PHOTOREGENERATION I

### The Alvarado Explanation of the Mechanism of SLT and its Practical Implications

Dr. Jorge A. Alvarado of the University of California San Francisco is one of the most prominent investigators of the biochemical and cellular regulation of aqueous circulation and of the related pathogenesis of glaucoma.

His contributions to the understanding of the IOP reduction mechanisms of SLT shed a new light not only on the way by which this modality treats glaucoma, used for years without its mechanism being known, but also on the mechanism of IOP regulation in general. The insight provided by Dr. Alvarado, in addition to being of profound basic science interest, has immediate practical applications.<sup>1-5</sup>



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#### To summarize Alvarado's findings:

- Trabecular meshwork endothelial cells act as pressure sensors, when detecting increased IOP they secrete soluble factors (cytokines) into the aqueous humor. These cytokines induce long-term increase in the permeability of the Schlemm's canal endothelial cells and thus the IP is reduced
- When SLT irradiation is applied to the trabecular endothelium it recruits monocytes of the innate immune system. These cells in turn activate the trabecular endothelium cells, causing the secretion of cytokines. These cytokines, as shown microscopically, increase the porosity of the Schlemm's canal endothelium thus reducing the IOP. It is likely that the monocytes also secrete cytokines which affect the porosity directly.
- The prostaglandin analogs, Latanoprost, travoprost and bimatoprost reduce IOP in much the same way – i.e., reducing the tightness of the intercellular thus increasing permeability of the Schlemm's canal endothelium cells. In this case however, the effect is of a much shorter duration.
- The differences in the duration of the IOP lowering effect between SLT and the prostaglandin analogs is explainable by the involvement of the immune system monocytes in the former's mechanism of action. These cells are probably involved in repairing the angle structures on a long term basis, until overcome by the processes causing the disease in the first place.

#### The practical implications of Alvarado's insights are:

- SLT will be successful in patients who responded positively to prostaglandin analogs and vice versa.
- There is no point in performing SLT on patients who do not respond to prostaglandin analogs.
- The effects of SLT and prostaglandin analogs are not cumulative and those two modalities better be not used together.
- Prostaglandin analogs should be discontinued for four weeks before SLT.
- Prostaglandin analogs can be used for a short duration after SLT to prevent pressure spikes.

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It must be mentioned in this context that there are clinical data indicating that there is no negative effect of previous prostaglandin analogs treatment on IOP reduction by SLT and that these two modalities of treatment can be used simultaneously.<sup>6</sup> This in no way refutes the basic SLT mechanism suggested by Dr. Alvarado..

### References:

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