Does optic nerve head surface topography change prior to loss of retinal nerve fiber layer thickness: a test of the site of injury hypothesis in experimental glaucoma

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**PURPOSE:** To test the hypothesis that optic nerve head (ONH) deformation manifesting as changes in its mean surface height precedes thinning of the peripapillary retinal nerve fiber layer (RNFL) in experimental glaucoma (EG).

**METHODS:** 68 rhesus macaque monkeys each had three or more baseline imaging sessions under manometric intraocular pressure (IOP) control to obtain average RNFL thickness (RNFLT) and the ONH surface topography parameter mean position of the disc (MPD). Laser photocoagulation was then applied to the trabecular meshwork of one eye to induce chronic, mild-to-moderate IOP elevation and bi-weekly imaging continued. Event analysis was applied to determine for each parameter when an 'endpoint' occurred (significant change from baseline) for eight different endpoint criteria. Specificity was assessed in the group of 68 fellow control eyes. Classical signal detection theory and survival analysis were used to compare MPD with RNFLT.

**RESULTS:** Regardless of the endpoint criterion, endpoints were always more frequent for MPD than for RNFLT. The discriminability index (d') was 2.7 ± 0.2 for MPD and 1.9 ± 0.2 for RNFLT (p<0.0001). Endpoints were reached by MPD an average of 1-2 months earlier than by RNFLT (p<0.01). At the onset of the first specific, detectable MPD change in EG eyes, there was still no significant change in RNFLT on average (p=0.29) and only 25% of individual eyes exhibited significant reduction. In contrast, at onset of significant RNFLT change, MPD had already changed an average of 101 µm from baseline (p<0.0001) and 71% of the individual eyes had exhibited significant change. The magnitude of MPD change was more than could be explained on the basis of axon loss alone.

**CONCLUSIONS:** This study demonstrates that the average surface height of the ONH changes prior to any detectable loss of average peripapillary RNFL thickness in non-human primate eyes with experimental glaucoma.


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