

Low-energy Stereotactic Radiosurgery of the Eye: Evaluation In a Yucatan Mini-pig Model

R. Danis¹, R. Singh², N. Mamalis³, E.M. Shusterman⁴, M. Gertner⁴

¹*Ophthalmology, University of Wisconsin, Madison, WI,* ²*Ophthalmology, Cleveland Clinic, Cleveland, OH,* ³*Ophthalmology, Pathology, University of Utah, Salt Lake City, UT,* ⁴*Oraya Inc, Newark, CA, USA*

Purpose: To evaluate the precision of low-energy X-rays delivered stereotactically to a retinal target with clinical examination, retinal imaging, and histopathology.

Methods: Low energy X-rays were applied to the retina across the pars plana in 3 sequential beams. Two eyes each received 0, 16, 24, 42, 60 or 90 Gy via a table-mounted device intended to provide radiotherapy for neovascular age-related macular degeneration (currently in Phase 1-2 human clinical trial; IRay™; Oraya Therapeutics, Inc., Newark, CA). Clinical evaluation was performed up to 9 months post-treatment by examination, color fundus photography, fluorescein angiography, indocyanine green angiography, and spectral domain OCT. MRI and CT scans of the head were also performed at 9 months. The eyes and orbital tissues were harvested for pathologic evaluation by light microscopy.

Results: The highest dose eyes (60-90 Gy) developed circular retinal white lesions subacutely by examination and photography. Later findings were confined only to the target site and included RPE atrophy, choroidal perfusion abnormalities, retinal vascular drop-out and leakage on angiography, and severe retinal atrophy and disorganization by OCT. A very abrupt transition from areas of injury within the target area to normal-appearing tissues was seen, consistent with radiologic dose calculations. Surrounding structures, including optic disk, cornea/sclera, lens, brain, and orbital bone demonstrated no radiation injury on examination or imaging. Histopathology was in accord with imaging findings, indicating well-defined areas of retinal damage at the high doses, with a sharp transition zone at the lesion boundary.

Conclusions: Low energy X-rays can be used to precisely target the retina while sparing other ocular and cephalic structures from undesirable effects of radiation.