Retrobulbar radiation, optic disc cupping, and neuroretinal rim thinning

Dear Editor,

Thank you for the opportunity to respond to Drs. Dalvin and Roddy's letter to the editor regarding our recently published original observations describing "Optic disc cupping after circumpapillary Pd-103 slotted plaque radiation therapy."[1] They point out that their recently published article in the *Journal of Neuroophthalmology* noted, "Post radiation optic atrophy is associated with intraocular pressure and may manifest with neuroretinal rim thinning."[2] We read their article (which was published within 30 days of ours) with great interest. They reported that their posteriorly placed radiation plaques resulted in either no optic neuropathy, or optic neuropathy without neuroretinal thinning or 19.2% with neuroretinal thinning (Table 1). In contrast, in our study, plaque therapy resulted in 88.5% with optic disc cupping.[1] Let's closely examine some of the differences between these two studies.

The tumors selected and methods of treatment were quite different.[1,2] For example, in Finger et al., we selected only peripapillary, juxtapapillary, and circumpapillary tumors. Due to their peripapillary location, treatment required 8 mm wide, variable-depth slots to be cut away from standard Collaborative Ocular Melanoma Study plaques to accommodate the retrobulbar optic nerve sheath within the plaque (thereby overcoming its obstruction).[1] These plaques covered the entire tumor plus a margin of normal-appearing tissue around the melanoma (American Brachytherapy Society [ABS] "normal" plaque position).[3] As a result, Finger's Slots uniquely allowed the plaques to be seated on the posterior pole to directly irradiate most or all of the posterior ocular circulation located immediately beneath the plaque.

In contrast, Dalvin and Roddy's tumors were selected to be within 6 mm of the optic disc.[2] It is unlikely that many tumors were juxtapapillary, peripapillary, or circumpapillary because most centers prefer not to treat them with the round Collaborative Ocular Melanoma Study plaques used in their study. In that the optic nerve sheath diameter extends 1.5 mm beyond the intraocular edge of the optic disc, there is no anatomical chance Dalvin and Roddy's round plaques could have achieved ABS "normal" plaque position, much less be seated over most or all the papillary and peripapillary circulation.

Studies have revealed, however, that round juxtaneural plaques tilt along their posterior extent and thus spray radiation in the direction of the posterior, typically uncovered melanoma and (of interest for this comparison) the neural and perineural circulation.[3,4] The use of plaque-tilt during radiation therapy challenges a medical physicists' ability to determine the actual dose to the optic nerve and emissary blood vessels. Dalvin and Roddy were likely considering this when adding transpupillary thermotherapy (TTT) at the time of plaque removal for 23 eyes (Table 1).[2] Clearly, the fact that TTT was used on 27% of the 15 nerves that went on to develop neuroretinal thinning is a confounding factor.[2]

Failure of local tumor control adds further evidence of plaque decentration seen with their approach. Though no reason was given, we noticed that three of their eyes came to enucleation (Table 1).[2] In contrast, in that Finger's slotted plaque technique allowed for "ABS normal" plaque positioning, there was no need to treat uncovered tumor margins with adjuvant peripapillary TTT, and there were no failures of local control.[1,5,6]

Our study does not suggest that neuroretinal rim thinning is unique to slotted plaque brachytherapy. Our research revealed a phenomenon where radiation was delivered directly to the papillary and peripapillary vasculature, which resulted in a greater incidence of optic nerve cupping (88.5%) versus (19.2%) neuroretinal thinning observed by Dalvin and Roddy (Table 1). We appreciate, however, that Dalvin and Roddy's research offers supporting evidence that neuroretinal rim thinning may occur with high radiation doses to the perineural circulation—and not simply in the setting of slotted plaques.

Lastly, Dalvin and Roddy suggest that radiation-induced optic nerve vasculopathy may have made the optic nerve

Table 1—Comparison of study methods and outcomes

Study	# of Patients	Position Tumor/Plaque	Plaque COMS - Shell	Radionuclide Seed-Source	Optic Disc Radiation Dose (mean)	Disc Cupping	Disc Pallor	IOP Increased	OCT-A	TTT- added	Enucleation Secondary
Galvin et. al. [2]	78	< 6 mm to disc	Round	iodine-125	84 Gy	19.2% (n = 15)	Yes	Yes	No	(n = 4/15, 27%)*	3
Finger et. al. [1]	39	< 1.5 mm, juxta, circumpapillary	8-mm Slotted#	palladium-103	113 Gy	88.5% (n = 35)	No	No	Yes	None	None

COMS, Collaborative Ocular Melanoma Study; IOP, intraocular pressure; OCT-A, optical coherence tomography-angiography; TTT, transpupillary thermotherapy; juxta, juxtapapillary, completely encircling and/or covering the optic disc; Gy, Gray

*This is the percentage of the 19.2% noted to exhibit neuroretinal thinning.

#See technique, all slots are 8 mm wide whereas slot depth depends on the distance required to circumnavigate the melanoma and margin. 6.

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head more sensitive to slight increases or even normal intraocular pressures. Though we did not find any raised intraocular pressure in our study, we agree this is certainly a theory worth investigating.

In summary, significant methodologic differences exist between the two studies that affect their relative ability to offer proof that radiation can induce optic nerve cupping.[1,2] Specifically, our study is the only one where quantifiable and reproducible measures of radiation were placed to cover the posterior neural and perineural circulation of the eye.[1] This is reflected by the numbers of patients who later developed progressive (optical coherence tomography-angiography—documented) ischemic radiation vasculopathy at the posterior pole along with secondary optic disc cupping.[1]

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Footnotes and Disclosure

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