

In response to their comments we would like to clarify how the high-density subthreshold micropulse laser (HSML) spots were applied to the retinas of patients treated in the PLACE trial. The laser spots were positioned adjacent to each other in a nonoverlapping fashion, as depicted in Figure 1 in the PLACE trial report and Figure 2 in PLACE trial report no. 3.<sup>1,3</sup>

The HSML device that was used in all centers during the PLACE trial and REPLACE trial was manufactured by Iridex, and no multispot pattern scan was used. A myriad of settings (for example frequency, spot size, exposure time, and duty cycle) can be used with HSML treatment, which might each theoretically alter the therapeutic effect. However, the site of the mechanism of action (activation/stimulation of the retinal pigment epithelium) is not altered by adjusting these settings. The vast majority of literature on CSC points toward the choroid as the root cause of accumulation of subretinal fluid; this observation is supported by the higher efficacy of a treatment that targets the choroid, such as photodynamic therapy.<sup>4</sup>

Drs Wu and Roca propose that further studies on the role of multispot micropulse laser treatment in CSC are warranted. To do this, a well-designed large, properly powered randomized controlled trial with a predefined study protocol is essential.<sup>4,5</sup>

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CONFLICT OF INTEREST DISCLOSURES: SEE THE ORIGINAL article for any disclosures of the authors.

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## Comment on: Evaluating Goldmann Applanation Tonometry Intraocular Pressure Measurement Agreement Between Ophthalmic Technicians and Physicians



EDITOR

WE READ WITH GREAT INTEREST THE ARTICLE BY MIHALovic and associates<sup>1</sup> on Goldmann applanation tonometry agreement between ophthalmic technicians and physicians. Authors looked into one of the important aspects of patient management in glaucoma, the intraocular pressure (IOP) measurement by Goldmann applanation tonometry (GAT), and concluded that the physician-technician disagreement while measuring IOP using GAT was higher than 2 physicians even after educational intervention. We agree with the authors that, because GAT is a subjective test, one of the important limitations was the intra- and interobserver variability. However, we would like to mention a few points which require further discussion.

First, IOP was measured using the same GAT between 2 physicians in the same chair, one after the other, but IOP was measured using different GAT among physician and technician. We assume that the patient was examined in 2 different rooms between the physicians and technicians and that there would be a time lag between the 2 measurements. We would like to know the time gap between these 2 readings and whether circadian rhythm has any influence on these measurements. The authors also mentioned that the measurement of IOP by 2 different tonometers would only have minimal impact on the outcome as the tonometers were calibrated every week. As authors have followed manufacturer's instructions for calibration, we would like to know the acceptable calibration error range. Because the manufacturers recommended an acceptable calibration

error of  $\pm 0.5$  mm Hg, this was considered to be very stringent, and studies have reported only 0% to 10.3% of GAT in institutions fall within this range.<sup>2,3</sup> The clinically acceptable calibration error range was less than  $\pm 2.5$  mm Hg.<sup>3</sup> If the latter was followed, then that might affect the outcome of this study significantly. Second, interobserver variability for GAT has been reported to be up to 4 mm Hg.<sup>4,5</sup> We believed choosing  $>4$  mm Hg as the standard would reveal the real disagreement beyond the interobserver test-retest variability.

We agree with the authors that IOP is just a surrogate measurement of glaucoma and that we need to consider the entire picture, such as structural and functional changes, before making any major decisions.

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ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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## Reply to Comment on: Evaluating Goldmann Applanation Tonometry Intraocular Pressure Measurement Agreement Between Ophthalmic Technicians and Physicians



EDITOR:

WE APPRECIATE THE THOUGHTFUL COMMENTS OF DR. SHU and associates. The authors raise the concern that circadian

rhythm may have partly contributed to the differences in intraocular pressure (IOP) when comparing clinicians to technicians. While it is theoretically possible, we doubt that this would have been the case in the present study as patients were evaluated by physicians within a short time of being screened by technicians. Although we did not collect data for the exact amount of time elapsed between IOP measurements taken by the technician and those taken by the physician, the longest it would have been was an hour, and most subjects would have been seen within minutes.

The authors also raise a concern about the calibration of tonometers in our clinics. We log these calibrations weekly, and all tonometers must meet a calibration error of  $\pm 0.5$  mm Hg or they are sent for repair.

Finally, the authors suggest that random noise can produce differences of  $\pm 2$  mm Hg when measuring IOP and suggest that a more appropriate cutoff value for the study would have been a difference of  $>4$  mm Hg. Although these larger fluctuations are sometimes seen, we continue to believe that differences  $>2$  mm Hg are important from a clinical standpoint and could result in altered treatment plans in some cases.

Once again, we thank Dr. Sahu and associates for raising these important considerations.

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DR. FRIEDMAN IS NOW AT: GLAUCOMA CENTER OF EXCELLENCE, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, USA.

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## Comment on: Rethinking the Hydroxychloroquine Dosing and Retinopathy Screening Guidelines



EDITOR:

WE READ WITH INTEREST THE STUDY BY BROWNING AND associates<sup>1</sup> and are writing to highlight the highly variable pharmacokinetics of hydroxychloroquine (HCQ) and its potential implications in HCQ-induced retinopathy (HCQR). The authors stated daily dosage was the most important and only modifiable risk factor for HCQR. Despite being the most important risk factor for HCQR, the dose itself does not completely predict HCQ exposure. HCQ has a variable and incomplete absorption (30%–100%).<sup>2</sup> The reported volume of distribution ranges from 153 liters to 47,247 liters.<sup>2,3</sup> HCQ is desethylated to *N*-desethylhydroxychloroquine (the major active metabolite), and 2 other metabolites in common with