

## Author Response: Smokers' Choroidal Changes

We would like to thank Marino et al. for their interest in our paper.<sup>1</sup>

First, it would be ideal in any research if the study group and control group were matched in as many aspects as possible to avoid confounding bias. Unfortunately, we were not able to have a perfect match for the age in this study. Data for axial length or refraction were also not available. We have acknowledged that the difference in ages between the two groups was one of the limitations in this study. We have tried to mitigate this by using linear mixed model in data analysis.<sup>1</sup> We also agree that axial length (AL) and refractive error may be confounding factors for choroidal thickness measurement. However, the main outcome measure in our study, choroidal vascularity index (CVI), was shown to be unaffected by most physiological variables, including AL and refractive error in a previous population study.<sup>2</sup> So it is unlikely that unavailability of AL and refraction data would significantly affect CVI results between smokers and nonsmokers.

Second, Marino et al. are correct that in CVI calculation, each pixel in the original gray-scale images is binarized into either black or white. This important step is carried out with specific thresholding strategies in various methods of calculating CVI. In our method, Niblack auto local threshold strategy is used because of its effectiveness in isolating vascular structures.<sup>3,4</sup> Unfortunately, to date, there is no direct proof that dark pixels in optical coherence tomography (OCT) images represent choroidal luminal area and that light pixels represent choroidal stromal area. However, there is abundance of published literature that strongly suggests the assumption is true.<sup>3,5,6</sup>

Third, Marino et al. are concerned that a variation in signal amplification during OCT image capture would change the relative proportion of light and dark pixels, therefore affecting CVI measurement. This is based on observation on ultrasonography studies and inferred to OCT studies.<sup>7</sup> We have tried to search the literature and did not find a clear description of "blooming effect" with OCT imaging of ocular structures. The fact that ultrasonography uses sound signal whereas OCT uses light signal also makes it difficult to conclude whether signal strength affects thresholding and

what is the effect size. However, we do acknowledge that future study on this aspect would be required.

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