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Effect of Intravitreal Anti–Vascular Endothelial Growth Factor Therapy on Choroidal Thickness in Neovascular Age-Related Macular Degeneration Using Spectral-Domain Optical Coherence Tomography

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A critical method of monitoring patients with neovascular age-related macular degeneration (AMD) being treated with anti–vascular endothelial growth factor (anti-VEGF) is optical coherence tomography (OCT), which uses low-coherence interferometry of light to examine the retina *in vivo* on a micrometer scale.¹

Recent advances in spectral-domain OCT make visualization of the choroid feasible. Using image averaging and enhanced depth imaging, successful examination and measurement of choroidal thickness in normal and pathologic states have been reported.^{2–4}

It has been hypothesized that anti-VEGF may affect choroidal vasculature.⁵ The goal of this study is to evaluate the effect of anti-VEGF on choroidal thickness using spectral-domain OCT in treatment-naive subjects.

Methods

Twenty-two patients (22 eyes) with neovascular AMD were identified prior to first-time treatment with anti-VEGF at New England Eye Center. All patients with concomitant ocular pathologies were excluded. Twenty age-matched healthy eyes were identified as a control group. This study was approved by the institutional review board of the Tufts Medical Center.

Patients were imaged with spectral-domain OCT prior to first-time treatment with anti-VEGF therapy and again at 3, 6, and 12 months (Figure 1). Control eyes were imaged at the time of identification and 6 months later. The scan pattern used was Cirrus high-definition 1-line raster (Carl Zeiss Meditec), which is a 6-mm line consisting of 4096 A-scans and 20 B-scans averaged together without tracking.

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Author Contributions: Dr Duker had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of Interest Disclosures: Dr Fujimoto receives royalties from intellectual property owned by Massachusetts Institute of Technology and licensed to Carl Zeiss Meditec Inc and has stock options in Optovue Inc. Dr Duker receives research support from Carl Zeiss Meditec Inc, Optovue Inc, and Topcon Medical Systems Inc.

Choroidal thickness was manually measured at 500- μm intervals, 2500 μm temporal and nasal to the fovea. Measurements were performed by 2 independent observers with a strong interobserver correlation ($r = 0.97$; $P < .001$). Two-way analysis of variance with Tukey multiple test was applied using Prism Mac 5.0 statistical software (GraphPad Software, Inc).

Results

A total of 22 eyes of 22 patients (11 male, 11 female) were included. The mean age was 79 years (range, 66–88 years). Five patients were lost to follow-up. Anti-VEGF therapy was not delivered in a standard fashion. Most eyes were treated with a “treat and extend” protocol. Fifteen patients were treated with ranibizumab and 7 were treated with bevacizumab. The average number of anti-VEGF treatments was 6.9 (range, 2–12). No correlation was found between the number of treatments and a decrease in choroidal thickness.

The mean (SD) subfoveal choroidal thickness at baseline and 3, 6, and 12 months' follow-up was 207.4 (22.1) μm , 194.7 (21.9) μm ($P > .05$), 164.9 (18.0) μm ($P < .05$), and 171.8 (17.4) μm ($P < .05$), respectively (Figure 2). The mean (SD) subfoveal choroidal thickness in the control group was 253.5 (4.1) μm at the first measurement and 255.3 (4.2) μm at 6 months ($P = .72$).

Comment

This study demonstrates significant choroidal thinning after 6 and 12 months of anti-VEGF treatment for neovascular AMD. Control eyes demonstrated no decrease in choroidal thickness over 6 months.

Histopathology of AMD is characterized by attenuation of the Bruch membrane and degeneration of the choriocapillaris.⁶ This suggests that there may be a component of choroidopathy in neovascular AMD. If antiangiogenic therapy affects the choroid, treatment could potentially have unforeseen adverse effects.

It is unclear whether the observed decrease in choroidal thickness is a consequence of anti-VEGF treatment or a component of AMD. Greater numbers of subjects are necessary to determine whether there is a dose response. Another limitation to this prospective investigation was that there was no standard protocol for the initiation of therapy or the timing and number of injections.

The use of anti-VEGF for the treatment of neovascular AMD has been shown to improve visual acuity and is currently being used extensively for this purpose. In our study, there was significant thinning of the choroid in patients with neovascular AMD treated with anti-VEGF. This may have implications for long-term choroidal function.

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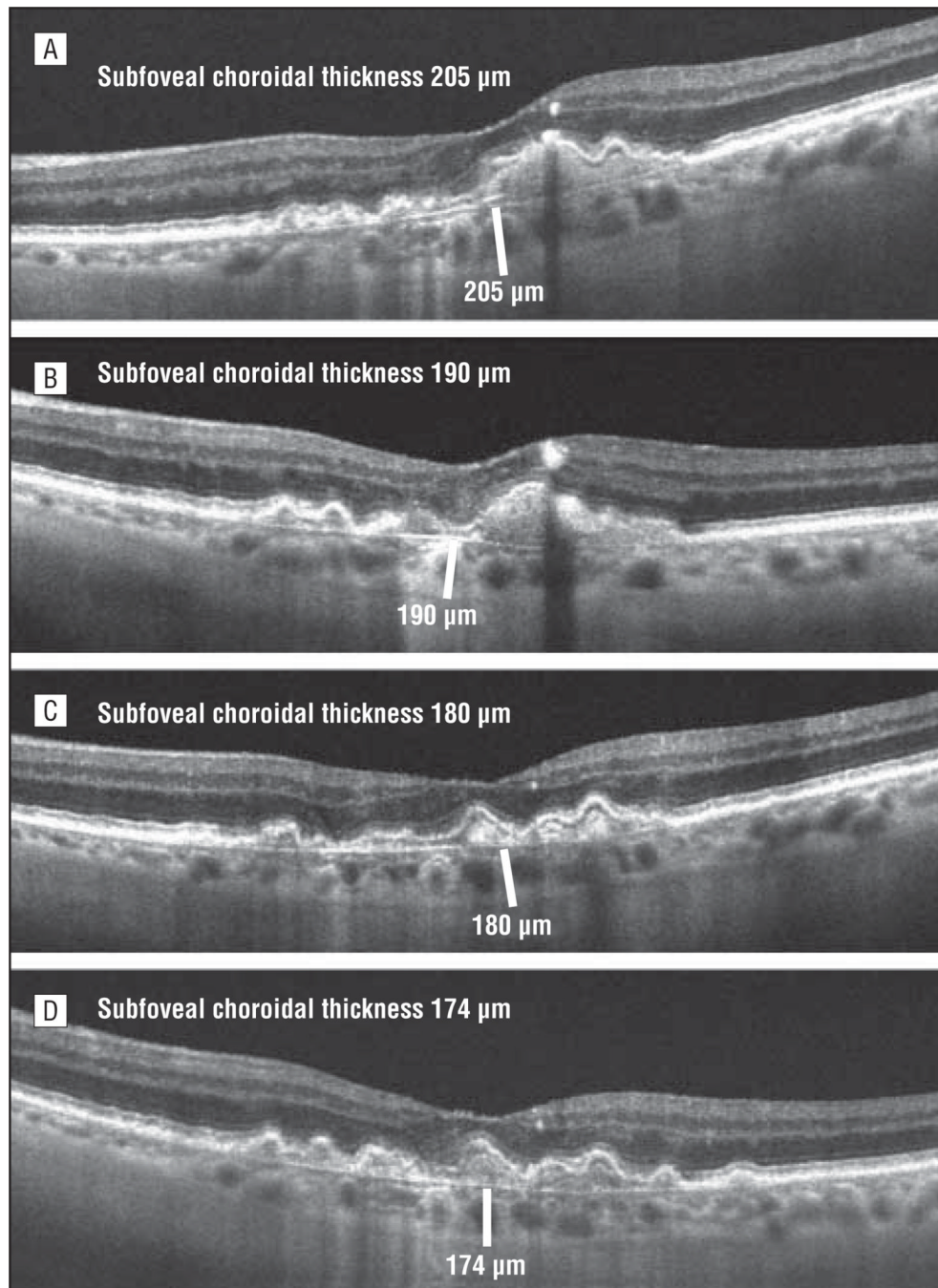


Figure 1. Spectral-domain optical coherence tomographic scans showing choroidal thicknesses of the same subject at 4 different times. Image averaging is used for choroidal visualization. Subfoveal choroidal thickness measurements were taken from the outer edge of the hyperreflective retinal pigment epithelium to the inner sclera. Red lines indicate subfoveal choroidal thickness. A, Before treatment with intravitreal anti-vascular endothelial growth factor. B, Three months after treatment with intravitreal anti-vascular endothelial growth factor. C, Six months after treatment with intravitreal anti-vascular endothelial growth factor. Note the decrease in choroidal thickness. D, Twelve months after treatment with

intravitreal anti-vascular endothelial growth factor. Note the decrease in choroidal thickness.

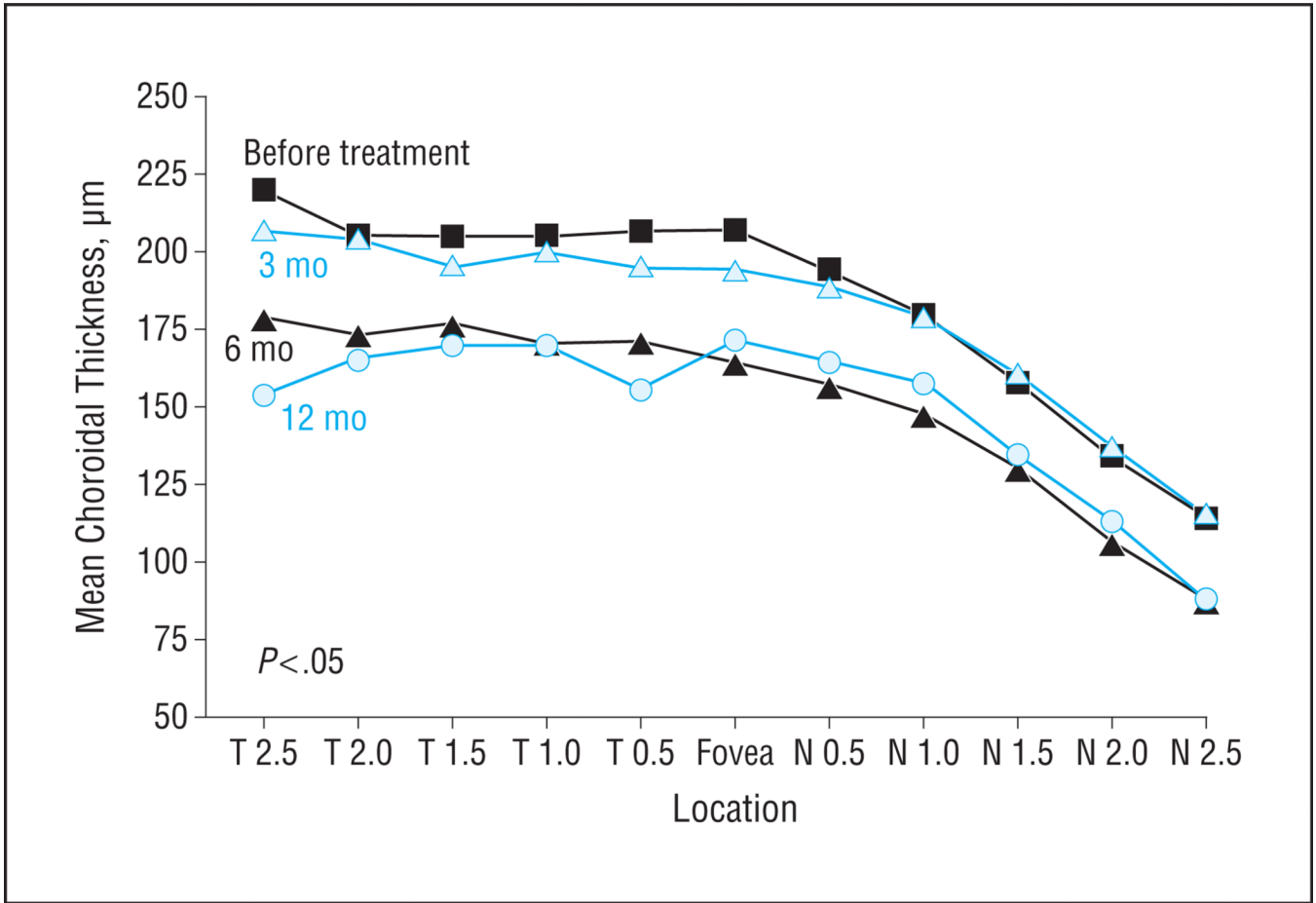


Figure 2. Mean choroidal thickness over all locations measured in 500-µm intervals, 2500 µm temporal (T) and nasal (N) to the fovea before treatment and 3, 6, and 12 months after the first treatment. Note that the N measurements are thinnest where the T measurements are thickest. The numbers next to the T and N locations indicate millimeters.