

Imaging of Laser-Photocoagulated Diabetic Microaneurysm with
Spectral-Domain Optical Coherence Tomography

Abbreviated title: Imaging of Microaneurysm with SD-OCT

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Summary Statement: Microaneurysms were evaluated with SD-OCT before and after photocoagulation. Focal photocoagulation may be a less invasive method for treating microaneurysms and that SD-OCT is useful for evaluating the efficacy of photocoagulation.

Abstract

Purpose: To analyze the morphology of microaneurysms before and after direct photocoagulation using spectral-domain optical coherence tomography (SD-OCT).

Methods: In 13 eyes of diabetic patients who underwent focal photocoagulation for clinically significant macular edema, microaneurysms were evaluated before and immediately, 1 month and 2 months after photocoagulation with SD-OCT. The microaneurysms were also evaluated by fluorescein angiography and color fundus photography. The patients underwent focal photocoagulation for microaneurysm.

Results: The microaneurysms before photocoagulation in SD-OCT were observed as circular or elliptical structures with hyper-reflective foci within vessel walls. Immediately after photocoagulation, the microaneurysms were changed to indistinct lesions with hyper-reflectivity around the microaneurysms. Acoustic shadows developed on the choroidal side of the microaneurysms. If photocoagulation for microaneurysms was appropriately done, retinal changes were limited to within the inner-retina around the microaneurysms and no changes were observed in retinal pigment epithelium. Within 2 months after

photocoagulation, the microaneurysms changed into fine scars, and the retinal structure normalized. Average retinal thickness of the fovea was 432 ± 70 μm before the procedure, but reduced to 373 ± 84 μm at 2 months post-surgery.

Conclusions: Focal photocoagulation may be a less invasive method for treating microaneurysms and that SD-OCT is useful for evaluating the efficacy of photocoagulation.

Introduction

Diabetic retinopathy (DR) is the leading cause of legal blindness in many countries.¹ When DR reaches an advanced stage, complications such as macular edema, vitreous hemorrhage, tractional retinal detachment, or neovascular glaucoma can be present. Diabetic macular edema (DME) is one of the common causes of visual loss, and it is normally treated by focal photocoagulation,^{2,3} pars plana vitrectomy (PPV),⁴ triamcinolone acetonide,⁵ and anti-vascular endothelial growth factor.⁶ The best treatment for DME has not yet been established. Of the current therapies, focal photocoagulation has the most support from medical evidence. In this study, focal photocoagulation was performed as described in the Early Treatment Diabetic Retinopathy Study (ETDRS).² ETDRS showed that focal photocoagulation of clinically significant macular edema (CSME) reduced the risk of visual loss.² Although it has been reported that microaneurysm treated by focal photocoagulation using fluorescein angiography had a closure rate of 75% at the end of 12 weeks, the detailed morphological changes were unknown.

However, recent technological development has provided new techniques for analyzing macular disease. Among these, spectral-domain optical coherence

tomography (SD-OCT) has allowed visualization of microaneurysms.

Hyper-reflective foci are visible within the anterior and posterior vessel walls of microaneurysms seen in SD-OCT.⁷

However, to the best of our knowledge, there are no reports of imaging of laser-photocoagulated microaneurysms using SD-OCT. Accordingly, we evaluated microaneurysms before and immediately, 1 month and 2 months after photocoagulation with SD-OCT.

Methods

This retrospective study conducted on 13 eyes of 13 diabetic patients who underwent focal photocoagulation for CSME between June 2009 and October 2009. The focal photocoagulation was performed with the following parameters²: wavelength 532nm, spot size 50 μ m, laser power 70-100 mW, and pulse duration 100 ms.

For each patient, we evaluated the microaneurysm before, immediately after, 1 month after, and 2 months after focal photocoagulation using SD-OCT (Spectralis[®], Heidelberg Engineering GmbH, Heidelberg, Germany). All images were acquired with an angle of 10°x20°, and comprised 96 sections with 30- μ m

spacing. Each image had 10 frames of automatic real time mean intensity with high resolution mode. The images acquired for follow-up (immediately, 1, 2 months after the photocoagulation procedure) used the same field of view as the original image. SD-OCT images were evaluated retrospectively, and thus we selected the images that included the microaneurysms. For each microaneurysm, we also evaluated the previous and next images in the SD-OCT sequence. The microaneurysms were also evaluated by fluorescein angiography and color fundus photography. The foveal average retinal thickness was measured as the central subfield mean thickness on optical coherence tomography (OCT) (Cirrus[®], Carl Zeiss Meditec, Dublin, CA). Best-corrected visual acuity (BCVA), fundus examinations, and foveal average retinal thickness before and 2 months after laser-photocoagulation were reviewed retrospectively using the patients' clinical records. Informed consent was obtained from all patients, and approval for this study was obtained from the Ethics Committee, Nagasaki University School of Medicine.

Statistical analysis: The results are expressed as means \pm standard deviation. The Mann-Whitney test was used to compare BCVA and foveal average retinal thickness before and after photocoagulation. Statistical analysis

was performed using Stafflex software version 5.0 (Artech Corporation, Osaka, Japan). P values <0.05 were considered to represent statistical significance.

Results

The study included 13 eyes of 13 patients (4 females, 9 males; mean age at operation, 63 ± 13 years). Foveal average retinal thickness was 432 ± 70 μm before laser photocoagulation, but reduced to 373 ± 84 μm at 2 months post-procedure ($p=0.003$) (Table 1).

Color fundus photography (Figure 1A) and fluorescein angiography (Figure 1B) before focal photocoagulation showed multiple microaneurysms in both photographs. Imaging of a microaneurysm before photocoagulation with SD-OCT was seen as a small hyper-reflective ring (Figure 1D). Immediately after focal photocoagulation, the microaneurysms changed to white when imaged with color fundus photography (Figure 1C). The lesions also became less distinct, with hyper-reflectivity around the microaneurysm and acoustic shadow on the choroidal side of the microaneurysm visible with SD-OCT (Figure 1E). All coagulated aneurysms changed to less distinct lesions with SD-OCT. In some cases, small scars were visible with SD-OCT after photocoagulation; others

were invisible. Normalized retinal layer structures were confirmed in 5 cases 2 months after photocoagulation.

Retinal changes were restricted to within the inner retina around the microaneurysms (compare Figure 2A and 2B). Although the microaneurysm changed to hyper-reflective lesion same as figure 1 immediately after photocoagulation (Figure 2B), the microaneurysm changed to an indistinct lesion with a small hyper-reflective scar 2 months after photocoagulation (Figure 2C).

Although microaneurysms mainly existed from the ganglion cell layer to the inner nuclear layers before photocoagulation, immediately after photocoagulation the ganglion cell layer became unclear (Figure 2B). Subsequently, the ganglion cell layer was almost normalized (Figure 2C). With photocoagulation, small scars developed in the retinal pigment epithelium and the junction between photoreceptor inner and outer segments was disrupted 2 months after the photocoagulation procedure (Figure 2C). Hyper-reflectivity around the microaneurysm remained 1 month after photocoagulation (Figure 3C; compare with Figure 3B). The scarring was less prominent 3 months after photocoagulation, and the structure of the inner nuclear layer and outer plexiform layer were normalized with SD-OCT (Figure 3D, compare with 3B).

Discussion

There have been several reports on imaging of diabetic microaneurysms with SD-OCT. Bolz et al. reported that hyper-reflective foci are visible within the anterior and posterior vessel walls of microaneurysms seen in SD-OCT.⁷ In the present study, microaneurysms were also visualized as circular or elliptical structures with hyper-reflective foci within vessel walls. Horii et al. reported on the status of the capsular structure called ring sign, shown in the sectional images of OCT, and classified microaneurysms as having complete ring signs, having an incomplete ring sign, or as having no structure.⁸ In the present report, many microaneurysms had incomplete ring signs. This suggests that microaneurysms with incomplete ring signs may induce macular edema. Sachdev et al. reported that a change in retinal thickness correlated significantly with a decrease in the number of leaking microaneurysms.⁹ In the current study, macular edema was reduced after photocoagulation for microaneurysm, similar to previous reports,^{2, 9} indicating that the photocoagulation procedures were successful and appropriately performed in our study population. Morphologic changes secondary to the retinal grid photocoagulation were similar to a

previous report.^{3,10} In a report on the morphology of retinal laser effects and their healing response using SD-OCT, the photoreceptor layers appeared to be eliminated in the photocoagulation area.¹¹ In the present report, photoreceptor layers seemed to maintain a normal structure and the retinal inner layers healed to an almost normal structure. These observations suggest that if photocoagulation for microaneurysms is appropriately done, it may be a less invasive method for treating microaneurysms.

To our knowledge, the imaging of photocoagulated microaneurysms in SD-OCT has not been previously reported. In the present report, we showed the effects of photocoagulation on microaneurysms immediately following the procedure. The microaneurysms changed to indistinct lesions with hyper-reflectivity, and acoustic shadows were present at the choroidal side of the microaneurysms.

One to 2 months after photocoagulation, the microaneurysms were less prominent and had changed into fine scars; retinal structure was also normalized.

These retinal structure changes were within the inner retinal layer, mainly from the inner nuclear layer to the nerve fiber layer. In 8 cases, the small scars from the microaneurysms were undetectable with SD-OCT 2 months after photocoagulation; we consider the microaneurysms as closed, but it is possible

that small scars existed between slices in SD-OCT.

In conclusion, we report observations of microaneurysms before and after photocoagulation with SD-OCT. Our results suggest that photocoagulation of only microaneurysms may be a less invasive method of treatment and that SD-OCT is useful for evaluating the success of photocoagulation of the microaneurysms.

References

1. Porta M, Bandello F. Diabetic retinopathy: A clinical update. *Diabetologia* 2002;45(12):1617-34.
2. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Early Treatment Diabetic Retinopathy Study research group. *Arch Ophthalmol* 1985;103(12):1796-806.
3. Scott IU, Danis RP, Bressler SB, et al. Effect of focal/grid photocoagulation on visual acuity and retinal thickening in eyes with non-center-involved diabetic macular edema. *Retina* 2009;29(5):613-7.
4. Kimura T, Kiryu J, Nishiwaki H, et al. Efficacy of surgical removal of the internal limiting membrane in diabetic cystoid macular edema. *Retina* 2005;25(4):454-61.
5. Yilmaz T, Weaver CD, Gallagher MJ, et al. Intravitreal triamcinolone acetonide injection for treatment of refractory diabetic macular edema: a systematic review. *Ophthalmology* 2009;116(5):902-11; quiz 12-3.
6. Scott IU, Edwards AR, Beck RW, et al. A phase II randomized clinical trial of intravitreal bevacizumab for diabetic macular edema. *Ophthalmology* 2007;114(10):1860-7.
7. Bolz M, Schmidt-Erfurth U, Deak G, et al. Optical coherence tomographic hyperreflective foci: a morphologic sign of lipid extravasation in diabetic macular edema. *Ophthalmology* 2009;116(5):914-20.
8. Horii T, Murakami T, Nishijima K, et al. Optical coherence tomographic characteristics of microaneurysms in diabetic retinopathy. *Am J Ophthalmol* 2010;150(6):840-8.
9. Sachdev N, Gupta V, Abhiramamurthy V, et al. Correlation between microaneurysm closure rate and reduction in macular thickness following laser photocoagulation of diabetic macular edema. *Eye (Lond)* 2008;22(7):975-7.
10. Bolz M, Kriechbaum K, Simader C, et al. In vivo retinal morphology after grid laser treatment in diabetic macular edema. *Ophthalmology* 2010;117(3):538-44.
11. Kriechbaum K, Bolz M, Deak GG, et al. High-resolution imaging of the human retina in vivo after scatter photocoagulation treatment using a semiautomated laser system. *Ophthalmology* 2010;117(3):545-51.

Figure Legends

Figure 1. (A) Color fundus photography and (B) fluorescein angiography before focal photocoagulation, showing multiple microaneurysms in both photographs. (C) Color fundus photography immediately after focal photocoagulation. The microaneurysms were changed to white. (D) Imaging of a microaneurysm before and (E) immediately after photocoagulation with SD-OCT. The microaneurysm became a lesion with hyper-reflectivity around the microaneurysm. An acoustic shadow developed at the choroidal side of the microaneurysm. (F) Axial imaging of a microaneurysm in another case before and (H) 1 week after photocoagulation with SD-OCT. The microaneurysm became a lesion with hyper-reflectivity. (G) Transversal imaging of the microaneurysm before and (I) 1 week after photocoagulation with SD-OCT.

Circle: Aneurysm shown with fundus photography and fluorescein angiography.

Arrow: microaneurysm.

Figure 2. Imaging of microaneurysm (A) before and (B) immediately and (C) 2 months after photocoagulation using SD-OCT. Hyper-reflectivity around the microaneurysm remained 1 month after photocoagulation and a small scar remained 2 months after photocoagulation (C). Macular edema was reduced.

The junction between photoreceptor inner and outer segment was distinct 2 months after photocoagulation.

Arrowhead: photocoagulation at RPE

Arrow: microaneurysm

Figure 3. Imaging of microaneurysm (A) before and (B) immediately, (C) 1, and (D) 3 months after photocoagulation in SD-OCT. Hyper-reflectivity around the microaneurysm remained 1 month after photocoagulation. The scar was not prominent 3 months after photocoagulation. Inner-retinal layers were clearly normalized in this case.

Arrow: microaneurysm

Figure 1.

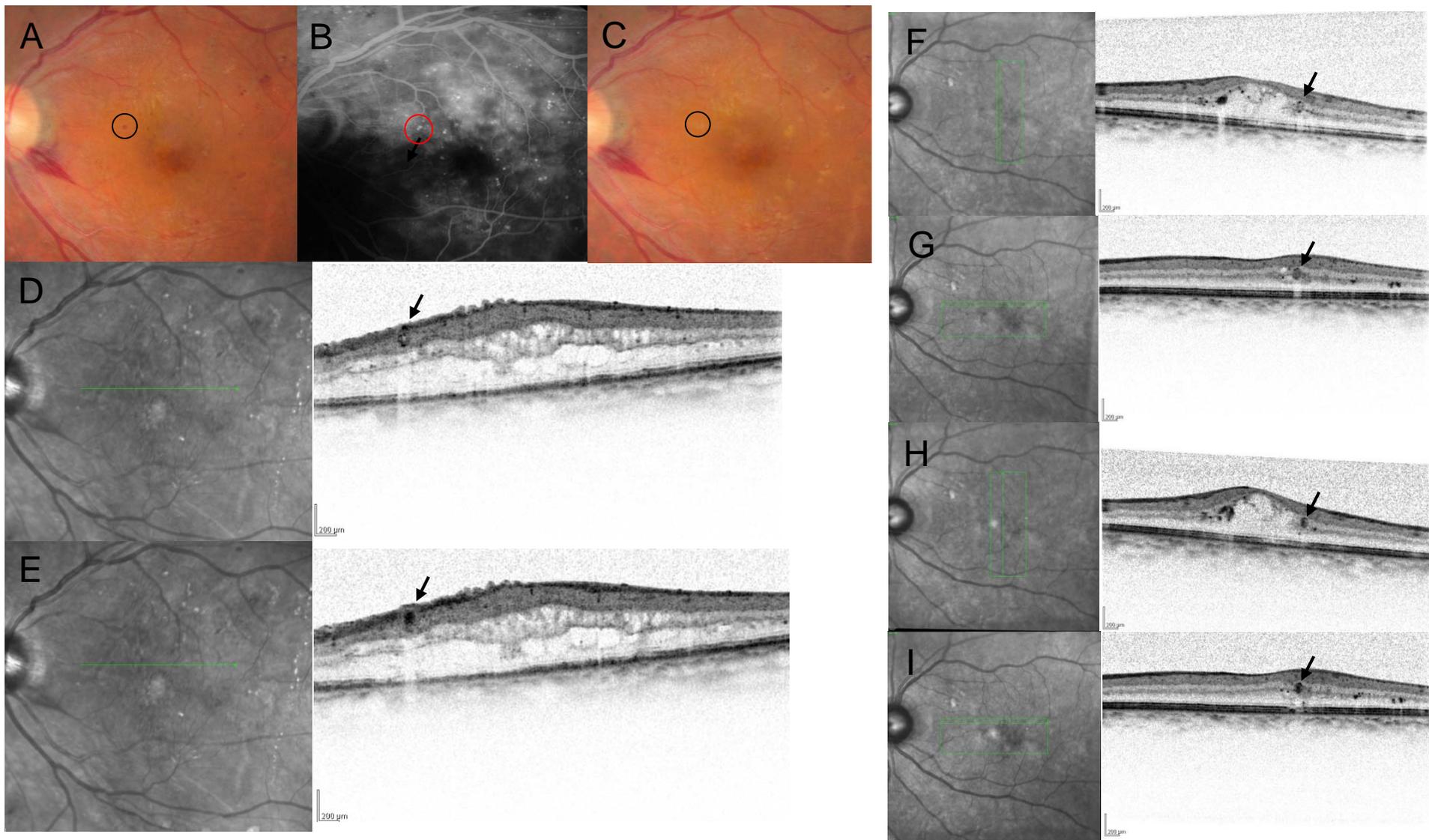


Figure 2.

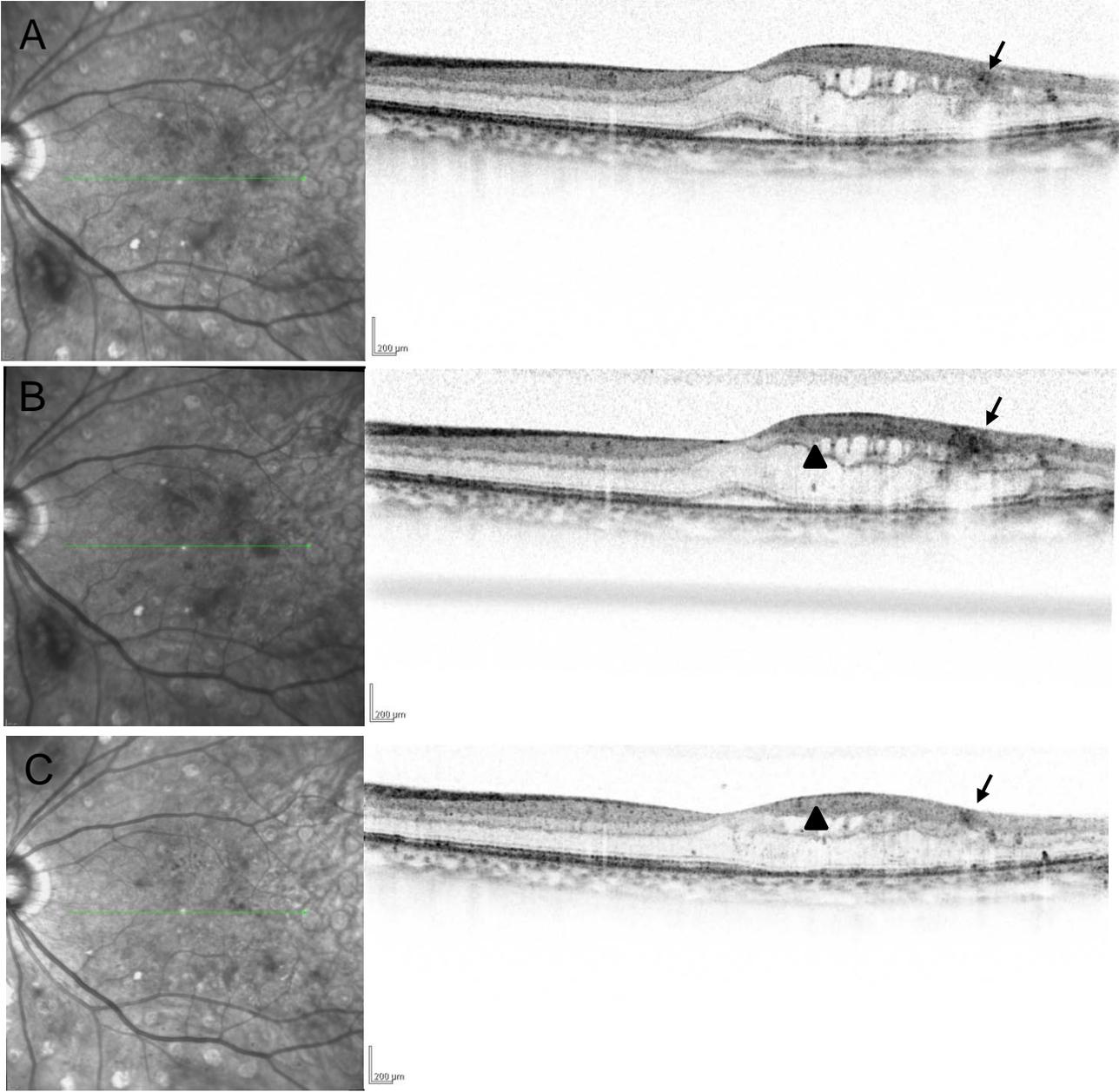


Figure 3.

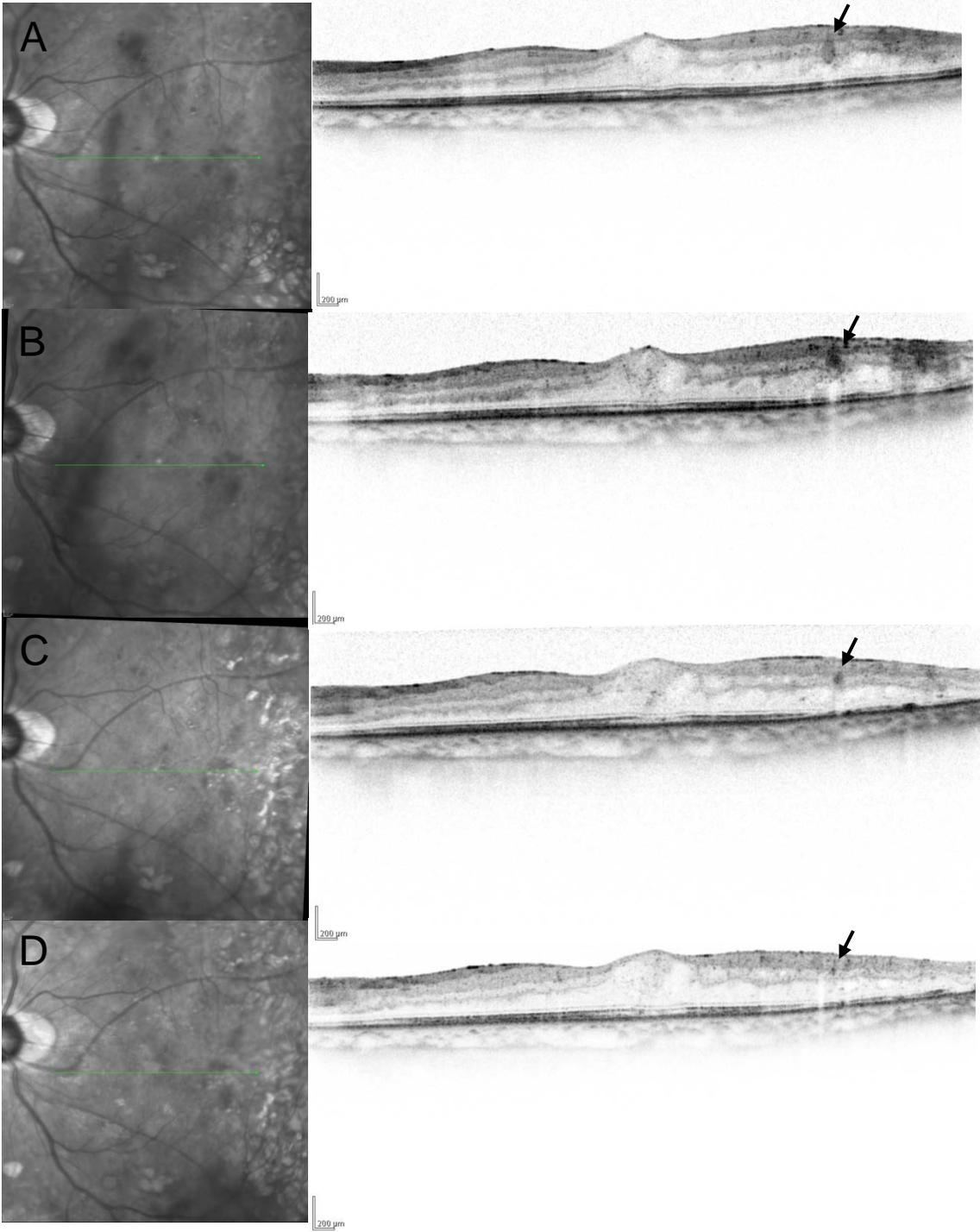


Table 1. Characteristics of patients with diabetic macular edema before and two months after photocoagulation

	Before photocoagulation (n=13)	Two months after photocoagulation (n=13)
Age (years, mean \pm SD)	63 \pm 13	
Sex (female : male)	4 : 9	
Foveal average retinal thickness (μ m; mean \pm SD)	432 \pm 70	373 \pm 84
Best corrected visual acuity (logMAR; mean \pm SD)	0.39 \pm 0.31	0.39 \pm 0.33
Number of microaneurysms detectable in SD-OCT	13 (100%)	5 (37%)

SD=standard deviation

logMAR=logarithm of the minimal angle of resolution

SD-OCT=spectral-domain optical coherence tomography