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Choroidal Thickness in Retinal Pigment Epithelial Tear as Measured by Spectral Domain Optical Coherence Tomography

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Abstract

Purpose—To evaluate choroidal thickness with spectral domain optical coherence tomography (SDOCT) in subjects with retinal pigment epithelial (RPE) tear as compared with the choroidal thickness of their fellow eye.

Methods—For this cross sectional investigation, 7 eyes of 7 patients with neovascular age-related macular degeneration and RPE tear in one eye imaged with SDOCT were identified. Choroidal thickness was measured from the posterior edge of the retinal pigment epithelium to the choroid/sclera junction at 500- μ m intervals up to 2500 μ m temporal and nasal to the fovea in both the eye with the RPE tear and the eye with intact RPE. All measurements were performed by 2 independent observers and averaged for the purpose of analysis. Measurements were compared using paired t-test.

Results—The average age of patients was 79 years (range 66-88). All subjects had dome-shaped pigment epithelial detachments (PED) prior to RPE tear and no dome-shaped PED in the unaffected eye. Average subfoveal choroidal thickness in the eye with the RPE tear was 154.9 μ m $\pm$ 10.1 μ m. Average subfoveal choroidal thickness in the eye with intact RPE was 212.9 μ m $\pm$ 10.6 μ m ($p=0.035$).

Conclusion—There is a significant decrease in subfoveal choroidal thickness in subjects with RPE tear as compared with their fellow eye with intact RPE. It is unclear if this thinning is a consequence of or precedes the RPE tear. Further studies are necessary to prospectively follow choroidal thickness in subjects with dome-shaped PED.

Keywords

choroidal thickness; retinal pigment epithelial tear; spectral domain optical coherence tomography

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Introduction

Retinal pigment epithelium (RPE) tears were first described by Hoskin et al in association with wet age-related macular degeneration (AMD) complicated by pigment epithelial detachment (PED).¹³ Subsequently, RPE tears have been noted to be associated with central serous chorioretinopathy, angioid streaks, idiopathic polypoidal choroidal vasculopathy, trauma, and age related macular degeneration.¹⁴⁻¹⁸ RPE tears have also been described to occur following various treatments for neovascular AMD such as laser photocoagulation, photodynamic therapy, and anti-vascular endothelial growth factor (anti-VEGF).²⁴⁻³⁶

RPE tears have been postulated to occur secondary to weakened intercellular connections between RPE cells that can develop following pigment epithelial detachment formation. Tears have a propensity for developing at the base of the PED near the junction of the detached and attached RPE and also at the temporal edge of the PED.¹⁹

The choroid is a highly vascular structure that fulfills the critical role of providing nourishment to the outer layers of the retina and RPE. Anatomically, the choroid is separated from the RPE only by a thin layer termed Bruch's membrane. Thus, alterations in choroidal structure and function can lead to dysfunction of the RPE and can play a role in many pathological processes.²⁴⁻⁴⁵

Optical coherence tomography (OCT) uses low coherence interferometry of light to examine the retina *in vivo* and enables visualization of the retina on a micron scale.⁶⁻⁷ Sufficient data regarding the OCT imaging characteristics of the choroid in these diseased states is lacking secondary to its posterior location and the presence of pigmented cells in the retinal pigment epithelium (RPE) which attenuates incident light. Recent advances using spectral domain OCT (SDOCT) technology make visualization of the choroid feasible using image averaging and enhanced depth imaging (EDI). Changes in choroidal thickness measured using SDOCT have been described in age related macular degeneration, choroidal melanoma, central serous chorioretinopathy, Vogt-Koyanagi-Harada and many others.^{3, 5-10}

The purpose of this study is to evaluate choroidal thickness with SDOCT in subjects with RPE tear as compared with the choroidal thickness of their fellow eye without RPE tear.

Methods

For this cross sectional investigation, 7 eyes of 7 patients with neovascular age-related macular degeneration and RPE tear in one eye were identified at the New England Eye Center between 2009 to 2011. All patients underwent a complete ophthalmic examination at New England Eye Center, including a slit-lamp examination and dilated fundus biomicroscopy. Each patient also underwent imaging with the Cirrus HD-OCT (Software version...Carl Zeiss Meditec, Dublin...). This study was approved by the institutional review board of the Tufts Medical Center. Inclusion criteria required the presence of a RPE tear in one eye, and the absence of it in the contralateral eye. All patients with concomitant ocular pathologies, including diabetic retinopathy, vascular occlusions, clinically significant macular edema, primary open angle glaucoma, and corneal disease including Fuchs' Dystrophy were excluded. Data from normal subjects was included from another study

which measured choroidal thickness in 42 eyes of 42 healthy subjects.¹² These subjects had no history of retinal or choroidal pathology, and patients with myopic refractive error of greater than 6.0 diopters were excluded.

Cirrus HD 1-line raster scans were used to obtain the measurements of choroidal thickness. These images were not inverted to bring the choroid adjacent to zero delay as image inversion utilizing Cirrus software results in a low-quality image. Choroidal thickness was manually measured from the posterior edge of the retinal pigment epithelium to the choroid/sclera junction at 500- μ m intervals up to 2500 μ m temporal and nasal to the fovea in both the eye with the RPE tear and the eye with intact RPE (figure 1). All measurements were performed by 2 independent observers and averaged for the purpose of analysis. This method has been previously described.¹²

Data are expressed as means $\pm$ standard error of the mean (SEM). Statistical analyses were performed using one way analysis of variance (ANOVA) followed by post test comparison with Bonferroni's Multiple Test. A 95% confidence interval and a 5% level of significance were adopted; therefore, the results with a *P*-value less than or equal to 0.05 were considered significant. All statistics were calculated using Graph Pad Prism 5.0 software for Mac.

Results

A total of 7 eyes of 7 patients with neovascular age-related macular degeneration and RPE tear in one eye were included in this study. The average age of these patients was 79 years (range 66-88). Of these subjects, 3 were male and 4 were female. In addition to exudative macular degeneration, the only other ocular comorbidity shared by these patients was the presence of nuclear sclerotic cataracts. Five patients had bilateral nuclear sclerotic cataracts. Two patients had a unilateral nuclear sclerotic cataract and uncomplicated cataract surgery with posterior chamber lens placement in the contralateral eye.

All subjects had dome-shaped pigment epithelial detachments (PED) prior to RPE tear and no dome-shaped PED in the unaffected eye. Four patients had bilateral neovascular age-related macular degeneration and three patients had dry age-related macular degeneration in the fellow intact eye with no dome-shaped PED. Five eyes with dome-shaped PED had active choroidal neovascularization by fluorescein angiography at the time of RPE tear formation. Of the four fellow eyes with neovascular macular degeneration and no dome-shaped PED, two of these eyes had active choroidal neovascularization and concurrent treatment with anti-VEGF therapy. All three eyes with dry age-related macular degeneration had mild to moderate disease without significant geographic atrophy and retained good visual acuity.

Four patients were treated with anti-VEGF therapy for wet macular degeneration prior to developing RPE tears, with an average of three pre-tear treatments of either bevacizumab (intra-vitreous 1.25 mg/0.05 ml) or ranibizumab (intra-vitreous 0.5 mg/0.05 ml) and range of 1-7 injections. One subject was found to have RPE tear formation four weeks following first treatment with intra-vitreous bevacizumab. In the remaining three subjects, RPE tear formation was the initial manifestation of their transformation to neovascular macular

degeneration and these patients had no previous history of therapy for wet macular degeneration. No subjects had been treated with laser, including photodynamic therapy (PDT), in either eye.

Reliable measurements of choroidal thickness were attained in all of the images that were analyzed. Intergrader reproducibility was assessed by intraclass correlation coefficient, and the measurements by the two independent observers were found to be significantly identical. The intraclass correlation coefficient (ICC) in mean choroidal thickness was between 0.907 and 0.997 in each area. The ICC was calculated to be 0.989 (95% confidence interval [CI], 0.932–0.998) in the subfoveal region, 0.964 (95% confidence interval [CI], 0.730–0.995) in the far nasal region, and 0.962 (95% confidence interval [CI], 0.776–0.994) in the far temporal region.

The mean choroidal thickness at each location was plotted (figure 2). Average subfoveal choroidal thickness in the eyes with the RPE tear was $154.9\mu\text{m} \pm 10.1\mu\text{m}$, and $212.9\mu\text{m} \pm 10.6\mu\text{m}$ in those with intact RPE ($p=0.035$, figure 3). Moreover, in the eyes with RPE tear, the measured choroidal thickness was thickest temporally, thinner in the subfoveal region, and progressed to be thinnest nasally. In eyes with intact RPE, the measured choroidal thickness was greatest in the subfoveal region. In the far nasal region, the average choroidal thickness was measured to be $108.2\mu\text{m} \pm 9.9\mu\text{m}$ in eyes with RPE tear and $101.8\mu\text{m} \pm 7.4\mu\text{m}$ in those with intact RPE ($p=0.05$). In the far temporal region, the average choroidal thickness was $200.4\mu\text{m} \pm 7.7\mu\text{m}$ in eyes with RPE tear and $203\mu\text{m} \pm 8.6\mu\text{m}$ in eyes with intact RPE ($p=0.05$).

The average age of normal subjects was 51.6 years (range 23–89). The average subfoveal, far nasal, and far temporal choroidal thickness measurements in normal subjects was found to be statistically greater compared to eyes with RPE tear and those with intact RPE ($p > 0.05$). The average subfoveal choroidal thickness in normal subjects was measured to be $256.8\mu\text{m} \pm 75.8\mu\text{m}$. In the far nasal and temporal regions, it was measured to be $243.2\mu\text{m} \pm 69.3\mu\text{m}$ and $255.0\mu\text{m} \pm 75.7\mu\text{m}$, respectively.

Longitudinal choroidal thickness data was available for eyes with RPE tear in four patients and for fellow, intact eyes in three patients. The average follow-up period was 29 months (range 25–36). There was no statistically significant difference between baseline choroidal thickness and follow-up measurements in tear and fellow eyes ($p = 0.08$). The mean choroidal thickness at baseline compared to follow-up in eyes with RPE tear was plotted (figure 4). There appeared to be a non-significant trend towards decreased choroidal thickness in all three locations (far nasal, subfoveal, far temporal) in tear eyes at follow-up. There was a non-significant trend towards decreased subfoveal choroidal thickness in eyes with tear compared to fellow eye with intact RPE. The average subfoveal choroidal thickness in the four eyes with the RPE tear was $129.0\mu\text{m} \pm 17.7\mu\text{m}$, and $212.9\mu\text{m} \pm 10.6\mu\text{m}$ in those with intact RPE ($p < 0.05$).

Discussion

RPE tears represent a potential severe complication of neovascular age-related macular degeneration which can lead to significant visual loss.^{19-20, 22} Our study detected a significant decrease in subfoveal choroidal thickness in subjects with RPE tear as compared with their fellow eye with intact RPE. Further, in comparison to normal eyes, those with RPE tear and fellow eyes with intact RPE had significant subfoveal thinning.

Subfoveal choroidal thinning may be a potential useful parameter in predicting risk of RPE tear in patients with PED associated with neovascular AMD in supplementation to other previously identified retinal OCT characteristics. One study described the formation of wavy RPE indentations or small interruptions and breaks in elevated RPE which was correlated with increased risk of developing an RPE tear in patients with pigment epithelium detachment following treatment with bevacizumab.²⁴ Chiang et al found large PED basal diameter and vertical height to be correlated with increased risk of developing RPE tear following anti-VEGF therapy.⁵⁴ Similarly, Chan et al measured preinjection vascularized PED height and found height > 400 μm to be a significant predictor for RPE tear formation following treatment with bevacizumab.⁵⁶ Subfoveal choroidal thickness in addition to such retinal OCT parameters could help stratify risk of developing RPE tear and dictate treatment in patients with wet macular degeneration.

In our study, four out of seven patients were treated with anti-VEGF therapy prior to developing a RPE tear, with one patient developing the tear four weeks after the first treatment was given. It has been hypothesized that in addition to decreasing the vascular permeability and rate of growth of abnormal blood vessels in neovascular AMD, anti-VEGF therapies may also affect the choroidal vasculature and structure.⁴⁶ Three patients had no previous history of anti-VEGF treatment and their choroidal thickness profiles did not significantly differ from those patients who had been treated. The choroidal thinning evident in these patients may be related to a process independent of an anti-VEGF mediated effect.

At present, it is unclear if this thinning of the choroid is a consequence of or precedes the RPE tear. Histopathology of AMD is characterized by attenuation of Bruch's membrane and degeneration of the choriocapillaris.^{45, 47} This suggests that there may be a component of choroidopathy in neovascular AMD. On fluorescein angiography, RPE tears do not typically exhibit leakage that may be expected in an exposed area of bare choroid and previous studies have suggested this may be secondary to concomitant atrophy of the choriocapillaris in the setting of AMD.¹⁹

The pathogenesis of RPE tear formation continues to remain controversial. Gass hypothesized that tears could occur due to rapid changes in vascular permeability which could induce sudden enlargement of the PED.²⁶ Krishan et al described the role of tangential force produced by shrinking choroidal neovascular membrane.⁶⁰ The role of contracting fibrovascular tissue was also illustrated by Spaide, who described reflective material suggestive of fibrovascular proliferation along the back surface of the RPE in PED by EDI OCT and subsequent contracture of the material following intravitreal ranibizumab.⁶¹ Our study detected significant subfoveal choroidal thinning in patients with RPE tear formation

and this decrease persisted two years later. We hypothesize that choroidal thinning could be associated with contracting choroidal neovascular tissue leading to increased risk of RPE tear formation.

Further prospective studies could address the limitations present in our study. First, due to the rarity of RPE tear formation, the sample size of our study was limited to only seven patients. Further, since all study subjects had dome-shaped pigment epithelial detachments (PED) prior to developing RPE tear, the results of this study may not be applicable to eyes with different types of PED. Future studies are needed to address the choroidal thickness patterns in eyes with dome-shaped PED versus other different types of PED. Also due to the rarity of RPE tear formation and retrospective design of the study, SDOCT scans were not performed prior to RPE tear development in our patients. Additionally, the scan pattern used can only provide anatomic information. Choroidal thickness measurements taken with SDOCT have yet to be correlated with any functional parameter of the choroid. One such way of addressing this in the future would be to employ Doppler OCT.⁴⁸⁻⁵³ Another limitation is that there was not a standard protocol for initiation of therapy or the timing and number of injections.

In this investigation, we observed a significant decrease in subfoveal choroidal thickness in subjects with RPE tear as compared with their fellow eye with intact RPE. Subfoveal choroidal thinning may be a potential useful parameter in predicting risk of RPE tear in patients with PED, particularly if future studies can show choroidal thinning precedes the development of RPE tear formation.

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Summary Statement

This study was conducted to evaluate choroidal thickness with SDOCT in 7 eyes of 7 patients with neovascular AMD and RPE tear in one eye compared to fellow eye with intact RPE. There is a significant decrease in subfoveal choroidal thickness in subjects with RPE tear.

Figure 1.
Cirrus HD 1 line raster of the macula in a patient with an RPE tear OD (A.) and intact RPE OS (B.).

Figure 2.

Graph of mean choroidal thickness in normal subjects and patients with RPE tear in one eye compared to the fellow eye at each of the 11 locations measured at 500 μm (0.5 mm) intervals temporal (T) and nasal (N). P -value represents the result of ANOVA.

Figure 3.

Graph of mean subfoveal choroidal thickness in patients with RPE tear in one eye compared to intact RPE in fellow eye.

Figure 4.

Graph of mean choroidal thickness in eyes with RPE tear at two year follow-up compared to baseline at each of the 11 locations measured at 500 μm (0.5 mm) intervals temporal (T) and nasal (N).