Evaluation of acute central serous chorioretinopathy using enhanced depth imaging OCT and multifocal electroretinography

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Research article

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Abstract

Background: To evaluate functional and structural abnormalities in patients with acute central serous chorioretinopathy (CSC) with multifocal electroretinography (mfERG) and enhanced depth imaging optical coherence tomography (EDI-OCT)

Methods: This prospective observational study included 57 patients with unilateral CSC. Both eyes underwent mfERG and EDI-OCT. Peak amplitudes and implicit times of the first kernel responses were analyzed and compared with those in 25 age-matched normal controls. Correlational analyses were performed between the mfERG results and EDI-OCT parameters. The thicknesses of the central retina, subretinal fluid, and choroid was measured at baseline and 3 months later.

Results: Compared with the normal controls, the amplitude and implicit time on mfERG were significantly impaired in the area with serous retinal detachment (SRD). The P1 amplitude and implicit time of the areas beyond the SRD were also found to be significantly impaired in the affected eyes. Eyes with a greater reduction in SRD had a less impaired mfERG response in fellow eyes than those whose retinal detachments were not spontaneously decreased by more than 90% after 3 months. Correlational analysis did not reveal any significant correlations between mfERG values and OCT parameters except for central choroidal thickness. The subfoveal choroidal thickness was negatively correlated with the mfERG parameters.

Conclusions: The findings of this study indicate diffuse functional impairment in acute CSC involving both eyes and areas beyond the SRD. The retinal response of the unaffected eye was associated with regression of SRD. Functional retinal abnormality was found to correlate with pathological changes in the choroid.

Background

Central serous chorioretinopathy (CSC) is a disease in which serous fluid spontaneously invades the space between the photoreceptor and retinal pigment epithelium (RPE) layers, leading to neurosensory detachment of the retina.[1] Although the cause of CSC has not been fully elucidated, individuals who have recently experienced a stressful life event and those with a type-A personality are known to be at higher risk and young-to-middle-aged men are most frequently affected.[1] Serous retinal detachment (SRD) in CSC is thought to originate from focal leakage from the RPE layer, and there is now increasing evidence suggesting that diffuse underlying abnormalities in the choroid layer have an important role in the development of CSC.[2] Furthermore, studies using indocyanine green angiography have demonstrated hyperpermeability and delayed filling of the choriocapillaris in areas outside the detachment area.[2-4]

The advent of optical coherence tomography (OCT) and multifocal electroretinography (mfERG) mean that retinal disorders can now be evaluated both anatomically and functionally. Retinal and choroidal measurements can now be obtained noninvasively using OCT with enhanced depth imaging (EDI).[5] EDI-OCT has revealed thickening of the choroid during the active phase of CSC, which regresses gradually as the subretinal fluid (SRF) and/or sub-RPE fluid decreases. [6] Moreover, it has been found that the subfoveal choroid is thicker in an eye with CSC than in the unaffected fellow eye.[7] The mfERG is an objective tool that reflects the focal electroretinographic responses at specific locations and allows functional assessment of multiple retinal areas simultaneously.[8] Previous mfERG studies in patients with active CSC have demonstrated reduced retinal response amplitudes and delayed latencies in locations with SRD.[9, 10] Furthermore, decreased retinal responses have been recorded from the posterior pole in eyes with active CSC and the unaffected fellow eyes.[11, 12]

Evaluation of the correlations between EDI-OCT and mfERG parameters might aid understanding of the relationships between the structural and functional changes in CSC. Therefore, the aim of this study was to evaluate the functional and structural abnormalities in patients with acute CSC using these assessment techniques. An attempt was also made to identify whether or not any OCT or mfERG parameters in affected and unaffected eyes with CSC were associated with spontaneous regression of SRD caused by CSC.

Methods

This observational study was performed in the Department of Ophthalmology at Dongtan Sacred Heart Hospital between December 2018 and December 2019. Patients with CSC were recruited prospectively for EDI-OCT and mfERG. Patients were included in the study if they had a diagnosis of unilateral CSC with a symptom duration of less than 1 month and had SRF involving the macula on OCT examination associated with leakage on fluorescein angiography. The following exclusion criteria were applied: (1) age older than 55 years or younger than 19 years; (2) myopia of more than -6 dioptres; (3) a history of ocular treatment or systemic corticosteroid therapy; (4) presence of a retinal disorder associated with SRF; (5) media opacity; (6) an abnormality in the fellow eye; (7) best-corrected visual

acuity (BCVA) <20/20 in the fellow eye; and (8) underlying disease or history of drug abuse. Twenty-five eyes of 25 age-matched individuals without any ophthalmic disease were enrolled as controls. The study was approved by the institutional review board and was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients.

At the time of presentation, all subjects underwent a complete ophthalmic examination, including measurement of BCVA with the Snellen chart, intraocular pressure, slit-lamp biomicroscopic examination, color fundus photography, fluorescein angiography, OCT examination, and mfERG recording. Patients were observed prospectively for 3 months without treatment (including laser photocoagulation, intravitreal injection, or photodynamic therapy to determine whether or not the CSC would regress spontaneously. Regression of CSC was defined as complete disappearance of SRF on fundus photographs and OCT scans.

OCT imaging

EDI-OCT images were obtained using a Spectralis OCT instrument (Spectralis; Heidelberg Engineering, Heidelberg, Germany) with seven horizontal lines of 20 × 20 degrees through the center of the fovea. The eye tracking system in this instrument was used to obtain each image and 100 scans were averaged to improve the signal-to-noise ratio. Considering the range of mfERG, the OCT image of the patient with an SRD of beyond 20 × 20 degrees through the center of the fovea was excluded. Using the built-in automated software, the distance between the inner surface of the retina and the inner border of the RPE at the central fovea was calculated manually as the central macular thickness (CMT). Two graders (IBJ, GSJ) measured the central height of the retina and choroid using built-in measurement software. The central height and diameter of the SRF were measured with the same method. The central retinal thickness (CRT) was measured from the anterior surface of the retinal nerve fiber layer to the outer border of the detached retina. The central SRF thickness (SRFT) was measured from the anterior surface of the RPE layer to the outer border of the detached retina and the central choroid thickness (CCT) was measured as the space between the outer portion of the hyperreflective line corresponding to the RPE layer and the choriosclera junction. The maximum width of the SRF on the OCT image was calculated as the SRF diameter (SRFD) (Fig. 1). Given the significant circadian fluctuations in CCT, all images were acquired on the same day within one hour between 10 am and 2 pm. [13] The graders were blinded to the patients' identities and the specific times of their visits.

mfERG recording

mfERG values were recorded using a Matrivision Monpack (Pérenchies, France) with reference to the ISCEV (International Society of Clinical Electrophysiology of Vision) guidelines.[14] A matrix of 61 hexagonal elements was generated by the visual stimulator and displayed on a cathode ray tube color monitor driven at a frame of 75 Hz. The white (luminance, 200 cd/m^2) and black (luminance, 1 cd/m^2) stimuli changed independently in each hexagon at a rate of 75 Hz. Before recordings were contained, the pupils were fully dilated by 1% tropicamide and 2.5% phenylephrine hydrochloride. mfERG recordings were obtained after 15 minutes of adaption to ordinary room light and before insertion of an ERG Jet corneal contact lens electrode. Proparacaine hydrochloride 0.5% drops were instilled for topical anesthesia. During mfERG testing, the N1, P1, and N2 peaks for each response were automatically identified in real time over a group of up to five rings from 0° to 25° of eccentricity. We analyzed the average amplitudes and implicit times of the first-order kernel mfERG responses (N1 and P1) from maps of N1, P1 and N2 wave peaks on each individual ring.

Statistical analysis

The Mann-Whitney *U* test was used to compare the mfERG values between the patients with CSC and the controls. Serial comparisons of the OCT and mfERG values were performed using the paired *t*-test. The correlations between the logMAR BCVA, OCT, and mfERG parameters were examined using Pearson's correlation coefficient. Multiple linear regression models were used to assess potential predictors for a decrease in SRFT. Statistical modeling was used to identify factors that were independently associated with the change in SRFT between baseline and 3 months. Only predictors that were statistically significant in exploratory analysis were included. A post hoc analysis was also performed to identify differences between patients who did and did not achieve a ≥90% reduction in SRFT. All statistical analyses were performed using SPSS version 19.0 (IBM Corp., Armonk, NY, USA). A *P*-value <0.05 was considered statistically significant.

Results

Sixty-one patients were enrolled in the study. Four of these patients were excluded because of loss to follow-up, leaving 57 patients with acute unilateral CSC and no history of other ocular disease for inclusion in the study. Both eyes of each patient were analyzed. The mean age at the time of the initial episode of CSC was 47.75 ± 7.98 (range, 36–55) years and the mean age of the control subjects was

45.88 ± 5.28 (range, 35–52) years. Fifty-three of the patients with CSC were male and four were female while 23 of 25 control subjects were male and two were female (Table 1).

The changes in BCVA and OCT parameters after 3 months of observation are shown in Table 1. The mean BCVA in affected eyes was 0.17 ± 0.21 logMAR at baseline, and improved significantly to 0.08 ± 0.11 logMAR after 3 months without treatment (P<0.0001). The mean CMT, SRFT and SRFD values were significantly decreased after 3 months of observation (P<0.0001) but there was no significant change in CRT (P=0.383). The mean CCT in the affected eyes decreased significantly from 385.79 ± 53.32 μm at baseline to 327.77 ± 46.5 μm at 3 months (P<0.0001). The mean CCT in the normal fellow eyes also decreased significantly after 3 months of observation (from 295.08 ± 54.97 μm to 281.17 ± 31.49 μm, P=0.045).

Tables 2 and 3 show the results of mfERG recordings from rings 1–5 of affected eyes and fellow eyes. Compared with normal controls, the mean amplitude and implicit times of retinal responses were significantly impaired in affected eyes, especially in the N1 and P1 response amplitudes (Table 2). There was a significant difference in the N1 amplitudes of rings 2–5 between control eyes and fellow normal eyes, but not in the other mfERG parameters.

Correlational analyses between logMAR BCVA, OCT, and mfERG parameters for eyes with CSC revealed no significant correlations between mfERG values and visual acuity (VA) or with OCT parameters except for CCT (Tables 4 and 5). The correlation analyses found significant negative correlations between CCT and the N1 amplitudes for rings 1–5 and the P1 amplitudes for rings 1,2, 4, and 5 (Table 4). Furthermore, a greater CCT was significantly associated with a delayed implicit time of N1 in rings 1–5 and P1 in ring 1 (Table 5).

Multiple and simple linear regression models were used to identify potential predictors of a decrease in SRFT at 3 months. In addition to the demographic data (sex and age) and baseline VA, baseline OCT parameters (SRFT, SRFD, CMT, CRT, CCT) were included in the multiple linear regression analysis. Statistical modeling identified the baseline VA to be the only significant predictor of SRFT reduction. A better VA at baseline predicted a better reduction in SRF at 3 months (coefficient -1.716, 95% CI -0.306, -3.126, P=0.045). The correlations between SRFT reductions and mfERG values in affected and unaffected eyes were calculated, and only the P1 implicit times at rings 3–5 of unaffected fellow eyes were negatively correlated with SRFT reductions (P<0.0001, P=0.019, and P=0.002, respectively).

Thirty-six of the 57 patients showed a more than 90% reduction in SRFT between baseline and 3 months and 21 patients achieved an SRFT reduction of less than 90% in the same period. Patients who achieved a more than 90% reduction in SRFT were defined as a group with regression and the patients who did not were defined as a group with less regression. Except for the baseline VA, there was no significant between-group difference (Table 6). The group with regression had a significantly better VA at baseline than the group with less regression. The mfERG results in the affected and unaffected eyes were compared between these two groups (Tables 7 and 8). There was no significant between-group difference in most of the mfERG parameters between the two groups of affected eyes (Table 7). However, the mean amplitude and implicit times in normal fellow eyes showed significant differences within rings 1–4 (Table 8). The retinal response in normal fellow eyes was better in the group with regression than in the group with less regression.

Discussion

This study evaluated a group of patients with acute CSC using mfERG and EDI-OCT. mfERG is an objective examination that provides a regional map of retinal function across the posterior pole.[11] Many studies have demonstrated abnormal mfERG responses in the detached retina in an affected eye.[9-12, 15-17] However, debate persists regarding the mfERG abnormalities in areas without serous detachment and in the normal fellow eye. Marmor and Tan were the first to show abnormal mfERG responses in the peripheral retina without SRD, but subsequent studies revealed that reductions in mfERG responses were limited to the central rings of affected eyes.[10, 11, 15-17] Unfortunately, these studies were not able to resolve this debate because of the relatively small numbers of patients enrolled. Timothy et al. performed a cross-sectional study in 45 eyes with acute CSC using mfERG and found a reduction in the second-order mfERG response for the more peripheral macular area. [17]

In the present study, mfERG examination in 57 patients with acute CSC showed that retinal responses and the implicit time of mfERG were significantly impaired in the area with SRD, which is consistent with previous reports. The P1 amplitude and implicit time of rings 4–5 was found to be significantly impaired in affected eyes when compared with the controls. This finding suggested that the area of retinal dysfunction in CSC is larger than the SRD observed clinically. In contrast with the mfERG results in affected eyes, the retinal response in fellow eyes was less severely impaired over the entire area examined. However, a post hoc analysis revealed that the patients with a better reduction in SRD showed a less impaired mfERG response in fellow eyes than the patients whose retinal

detachments were not spontaneously decreased by more than 90% after 3 months. This finding means that some of the patients with unilateral CSC had fellow eyes with good retinal responses and others did not. For this reason, whether normal fellow eyes in patients with CSC have abnormal retinal responses on mfERG examination remains controversial. This study clearly indicates that the pathogenesis of CSC involves areas beyond the SRD in affected eyes and areas throughout the posterior pole of non-affected eyes; this finding support the view that CSC is a disease affected by systemic humoral factors or by diffuse underlying choroidal vascular disease.[18, 19]

The advent of EDI-OCT has provided a non-invasive method for examination of the choroid and has contributed greatly to current understanding of the pathogenesis underlying CSC.[2] EDI-OCT imaging has shown that the choroid is abnormally thickened in both the affected and non-affected eye during the acute phase of CSC and that the choroidal thickness gradually decreases with regression of the disease. The EDI-OCT imaging measurements in this study also showed that the choroid thickness was increased in both the affected and normal fellow eyes but decreased significantly as SRD regressed. In addition to measuring choroidal thickness, various parameters from the OCT images, including SRFT, SRFD, CRT, and CMT were measured manually and correlations were sought between the mfERG and OCT parameters. Previous studies that investigated patients with CSC using mfERG and OCT performed similar analyses to identify associations between the functional and structural changes in CSC.[9, 20] Such studies found no significant association of OCT parameters, including SRFT, CCT, and CMT, with mfERG parameters, and none performed correlation analyses, including of choroidal thickness, in patients with CSC because EDI-OCT was not available when the studies were conducted. In the present study, subfoveal choroidal thickness was the only OCT parameter that was negatively associated with mfERG. The choroid has reportedly been implicated in the pathogenesis of CSC, which is thickened and thought to be hyperpermeable due to inflammation or vascular congestion, [2] Because the choroid dissipates heat from retinal metabolism and supplies nutrients and oxygen to the outer retina, [21] a pathologically thickened choroid implies compromised photoreceptor metabolism, diminished supply to the outer retinal layer, and consequent retinal dysfunction. Ignacio et al. also reported significant correlations between choroidal thickness and mfERG results. [22] This study found retinal dysfunction to have become more prominent as the choroid thickened.

The major limitation of this study is the lack of follow-up mfERG results. There has been debate as to whether retinal dysfunction is fully recovered after resolution of SRD.[10, 11] This study was not able to answer this question. A further prospective study that includes follow-up mfERG evaluation in a large number of patients with CSC is needed for a better understanding of retinal dysfunction in CSC. The study is further limited by the possible influence of light scattering on mfERG, as light scattering can reduce the macular mfERG response and elevate the peripheral mfERG response. [23, 24] The scattering effect may be linked to the presently observed results that decreased retinal responses in ring 4-5. Furthermore, while previous research revealed a significant correlation between SRFD and the mfERG response, our study did not. [9] The scattering phenomenon may explain this discrepancy. We only measured the thickness of the choroid, in spite of EDI-OCT allowing for in-depth observation of the choroid and the analysis was unable to compare the exact location between OCT images and mfERG measurements. [6] These limitations may have contributed to the lack of a significant correlation between the choroidal thickness of fellow eyes and the mfERG results (data not presented), unlike with affected eyes. The mfERG results and choroidal thickness in the fellow eye were not perfectly normal, and the gross measurement of choroidal thickness could not detect subtle differences, which may have resulted in failure to identify a correlation between OCT and mfERG in fellow eyes. Possibly due to the limitation of measuring choroidal thickness, this may also have compromised the identification of a correlation between OCT and mfERG in fellow eyes. [25] The choroid can be affected by circadian rhythms, and the repeatability of measurements remains questionable. [26] Kim et al. reported intra-observer and inter-observer differences in choroidal thickness measurements to be 32-38 μm and 46-57 μm, respectively. [27] These limitations may be linked to the remarkable decrease in choroidal thickness after 3 months. The small number of control subjects and short follow-up period were further weaknesses of this study.

In spite of these limitations, this study is the first to examine patients with acute CSC using a combination of EDI-OCT and mfERG and found bilateral diffuse impairment of the retinal response. The retinal response of the unaffected eye was associated with the regression of SRD, suggesting that the mfERG results for the unaffected eye may serve as an indicator of spontaneous regression. By applying the mfERG in the routine clinical examination of CSC, patients will be able to obtain more precise information regarding the course of their disease. Furthermore, pathological changes in the choroid identified by EDI-OCT had a negative correlation with retinal function measured with mfERG. These findings imply that structural and functional impairment of the choroid plays an important role in the pathogenesis of CSC. Further evaluation using EDI-OCT and mfERG will improve current understanding of the choroid in patients with CSC and explain the subtle variation in disease progression from patient to patient.

Declarations

Ethical approval and consent to participate

The study was approved by the ethical committee of Dongtan Sacred Heart Hospital. All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee, as well as with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed in the current study are available from the corresponding author on reasonable request.

Competing interest

None.

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Author contributions

In Hwan Hong and Jae Ryong Han designed and conducted the study.

In Boem Chang and Gang Seok Jeon collected the data.

In Hwan Hong analyzed and interpreted the data.

In Hwan Hong, In Boem Chang, Gang Seok Jeon and Jae Ryong Han prepared, reviewed, and approved the manuscript.

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Not applicable.

References

1. Yannuzzi LA: Type-A behavior and central serous chorioretinopathy. *Retina (Philadelphia, Pa)* 1987, 7(2):111-131.
2. Nicholson B, Noble J, Forooghian F, Meyerle C: Central serous chorioretinopathy: update on pathophysiology and treatment. *Surv Ophthalmol* 2013, 58(2):103-126.
3. Prünte C, Flammer J: Choroidal capillary and venous congestion in central serous chorioretinopathy. *Am J Ophthalmol* 1996, 121(1):26-34.
4. Iida T, Kishi S, Hagimura N, Shimizu K: Persistent and bilateral choroidal vascular abnormalities in central serous chorioretinopathy. *Retina* 1999, 19(6):508-512.
5. Spaide RF, Koizumi H, Pozonni MC: Enhanced depth imaging spectral-domain optical coherence tomography. *Am J Ophthalmol* 2008, 146(4):496-500.
6. Sonoda S, Sakamoto T, Kuroiwa N, Arimura N, Kawano H, Yoshihara N, Yamashita T, Uchino E, Kinoshita T, Mitamura Y: Structural changes of inner and outer choroid in central serous chorioretinopathy determined by optical coherence tomography. *PloS one* 2016, 11(6).
7. Maruko I, Iida T, Sugano Y, Ojima A, Sekiryu T: Subfoveal choroidal thickness in fellow eyes of patients with central serous chorioretinopathy. *Retina* 2011, 31(8):1603-1608.
8. Sutter EE, Tran D: The field topography of ERG components in man—I. The photopic luminance response. *Vision Res* 1992, 32(3):433-446.

9. Yip YW, Ngai JW, Fok AC, Lai RY, Li H, Lam DS, Lai TY: Correlation between functional and anatomical assessments by multifocal electroretinography and optical coherence tomography in central serous chorioretinopathy. *Doc Ophthalmol* 2010, 120(2):193-200.
10. Vajaranant TS, Szlyk JP, Fishman GA, Gieser JP, Seiple W: Localized retinal dysfunction in central serous chorioretinopathy as measured using the multifocal electroretinogram. *Ophthalmology* 2002, 109(7):1243-1250.
11. Marmor MF, Tan F: Central serous chorioretinopathy: bilateral multifocal electroretinographic abnormalities. *Archives of Ophthalmology* 1999, 117(2):184-188.
12. Chappelow AV, Marmor MF: Multifocal electroretinogram abnormalities persist following resolution of central serous chorioretinopathy. *Arch Ophthal* 2000, 118(9):1211-1215.
13. Usui S, Ikuno Y, Akiba M, Maruko I, Sekiryu T, Nishida K, Iida T: Circadian changes in subfoveal choroidal thickness and the relationship with circulatory factors in healthy subjects. *Invest Ophthalmol Vis Sci* 2012, 53(4):2300-2307.
14. Hood DC, Bach M, Brigell M, Keating D, Kondo M, Lyons JS, Marmor MF, McCulloch DL, Palmowski-Wolfe AM, Vision ISFCEo: ISCEV standard for clinical multifocal electroretinography (mfERG)(2011 edition). *Documenta Ophthalmologica* 2012, 124(1):1-13.
15. Huang S, Wu D, Jiang F, Wu L, Liang J, Luo G, Wen F, Ma J: The multifocal electroretinogram in central serous chorioretinopathy. *Ophthalmic and Physiological Optics* 2002, 22(3):244-247.
16. Zhang W, Zhao K: Multifocal electroretinography in central serous chorio-retinopathy and assessment of the reproducibility of the multifocal electroretinography. *Doc Ophthalmol* 2003, 106(2):209-213.
17. Lai TY, Lai RY, Ngai JW, Chan W-M, Li H, Lam DS: First and second-order kernel multifocal electroretinography abnormalities in acute central serous chorioretinopathy. *Doc Ophthalmol* 2008, 116(1):29-40.
18. Roybal CN, Sledz E, Elshatory Y, Zhang L, Almeida DR, Chin EK, Critser B, Abramoff MD, Russell SR: Dysfunctional autonomic regulation of the choroid in central serous chorioretinopathy. *Retina* 2018, 38(6):1205-1210.
19. Iida T, Hagimura N, Sato T, Kishi S: Evaluation of central serous chorioretinopathy with optical coherence tomography. *American journal of ophthalmology* 2000, 129(1):16-20.
20. Moschos M, Brouzas D, Koutsandrea C, Stefanos B, Loukianou H, Papantonis F, Moschos M: Assessment of central serous chorioretinopathy by optical coherence tomography and multifocal electroretinography. *Ophthalmologica* 2007, 221(5):292-298.
21. Nickla DL, Wallman J: The multifunctional choroid. *Prog Retin Eye Res* 2010, 29(2):144-168.
22. Flores-Moreno I, Arias-Barquet L, Rubio-Caso MJ, Muñoz-Blanco A, Vidal-Martí M, Catala-Mora J, Ruiz-Moreno JM, Duker JS, Caminal JM: Structure versus function: correlation between outer retinal and choroidal thicknesses measured by swept-source OCT with multifocal electroretinography and visual acuity. *International journal of retina and vitreous* 2017, 3(1):29.
23. Tam W-k: Effects of light scattering on the multifocal electroretinogram (mfERG): Hong Kong Polytechnic University (Hong Kong); 2005.
24. Tam A, Chan H, Brown B, Yap M: The effects of forward light scattering on the multifocal electroretinogram. *Current eye research* 2004, 28(1):63-72.
25. Mrejen S, Spaide RF: Optical coherence tomography: imaging of the choroid and beyond. *Survey of ophthalmology* 2013, 58(5):387-429.
26. Daruich A, Matet A, Dirani A, Bousquet E, Zhao M, Farman N, Jaisser F, Behar-Cohen F: Central serous chorioretinopathy: recent findings and new physiopathology hypothesis. *Prog Retin Eye Res* 2015, 48:82-118.
27. Kim J, Kang S, Kim J, Kim S: Variability of subfoveal choroidal thickness measurements in patients with age-related macular degeneration and central serous chorioretinopathy. *Eye* 2013, 27(7):809-815.

Tables

Table 1. Baseline demographics and ophthalmic characteristics seen on optical coherence tomography

Characteristics			
Number of eyes/patients	57 eyes/57 patients		
Sex (male/female)	53/4		
Age (years)	47.75 ± 7.98		
	Baseline	3 mon	*P* value*
Visual acuity	0.75 ± 0.25	0.86 ± 0.19	<0.0001
Central retinal thickness (㎛)	237.15 ± 54.55	243.40 ± 41.34	0.383
Central subretinal fluid thickness (㎛)	251.16 ± 115.99	70.44 ± 100.83	<0.0001
Central macular thickness (㎛)	492.67 ± 112.98	329.33 ± 101.91	<0.0001
Central choroidal thickness (㎛)	385.79 ± 53.32	327.77 ± 46.5	<0.0001
Central choroidal thickness of fellow eye (㎛)	295.08 ± 54.97	281.17 ± 31.49	0.045

*Paired t-test

Table 2. Comparison of multifocal electroretinography parameters between affected eyes and control eyes

mfERG parameters	Affected eyes (57 eyes)	Control eyes (25 eyes)	*P* value*	mfERG parameters	Affected eyes (57 eyes)	Control eyes (25 eyes)	*P* value*
N1 amplitude				N1 implicit time			
Ring 1	487.49 ± 192.74	1069.08 ± 242.58	<0.0001	Ring 1	32.42 ± 3.01	29.48 ± 1.04	<0.0001
Ring 2	445.18 ± 147.44	726.84 ± 65.73	<0.0001	Ring 2	30.50 ± 1.92	28.99 ± 0.78	<0.0001
Ring 3	461.68 ± 123.34	634.80 ± 54.53	<0.0001	Ring 3	28.81 ± 1.11	27.90 ± 0.54	0.001
Ring 4	458.74 ± 92.84	592.52 ± 57.92	<0.0001	Ring 4	28.45 ± 1.18	27.68 ± 0.74	0.004
Ring 5	474.02 ± 105.82	564.56 ± 44.83	0.003	Ring 5	28.80 ± 4.60	27.57 ± 0.68	0.059
P1 amplitude				P1 implicit time			
Ring 1	820.54 ± 327.24	1956.96 ± 387.99	<0.0001	Ring 1	52.89 ± 4.25	49.92 ± 0.98	0.001
Ring 2	837.51 ± 258.41	1246.56 ± 149.38	<0.0001	Ring 2	48.99 ± 2.98	47.03 ± 1.25	0.003
Ring 3	932.16 ± 201.30	1084.04 ± 138.32	0.03	Ring 3	47.16 ± 1.63	45.50 ± 0.94	0.008
Ring 4	930.44 ± 208.91	1067.40 ± 149.15	0.022	Ring 4	46.28 ± 1.48	45.31 ± 0.87	0.048
Ring 5	999.74 ± 263.29	1138.76 ± 200.91	0.04	Ring 5	46.29 ± 1.51	45.32 ± 1.05	0.198

mfERG; multifocal electroretinography, *Mann-Whitney U test

Table 3. Comparison of multifocal electroretinography parameters between non-affected eyes and control eyes

mfERG parameters	Fellow eyes (57 eyes)	Control eyes (25 eyes)	*P* value*	mfERG parameters	Fellow eyes (57 eyes)	Control eyes (25 eyes)	*P* value*
N1 amplitude				N1 implicit time			
Ring 1	930.44 ± 289.80	1069.08 ± 242.58	0.112	Ring 1	30.79 ± 1.69	29.48 ± 1.04	0.224
Ring 2	560.14 ± 156.04	726.84 ± 65.73	0.003	Ring 2	29.24 ± 1.46	28.99 ± 0.78	0.142
Ring 3	500.51 ± 98.03	634.80 ± 54.53	0.001	Ring 3	28.75 ± 1.12	27.90 ± 0.54	0.346
Ring 4	491.46 ± 96.18	592.52 ± 57.92	0.11	Ring 4	28.41 ± 1.06	27.68 ± 0.74	0.448
Ring 5	488.35 ± 90.85	564.56 ± 44.83	0.001	Ring 5	28.38 ± 1.10	27.57 ± 0.68	0.106
P1 amplitude				P1 implicit time			
Ring 1	1610.30 ± 532.61	1956.96 ± 387.99	0.537	Ring 1	51.06 ± 1.78	49.92 ± 0.98	0.241
Ring 2	1104.04 ± 217.99	1246.56 ± 149.38	0.476	Ring 2	47.83 ± 1.48	47.03 ± 1.25	0.158
Ring 3	1003.96 ± 159.75	1084.04 ± 138.32	0.397	Ring 3	46.50 ± 1.23	45.50 ± 0.94	0.085
Ring 4	1021.40 ± 152.09	1067.40 ± 149.15	0.468	Ring 4	45.96 ± 1.29	45.31 ± 0.87	0.396
Ring 5	1072.70 ± 176.15	1138.76 ± 200.91	0.468	Ring 5	45.89 ± 1.27	45.32 ± 1.05	0.627

mfERG; multifocal electroretinography, *Mann-Whitney U test

Table 4. Pearson's correlation analyses between amplitude of multifocal electroretinography, best-corrected visual acuity, and retinal thickness

	Visual acuity		Central subretinal fluid thickness		Central retinal thickness		Central macular thickness		Central choroidal thickness	
	r	*P* value	r	*P* value	r	*P* value	r	*P* value	r	*P* value
N1 amplitude										
Ring 1	0.030	0.826	-0.09	0.506	-0.093	0.497	-0.114	0.409	-0.373	0.005
Ring 2	0.010	0.998	-0.05	0.729	-0.11	0.417	-0.043	0.752	-0.457	<0.001
Ring 3	-0.041	0.763	0.08	0.552	-0.028	0.835	0.075	0.578	-0.365	0.005
Ring 4	0.021	0.879	-0.11	0.4	-0.068	0.616	-0.191	0.154	-0.265	0.046
Ring 5	-0.039	0.776	-0.05	0.712	-0.021	0.876	-0.073	0.587	-0.263	0.048
P1 amplitude										
Ring 1	0.086	0.524	0.05	0.716	-0.089	0.049	-0.01	0.938	-0.302	0.023
Ring 2	0.184	0.17	-0.27	0.045	0.102	0.45	-0.261	0.05	-0.263	0.048
Ring 3	0.084	0.535	-0.09	0.491	-0.065	0.632	-0.16	0.235	-0.249	0.062
Ring 4	0.026	0.848	-0.06	0.656	-0.12	0.375	-0.115	0.392	-0.353	0.007
Ring 5	0.087	0.522	-0.20	0.143	0.05	0.71	-0.169	0.209	-0.279	0.035

Table 5. Pearson's correlation analyses between implicit time of multifocal electroretinography, best-corrected visual acuity, and retinal thickness

	Visual acuity		Central subretinal fluid thickness		Central retinal thickness		Central macular thickness		Central choroidal thickness	
	r	*P* value	r	*P* value	r	*P* value	r	*P* value	r	*P* value
N1 implicit time										
Ring 1	-0.033	0.813	-0.152	0.266	0.091	0.508	-0.176	0.199	0.292	0.03
Ring 2	0.003	0.984	0.039	0.771	0.053	0.697	0.036	0.791	0.451	<0.001
Ring 3	0.005	0.968	-0.024	0.862	0.016	0.905	-0.052	0.7	0.370	0.005
Ring 4	-0.021	0.876	-0.045	0.738	0.049	0.715	-0.079	0.557	0.262	0.049
Ring 5	-0.018	0.896	0.044	0.745	-0.036	0.79	-0.011	0.935	0.268	0.044
P1 implicit time										
Ring 1	-0.08	0.557	-0.086	0.53	0.066	0.631	-0.082	0.548	0.277	0.038
Ring 2	-0.185	0.173	0.001	0.993	0.143	0.292	0.001	0.985	0.24	0.074
Ring 3	-0.291	0.03	0.167	0.218	0.053	0.7	0.144	0.291	0.22	0.104
Ring 4	-0.415	0.002	0.122	0.376	-0.094	0.496	0.041	0.766	0.069	0.618
Ring 5	-0.277	0.038	0.116	0.396	-0.007	0.958	0.052	0.706	0.107	0.431

Table 6. Comparison of baseline characteristics and optical coherence tomography parameters between the group with regression and the group with less regression

Characteristics	Regression (36 patients)	Less-regression (21 patients)	*P* value*
SRF reduction (%)	97.08 ± 8.32	36.52 ± 26.66	<0.001
Age (years)	45.94 ± 6.63	50.86 ± 9.34	0.083
Baseline VA (logMAR)	0.13 ± 0.18	0.25 ± 0.24	0.017
Baseline SRFT (□)	248.97 ± 132.71	273.10 ± 98.97	0.313
Baseline CRT (□)	236.22 ± 43.70	230.81 ± 71.07	0.513
Baseline CMT (□)	493.89 ± 121.96	507.19 ± 111.05	0.546
Baseline CCT (□, affected eye)	380.14 ± 57.28	388.29 ± 56.20	0.579
Baseline CCT (□, fellow eye)	290.00 ± 54.38	302.38 ± 56.77	0.549

SRF, serous retinal fluid; VA, visual acuity; SRFT, serous retinal fluid thickness; CRT, central retinal thickness; CMT, central macular thickness; CCT, central choroid thickness; *Mann-Whitney U test

Table 7. Comparison of multifocal electroretinography parameters in affected eyes between the group with regression and the group with less regression

mfERG parameters	Regression (36 patients)	Less-regression (21 patients)	*P* value*	mfERG parameters	Regression (36 patients)	Less-regression (21 patients)	*P* value*
N1 amplitude				N1 implicit time			
Ring 1	497.23 ± 175.27	470.46 ± 223.89	0.546	Ring 1	32.31 ± 2.40	32.62 ± 3.93	0.478
Ring 2	462.50 ± 150.32	415.48 ± 140.92	0.286	Ring 2	30.42 ± 1.60	30.65 ± 2.41	0.362
Ring 3	478.53 ± 114.62	432.81 ± 134.92	0.212	Ring 3	28.69 ± 0.95	29.01 ± 1.35	0.188
Ring 4	462.39 ± 87.06	452.48 ± 103.95	0.551	Ring 4	28.29 ± 0.99	28.73 ± 1.42	0.090
Ring 5	477.08 ± 94.15	468.76 ± 125.67	0.817	Ring 5	27.97 ± 1.76	30.21 ± 7.11	0.085
P1 amplitude				P1 implicit time			
Ring 1	828.25 ± 370.59	807.33 ± 243.32	0.882	Ring 1	52.41 ± 3.89	53.75 ± 4.80	0.586
Ring 2	864.19 ± 272.89	791.75 ± 23.59	0.203	Ring 2	48.69 ± 2.78	49.53 ± 3.30	0.086
Ring 3	951.25 ± 206.87	899.43 ± 191.80	0.141	Ring 3	46.67 ± 1.53	47.98 ± 1.49	0.002
Ring 4	937.36 ± 204.05	918.57 ± 221.58	0.679	Ring 4	45.85 ± 1.04	47.03 ± 1.84	0.023
Ring 5	1014.44 ± 237.02	974.52 ± 307.79	0.418	Ring 5	45.77 ± 1.15	47.16 ± 1.67	0.001

mfERG; multifocal electroretinography, *Mann-Whitney U test

Table 8. Comparison of multifocal electroretinography parameters in non-affected eyes between the group with regression and the group with less regression

mfERG parameters	Regression (36 patients)	Less-regression (21 patients)	*P* value*	mfERG parameters	Regression (36 patients)	Less-regression (21 patients)	*P* value*
N1 amplitude				N1 implicit time			
Ring 1	1043.58 ± 273.88	720.24 ± 174.27	<0.0001	Ring 1	30.13 ± 1.65	31.89 ± 1.23	<0.0001
Ring 2	605.83 ± 136.95	481.81 ± 158.59	0.003	Ring 2	28.78 ± 1.23	30.02 ± 1.53	0.002
Ring 3	521.72 ± 96.95	464.14 ± 90.90	0.030	Ring 3	28.31 ± 0.97	29.50 ± 0.95	<0.0001
Ring 4	518.72 ± 97.27	444.71 ± 75.55	0.007	Ring 4	28.04 ± 0.92	29.05 ± 1.00	0.001
Ring 5	490.36 ± 86.17	484.90 ± 100.49	0.869	Ring 5	28.16 ± 0.97	28.74 ± 1.22	0.058
P1 amplitude				P1 implicit time			
Ring 1	1866.47 ± 467.26	1171.14 ± 302.60	<0.0001	Ring 1	50.36 ± 1.48	52.31 ± 1.55	<0.0001
Ring 2	1176.53 ± 203.88	979.76 ± 186.11	0.001	Ring 2	47.37 ± 1.18	48.68 ± 1.59	0.001
Ring 3	1056.94 ± 154.66	913.76 ± 126.03	0.001	Ring 3	46.02 ± 0.80	47.26 ± 1.45	<0.0001
Ring 4	1056. 08 ± 141.94	961.95 ± 153.75	0.012	Ring 4	45.51 ± 0.87	46.72 ± 1.54	<0.0001
Ring 5	1106.06 ± 166.35	1015.52 ± 181.70	0.024	Ring 5	45.45 ± 0.87	46.58 ± 1.54	0.004

mfERG; multifocal electroretinography, *Mann-Whitney U test

Figures

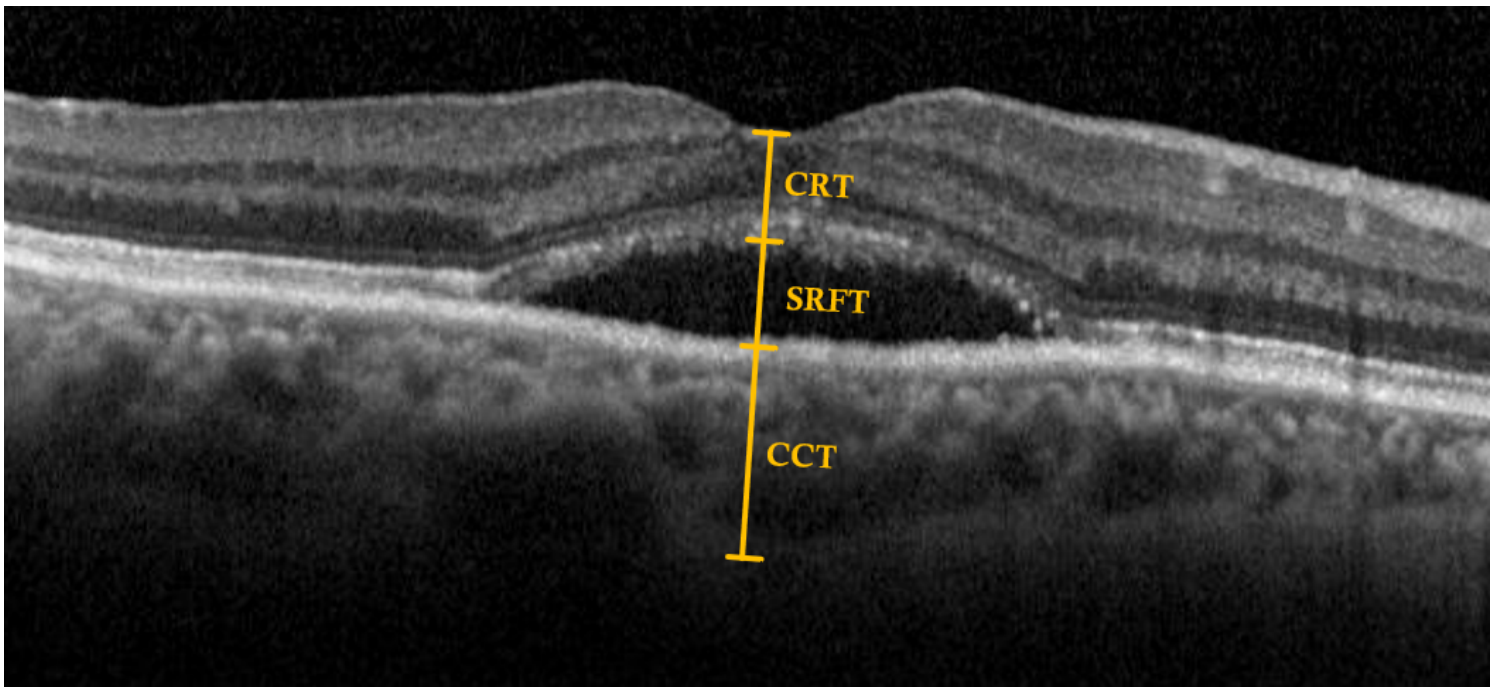

Figure 1

A representative horizontal optical coherence tomography scan of an eye with central serous chorioretinopathy. Central retina thickness (CRT), subretinal fluid thickness (SRFT), subretinal fluid diameter (SRFD) and central choroidal thickness (CCT) were measured manually.