

## Continuing Medical Education:

# Half-dose vs one-third-dose photodynamic therapy for chronic central serous chorioretinopathy

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**Release date: 10 May 2012; Expiration date: 10 May 2013**

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### Learning Objectives

Upon completion of this activity, participants will be able to:

1. Evaluate the diagnosis of CSC
2. Compare a 50% dose of verteporfin with a 30% dose of verteporfin in the resolution of subretinal fluid in CSC
3. Compare a 50% dose of verteporfin with a 30% dose of verteporfin in other outcomes following PDT for CSC
4. Assess the relationship between choroidal thickness and subretinal fluid resolution in the current study of CSC

### Authors/Editors disclosure information

Andrew J Lotery has disclosed the following relevant financial relationships: Received grants for clinical research from: Novartis Pharmaceuticals Corporation. Served as an advisor or consultant for: Allergan, Inc. and Novartis Pharmaceuticals Corporation. Served as a speaker or a member of the speaker's bureau for: Novartis Pharmaceuticals Corporation.

Uetani Ruka has disclosed no relevant financial relationships.

Yasuki Ito has disclosed no relevant financial relationships.

Kazuhiro Oiwa has disclosed no relevant financial relationships.

Kohei Ishikawa has disclosed no relevant financial relationships.

Hiroko Terasaki has disclosed no relevant financial relationships.

### Journal CME author disclosure information

Charles P Vega has disclosed no relevant financial relationships.

# Half-dose vs one-third-dose photodynamic therapy for chronic central serous chorioretinopathy

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## Abstract

**Purpose** To prospectively compare the effects of half-dose verteporfin (3 mg/m<sup>2</sup>) photodynamic therapy (1/2 PDT) with those of one-third-dose verteporfin (2 mg/m<sup>2</sup>) PDT (1/3 PDT) for chronic central serous chorioretinopathy (CSC).

**Methods** Sixteen eyes of 16 consecutive patients with chronic CSC were enrolled and followed up for a 3-month study period. The first 10 patients received 1/2 PDT and the next 6 patients received 1/3 PDT. The resolution rate of subretinal fluid (SRF) was compared between the two groups. The changes in the choroidal thickness inside and outside the PDT-applied area in both groups were also evaluated.

**Results** SRF disappeared in all eyes (100%) in the 1/2 PDT group and in two eyes (33%) in the 1/3 PDT group. In the 1/2 PDT group, choroidal thickness inside and outside the PDT-applied area reduced significantly from the baseline (inside, from 387 ± 24 to 325 ± 25 μm; outside, from 292 ± 25 to 249 ± 19 μm; both *P* = 0.005). In the 1/3 PDT group, choroidal thickness decreased in two eyes where SRF disappeared (inside, 87.2 and 90.9% of the baseline; outside, 91.4 and 92.6% of the baseline), but did not change in the other four eyes where SRF remained (inside, 104.1, 100.0, 105.1, and 100.5% of the baseline; outside, 98.9, 103.0, 100.0, and 99.0% of the baseline).

**Conclusions** 1/2 PDT is more effective than 1/3 PDT in the resolution of SRF for chronic CSC. Decrease in the choroidal thickness after PDT may be related to the resolution of SRF in chronic CSC.

*Eye* (2012) 26, 640–649; doi:10.1038/eye.2012.66

**Keywords:** central serous chorioretinopathy; photodynamic therapy; verteporfin; choroidal thickness; subretinal fluid; choroidal vein

## Introduction

Central serous chorioretinopathy (CSC) is characterized by an accumulation of subretinal fluid (SRF) in the posterior pole and is a common condition in middle-aged men with a so-called A-type personality.<sup>1,2</sup> Although acute CSC could be resolved spontaneously, approximately half of the patients have recurrence or persistence of SRF and require treatment.<sup>3</sup> Laser photocoagulation (LP) is generally used to treat CSC. However, CSC with subfoveal or parafoveal leakage points, and chronic CSC with broad and indistinct leakage are difficult to treat with LP because of the complication of scotoma.<sup>4</sup> Choroidal neovascularization (CNV) is also known as a serious complication of LP.<sup>5–8</sup>

Recently, photodynamic therapy (PDT) with verteporfin has been shown to be effective in reducing SRF and improving visual acuity for chronic CSC.<sup>9–12</sup> However, post-PDT complications such as secondary CNV, pigmentary changes of the retinal pigment epithelium (RPE), and persistent choriocapillaris hypoperfusion have been reported.<sup>10,13–15</sup> To minimize these side effects and to obtain the maximum effects, half-dose verteporfin PDT has been conducted successfully in chronic CSC without serious complications.<sup>16–19</sup> However, the optimal dosage of verteporfin required to treat chronic CSC has not been established. The lowest dose of verteporfin required to treat acute CSC successfully was reported to be 30% of the conventional dosage.<sup>20</sup> Thus, the purpose of this study was to prospectively compare the results of half-dose verteporfin (3 mg/m<sup>2</sup>) PDT (1/2 PDT) with those of one-third-dose verteporfin (2 mg/m<sup>2</sup>) PDT (1/3 PDT) for chronic CSC. The primary outcome measure was the disappearance rate of SRF. Secondary outcome

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Received: 2 December 2011  
Accepted in revised form: 12 February 2012

measures were the changes in best-corrected visual acuity (BCVA) and central retinal sensitivity. In addition, we studied the changes in the anatomical structure of the choroid after PDT to find the factors associated with the resolution of SRF.

## Materials and methods

### *Study design and patient recruitment*

This study was a prospective, non-randomized, consecutive, open-label case series conducted in the Department of Ophthalmology, Nagoya University Graduate School of Medicine. Sixteen eyes of 16 patients with chronic CSC were recruited from July 2009 to January 2010. The first ten patients received 1/2 PDT and the next six patients received 1/3 PDT. Because there was no previous report that showed the effects of 1/3 PDT on chronic CSC, we set the number of patients in the 1/3 PDT group ( $n = 6$ ) lesser than that of the 1/2 PDT group ( $n = 10$ ). CSC was diagnosed if SRF caused by idiopathic leakage from the RPE was present at the macula. Leakage from the RPE was detected by fluorescein angiography. Indocyanine green angiography (ICGA) was used to confirm the presence of choroidal vascular hyperpermeability. The inclusion criteria were the following: (1) presence of SRF involving the foveal region persisting for 3 months or more, (2) difficulty to treat with LP because of leakage from the subfovea, parafovea, or broad area, (3) BCVA between 35 and 85 Early Treatment of Diabetic Retinopathy Study (ETDRS) letters, and (4) age between 20 and 70 years. The exclusion criteria were as follows: (1) previous PDT or focal thermal LP to treat CSC, (2) CNV or other maculopathy, (3) choroidopathy that may affect the choroidal thickness, (4) previous intravitreal injections of anti-vascular endothelial growth factor drugs, and (5) intake of medication such as corticosteroids, adrenergic agonists, or adrenergic antagonists.

### *Photodynamic therapy*

When performing 1/2 PDT and 1/3 PDT, only the dosage of verteporfin (Visudyne; Novartis AG, Bülach, Switzerland) was changed from the conventional PDT recommended by the Age-Related Macular Degeneration with Photodynamic Therapy investigation.<sup>21</sup> In 1/2 PDT 3 mg/m<sup>2</sup> of verteporfin was infused, and in 1/3 PDT 2 mg/m<sup>2</sup> of verteporfin was infused. After treatment, patients were instructed to avoid strong light for 5 days.

### *Baseline and follow-up examinations*

Patients were assessed at baseline and followed up at 4 days, 1 month, and 3 months after PDT. BCVA and

macular sensitivity were measured, and optical coherence tomography (OCT) was performed at each visit. The examiners were masked to the type of the treatment that patients received. BCVA was measured using the ETDRS charts at 4 m. Macular sensitivity was evaluated after pupil dilatation using microperimeter-1 (Nidek, Vigonza, Italy). A white Goldmann III spot size was used in a 4-2-1 staircase strategy. Thirty-three stimulus points covering the area of the central 15° diameter around the macula were examined. The average sensitivity of the 33 points was defined as the central retinal sensitivity. At post-PDT visits, the same locations as baseline were examined using the eye-tracking function of microperimeter-1. OCT images were obtained using spectral-domain OCT (Spectralis HRA + OCT, Heidelberg Engineering, Heidelberg, Germany). A series of horizontal scans were taken through the fovea and the area to be treated. The enhanced depth-imaging technique<sup>22-24</sup> was used to obtain the clear images of the choroid. OCT images were used to measure the choroidal thickness, the cross-sectional area of the large choroidal veins, and the vertical and the horizontal diameters of the large choroidal veins. These were measured both inside and outside the PDT-applied area. Fovea was included in the PDT-applied area in all cases. The location examined as inside the PDT-applied area was the subfovea. The location examined as outside the PDT-applied area was one at 1.0 mm temporal distance from the temporal edge of the PDT spot line. Choroidal veins were identified during the venous phase of ICGA. Large veins running perpendicularly to horizontal OCT scans and having a horizontal diameter of >200 μm were defined as the large choroidal vein. The choroidal thickness and the cross-sectional area of the large choroidal veins were evaluated in both treatment groups. The diameters of the large choroidal veins were evaluated in the 1/2 PDT group. The choroidal thickness and the diameters of the large choroidal veins were measured using the built-in caliper function of the Heidelberg Eye Explore software. The cross-sectional area of the large choroidal veins was measured using the NIH Image 1.61 software (developed at the US National Institutes of Health and available on the Internet at <http://rsb.info.nih.gov/nih-image/>). At post-PDT visits, OCT was performed at the same locations as at baseline by using the eye-tracking function of Spectralis OCT.

The protocol for this prospective study was approved by the Institutional Review Board of Nagoya University Graduate School of Medicine before the study initiation, and written informed consent was obtained from all patients. The procedures of this study followed the tenets of the Declaration of Helsinki.

### Statistics

Statistical analyses were performed using PASW statistics version 18.0 (SPSS Inc., IBM Corporation, Chicago, IL, USA). Comparisons were made between the two treatment groups using Fisher's exact test for gender and the disappearance rate of SRF, and using Mann-Whitney *U* test for the other clinical data. *P* values of less than 0.05 were considered to be statistically significant.

Wilcoxon signed-rank test with Bonferonni correction was used to compare the baseline clinical data with those of 4 days, 1 month, and 3 months. *P* values of <0.017 were taken to be statistically significant.

### Results

#### Patients' baseline demographics and clinical data

The baseline demographic and clinical data of the two treatment groups are summarized in Table 1. No significant differences were found in age, gender, baseline BCVA, baseline retinal sensitivity, duration of symptoms, foveal thickness at baseline, choroidal thickness at baseline, size of the choroidal vein at baseline, and PDT spot size between the two treatment groups. The representative cases of the 1/2 and 1/3 PDT groups are shown in Figures 1 and 2, respectively.

#### Disappearance rate of SRF

At 1 month, 7 eyes (70%) in the 1/2 PDT group had complete resolution of SRF compared with 2 eyes (33%) in the 1/3 PDT group. At 3 months, all 10 eyes (100%) in the 1/2 PDT group had complete resolution of SRF, and the same 2 eyes (33%) in the 1/3 PDT group maintained

the complete resolution. The SRF disappearance rate of the 1/2 PDT group was significantly greater than that of the 1/3 PDT group at 3 months (*P* = 0.008).

#### Changes in visual acuity

In the 1/2 PDT group, significant improvement was seen at 3 months compared with the baseline (*P* = 0.007). In the 1/3 PDT group, no significant improvement from the baseline was seen at any visit after PDT. No significant difference in gained ETDRS was found between the two groups at any visit after PDT (Table 2).

#### Changes in central retinal sensitivity

In the 1/2 PDT group, significant improvements were seen at 1 month and 3 months compared with the baseline (both, *P* = 0.005). In the 1/3 PDT group, no significant improvement from the baseline was seen at any visit after PDT. At 1 month and 3 months, gained retinal sensitivities of the 1/2 PDT group were significantly greater than those of the 1/3 PDT group (Table 2).

#### Changes in choroidal thickness inside the PDT-applied area

In the 1/2 PDT group, significant reductions were seen at 1 month and 3 months compared with the baseline (both, *P* = 0.005). In the 1/3 PDT group, there was no significant change from the baseline at any visit after PDT. At 1 month and 3 months, the reduction rates of the 1/2 PDT group were significantly greater than those of the 1/3 PDT group (Table 2). Within the 1/3 PDT group,

**Table 1** Baseline demographics and clinical data of the two treatment groups

	Half-dose PDT group (n = 10)	One-third-dose PDT group (n = 6)	<i>P</i> value
Mean ± SEM age (years)	50.1 ± 3.5	52.5 ± 2.6	NS <sup>a</sup>
Gender (male/female)	8/2	5/1	NS <sup>b</sup>
Mean ± SEM BCVA (ETDRS letters)	76.0 ± 3.1	72.7 ± 4.0	NS <sup>a</sup>
Mean ± SEM retinal sensitivity (dB)	14.8 ± 0.8	15.1 ± 0.8	NS <sup>a</sup>
Mean ± SEM duration of symptoms (months)	30.5 ± 6.2	30.5 ± 7.9	NS <sup>a</sup>
Mean ± SEM foveal thickness (μm)	357 ± 26	325 ± 21	NS <sup>a</sup>
Mean ± SEM choroidal thickness inside the PDT-applied area (μm)	387 ± 24	351 ± 17	NS <sup>a</sup>
Mean ± SEM choroidal thickness outside the PDT-applied area (μm)	292 ± 25	253 ± 32	NS <sup>a</sup>
Mean ± SEM size of the choroidal vein inside the PDT-applied area (× 10 <sup>3</sup> μm <sup>2</sup> )	75.4 ± 13.9	72.3 ± 12.6	NS <sup>a</sup>
Mean ± SEM size of the choroidal vein outside the PDT-applied area (× 10 <sup>3</sup> μm <sup>2</sup> )	65.8 ± 7.3	62.2 ± 6.4	NS <sup>a</sup>
Mean ± SEM PDT spot size (μm)	3000 ± 213	2775 ± 268	NS <sup>a</sup>

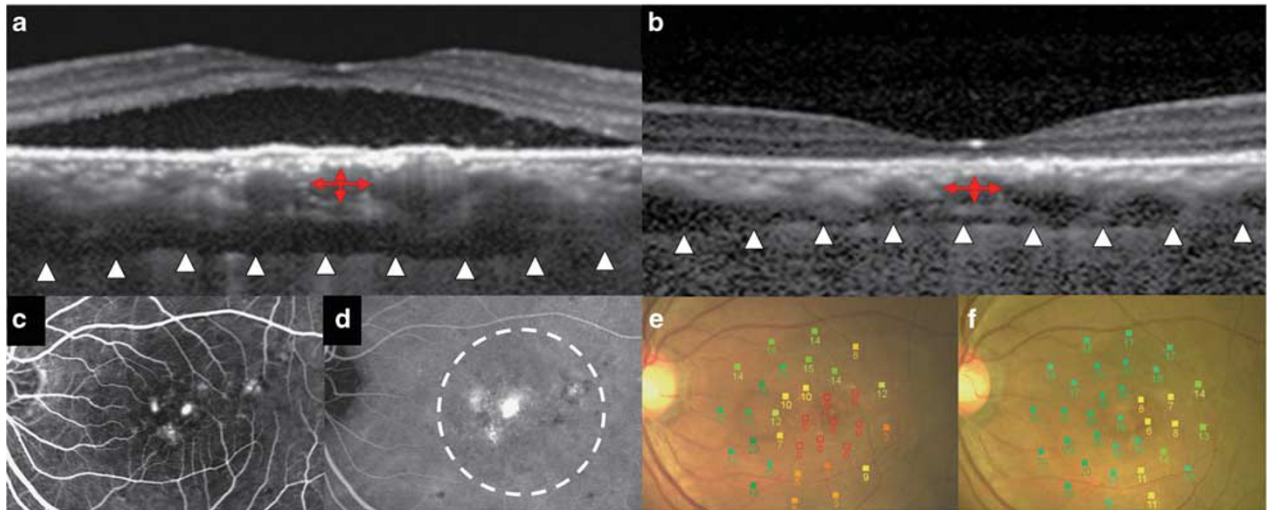
Abbreviations: PDT, photodynamic therapy; BCVA, best-corrected visual acuity; ETDRS, Early Treatment of Diabetic Retinopathy Study; NS, not statistically significant; SEM, standard error of the mean.

*P* values <0.05 were considered to be statistically significant.

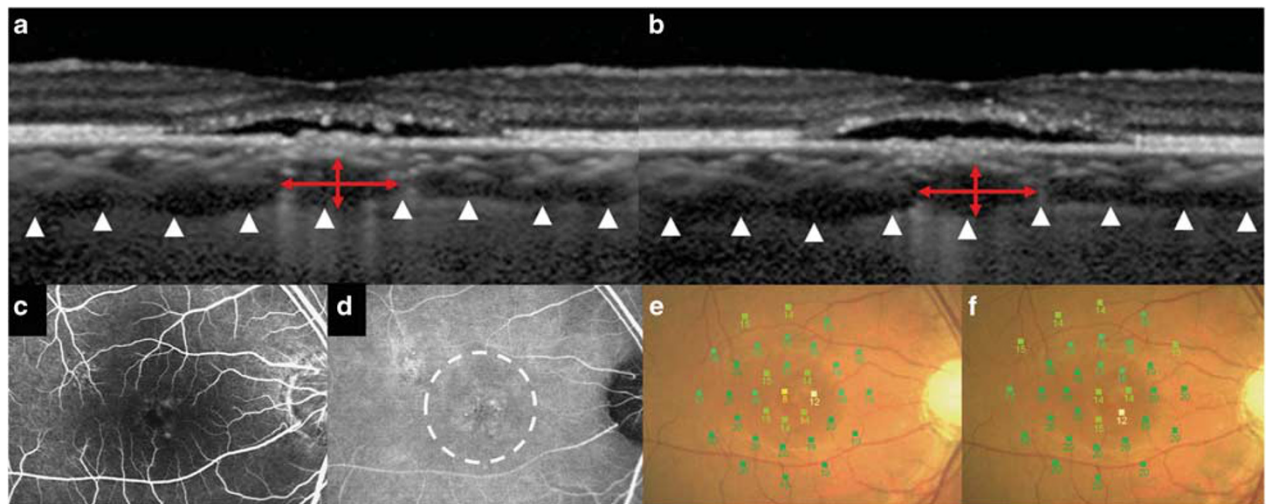
<sup>a</sup>Comparisons between the two groups were made using Mann-Whitney *U* test

<sup>b</sup>Comparisons between the two groups were made using Fisher's exact test.





**Figure 1** Images of a 49-year-old man with chronic central serous chorioretinopathy treated with half-dose verteporfin photodynamic therapy (PDT). Blurred vision of 30 months duration was noted in his left eye. The best-corrected visual acuity measured by Early Treatment of Diabetic Retinopathy Study charts was 52 letters before PDT, which increased to 62 letters at 3 months after PDT. Spectral-domain optical coherence tomography images before (a) and 3 months after PDT (b). Red double arrows indicate the vertical and horizontal diameters of the subfoveal choroidal vein. White arrowheads indicate the inner sclera border. Subretinal fluid was completely resolved, and the subfoveal choroidal thickness reduced from 398 to 352  $\mu\text{m}$  after PDT. Reduction in the vertical diameter and no change in the horizontal diameter were seen after PDT. Early-phase fluorescein angiogram before PDT (c) showed focal leakages from the retinal pigment epithelium at the macula. Middle-phase indocyanine green angiogram before PDT (d) showed hyperfluorescence secondary to vascular hyperpermeability at the macula. The white dashed circle indicates the PDT spot area of 4000  $\mu\text{m}$  diameter. Results of microperimeter-1 before (e) and 3 months after PDT (f). The mean retinal sensitivity of the central 15° around the macula increased from 9.2 to 16.0 dB after PDT.



**Figure 2** Images of a 49-year-old man with chronic central serous chorioretinopathy treated with one-third-dose verteporfin photodynamic therapy (PDT). He complained of image distortion of 12 months duration in his right eye. The best-corrected visual acuity measured by Early Treatment of Diabetic Retinopathy Study charts was 80 letters before PDT and 79 letters at 3 months after PDT. Spectral-domain optical coherence tomography images before (a) and 3 months after PDT (b). Red double arrows indicate the vertical and horizontal diameters of the subfoveal choroidal vein. White arrowheads indicate the inner sclera border. Subretinal fluid persisted, and there was no change in the subfoveal choroidal thickness (303  $\mu\text{m}$ ) after PDT. Neither the vertical nor the horizontal diameter changed significantly after PDT. Early-phase fluorescein angiogram before PDT (c) showed focal leakages from the retinal pigment epithelium at the macula. Middle-phase indocyanine green angiogram before PDT (d) showed hyperfluorescence secondary to vascular hyperpermeability at the macula. The white dashed circle indicates the PDT spot area of 2600  $\mu\text{m}$  diameter. Results of microperimeter-1 before (e) and 3 months after PDT (f). The mean retinal sensitivities of the central 15° around the macula were 17.0 dB before PDT and 17.7 dB after PDT.

**Table 2** Changes in the clinical data after PDT in the two treatment groups

	Day 4			Month 1			Month 3		
	Half-dose PDT group	P value	One-third-dose PDT group	Half-dose PDT group	P value	One-third-dose PDT group	Half-dose PDT group	P value	One-third-dose PDT group
Mean ± SEM gained BCVA (ETDRS letters)	0.4 ± 0.7 (76.4 ± 2.9)	NS	0.0 ± 0.9 (72.7 ± 4.0)	2.7 ± 1.6 (78.7 ± 2.5)	NS	1.7 ± 1.7 (74.3 ± 4.0)	5.4 ± 1.0 (81.4 ± 3.0)	NS	1.7 ± 2.2 (74.3 ± 4.4)
Mean ± SEM gained retinal sensitivity (dB)	0.3 ± 0.4 (15.1 ± 0.7)	NS	0.9 ± 0.3 (15.9 ± 0.8)	2.4 ± 0.3 (17.2 ± 0.5)	0.011	0.8 ± 0.5 (15.8 ± 1.2)	3.4 ± 0.6 (18.1 ± 0.3)	0.030	0.9 ± 0.8 (15.9 ± 1.4)
Mean ± SEM relative choroidal thickness (%)	96.8 ± 1.9 (374 ± 23)	NS	98.1 ± 2.8 (345 ± 20)	83.3 ± 2.9 (324 ± 25)	0.023	97.3 ± 3.7 (343 ± 25)	83.5 ± 2.8 (325 ± 25)	0.013	98.0 ± 3.0 (345 ± 22)
the PDT-applied area									
Mean ± SEM relative choroidal thickness (%)	97.9 ± 1.3 (284 ± 22)	NS	99.5 ± 0.6 (252 ± 31)	87.2 ± 2.4 (253 ± 20)	0.013	98.9 ± 3.1 (252 ± 34)	86.1 ± 1.4 (249 ± 19)	0.001	97.5 ± 1.9 (248 ± 33)
the PDT-applied area									
Mean ± SEM relative size of the choroidal vein (%)	84.8 ± 3.0 (64.3 ± 11.9)	0.039	95.8 ± 2.8 (69.2 ± 12.3)	70.5 ± 3.5 (52.1 ± 8.6)	0.003	93.3 ± 3.8 (67.7 ± 12.4)	69.0 ± 4.6 (50.4 ± 9.0)	0.001	97.0 ± 2.3 (69.7 ± 12.2)
(× 10 <sup>3</sup> μm <sup>2</sup> ) inside PDT Applied Area									
Mean ± SEM relative size of the choroidal vein (%)	91.2 ± 1.8 (60.0 ± 6.6)	0.030	98.2 ± 1.5 (61.3 ± 6.8)	80.6 ± 2.4 (53.3 ± 6.8)	0.002	97.6 ± 2.9 (61.0 ± 7.1)	80.0 ± 2.2 (52.7 ± 6.5)	0.001	98.9 ± 2.2 (61.5 ± 6.4)
(× 10 <sup>3</sup> μm <sup>2</sup> ) outside the PDT-applied area									

Abbreviations: BCVA, best-corrected visual acuity; ETDRS, Early Treatment of Diabetic Retinopathy Study; SEM, standard error of the mean; PDT, photodynamic therapy; NS, not statistically significant. Relative choroidal thickness and relative size of the choroidal vein show the percentage change of choroidal thickness and size of the choroidal vein after PDT compared with baseline. Comparisons between the two treatment groups were made using Mann–Whitney U test. P values <0.05 were considered to be statistically significant.

choroidal thickness inside the PDT-applied area decreased in two eyes where SRF disappeared (87.2 and 90.9% of the baseline at 3 months), but did not decrease in the other four eyes where SRF remained (104.1, 100.0, 105.1, and 100.5% of the baseline at 3 months).

**Changes in choroidal thickness outside the PDT-applied area**

In the 1/2 PDT group, significant reductions were seen at 1 month and 3 months compared with the baseline (both,  $P=0.005$ ). In the 1/3 PDT group, there was no significant change from the baseline at any visit after PDT. At 1 month and 3 months, the reduction rates in the 1/2 PDT group were significantly greater than those of the 1/3 PDT group (Table 2). Within the 1/3 PDT group, choroidal thickness outside the PDT-applied area decreased in two eyes where SRF disappeared (91.4 and 92.6% of the baseline at 3 months), but did not decrease in the other four eyes where SRF remained (98.9, 103.0, 100.0, and 99.0% of the baseline at 3 months).

**Changes in cross-sectional area of the large choroidal vein**

Both inside and outside the PDT-applied area, the reduction rates of the 1/2 PDT group were significantly greater than those of the 1/3 PDT group at all visits after PDT (Table 2).

**Changes in the diameters of the large choroidal vein in the 1/2 PDT group**

Both inside and outside the PDT-applied area, the reduction rates of the vertical diameter were significantly greater than those of the horizontal diameter at all visits after PDT (Table 3).

**Safety**

None of the patients developed any systemic adverse event associated with verteporfin infusion. No ocular side effects, including development of CNV, were seen in any cases throughout the follow-up period.

**Discussion**

As CSC is a benign disorder and patients usually have a good baseline visual function, it is important to seek the best PDT protocol in order to obtain the maximum effect and the minimum complications. Half-dose PDT has been conducted to chronic CSC with relative safety,<sup>16-19</sup> but treatment with verteporfin at less than 50% of the conventional dosage has not been attempted for chronic

**Table 3** Changes in the diameters of the choroidal vein after PDT in the half-dose PDT group

	Day 4			Month 1			Month 3		
	Vertical diameter	P value	Horizontal diameter	Vertical diameter	P value	Horizontal diameter	Vertical diameter	P value	Horizontal diameter
Mean ± SEM relative diameter of the choroidal vein (%)	84.6 ± 3.0	0.003	100.1 ± 1.1	73.4 ± 3.4	<0.001	95.8 ± 2.8	70.8 ± 4.2	<0.001	96.2 ± 1.8
(Mean ± SEM diameter of the choroidal vein) (µm) inside the PDT-applied area	(198 ± 21)		(396 ± 52)	(169 ± 16)		(383 ± 55)	(163 ± 16)		(382 ± 53)
Mean ± SEM relative diameter of the choroidal vein (%)	91.2 ± 1.8	<0.001	100.2 ± 0.3	80.9 ± 2.3	<0.001	99.8 ± 0.3	80.8 ± 1.9	<0.001	97.1 ± 1.8
(Mean ± SEM diameter of the choroidal vein) (µm) outside the PDT-applied area	(186 ± 12)		(401 ± 27)	(165 ± 12)		(400 ± 28)	(164 ± 10)		(389 ± 29)

Abbreviations: SEM, standard error of the mean; PDT, photodynamic therapy. Relative diameter of the choroidal vein shows the percentage change in diameter of the choroidal vein after PDT compared with baseline. Comparisons between the vertical diameter and the horizontal diameter were made using Mann-Whitney U test. P values <0.05 were considered to be statistically significant.

CSC. Previous studies have shown that cytotoxicity and vascular damage associated with PDT are dose dependent.<sup>25,26</sup> In this prospective clinical trial, we compared the efficacy and safety of 1/2 PDT with those of 1/3 PDT for chronic CSC.

Zhao *et al*<sup>20</sup> conducted PDT with verteporfin at 30% of the conventional dosage in 8 eyes with acute CSC, and all eyes (100%) had resolution of SRF. In this study, one-third dose was effective in only 2 out of 6 eyes (33%) with chronic CSC. In eyes with CSC, SRF accumulates when the exudation of serous fluid from choroidal vessels exceeds the barrier and the pump functions of RPE.<sup>27</sup> Because retinal atrophy occurs in chronic stage of CSC,<sup>28</sup> the barrier and the pump functions of RPE may be weaker and SRF may accumulate with less exudation in chronic CSC compared with acute CSC. Stronger suppression of the exudation from the choroid may be necessary for the resolution of SRF in chronic CSC than in acute CSC.

The mechanism of the action of PDT in CSC has not been fully understood, but the changes in choroidal structures after PDT in this study provide a useful clue. Choroidal thickness and the cross-sectional area of the large choroidal vein significantly decreased after PDT in the 1/2 PDT group, but did not change in the 1/3 PDT group. The SRF disappearance rate was greater in the 1/2 PDT group than in the 1/3 PDT group. Within the 1/3 PDT group, choroidal thickness decreased in two eyes where SRF disappeared, but did not change in the other four eyes where SRF remained. Considering these facts, the thinning of the choroid and the reduction of the size of the choroidal vein may be related to the resolution of SRF. To the best of our knowledge, this is the first study reporting the unchanged choroidal thickness after ineffective PDT.

In chronic CSC, the speed of the SRF resolution after PDT is relatively fast. SRF disappeared in 1 month in all successful cases in this study. There are two reports<sup>19,24</sup> that compared the efficacy of half-dose PDT with LP in treating chronic CSC. Both studies reported that SRF disappeared in all eyes in both the PDT group and the LP group. But faster SRF resolution was observed in the PDT group compared with the LP group. In the study of Lim *et al*,<sup>19</sup> 1 out of 14 eyes (7%) in the PDT group and 5 out of 12 eyes (42%) in the LP group had residual SRF at 1 month after PDT. In the study of Maruko *et al*,<sup>24</sup> 2 out of 8 eyes (25%) in the PDT group and 9 out of 12 eyes (75%) in the LP group had residual SRF at 1 month after PDT. Maruko *et al*<sup>24</sup> also reported that choroidal thickness decreased after half-dose PDT, but did not change after LP. Faster resolution of SRF after half-dose PDT may be related to the thinning of the choroid.

Pryds and Larsen<sup>29</sup> reported that the reduction of choroidal thickness occurred not only inside the PDT-applied area but also outside the PDT-applied area after a half-light dose PDT for chronic CSC. In this study,

choroidal thickness and the cross-sectional area of the large choroidal vein significantly decreased both inside and outside the PDT-applied area after 1/2 PDT. These findings suggest that the PDT affects the choroid not only inside but also outside the PDT-applied area. We speculated that PDT first decreases the size of the large choroidal veins and choroidal blood flow in the PDT-applied area. As the choroidal vascular system is an anastomosing network, the influence of the reduction of choroidal blood flow spreads through the posterior pole and the decrease in the size of the large choroidal veins occurs outside the PDT-applied area secondarily.

In this study, the reduction rate of the vertical diameter of the large choroidal veins was greater than that of the horizontal diameter in the 1/2 PDT group. Our previous study has demonstrated that a significant correlation exists between choroidal thickness and the ratio of vertical/horizontal diameter of the large choroidal veins in normal eyes.<sup>30</sup> The higher mobility of the vertical diameter compared with that of the horizontal diameter may be the characteristic of the large choroidal veins. Observing the change in the shapes of the choroidal veins may provide a clue on the integrity of the choroidal circulation.

This study has several limitations, including small sample size and short-term follow-up period. Patients were consecutive and were not matched for the degree of hyperpermeability on ICGA. A randomized clinical trial with larger sample size and longer follow-up period is necessary to draw definitive conclusions.

To determine the optimal dose of verteporfin for chronic CSC, another dosage, such as between 2 and 3 mg/m<sup>2</sup>, needs to be evaluated. In addition, there are many parameters of PDT besides dosage, such as light energy, time interval between injection and irradiation, duration of photosensitization, and PDT spot size. We need to conduct a head-to-head comparison of each parameter of PDT to decide the optimal protocol of PDT for chronic CSC.

## Summary

### What was known before

- The lowest dose of verteporfin required to treat acute CSC successfully was reported to be 30% of the conventional dosage. However, the optimal dosage of verteporfin required to treat chronic CSC has not been established.

### What this study adds

- 1/2 PDT was more effective than 1/3 PDT in the resolution of SRF for chronic CSC. This study also showed that decrease in the choroidal thickness after photodynamic therapy may be related to the resolution of SRF in chronic CSC.

## Conflict of interest

The authors declare no conflict of interest.



## Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan (Dr Ito, C2159225).

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# Half-dose vs one-third-dose photodynamic therapy for chronic central serous chorioretinopathy

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- You are called to evaluate a patient with central serous chorioretinopathy (CSC). What should you consider regarding this diagnosis as you begin the encounter?
  - It occurs most commonly among women
  - It nearly never occurs among adults less than 60 years old
  - Approximately half of the patients require treatment
  - Chronic CSC with broad leakage responds best to laser photocoagulation (LP)
- After a thorough evaluation, you decide to treat this patient with photodynamic therapy (PDT). Based on the results of the current study, what should you expect regarding the disappearance of subretinal fluid after treatment with 1/2 PDT vs 1/3 PDT?
  - There will be less than 50% resolution of subretinal fluid (SRF) in 3 months, regardless of dose
  - 1/2 PDT results in better resolution of SRF at 1 month, but not at 3 months
  - 1/2 PDT results in better resolution of SRF at 1 and 3 months
  - There is no difference between 1/2 PDT and 1/3 PDT in the resolution of SRF
- What should you consider regarding other outcomes associated with 1/2 PDT vs 1/3 PDT in the current study?
  - There was no difference in visual acuity between treatments
  - Choroidal neovascularization (CNV) was more common with 1/2 PDT than with 1/3 PDT
  - Gained retinal sensitivities were higher for 1/2 PDT than for 1/3 PDT
  - Neither treatment had an effect on the cross-sectional area of the large choroidal vein

- What was the relationship between study treatment and choroidal thickness in the current study?
  - Reductions in choroidal thickness were associated with resolution of SRF in both treatment groups
  - Only 1/2 PDT significantly influenced choroidal thickness
  - There was no difference between 1/2 PDT and 1/3 PDT in their effects on choroidal thickness
  - Neither treatment affected choroidal thickness outside of the treatment area of PDT

### Activity evaluation

- The activity supported the learning objectives.
 

Strongly disagree				Strongly agree
1	2	3	4	5
- The material was organized clearly for learning to occur.
 

Strongly disagree				Strongly agree
1	2	3	4	5
- The content learned from this activity will impact my practice.
 

Strongly disagree				Strongly agree
1	2	3	4	5
- The activity was presented objectively and free of commercial bias.
 

Strongly disagree				Strongly agree
1	2	3	4	5