

# Comparison of foveal-sparing with foveal-involving photodynamic therapy for myopic choroidal neovascularization

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CLINICAL STUDY

## Abstract

**Purpose** To evaluate the visual outcomes of choroidal neovascularization (CNV) secondary to pathological myopia in eyes treated with photodynamic therapy (PDT), and to determine the effect of lesion location and foveal involvement on visual prognosis.

**Methods** Interventional case series of 24 consecutive patients with myopic CNV treated with PDT. The main outcome measure was final LogMAR visual acuity (VA).

**Results** Of 24 eyes, the CNV lesion was subfoveal in 11 and extrafoveal in 13. Overall, the mean LogMAR VA at 24 months was 0.72. Extrafoveal CNV lesions achieved significantly better final VA compared with subfoveal CNV (LogMAR 0.45 vs 1.05,  $P=0.012$ ). Eyes with extrafoveal CNV lesions were subdivided into foveal-sparing PDT (where the PDT laser spot did not involve the foveal center) and foveal-involved PDT (where the PDT laser covered the fovea). At all time points, the group with foveal-sparing PDT had significantly better VA compared with the foveal-involved group. The final LogMAR VA for the foveal-sparing PDT group was 0.26 compared with 1.00 for the foveal-involved PDT group ( $P=0.003$ ). At 24 months, 77.8% of foveal-sparing PDT cases achieved VA of  $\geq 20/40$ , compared with 25% of foveal-involved PDT cases and 9.1% of subfoveal CNV lesions ( $P=0.006$ ).

**Conclusion** For patients with myopic CNV, foveal-sparing PDT results in significantly better long-term visual outcomes compared with those with foveal-involved PDT. Foveal-sparing PDT may be of value for treatment of myopic CNV patients who are not suitable

for treatment with anti-vascular endothelial growth factor injections.

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**Keywords:** myopic choroidal neovascularization; pathologic myopia; photodynamic therapy; visual acuity; foveal sparing

## Introduction

The prevalence of myopia is increasing among the younger age groups and also varies by population, with higher rates of myopia reported among populations of Asian descent. Pathologic myopia is a major cause of irreversible vision loss<sup>1,2</sup> and choroidal neovascularization (CNV) secondary to pathological myopia is the leading cause of CNV in people aged younger than 50.<sup>3</sup>

Among patients with myopic CNV, between 50 and 60% of eyes experience deterioration of vision within 2 years.<sup>4</sup> The long-term visual outcome for myopic CNV is poor, and many patients have visual acuity (VA) of 20/200 or worse within 5–10 years.<sup>3</sup>

The Verteporfin in Photodynamic Therapy (VIP) study<sup>5</sup> evaluated the efficacy of photodynamic therapy (PDT) in patients with subfoveal CNV secondary to pathologic myopia, and reported that VA stabilized in 72% of patients at 1 year. More recently, studies on treatment of myopic CNV with intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) agents have reported good clinical outcomes.<sup>6–12</sup> However, anti-VEGF

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agents are associated with systemic risks such as cerebrovascular accidents and other arterial thromboembolic events, especially for patients with pre-existing disease.<sup>13–16</sup> In addition, intravitreal injections carry the risk of infectious endophthalmitis.<sup>17</sup> Therefore, PDT may still have a role in the management of patients with myopic CNV where anti-VEGF agents are contraindicated due to the systemic risks or where patients are unwilling to accept the systemic or ocular risks associated with this treatment.

We aimed to evaluate the visual outcome of patients with myopic CNV and to determine the role of lesion location and foveal involvement by the PDT laser spot in determining the visual prognosis.

### Materials and methods

This was an interventional case series of 24 consecutive patients with pathologic myopia treated for myopic CNV at the Ophthalmology Clinic at Tan Tock Seng Hospital, National Healthcare Group Eye Institute, Singapore. This study was approved by the Institutional Review Board of the National Healthcare Group, Singapore, and complied with the Tenets set forth in the Declaration of Helsinki.

The inclusion criteria were spherical equivalent of  $-6$  D or worse or features of pathological myopia on retinal examination. Patients with co-existing ocular pathology, especially CNV secondary to age-related macular degeneration, were excluded.

Confocal scanning laser ophthalmoscopy fluorescein angiography (FA) and indocyanine green angiography (ICGA) were performed for all patients using the Heidelberg HRA2 (Heidelberg Engineering, Heidelberg, Germany) using a standardized imaging protocol.

The angiograms were independently reviewed by two ophthalmologists to confirm the diagnosis of myopic CNV and its location. ICGA was used to exclude polypoidal choroidal vasculopathy, which is more common among Asian populations, and retinal angiomatous proliferation. The CNV lesions were classified according to their location on FA (subfoveal, juxta-foveal, or extra foveal).<sup>5</sup> The non-subfoveal CNV lesions were further analyzed according to whether or not the laser spot used during PDT treatment covered the foveal center. If the PDT laser spot did not cover the foveal center, this was termed foveal-sparing PDT (Group 1) (Figures 1a and b), whereas if the laser spot covered the foveal center, this was classified as foveal-involved PDT (Group 2). Patients with subfoveal CNV lesions (Figures 1c and d), where the PDT laser spot would definitely cover the foveal center, were classified as Group 3.

During the period these patients initially presented, PDT was the standard of care for patients with myopic

CNV and anti-VEGF injections were not commonly in use in our institution. Patients were treated by a single ophthalmologist (THL) and received full-fluence PDT with Verteporfin following the guidelines of the VIP study and Treatment of Age-Related Macular Degeneration with Photodynamic Therapy study.<sup>5,18</sup> All patients were followed up for 2 years and the main outcome measure was LogMAR VA.

Statistical analysis was performed using SPSS for Windows version 16 (SPSS Inc., Chicago, IL, USA), with  $P$  values  $<0.05$  taken as significant.

### Results

There were 11 males (45.8%) and 13 females (54.2%), with a mean age of 58.7 years (SD  $\pm 13.7$ ) and mean spherical equivalent of  $-11.3$  D (SD  $\pm 4.8$  D). In 11 patients (45.8%), the right eye was affected.

In 11 patients (45.8%), the CNV lesion was subfoveal. Of the remaining 13 (54.2%) with extrafoveal CNV lesions, 4 had foveal involvement by PDT laser whereas the remaining 9 were foveal-sparing cases. The mean number of PDT treatments for all patients was 1.7 (range, 1–4 treatments) and there was no significant difference in mean number of PDT among the three groups of patients.

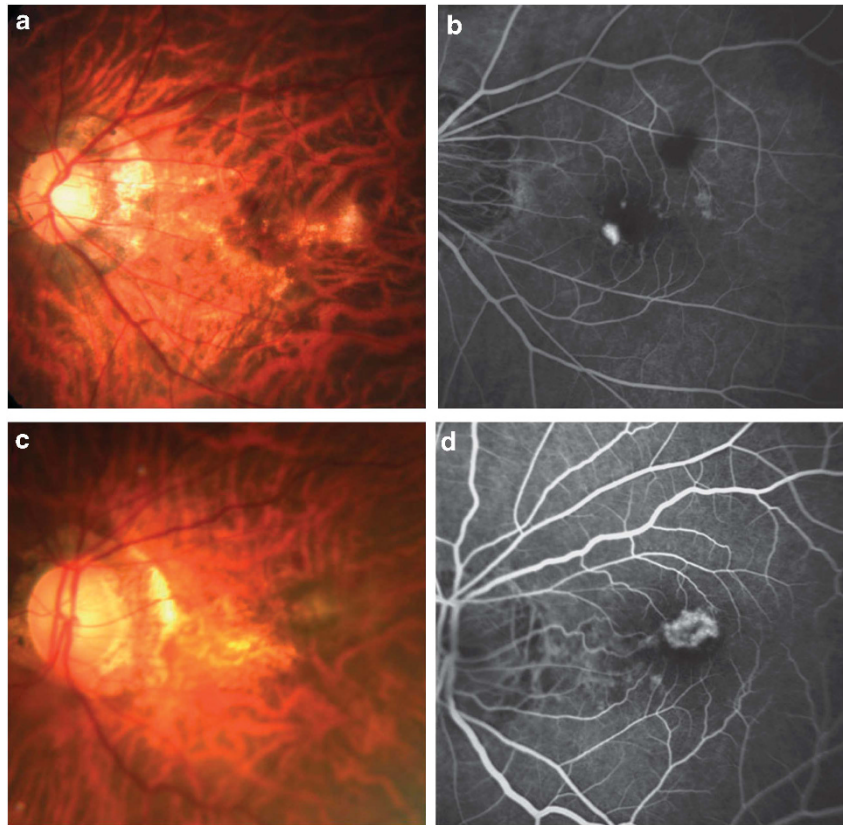
The mean best-corrected logMAR VA (BCVA) was 0.67 ( $\pm 0.51$ ) on presentation and 0.72 ( $\pm 0.62$ ) at the final review. At all follow-up visits up to 24 months, mean VA was better for extrafoveal lesions compared with subfoveal CNV lesions (all  $P < 0.05$  except for 3 and 18 months) (Table 1). At the final visit, the mean LogMAR VA was 0.45 for extrafoveal lesions compared with 1.05 for subfoveal CNV lesions ( $P = 0.012$ ).

Visual outcomes were not associated with gender, initial BCVA, number of PDT treatments, or severity of myopia.

Of the 24 patients, 20 had subsequent FA performed at a mean of 12.9 months (range, 4–24 months). Among eyes with extrafoveal CNV lesions on presentation, 4 of 13 (30.8%) developed expansion of the CNV lesion to involve the fovea, whereas the remainder were either quiescent or had lesions that remained non-subfoveal. Of the four eyes with subsequent subfoveal extension, all experienced worsening of VA after involvement of the fovea by the CNV lesion.

### Analysis of visual outcomes based on foveal involvement by PDT laser spot

Upon further analysis of patients according to foveal involvement by the PDT laser spot (Figure 2), we found that among patients with foveal-sparing PDT (Group 1), the mean LogMAR VA varied from 0.22 to 0.30 at the



**Figure 1** (a) Color fundus photograph of extrafoveal myopic CNV. (b) Fluorescein angiogram demonstrating the CNV lesion in an extrafoveal location. (c) Color fundus photograph of subfoveal myopic CNV. (d) Fluorescein angiogram demonstrating the subfoveal CNV lesion.

**Table 1** Comparison of visual outcome for myopic choroidal neovascularization based on lesion location

Follow-up interval	Lesion location <sup>a</sup>		P-value
	Subfoveal	Extrafoveal	
Baseline	0.95	0.42	0.008
1 month	0.86	0.32	0.005
3 months	0.85	0.46	0.080
6 months	0.84	0.33	0.002
9 months	1.07	0.47	0.011
12 months	0.97	0.49	0.030
18 months	1.02	0.54	0.063
24 months (final visit)	1.05	0.45	0.012

<sup>a</sup> Lesion location is based on fluorescein angiography.

various follow-up time points and did not worsen over time. In contrast, the mean LogMAR VA of patients with foveal-involved PDT (Groups 2 and 3 combined) ranged from 0.73 to 1.05, and gradually worsened over the follow-up period. The differences between the two groups was statistically significant at all time points (all  $P < 0.05$ ).

At the final visit (24 months), mean LogMAR VA was 0.26 for the foveal-sparing PDT group compared with 1.00 for the foveal-involved group ( $P = 0.003$ ), and seven of nine patients in Group 1 had VA 20/40 or better, compared with one patient each in Groups 2 and 3 (77.8% vs 25.0% vs 9.1% for groups 1, 2, and 3, respectively,  $P = 0.006$ ).

### Discussion

In this study, we have demonstrated that among patients with myopic CNV, those treated with foveal-sparing PDT had significantly better VA compared with those treated with foveal-involving PDT.

The mean LogMAR VA for myopic CNV lesions treated with PDT ranges from 0.25 to 0.72 in the literature (Table 2),<sup>19–30</sup> which is comparable to the overall results in this series (mean LogMAR VA 0.72 at 2 years). In studies that have analyzed visual outcomes based on the location of the CNV lesion, final VA for subfoveal myopic CNV ranged from 0.43 to 0.92,<sup>20,22,24,29</sup> whereas the final VA for extrafoveal myopic CNV was slightly

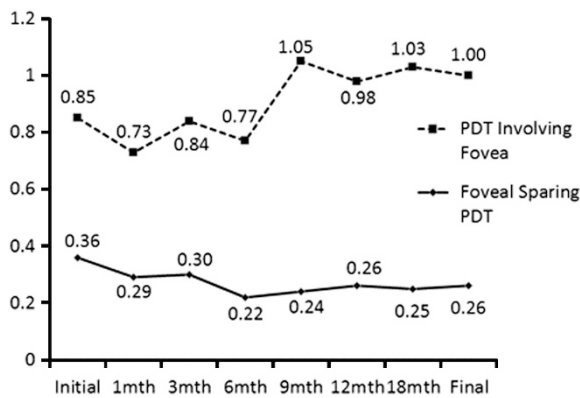
better, ranging from 0.25 to 0.72.<sup>19,20,23</sup> Similar to these earlier studies, our results showed a significant difference in visual outcomes based on the location of the CNV lesion, with extrafoveal CNV having better outcomes compared with subfoveal CNV (LogMAR VA 0.45 vs 1.05 at 24 months).

With the advent of anti-VEGF drugs, ophthalmologists now have a newer modality to treat patients with myopic CNV.<sup>6,8-12</sup> The mean final VA in patients treated with anti-VEGF drugs reported in the literature ranges from 0.23 to 0.55 (Table 2).<sup>6-12,31-36</sup> More importantly, in studies which have compared anti-VEGF with PDT treatment for myopic CNV, patients treated with anti-VEGF generally achieved better visual outcomes compared with the group treated with PDT.<sup>7,24,25</sup> It is important to note, however, that in these studies, patients

were not randomized to the two treatment groups. To the best of our knowledge, there are currently no results from randomized controlled trials comparing the two treatment modalities.

It has been suggested that PDT may damage the underlying choroid and photoreceptors, causing chorioretinal atrophy,<sup>19,20</sup> which accounts for the long-term visual loss. Hence some authors have suggested that anti-VEGF therapy is advantageous compared with PDT. However, anti-VEGF injections are associated with both ocular and systemic risks to patients.<sup>13-17</sup> Some patients with previous history of thromboembolic events may not be willing to accept the higher risk of cerebrovascular accidents or other arterial thromboembolic events. In addition, the risk of endophthalmitis associated with intravitreal injections,<sup>17</sup> although rare, is an ever-present consideration each time the injections are performed. Some patients are not keen to take this risk, especially if the fellow eye has already lost functional vision. For this group of patients who are unwilling to accept the risks of anti-VEGF therapy, PDT may offer an alternative treatment modality. We believe that PDT may still have a useful role in the management of myopic CNV, if patients are carefully selected.

Our results have shown that among patients with extrafoveal CNV in which the PDT laser spot does not involve the center of the fovea, the visual outcomes are good, with a mean LogMAR VA better than 0.26. Also, 78% of patients with foveal-sparing PDT had VA 20/40 or better at 2 years. These visual outcomes are comparable to, or in some cases better than, those reported from studies using anti-VEGF drugs. We believe



**Figure 2** LogMAR Visual acuity of foveal-sparing and foveal-involved groups over the course of 2 years.

**Table 2** Visual outcome of myopic CNV treated by photodynamic therapy and anti-vascular endothelial growth factor

Study	Follow-up duration	VA outcomes for subfoveal CNV lesions		VA outcomes for non-subfoveal CNV lesions		VA outcomes (all cases)	
		Initial	Final	Initial	Final	Initial	Final
<i>Treatment with photodynamic therapy</i>							
Coutinho et al <sup>21</sup>	5 years	—	—	—	—	0.78	0.70
Hayashi et al <sup>20</sup>	3 years	0.76	0.82	0.39	0.25	0.63	0.74
Hayashi et al <sup>19</sup>	2 years	0.56	0.70	0.43	0.30	0.59	0.56
Pece et al <sup>26</sup>	3 years	—	—	0.44	0.34	—	—
Parodi et al <sup>27</sup>	2 years	—	—	0.52	0.72	—	—
Lam et al <sup>23</sup>	1 year	—	—	0.57	0.39	—	—
Ruiz Moreno et al <sup>28</sup>	4 years	9.0 lines	9.6 lines	—	—	—	—
Giansanti et al <sup>29</sup>	3 years	0.50	0.61	—	—	—	—
Lam et al <sup>22</sup>	2 years	0.61	0.56	—	—	—	—
Axel-Siegel et al <sup>30</sup>	1 year	0.68	0.74	—	—	—	—
<i>Treatment with anti-vascular endothelial growth factors</i>							
Oishi et al <sup>32</sup>	2 years	—	—	—	—	0.76	0.54
Voykkov et al <sup>33</sup>	2 years	—	—	—	—	0.64	0.55
Ruiz-Moreno et al <sup>34</sup>	1 year	—	—	—	—	0.72	0.53
Vadala et al <sup>35</sup>	1 year	—	—	—	—	0.68	0.27
Yoon et al <sup>36</sup>	1 year	—	—	—	—	0.51	0.23

that PDT may be useful in treating extrafoveal CNV lesions, especially if the laser spot can be adjusted to avoid the foveal center.

Patients with foveal-involving PDT included those with subfoveal and extrafoveal CNV lesions. As this is a heterogeneous group, it remains unknown whether the poorer visual outcome in this group is due to the CNV location or involvement of the foveal center by the PDT laser spot. It is likely that both factors contributed to the final VA, and further studies are required to evaluate this in greater detail.

The strengths of this study include a long duration of follow up and treatment of all patients by a single experienced ophthalmologist, thus ensuring that PDT technique does not confound the results. The limitations of this study include the lack of a control group for comparison of visual outcomes. Currently, we are not aware of any published results of randomized controlled trials comparing PDT with anti-VEGF drugs.

The results of earlier randomized studies on myopic CNV have focused on subfoveal lesions, whereas it has been shown that extrafoveal CNV lesions occur in between 18.5 and 32% of myopic CNV patients.<sup>3,4</sup> We believe that our results may provide the impetus to perform randomized controlled trials not only for subfoveal CNV lesions, but also to examine the role of foveal-sparing PDT in the management of extrafoveal myopic CNV.

In summary, this study demonstrates that in patients where foveal-sparing PDT can be performed, patients can have good visual outcomes and PDT may be an alternative treatment for patients who are unwilling to accept the risk of anti-VEGF therapy.

#### Contributorship statement

Each author (CS Tan, MC Chew, and TH Lim) certifies that they have met all of the following criteria: (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published.

#### Summary

##### What was known before

- Patients with myopic CNV treated with anti-VEGF agents generally achieve better visual outcomes compared with photodynamic therapy (PDT).

##### What this study adds

- In patients where foveal-sparing PDT can be performed, good visual outcomes can be achieved. The VA at 2 years is comparable to those reported from eyes treated using anti-VEGF agents.

#### Conflict of interest

Dr Tan receives travel support from Novartis and Bayer. Professor Lim receives travel support from Novartis, Bayer, and Heidelberg Engineering.

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