Radiotherapy for subfoveal neovascularisation associated with pathological myopia: a pilot study

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Abstract

Background/aim—Limited treatments are available for this disease process. A pilot study was performed to determine the toxicity and efficacy of external beam radiotherapy for subfoveal neovascular membranes and subretinal haemorrhage associated with pathological myopia.

Methods—A randomised, prospective study was carried out on 39 patients with subfoveal neovascularisation associated with high myopia. 20 patients underwent radiotherapy and the remaining 19 were observed as a randomised comparison group. All patients were followed up for at least 24 months. Subfoveal choroidal neovascular membranes (CNVMs) were treated with a single lateral 6 MV photon beam to a dose of 10 Gy in five fractions over 5–7 days. Post-treatment measurements included corrected visual acuity, area of CNVM, and occurrence of radiotherapy related complications, and adverse reactions. To assess changes of area of CNVM, the initial (pretreatment) size of the CNVM was set to 100%, and all post-treatment measurements were normalised relative to the initial size.

Results—No significant acute morbidity was noted. There was no significant difference in age, sex, refractive error, visual acuity, and area of CNVM at baseline between the treatment group and control group. The mean change of the size of the CNVM for 2 years was 155% (SD 156%) in the treatment group and 249% (124%) in the control group. The increase in the size of CNVM in the treatment group was significantly smaller than that in the control group ($p = 0.0452$). In the treated eyes, the visual acuity before and 1 and 2 years after radiotherapy were 0.111 (22.2/200), 0.091 (18.2/200), and 0.086 (19.2/200), respectively. In the control eyes, visual acuity before and 1 and 2 years after the start of the follow up were 0.141 (34.2/200), 0.089 (17.8/200), and 0.063 (12.6/200). The patients in the treatment group showed no significant change for 2 years, and those in the control group showed a significant decrease in the visual acuity ($p = 0.0033$). The changes of logMAR of visual acuity for 2 years after the start of the follow up were +0.019 (0.443) in the treatment group and +0.347 (0.374) in the control group. There was a statistically significant difference between them ($p = 0.0173$). Multiple regression analysis on the treatment group showed that the most

significant predictive variable for the visual acuity 2 years after the treatment was the combination of pretreatment visual acuity and refractive error.

Conclusions—Radiotherapy appeared to have a favourable treatment effect in eyes with subfoveal neovascular membranes and haemorrhage associated with pathological myopia. Further investigation is needed to evaluate the efficacy of radiotherapy for subfoveal neovascularisation associated with pathological myopia.

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Patients with pathological myopia frequently develop slowly progressive loss of central acuity associated with myopic degenerative changes in the fifth or sixth decade.¹ Fucks described a raised, circular, pigmented lesion that develops in the macula of middle aged patients (Foerster–Fucks spot).^{2,3} This lesion consists of a localised ingrowth of fibrovascular tissue from the choroid and proliferation of pigment epithelial cells. In addition, bleeding from the subretinal neovascular membranes causes blurring or loss of central vision. No efficacious treatment for the subfoveal neovascularisation and its associated subretinal haemorrhage has been available.^{4–7}

Several investigators demonstrated the efficacy and safety of low dose irradiation (10–20 Gy) for subfoveal choroidal neovascular membranes of age related macular degeneration.^{8–20} This study, for the first time, assesses low dose radiotherapy for subfoveal neovascular membrane and subretinal haemorrhage associated with pathologic myopia.

Subjects and methods

PATIENTS

Patients with high myopia were eligible for study when they had subfoveal neovascularisation. Indications for radiotherapy were (1) subfoveal choroidal neovascular membranes (CNVMs), (2) newly formed or exacerbated CNVMs, (3) visual acuity of 0.4 (80/200) or less, (4) age of 60 and over, and (5) high myopia. High myopia was defined as the presence of myopic refraction of -8 D or over and axial length of 26 mm or longer in the presence of typical fundal changes of high myopia. Thirty nine patients with subfoveal neovascularisation on fluorescein angiography were identified for inclusion into the study. The angiograms of all these patients showed early leakage of dye seen as hyperfluorescence which involved the foveal avascular zone. Any patient with pre-existing ocular disease (glaucoma, chronic inflammatory, or neoplastic disorders) was excluded as

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were those with systemic disorders (diabetes, uncontrolled hypertension) or a known life threatening disease at enrolment into the study. Patients with signs consistent with age related macular degeneration, including soft drusen and retinal pigment epithelium (RPE) abnormalities, were excluded.

The study protocol and consent forms were approved by the human subjects committee of Amagasaki Hospital. Patients were informed of the purpose of our study, and provided their signed consent to participate. Thirty nine patients were prospectively randomised to radiotherapy or no treatment, with only one eye of a patient to be randomised. For cases in which we believed that both eyes of a patient were eligible, we and the patient made a subjective judgment as to which eye would be enrolled in the study. Within 24 hours after enrolment, the patients were randomised using computer generated numbers; 0 is to receive low dose radiotherapy and 1 is to receive no treatment. The patients' randomisation state was masked to the treating doctor (HK). Twenty patients underwent radiotherapy, and the remaining 19 patients who did not undergo radiotherapy were followed up as a randomised group. Within a week after random assignments treatment was to begin.

All recruited patients underwent a complete ophthalmological examination, including measurement of the corrected visual acuity, near vision, slit lamp biomicroscopy, and indirect ophthalmoscopy. Fully corrected distance visual acuity was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. The logarithm of the minimum angle of resolution (logMAR) was calculated and used for all statistical analysis. An immediate pretreatment fluorescein angiogram was obtained within 1 week of commencing radiotherapy. Radiotherapy was carried out as described as below. After radiotherapy the patients were reviewed at 2 weeks, 1, 2, 3, 6, 9, 12, 18, 24 months, and then yearly. Safety was evaluated by determining the incidence of radiotherapy related complications and adverse reactions for both treatment and control groups. The patients were regularly questioned and examined for side effects. The control group received the same follow up as the treatment group. Visual function was assessed at every visit and angiography scheduled for the 3, 6, 12, 18, and 24 month visits. Assessment of outcomes including visual acuity, angiographic interpretation, assessment of complications, and adverse events was performed in a masked fashion. To detect adverse events, all patients were examined by the same examiner (HK) to avoid interobserver variation. For assessment of cataract, nuclear sclerosis was assessed as described by Emery *et al.*²¹ Anterior and posterior subcapsular cataract and cortical opacity were scored according to Heckenlively.²²

RADIOTHERAPY

Patients were immobilised with a thermoplastic mask with the head in normo-extension. The isocentre was determined in the centre of the radiotherapy eye, 15 mm behind the

cornea. Irradiation was administered with 6 MV photons with a gantry position of 90 degrees. A high definition computed tomography (CT) scan of the orbit was obtained. Cursor measurements were made from surface markers placed on the Perspex shell at the temporal region and the position of the posterior pole of the eye plotted from these measurements. Computer generated isodose curves for a single 6 MV photon beam, given to 90% of the maximum dose, were superimposed onto the CT scan images. The 90% isodose encompassed the macula of the affected eye. All patients received a dose of 10 Gy prescribed to the 90% isodose, delivered as five fractions of 2 Gy over 5–7 days. All eyes were irradiated through a single lateral port.

DETERMINATION OF AREA OF CNVM

A CNVM associated with pathological myopia showed the area of hyperfluorescence with well boundaries, allowing for accurate determination of the location and size of the lesion. Measurements of the CNVM included only CNVM, but not contiguous blood, fibrosis, or atrophy. In pathological myopia, subretinal blood was thin and did not obscure the boundaries of the CNVM, whereas subretinal blood was thick and obscured the CNVM in age related macular degeneration. Subretinal blood was considered to be present if blood was under the retina in a location immediately contiguous with the area of CNVM or within a serous sanguineous detachment of the retina contiguous with the area of CNVM. Fundus angiograms were obtained using a high resolution digital fundus imaging system based on a UVi fundus camera (Canon, Tokyo, Japan). In each angiogram, one picture was selected that gave the extent of the CNVM and the optic disc. The image was analysed with UTHSCSA Image Tool 32 bit image analysis program (developed at the University of Texas Health Science Center at San Antonio, TX, USA). After applying sharpening and contrast enhancing image filters, the outline of the membrane was drawn on the image manually and the membrane surface was calculated. The outline of the optic disc was simultaneously drawn and saved. To calculate for magnification errors, the disc/CNVM ratio was calculated for each image. The initial (pretreatment) size of the CNVM was set to 100%, and all post-treatment measurements were normalised relative to the initial size. When repeated measurement done on the same picture, statistical analysis of the reproducibility of this measuring method showed a high correlation coefficient of 0.995. A change of less than 20% was considered as unchanged.

STATISTICAL ANALYSIS

Values are presented as the mean (SD) and range. Unless otherwise specified, data were analysed by paired, unilateral *t* tests. A level of $p < 0.05$ was accepted as statistically significant.

Stepwise regression analysis on both the treatment group and control group was used to determine which factors the visual acuity, age, refractive error, and area of CNVM at baseline

would predict the visual acuity and area of CNVM at 2 years after the start of the follow up. Regression analysis was performed to determine the precise relation between variables. For regression analysis, a level of $p < 0.01$ was accepted as statistically significant.

Results

AT BASELINE

Table 1 shows a comparison of age, sex, and refractive error in the treatment group and control group at baseline, and there was no significant difference between two groups. Baseline visual acuity was slightly poorer in the treatment group compared with untreated, but this difference was not statistically significant. Mean area of pretreatment CNVM was 1.472 (1.055) mm² in the treatment group and 1.549 (1.065) mm² in the control group. No difference was found between two groups. Fourteen patients (70%) in the treatment group and 16 patients (84%) in the control group exhibited lacquer cracks at the site of the CNVM.

POSSIBLE ADVERSE REACTIONS

Throughout the study, patients were monitored for any possible adverse side effects which could be attributed to radiotherapy. In the treatment group, one patient suffered transient conjunctival irritation with resolution with 2 weeks and thereafter has remained asymptomatic. No significant progression of cortical and posterior subcapsular lens opacities was observed. Radiation induced retinal vasculopathy (microvascular abnormalities,

leakage, and cotton wool spots) or optic neuropathy (disc pallor) were not observed clinically. Angiograms were scrutinised for evidence of retinal microvascular abnormalities and none was found. In the control group, no complication or adverse reaction was found.

AT FOLLOW UP

Mean changes of area of the CNVM for 1 and 2 years after the start of the follow up were 145% (95%) and 155% (156%) in the treatment group and 208% (98%) and 249% (124%) in the control group, respectively (Table 2). The increase in the area of CNVM in the treatment group for 2 years was significantly smaller than that in the control group ($p = 0.0452$). Of 19 patients in the control group, one patient showed regression of the CNVM and four patients showed stable fluorescein angiographic appearance at 2 years after the start of the follow up (Table 2). Of 20 patients in the treatment group, seven patients showed significant regression and six patients showed stable fluorescein angiographic appearance at 2 years after the radiotherapy. All patients with subretinal haemorrhage showed complete resolution in the treatment group (Table 2).

In the treated eyes, mean visual acuity before and 1 and 2 years after radiotherapy were 0.111 (22.2/200), 0.091 (18.2/200), and 0.086 (19.2/200), respectively (Table 1). No significant difference was found between each two of three examinations. In the control eyes, mean visual acuity before and 1 and 2 years after the

Table 1 Demographics of patient groups

	Treatment group	Control group	<i>p</i> Value
No of patients	20	19	
Baseline			
Men	6 (30%)	5 (26%)	0.7982
Women	14 (70%)	14 (74%)	
Right eye	11 (55%)	11 (58%)	0.8554
Left eye	9 (45%)	8 (42%)	
Age (years)			
60–69	8 (40%)	9 (47%)	
70–79	10 (50%)	9 (47%)	
80–89	2 (10%)	1 (5%)	
Mean (SD)	72.90 (6.52)	72.37 (7.16)	0.8102
(range)	(60–89)	(60–89)	
Refractive error (D)			
–8 to –10	9 eyes (45%)	10 eyes (53%)	
–10.1 to –15	8 eyes (40%)	7 eyes (37%)	
–15.1 to –20	2 eyes (10%)	1 eye (5%)	
<–21	1 eye (5%)	1 eye (5%)	
Mean (SD)	–11.73 (3.89)	–11.33 (4.74)	
(range)	(–22.0 to –8.0)	(–28.0 to –8.0)	0.7744
Pretreatment area of CNVM			
0–0.250 mm ²	2 eyes (10%)	2 eyes (11%)	
0.251–0.500 mm ²	4 eyes (20%)	2 eyes (11%)	
0.501–1.000 mm ²	3 eyes (15%)	4 eyes (21%)	
1.001–2.000 mm ²	5 eyes (25%)	4 eyes (21%)	
2.001–3.000 mm ²	3 eyes (15%)	3 eyes (16%)	
3.001–4.000 mm ²	3 eyes (15%)	4 eyes (21%)	
Mean (SD)	1.472 (1.055)	1.549 (1.065)	0.8218
(range)	(0.221 to 3.554)	(0.105 to 3.331)	
Subretinal haemorrhage			
(+)	11 (55%)	9 (47%)	0.6336
(–)	9 (45%)	10 (53%)	
Visual acuity			
0.1–0.5 (20/200–20/40)	7 eyes (35%)	9 eyes (47%)	
0.05–0.09 (20/400–20/222)	5 eyes (25%)	5 eyes (26%)	
0.01–0.04 (20/2000–20/500)	8 eyes (40%)	5 eyes (26%)	
Mean	0.111 (22.2/200)	0.141 (34.2/200)	
(range)	(0.01 to 0.4)	(0.02 to 0.4)	
Mean (SD) (logMAR)	0.954 (0.595)	0.851 (0.403)	0.5329

LogMAR of visual acuity = logarithm of the minimal angle resolution of visual acuity. CNVM = choroidal neovascular membrane. Refractive error was the spherical equivalent.

Table 2 Changes of visual acuity and area of CNVM after follow up

	Treatment group	Control group	p Value
No of patients	20	19	
Duration of follow up (months)	27.2 (4.6) (24 to 36)	28.9 (5.2) (24 to 38)	0.2859
Area of CNVM (mm ²)			
Baseline	1.472 (1.055) (0.221 to 3.554)	1.549 (1.065) (0.105 to 3.331)	0.8218
3 months	1.584 (1.097) (0.245 to 3.983)	1.956 (1.332) (0.235 to 4.244)	0.3488
6 months	1.601 (1.102) (0.287 to 4.488)	2.133 (1.367) (0.332 to 5.301)	0.1880
12 months	1.619 (1.122) (0.301 to 4.807)	2.201 (1.439) (0.406 to 5.396)	0.1661
24 months	1.317 (1.435) (0.422 to 5.533)	2.717 (1.974) (0.496 to 7.395)	0.0153
Change of area of CNVM			
3 months	117.61 (78.36) % (78 to 188 %)	136.28 (80.28) % (83 to 287 %)	0.4670
6 months	138.76 (84.22) % (71 to 245 %)	156.35 (87.72) % (83 to 332 %)	0.5271
12 months	144.67 (94.59) % (54 to 351 %)	208.37 (98.32) % (78 to 411 %)	0.2823
24 months	154.87 (156.49) % (35 to 632 %)	248.84 (123.83) % (77 to 472 %)	0.0452
Eyes with change of area of CNVM 24 months after the start of the follow up			
Decreased ($\geq 20\%$)	7 eyes (35 %)	1 eyes (5 %)	
Unchanged	6 eyes (30 %)	4 eyes (21 %)	
Increased ($\geq 20\%$)	7 eyes (35 %)	14 eyes (74 %)	
Area of CNVM 24 months after the start of the follow up			
0–0.250 mm ²	1 eye (5%)	0 eye (0%)	
0.251–0.500 mm ²	3 eyes (15%)	1 eye (5%)	
0.501–1.000 mm ²	4 eyes (20%)	4 eyes (21%)	
1.001–2.000 mm ²	9 eyes (45%)	4 eyes (21%)	
2.001–3.000 mm ²	2 eyes (10%)	2 eyes (11%)	
3.001–4.000 mm ²	0 eye (0%)	3 eyes (16%)	
4.001–5.000 mm ²	1 eye (5%)	2 eyes (11%)	
>5.000 mm ²	0 eye (0%)	1 eye (5%)	
Visual acuity			
Baseline	0.111 (22.2/200) (0.01 to 0.4)	0.141 (34.2/200) (0.02 to 0.4)	
LogMAR	0.958 (0.470)	0.851 (0.403)	
3 months	0.120 (24/200) (0.02 to 0.4)	0.120 (24/200) (0.03 to 0.4)	
LogMAR	0.922 (0.362)	0.921 (0.394)	
6 months	0.108 (21.6/200) (0.02 to 0.4)	0.106 (21.2/200) (0.04 to 0.4)	
LogMAR	0.964 (0.333)	0.971 (0.319)	
12 months	0.091 (18.2/200) (0.02 to 0.6)	0.089 (17.8/200) (0.01 to 0.2)	
LogMAR	1.006 (0.338)	1.049 (0.278)	
24 months	0.086 (19.2/200) (0.02 to 0.6)	0.063 (12.6/200) (0.01 to 0.2)	
LogMAR	0.977 (0.353)	1.198 (0.264)	
Change of logMAR visual acuity after the start of the follow up			
3 months	–0.035 (0.262) (–0.602 to +0.523)	+0.070 (0.237) (–0.699 to +0.477)	0.1982
6 months	+0.007 (0.365) (–0.477 to +0.903)	+0.120 (0.253) (–0.699 to +0.)	0.2708
12 months	+0.048 (0.426) (–0.477 to +1.125)	+0.198 (0.290) (–0.301 to +0.699)	0.2090
24 months	+0.019 (0.443) (–0.477 to 1.301)	+0.347 (0.374) (–0.477 to +0.602)	0.0173
Eyes with change of visual acuity during 24 months			
Improved (≥ 2 lines)	9 eyes (45 %)	3 eyes (16 %)	
Unchanged	4 eyes (20 %)	3 eyes (16 %)	
Deteriorated (≥ 2 lines)	7 eyes (35%)	13 eyes (68%)	
Visual acuity 24 months after the start of the follow up			
≥ 0.6 (120/200)	1 eye (5%)	0 eye (0%)	
0.1 to 0.5 (20/200 to 100/200)	12 eyes (60%)	5 eyes (26%)	
0.06 to 0.09 (12/200 to 18/200)	3 eyes (15%)	4 eyes (21%)	
0.01 to 0.05 (2/200 to 10/200)	4 eyes (20%)	10 eyes (53%)	

LogMAR of visual acuity = logarithm of the minimal angle resolution of visual acuity. CNVM = choroidal neovascular membrane.

start of the follow up were 0.141 (34.2/200), 0.089 (17.8/200), and 0.063 (12.6/200), respectively. The visual acuity significantly de-

creased for 2 years ($p = 0.0033$). The changes of logMAR of visual acuity for 2 years after the start of the follow up were +0.019 (0.443) in the treatment group and +0.347 (0.374) in the control group. There was a statistically significant difference between them ($p = 0.0173$).

Table 3 Regression analysis and correlation coefficients for visual acuity and area of CNVM 2 years after the start of the follow up, and their changes

	Treatment group (N=20)		Control group (N=19)	
	r	p Value	r	p Value
LogMAR of visual acuity 2 years after the start of the follow up				
LogMAR of pretreatment visual acuity	0.598	0.0323	0.532	0.0247
Age	0.360	0.1872	0.030	0.9018
Refractive error	0.432	0.1076	0.283	0.2412
Area of CNVM	0.101	0.7195	0.297	0.2170
Change of logMAR of visual acuity for 2 years				
LogMAR of pretreatment visual acuity	0.713	0.0028	0.796	0.0001
Age	0.408	0.1308	0.115	0.6381
Refractive error	0.354	0.1949	0.054	0.8262
Area of CNVM	0.532	0.0411	0.371	0.1176
Area of CNVM 2 years after after the start of the follow up				
LogMAR of pretreatment visual acuity	0.116	0.6811	0.013	0.9565
Age	0.012	0.9661	0.147	0.5437
Refractive error	0.352	0.1984	0.394	0.0947
Area of CNVM	0.630	0.0180	0.718	0.0005
Change of area of CNVM for 2 years				
LogMAR of pretreatment visual acuity	0.256	0.3569	0.506	0.0272
Age	0.270	0.3313	0.268	0.2627
Refractive error	0.366	0.1795	0.113	0.6443
Area of CNVM	0.540	0.0378	0.538	0.0175

LogMAR of visual acuity = logarithm of the minimal angle resolution of visual acuity. CNVM = choroidal neovascular membrane.

FACTORS INFLUENCING CHANGES OF CNVM SIZE AND VISUAL ACUITY AFTER RADIOTHERAPY

In the treatment group, there were a significant correlation of changes in visual acuity and pretreatment visual acuity ($r = 0.713$; $p = 0.0028$), as shown in Table 3. Multiple regression analysis showed that the most significant predictive variable of visual acuity at 2 years after the treatment was the combination of pretreatment visual acuity and refractive error and then pretreatment visual acuity only (Table 4). The strongest factor for the prediction of area of CNVM at 2 years after the treatment was pretreatment of the CNVM area.

Discussion

We demonstrated the safety and efficacy of radiotherapy for a subfoveal neovascular membrane associated with pathological myopia.

Table 4 Multiple regression analysis of predictors of visual acuity and area of CNVM 2 years after the start of the follow up, and their changes

Variable entered	r	F test	Correlation equation
<i>Treatment group (N=20)</i>			
Visual acuity at 2 years after radiotherapy	0.598	4.295	[LogMAR of post-treatment visual acuity] = +0.649 + 0.361 × [logMAR of pretreatment visual acuity]
	0.661	4.660	[LogMAR of post-treatment visual acuity] = +0.649 + 0.362 × [logMAR of pretreatment visual acuity] - 0.043 × [refractive error]
Change of visual acuity	0.713	13.47	[Change of logMAR of post-treatment visual acuity] = +0.649 - 0.369 × [logMAR of pretreatment visual acuity]
	0.795	10.31	[Change of logMAR of post-treatment visual acuity] = +1.178 - 0.638 × [logMAR of pretreatment visual acuity] - 0.043 × [refractive error]
Area of CNVM at 2 years after radiotherapy	0.630	8.561	[Post-treatment area of CNVM] = 0.648 + 0.479 × [pretreatment area of CNVM]
Change of area of CNVM	0.540	5.349	[Change of area of CNVM] = 259.732 - 69.54 × [pretreatment area of CNVM]
<i>Control group (N = 19)</i>			
Visual acuity at 2 years after the start of the follow up	—	—	—
Change of visual acuity	0.796	29.37	[Change of logMAR of post-treatment visual acuity] = +0.994 - 0.748 × [LogMAR of pretreatment visual acuity]
Area of CNVM at 2 years after the start of the follow up	0.839	40.40	[Post-treatment area of CNVM] = 1.171 + 1.403 × [pretreatment area of CNVM] - 1.344 × [LogMAR of pretreatment visual acuity]
	0.898	33.15	[Post-treatment area of CNVM] = 0.445 + 1.133 × [pretreatment area of CNVM]
Change of area of CNVM	0.538	6.924	[Change of area of CNVM] = 315.7 - 62.6 × [pretreatment area of CNVM]

LogMAR of visual acuity = logarithm of the minimal angle resolution of visual acuity. CNVM = choroidal neovascular membrane.

The increases in the area of CNVM in the treatment group for 2 years were significantly smaller than those in the control group. The patients in the treatment group showed no significant change in the visual acuity for 2 years, and those in the control group showed a significant decrease.

Tokoro showed that 50% of eyes with CNVM had visual acuity less than 0.1 and 75% had visual acuity less than 0.3, although the percentage of CNVM is low in eyes with visual acuity less than 0.01.³ Because the distribution of visual acuity of eyes in this study was similar to those reported by Tokoro, visual acuity at baseline was relatively low.

There is a potential risk of development of malignancy induced by radiotherapy in younger patients in spite of the low dose. We enrolled patients at the age of 60 or over, because these patients have a minimal risk for carcinogenesis.

The guidelines for laser photocoagulation treatment for subretinal neovascularisation caused by other diseases may not be applicable to treatment of this complication in patients with myopic degeneration.⁴ The extreme thinness of the choroid and Bruch's membrane in eyes with myopic degeneration makes them particularly vulnerable to mechanical effects, including those induced by photocoagulation. This together with our success with radiotherapy suggests that a CNVM associated with pathological myopia may be treated with radiotherapy.

Although a CNVM associated with age related macular degeneration needs a dose of 15–20 Gy of irradiation,^{8–20} a dose of 10 Gy may be enough dose to treat the subretinal neovascular membrane with pathological myopia because of the relatively limited size of the membrane.^{1–3} In this study, we used a dose of 10 Gy in fraction of 2 Gy. The risk of optic neuropathy and radiation induced retinopathy is significantly increased with larger fraction sizes. If recurrence is observed, radiotherapy can be performed again. One patient in the treatment group showed regrowth of CNVM

with subretinal haemorrhage 26 months after radiotherapy. The patient underwent an additional irradiation of 10 Gy, which induced regression of the CNVM and resolution of the haemorrhage. However, it is not still clear whether a dose of 10 Gy is enough for the treatment of a CNVM. A further investigation regarding dose, including an escalation study, is required to determine the dose effective for the CNVMs.

To evaluate the efficacy of radiotherapy for subfoveal CNVM associated pathological myopia is more difficult than for CNVM associated with age related macular degeneration. In a natural course, no patient with age related macular degeneration show regression of CNVM.¹ Of 19 patients in this study, one patient with high myopia showed spontaneous regression of CNVM and eight showed resolution of subretinal haemorrhage. There is little literature regarding to the long term observation of the subretinal CNVM associated pathological myopia. Before new formation or exacerbation of CNVMs, eyes with high myopia usually show myopic degenerations and loss of vision. In the course of the follow up, the progression of the degenerations may lead to further decrease of visual acuity and make it difficult to evaluate the effects of treatment. Therefore, more cases are needed to evaluate the efficacy of radiotherapy.

In this study, multiple regression analysis demonstrated that the most significant predictive factor for visual acuity 2 years after the treatment was the combination of pretreatment visual acuity and refractive error and then pretreatment visual acuity only. The strongest variable for the prediction of change of CNVM area was pretreatment CNVM area. The ability to predict the post-treatment visual results would be helpful in treating patients with subfoveal neovascularisation associated with pathological myopia.

In this study, we demonstrated the safety and efficacy of radiotherapy for subfoveal neovascularisation and subretinal haemorrhage associated with pathological myopia. Long term

follow up is required to assess side effects, including cataract, radiation induced retinopathy, and optic neuropathy, as well as recurrence of subretinal neovascularisation.

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