

# EyeSEA Eye South East Asia

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#### Editor's Letter Proud of the past, driven for the future.

Dear esteemed readers,

It is my greatest pleasure in this editorial letter to announce the first ever issue of Eye South East Asia to be published this June 2017. Firstly please allow me to express my most heartfelt thanks to everyone involved for making the dream of EyeSEA possible. It is also worth saying that this is issue is the most voluminous issue ever produced by Thammasat Eye Center (TEC) ever since our original journal was released 10 years back, then known as the Thammasat Thai Journal of Ophthalmology (TTJO).



I would like to tell you the story of the origins of EyeSEA. One decade ago, my department of ophthalmologists our colleagues from all over Thailand connected via the Royal College of Ophthalmologists Thailand to form TTJO. The journal was released biannually, exclusively in Thai language with English abstracts and peer reviewed which published twenty issues over the span of a decade containing a variety of articles from submissions all around Thailand. In that time TTJO grew in reputation and accreditation, reaching the first tier of the Thai Citation index (TCI), a subsidiary organization of the ASEAN Citation Index (ACI) – a partnership database with Scopus (Elsevier). This proved our editorial and production team's abilities and dedication that we were consistently able to publish a bi-annual peer reviewed journal and maintain an updated website for 10 years.

TTJO had its ups and downs. Thammasat University Hospital suffered a massive flooding in 2011, and with the chaos that ensued, our team's clinical duties were greatly affected and the necessarily reduced attention to TTJO resulted in a degradation to the second tier of TCI. However, rain or shine, the relentlessly hardworking staff of TEC pushed TTJO's standing back into tier 1 of TCI in 2016. But we could never stop there. Growing in parallel with TTJO was another of TEC's brainchild initiative – the ASEAN Economic Community Ophthalmology Meeting (AECOM) - an ophthalmology academic society supported by TEC and the Faculty of Medicine at Thammasat University aimed at bringing together ophthalmology health professionals to improve healthcare in the region. AECOM hosted four annual scientific conferences in Thailand, Cambodia and Lao PDR, garnering a growing network of international ophthalmologists who attend not only for scientific reasons, but also for a chance in international collaboration for research, training and clinical service. More information can be found at aecomeye.org

With AECOM's success, my junior colleague and managing editor Dr. Tayakorn Kupakanjana spearheaded the idea of merging our existing journal TTJO with the concept of AECOM, using our international annual conferences as a platform for recruiting and forming a community of authors, editors and reviewers to produce clinical research and academic publishing that represents the needs and interest the South East Asian population and ophthalmology society. I strongly believe that EyeSEA marks an important keystone in the new era of strengthened collaboration between ophthalmologists in south east Asia and higher quality research with more robust methodology, and widened perspectives in all areas and controversial topics of ophthalmology - not only for us readers in the region but also the international community. We hope to see articles published in EyeSEA bring clinical innovations and new knowledge to fruition for the greater good of eye healthcare for all. In parting, I would like to take this chance to cordially invite all readers to our fifth annual AECOM scientific meeting set for 24th-26th November 2017 in Hanoi, in conjunction with the Vietnam National Ophthalmology Conference. And last but not least, my final message to you is to encourage you all to contribute your opinion in EyeSEA through the editorial letters section - it is your chance to interact with the authors and help create a lively community of thoughtful ophthalmologists. Did you not agree with a point made in a previous article? Or you have a different perspective to share about the same topic from the last issue? No problem - just write us an email to accomeye@gmail.com with the subject line 'Editorial letter' and we will publish your letter in the next issue and encourage the relevant author or editor to respond in the following issue. Thank you for your attention, see you at the 5th AECOM 2017 at Hanoi, and be in touch again on December 2017 for the next issue of EyeSEA.

> Associate Professor Sakchai Vongkittirux, MD Head of Thammasat Eye Center, Faculty of Medicine Thammasat University and Former President of The Royal College of Ophthalmologists Thailand

#### Aims and Scope

Eye South East Asia (EyeSEA) strives to promote the dissemination of regionally relevant academic publications and discourse in the field of Ophthalmology. The South East Asian population has a unique spectrum of eye diseases due to pathophysiologic, geographic, socioeconomic and cultural contexts – although often underrepresented in literature. EyeSEA supports the growing number of ophthalmic healthcare professionals in the region seeking to produce and disseminate academic publications, developing robust clinical methodology and quality of original publications in Ophthalmology from South East Asia to the world.

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- Issue 1: January - June
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- Issue 2: July - December Author Submission Deadline: 30<sup>th</sup> of September
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Abbreviations should be defined at the first mention in the text and also in each table and figure. For a list of standard abbreviations, please consult the Council of Science Editor Style Guide or other standard sources. Write out the full term for each abbreviation at the first use unless it is a standard unit of measure.

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<u>https://publicationethics.org/files/COPE\_plagiarism\_discussion\_%20doc\_26%20Apr%2011.pdf</u> EyeSEA will also refer to the following flow chart for the management of suspected plagiarism <u>https://publicationethics.org/files/plagiarism%20A.pdf</u>

#### Subject to Change

EyeSEA strives to improve its author's guidelines and publication policy in line with international governing authorities regarding ethical and trustworthy scientific publication. We attempt to constantly improve our adherence to reccommendations by COPE, DOAJ and ICMJE. As this is a work in progress, the author's guideline will be subject to change in each issue, the changes will be reflected in the NEWS section and the relevant policies section in the website and each printed issue.

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## **Case report: Choroidal melanoma: experience from a tertiary referral centre in Malaysia.**

#### Long Li Ying MD<sup>1</sup>, Roslin Azni Abdul Aziz MD<sup>2</sup>.

<sup>1</sup>Department of Ophthalmology, Hospital Selayang, Selangor, Malaysia.

<sup>2</sup>Master trainee, Department of Ophthalmology, Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Kuala Lumpur, Malaysia.

<sup>1</sup>Department of Ophthalmology, Hospital Shah Alam, Selangor, Malaysia.

**Background**: Choroidal melanoma is known as the most common primary intraocular malignancy in adults. Nevertheless, it is more commonly found in Caucasians and rarely found in Malaysian population.

**Objective**: We present eight cases of choroidal melanoma referred to Hospital Selayang, a tertiary centre for medical retinal cases, from year 2012 to 2016.

Methods: Retrospective case series.

**Results**: There were seven females and one male with a mean age was 53.9 years old. Five patients were Chinese and three were Malay. The presenting complaints were visual field defect (n=3), distorted vision (n=2), photopsiae (n=2) and decreased vision (n=1). The tumour thickness ranged from 3.00 to 13.94 mm (mean=8.93mm). One case had exudative retinal detachment while the remaining had adjacent sub-retinal fluid. Three patients had undergone globe-preserving therapy (plaque brachytherapy and stereotactic radiotherapy) while the remaining had undergone enucleation or exenteration. The histopathological examinations showed three cases of spindle B cells, one with epitheliod cells and one with mixed features. One patient died due to tumour recurrence and complications of multiple distant metastasis while the rest were well under regular follow-up.

**Conclusions**: Although choroidal melanoma is very rare among Malaysian population, it is a crucial diagnosis to make in view of its metastatic risks. Early presentation and diagnosis of choroidal melanoma is significant to save lives.

Keywords: Choroidal melanoma, case series, melanoma, Malaysia, primary, uvea

*EyeSEA 2017*; *12 (1)*: *1-8 Full text.* <u>https://www.tci-thaijo.org/index.php/eyesea/index</u>

#### Introduction

Choroidal melanoma is known as the most common primary intraocular malignancy in adults. The incidence of primary choroidal melanoma is approximately 6 cases per million population in United States and 7.5 cases per million per year in Denmark and other Scandinavian countries.<sup>1</sup> However, it is commonly found in Caucasians and rarely found in Malaysian population. The risk factors for choroidal melanoma includes fair skin, lighter iris color, ultraviolet light exposure and smoking.

#### Materials and Methods

A retrospective analysis of patients referred to the Medical Retinal Clinic, Department of Ophthalmology, Hospital Selayang from year 2012 to 2016 and diagnosed with choroidal melanoma were identified. Patients' demographic data, tumour characteristics, treatment, outcome and complications were reviewed and tabulated.

The diagnosis of choroidal melanoma was made by thorough clinical evaluation, ophthalmic examination. supported by ultrasound, fundus fluorescein angiograph, optical coherence tomography and reviewed by ophthalmic oncology subspecialist.

#### Results

A total of eight cases diagnosed with choroidal melanoma were identified and analysed. Among the eight patients, there were seven females and one male. The mean age was 53.9 years old which ranged from 33 to 66 years old. Five patients (62.5%) were Chinese and another three (37.5%) were Malay. The presenting complaints include visual field defect (n=3, 37.5%), distorted vision (n=2, 25%), photopsiae (n=2, 25%) and blurring of vision (n=1, 12.5%). Three of them had family history of malignancy in first-line relatives, but none of them had family history of ocular malignancy. One of the patients was an ex-smoker who smoked 40 packs/ year but quit smoking 10 years ago and the rest were nonsmokers. Their occupations did not involve prolonged sunlight exposure. None of them had other pre-existing ocular comorbidity prior to presentation. Table 1 summarized the demographic data including age, gender, ethnicity, occupation, ocular presentation, presenting visual acuity, co-morbidity, family history of cancer and smoking history.

Table 2 showed tumour characteristics of the eight cases which were analysed based on the mnemonic device "To find small ocular melanoma using helpful hints daily", representing thickness, fluid, symptoms, orange pigment, margin, ultrasonographic hollowness, halo absence and drusen absence.<sup>2</sup> The tumour thickness ranged from 3.0 to 13.94 mm (mean=8.93mm). One case had exudative retinal detachment while the remaining were associated with adjacent sub-retinal fluid. Three out of eight cases had orange pigment on the tumour. All of the tumours were more than 3 milimeter or 2 disc diameter (DD) away from the optic disc and were not associated with halo or drusen.

Treatment with plaque brachytherapy was not available in Malaysia. Two patients deemed suitable for plaque brachytherapy were referred to centres offering the above treatment. One patient underwent stereotactic radiotherapy. Five patients required more radical treatments like enucleation or

No.	Age	Gender	Ethnicity	Occupation	Ocular	Present	Co-	Family	Smoking
					presentati	ing	morbidity	history	history
					on	vision		of cancer	
1	60	Female	Chinese	Housewife	Visual	6/9	Nil	No	No
					field				
					defect for				
					1 month				
2	52	Female	Chinese	Housewife	Visual	6/18	Hypertens	Yes	No
					field	PH:6/1	ion		
					defect	2			
					with	_			
					floaters				
					for 3				
					months				
3	53	Female	Chinese	Waitress	Decreased	6/18	Diabetes	Ves	No
		Tennare	Chinese		vision	0/10	hypertensi	105	110
					with		on		
					floaters		dyclinide		
					for 2		min		
					norths		IIIId		
4	22	Famala	Chinasa	Dharmagist	Degranged	6/12	NG	No	No
4	33	remaie	Chinese	Filarinacist	Decreased	0/12 DIL6/0	1811	INO	INO
					vision	F11.0/9			
					distantian				
					for 2				
					101 2				
5	50	F 1	N ( 1	T 1	Weeks	(/10	T C	N	N
5	28	Female	Ivialay	Teacher	Decreased	0/18	Len	INO	INO
					Vision		tentorium		
					with		cerebelli		
					Visual		meningio		
					field		ma		
					defect for				
	4.1	F 1			2 months	6150		37	N.
6	44	Female	Malay	Housewife	Distorted	6/60	Nıl	Yes	No
					vision for				
				~	2 weeks				
7	66	Male	Malay	Computer	Decreased	HM	Diabetes,	No	Ex-
				manager	vision for		hypertensi		smoker
					1 year		on, treated		
							renal		
							carcinoma		
8	65	Female	Chinese	Housewife	Flashes	6/18	Dyslipide	No	No
					for 6	PH:6/9	mia, left		
					months		deep vein		
							thrombosi		
							S		

 Table 1: Patients' demographic data

exenteration. Lid-sparing exenteration was performed in case no. 3 due to radiological evidence of lateral rectus and lateral orbital wall involvement. The histopathological examinations showed three cases of spindle cells type B, one with epitheliod cells and one with mixed features.

The two patients that underwent plaque brachytherapy developed foveal atrophy and cystoid macular edema. The cystoid macula edema did not respond very well to treatment with orbital floor triamcinolone. Intravitreal Anti-Vascular Endothelial Growth Factor (anti-VEGF) was not performed in this patient due to presence of significant macular ischaemia found in fundus fluorescein angiography. who had stereotactic The patient radiotherapy developed radiation

retinopathy which was treated with laser retinal photocoagulation and intravitreal anti-VEGF injection. The visual outcome of all these patients were poor.

One patient had tumor recurrence with multiple distant metastasis to the brain and liver which was diagnosed at eight months after enucleation. This patient died two weeks after the diagnosis of metastasis. Otherwise, other patients were well under regular follow-up without recurrence or distant metastasis. The mean duration of follow-up till date was 26.5 months (ranged from 8 months to 50 months). Table 3 summarized the treatment, histopathological findings, complications, final vision outcome, duration of follow-up and current general status.

Ν	Tumour	Subretin	Sympto	Orange	Margin	Ultrasono-	Halo	Druse
0.	thickness	al fluid	ms	pigme	from	graphic		n
	(mm)			nt	optic disc	hollownes		
						S		
1	6.1	Yes	Yes	No	4DD	Yes	No	No
2	5.87	Yes	Yes	No	5DD	Yes	No	No
3	13.07	Yes	Yes	No	Unable	Yes	No	No
					to			
					visualise			
4	3.0	Yes	Yes	Yes	4DD	Yes	No	No
5	11.4	Yes	Yes	Yes	3DD	Yes	No	No
6	13.94	Yes	Yes	No	Unable	No	Unable	No
					to		to	
					visualize		visualize	
7	9.36	Yes	Yes	No	-	Yes	No	No
8	8.69	Yes	Yes	Yes	4DD	Yes	No	No

 Table 2: Tumor characteristics



**Figure 1:** Case 4: left eye fundus. (A) Dome-shaped pigmented mass temporal to macula measuring 2DD with sub-retinal fluid. Patient underwent 5 sessions of stereotactic radiotherapy. (B) Post-treatment photo showing shrinkage of tumour size.

Table 3: Treatment, or	tcome and complicatio	n
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No.	Treatment	HPE	Complication	Final vison	Duration of follow- up (months)	Current status
1	Plaque brachytherapy	-	Foveal atrophy	CF 2 feet	22	Well
2	Plaque brachytherapy	-	Cystoid macular oedema	6/60 PH:6/36	18	Well
3	Lid-sparing exenteration	Spindle B cells	Wound breakdown	-	21	Well
4	Stereotactic radiotherapy	-	Radiation retinopathy	CF 2 feet	50	Well
5	Enucleation	Spindle B cells	Nil	-	42	Well
6	Enucleation	Epitheloid cells	Recurrence with metastasis to brain and liver	-	8	Dead
7	Enucleation	Mixed cells	Nil	-	24	Well
8	Enucleation	Spindle B cells	Nil	-	27	Well



#### Figure 2: Case 6

Fast growing choroidal melanoma with sentinel vessel (A & B). Enucleation was performed which showed pigmented lesion on posterior sclera (C). Optic nerve and rectus muscles margin were free of tumour cells. Unfortunately, patient had recurrence eight months later and died due to complications of distant metastasis to brain and liver.

#### Discussion

Melanoma appears as a unifocal mass with variable pigmentation arising from melanocytes of choroid, ciliary body or iris. Choroidal melanoma accounts for about 80% of all uveal melanoma. In this case series review, majority of cases involve the Chinese population. This is likely related to host factor that Chinese has fairer skin color and inability to tan. Shah et al.<sup>3</sup> found that chronic ultraviolet exposure and occupational sunlight exposure were borderline factors.

Typically starts as dome-shaped lesion, choroidal melanoma acquires a mushroom or collar-button shape as it grows and breaks through the Bruch membrane. It often associates with subretinal fluid and causes retinal detachment. It can also develop vitreous haemorrhage and secondary glaucoma. Choroidal melanoma can be grouped into three sizes based on the tumour thickness, including small (0-3.0 mm), medium (3.1-8.0 mm) and large (8.1 mm or greater).<sup>4</sup>



Figure 3: Case 2 Dome shaped raised mass at superotemporal retina measuring 5DD associated with sub-retinal fluid.

The management of choroidal melanoma depends on patient's age, general health, preference, status of fellow eye, tumour size and location. Options of management including eyepreserving techniques such as transpupillary thermotherapy, plaque brachytherapy, proton-beam radiotherapy, transcleral resection and endoresection, and radical treatment such as enucleation or orbital exenteration.

The use of focal radiotherapy such as proton beam irradiation or plaque brachytherapy can generally achieve good local tumour control, but it may be associated with poor visual outcome. Gunduz et al studied 1,300 eyes with posterior uveal melanoma treated with plaque brachytherapy, showed that 42% patients subsequently developed radiation retinopathy by 5 years after treatment.<sup>4</sup> Sagoo et al analysed 650 consecutive eyes with juxtapapillary choroidal melanoma (<1mm to optic disc) treated with plaque brachytherapy and found that this treatment modality commonly leads to retinopathy and papillopathy, and visual loss should be anticipated in 45% by 5 years. Nevertheless, they concluded that plaque brachytherapy remains a suitable treatment of juxtapapillary melanoma in view of high globe retention rate, which was 84% at 5 years.<sup>5</sup>

The Collaborative Ocular Melanoma Study (COMS) was a prospective study designed to evaluate the management of choroidal melanoma. COMS consists of three substudies including the large, medium and small choroidal melanoma trials. The large tumor trial showed no difference in patient's survival when comparing enucleation and preenucleation radiation groups.<sup>6</sup> The medium tumor trial showed no difference in patient's survival when comparing enucleation and plaque brachytherapy up to 12 years follow-up.<sup>7</sup> The cumulative all- cause mortality at 12 vears was 43% in the plaque brachytherapy group and 41% in the enucleation group.

According to American Joint Committee on Cancer (AJCC) TNM Staging, the clinical features that is associated with poor prognosis is usually related to tumor size of more than 15mm, tumor location in ciliary body, extrascleral tumor extension, older age at diagnosis and regrowth after globeconserving therapy. Histopathological and cytogenic factors associated with poorer prognosis includes epithelioid cell increased mitotic type, activity. infiltrating lymphocytes, tumor vascular networks and chromosomal mutations (monosomy 3 and trisomy 8).<sup>8</sup> Shield et al, found that each milimeter increase in tumor thickness is related to 5% increased rate of metastasis.9

Distant metastasis usually occurs hematogenously by penetration into vortex veins and at risk of spreading to liver, lungs, bone, skin or brain.<sup>8</sup> Lymphatic spread is usually rare. Subsequent follow-up are required to watch out for recurrence and monitoring of metastasis. Thorough physical examination, twice yearly liver function tests, yearly chest radiograph and liver imaging are advisable.

#### Conclusion

Choroidal melanoma has a very low incident in Malaysia. Nevertheless, it is an important diagnosis to make as it leads to life-threatening consequences. Early presentation and diagnosis of choroidal melanoma is significant to save lives.

## Acknowledgements and conflict of interest

None.

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## Case report: Excimer laser phototherapeutic keratectomy (PTK) in gelatinous drop-like dystrophy.

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**Background**: Gelatinous drop-like corneal dystrophy (GDLD) is a rare corneal dystrophy, characterized by amyloid deposition in subepithelium and stroma of cornea, causing reduction in vision, photophobia and irritation because of irregularity in corneal surface. Excimer Laser Phototherapeutic Keratectomy (PTK) using Argon-fluoride laser is used to reshape, smoothen the corneal surface and removal of corneal opacity with minimal adverse reaction to the surrounding corneal tissue. A 19 year-old patient complained of irritation in both eyes for 3 months. She noticed whitish nodules on her cornea for about 5 years. After which she gradually suffered a progressive loss of her vision on both eyes.

**Results**: right eye BCVA is 20/70, and counting fingers at 1 foot on left eye. Slit lamp examination revealed 2 grayish protruding subepithelial nodules at the central cornea of the right eye and multiple protruding subepithelial nodules that coalesce to a large lesion at the central cornea of the left eye. The patient was diagnosed as GDLD by clinical appearance. PKP was planned to restore vision, however the queue in Thailand for the procedure was 4-5 years. Thus Excimer laser PTK and fluid masking technique was performed for relieving the symptoms and temporary restoring the vision. Left eye laser setting was 6.8 mm zone of ablation with 45 microns in depth, performed after epithelium removal, the material deposit was reported as amyloid material.

**Discussion**: The patient showed improving visual acuity and decreasing in eye symptoms following treatment. Duration of follow up was 2 months at time of writing with no clinical sign of recurrence of disease after laser operation.

*Keyword:* Excimer Laser Phototherapeutic Keratectomy, PTK, Gelatinous drop-like corneal dystrophy, GDLD, PKP

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#### Background

Gelatinous drop-like corneal dystrophy (GDLD) is a rare corneal dystrophy, characterized by deposition of amyloid in subepithelium and stroma of cornea. Clinical manifestation of GDLD usually present in first 2 decades of life with bilateral multiple white gelatinous subepithelial nodules (mulberry-like configuration) or band keratopathy-like lesion. With time. superficial vascularization has occurred and the lesion progresses to become larger and deeper which cause stromal nodules (kumquat-like lesion) and /or stromal opacifications

GDLD is classified as category I by IC3D Classification of Corneal Dystrophies<sup>2</sup>, in which causative gene is Tumor-associated calcium signal transducer 2 (TACSTD2, previously M1S1), located in chromosome 1(1p32)<sup>3</sup>. Approximately about 25 mutations are reported on TACSTD2 gene. Loss of TASCSTD2 gene function resulting in loss of epithelial tight junction, allow the tear fluid influx into corneal tissue, and then lactoferrin in tear fluid turns to amyloid deposition in corneal tissue<sup>4</sup>.

On Histopathology, GDLD is characterized by deposition of amyloid in subepithelial and stromal layer, area of epithelial hyperplasia and epithelial atrophy<sup>5</sup>, destruction of Bowman's layer, stromal fibrosis and neovascularization. Descemet's membrane and endothelium are clearly visible. Transmitting electron microscopy reveals disruption of epithelial tight junction and amyloid deposit in basal epithelial layer.

GDLD can cause significant reduction in vision, photophobia and

irritation because of irregularity in corneal surface. Wearing of soft contact lens in GDLD is proposed to relieve the ocular irritation. Surgical treatments are performed for visual restoration and rehabilitation including various type of keratoplasty. Limbal stem cell transplantation combined with keratoplasty or superficial keratectomy is an alternative option of tratment. However, recurrence after surgery is common within few years.

Boston type I keratoprosthesis<sup>6</sup> could be an option for advanced case of GDLD which required multiple keratoplasty.

Excimer Laser Phototherapeutic Keratectomy (PTK) using Argon-fluoride laser, emitting pulse at 193 nanometers is used to reshape, smoothen the corneal surface and remove corneal opacity with reaction minimal adverse to the surrounding corneal tissue. This technique has been used in many corneal disorders including recurrent corneal erosion. Reis-Buckler's dystrophy. anterior granular and lattice dystrophy. However it is not indicated in deep stromal lesions.

Recurrence after PTK is common in corneal dystrophy and may require repeating in PTK or corneal transplantation.

#### Case report

A 19 year-old patient presented to our eye clinic complaining of irritation on both sides of her eyes for 3 months. She denied any previous history of ocular trauma and surgery in addition to any underlying medical conditions. She also denied any family history of corneal dystrophy and reported none of her relatives had the same symptoms. She has mild degree of eye irritation on both sides for about 10 years, and has noticed some whitish nodules on her cornea for about 5 years. After noticing the white nodules on the cornea, she reported a gradual progressive loss of vision on both eyes.

On ophthalmic examination, her right eye visual acuity is 20/100 which improved to 20/70 after pinhole

correction and counting fingers at 1 foot on left eye which is not improved with pinhole. Slit lamp examination revealed 2 grayish protruding subepithelial nodules at central cornea on right eye and multiple protruding subepithelial nodules that coalesce to be a large lesion at central cornea on left eye. No epithelial defects on both eyes. Normal anterior chamber depth, lens and pupillary light reaction.<sup>3</sup>



Fig 1: Right eye of patient demonstrates grayish subepithelial deposition at central cornea



Fig 2: Left eye of patient demonstrates multiple grayish subepithelial deposition with haziness of central cornea

The patient was diagnosed as having gelatinous drop-like corneal dystrophy based upon clinical appearance. Plan of treatment is to perform penetrating keratoplasty to restore vision. But in Thailand, the waiting time is at least 4-5 years in surgical listing queue to receive the donor-cornea for transplantation. Thus Excimer laser PTK and the fluid masking technique were performed to temporarily restore vision and relieve the symptoms.

A decision was made to perform the laser operation on her left eye first and the laser setting was 6.8 mm zone of ablation with 45 microns in depth, performed after epithelium removal. Operation was successfully completed without complications. The material deposit on the cornea which we sent to identify was reported back as amyloid material.

One week after the laser operation, the corneal epithelial defect closed, left eye visual acuity has improved to 20/200 and 20/70 with pinhole correction. Her eye symptoms improved significantly, in particular, the symptom of photophobia has almost completely subsided.

#### Discussion

This is a case of a young female patient who presented with visual loss, eye irritation, photophobia and grayish subepithelial nodules on cornea of both eyes. A diagnosis of Gelatinous drop-like dystrophy of cornea was made. The management plan was to perform penetrating keratoplasty. Whilst waiting for the surgical listing queue, the patient received excimer laser PTK to relieve the eye symptoms and temporarily restore vision.

GDLD is a rare corneal dystrophy occurring in the young population. It still proves a challenge to today's ophthalmologists in diagnosis and providing treatment. Almost every patient will experience a recurrence within a few years following keratoplasty and superficial keratectomy techniques, thus patients may need multiple surgical intervention.

From literature review, there were few reports about excimer laser PTK for treatment of primary GDLD. T. Yamaguchi<sup>8</sup> reported direct ablation with excimer laser on the surface of cornea produces more surface irregularities. While Mouamen M. Seleet report lesion peeling and Phototherapeutic Keratectomy (PTK) and followed by Mitomycin C application appeared to be effective for GDLD for 6 months. Due to the rarity of disease, only reports in small case series with limited time of follow-up period are available.

Sustainability of treatment was also questioned, from case series reported by Shimazaki,<sup>9</sup> GDLD patients who received keratoplasty almost all developed subepithelial haziness on the graft's location within 1 year and amyloid deposition typically recurred within a few years.

This case demonstrated improving visual acuity and decreasing in eye symptoms following excimer laser PTK with fluid masking technique. Duration of follow up is currently about 2 months with no clinical sign of recurrence of disease after laser operation.

#### Conclusion

Excimer laser PTK appears to be effective for treatment of primary Gelatinous drop-like corneal dystrophy with good initial response in visual improvement and relieving of eye symptoms.

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# Case Report: An outlook on outreach vision screening.

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**Background**: Alport syndrome, a hereditary nephritis accompanied by high tone sensorineural deafness and distinctive ocular signs, was first reported in the early 1900s by Dr. Cecil A. Alport in 1927. Studies have demonstrated that it is caused by a genetic defect within one of the alpha chains of the type IV collagen, the major component of basement membranes (BM) in the kidney, inner ear, and eye. Pathologic biopsy studies and genotyping play an important role in evaluating patients with Alport syndrome. Difficulties still exist to confirm the diagnosis of Alport syndrome (AS) exactly (Xu et al. 2010).

**Case Report**: A middle aged male presented with bilateral reduced vision. His vision was not improved with refraction and anterior lenticonus and retinal flecks were significant during dilated fundus examination. We noticed facial puffiness and pallor. Then we obtained hypertension and reduced hearing from history. There was no known family history. We decided to do the investigations to confirm the diagnosis of Alport syndrome and to know the severity.

**Conclusion**: This is an unexpected case seen in the outreach vision screening. With the help of slitlamp findings, Alport syndrome was diagnosed and associated nephropathy and sensorineural deafness were referred for the appropriate treatment. It is fascinating that eye screening can save a life for lifelong treatment.

**Keywords:** Anterior lenticonus, Alport Syndrome, Hereditary Nephritis, X-linked Alport syndrome (XLAS), autosomal recessive Alport syndrome (ARAS), autosomal dominant form (ADAS)

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#### Introduction

According to the annual report of Prevention of Blindness Myanmar, cataract is the number one cause of blindness in our country and refractive error is the commonest cause of the visual impairment. Every year, there are more than 10 outreach screening performed. With the support from Government and local well-wisher, slit-lamp microscope is an essential equipment to find out the anterior and the posterior segment pathology like this case. All the team members are happy to catch the problem which needs to proceed surgery. However, when ophthalmologist can find out the clues which threaten the life of patient, we all are pleased and this is the one incentive to update the carrier.

#### **Case Report**

A 35 year-old man presented in an outreach eye screening with reduced vision in both eyes over couple of years. He is a healthy working farmer with only history of hypertension for more than 5 years. Also he said hard of hearing for the same duration. He has two elder sisters and one younger sister who are all healthy. His mother died of probably ascites 20years ago and did not know the cause of death. His father is still alive and healthy. On examination, he had a vision of 20/200 OU with best correction. There was no abnormality in pupils and EOM testing. IOP Intraocular pressure was 15mmHg with NCT noncontact Slit-lamp examination tonometry. bilateral showed marked anterior lenticonus. Both disc and macula are pretty good except flecks found all over the retina. On general examination his blood pressure was 170/100 mmHg with marked pallor. Blood haemogram revealed haemoglobin 5.1 g/dl which was consistent with marked anaemia. His creatinine was 12.7 mg/dl which is 10 times more than normal. There was albuminuria and haematuria in microscopic examination of urine. In addition sensorineural hearing loss was found in audiometry test. In ultrasound (abdomen), both kidneys are small in size 5.9 into 2.7 cm, right kidney and 7 into 3.1 cm, left kidey with bilateral chronic nephropathies.

We referred the patient to the nephrologists for this life threatening condition and they planned to do dialysis.

#### Discussion

Alport syndrome is a rare genetic disorder characterized by progressive kidney disease and abnormalities of the ears and eyes. There are three genetic types. X-linked Alport syndrome (XLAS), autosomal recessive Alport syndrome (ARAS), autosomal dominant form (ADAS).

The hallmark of the disease is the appearance of blood in the urine (haematuria) with early in life. progressive decline in kidney function (kidney insufficiency) that ultimately results in kidney failure, especially in affected males. XLAS is caused by mutations in the COL4A5 gene. ARAS is caused by mutations in both copies of either the COL4A3 or the COL4A4 gene. ADAS caused by mutations in one copy of the COL4A3 or COL4A4. . Individuals with heterozygous COL4A3 or COL4A4 mutations usually have thin basement membrane nephropathy with normal renal function but some develop renal impairment (Savige et al. 2016). The next stage in progression is gradual loss of kidney function, frequently associated with high blood pressure (hypertension), until, the kidneys fail to work (Kashtan, 2017).

Progressive hearing loss (sensorineural deafness) occurs frequently in people with Alport syndrome. The deafness results from impaired transmission of sound input from the inner ears (cochleae) to the brain via the auditory nerves. Diminished hearing is usually evident by late childhood in males with XLAS although it may be mild or subtle. In males with XLAS the frequency of hearing loss is approximately 50% by age 15, 75% by age 20 and 90% by age 40 (Kashtan, 2017). Individuals diagnosed with Alport syndrome should undergo hearing tests that determine a person's audible range for tones and speech (audiometry).

Individuals with Alport syndrome mav also develop abnormalities in several parts of the eyes including the lens, retina and cornea. Eye abnormalities in XLAS and ARAS are very similar in presentation. Eve abnormalities are uncommon in ADAS. Anterior lenticonus is a condition in which the lenses of the eyes are shaped abnormally, specifically the lens bulges forward into the space (anterior chamber) behind the cornea. Anterior lenticonus can result in the need for glasses and sometimes leads to cataract formation. Anterior lenticonus occurs in about 20% of males with XLAS and often becomes apparent by late adolescence or early adulthood (Kashtan, 2017).

The retina, may also be affected, usually by pigmentary changes caused by the development of yellow or white flecks superficially located on the retina (Kashtan, 2017).

The cornea, may also be affected, although the specific abnormalities can vary. Recurrent corneal erosions and posterior polymorphous corneal dystrophy may occur (Kashtan, 2017).

Tissue studies (kidney or skin biopsy) are very useful tools in the evaluation of patients with Hematuria. With immunostaining, an antibody that reacts against collagen type IV alpha-5 chain proteins is added to the skin sample. Normally, alpha-5 chains are found in skin samples, but in males with XLAS they are nearly completely absent. Alpha-3 and alpha-4 chains are not present in the skin and, therefore, skin biopsies cannot be used to diagnose ARAS or ADAS (Kashtan, 2017).

A kidney biopsy may be also performed. Abnormalities of the glomerular basement membrane (GBM) that can be detected by an electron microscope. In addition to detecting alpha-5 chains, kidney samples can be assessed to determine whether type IV collagen alpha-3 or alpha-4 chains are present and in what quantity (Kashtan, 2017).

The treatment of Alport syndrome is directed toward the specific symptoms. The current standard of care for patients with Alport syndrome is angiotensin blockade in those with overt proteinuria (Kashtan, 2017).

Dialysis is to control blood pressure, and helping to maintain proper levels of essential chemicals such as potassium. End-stage renal disease is not reversible so individuals will require lifelong dialysis and kidney transplant (Kashtan, 2017).

Because of unavailable genetic testing and limited immunoassay for skin biopsy, we diagnose this rare genetic disorder, Alport syndrome by only clinical in general and ophthalmologist points.

#### Conclusion

This is the proof that the eye is the window of not only for the Soul/Brain actually of the whole body.



**Fig.** 1 35 yr-old male with reduced vision in both eyes on slit lamp examination, anterior lenticonus: bilateral axial projection of the anterior surface of the lens into the anterior chamber (A) Right eye (B) Left eye



Fig. 2 pallor of the nail beds showing marked anaemia due to chronic renal insufficiency.

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## Comparing Bevacizumab PRN and focal/grid laser for naive diabetic macular edema. One year results of an open-label randomized controlled trial.

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**Background:** Diabetic retinopathy is an emerging challenge and burden worldwide and in Viet Nam. Among those patients, diabetic macular edema (DME) is disabling for patients in working ages. Bevacizumab is a popular anti-VEGF using in DME with a relative safety profile and good efficacy in clinical use. However, clinical randomized trials using Bevacizumab PRN in DME treatment is somewhat lacking, especially in Viet Nam population. We conducted an open-label clinical randomized trial comparing Bevacizumab PRN to modified ETDRS focal/grid laser in treating naive DME patients.

**Objectives:** Intravitreal injection of Bevacizumab is non-inferior to modified ETDRS focal/grid laser in treating naive DME using BCVA and central retinal thickness (CRT) change from baseline at 12 months.

**Methods:** This was an open-label randomized controlled trial. We recruited type 2 diabetes patients with vision loss from naïve DME having BCVA from 20/25 to 20/320 (Snellen equivalent) and  $CRT \ge 225$  micron on spectral domain optical coherence tomography. Each eye was randomized to at least 3 monthly intravitreal Bevacizumab (1,25 mg) injections until BCVA stabilization then PRN or standard modified ETDRS focal/grid laser protocol. BCVA change within 5 letters was considered stable. Bevacizumab group was followed up with BCVA and CRT every month while Laser group was followed up every three months and both were treated PRN accordingly.

**Results:** There were 112 eyes of 79 patients were randomized (55 to Bevacizumab, 57 to focal/grid laser). Among those eyes, 39.62% bevacizumab-treated eyes vs 8.93% laser-treated eyes gained at least 15 letters at 12 months (p < 0.001). Average letters gained were  $12.17 \pm 6.65$  and  $2.11 \pm 11.84$  accordingly. Average change in CRT were -143.89  $\pm$  127.54 and -89.96  $\pm$  127.62 micron respectively (p < 0.001). No serious systemic adverse events were recorded. The most common adverse event in bevacizumab-treadted patients was subconjunctival hemorrhages 37%.

**Conclusions**: Bevacizumab PRN was non-inferior to or better than focal/grid laser in treating naive DME patients in terms of BCVA and RCT change at 12 months.

Keywords: anti-VEGF, Bevacizumab, Diabetic macula edema, Focal/grid Laser

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#### Introduction

According to the latest data from the American Diabetes Association, diabetic retinopathy is the leading cause of blindness in adults aged 20 to 74 years. The incidence of diabetes mellitus in the world is also increasing worldwide, which means that diabetic retinopathy will continue to be a major burden of visual loss and blindness in the coming years. Diabetic macular edema is the leading cause of vision loss in diabetic retinopathy patients. Once the edema has involved macular center, the risk of vision loss is even higher. The risk of severe vision loss (loss of at least three lines) after three years was 33% in the ETDRS study.10

standard treatment The for diabetic macular edema during the past five decades is focal/ grid photocoagulation. However. the therapeutic effect of this method is relatively low, which only reduces the risk of moderate and severe vision loss by 50%.<sup>10</sup> In addition, photocoagulation was significantly less effective with diffuse macular edema with only 14.5% visual improvement.<sup>7</sup> The DRCR.NET study also found that proportion of visual acuity improvement  $\geq$  5 letters were 51%, 47%, and 62% at 1, 2 and 3 years, respectively.<sup>2</sup> The anti-VEGF therapy has recently been shown to have good short-term efficacy by multiple clinical trials.<sup>1,9</sup> The standard of care of anti-VEGF for diabetic macula edema is Ranibizumab and Aflibercept. Although not officially approved for use in the eye, Bevacizumab, with its cheap and widely available advantage, is one of the most used anti-VEGF drug in developing world. In CATT study, monthly dosing Bevacizumab has been shown to be non-inferior to Ranibizumab for the treatment of wet AMD. There are some clinical trials using Bevacizumab for the treatment of diabetic macular edema<sup>11</sup> and have shown encouraging visual results. In Vietnam, most physicians use the Bevacizumab PRN regimen for diabetic macula edema but robust clinical trials data to support its use are still lacking. To provide evidencebased data on this subject, we compared Bevacizumab PRN regimen with open-label focal/grid laser in an randomized, one center study.

#### Material(s) and method(s) Objective

Visual gain (ETDRS letters) and the reduction in CRT (central retinal thickness) compared to baseline at 12 months.

#### **Inclusion criteria**

The study subjects will be selected from diabetic macula edema Patients visiting Ho Chi Minh City Eye Hospital from December 1<sup>st</sup>, 2011 to April 30<sup>th</sup>, 2014. Patients must be 18 years or older and consent to participate in the study. Eligible criterion for each eye included in the study are the followings:

- Never treated DME before
- BCVA  $\geq$  19 letters (20/400 Snellen equivalent) and  $\leq$  80 letters (20/25).
- Clinical significant macula edema
- Central retinal thickness  $\geq$  225  $\mu$ m

Both eyes of the same patient were included in the study only when both eyes met the criteria for inclusion and exclusion at the time of randomisation.

#### **Exclusion criteria**

- Previous history of renal failure, kidney transplant or dialysis
- One eye patient
- PRP within 4 months or expected to have PRP in the next 4 months
- YAG laser capsulotomy within 2 months
- Vitrectomy within 6 months

#### Study design

This was an open-label randomized controlled trial. Baseline characteristics included BCVA, CRT, hypertension, hyperlipidemia, insulin use, smoking history, gender, severity of diabetic retinopathy, lens status. Each eligible eye was then randomized to at least 3 monthly intravitreal Bevacizumab (1,25 mg) injections until BCVA stabilization then PRN or standard modified ETDRS focal/grid laser protocol. In cases where both eyes were eligible then one eye will be randomized to a treatment arm and the other eye belonged to the remaining arm. BCVA was measured with ETDRS chart and CRT were measured by Cirrus SD OCT at baseline, 3, 6 and 12 months. All procedures including laser photocoagulation, Bevacizumab injections and treatment for complications, if any, were performed by the investigators. Bevacizumab group was followed up with BCVA and CRT every month while Laser group was followed up every three months and both were treated PRN accordingly. Treatment protocols are summarized in Figure 1



Figure 1 Treatment protocol
Patients in the laser group received focal/ grid laser treatment on Day 1 right after randomization. In the case of failure to receive treatment within the day, the treatment must be completed within 2 weeks from randomisation. After the first treatment, the patient was followed up every 3 months and the investigator would classify the status of macular edema as persistent, recurrent or new. Patients received additional treatment if they met one of the following criteria:

- Macula edema worsens.
- Macula edema recurs.
- Appearance of a new macular edema area.
- Macula edema persists within 500 µm from the fovea. Except when the investigator believed there was improvement from previous visit as > 50% reduction in total macular edema area or > 50% reduction in total thickening retina area.

In the following cases, there will be no further treatment:

- Macula edema resolved
- Macula edema regressed

The re-treatment time for Laser group should occur only at month 3 or 6. Thus, the number of focal/grid laser treatments for each patient in the Laser group should be at least 1 and a maximum of 3.

In the Bevacizumab group, the patient will be given a monthly injection of Bevacizumab, beginning on Day 1 and continuing until BCVA no longer improving or stable (BCVA change within 5 letters). Stable BCVA was determined through three consecutive monthly follow-up visits during the treatment period (the earliest assessment of visual stabilization was done in the third month when comparing the 1, 2 and 3 months). If the patient has stable BCVA (at 3 months or any time afterwards), treatment may be discontinued. Patients are monitored monthly for BCVA and desease activity on OCT. If the disease activity was documented, then treatment will be resumed. Desease activity are defined as the followings:

- Visual loss  $\geq 5$  letters
- Increase CRT >=10% comparing to previous visit
- Recurrent of cystoid macula edema or subretinal fluid
- Recurrent of leakage on FFA

In those cases, patients would be treated monthy with Bevacizumab until VA stabilized again. For VA stability, patient's BCVA needed to be stable in 3 consecutive visits which required at least 2 more treatments. The last treatment was at month 11. The minimum number of injection in this study is 3 and maximum possible injection is 11.

#### Results

#### **Baseline characteristics**

There were 203 patients with diabetic macular edema were eligible for inclusion during screening visits. Of these, 86 patients agreed to participate in the study and signed consent forms. Seven patients were excluded due to exclusion criteria, so the number of patients in the sample was 79. The mean age of the patients was  $53.72 \pm 9.96$  years (32 to 77 years). There were 41 patients (51.89%) were female. The mean diabetes mellitus time was  $8.92 \pm 4.10$  years (2 to 20 years). The mean HbA1C was  $8.10 \pm 1.74$  (4.8 to 13.2). Of the 79 patients mentioned above, 33 (41.77%)

patients had both eyes and 46 (58.23%) patients had one eye being included in the study. Thus, the total number of eyes included in the study was 112 eyes with 79 patients. After randomisation, there were 55 (49.10%) eyes in the Bevacizumab group and 57 (50.90%) eyes in the laser group. The following table (Table 1) will give more details about the characteristics of the study sample.

Table 1. Baseline characteristics						
Patients characteristics	79 patients					
Both eyes included: n (%)	33 (41,77)					
Female: n (%)	41 (51,89)					
Age: Mean ± SD (min-max)	$53,72 \pm 9,96 (32-77)$ year					
Diabetes time: Mean ± SD (min-max)	$8,92 \pm 4,10$ (2-20) year					
HbA1C: Mean $\pm$ SD (min-max)	8,10 ± 1,74 (4,8 - 13,2)					
Smoking history: n (%)	33 (41,77)					
Insulin user: n (%)	28 (35,44)					
Hyperlipidemia: n (%)	49 (62,02)					
Hypertension history: n (%)	50 (63,29)					
Eye characteristics	112 eyes					
OD: n (%)	54 (48,21)					
Phakia: n (%)	82 (73,21)					
Pseudophakia: n (%)	30 (26,79)					
Number of eyes in Bevacizumab group: n (%)	55 (49,10)					
Number of eyes in Laser group: n (%)	57 (50,90)					
Snellen equivalent: n (%)	, í					
<20/100	12 (10,71)					
20/100-20/50	38 (33,93)					
20/40-20/25	62 (55,36)					
BCVA Mean $\pm$ SD (min-max, median)	$64,94 \pm 10,37 (35-80, 66,50)$ letters					
BCVA (Snellen): Mean ± SD	$20/50 \pm 2$ hàng					
Number of treatments: Mean $\pm$ SD (min-max, median)						
Bevacizumab group	7,29 ± 2,33 (3-11,7)					
Laser group	$1,93 \pm 0,75 \ (1-3,2)$					
CRT						
226-275 μm	23 (18,75)					
276-400 μm	49 (43,75)					
>400 μm	40 (37,50)					
CRT: Mean $\pm$ SD (min-max, median)	$383,04 \pm 123,36 (202 - 861, 363,00) \mu\text{m}$					
Leakage in FFA: n (%)						
Focal	42 (37,50)					
Diffuse	44 (39,29)					
Intermediate	26 (23,21)					
Diabetic Retinopathy Severity: n (%)						
No Apparent Retinopathy	2 (1,80)					
Mild/ Moderate Non-Proliferative Diabetic Retinopathy	73 (65,18)					
Severe Non-Proliferative Diabetic Retinopathy	20 (15,16)					
Proliferative Diabetic Retinopathy	17 (17,86)					

#### BCVA and CRT at baseline

Mean BCVA at baseline of Bevacizumab and Laser groups were  $63.80 \pm 10.71$  and  $66.04 \pm 10.01$  letters respectively. Mean CRT at baseline were  $398.75 \pm 137.50$  and  $367.89 \pm 107.05 \mu m$ respectively. The difference between treatment groups in BCVA (p = 0.31) and CRT (p = 0.37, Mann-Whitney U test) was not statistically significant. In other words, the two groups Bevacizumab and Laser share similarities in BCVA and CRT before treatment.

#### **BCVA** after treatment

The mean BCVA of the Bevacizumab group compared with Laser group was as follows:

• 3 months:  $8.53 \pm 6.49$  vs.  $0.61 \pm 10.3$  letters

- 6 months:  $9.78 \pm 7.86$  vs.  $2.33 \pm 11.89$  letters
- 12 months: 12.17 ± 6.65 vs. 2.11 ± 11.84 letters

BCVA in Laser group increased slowly while BCVA in Bevacizumab group increased quickly from month 3. Repeated measures ANOVA showed there was significant difference between the two groups (p < 0.0001), between visits (p = 0.0011) and no interaction between treatment groups over time (p =0.13). Eyes treated with Bevacizumab had better visual acuity than the Laser treated eyes. By the end of the study at month 12, Bevacizumab group gained +10 letters more than Laser group (p = 0.0003; Wilcoxon signed rank test). The following figure (Figure 2) shows BCVA changes comparing to baseline.



Figure 2. BCVA change comparing to baseline by groups

In this study, thirty-three (41.77%) had both eyes participating in the study, with one eye in the Bevacizumab group and the other in the laser group. Mean BCVA in Bevacizumab and Laser groups in these patients was  $65.73 \pm 10.41$  and  $64.85 \pm$ 9.94 letters respectively. Thus, baseline BCVA of the two groups was similar (p = 0.50, Wilcoxon signed rank test).

The mean BCVA of the Bevacizumab group compared with the laser group was as follows:

- 3 months: 8.27 ± 7.09 vs. 1.52 ± 9.16 words
- 6 months: 9.58 ± 8.85 vs. 5.45 ± 8.48 words
- 12 months: 11.69 ± 7.46 vs. 4.25 ± 8.64 words

Repeated measures ANOVA showed that there was a significant difference in BCVA between the two groups (p = 0.0011), between visits (p=0,0062), There was no interaction between treatment groups over time (p = 0.67). In addition, eyes treated with Bevacizumab gained +7.5 more letters comparing to laser treated eyes at month 12 (p = 0.0003, Wilcoxon signed rank test).

At month 12, BCVA gained 15 letters or more in Bevacizumab group was 39.62% while that of the laser group was 8.93% (p = 0.0004, Chi-squared test). BCVA gain 10 letters or more was 64.15% in Bevacizumab group, and 26.79% in Laser group (p = 0.0002, Chi-squared test). BCVA gain 5 letters or more in the Bevacizumab group was 88.68% and that of the Laser group was 48.21% (p <0.0001, Chi-squared test). In the Bevacizumab group, none of the eyes lost 15 or more letters while the laser group had 8.93%, but the difference between the two groups was not statistically significant (p = 0.057, Fisher Exact Test). These statistics are detailed in Table 2.

Table 2. Proportion of BVCA change by groups									
Proportion % (n/ Total)	Bevacizumab	Laser	P value						
BCVA gain $\geq 15$ letters	39,62 (21/53)	8,93 (5/56)	0,0004 (Chi-squared)						
BCVA gain $\geq 10$ letters	64,15 (34/53)	26,79 (15/56)	0,0002 (Chi-squared)						
BCVA gain $\geq$ 5 letters	88,68 (47/53)	48,21 (27/56)	<0,0001 (Chi-squared)						
BCVA loss $\geq$ 15 letters	0 (0/53)	8,93 (5/56)	0,057 (Fisher Exact)						

#### **CRT change after treatment**

The mean CRT change of the Bevacizumab group compared with the laser group was as follows:

- 3 months: -112,8 ± 123,67 vs
   -34,63 ± 89,98 μμm
- 6 months:  $-135,72 \pm 121,93$  vs  $-71,37 \pm 127,55 \ \mu\mu m$
- 12 months: -143,89 ± 127,54
   vs -89,96 ± 127,62 μμm

CRT in Lasergroup slowly regressed while CRT in Bevacizumab group regressed significantly from month 3 (Chart 2). Repeated measures ANOVA showed that there was a significant difference in CRT change between the two groups (p = 0.03, between visits (p < 0,0001), There was no interaction between treatment groups over time (p = 0.10).



Figure 3. CRT change comparing to baseline by groups

#### Discussion

In this study, there were 79 patients with 112 eyes participating in the study. The Bevacizumab group had 55 eyes and the Laser group had 57 eyes. Follow-up completion rate at 6 and 12 months were 99.11% and 97.32% respectively. The proportion of men and women in this study is similar. Mean age in the sample was 53.72. There were 72% of patients enrolled in the study with HbA1C> 7. This indicated a poor glycemic control. In addition, about 50% of patients have hyperlipidemia and/or hypertension. Of the 79 patients enrolled in the study, 28 (35%) were treated with insulin. Mean visual acuity of patients in the study was 65.95 ETDRS letters (20/50 Snellen equivalent). Sixty-seven percent of patients had mild/moderate diabetic retinopathy. Median number of treatments for Bevacizumab group was 7 and Laser group was 2.

BCVA of the two groups Bevacizumab and Laser were similar before treatment. The treatment outcome of the Bevacizumab group was better than that of the laser group at all time points in the study at 3,6 and 12 months. BCVA gain in Bevacizumab group was two lines (10 letters) better than that of the laser group at 12 months. There were 77.36% (approximately 4/5) patients treated with Bevacizumab had BCVA at 12 months  $\geq$ 20/40 vs 51.49% in the laser group. This level of BCVA is an important milestone in which the patient could function normally, such as driving a car, watching television and reading. The number of eye gain at least 3 lines (15 letters) in the Bevacizumab group was 39.62% which was 4.4 times higher than the laser group at 8.93%. No patients in the Bevacizumab group lost three or more lines compared with 8.93% of the laser group. Thus, treatment with bevacizumab has a significantly higher rate of visual acuity gain and visual loss reduction compared with laser treated eyes. These observations are well comparable to many other studies in the literature. <sup>5,8,12</sup>.

#### Conclusion

Bevacizumab PRN was more effective in treating diabetic macular edema than a focal/grid laser in this 12month period study for both visual acuity and reduction in CRT for diabetic macular edema treatment.

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## Clinical features of neuromyelitis opticarelated atypical optic neuritis in Thammasat hospital.

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**Purpose:** To study the clinical features of optic neuritis in patients with neuromyelitis optica (NMO) in Thammasat Hospital.

**Design**: Retrospective case series

*Material and Method*: The author reviewed the medical records of 12 patients who had optic neuritis with atypical features managed at Thammasat Hospital between October 1, 2015 and June 30, 2016. The baseline characteristics including age, gender, underlying systemic diseases, laterality of visual loss, best corrected visual acuity (BCVA), optic disc appearance, color vision, visual fields, positive laboratory investigations, visual evoked potential (VEP), cerebrospinal fluid (CSF) analysis, magnetic resonance imaging (MRI) findings, and serostatus of aquaporin 4-Immunoglobulin G (AQP4-IgG) were analyzed.

**Results**: Five from 12 patients had clinical features of neuromyelitis optica spectrum disorder (NMOSD) diagnostic criteria for adult patients. All were healthy female and they had a mean age of 42.2 years (range 13 to 54 years). Two patients had bilateral simultaneous involvement, one patient had bilateral sequential involvement within 2 years, and another two patients had unilateral involvement. All had severe visual loss, initial BCVA worse than 20/200. Three patients had retrobulbar optic neuritis and two patients had anterior optic neuritis. We cannot perform the color vision and visual field due to the patient. VEP showed evidence of demyelinating optic neuropathy. The CSF analysis was all normal. All patients had normal brain MRI findings with two patients had bilateral optic nerve enhancing lesions. One patient developed acute transverse myelitis following optic neuritis. All had positive test for AQP4-IgG by using available detection method.

**Conclusions**: The present study demonstrated that patients with atypical clinical features are more likely to develop NMOSD 5 from 12 patients. NMOSD should be suspected in patients with the clinical signs revealed aspects that were not typical for demyelinating optic neuritis.

Keywords: Neuromyelitis optica, Optic neuritis, Aquaporin-4, Multiple sclerosis EyeSEA 2017; 12 (1): 29-39 Full text. <u>https://www.tci-thaijo.org/index.php/eyesea/index</u>

#### Introduction

Typical optic neuritis is a demyelinating inflammation of the optic nerve that often occurs in isolated or association with multiple sclerosis (MS). Typical clinical features will present as subacute unilateral visual loss that is progressive over several days associated with periorbital pain that precedes visual loss or occur simultaneously.<sup>1</sup> Atypical optic neuritis often occurs in association with infectious, autoimmune, or systemic inflammatory diseases. Atypical clinical features may present as bilateral visual loss, lack of pain, severe pain or severe visual loss, signs of ocular inflammation, or lack of spontaneous visual recovery within one month.

Neuromyelitis optica (NMO) or the new term; neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune demyelinating CNS disorder which primarily attack the optic nerve, spinal cord and causing some part of the brain lesions at certain sites such as the hypothalamus.<sup>2</sup> NMOSD has a higher non-Caucasians.<sup>3-4</sup> among incidence NMOSD-related optic neuritis is most often characterized by episodes of bilateral onset, chiasmal involvement, altitudinal visual field defect, or visual acuity 20/200 or worse. Most patients have serum AQP4-IgG and these specific antibodies are required as one of diagnostic criteria. The criteria for diagnosis of **NMOSD** are the manifestation at least 1 of 6 CNS regions: optic nerve, spinal cord, area postrema of the dorsal medulla, brainstem, diencephalon, or cerebrum.<sup>5</sup> NMOSD must be differentiated from MS in patients with optic neuritis because no

clinical characteristic is pathognomonic of NMOSD such as bilateral simultaneous optic neuritis may also occur in MS. Whether all optic neuritis patients should be tested for AQP4-IgG remains controversial.<sup>6-7</sup>

The objective of the present study was to review the clinical features of optic neuritis in patients with NMO in Thammasat Hospital for the planning of investigations in patients presenting with atypical optic neuritis.

#### **Materials and Methods**

The study was approved by the Medical Ethics Committee of Thammasat University (MTU-EC-OP-0-141/58), Pathum thani, Thailand, and was conducted in accordance with the tenets of the Declaration of Helsinki. The author reviewed the medical records of 12 patients who had optic neuritis with atypical features managed at Thammasat Hospital between October 1, 2015 and June 30, 2016. Patients with unilateral or bilateral optic neuritis with visual symptoms for 14 days or less were enrolled. The inclusion criteria included the diagnosis of NMOSD following the International Panel for NMO Diagnosis (IPND) either (1) Diagnostic criteria for NMOSD with AQP4-IgG require at least one of six core clinical characteristics plus AQP4-IgG seropositivity. Six core clinical characteristics included optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with typical diencephalic MRI lesions, and symptomatic cerebral syndrome with typical brain lesions. (2) Diagnostic criteria for NMOSD without AQP4-IgG or unknown AQP4-IgG status require at least two of six core clinical characteristics in which at least one core clinical characteristic must be optic neuritis, acute myelitis with longitudinal extensive transverse myelitis (LETM), or area postrema syndrome. AQP4-IgG were negative test by using best available detection method. Additional findings for acute optic neuritis in NMO requires brain MRI showing normal findings or only nonspecific white matter lesions, or orbital MRI showing T2-hyperintense or T1-weighted gadoliniumlesion enhancing lesion extending over 1/2 optic nerve length or involving chiasm.

The patients who had any incomplete medical records, duration of follow-up less than 6 months, infectious disease that can cause infectious optic neuropathy such as syphilis, tuberculosis and evidence of alternative diagnoses such as other demyelinating diseases were excluded. The patient data including systemic age, gender, underlying diseases, laterality of visual loss, BCVA, optic disc appearance, color vision, visual fields, positive laboratory investigations, VEP, CSF analysis, MRI findings, and serostatus of AQP4-IgG were collected. The optic disc appearance and the retinal nerve fiber layer (RNFL) were analyzed by stereo optic disc photography and the optical coherence tomography (OCT). Contrast-enhanced MRI brain and orbit with gadolinium were performed in all cases and the enhancing optic nerve lesion interpreted was by а neuroradiologist. Contrast-enhanced MRI spine did was not performed in all cases because the decision to investigate will

depend upon the signs and symptoms of spinal cord lesions. Examination of serum AQP4-IgG was done at the Prasart Neurological Institute by using cell-based indirect immunofluorescence assay (CBA) method. The available commercial CBA assay vielded sensitivity of 68% and specificity of 100%. The time to interpretation is about 5 working days. Statistical analysis was performed with SPSS software version 20.0 (IBM Inc, Chicago, IL). Data described in number and range.

#### Results

Five from 12 patients had clinical features of NMOSD diagnostic criteria for adult patients. All were healthy female and they had a mean age of 42.2 years (range 13 to 54 years). One patient had retrobulbar pain with eye movement. Two had bilateral patients simultaneous involvement, one patient had bilateral sequential involvement within 2 years, and another two patients had unilateral involvement. All had severe visual loss, initial BCVA worse than 20/200. Three patients had normal disc appearance (retrobulbar optic neuritis) and two patients had swollen disc (papillitis or anterior optic neuritis). We cannot perform the color vision and visual field in some patient which had severe visual impairment. VEP showed prolong P100 latency and decreased amplitude in affected eye. One patient had no P100 response in the affected eye with BCVA of no light perception. Investigations of serum inflammatory markers include erythrocyte sedimentation rate. Creactive protein, and serum autoimmune markers include rheumatoid factor, lupus

anticoagulant, anti-cardiolipin IgM and IgG, anti-double stranded DNA antibody, anti-neutrophil cytoplasmic antibody, and anti-nuclear antibody revealed negative, except one patient was positive for anticardiolipin IgM. Routine laboratory tests for starting systemic corticosteroids were all normal. All patients were consulted with neurologist and underwent a lumbar puncture procedure. The CSF analysis revealed normal opening CSF pressure, protein level, sugar level, oligoclonal bands, and cytology. All patients had normal brain MRI findings with 2 patients had bilateral optic nerve enhancing lesions. MRI of whole spine showed no hyperintense intramedullary lesion or cord enlargement in 4 patients, but in one patient who developed episode of numbness and paraparesis of both legs following optic neuritis had hyperintense

lesions with focal cord enlargement in cervical 2<sup>nd</sup>-6<sup>th</sup> segments which correlated with acute transverse myelitis. All had positive test for AQP4-IgG by using available commercial CBA assay method.

All patients received high-dose intravenous methylprednisolone (IVMP) (1 gram/day) for 3 days in 4 patients and extend for 5 days in one patient. Then patients were received oral prednisolone (1 mg per kg body weight). After the diagnosis of NMO was confirmed by AQP4-IgG seropositivity, the patient was scheduled to continue oral prednisolone for several months then tapered over to azathioprine for long-term treatment. During the follow-up period, one patient developed erythematous skin rash from azathioprine-induce photodermatosis, the drug was stopped and the patient was received long-term corticosteroid instead

Table	1	Patients	data	
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Case	Age	Gender	Laterality	Visual	Initial	Final BCVA	Optic	MRI
				symptoms	BCVA		disc	findings
1	13	F	Bilateral	10 days	20/20,	20/20,20/20	Swollen	Enhancing
			sequential		PL		disc	nerve(s), cervical cord lesions
2	38	F	Unilateral	5 days	5/200,	20/50,20/20	Swollen	Normal
					20/20		disc	
3	52	F	Unilateral	5 days	HM,	5/200,20/50	Normal	Normal
					20/50		disc	
4	54	F	Bilateral	3 days	NPL,	HM,20/200	Normal	Enhancing
			simultaneous		Fc1foot		discs	optic nerves
5	54	F	Bilateral	1 day	PJ, PJ	5/200,Fc 1ft	Normal	Enhancing
			simultaneous				discs	optic nerves

#### **Selected Case Summaries**

Case 1: A 13-year-old female presented with acute visual loss in the left eye preceded by periorbital pain which worsened on eye movement followed by a decreased vision in the right eye vision 2 years later. Initial BCVA were was 20/20 OD and light perception (PL) OS with relative afferent pupillary defect (RAPD) in the left eye. The left optic disc was swollen. MRI of the brain and orbit with gadolinium contrast showed mild enhancement of left optic nerves in T1weighted images. No evidence of periventricular white matter lesion in FLAIR T2-weighted images (Figure 1).

Investigations of serum inflammatory markers revealed to be negative. Lumbar puncture revealed normal CSF analysis and negative oligoclonal bands. We suspected idiopathic demyelinating optic neuritis. The patient received high-dose IVMP (1 gram/day) for 3 days followed by oral prednisolone (1 mg per kg body weight) then taper within few weeks. The BCVA of her left eye was improved to counting fingers at 3 feet and 20/20 at 6 months. Two years later, the patient developed recurrent optic neuritis in her right eye and numbness and paraparesis of both legs. Repeat CSF analysis was all normal. Repeat MRI brain and orbit revealed mild enhancement of right optic nerve without brain lesions (Figure 2). MRI spine revealed hyperintense lesions with focal cord enlargement in cervical 2<sup>nd</sup>-6<sup>th</sup> segments which correlated with acute transverse myelitis (Figure 3). Serum AQP4-IgG was positive. The patient received pulse IVMP again and continued oral prednisolone for several months then tapered over to azathioprine for long-term treatment. The final visions were 20/20 OU with bilateral optic atrophy. The color visions were normal in both eyes. The visual field defects were inferior altitudinal defect in the right eye and normal field in the left eye (Figure 4).



Figure 1 shows gadolinium-enhancing left optic nerve lesions in fat-suppressed T1weighted orbital MRI.



Figure 2 shows gadolinium-enhancing right optic nerve lesions in fat-suppressed T1weighted orbital MRI.



Figure 3 show hyperintense lesions with focal cord enlargement in cervical 2<sup>nd</sup>-6<sup>th</sup> segments in whole spine MRI.



Figure 4 shows visual field of inferior altitudinal defect in the right eye and normal field in the left eye

54-year-old Case 2: female А presented with acute bilateral simultaneous painless visual loss. Initial BCVA were was no light perception (NPL) OD and counting fingers at 1 foot OS with RAPD in the right eye. The optic discs were normal appearance. MRI of the brain and orbit with gadolinium contrast showed enhancement of intraorbital part of bilateral optic nerves without brain lesions (Figure 5). Investigations of serum inflammatory markers revealed positive for anti-cardiolipin IgM. Lumbar puncture revealed normal CSF analysis and negative oligoclonal bands. We suspected NMOSD-related optic neuritis. VEP showed no P100 response in the right eye and prolong P100 latency in the left eye. The

patient received high-dose IVMP (1 gram/day) for 5 days followed by oral prednisolone (1 mg per kg body weight). After the diagnosis of NMO was confirmed by AQP4-IgG seropositivity, the patient was scheduled to continue oral prednisolone for several months then tapered over to azathioprine for longterm treatment. At 6 months, the BCVA were NPL OD, count finger counting fingers at 2 feet OS. At one year after initial attack, the BCVA were improved to hand motion (HM) OD and 20/200 OS with bilateral optic atrophy (Figure 6). We cannot could not perform the color vision and visual field tests due tobecause the patient still had suffered from severe visual impairment.



Figure 5 shows bilateral gadolinium-enhancing optic nerve lesions in fatsuppressed T1-weighted orbital MRI.



Figure 6 shows bilateral optic atrophy

#### Discussion

Optic neuritis was characterized with decreased vision, dyschromatopsia, RAPD and visual field defect. The optic disc may appear normal or swelling, the term retrobulbar optic neuritis and papillitis was used respectively. When the clinical features suggest typical optic neuritis, at young ages (18-45 years old) patients will present with acute/subacute unilateral visual loss that progressive over several days. Most patients (92%) have associated periorbital pain which may precede the visual loss by days or occur simultaneously, and pain was worsened by eye movement. These features can help for help in the clinical diagnosis in that typical optic neuritis is mostly related to isolated or demyelinating disorders particularly MS.

In NMOSD. the immunemediated inflammation primarily attacks the AQP4 water channels resulting in loss of astrocytic AOP4 and disruption of water homeostasis. The pathophysiology features of NMOSD include perivascular of immunoglobulin deposition and activated complement, leukocytes migration and macrophage infiltration and secondary demyelination with axonal loss. NMOSD had characterized by optic neuritis and transverse myelitis and some part of the brainstem involvement. The disease can be monophasic or relapsingremitting form.<sup>8</sup> In monophasic form, optic neuritis and transverse myelitis occur simultaneously or within days of each other. In relapsing form, patients often have a relapse weeks or months after the initial attack.9 NMOSD rarely has a secondary progressive phase without remission. Optic neuritis are often more severe after an NMO attack than an MS attack and some patients have permanent visual loss.<sup>10</sup> Acute treatment is high-dose corticosteroids; IVMP 1 g for 5 days followed by prednisolone (1 mg per kg body weight). If the AQP4-IgG titers return as positive, prednisolone should be continued and immunosuppressant agents should be considered to prevent relapse. Some patients may need a low dose of prednisolone to maintain remission. Most patients need prednisolone at dose 0.5-1 mg/kg for up to 3 months after an attack, and then a slow tapering off over 6-12 months.11

We reported five cases of seropositive NMOSD related-optic neuritis. All were healthy female and they had age range of 13-54 years which is correlated to the demographic data of NMOSD including a predilection of female gender and the typical age range usually 15-50 years. Four patients lacked retrobulbar pain with eye movement which could be related to the clinical features of atypical optic neuritis. Most cases had bilateral involvement; one of five patients had recurrent episode of visual loss in the fellow eye (relapsing form) and this patient also had optic neuritis and transverse myelitis which occur simultaneously. These findings could be related to the clinical features of frequency of the high bilateral involvement and lack of the retrobulbar pain with eye movement in the early phase of NMOSD, respectively. All had severe visual impairment in the initial phase, two patients had delayed good visual recovery and three patients had delayed insufficient visual recovery

which could be related to the clinical features of severe disability in NMOSD.<sup>12</sup> All had no underlying systemic disease, but one patient was positive for anticardiolipin IgM which could be related to the clinical features of NMOSD that is frequently associated with systemic autoimmune disorders, or with the presence of serum autoantibodies. All patients had normal brain MRI findings with 2 patients having bilateral optic nerve enhancing lesions although the enhancing lesions not extending did not extend over 1/2 optic nerve length or chiasm. Enhancing involving the gadolinium of optic nerve lesion is found about 90 percent of optic neuritis, which can be found on average 30 days after the onset of visual symptoms.<sup>13</sup> The duration ofqueue for an the MRI order in our hospital sometimes can be as long it's quite a long time can is long, at times lasting about 1 to 2 weeks. Some patients in the present study received intravenous corticosteroids treatment before they underwent MRI, so only 2 patients had optic nerve enhancing lesions. One patient had hyperintense lesions with focal cord enlargement equal or more than 3 contiguous vertebral segments which could be related to the clinical features of longitudinal extensive transverse myelitis (LETM) in NMOSD.<sup>14</sup> All had positive test for using AOP4-IgG by available commercial CBA assay method which could be indicate that AQP4-IgG is directly related to optic neuritis in our cases.

The major limitation of the present study is the small sample size. Only 12 participants enrolled within 9 months, which may be explained from by the insufficient numbers of number of case of optic neuritisoptic neuritis cases in our hospital is still insufficient and we should extend the time period for the further study. In conclusion, the present study demonstrated that patients with atypical clinical features are more likely to develop NMOSD in 5 from 12 patients. NMOSD should be suspected in patients with the clinical signs revealed aspects that were not typical for demyelinating optic neuritis.

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# Measurement of choroidal thickness and volume with spectral domain optical coherence tomography: variation with age, gender and ethnicity.

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**Objective**: To evaluate the subfoveolar choroidal thickness (SFCT) and choroidal volume (CV) in variation to age, gender and ethnicity among healthy individuals.

**Study design and method**: This was a cross sectional hospital based study done in Selayang Hospital. A total number of 113 healthy subjects were recruited. All subjects were scanned using the spectral domain-optical coherence tomography (SD-OCT) machine using the enhance depth imaging (EDI) mode. The subfoveolar choroidal thickness and choroidal volume were then measured using the build-in thickness map software of the proprietary machine and were then evaluated in variation to age, gender and ethnicity.

**Results**: The overall mean age was 39.58 ( $\pm$ 14.71) years. Mean SFCT was 320.08 ( $\pm$ 56.08) µm and mean CV was 8.10 ( $\pm$ 1.212) mm<sup>3</sup>. Linear regression analysis showed reduction of 1.78 µm of thickness and 0.042 mm<sup>3</sup> of volume respectively per year of age. The mean SFCT in males was 335.13( $\pm$ 58.93) µm and 307.25( $\pm$ 50.55) µm in females. Mean CV was 8.52( $\pm$ 1.35) mm<sup>3</sup> for males and 7.74( $\pm$ 0.96) mm<sup>3</sup> for females. Indians had mean SFCT 342.18 ( $\pm$ 55.08) µm and CV 8.58( $\pm$ 1.01) mm<sup>3</sup>. There were no significant differences of these values between Malay and Chinese groups with p values >0.95.

**Conclusion**: SFCT and CV decreases with age. Females had generally thinner SFCT and lesser CV as compared to males. There were no significant variations of SFCT and CV between ethnic groups. However Indian subgroup had a greater SFCT and CV.

Keywords: choroidal thickness; choroidal volume; enhance depth imaging; OCT

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#### Introduction

Adequate visualization of the choroid using OCT has been made possible by using the enhanced depth imaging (EDI) mode. Spaide et al<sup>1</sup> reported successful examination and measurement of choroidal thickness with this technique using the Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany) OCT instrument.

The EDI employs the ability of the spectral domain (SD) OCT systems to show an inverted image when the device is moved close to the patients' eye, allowing images of deeper structures such as the choroid to be closer to the zerodelay line. This technique produced an enhanced sensitivity for the deeper ocular structures which increase the imaging depth and the resultant visibility of the choroidal layer.

Previous reports had demonstrated variations of choroidal parameters in normal and pathologic states using the SD-OCT instruments. The choroid thickness is found to be increased in cases of active Vogt-Koyanagi-Harada disease and central serous chorioretinopathy. In age related degeneration and macular diabetic macula edema, the choroidal thickness is decreased. often These variations suggested that the choroidal thickness and volume could be important parameters in the evaluation of ocular disease.

To understand the significance of these potential differences, normative values for choroidal thickness and volume would appear to be important for reference purposes. Accordingly, a number of investigators have studied and reported normative values for choroidal thickness and volume in different populations.<sup>2,3,4,5,6</sup> The values between different studies were observed to be variable. This limits application of the available data on patients from different backgrounds and thus difficult to establish a clear threshold between normal and pathologically choroidal profile in a clinical setting

Therefore, our study was done to contribute in developing a locally based normative data to help clinicians in evaluating patients with various chorioretinal disorders by providing them a normative value for references. In this study, we measured the subfoveal choroidal thickness and choroidal volume as well as to evaluate its relation to age, gender, and ethnicity among healthy individuals.

#### Methodology

This cross sectional study was performed between 1<sup>st</sup> November 2014 until 30th October 2015 with subjects randomly recruited from staffs and visitors of Selayang Hospital, Selangor, Malaysia. Eligible individuals were selected and written consent was obtained from each volunteers. The study was conducted in accordance to the Malaysian Guidelines for Good Clinical Practice (GCP) and the Declaration of Helsinki. and the Declaration of Helsinki. Sample size was calculated using Power and Sample Size Calculation software version 3.0.43 (Dupont WD, Plummer WD: 'Power and Sample Size Calculations: A Review and Computer Program', Controlled Clinical Trials 1990; 11:116-28). Based on mean differences from previous studies<sup>5,8</sup> with the Confidence Interval of 95%, Power 80% and ratio of sample size 1, the calculated sample size was 114 subjects.

All volunteers underwent screening test for blood pressure, sugar level and ophthalmologic examination. Accepted blood pressure level was ≤140/90mmHg and blood sugar level  $\leq$ 11.1mmol/l. The inclusion criteria were individuals aged 18 years old and above of either gender. Subjects were either Malay, Chinese or Indian ethnicity with ocular axial length between 23.00 to 24.50 mm. Exclusion criteria were individuals who were diagnosed with systemic illness such as diabetes mellitus, hypertension, connective tissue diseases and malignancies; any co-existing ocular disease except age related cataract with good fundus view and subjects who had undergone any form of previous ocular surgery, laser procedures or intra/peri ocular injections. Subjects with poor image quality scans i.e poor demarcation of choroidoscleral interface and signal strength of less than 7 were excluded as well.

Eligible subjects had their eyes scanned by an experienced operator using the Heidelberg Spectralis Spectral Domain Optical Coherence Tomography, Software version 1.9.10.0 (Heidelberg Engineering, Heidelberg, Germany). Data from either the right or left eye were used and analyzed for the study purposes.

All subjects were scanned twice, each for choroidal volume and subfoveal choroidal thickness evaluation. Scanning for choroidal volume were done using a standardized scanning protocol as described previously by Barteselli G et al<sup>7</sup>. A 31 high-resolution B- scans (9.0mm in length) covering an area of 30° x 25  $^{\circ}$ centered on the fovea spaced 240µm apart from each other was performed in each eye. An internal fixation light was used to center the scanning area on the fovea. A minimum of 50 frames were automatically averaged and used to obtain a choroidal image using the built-in TruTrack Active Eye Tracking software of the device (Heidelberg Engineering). The enhanced depth imaging (EDI) mode optimize were used to choroidal sensitivity and enhance visualization of the full choroidal thickness.

For subfoveal choroidal thickness, a standardized scanning protocol of 7 high resolution B-scans, covering an area of  $30^{\circ} \times 5^{\circ}$  centered at the fovea with 100 frames averaged were done using the EDI mode.

To assess the choroidal volume. choroidal segmentations were performed manually after the automated retinal layer segmentation software was disabled. The reference lines of the built- in automated segmentation were moved from the retinal boundaries to the choroidal boundaries. The internal limiting membrane line was moved to the outer part of the hyper- reflective line of Bruch's membrane. The basement membrane line, which was the reference line for the posterior edge of the retina, was shifted to the posterior edge of the choroid as demarcated by the hyperreflective margin line corresponding to choroidoscleral the interface. This method would allow the use of the automatic retinal thickness/volume map of the proprietary built-in features software to calculate the choroidal volume.

The standardized grid which followed the ETDRS grid that divides the macula into three circles with diameters of 1 mm (central), 3 mm (inner), and 6 mm (outer) were positioned automatically by the Spectralis OCT software that designed to map macular thickness. Both inner and outer rings were further divided into nasal, temporal, superior and inferior quadrants. The values for overall total average choroidal volume and volume within each subfield of the standardized grid were then evaluated. Refer Figure 1.

The subfoveal choroidal thickness was assessed by selecting the horizontal section of choroid corresponding at the foveal center. Manual segmentation of the choroidal layer was done in the similar manner as



described for choroidal volume measurement. The choroidal thickness were measured perpendicularly from the Bruch membrane line to the choroidoscleral interface line at the subfoveola region using the automatic built in measurement software.

22 eyes were selected randomly for a repeat measurement of choroidal parameters to assess the reproducibility and reliability of method of measurement. The choroidal parameters were measured by the principle researcher and

medical retina specialist, in which both were masked from each other's measurements.

All data were analyzed using SPSS V 22 (SPSS Inc, Cary, NC), with the level of significance set at less than 0.05%.

Figure 1 EDI OCT macula A: 31 B scans protocol. B: Standardized grid including three concentric rings with a total of nine subfields centered on the fovea. C: Automated retinal segmentation and manual choroidal segmentation. Internal limiting membrane line (red arrows) and basement membrane line (blue automated retinal arrows) on segmentation is moved to the base of retinal pigment epithelium (orange arrows) and choroidoscleral interface (green arrows) to demarcate choroidal boundaries. D: Delineation of posterior edge of choroid. A curve line is constructed at the inner most zone of the hyper-reflective margin line corresponding to the choroidoscleral interface using the built in segmentation software.

#### Results

113 out of 118 healthy eyes were included. Five were excluded due to poor delineation of choroidoscleral junction. There were 61 females and 52 males. 41 were Malays, 39 Chinese and 33 Indians respectively. Mean age was  $39.58 (\pm$ 14.71) years old.

The overall mean subfoveal choroidal thickness was  $320.08 \ \mu m$  (±56.08) and choroidal volume was 8.10 (± 1.212) mm<sup>3</sup>.

The mean subfoveal choroidal thickness (SFCT) of subjects <40 years old was  $335.42\mu$ m, between 40 to 60 years old was  $302.85\mu$ m and > 60 years old was  $262.22\mu$ m. Further Post hoc (Bonferroni) analysis test noted a significant difference between subjects <40 years old compared to subjects in the other two groups of  $\geq$ 40 years old with p value of 0.011 and p<0.001 respectively.

The mean choroidal volume (CV) among subjects of <40 years old was 8.47 mm<sup>3</sup>. Subjects within the 40-60 years old group had a mean CV of 7.74 mm<sup>3</sup> whereas the older age group >60 years old had a lower CV, with mean of 6.46 mm<sup>3</sup>. These differences of mean values were statistically significant in all 3 groups with p< 0.05.

Linear regression analysis showed that subfoveal choroidal thickness declined by  $1.78 \mu m$  and choroidal volume decline by 0.042 mm3 with every year increase in age.

The mean SFCT in males was significantly thicker as compared to females with the value of 335.13um ( $\pm$ 58.93) µm and 307.25 ( $\pm$ 50.55) µm respectively, p = 0.008. The mean CV in males was also significantly higherµ at 8.52 ( $\pm$ 1.35) mm<sup>3</sup> in comparison to 7.74 ( $\pm$ 0.96) mm<sup>3</sup> in females, p= 0.001.

Indian subjects had mean SFCT 342.18 ( $\pm$ 55.08) µm and CV 8.58( $\pm$ 1.01) mm<sup>3</sup>. There were no significant differences of these values between Malay and Chinese subjects with p values >0.95.

Refer table 1 for summary of results.

Variables	n (%)	Mean SFCT (SD)	Mean CV (SD)
		μm	mm <sup>3</sup>
Age group			
< 40 years old	71 (62.8)	335.42(50.48)	8.47 (1.08)
40-60 years old	33 (29.2)	302.85 (54.68)	7.74 (1.11)
> 60 years old	9 (8.0)	262.22 (51.99)	6.46 (0.84)
Gender			
Female	61 (54.0)	307.25 (50.55)	7.74 (0.95)
Male	52 (46.0)	335.13 (58.93)	8.52 (1.35)
Ethnic group			
Malay	41 (36.3)	311.56 (51.38)	7.84 (1.26)
Chinese	39 (34.5)	310.33 (9.24)	7.97 (1.23)
Indian	33 (29.2)	342.18 (55.08)	8.58 (1.01)

Table 1 Demographic characteristic, mean SFCT and mean CV of study subjects

#### Discussion

Many studies measuring the choroid using SD OCT had been done in both healthy and in various ocular diseases over recent years. However, only a handful of studies on healthy Asian subjects had been published. These previous studies had observed the healthy mean subfoveal choroidal thickness, as scanned by Spectralis SD-OCT, to be ranging from 261.93µm to 340 µm.<sup>8,9,10,11</sup> Please refer Table 2.

Our study produced the mean SFCT of  $320.08 \pm 56.08 \mu m$  which is within the normal variations of choroidal thickness values reported. These variations between studies could be due to the difference in study population in which choroidal thickness was influenced by age, gender, refraction, axial length as well as ethnicity.12

It had been suggested in literature that choroidal thickness decreased with increasing age.<sup>8,12,13</sup> Margolis and Spaide<sup>13</sup> quoted 15.6  $\mu$ m decrease in choroidal thickness for every 10 years. The current study also showed similar results in which a reduction of SFCT of 1.78  $\mu$ m per year was observed across both gender and all ethnic groups when the entire cohort was compared.

We found that the SFCT was significantly thicker in males as compared to females, similar to studies done by Li<sup>5</sup> in 93 Danish students and Ding and colleagues.<sup>8</sup> In contrast, some studies did not observe any gender-related differences in choroidal thickness.<sup>11,14</sup>

Our results have also shown that Indian subjects had thicker SFCT as compared to Chinese with P value of 0.046. We propose a study with larger sample size to look further into the ethnicity factor. Bafiq et al<sup>11</sup> had categorized their subjects into white, black and south Asian (Indian subcontinents) with 30 subjects in each group. They observed no difference of SFCT between those groups but noted that the temporal choroid in eyes of black to be significantly thinner compared to whites and South Asians.

Sanchez et al<sup>14</sup> reported overall mean choroidal volume of  $8.99 \pm 1.88$ mm3 (mean age  $23.8 \pm 3.2$  years), similar to our results  $8.10 \pm 1.212$  mm<sup>3</sup> (mean age  $39.58 \pm 14.71$  years). Hirata and associates<sup>6</sup> reported lower values of 5.411 $\pm 2.097$ mm<sup>3</sup> (mean age 65 years), The variations in the mean value between these studies could be related to the difference in the mean age of the study population.

We found that similar to the SFCT, the choroidal volume was negatively related to age as noted in other studies.<sup>4,14,15</sup> The exact mechanisms behind choroidal thinning with age are still not clear. Previous studies on histologic evaluation had shown a reduction in vascular density, luminal area, and diameter of the choriocapillaries in aging eyes.<sup>16</sup>

The choroidal volume in males were observed to be higher when compared to females. The difference of these values could be related to the influence of sex hormones on the choroidal blood flow. Kavroulaki D et al<sup>17</sup> had observed that premenopausal females have higher choroidal blood flow as compared to postmenopausal females.

Our study has provided normative data on subfoveal choroidal thickness and choroidal volume amongst healthy individuals of Malay, Chinese and Indian ethnicity in a single tertiary hospital in Selangor, Malaysia. Strengths of this study include the inclusion criteria for subjects with axial length between 23.00-24.50 mm (mean 23.76 ±0.46mm), which was within the range of emmetropic eyes. Readings of blood pressure and random blood sugar level were also taken, apart from the subject's self-declaration that they were healthy.

Another limitation of this study was a small sample size among subjects above 60 years old.

this In current study, the choroidal segmentations were done manually and thus would subject to error compared to automatic segmentations technique. However, although the choroidoscleral junctions were delineated manually, our data showed good intergrader agreements with the ICC values ranging between 0.83 to 0.99 indicating a high degree of reliability. Refer Table 3.

We recommend future studies with larger sample sizes to establish a local choroidal normative database including pediatric and elderly age group.

	X Ding et al <sup>8</sup>	Kim MK et al <sup>10</sup>	Tan CSH et al <sup>9</sup>	Bafiq R et al <sup>11</sup>	Our study
Mean Age (SD) years	49.73(±17.9)	40.18 (±17.9)	23.0 (±1.9)	35.0 (±15)	39.58(± 14.7)
Ethnicity	Chinese	Korean	Chinese	Indian	Malay, Chinese,
	(China)	(Seoul)	(Singapore)	(UK)	Indian (Malaysia)
Mean SFCT (SD) μm	261.93 (±88.42)	307.26 (±95.18)	326.4 (±95.2)	340.0 (±44.6)	320.08 (±56.08) *M-311.56 (±51.38) *C- 310.33 (±57.71) *I- 342.18 (±55.14)
OCT type	Spectralis	Spectralis	Spectralis	Spectralis	Spectralis
	SD OCT	SD OCT	SD OCT	SD OCT	SD OCT
Scan	EDI: 100	EDI: 100	EDI:25-35	EDI: 24	EDI: 100 ART
Protocol	ART	ART	ART	ART	

Table 2	: Com	parison	of mean	SFCT	in d	lifferent	studies	among	healthy	Asians
								0	2	

• M-Malay C-Chinese I-Indian

Measurements	ICC*	95% CI	P-value
SFCT100	0.83	0.59, 0.93	< 0.001
SFCT50	0.94	0.80, 0.98	< 0.001
Central CV	0.97	0.92, 0.99	< 0.001
Inner nasal (IN)	0.98	0.94, 0.99	< 0.001
Inner temporal (IT)	0.98	0.93, 0.99	< 0.001
Inner superior (IS)	0.97	0.94, 0.99	< 0.001
Inner inferior (II)	0.83	0.60, 0.93	< 0.001
Outer nasal (ON)	0.97	0.89, 0.99	< 0.001
Outer temporal (OT)	0.99	0.97, 1.00	< 0.001
Outer superior (OS)	0.98	0.95, 0.99	< 0.001
Outer inferior (OI)	0.98	0.96, 0.99	< 0.001
Total CV	0.99	0.92, 1.00	< 0.001

 Table 3 Reliability of measurements by two raters

\*ICC (2,k): Two way random, average measures

The ICC values for all the measurements were high (ranges from 0.83 to 0.99) indicating a high degrees of reliability.

#### Conclusion

This study has profiled the choroidal thickness and volume among healthy adults which has been evaluated by age, sex, and ethnicity. We found that the subfoveal choroidal thickness and choroidal volume decreases with age. Females had generally thinner SFCT and lower CV as compared to males. There were little variations between ethnic groups however Indian subgroup has a slightly greater subfoveal choroidal thickness and volume. We hope that this will provide basic information that could be useful for further studies evaluating choroidal changes and for facilitation in managing patient with various choroidal disorder.

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# Visual field recovery after pars plana vitrectomy procedure for rhegmatogenous retinal detachment.

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**Objective:** To evaluate visual field recovery after pars plana vitrectomy procedure for rhegmatogenous retinal detachment.

Design: Prospective case series.

*Method:* The series was conducted in 8 patients (8 eyes) with rhegmatogenous retinal detachment at Thammasat eye center. Each patient who was diagnosed rhegmatogenous retinal detachment had to perform visual field test (CTVF 24-2 and CTVF120 degree) on the first visit, and postoperatively at 1<sup>st</sup> and 3<sup>rd</sup> month. The number of threshold spots were recorded as visual field scores, then calculated and compared statistically.

**Results:** After successful reattachment surgery, the visual field score increased mostly within the first postoperative month and then gradually raised through the third month in both CTVF 24-2 and CTVF 120 degree strategies. The CTVF 24-2 and CTVF 120 degree visual fields significantly increased (P < 0.05) when compared to pre-operation and 1<sup>st</sup> month-post operation. However, the CTVF 120 degree visual field group did not significantly increase when compared to 1<sup>st</sup> month and 3<sup>rd</sup> month-post operation (P = 0.396). There was an unexpected observation that in cases of macular-on rhegmatogenous retinal detachment the visual field might not improve, when compared to macular-off rhegmatogenous retinal detachment. This may be due to good baseline visual function including visual field, hence after surgery the visual function tended to see little improvement.

**Conclusion:** Visual field recovery was significantly increased in the first month after successful retinal reattachment surgery and steadily through the third month.

Keywords: visual field recovery, rhegmatogenous retinal detachment surgery

*Ethics:* This study was approved for ethical research in human with the human research ethics committee of Thammasat university, Thailand (Research ID : MTU-EC-OP-1-152/58).

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#### Background

Rhegmatogenous retinal detachment (RRD) is the most common type of retinal detachment. It occurs after the retina was torn by traction force such as from posterior vitreous detachment (PVD) which leads to subretinal fluid accumulation and separation of the neurosensory retina from the underlying retinal pigment epithelium (RPE). The incidence is about 10-15 per 100,000 cases<sup>1</sup> with a prevalence of about 0.3% of the general population and a lifetime risk of 3% by the age of  $85^2$ . It is more common in males than in females.<sup>3,4</sup> The classic symptom is photopsia (flashing lights) which occurs in about 60% of patients<sup>10</sup>. This tends to be induced by eye movement and is best seen in dim lighting condition, particularly in the temporal, peripheral visual field. It arises as a result of the vitreous traction on the retinal surface from preexisting PVD. Photopsia is commonly associated with floaters which may be described as a solitary opacity, a cobweb-like opacity or a shower of little spots<sup>11</sup>. Patients often describe a black curtain (visual field defect) once the retinal detachment extends posterior to the equator. When the macula becomes detached (i.e. extension of subretinal fluid into the macula), the patient will experience a drop in visual acuity and feel the loss of central vision. On eye examination, a detachment can be seen as a sheet of sensory retina billowing towards the center of the globe, over which the vessels pass like paths over a hill and there may be an associated visible tear. The surgical goals are to identify and close all retinal breaks with minimum iatrogenic damage.

Closure of the breaks occurs when the edges of the retinal break are brought into contact with the underlying RPE. This is accomplished either by bringing the eye wall closer to the detached retina (a scleral buckle) or by pushing the detached retina toward the eye wall (by intraocular tamponade with a gas bubble). Sealing of the breaks is accomplished by creating a strong chorioretinal adhesion around the breaks. This may be completed with cryotherapy, diathermy, or laser photocoagulation. Untreated rhegmatogenous retinal detachments (RRD) may lead to blindness. But early and appropriate intervention can do excellent outcome.<sup>5,6</sup> For those requiring surgery, prognosis is related inversely to the degree of macular involvement and the duration of retinal detachment.<sup>7</sup> Recovery depends on the site and extent of the retinal detachment. Most series report an anatomical success rate of 90-95%. Of the eyes that are successfully reattached, about 50% obtain a final visual acuity of 20/50 or better.8 There are many studies that evaluate the visual recovery after surgical repair in term of contrast visual acuity. sensitivity, electroretinogram and anatomical outcome.<sup>9</sup> In this study we focus on visual field recovery after surgical repair by pars plana vitrectomy technique.

#### **Material and Method**

This prospective case series was approved by the human ethics committee of Thammasat university, Thailand (Research ID : MTU-EC-OP-1-152/58) and the study was conducted from 1 August 2015 to 31 May 2016. Each visual field test was performed by experienced staff at the Out Patient Department (OPD) using CTVF 24-2 and 120 degree strategy. Humphrey automated visual field perimetry was used in this study. On the first visit, if the patients were not able to perform visual field test due to poor visual acuity, this was given a zero score. On the first month and the third month visit, we calculated the score by counting the threshold spots on each strategy.

Figure 1: Recruitment flow of 8 patients (8 eyes) assigned to perform visual field test from 1 August 2015 to 31 May 2016: Faculty of Medicine, Thammasat University



The patients have the opportunity to ask an investigator (J.C.) questions regarding the study and then signs the participation information and consent forms before starting the study. We excluded patients who had any history of ocular vitreoretinal surgery or has underlying ocular disease which may affect visual field evaluation eg. glaucoma or glaucoma suspected, corneal scar, optic neuropathy. Eight patients (8 eyes) were included in this study.

#### **Intervention and evaluation**

Each patient who was diagnosed with rhegmatogenous retinal detachment in their eye was assigned to perform visual field test using Humphrey automated visual field perimetry 24-2 and 120 degree strategy on the first visit and then on the first and third post-operative month. By using 24-2 strategy each threshold spot (white spot) represent 1 mark, each subthreshold spot represents a 0.5 mark and each black spot represents a 0 mark. Total spots should be In a normal person, there should be a total of 52 threshold spots. in normal person. By using 120 degree strategy we used "seen spots" as a score. Total spots should be 120 seen spots in normal person. On the first visit, if the patients could not perform visual field test due to poor visual acuity we marked asgave a zero score.

 Table 1: Baseline characteristic

#### Statistical analysis

Based on the data provided by previous studies.<sup>12</sup> A sample size of 12 was calculated as being necessary to provide 90% power at the 5% two-sided level to detect a difference in means characterized. Eight participants were allocated. The statistical analysis were performed using STATA version 7 (Stata coop, Texas, USA). The descriptive analysis included mean  $\pm$  standard deviation depend on the data distribution. A P-value equal to or less than 0.05 was considered statistically significant.

#### Result

There were 8 patients included in this study (Table 1). The mean age was 52 years and there were 4 (50%) males. The mean onset was 2.88 weeks. 2 patients (25%) had macula-on status and 6 patients (75%) were phakic eye. The visual acuity ranged from hand motion to 20/30.

Case (no.)	Sex	Age (yrs)	Eye	Onset (wks)	Macular status	Extension (quadrant)	Lens status	Visual acuity
1	F	59	OD	4 WK	OFF	3 Q	PHAKIC	HM
2	М	24	OD	1 WK	OFF	3 Q	PHAKIC	FC
3	F	49	OS	2 WK	ON	2 Q	PHAKIC	20/30
4	М	40	OD	2 WK	OFF	3 Q	PHAKIC	20/200
5	F	64	OS	8 WK	ON	2 Q	PHAKIC	20/70
6	F	56	OD	1 WK	OFF	3 Q	PHAKIC	10/200
7	М	62	OS	1 WK	OFF	2 Q	PSEUDOPHAKIC	HM
8	М	63	OD	4 WK	OFF	2 Q	PSEUDOPHAKIC	FC

The mean threshold spots in visual field test using Humphrey automated visual field perimetry 24-2 strategy at pre-operative period was 4.13 spots (range from 0-33 spots), at 1-month post-operative period was 23.79 spots (range from 0-44 spots), at 3-months post-operative period was 37.14 spots (range from 22.5-50 spots) (table 2)

case		CTVF 24-2		CTVF 120 degree			Vitreous
	(0-	52 threshold sp	ots)	(0-	-120 threshold s	spots)	Substitute
No.	Pre-op	1mo	3mo	Pre-op	1mo	3mo	
1	0	MISS	41	0	0	14	C3F8
2	0	44	44	4	75	99	C3F8
3	33	23.5	26	58	55	50	SO
4	0	21.5	40	10	36	33	C3F8
5	0	10.5	OR	0	0	OR	C3F8
6	0	40	50	0	95	MISS	C3F8
7	0	27	36.5	0	5	MISS	C3F8
8	0	0	22.5	0	3	36	SO
Mean	4.13±11.67	23.79±15.43	37.14±9.78	9±20.11	33.63±37.72	46.4±32.08	

**Table 2:** Clinical data of the patients before and after surgery

MISS ; patient did not perform visual field testing in that visit.

OR ; patient has redetachment of retina at that visit

The mean threshold spots in visual field test using Humphrey automated visual field perimetry 120 degree at pre-operative period was 9 spots (range from 0-58 spots), at 1-month post-operative period was 33.63 spots (range from 0-95 spots), at 3-month post-operative period was 46.4 spots (range from 14-99 spots) (table 2).

Visual field threshold spots in 24-2 strategy were improved from pre-operative period to 1-month post-operative period significantly (P value =0.001) and continued improvement at 3-month post-operative period (P-value =0.026) (table 3).

		CTVF 24-2 (threshold spots)					
	Mean	Mean change from pre-	Mean change from 1				
		ор	month				
Pre-operative	37.14±9.78						
1 month	37.14±9.78	19.66 (P value = 0.001)					
3 month	37.14±9.78		13.35 (P value = 0.026)				

**Table 3**: Summaries of outcomes for CTVF 24-2

Visual field threshold spots in 120 degree strategy were improved from preoperative period to 1-month post-operative period significantly (P value =0.03) but not be significant improved at 3-month post-operative period (P value = 0.396) (table 4).

Table 4:	Summaries	of outcomes	for CTVF	120 degree
				0

	CTVF 120 degree (threshold spots)		
	Mean	Mean change from pre-	Mean change from 1 month
		ор	
Pre-operative	9±20.11		
1 month	33.63±37.72	24.63 (P value =0.03)	
3 month	46.4±32.08		12.77 (P value = 0.396)

#### Discussion

Rhegmatogenous retinal detachment (RRD) occurs when the retina was torn by traction force such as from posterior vitreous detachment (PVD) which leads to fluid accumulation and separation of the neurosensory retina from the underlying retinal pigment epithelium (RPE). Patients often describe a black curtain (visual field defect) once the subretinal fluid extends posterior to the equator. When the macula becomes detached (ie, extension of subretinal fluid into the macula), the patient experiences a drop in visual acuity and loss of central vision. There are many studies that evaluate the visual recovery after surgical repair in term of visual acuity, contrast sensitivity, electroretinogram and anatomical outcome.

In the current study we focus on visual field recovery. After successful reattachment surgery, the visual field score mostly increased within the first post-operative month and then slowly raised through the third month in both CTVF 24-2 and 120 degree strategy. The 1-month post-operative visual field were significantly increase in both 24-2 and 120 degree strategy (p = 0.01 and 0.03). However the 120 degree visual field doesn't show significant increases when compared to 1<sup>st</sup> month and 3<sup>rd</sup> month-post operatively (P = 0.396). The 24-2 visual field test strategy may represent central visual field and 120 degree strategy visual field test may represent periphery visual fields. These findings were comparable with previous studies<sup>12,13</sup> which show the improvement of visual acuity and other visual function within three months. There was an unexpected observation that in cases of macular-on rhegmatogenous retinal detachment the visual field may not improve when compared with macular-off cases. This may be from the good baseline visual function include visual field so when after surgery the visual function tend to be a little improvement.

Some experimental studies have shown that there may have been some defects in the outer segment, especially in the outer segment of cone cells after retinal reattachment surgery. In cases with detachment of short duration (less than 1 week), morphological recovery in the reattached retina is complete while with detachments longer than 1 month in duration, recovery is usually incomplete<sup>14,15</sup>. This may explain why visual function including visual fields are not full recovered despite anatomical reattachment.

This study has several limitations. First, the lens status may be the confounding factors for this study. After vitreoretinal surgery the cataract may come faster than usual and disturb the visual field test result. Second, the vitreous substitute (eg. C3F8 and silicone oil) may affected the visual field results especially at 1-month post operative period due to the gas level may confound the visual field test. Further studies should separate lens status and enroll more sample size to find the correlation between visual field recovery correctly.

#### Conclusion

Visual field recovery in primary rhegmatogenous retinal detachment surgery can be found as early in the first month through the third month after surgery. Both central and periphery visual field were recovered. Incomplete recovery of visual field indicated the incomplete recovery of photoreceptor cell.

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# Post-operative refraction in the patients with out-of-the-bag intraocular lens implantations.

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**Objective:** To study the association between the estimated refraction for in-the-bag intraocular lens (IOL) implants and the post-operative refraction in the patients with out-of-the-bag implants.

**Methods:** This retrospective study examined medical records of all patients who had undergone complicated cataract surgery with out-of-the-bag IOL implants in Thammasat university hospital from January 1<sup>st</sup> 2013 to December 31<sup>st</sup> 2015. We recorded sex, age, diagnosis, type of cataract surgery, type of IOL, implantation position, estimated post-operative refraction for in-the-bag implants and actual post-operative refraction at the 1<sup>st</sup> and 3<sup>rd</sup> months. The estimated and the post-operative refraction association was evaluated by linear regression analysis.

**Result:** We identified 51 patients (51 eyes) who underwent complicated cataract surgery with out-of-the-bag IOL implants; 27 in-the-sulcus implants and 24 sclera-fixed implants. For the in-the-sulcus group, the estimated pre-operative refraction was -0.89 to +0.86 D (mean=+0.08, SD  $\pm$ 0.43) and the actual post-operative refractions at the 1<sup>st</sup> and 3<sup>rd</sup> months were -3.00 to + 1.50 D (mean= -0.51, SD  $\pm$ 0.99) and -3.25 to +0.50 D (mean= -0.54, SD  $\pm$ 0.95), respectively. The pre- and 3 months post-operative refractions were significantly (p=0.0391) correlated. For the sclera-fixed group, the estimated pre-operative refraction was -0.34 to +1.22 D (mean=+0.33, SD  $\pm$ 0.37) and the actual post-operative refraction 1<sup>st</sup> and 3<sup>rd</sup> months were -4.00 to +1.00 D (mean= -0.99, SD  $\pm$ 1.31) and -2.75 to +0.75 D (mean= -0.83, SD  $\pm$ 1.06), respectively but there was no significant pre- and post-operative correlation.

**Conclusion:** Out-of-the-bag IOL implants are associated with postoperative myopic shifts, -0.54D in in-thesulcus group and -0.83 D in scleral-fixed group. Base on our derived linear regression equation, the IOL power selection for in-the-sulcus implants should be +0.77 to achieve the post-op emmetropia.

**Keyword**: Post-operative refraction, Out-of-the-bag intraocular lens implant, In-the-sulcus implant, Sclerafixed implant

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#### Introduction

Cataracts are common in the developing world and an increasing cause of blindness.<sup>1, 2</sup> Up to 19 million cataract removal surgeries are performed each year around the world and the WHO projects this figure will rise to 32 million by 2020.<sup>3</sup>

During cataract surgery, the lens is removed from the capsular bag and replaced with a new intraocular lens (IOL). The desired result is a great improvement of the affected individual's sight and the majority of cataract surgeries are generally successful in achieving post-operative emmetropia. Pre-operatively, all patients need to be evaluated and ocular parameters; such as keratometry and axial length; measured to determine the proper IOL power necessary for the in-the-bag implantation.

Unfortunately, a small portion of patients may encounter operative difficulties e.g. the IOL could not be implanted into the capsular bags due to posterior capsular tear,<sup>4</sup> lens dislocation, and zonule lysis.<sup>5</sup> In order to overcome these complications, surgeons often choose to implant the intraocular lens outside of the capsular bags via sulcus or sclera-fixated implantation but these surgeons still need to be refer to the IOL power calculation as if for an in-the-bag implantation.<sup>6</sup> By reducing the IOL power, surgeons may estimate the postoperative refraction they hope to achieve. However, this method rarely results in post-operative emmetropia. Therefore, this paper aims to increase the chance of post-operative emmetropia for out-of-thebag implantation by constructing a new

equation for finding a more accurate value of estimated refraction value.

#### **Materials and Methods**

This was a retrospective review of the medical charts of patients who had undergone the out-of-the-bag cataract surgery from January 1<sup>st</sup>, 2013 to December 31<sup>st</sup>, 2015 at Thammasat University Hospital, Thailand.

The Inclusion criteria were:

- 1. The patients who have undergone cataract surgery with out-of-thebag IOL implantation using an IOL power calculation based on the in-the-bag implantation
- 2. The patients were seen after the 1<sup>st</sup> and 3<sup>rd</sup> months post-operatively
- 3. The absence of concomitant eye pathology that could interfere the patient's refraction (e.g. corneal scar, pterygium with corneal invasion, severe ocular surface diseases.)

# Sample size calculation and data analysis

In this study, Stata 12.1 was used to calculate the sample size. To obtain a statistically significant outcome between estimated and post-operative refraction for 2 implant techniques, 2 sample groups are required: 21 patients for the in-thesulcus group, and 31 patients for the sclera-fixed group. With these sample sizes, it would be possible to achieve 2sided test of 95% confidence interval with the p-value less than 0.05.

We collected data using a standard case record form: sex, age, diagnosis, type of cataract surgery, type of IOL, implantation position, estimated

post-operative refraction for in-the-bag and implants actual post-operative refraction at 1<sup>st</sup> and 3<sup>rd</sup> months. Preoperatively, all patients were evaluated the ocular parameters; such as keratometry by the ZEISS VISUREF 100 Auto Refractor/Keratometer, Germany and axial length by the Tomey AL-100 Biometer, Germany and then these parameters were used to calculate the IOL power by the SRK/T formula. Postoperatively, the estimated refraction data corresponding to the implanted IOL power were recorded. The actual refraction data at 1<sup>st</sup> and 3<sup>rd</sup> month were determined by the ZEISS VISUREF 100 Auto Refractor/Keratometer, Germany and were expressed in spherical equivalents. The association between estimated refraction and the postoperative refraction at 1<sup>st</sup> and 3<sup>rd</sup> months was evaluated by linear regression analysis via Stata 14. The regression equations at 3<sup>rd</sup> months from each group were calculated and used to predict the proper IOL power for aiming emmetropia in both techniques.

#### Results

We retrieved notes from 27 patients who made up the in-the-sulcus implantation group. Their mean age was 72.5 years, 14 were males and 14 underwent operations in their left eyes. Twenty three eyes underwent phacoemulsification (PE) and the intraoperative complications were posterior capsular rupture with vitreous loss in 14 eyes, posterior capsular rupture without vitreous loss in 2 eyes, partial zonule lysis in 1 eye and nucleus drop in 6 eyes. Four eyes underwent extracapsular cataract extraction (ECCE) and the intra-operative complications were posterior capsular rupture with vitreous loss in all. The measured pre-operative refraction values (Table1) range from +0.86 to – 0.89 for a mean, (standard deviation [SD]) of +0.08 (0.43). The post-operative refraction values at the first month were +1.50 to -3.00 (mean, SD= -0.51, 0.99), and the 3<sup>rd</sup> month were + 0.5 to - 3.25 (mean, SD= -0.54, 0.95).

There were 24 patients in the sclera-fixated group, but 7 of them were excluded, as they did not have the IOL power calculations from in-the-bag implantations. Of the remaining 17 patients, 11 were males and 9 had surgery on their right eye (Table 1). One eye underwent extracapsular cataract extraction (ECCE) and the intra-operative complication was posterior capsular rupture with vitreous loss. Ten eyes underwent intracapsular cataract extraction (ICCE) and the intra-operative complications were posterior capsular rupture with vitreous loss in all. Six eyes underwent pars plana lensectomy (PPL). Their estimated refraction values ranged from + 1.22 to - 0.34 (mean, SD= +0.33, 0.37). The post-operative refraction values for the 1<sup>st</sup> month ranged from + 1.00 to - 4.00 (mean, SD= -0.99, 1.31), and for the  $3^{rd}$  month were + 0.75 to - 2.75 (mean, SD = -0.83, 1.06).

	In-the-sulcus group	Scleral-fixated group
	N=27	N=17
Age (years)		
Mean (SD)	72.52 (8.73)	59.18 (14.54)
Sex, N (%)		
Male	14 (51.85%)	11 (64.71%)
female	13 (48.15%)	6 (35.29%)
Laterality, N (%)		
Right	14 (51.85%)	9 (52.94%)
Left	13 (48.15%)	8 (47.06%)
Estimated refraction (D)		
Range	+0.86 to-0.89	+1.22 to -0.34
Mean (SD)	0.08 (0.43)	0.33 (0.37)
Post-op refraction 1 month (D)		
Range	+1.50 to-3.00	+1.00 to-4.00
Mean (SD)	-0.51 (0.99)	-0.99 (1.31)
Post-op refraction 3 months (D)		
Range	+0.5 to-3.25	+0.75 to -2.75
Mean (SD)	-0.54, 0.95	-0.83 (1.06)

Table 1: demographic data and estimated pre- and postoperative refraction values.

The distribution from the bar graph (figure 2A), it has shown the data distribution of these two groups; for in-the-sulcus group, estimated refraction was between -1.00 to+1.00, and for sclera-fixated group the estimated refraction was more positive value than in the sulcus group



Figure 2: Histograms showing the distributions of the preoperative and postoperative distributions (A) of the refraction values at one month (B) and three months (C).

By the  $3^{rd}$  month, 16 of 27 patients (59.3%) in the sulcus group achieved emmetropia (>-0.50 to  $\leq$ +0.50 D), however, the 9 of 27(33.3%) patients had myopic shifts. By contrast, postoperative myopic shift tended to be greater in the sclera-fixated group (10 of 17 patients (58.8%)). (Figure 2 C)

For the in-the-sulcus group (Figure 3), there was not a significant correlation between the pre- and post-operative refraction at  $1^{st}$  month (p=0.1527) but there was a significant correlation at 3 months (p=0.0391) as well as between the month 1 and 3. (p=0.0001)



Figure 3: Scatter plots of the pre- and post-operative refraction values for the in-the-sulcus group at one month (A) and three months (B). Figure C is between months one and three.

The regression equation for the in-the-sulcus groups is "SE3 = 0.88 \* estimate AR – 0.61", where SE3 is the 3<sup>rd</sup> month postoperative refraction, and estimated AR means the preoperative refraction values. When emmetropia which is SE3 = zero, the estimated AR is 0.69. (Figure 4)



Figure 4: The linear regression line of the pre- and post-operative refraction values for the in-the-sulcus group.

For the sclera-fixated group (Figure 5), there were no statistically significant association between the estimated refraction and the  $1^{st}$  or  $3^{rd}$  month post-operative refraction values (p=0.5051, 0.7502, respectively). But there was between the two postoperative refraction values (p=0.0001).



Figure 5: Scatter plots of the pre- and post-operative refraction values in the sclera fixation group at one month (A) and three months (B). Figure C is between months one and three.

#### Discussion

Our retrospective study has demonstrated that patients who underwent IOL implantation using either the in-the-sulcus or sclera-fixated technique experienced a myopic shift in refraction three months post implantation.

These are the two most common techniques for IOL implantation and choosing which technique to perform depends on the stability of the residual capsular bag, in-the-sulcus technique for stable anterior capsular ring or sclerafixated technique for inadequate lens capsule. In these operations, the exact IOL power that results in emmetropia was unknown. Most surgeons prefer to estimate the approximate value by reducing the power for achieving the postoperative emmetropia.

In our study, the myopic shift at three months was -0.54 and -0.83 diopter (D) for in-the-sulcus and sclera-fixated group, respectively, which were similar to other studies<sup>7-10</sup> that have reported approximately -1.00 D myopic shift after out-of the-bag IOL implants. The mean refraction for in-the-sulcus group was less than the previous studies, this may due to a shorter follow up period and there may be a more myopic shift in the long term. for sulcus-fixated Therefore, IOL implants, these authors recommended reducing the power by about 1.00 to 1.50 D less than in-the-bag implant.<sup>8-9</sup>

However, in our study, we found a significant association between the preand 3 month post-operative refraction for in-the-sulcus group (p=0.0391), expressed by the linear equation, SE3 = (0.88 \* estimate AR) - 0.61. To achieve emmetropia, SE3 should equal to zero, resulting in an AR of 0.69. We suggest increasing this by the mean of estimated refraction of 0.08 D, giving a final estimated refraction value of +0.77 D.

In the sclera-fixated group, the mean post-operative myopic shifts were  $\sim$ -1.00 and -0.83 D at one and three months, respectively, which were similar to results from Mimura et al<sup>10</sup>. They also reported the long term post-operative refraction. They found that the immediate post-operative refraction was -0.95 D, -1.16 D after two years, and -1.37 D after 12 years. In our study, we found no statistically significant association between pre-and post-operative refraction values at both time points and cannot calculate the regression equation to predict the proper power. These may have resulted from e.g. heterogeneity of the surgical techniques and imprecise location of the IOL. However, for sclerafixated IOLs, Han et al. advise a reduction of IOL power of 1.00 D.<sup>11</sup>

The limitations of this study include its small sample size and retrospective design, different sclerafixated techniques performed by the surgeons, and imprecise location of IOL. A prospectively designed study following standard operative techniques would provide better quality data.

#### Conclusion

Post IOL, the in-the-sulcus group and scleral-fixated group experienced postoperative myopic shifts: -0.54 D and -0.83 D, respectively. The pre- and postoperative refractions were positively related in the in-the-sulcus group and the regression equation suggested that the IOL power for such implants should be +0.77 to achieve the post-operative emmetropia.

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# Outcome of vitrectomy for intraocular foreign bodies at Thammasat university hospital.

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*Aim:* to study the postoperative outcomes of vitrectomy for retained posterior segment intraocular foreign bodies (IOFB) in patients with ocular injury

Study Design: Retrospective Case Series

**Methods:** Patient registry of patients with cases of retained posterior segment IOFB in patients with ocular injury who received vitrectomy at Thammasat University Hospital between October 2012-September 2016 were examined. Statistical analysis exact fisher's test to examine the treatment outcome and the relationship of different factors that may affect the treatment outcome.

**Results:** Of all 25 patients, 23 were male (92%), 2 were female (8%) mean age  $34.04\pm 8.97$  years. Twelve right eyes (48%) and 13 left eyes (52%). Mean duration between injury and operation was  $23.24\pm46.18$  days.19 patient's eyes (76%) had postoperative visual acuity (VA) of 20/200 or better. 6 patient's eyes had postoperative VA lesser than 20/200 (24%). One eye resulted in no light perception. No factor was found to have statistically significant association.

*Conclusion:* The study results have not found any other statistical significance in occurrence relations between postoperative visual outcomes and other examined factors.

Keywords: Penetrating ocular injury, Intraocular foreign body, Pars plana vitrectomy

*Ethical Considerations:* this study has been approved by the Human Research Ethics Committee of Thammasat University Faculty of Medicine (Research ID:MTU-EC-OP-1-038/60)

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#### Introduction

Open globe injuries with retained intraocular foreign bodies are a major cause for blindness<sup>1</sup> found between 17-41% of ruptured globes. Risk factors are age groups 21-40 years, occupational hazards (54-72%) with 60-80% of globe rupture cases caused by metal hammering.<sup>2,3,4</sup> Management of intraocular foreign bodies (IOFB) requires surgery to remove the foreign object which often carries a poor prognosis. Multiple factors contribute to the prognosis such as endophthalmitis, retinal detachment, site of injury and visual acuity (VA) prior to surgery, <sup>2,5,6,7,8</sup> afferent pupillary defect<sup>9,10</sup>, size of IOFB; where larger sizes are associated with poor visual outcomes.<sup>7,9,11</sup> Duration of injury prior to surgical IOFB removal have been found not to affect visual outcomes.<sup>12,13</sup>

#### **Materials and Methods**

Patient records at Thammasat University Hospital between October 2012 - September 2016 were examined for cases of retained posterior segment IOFB that also required vitrectomy to remove foreign bodies. Exclusion criteria were patients lost to follow up, patients with history of visual loss prior to injury. collection parameters Data include gender, age, cause of IOFB, site and side of globe rupture, type and size of IOFB, VA before and after surgical management. Patients included in this study have stable VA with pinhole for two consecutive follow up sessions, we did not use BCVA. Every patient who had cataracts affecting vision will have received cataract surgery and IOL

implantation. Occurrence of associated complications such as endophthalmitis, retinal detachment, and vitreous hemorrhage are also recorded. All of the above parameters are analyzed for statistical significance for their effects on postoperative visual outcomes in cases of IOFB receiving vitrectomy. Favorable postoperative visual outcome is defined in this study as a visual acuity reading of 20/200 or better using the Snellen chart.<sup>5</sup>

#### Statistical analysis

Collected parameters specified in the methods section are analyzed by the SPSS software, using Fisher's Exact Test to determine which independent nominal variables are statistically significant in affecting postoperative visual outcomes for cases of IOFB receiving vitrectomy. A p-value of less than 0.05 was accepted as having statistical significance.

#### Results

Of all 29 patients, 4 were excluded (one was loss to follow up, one was due to being aphakic, another was referred back to their original point of care, and one due to a loss of medical history records. Of the remaining 25 patients. all received intravenous ceftazidime 2 grams every 8 hours and vancomycin 1 gram every 12 hours after having received 72 hours topical ceftazidime (2 mg / 0.1 ml) and vancomycin (1 mg / 0.1 ml) every 1 hour from start of treatment until discharge. Twenty three patients are male (92%) and 2 were female (8%) with a mean age of  $34.04 \pm 8.97$  years. Twelve right eyes (48%) and 13 left eyes (52%) were analyzed. The causes for IOFB injuries

were; 7 steel extractions (28%), 5 grass cuttings (20%), 5 metal shearings (20%), 4 nail hammerings (16%) and 4 other causes (16%). All IOFBs were found to be metal (100%). Site of IOFB injury entry points were; 18 cornea (72%), 6 sclera (24%), 1 corneoscleral (4%). Sizes of IOFB were; 3 millimeters or smaller in 12 eyes (48%), larger than 3 millimeters in 13 eyes (52%). Duration between injury and operation was found to be between 0-195 days, averaging 23.24± 46.18 days. 4 eyes (16%) received surgery within 24 hours, whilst 21 eyes (84%) received surgery after 24 hours. 7 eyes (28%) had visual acuity prior to surgery of better than or equivalent to 20/40, 6 eyes (24%) had visual acuity between 20/50 and 20/200, 12 eyes (48%) had visual acuity of less than 20/200. All cases underwent pars plana vitrectomy to remove IOFBs. Postoperatively, 14 eyes (56%) had visual acuity of greater than 20/40, 5 eyes (20%) had visual acuity between 20/50 and 20/200, 6 eyes (24%) had visual acuity of less than 20/200 and 1eye had no light perception. Complications observed were 8 retinal detachments (32%),6 vitreous hemorrhages (24%), 6 endophthalmitis (24%). Demographic information is shown in table 1.

		Mean (range, SD)
Age		34.04 (18-57, 8.97)
		Number (%)
Gender	Male	22 (02)
Gender	Female	23(92)
Eve	Diaht	2 (8)
Еус	Laft	12(40) 12(52)
Injum machanism	Motol Extraction	7 (28)
injury mechanism	Gross Cutting	7 (28) 5 (20)
	Motol Shooring	5 (20)
	Neil Hammarina	3(20)
	Others	4(16)
Turna of IOEP	Matallia	4(10)
Site of initian	Metallic	23 (100)
Site of injury	Comea	18(72)
	Scieral	6 (24) 1(4)
C' CLOED	Corneoscieral	1(4)
Size of IOFB	$\leq 3$ mm.	12 (48)
	> 3mm.	13 (52)
Time of surgery Number (%)	$\leq 24$ hours	4 (16)
	> 24 hours	21 (84)
Initial VA	$\geq 20/40$	7 (28)
	20/50 - 20/200	6 (24)
	< 20/200	12 (48)
Final visual acuity	≥20/40	14 (56)
	20/50 - 20/200	5 (20)
	<20/200	6 (24)
Complication	Retinal detachment	8 (32)
*	Vitreous hemorrhage	6 (24)
	Endophthalmitis	6 (24)

**Table 1**.Demographic data of patients with retained intraocular foreign body) total 25 eyes)

Results suggest none of the factors investigated are significantly related to visual prognostic outcomes for retained posterior segment IOFB after vitrectomy. Prognostic factors for visual outcome shown in Table 2.

Table 2. Prognostic factors for visual	outcome in patients	with penetrating	ocular injury with
retained intraocular foreign body			

Prognostic factors	Final VA $\geq 20/200$	Final VA < 20/200	p-value
C .	total 19 eye	total 6 eye	1
	Number/total (%)	Number/total (%)	
Initial VA < 20/200			0.732
Yes = 12	6/19 (31.58)	6/6 (100)	
No = 13	13/19 (68.42)	0/6 (0)	
Time of surgery < 24 hours			0.208
Yes = 4	4/19 (21.05)	0/6 (0)	
No = 21	15/19 (78.95)	6/6 (100)	
Size of IOFB < 3 mm			0.076
Yes = 12	9/19 (47.37)	3/6 (50)	
No = 13	10/19 (52.63)	3/6 (50)	
Presence of corneal injury			0.404
Yes = 18	13/19 (68.42)	5/6 (83.33)	
No = 7	6/19 (31.58)	1/6 (16.67)	
Presence of scleral injury			0.638
Yes = 6	5/19 (26.32)	1/6 (16.67)	
No = 19	14/19 (78.95)	5/6 (83.33)	
Presence of retinal detachment			0.679
Yes = 8	4/19 (21.05)	4/6 (66.67)	
No = 17	15/19 (78.95)	2/6 (33.33)	
Presence of vitreous			0.316
hemorrhage			
Yes = 6	6/19 (31.58)	0/6 (0)	
No = 19	13/19 (68.42)	6/6 (100)	
Presence of endophthalmitis			0.638
Yes = 6	2/19 (10.53)	4/6 (66.67)	
No = 19	17/19 (89.47)	2/6 (33.33)	

#### Discussion

This study found that there are no significant factors that affect postoperative visual outcomes in vitrectomy for retained posterior segment IOFB, in the contrary to previous literature.<sup>2,5,6,7,8</sup> This may be due to a small sample size that was analysed for statistical significance in finding associative factors affecting post-operative visual outcomes. The size of IOFB has also been a known determinant for post-operative visual outcomes in vitrectomy for retained posterior segment IOFB<sup>7,9,11</sup> with larger foreign bodies causing more tissue damage to the eye and consequently causing other complications such as retinal detachment, vitreous hemorrhage, proliferative vitreoretinopathy (PVR).<sup>14</sup> These complications are significant to the prognosis of the patient, however this

study found no association between IOFB size and postoperative visual outcomes (p=0.076) and all patients had IOFBs in the retina or vitreous without involving the center of the macula.

The time to surgery for removal of IOFB within the first 24 hours of injury was not found to have any significant associations for postoperative visual outcomes (p=0.208), which is mentioned literature.<sup>12,13</sup> However, all four patients in our study who received treatment within the first 24 hours of injury were found to have favourable postoperative visual outcomes, suggesting early IOFB vitrectomy removal with mav significantly reduce rates of infection.<sup>14,15</sup> Furthermore, patients receiving early surgical intervention may be more likely to have a lesser severity of injury, as smaller injuries do not require as much time for preoperative preparation and can be operated on almost immediately after injury - leading to better postoperative visual outcomes. Nevertheless, this theory requires larger samples sizes for matched and correlated data analysis to prove the association.

The presence of vitreous hemorrhage suggests a high severity of traumatic injury to the eye and is associated to less favorable postoperative visual outcomes, and is a risk factor for proliferative vitreoretinopathy that may follow. Thus, patients receiving early surgical removal of IOFB following injury may also reduce risk of fibrotic sequelae. In our study, patients who suffered with vitreous hemorrhage were all found to be mild in severity and has favorable VA prior to surgery; data for this group was found to have no

association with postoperative visual outcomes, contrary to other literature, this may be due to the small sample size of the study.

The presence of retinal detachment in IOFB injuries is a known factor associated with poorer postoperative visual outcomes; however, this study does not suggest there is an association (p = 0.679) potentially due to a small sample size. Furthermore, the cause of all cases of retinal detachment following IOFB injuries in this study do not appear to be related to the injuries themselves.

Endophthalmitis is not found to be significantly associated with postoperative visual outcomes, contrary to other literature. This could be attributed to the fact that all patients received topical, oral and intravenous antibiotics during their treatment to reduce the rate of infection. However, this group may be at risk of poorer postoperative visual comes similarly to that of retinal detachment.

The patient's baseline visual acuity prior to surgery was not significantly associated with postoperative visual outcomes. Due to the fact that some injuries may have simultaneously caused cataracts which may be the cause of a sudden and severe worsening of visual acuity. Nevertheless cataracts can be curatively treated by surgery and intraocular lens implantation.

The site of injury, whether it is the cornea or sclera does not appear to be significantly associated with postoperative visual outcomes in our study. This may be due to a small sample size, however, cornea injuries are more likely to have worse postoperative outcomes.

Site of IOFB injury entry point is not associated with postoperative visual outcomes, regardless of entry point being corneal or scleral. This may be due to a limited sample size. However, corneal entry points are known to cause worse postoperative visual outcomes due to cornea damage or astigmatism as a result of corneal repair surgery.

In conclusion, our study did not find preoperative and intraoperative factors to be significantly associated with postoperative visual outcomes in cases of IOFB with vitrectomy. The potential reasons for the lack of associations in our data may be due to a small sample size and its retrospective nature in which only visual acuity with pinhole correction was made and may not be suitable for analysis for associations.

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## Comparing the effectiveness of printed versus iPad Ishihara plates in diagnosis of congenital red-green color deficiency in Thai male population.

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**Objective:** To compare the Effectiveness Between Ishihara plates on iPad Air2 and traditional printed standard Ishihara test for screening red-green color vision deficiency in male population

Design: Case-control Diagnostic Study

**Methods:** Male volunteers (patients and relatives) from Thammasat hospital and students from grades 3-6 at Buengkhaoyorn school, Pathumtani province were recruited. All volunteers were examined for red-green color deficiency by standard Ishihara test, and Pseudochromatic color test application on iPad Air2 at 100% brightness in a room without or less sunlight, comparing the two results to determine the latter test's effectiveness in screening red-green color deficiency.

**Results:** A total of 313 selected volunteers were examined, age ranged from 6 to 80 years old. Fourty - nine participants who tested positive for red-green color vision deficiency using the Standard Ishihara test were also positive for red-green color vision deficiency using the Pseudochromatic color test application in iPad Air2. Another 264 volunteers who tested negative red-green color vision deficiency using the Standard Ishihara test also had negative red-green color vision deficiency using the Pseudochromatic color test application in iPad Air2. The sensitivity, specificity and positive predictive value for the Pseudochromatic color test was 100%, 100% and 100%.

**Discussion:** The Pseudochromatic color test is a suitable substitute to the standard Ishihara test when used on an iPad Air2 at optimal lighting conditions. The use of free standard Ishihara test substitute applications on tablets may be suitable for screening color deficiency in resource limited settings.

Keywords: color vision testing, cone dystrophy, color deficiency, Ishihara test

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#### Introduction

The normal capacity to perceive colors in humans requires the ability to receive and discriminate colors by cone cells in the retina. Cells of the retina are classified into 3 types, according to sensitivity in perceiving primary colors red green and blue. Abnormalities in particular type of cone cells may decrease the ability to perceive colors in normal lighting conditions, this state is also known as color deficiency.

There is a system of classification for color deficiency, based on which colors are unable to be perceived. Color deficiency may be congenital or acquired. Existing literature reported red-green color deficiency as the most common form, which is a congenital x-linked recessive condition. As a result, females are often found to be carriers whilst manifesting as the condition in males. Studies from around the world suggest color deficiency is found in 5-8% of males and 0.5% of females, with some variation of this proportion around in each region.<sup>1-5</sup> A previous study in Thailand found prevalence of color deficiency in Thailand to be 7.7% in males and none in females, similar to findings from studies abroad.<sup>6</sup>

A commonly used screening method to detect color deficiency in modern practice uses а Pseudosochromatic chart, also known as the standard Ishihara test (figure 1.) which consists of color plates designed to confuse patients with red-green color deficiency. For example a patient with red color deficiency would be unable to perceive red and blue-green dots if there is a red number on a blue-green background, or an affected patient may not be able to perceive the number indicated on the plate. Present literature suggests the sensitivity, specificity and positive predictive values for the standard Ishihara test are 100%, 97% and 97% respectively.<sup>7</sup>



Figure 1. Standard Ishihara Test

Although the standard Ishihara test is a commonly used method of screening<sup>7</sup> it is an expensive method, costing 10,000 Thai baht, hence it is only used in large hospitals. In current practice it is common for healthcare workers to download the standard Ishihara test applications onto tablets such as the iPad or smart phones such as the Pseudochromatic color test which is created to assist in screening (figure 2). This cost reducing improvisation is an interesting prospect, assuming these applications can reliably screen for color deficiency as the standard Ishihara test.



Figure 2. illustrates Application Program Ishihara Color Test on iPad

#### Methods

313 Male patients and relatives at Thammasat University Hospital and Primary school children from 3rd- 6th grade at Bungkhaoyorn, Pathumthani province are recruited for color deficiency screening between June and December 2016. The sample size was calculated to be 49 patients with positive standard Ishihara test result, and 264 patients with negative standard Ishihara test result, with sufficient statistical power of 0.9, in proving the sensitivity and specificity of the Pseudochromatic Color test free application comparable to the standard Ishihara test using a one sample test of proportion.<sup>8</sup>

$$n = \left[\frac{z_{1-\alpha/2} \{p_0(1-p_0)\}^{1/2} + z_{1-\beta} \{p_A(1-p_A)\}^{1/2}}{p_A - p_0}\right]^2$$

Each patient undertakes а standard Ishihara test (24 plate variant, 17 plates consisting of numbers) and screened for red-green color deficiency if 4 or more plates containing numbers are incorrectly interpreted. Patients are then asked to take the Pseudochromatic color test, a free application available on iPad Air2 which displays the same pictures of the standard Ishihara test, at 100% brightness in a room with less sunlight. We shuffled pictures in Pseudochromatic color test to reduce recall bias in every patient. We standardized the screen contrast at 100% and used the same methods as the standard Ishihara test. The results are analysed for sensitivity and specificity.

#### **Inclusion** Criteria

Subjects who are able to verbally communicate and interpret Arabic numerals who have given written consent, and does not have any ophthalmological past history hindering the ability to perceive numbers in both types of tests.

#### **Exclusion Criteria**

Subjects who decline to agree to the terms stated in the written consent form

#### Results

313 male patients aged 6-80 underwent both the standard Ishihara test and the Pseudochromatic color test on the iPad Air2. Results are shown in table 1. All 49 patients who tested positive for red-green color deficiency using the standard Ishihara test also tested positive for the Pseudochromatic color test on iPaid Air2. Consequently, the remaining 264 patients tested negative for both tests as seen in table 2. The results suggest a sensitivity, specificity and positive predictive value of 100% for the Pseudochromatic color test on iPad Air2 using the standard Ishihara test as a standard.

Standard Ishihara Test	Number of patients
Positive	49
Negative	264
Total	313

Table 1 showing results of patients taking the standard Ishihara test

Standard Ishihara Test Pseudochromatic color test iPad Air2	Positive	Negative
Positive	49	0
Negative	0	264

 Table 2 comparing the results between the standard Ishihara test and the Pseudochromatic color test on the iPad Air 2

#### Discussion

Our study suggests the Pseudochromatic color test application, a red-green color deficiency screening program on the iPad Air2 on 100% brightness has a screening performance equivalent to that of a the standard Ishihara test with statistical significance. Implying that the application can be used as a substitute to the standard Ishihara test. The use of free standard Ishihara test substitute applications on tablets may be suitable for screening color deficiency in resource limited settings.

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# Results of student vision screenings at primary schools in Oudomxay province, Lao PDR.

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**Purpose:** To evaluate and implement a school based child vision screening program, which would identify the causes of blurred vision, improve vision with glasses, and increase teachers' awareness of eye care.

**Methods**: Primary school vision screenings took place in 155 schools in two districts of Oudomxay Province in November and December 2016. The children were initially screened by teachers trained in vision screening using the Snellen chart at 6 meters and trained in how to prevent conditions such as conjunctivitis and eye injury. The results of the screening vision tests of all children were sent to Oudomxay Provincial Hospital Eye Unit by teachers. A team comprising of one ophthalmologist and one optometrist followed up with students identified with vision impairment at the schools to perform additional vision tests and eye exams. Children confirmed with refractive errors were provided glasses and those diagnosed with cataract and glaucoma were referred to the Ophthalmology Unit of the hospital.

**Results**: In total, 16,982 children (Female 8,273) aged 5-14 years old were screened. The vision impairment with available correction (one and both eyes) of 133 children (0.78%), and included 40.60% of children requiring spectacle provision. Other ocular abnormalities included corneal scar (32.22%), posterior segment disease (23.08%), cataract (3.76%), and glaucoma (1.50%). 155 primary schools teachers were trained in vision screening. The vision of 45 children was improved with eyeglasses for refractive error. This number is lower compared to that of neighboring countries.

Conclusion: Trained school teachers can play an important role in the prevention of childhood blindness.

*Keywords*: Vision screening, rural health care, visual impairment, children, pediatric ophthalmology, amblyopia, refractive error, corneal scar.

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#### Introduction Background Information

Children's eyes are very sensitive and are easily affected by infections and nutritional deficiencies. Childhood blindness is caused by a number of diseases and conditions in low-income countries, such as vitamin-A deficiency, cataracts from rubella, corneal scarring from measles, strabismus, and retinopathy of prematurity.

Vision impairment means that a person's eyesight cannot be corrected to a "normal" level (VA is less than 6/18 to 6/60). Vision impariment may be caused by a loss of visual acuity, where the eye does not see objects as clearly as usual. It may also be caused by a loss of visual field.

Generally, visual disability and blindness are caused by eye diseases or/and related to systemic diseases, which might happen prenatally, or postnatally in childhood.

#### **Statement of Problem**

In the past there has been no National Student Vision Screening in Laos, the number of children with visual disability are still found in great quantities in rural areas, they have insufficient access to care, because the recognition of importance for primary eye care is still low and the condition of the environment still confront difficulties for examination.

In 2016, there were 458 primary schools with a total of 49,117 students (F 23,681) in Oudomxay Province, Lao PDR.

No	District	Otr, of schools	Qty. of s	student
INU	District	Qty. of schools	Total	Female
1	Xay	71	11,105	5,506
2	La	40	1,977	888
3	Namor	59	6,692	3,192
4	Nga	62	5,598	2,706
5	Beng	59	5,099	2,418
6	Houn	103	12,930	6,255
7	Pakbeng	64	5,716	2,716
	Total	458	49,117	23,681

**Table 1.** The number of schools and students in primary school in Oudomxay province

 (2016)

The children at primary school are mostly in the age group of 5-14 years, these children's eye and vision are sensitive during growth development. If a child with vision impairment is not treated it can progress to become low vision or blindness.

The National Ophthalmology Center works with very few numbers of schools in four provinces (Louangprabang, Xiengkhuang, Savannakhet, and Champasak) to target screening school children.

Therefore, vision screening for students at primary school and finding out the causes of visual disability leading to a set of necessary and important data for measuring indices for the treatable and preventable of blindness for children at primary schools. The ophthalmologists and teachers collaborate in providing an adequate team in quantifying and analyzing the eye health of Lao PDR's children and identifying those at risk of blindness.

This study is aimed to evaluate and implement a school based child vision screening program, which would identify the causes of blurred vision, improve vision with glasses, and increase teachers' awareness of eye care. This information will enable us to find methodologies for prevention of blindness in the next phase.

#### Objective

#### **General Objective**

To study the percentage of vision impairment in students at primary schools in two districts of Oudomxay province.

#### **Specific Objective**

- To increase school teachers' awareness of eye care
- To determine the number/percentage of children with vision impairment
- To determine the major cause of vision impairment
- To improve vision with glasses

#### **Expected Outcome**

After the completion of this study, we hope to gain data and identify the cause of vision impairment in students attending the primary schools in two districts of Oudomxay province. In order to find preventive measures to reduce the number of childhood blindness and help children with refractive error who have not yet received treatment in these highly remote areas.

#### Materials and Methods Study Design

This was a cross-sectional descriptive study, in collaboration with school teachers by trained in vision screening and trained in how to prevent conditions such as conjunctivitis and eye injury for schools teachers, applying quantitative method to obtain data visual disability, was carried out in 155 primary schools in two districts.

#### **Study Site**

This study sites are selected in 155 schools in two districts of Oudomxay province

- Xay district (92 schools)
- Namor district (63 schools)

#### **Duration of Study**

Between November, 2016 to December, 2016

#### **Sampling Techniques**

All students in 155 schools were screened vision by teachers using Snellen chart at 6 meters, the results of the screening vision tests of all children were sent to Oudomxay Provincial Hospital Eye Unit. A team comprised of one ophthalmologist and one optometrist followed up with students identified with vision impairment at the schools to perform additional vision tests and eye exams.

#### • Inclusion Criterion

Children who as been studying in 155 primary schools in two districts (class room 1-5) with no

Figure 1. E chart and Snellen chart

regard to sex, age, tribe, religion, caste.

- **Exclusion** Criterion
  - ➢ Mental retardation
  - Student who is noncompliance to join in the study

#### **Sample Size**

All students enrolled in the 155 primary schools in two districts in 2016 were included in the study.

#### **Data Collection**

During the academic year, 155 primary schools were screened for vision impairment by teachers trained by ophthalmologists. Data collected (form record) included: a name, age, visual acuity (right eye / left eye), which used Echart, Snellen chart (figure 1)



There are 60 primary schools where there are students with vision impairment, clinical/ophthalmic examination was performed on the eyes of children who suffered vision impairment by ophthalmologist and optometrist, included:

- Redo visual acuity test, which used E-chart, Snellen chart. The visual loss graded according to WHO classification of blindness and visual impariment.
- Intraocular pressure was measured by Schiotz tonometer for children who presented with signs and symptoms of glaucoma.
- Anterior segment examination was performed using a flashlight and portable slit lamp
- Posterior segment examination was performed using an indirect or direct ophthalmoscope after mydriasis by tropicamide 1%.
- Auto-refraction or refraction was performed for children who vision impairment with anterior and posterior segment were normal or/and better vision with pinhole. Optometrist has recorded the result of refraction. Children confirmed with refractive errors were provided glasses.
- Those diagnosed with cataract and glaucoma were referred to the Ophthalmology Unit of the hospital.

#### **Data Analysis**

The data was recorded on the vision test record form for children including the name, age and visual acuity (right/left eye).

All children with vision impairment were recorded on PBL eye examination record form including personal details of the child, visual assessment, eye examination, major site of abnormality leading to visual loss, prognosis for vision and full diagnosis. Data was entered analysed into a database in Excel version 2007.

The dada was analysed to find out the percentage of the following:

- The distribution of sex and age
- The catergories of visual impairment (graded according to WHO classification)
- An onset of visual impairment during infacy/childhood or before
- The cause of visual impariment or blind
- Number of students which could be improved vision by glasses

#### Results

#### **Demographic Factors**

In all 16,982 students participated, with a median age 9 years (rang, 5 years-15 years). Total enrollment numbered 16,982, with 8,709 (48.72%) were males and 8,273 (51.28%) were females, shows in (Table 2.). The vision impairment with available correction (one and both eyes) of 133 children (0.78%)

with 62 (46.62%) were males and 71 (53.38%) were females, shown in (table 3.)





Table 2. The percentage of age and sex distribution

Age group	Male	Female	Total
1-5 years	821 (4.83%)	741(4.36%)	1,562 (9.20%)
6-10 years	6,012 (35.40%)	5,845 (34.42%)	11,857 (69.82%)
11-16 years	1,876 (11.05%)	1,687 (9.93%)	3,563 (20.98%)
Total	8,709 (51.28%)	8,273 (48.72%)	16,982 (100.00%)

Table 3. The age and sex distribution of children with visual impairment

Age group	Male	Female	Total
1-5 years	4	5	9
6-10 years	45	55	100
11-16 years	13	11	24
Total	62	71	133

WHO category	Level of visual	Freq.	Percent
	acuity		
No impairment	6/18 or better	16,849	99.22%
Viual impairment	<6/18-6/60	64	0.38%
Severe visual impairment	<6/60-3/60	44	0.26%
Blindness	<3/60-PL	14	0.08%
Absolute blindness	No PL	11	0.06%
Total		16,982	100.00%

The distribution of the visual acuity, based on WHO category, in worst eye (133 children) with available correction is shown in table 4.

(No PL=no perception of light; PL= perception of light)

The distribution of the visual acuity base the WHO category, in better eye (44 children) with available correction is shown in table 5.

WHO category	Level of visual	Freq.	Percent
	acuity		
No impairment	6/18 or better	16,938	99.74%
Viual impairment	<6/18-6/60	19	0.11%
Severe visual impairment	<6/60-3/60	22	0.13%
Blindness	<3/60-PL	3	0.02%
Absolute blindness	No PL	0	0.00%
Total		16,982	100.00%

(*No PL=no perception of light; PL= perception of light*)

#### Cause of Visual Impairment in worst eye (133 children)

Overall 80% of children with visual impairment has potentially avoidable (preventable and treatable), which refractive error was the first and most important cause followed by corneal scars. (table 6.)

Cause	Freq.	Percent
Refractive error	54	40.60%
Corneal scar	43	32.33%
Posterior segment diseases	29	21.80%
(traumatic 18 and other 11)		
Cataract	5	3.76%
Glaucoma	2	1.50%
Total	133	100.00%

Those diagnosed with cataract and glaucoma were referred to the Ophthalmology Unit of the hospital.

#### **Prognosis for Vision**

In this study, the number of cases where prognosis for vision could be improved and was treated was 60 (45.11%). These cases could be improved if it has been treated or with the best correction

- Refraction performed, distance visual acuity with corrective lenses provided to 45 children
- Cataract surgery performed on 5 children.
- Others, the visual acuity could be improved were corneal scaring if the eye has been treated by penetrating keratoplasty (PKP).

#### **Discusion And Conclusion**

This is the first study to screen vision and examine students enrolled in 155 primary schools in two districts in Oudomxay province. Although the initiative has not covered all schools, it is very helpful to detect cases at an early stage for prompt treatment in preventing amblyopia.

The results of this study shows refractive error (40.60%) to be the main cause of children with visual impairment. Our data also suggests that many children were never examined before and a lot of children do not like to wear glasses. However, we should advise the school teacher and the children's parents to become aware of this issue and involve them in improving vision for children.

Corneal scarring is the second most prominent cause of visual impairment in this study, corneal scaring in almost all cases occur when the child was by eye injury, infection, harmful traditional eye medicines predominate and from vitamin A deficiency. The pattern of children with visual impairment in this study almost certainly reflects from primary healthcare, teachers' awareness of eye care and socioeconomic status of Laos, there is a need for promote primary eye care to community.

Trained school teachers can play an important role in the prevention of childhood blindness. Visual screening among school children should be one of the indicators that National Ophthalmology Center should assign primary school teachers to conduct visual screening in children every year at the beginning of school year to detect children with impairment vision.

#### Recommendations

The results of this study created a data base that contributes to a creation of a recommendation guideline for the prevention of blindness in children of Lao PDR:

- Screening of preschool children
- Strengthening primary eye care programs

Screening of preschool children is aimed at the early detection of certain disorders such as ocular deviation and amblyopia.

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# Risk factors for pterygium in Cambodian people.

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**Introduction**: Pterygium is one of the most common eye diseases around the world especially in Aasia. Many studies on pterygium show that residence; age, race, sex, sunlight exposure, and education level were with risk for pterygium. Currently, the exact the pathogenesis of pterygium remains unclear, however the number of people working in agriculture related fields and regions are seen with a much higher risk of developing pterygium.

*Objective:* To determine the risk factors for pterygium in a group of Cambodian people.

*Materials and Methods:* Data were analyzed from 183 participants, in Preah Ang Doung Hospital and Takeo Eye Hospital, age ranged from 20-80 years old. Participants were asked to answer a questionnaire related to their everyday activities.

**Results**: Males were affected more than females. The most affected age range was 50-59 years old. The participants who live and work in rural areas were more populated with pterygium than that from the cities. More than 70% of the participants never have protection during work.

**Conclusion:** Pterygium was positively associated with older age and outdoor time and use of hat and/or sunglasses.

Keywords: pterygium, risk factors, outdoor time, sunlight exposure

*EyeSEA 2017*; *12 (1)*: *87-93 Full text.* <u>https://www.tci-thaijo.org/index.php/eyesea/index</u>

#### Introduction

Pterygium is a fibrovascular external disease of the globe involving the cornea. The wedge-shaped lesion usually found overhanging the nasal, temporal or rarely both side of the limbus and is directed centrally, give rise to many visual problem such as astigmatism or blindness if interfere with visual axis and can sometimes be a cosmetic complain. Treatment is consider because of these factors above and techniques have been modified over the years. As an external ocular disorder. "Pterygium" is commonly seen with a global prevalence of 0.7% to 33%.<sup>1</sup> About 30% to 90% of recurrences are seen after excisional surgery.<sup>2</sup> It is seen that a number of theories have proven the pathogenesis involving genetic, environmental, infective and immunological factors.<sup>3</sup> The exact etiology of pterygium still cannot be well explained although ultraviolet radiation (UVR) is а hypothetical risk factor that has been well studied before.<sup>4</sup> However, the risk factors for pterygium in Cambodia have not been sufficiently investigated. Since the majority of Cambodians work in agricultures and are highly exposed to sunlight, it would be interesting to study about how work fields correlate with the risk of developing pterygium.

#### **Objectives**

This study was performed to provide informative resources of pterygium related to work and their protection. It aims to study the risk factor of pterygium related to age, sex, geographic area, working time exposure to sunlight and their protection.

#### **Materials and Methods**

This study was a retrospective, hospital based study on pterygium in people aged from 20 to 80 years who receives the ophthalmic examination from January to June 2015 at Preah Ang Doung Hospital and Takeo Eye Hospital. The total population of the Study was 183. After the consultation, patients were asked to answer a questionnaire related to their everyday work. Questionnaire consists of: Age, Location, Occupation, Duration of sunlight exposure per day, and Protection against sunlight, which were taken at time of first consultation as a routine history taking for every patients. The Data was analyzed using Microsoft Excel for Mac 2008 version 12.0 (071130).

#### Result

The majority of patients studied were aged from 50-59 years (21.41%) which is an active age of doing outdoor activities. About 13.66% were 70-79 years which are senior therefore limit work ability. There was their predominance of Male patients: 107 (58.47%) of the total 183 being male versus 76 (41.53%) being female. Most of the patients are from Phnom Penh (19.87%) and Takeo Province (37.15%). Subsequently if we compare city to provincial residence in percentage it equals to City (19.87%) and Provenance (80.13%)



Figure 1: Age Distribution of Pterygium prevalence based on the average working age and sunlight exposure



Figure 2: Sex Distribution



Figure 3: Provenance Distribution

Among all the population in the study, 61.2% of them *always* work under the sunlight or high exposure to the sunlight. 24.59% rate their work with *often* and 14.2% *sometimes* work with sunlight exposure.

70.49% of the patients didn't have any protection during work. Whereas 3.82% can protect their eye from the sunlight and 25.68% can sometimes protect their eye with sunglasses or hat.

Work related to Sunlight exposure	Number	Percentages
Always	112	61.2%
Often	45	24.59%
Sometimes	26	14.2%

Table 1:	Work	related	to	sunlight	Exposure
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Sunglasses/Hat	Number	Percentages
Always	7	3.82%
Never	129	70.49%
Sometimes	47	25.68%

Table 2: Protection from sunlight with sunglasses or hat

#### Discussion

The results of this survey were in accordance with the notion that the prevalence of pterygium increased with age and it may be attributed to the accumulated sunlight exposure. In this survey, participants aged between 50 and 59 years had the highest prevalence of 21.41%, followed by the group of 60-69 years with a prevalence of 17.48%. The slightly lower pterygium prevalence in participants aged 80 years or above may be ascribed to a smaller sample size of 183 people. 4,564 people were studied by Fotouhi and results showed that pterygium prevalence increased by 0.1% in younger people aged from 1-19 years old to about 7.8% in the group older than 60 years old.<sup>5</sup> Another study was done in Indonesia,<sup>6</sup> revealed that there is a significant prevalence increase all around in all the different age group, ranging from 2.9% in people under 30 years old to 17.3% in people over 50 years old.

However associating gender as a risk factor is still controversial. Previous studies in Doumen County<sup>7</sup> suggest that women are at higher risk compared to men. However other studies have shown the opposite, as men are more prone to developing pterygium than women.<sup>8</sup> In the present study, the prevalence is slightly higher in men than that of women but not significantly different. The reason for a nearly equal sex distribution is that,

in order to improve their economic status, women have to do outdoor farming work rather than staying at home and depend on men as the sole breadwinner of the family.

In the provinces, the majority of residents take part in outdoor farming work and agricultural income is the exclusive economic source for their family. In our study, the prevalence of the patient who lives in the province (80.33%) is much higher than that of the people in the city (19.67%).

In the present study, outdoor work time is association with increased risk of developing pterygium. A large number of participants were occupied with working activities under the sunlight and they spent most of their day time In accordance outdoors. with the Barabasos Eye Study<sup>9</sup> and Rosenthal,<sup>10</sup> we agreed that UV radiation exposure increase pterygium prevalence and protection such as sunglasses and/or hats can prevent the disease. In our current studies we saw that the higher the exposure time to sunlight the higher this risks are and protection could also help reduce the incident of pterygium. Therefore these two factors should play a key role in providing us details of the risk factors of pterygium in correlation with work. How it protects and prevents eyes from pterygium rate is hypothetical but blocking of UVR and dust should be

important factors.<sup>11</sup> Therefore, people using hats or sunglasses had lower prevalence of pterygium. However, because a large proportion of the population depend on working outside for a living and sunlight exposure is inevitable, getting protection like hats and especially sunglasses is key in preventing as well as reducing the prevalence of pterygium.

The limitation of our study included the characteristics of a hospitalbased approach; small sample size and the severity of pterygium were not recorded during the survey. Regarding the UVR exposure, which may be the main cause for pterygium, was estimated by outdoor time in a questionnaire, rather than an objective measurement. Finally, not all the refractive statuses of participants were available in this study; the relationship between pterygium and astigmatism was unsure.

#### Conclusion

In conclusion, pterygium was positively associated with older age and outdoor time and use of hat and/or sunglasses. Because severe pterygium can result in visual impairment and blindness, it is important to take some preventive measures to diminish the prevalence of pterygium, such as suggesting people wear a hat and/or sunglasses whenever they are outside in the sunshine, educating farmers to raise their awareness for pterygium, and service providing surgery when pterygium is diagnosed. We hope that every effort will be taken to avoid the blindness caused by severe pterygium.

#### **Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this paper.

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