การวัดเชิงสัณฐานของปมประสาทซีลีอารี่ที่เกี่ยวข้องกับการประยุกต์ทางคลินิก

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วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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The morphometric study of the ciliary ganglion and its related clinical application

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หัวข้อวิทยานิพนธ์	การวัดเชิงสัณฐานของปมประสาทซีลีอารี่ที่เกี่ยวข้องกับการประยุกต์ทางคลินิก
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ปมประสาท ซีลีอารี่ เป็นปมประสาทในเบ้าตาที่โดนทำลายหรือทำให้บาดเจ็บได้ง่ายจากการทำหัตถการต่างๆ ในเบ้าตา ปมประสาทซีลีอารี่จะอยู่ทางด้านหลังในเบ้าตาที่ค่อนมาทางผนังเบ้าตาส่วนนอกเป็นผลให้หัตถการต่างๆที่เข้าทางเบ้าตาส่วนนอกมักส่งผลให้ปมประสาทโดนทำลายหรือบาดเจ็บ ซึ่งการที่ปมประสาทนี้เกิดการบาดเจ็บจะทำให้เสียหน้าที่การทำงานที่ทำให้เกิดม่านตาขยาย หรือ ภาวะรูม่านตาค้าง (tonic pupil) การศึกษารายละเอียดของปมประสาทซีลีอารี่ใน 40 ลูกตา จากอาจารย์ใหญ่ 40 ท่าน ทำโดยใช้แว่นขยายสำหรับผ่าตัดที่มีกำลังขยาย 3.5 เท่า เพื่อศึกษาลักษณะของรากที่เข้าสู่ปมประสาทซีลีอารี่ จำนวนของเส้นประสาทชอทซีลีอารี่ (short ciliary nerves) ตำแหน่งของปมประสาทซีลีอารี่ ขนาดของปมประสาทซีลีอารี่ และระยะห่างระหว่างปมประสาทซีลีอารี่กับโครงสร้างอื่นๆในเบ้าตา ปมประสาทซีลีอารี่ถูกพบว่าอยู่ที่ยอดหลังสุดของเบ้าตา ด้านข้างทางด้านนอกต่อเส้นประสาทออพติก ด้านข้างทางด้านในต่อกล้ามเนื้อตา lateral rectus ปมประสาทซีลีอารี่มีความกว้างประมาณ 2.24 มิลลิเมตร และความยาวประมาณ 3.50 มิลลิเมตร ระยะห่างโดยเฉลี่ยระหว่างปมประสาทซีลีอารี่และส่วนท้ายสุดของลูกตามีขนาด 16.04 มิลลิเมตร ระยะห่างโดยเฉลี่ยระหว่างปมประสาทซีลีอารี่และกล้ามเนื้อตา lateral rectus มีขนาด 2.88 มิลลิเมตร ระยะห่างโดยเฉลี่ยระหว่างปมประสาทซีลีอารี่และเส้นประสาทออพติก มีขนาด 1.47 มิลลิเมตร ระยะห่างโดยเฉลี่ยระหว่างปมประสาทซีลีอารี่และจุดเกาะที่ตาขาวของกล้ามเนื้อตา lateral rectus มีขนาด 31.53 มิลลิเมตร นอกจากนี้ความสัมพันธ์ระหว่างระยะห่างจากปมประสาทซีลีอารี่ถึงจุดที่อยู่ท้ายสุดของลูกตาเป็นแบบผกผันกัน กับ ระยะห่างจากปมประสาทซีลีอารี่ถึงกล้ามเนื้อตา lateral rectus นั่นหมายถึงยิ่งปมประสาทอยู่ห่างจากลูกตาจะยิ่งอยู่ใกล้กล้ามเนื้อ lateral rectus ส่วนจำนวนของรากประสาทมอเตอร์ (motor root) ถูกพบว่ามี 1 ราก 2 ราก และ ยังพบถึง 3 รากโดยที่ยังไม่มีรายงานมาก่อน รากประสาทรับความรู้สึกพบว่ามี 1 ราก รากประสาทซิมพาเทติก (sympathetic root) พบ 1 รากเช่นเดียวกับรากประสาทรับความรู้สึก จำนวนของเส้นประสาทชอทซีลีอารี่จะพบประมาณ 6-14 เส้น แพทย์ผู้ทำหัตถการในส่วนเบ้าตาควรตระหนักถึง ความรู้ทางด้านกายวิภาคและลักษณะต่างๆของปมประสาทซีลีอารี่เพื่อลดการเกิดผลแทรกซ้อนจากปมประสาทนี้บาดเจ็บเช่น ม่านตาขนาดผิดปกติ ในรายงานฉบับนี้ยังแสดงถึงระยะห่างระหว่างปมประสาทซีลีอารี่กับจุดเกาะของกล้ามเนื้อตา lateral rectus ที่ตาขาวซึ่งยังไม่มีรายงานมาก่อนและควรคำนึงเพื่อลดการบาดเจ็บของปมประสาทซีลีอารี่ในหัตถการฉีดยา โบทูลินัม (botulinum toxin) เข้ากล้ามเนื้อตา lateral rectus ในการรักษาภาวะตาเข

สาขาวิชา	วิทยาศาสตร์การแพทย์		ลายมือชื่อนิสิต ....
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Lita Tesapirat : The morphometric study of the ciliary ganglion and its related clinical application. Advisor: Prof. VILAI CHENTANEZ, MD. Ph.D.

Ciliary ganglion can be easily injured without notice in many intraorbital procedures. It lays posterolateral in the orbit; the surgical procedures approaching lateral side of the orbit are always associated with the ciliary ganglion injury which may results in transient mydriasis and tonic pupil. 40 embalmed cadaveric globes were dissected under surgical loupe to observe characteristics of roots reaching the ciliary ganglion, number of short ciliary nerve, location of the ciliary ganglion in the orbit. Morphometry of the ciliary ganglion and distances between the ciliary ganglion and important landmarks were measured. The ciliary ganglion located near orbital apex, lateral to optic nerve and medial to lateral rectus muscle. The mean width of the ciliary ganglion was 2.24 mm and the mean diameter from anterior edge to posterior edge was 3.50 mm. The mean distances from the ciliary ganglion to posterior end of globe, lateral rectus muscle, optic nerve and the scleral insertion of the lateral rectus muscle were 16.04 mm, 2.88 mm, 1.47 mm and 31.53 mm, respectively. Moderate inverse correlation was found between the distance from the ciliary ganglion to posterior end of globe and the distance between the ciliary ganglion and the lateral rectus muscle. The number of motor root could be 1,2 and also 3 roots which had not been reported. Sensory root was found only 1 root in every specimen. Sympathetic root could be observed 1 root in most of the specimens. The number of short ciliary nerves was 6-14 nerves. This anatomical knowledge should be concerned in intraorbital procedures to reduce complication of the ciliary ganglion injury. The new measurement from the ciliary ganglion to scleral insertion of lateral rectus muscle could be applied in intraorbital surgeries and also in botulinum toxin injection to ocular muscles.

Field of Study:	Medical Sciences	Student's Signature ....
Academic Year:	2019	Advisor's Signature ....

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สารบัญ

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สารบัญตาราง

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Chapter I Background and rationale

Ciliary ganglion is 3 mm in size and easily injured without notice in many procedures[1]. It lays posterolateral in the orbit, so the surgical procedures approaching lateral side of the orbit are always associated with the ciliary ganglion injury such as lateral orbitotomy, inferolateral endoscopic orbital approach (IL-EOA), transmaxillary approach to the orbit, lateral approach of optic nerve sheath fenestration and inferior oblique muscle surgery [2-7]. Therefore, the morphometric study of the ciliary ganglion is essential for surgeons in order to make preferable results of these operations including the distance between: the ciliary ganglion and the optic nerve, the ciliary ganglion and the lateral rectus muscle, and the ciliary ganglion and posterior end of the globe. Botulinum toxin A (BTX-A) injection is used for treatment of strabismus, blepharospasm and cosmetic purpose. There are some reports of transient mydriasis as a complication of these procedures. The cause of transient mydriasis is either by means of trans-scleral diffusion or by ciliary artery perfusion if the injection was superficial to the muscle or to anticholinergic toxicity or direct injury at the level of the ciliary ganglion if the injection was deep to the muscle [8-10]. As a result, the knowledge about morphometric studies of the ciliary ganglion can help surgeons the chance of the ciliary ganglion injury during BTX-A injection procedure.

Ciliary ganglion is posterolaterally located in orbital apex, between optic nerve and lateral rectus muscle and close to lateral side of ophthalmic artery. It has vital functions in autonomic control of eyes such as controlling pupil size and accommodation reflex. Three types of nerve fibers run into the ciliary ganglion including parasympathetic root from Edinger Westphal nucleus, or called motor root, sympathetic root from internal carotid plexus or plexus around the ophthalmic artery, and sensory root from nasociliary nerve[1]. Because it is small and is obscured by the similar color orbital fat between the lateral rectus muscle and the optic nerve, it is difficult to be identified during surgery.

The ciliary ganglion injury can cause mydriasis of the affected eye which is the local type tonic pupil. This tonic pupil involves in both the ciliary ganglion and the short ciliary nerve injury. The patients have unilateral pupil dilation, poor or absent light reflex response and light near dissociation[11]. Some of the patients with the ciliary ganglion injury can be recovered.

There are two studies depicting morphology or morphometry of the ciliary ganglion and also its relation with the surrounding structures. The first study, Sinnreich and Nathan (1980), described morphology and location of the ciliary ganglion. The interesting part of their study is observation of the root reaching the ciliary ganglion including motor parasympathetic root, sympathetic root and sensory root. They told about the number of each root and varied sites where the roots branching from but they did not measure distance between the ciliary ganglion and its surrounding structures[12]. Izci and Gonul (2006), is the first publication about the morphometric study of the ciliary ganglion. They showed width and length (largest diameter paralleling to the optic nerve) of the ciliary ganglion, and also the distance between it and other structures including posterior end of the globe, site of the ophthalmic artery crossing the lateral side of the optic nerve, the optic nerve, superior ophthalmic vein, inferior ophthalmic vein and the lateral rectus muscle[1]. But, they did not show the distance between the ciliary ganglion and the scleral insertion point of the lateral rectus muscle which is quite important for BTX-A procedure as mentioned before. Girijavallabhan and Ramakrishna (2008), reported about the position variation of the ciliary ganglion. They discovered that the ciliary ganglion lied between the medial rectus and the optic nerve[13]. So, this variation location of the ciliary ganglion must be observed and considered during any medial approach procedure.

As aforementioned, the anatomical knowledge of the ciliary ganglion is essential for surgeons operating surgery or procedure in the posterolateral area of the orbit. The morphometric study can be benefit for surgeons to be aware of the ciliary ganglion injury. Therefore, this study will focus on the distance between the ciliary ganglion and other structures which are believed to be principal landmark for conducting the procedures consisting of the scleral insertion point of the lateral rectus muscle, the optic nerve, the lateral rectus muscle, and posterior end of the globe. In addition, the number of the short ciliary nerves, the number of each root reaching the ciliary ganglion and position variation of the ciliary ganglion location in Thai cadavers will be observed. This knowledge will be useful information for any related procedure especially in Asian patients.

Research questions

Primary research question

1. What are the distance between the ciliary ganglion and surrounding structures in Thai cadavers?

Secondary research questions

1. Are there any variations of the ciliary ganglion position in the orbit in Thai cadavers?
2. What is the size of the ciliary ganglion of Thai cadavers?
3. What are the characteristic of the ciliary ganglion's roots in Thai cadavers?
4. How many numbers of short ciliary nerves given off from the ciliary ganglion in Thai cadavers?

Objectives

1. To measure distance between the ciliary ganglion and posterior end of the globe (site where optic nerve exits the eyeball)
2. To measure distance between the ciliary ganglion and the scleral insertion of lateral rectus muscle
3. To measure shortest distance from the ciliary ganglion to the lateral rectus muscle

4. To measure distance from the ciliary ganglion to the optic nerve

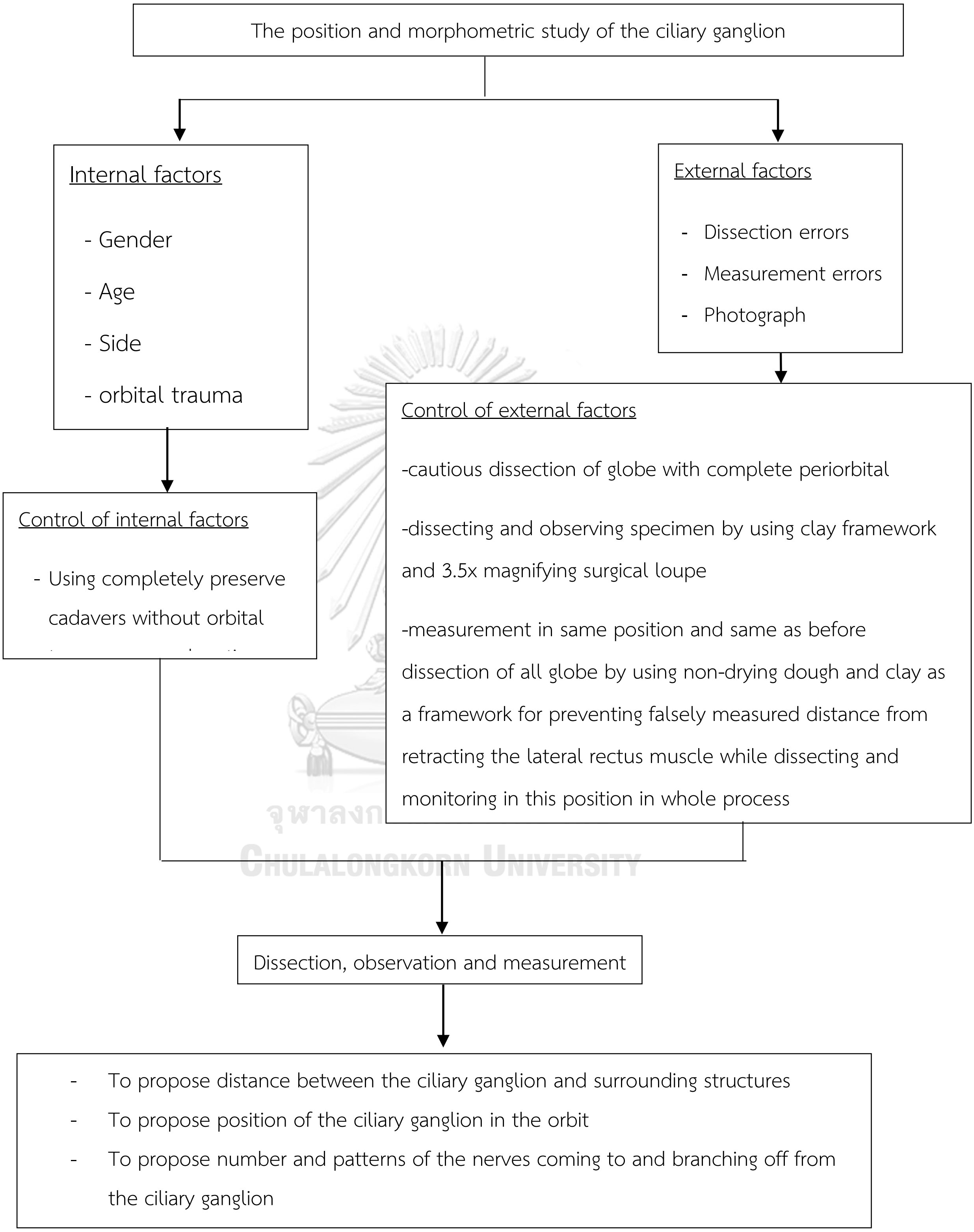
5. To investigate the position variation of the ciliary ganglion in the orbit

6. To measure size of the ciliary ganglion

7. To study pattern and number of motor parasympathetic root, sensory root and sympathetic root reaching the ciliary ganglion

8. To evaluate the number of short ciliary nerves branching from the ciliary ganglion

Conceptual framework



Key words: ciliary ganglion, short ciliary nerves, tonic pupil

Research design: Descriptive study

Expected benefits and applications

This current study will explain more anatomical knowledge in detail of morphometric study of the ciliary ganglion and surrounding structures which are believed to be important surgical landmarks in Thai cadavers. This reinvented knowledge will help surgeons diminish postoperative or post-procedural complications which are resulted from the ciliary ganglion injury.

Chapter II Literature review

Ciliary ganglion, 3 mm in size, locates in orbital apex, lying in posterolateral to eyeball in loose areolar tissue. This ganglion places in inferolateral aspect of optic nerve, medial to lateral rectus muscle, lateral to ophthalmic artery, approximately 1 cm in front of annular tendon and about 1.5 cm through 2 cm behind the eyeball[1, 12, 14]. There is a study by Izci and Gonul (2006) which reveals distance between the ciliary ganglion and important structure in the orbit related to ciliary ganglion injury, for instance optic nerve and lateral rectus muscle. The mean distance between the ganglion and optic nerve is 2.9 mm (range 2.7-3.1 mm)[1]. The mean distance between the ganglion and lateral rectus muscle is also measured as 10.4 mm (range 9.2-11.2 mm)[1]. The ganglion is the site to which three types of fiber going ahead with two types just passing through and forming only one synapse. The motor parasympathetic fibers from oculomotor branch to inferior oblique muscle forms synapse with post ganglionic neurons. They carry parasympathetic fibers from Edinger-Westphal nucleus and anteromedian nuclei of midbrain. They arrive ciliary ganglion in postero-inferior angle. The post ganglionic fibers leave by the route of short ciliary nerves which pass through the lamina cribosa sclerae to innervate ciliary muscle and iris sphincter muscle. The sensory root reaches the ganglion at its postero-superior angle by means of nasociliary nerve (ophthalmic nerve branch) without forming synapse. The sensory fibers carry information from iris, ciliary body and mainly cornea to the ciliary ganglion by short ciliary nerve. After leaving from the ciliary ganglion, the sensory fibers join the nasociliary nerve and then join the ophthalmic nerve. From there, the sensory signal will come back to the brainstem by trigeminal nerve. The sympathetic fibers are formed by post ganglionic fiber from neurons located at the superior cervical ganglion. The sympathetic preganglionic fibers come from neurons located in the intermediolateral cell column (IML) in the C8-T2 segments of the spinal cord running through first thoracic spinal nerve, ascend through the inferior and middle cervical ganglion, and form synapse when reaches superior cervical ganglion. The postganglionic fibers leave superior cervical ganglion via internal and external carotid nerve, then form the carotid plexus around internal carotid artery as seen in figure 1. The sympathetic root to the ciliary ganglion originate either directly from the carotid plexus or cavernous plexus in cavernous sinus and come to the orbit via superior orbital fissure, or from plexus around the ophthalmic artery which is already in the orbit[15]. Natori and Rhoton (1995), found the sympathetic root coming from both sources[16]. The sympathetic root passes through without forming synapse and reaches the ciliary ganglion at its posterior border between the other two roots. They go to the globe by the short ciliary nerve and arrive at the eyeball vessel for controlling vasoconstriction and pupil dilator muscle for sympathetic response of iris [12, 16].

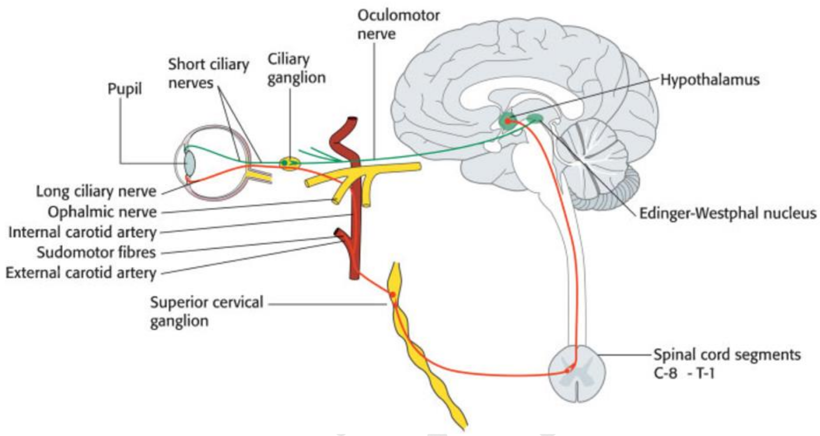


Figure 1. Sympathetic innervation to the pupillodilator. (Yeo et al. 2010)[17]

The ciliary ganglion branches out 6 to 10 short ciliary nerves in number, but approximately 12 to 20 filaments. These branches penetrate sclera at the exit site of the optic nerve, running ahead along with ciliary arteries above and below the optic nerve [1, 12].

The previous morphometric study of the ciliary ganglion

Sinnreich and Nathan (1981), described about anatomical observation of the ciliary ganglion[12]. They studied in 30 cadavers and found that the ciliary ganglion had an irregular, ovoid or rectangular shape with its largest diameter locating along the lateral aspect of optic nerve in the posterior part. The structures on the lateral side of the ganglion are the abducens and the lateral rectus muscle, separated by a thin layer of orbital fat. They did not measured distance of the ciliary ganglion with other structures in the orbit, but made observation about the roots reaching the ciliary ganglion. Motor parasympathetic root presented in 28 cases in form of one root, but some had double root. The other 2 cases did not have motor root, in one of these cases the ganglion was directly attach to the inferior oblique muscle branch of oculomotor nerve, and in the other the ciliary ganglion lay in direct opposition to the inferior branch of oculomotor nerve. Every case had sensory root from nasociliary nerve. The sympathetic root was identified in 22 specimen; 20 cases had the sympathetic root originated from internal carotid plexus, in the other 2 cases the sympathetic root derived from the plexus surrounding the ophthalmic artery or one of its branches. In 3 of 20 cases, there were two sympathetic roots derived from both internal carotid artery and ophthalmic artery. From their study, they recommended that the ciliary ganglion could be found by following the oculomotor branch to inferior oblique muscle backwards up to the motor root of the ganglion. The oculomotor branch to the inferior oblique runs parallel and close to the inferior border of the lateral rectus muscle[12].

Izci and Gonul (2006), depicted the ciliary ganglion width and length in parallel axis to the optic nerve and the distance between the ciliary ganglion and other structures including the posterior end of the globe, site of the ophthalmic artery crossing the lateral side of the optic nerve, the optic nerve, superior ophthalmic vein, inferior ophthalmic vein, lateral rectus muscle. They also concentrated on the number of the short ciliary nerve[1]. Their study is the first to describe specific and detailed study about morphological aspects, and also morphometric study of the ciliary ganglion as shown in table 1 and table 2.

Distance	**from**	**to**
A – B	Posterior end of the globe	Anterior edge of the ciliary ganglion
B – C	Anterior edge of the ciliary ganglion	Posterior edge of the ciliary ganglion
C – D	Posterior edge of the ciliary ganglion	Site of the ophthalmic artery crossing the lateral side of the optic nerve
A – C	Posterior end of the globe	posterior edge of the ciliary ganglion
A – D	Posterior end of the globe	Site of the ophthalmic artery crossing the lateral side of the optic nerve

Table 1. The landmarks of the morphometric measurements (Izci et al. 2016)[1]

Measurement sites	**Mean [mm]**	**Range [mm]**
A – B	12	7.75 – 19.80
B – C	5.25	4.15 – 6.45
C – D	4.1	3.25 – 9.70
A – C	18.08	12.80 – 23.50
A – D	18.16	15.10 – 23.50
Width of CG	3.04	2.75 – 3.40
CG – ON	2.90	2.70 – 3.10
CG – SOV	5.1	4.70 – 5.60
CG – IOV	4.5	3.70 – 4.90
CG – LRM	10.4	9.20 – 11.20
Number of SCN	7	6 – 10

CG = ciliary ganglion, ON = optic nerve, SOV = superior ophthalmic vein, IOV = inferior ophthalmic vein, LRM = lateral rectus muscle, SCN = short ciliary nerves.

Table 2. Measurements of the anatomic structures related to the CG (Izci et al. 2016)[1]

Girijavallabhan and Ramakrishna (2008), reported about the position variation of the ciliary ganglion. They found the right eye ciliary ganglion of 62 years old, south Indian female cadaver positioned between the optic nerve and medial rectus muscle, lateral to the ophthalmic artery. It is close contact to the ophthalmic artery and locating superomedial to the optic nerve, beneath the superior rectus muscle. On the other hand, in the left eye ciliary ganglion, the position, branching pattern and its association with other structures are normal[13].

Moreover, orbit composes of four sides, like pyramidal shape, with the narrowest part of orbital apex. It is rich in neurovascular structure in the confined space[18]. Most of these compact structures have important roles for ocular function such as eye movement, light reflex, accommodation reflex and regulation of ocular blood flow[15].

As oculomotor nerve, abducen nerve, trochlear nerve, which innervate extraocular muscle of eyes, are essential nerves for eye movement[14]. These come from nuclei in midbrain and pons and pass through superior orbital fissure to synapse their targets. Most of extraocular muscles are innervated by oculomotor nerve. In addition, oculomotor nerve and its branches also play important roles in autonomic system function of eye[18].

Oculomotor nerve departs from midbrain originating from two nucleus which are oculomotor nucleus at the level of superior colliculus, and Edinger-Westphal nucleus as seen in figure 2. Oculomotor nucleus consists of five subnuclei. Each nuclei gives general somatic efferent axon to innervate different extraocular muscle, and also levator palpebrae superioris muscle. Edinger-Westphal nucleus, or called accessory oculomotor nucleus, is a combination of preganglionic parasympathetic neuron. General visceral efferent axons are fibers that come out from this nucleus. They mainly control parasympathetic autonomic system including pupil constriction in light reflex and accommodation reflex. They give branch to innervate sphincter pupillae muscle and ciliary muscle for controlling light reflex and accommodation reflex respectively. These nucleus give fibers together with fibers from oculomotor nucleus to form oculomotor nerve[19]. Oculomotor nerve leaves midbrain via cerebral peduncle forward to interpeduncular cistern. After entering interpeduncular cistern, it passes through cavernous sinus going ahead to enter the orbit by superior orbital fissure[20]. Superior orbital fissure is the site assembling of dura, periorbital of orbital apex and annular tendon. The annular tendon is the origin of extraocular muscle and covers upper-medial portion of superior orbital fissure[21]. As oculomotor nerve come into annular tendon, then it is separated into two branches including superior and inferior division in oculomotor foramen. Oculomotor foramen is the central part of superior orbital fissure and surrounded by some parts of annular tendon and lesser wing of sphenoid bone[16].

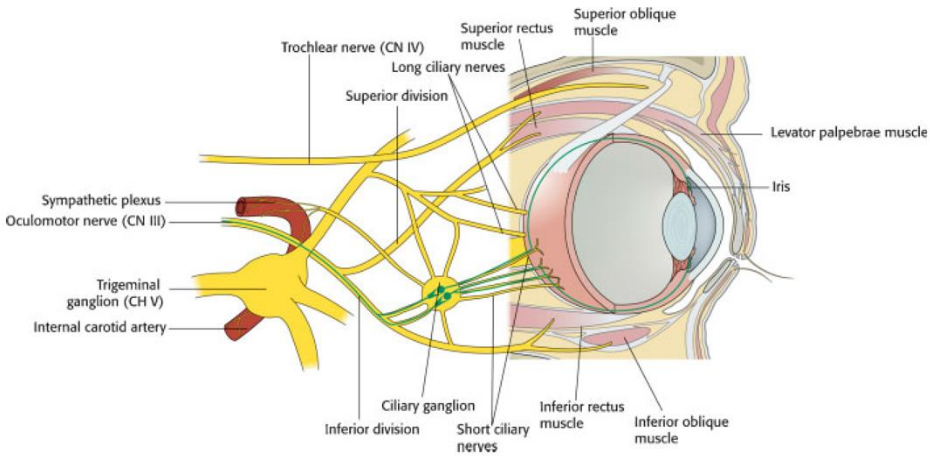


Figure 2. Ciliary ganglion and innervation to the muscle of the eye. (Yeo et al. 2010)[17]

The superior division of oculomotor nerve runs beneath the lesser wing of sphenoid bone, then gets into the orbit at which is the origin of superior rectus muscle and above ophthalmic artery. At this site superior division of oculomotor nerve gives innervation to levator palpebrae superioris and superior rectus muscle[14].

Meanwhile, the inferior division of oculomotor nerve passes through the inferomedial part of superior orbital fissure locating medial to abducens nerve and nasociliary nerve which is the branch of ophthalmic nerve. It gives 3 branches to innervate inferior oblique muscle, inferior rectus muscle and medial rectus muscle. Innervation to the inferior oblique muscle is found to be the longest branch as seen in the figure3[14].

The branch to inferior oblique muscle also brings general visceral efferent fibers from parasympathetic preganglionic neuron of Edinger-Westphal nucleus, to form synapse in ciliary ganglion[18].

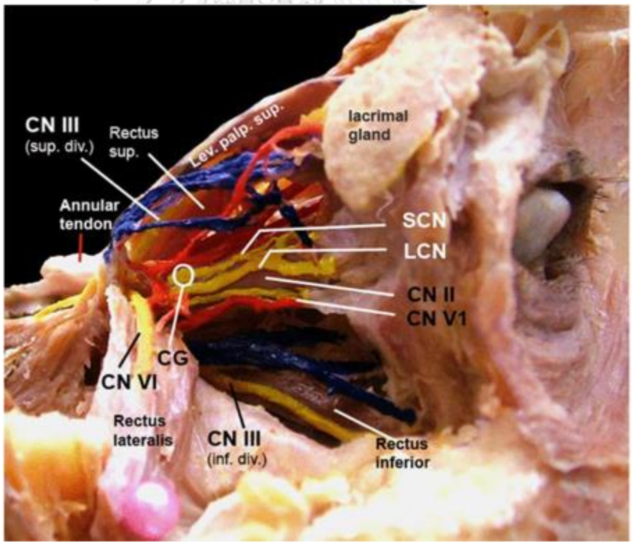


Figure 3. Contents of the orbit, lateral view of right side. The ciliary ganglion is located just lateral to the optic nerve. The rectus inferior is innervated by the inferior division of the oculomotor nerve. The long ciliary nerves which are branches of nasociliary nerve of ophthalmic nerve are by passing ciliary ganglion to enter the orbit. The relation of the nerves with the branches of the ophthalmic artery (colored red) and vein (colored blue) can be noted. CG: ciliary ganglion; LCN: long ciliary nerves; SCN: short ciliary nerves (Apaydin et al. (2018))[18]

The surgical technique of orbital surgery and the ciliary ganglion injury

Lateral orbitotomy is adequate exposure for tumors located in superior, lateral or inferior to optic nerve seen in figure 4. It is not associated with intracranial compartment, simply performed, safe and flexible to the lesion in more anterior. I t is possible to approach by a 35 mm skin incision or using coronal flap[2]. In superior approach, inferior approach and central approach of this procedure, the lateral rectus muscle is retracted inferiorly, superiorly and disinserted respectively. The ciliary ganglion and ciliary nerves which locate in posterolateral in the orbit, lateral to optic nerve can be easily accesses or injured because retracted lateral rectus muscle not any longer protect these structure. In addition, in the inferior and central approach, there is exposure to not only ciliary ganglion and its nerve, but also inferior division of oculomotor nerve to inferior oblique muscle which send branch to form synapse in the ciliary ganglion[2]. Many large lesions which occupy both the muscle cone and inferior nasal portion of the orbit; inferolateral orbitotomy is required for complete excision as it provides more exposure. For the inferolateral approach, the globe is retracted superiorly and the inferior rectus is retracted laterally and superiorly or disinserted and retracted. The contents of inferior and inferomedial compartment of the orbit and inferior surface of the optic nerve will be exposed including the short ciliary nerve, the ciliary ganglion, the inferior ophthalmic vein and the inferior oblique muscle branch of inferior division. During this approach the ciliary ganglion, the short ciliary nerve and the long course of nerve to the inferior oblique are high risk to be injured and cause unilateral mydriasis[22]. Besides, in Inferolateral endoscopic orbital approach (IL-EOA), an alternative microsurgical procedure of lateral obitotomy, the ciliary ganglion and short ciliary nerve are in peril since the lateral rectus muscle is disinserted and retracted posteriorly, then not blocks these structure[3].

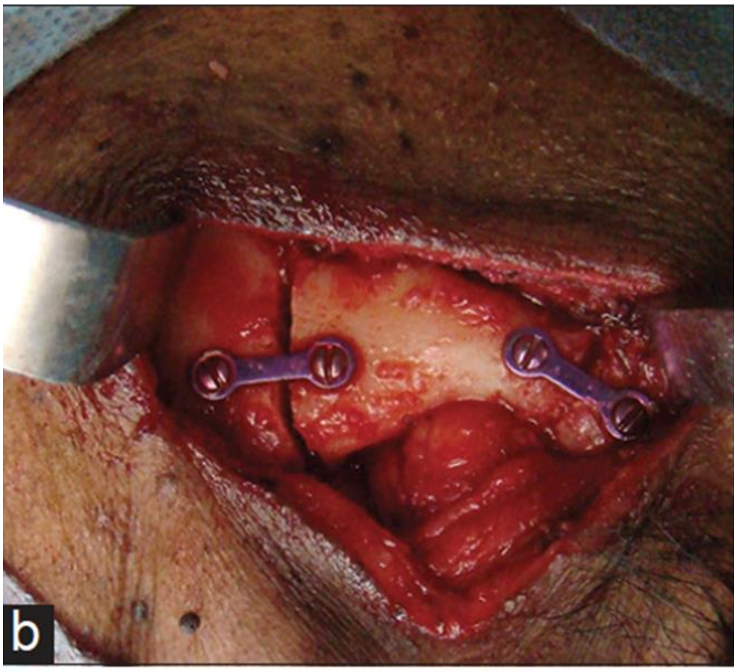


Figure 4. Process of the zygomatic bone and frontal bone were removed during lateral orbitotomy[23]

Gonul et al. (2003) performed transmaxillary approach to the orbit which offered access to the inferomedial and inferolateral orbit and to the inferior aspect of the optic nerve (figure 5). It is an alternative technique for orbital surgery. Furthermore, It provides a less invasive extradural approach to the orbit with avoiding the use of craniotomy and brain retraction and is cosmetically acceptable. Although this technique looks safe and preferable, it takes some risks for the ciliary ganglion and other neural structures injury, especially via the lateral route of approach. The inferior oblique muscle branch of the oculomotor nerve, the motor root to the ciliary ganglion, and the short ciliary nerves can also be damaged because these neural structures often escape notice within the orbital fat[4].

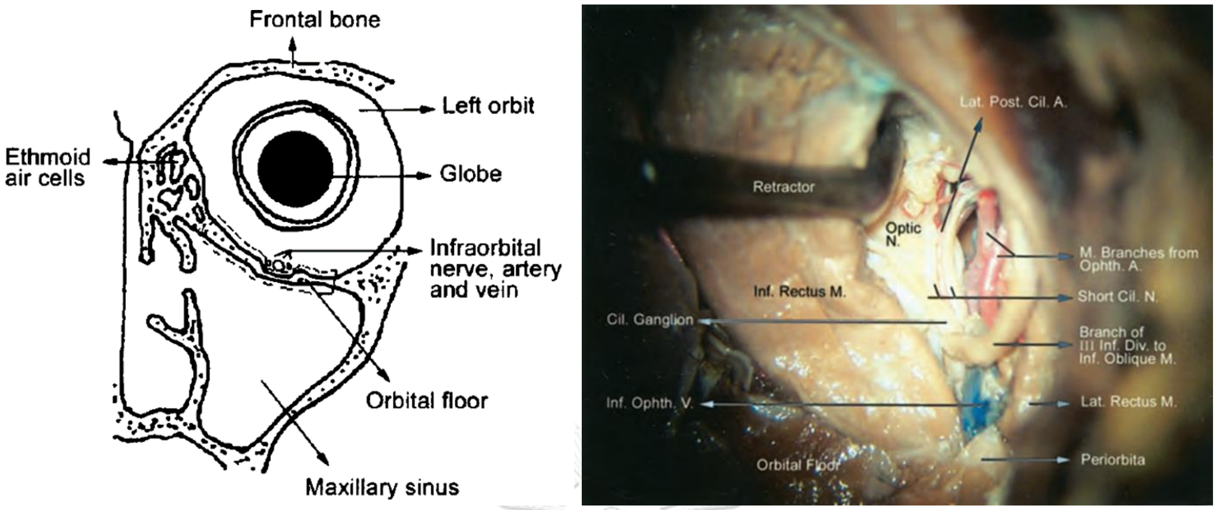


Figure 5. Orbital floor was removed during transmaxillary approach. By inferolateral approach, the ciliary ganglion could be found. [4]

Kyung Ah (2017) and Jae Il (2016) report cases about manipulation of inferior oblique muscle during medial orbital floor fracture reconstruction can cause unilateral mydriasis because of interruption of parasympathetic pathway[24, 25]. Since, the medial orbital floor fracture itself is low possibility of direct nerve or ganglion injury but inferior oblique muscle, which joins the capsulopalpebral fascia with inferior rectus muscle, is always aggressively manipulated during medial/inferior rim of orbit fracture reconstruction and then results in motion of inferior rectus muscle. As inferior division of oculomotor nerve travels on inferior rectus muscle, it will also be interrupted[17]. It is believed that in posterior orbital fracture cases, surgical manipulation of or around the ciliary ganglion also accounts for mydriatic pupil[7]. Horn Blast and Still Water also reported the association of posterior orbital floor fracture and unilateral mydriasis pupil[26]. Moreover, during inferior oblique muscle surgery as a treatment of strabismus especially in denervation-extirpation, excessive traction on it can cause excessive traction on the ciliary ganglion. As a result, excessive traction of this muscle can cause injury to the ciliary ganglion directly[6]. There was a presumption that intraoperative manipulation of the nerve to the inferior oblique muscle, inferior rectus muscle, ciliary ganglion, or short ciliary nerves, causing disturbance formation of the parasympathetic fibers with subsequent transient conduction block, and will result in the anisocoria[26, 27]. As a result, medial or posterior orbital floor fracture patients who will undergo reconstruction and strabismus patients who will have inferior oblique muscle surgery should be warned before operation about possible anisocoria complication. Moreover, surgeons should avoid placing retractor too posterior along lateral side of orbit to evade the ciliary ganglion manipulation[17].

Some ophthalmologists introduce botulinum toxin (BTX-A) injection into the antagonist muscle of the paretic muscle to decrease adduction tone of antagonist muscle as one of the treatment choices of strabismus. Moreover, BTX-A is used for treatment of blepharospasm and cosmetic purpose. Five cases of transient mydriasis from botulinum toxin (BTX-A)injection to extraocular muscles were reported in humans[8]. In these five cases, after botulinum toxin injection, mostly to the lateral rectus muscles, transient mydriasis was shown with tonic pupils. The most likely suggested cause was injury to the ciliary ganglion, resulting in weakened accommodation. All of these cases, mydriasis were showed temporary and only for a few weeks[8]. Hemmerdinger et al, 2006 showed one of those five cases included a case of 69-year old man patient with horizontal hypometric saccades (secondary to his cerebrovascular accident) injected with BTX-A 1.25 international units (IU) to the lateral rectus muscle of right eye. He received similar dose of BTX-A a month later and was repeated twice at quarterly intervals. Three months after first BTX-A injection, he got mydriasis of the right eye and resolved by 20 weeks. He was suspected to have the ciliary ganglion injury during BTX-A injection[10]. On the other hand, there was also a report about BTX-A injection to medial rectus and then causing transient mydriasis of affected eye. Christiansen et al (2016) reported 3 cases out of 27 participants developed left eye tonic pupil after they were performed BTX-A injection to medial rectus muscle as a treatment of esotropia. All 3 cases tonic pupil occurred in the left eye of participants who underwent bilateral BTX-A injection by the same surgeon. Anisocoria was found at the 2 week visit post injection. BTX-A injection was not standard performed using a closed conjunctival technique without electromyography control because this study was conducted in the part of the routine care. One possible reason for left eye tonic pupil may be inaccurate needle placement in muscle because the surgeon was right handed. Akkaya et al, 2015 found unilateral transient mydriasis and ptosis after botulinum toxin injection for a cosmetic procedure in 36-year-old patient(8). The most likely suggested cause was cumulative high dose of BTX-A injection which resulted in pharmacological blockage.

The cause of tonic pupil in these procedures was suspected to be pharmacological blockade of the cholinergic terminals in the iris by means of trans-sclera diffusion or by ciliary artery perfusion if the injection was superficial to the muscle or to anticholinergic toxicity or direct injury at the level of the ciliary ganglion if the injection was deep to the muscle(9). This procedure, the tip of needle may cause ciliary ganglion injury as it lays medial to lateral rectus muscle.

Optic nerve sheath fenestration (ONSF) is most commonly indicated in for optic neuropathy in the setting of raised intracranial pressure, especially in patients with severe or progressive visual loss due to pseudotumor cerebri syndrome (PTSC). The greatest morbidity from this disorder is visual loss related to optic disc swelling. PTSC is classified to primary pseudotumor cerebri syndrome or idiopathic intracranial hypertension (IIH), and secondary pseudotumor cerebri syndrome which include etiologies such as medications, medical conditions, and cerebral venous abnormalities. In 1964, Hayreh first depicted that papilledema was a sequence of increase intracranial pressure and could be relieved by reducing the CSF pressure in subarachnoid space of optic nerve(28). Management of both types of PTSC depends on the level of visual loss.

In addition, other indications for ONSF are severe visual loss at presentation, inability to comply with medications, poor follow-up, or inability to cooperate with visual field testing. In ONSF, windows or slits, followed by blunt lysis of subarachnoid adhesions, are created through the dura and arachnoid surrounding the optic nerve or a window of dura can be excised. The lateral orbitotomy approach of optic nerve sheath fenestration is depicted in figure 6. This procedure allows CSF release which makes CSF pressure decrease.

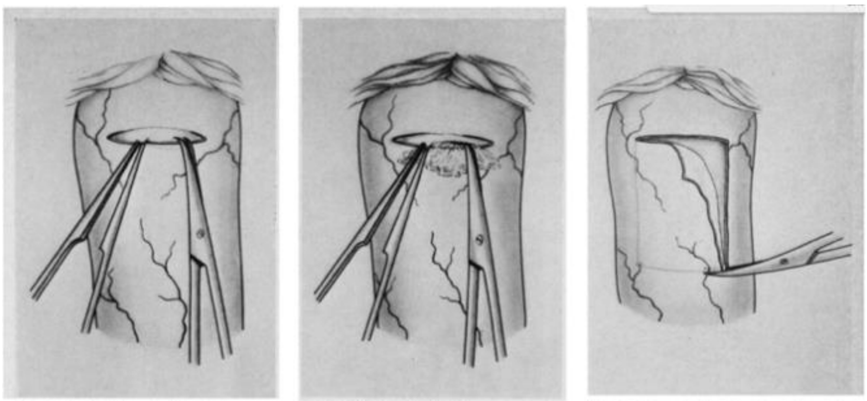


Fig 1.—Arachnoid and edge of dura are grasped with forceps.

Fig 2.—Cerebrospinal fluid escapes once arachnoid is incised.

Fig 3.—One blade of microscissors is inserted into subarachnoid space, and rectangular window is excised from sheath.

Figure 6. The lateral orbitotomy approach of optic nerve sheath fenestration (Tse et al. 1988)[5]

There are many surgical approach techniques, for instance the lateral orbitotomy approach, the medial approach and anterior medial upper eyelid crease approach[29]. The medial approach (transconjunctiva and under the medial rectus muscle) is more popular due to less complicated technique. Each approach has technical advantages and disadvantages, depended on surgeon preferences. One of the lateral orbitotomy approach disadvantages is that there is a chance to injure ciliary ganglion and posterior ciliary nerve resulting in anisocoria and accommodative dysfunction.

As a result, the surgeon who uses these techniques must have good knowledge about the ciliary ganglion and its surrounding structures to diminish risk of the ciliary ganglion injury.

The affects of the ciliary ganglion and its branches injury

Following the injury to the nerve to inferior oblique muscle, the ciliary ganglion and the short ciliary nerve, there will be mydriasis on the affected eye because of disruption of parasympathetic pathways. Furthermore, injury to this pathway can also cause tonic pupil. There are three type of tonic pupil including: Adie tonic pupil, neuropathic tonic pupil and local tonic pupil[30]. The local tonic pupil, which is one of the three types, involves in the ciliary ganglion and the short ciliary nerve injury. Furthermore, the local tonic pupil has some characteristics which observation may include: unilateral dilation of pupil; light near dissociation (LND) which is poor or absent response to light but response to near; segmental palsy of the iris sphincter; and denervation hypersensitivity to the dilute cholinergic agents. Due to disruption of parasympathetic innervation to the iris sphincter, there is anisocoria with the affected pupil larger than the other side. The affected pupil fails to react to light, but constrict slowly and long-lasting when focusing on the near object. This is light near dissociation (LND) which can be developed after the ciliary or the short ciliary nerve injury about weeks to month. The tonic pupil examination can be seen as in figure 7.

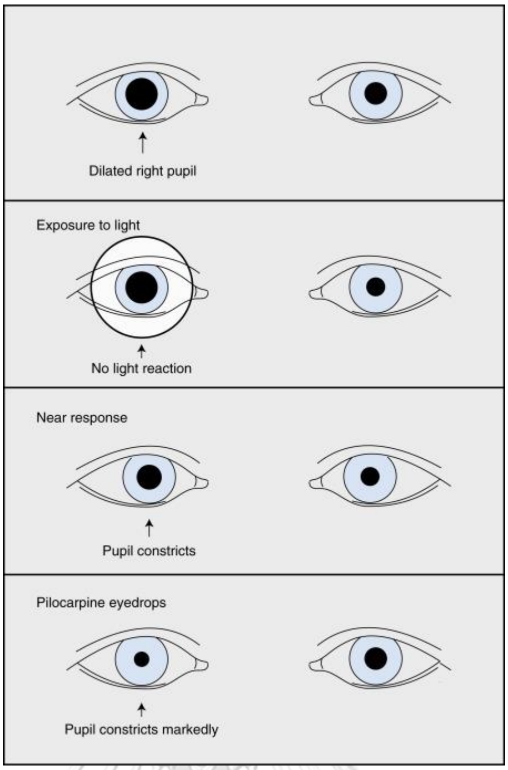


Figure 7. The patient in this figure has a right tonic pupil. At baseline, there is anisocoria with the right pupil larger than the left (first row). The dilated pupil fails to react to light (second row) but constricts slowly (i.e., tonic contraction) when the patient focuses on a near object (third row). After instillation of dilute pilocarpine eyedrops (fourth row), the pupil constricts markedly. (Evidence-Based Physical diagnosis, 4th edition(2018))[11]

The pathogenesis of LND is that after the parasympathetic nerve fiber from ciliary ganglion are disrupted, the regenerating fiber come to innervate iris instead of their originally destination for ciliary body. The reinnervation may be aberrant (aberrant regeneration) and runs to iris instead of the ciliary body in 30 times the number of fibers to the fibers for controlling light reaction of iris. As the fact that the sphincter pupillae consists of 70 to 80 separate motor unit and each served by a separated parasympathetic nerve fiber, when injury occurs in some nerve fibers, it will cause segmental palsy of the iris sphincter which leads to oval pupil. After damage to the ciliary ganglion, reinnervation and upregulation of the postsynaptic receptors occurs, a process known as denervation supersensitivity which can be found within days to weeks[11, 31].

However, it was once believed that the ciliary ganglion injury also led to Argyll Robertson Pupils which also has LND as one of its manifestations. From recent study, the syphilis does not commonly produce a peripheral neuropathy such as the ciliary ganglion and the short ciliary nerve. Moreover, the postmortem study of the ciliary ganglion in the AR patients are invariably normal[30]. It also has different characteristics and origin. The Argyll Robertson Pupils have four characteristic finding including: 1.bilateral involvement, 2. small pupils in baseline that fail to dilate fully in dim light, 3. no light reaction, and 4. brisk constriction to near vision and brisk redilation to far vision. This pathology was first described by Douglas Moray Cooper Lamb Argyll Robertson in 1868, but the association between this pathology and neurosyphillis was provedby means of Wasserman serologic test for syphilis which was launched in 1906. In addition to neurosyphillis, the other causes of Argyll Robertson Pupils are diabetes mellitus, neurosarcoidosis, and Lyme disease[32]. The lesion in dorsal midbrain, which preserves more ventrally located accommodative fiber innervating Edinger-Westphal nucleus but disrupts the light reflex fibers, is believed to bring about this pathologic pupil. The Argyll Robertson pupils already constrict in baseline, and they does not become smaller when doing the light reflex and swinging flash light test. Nonetheless, the pupil become smaller than base line and long-lasting[11].

Here is the table show the comparison between the tonic pupil and the Argyll Robertson Pupil[11](table 3).

Finding	Tonic Pupil	Argyll Robertson Pupil
Pupil size	Large	Small
Laterality	Mostly unilateral	Mostly bilateral
Reaction to near vision	Extremely slow and prolonged with slow redilation	Normal with brisk redilation

Table 3. Comparison of Tonic Pupil and Argyll Robertson Pupil (Evidence-Based Physical diagnosis, 4^{th} edition(2018))[11]

Chapter III Material and methods

Target population and sample population

This current study will used the embalmed cadavers in the department of anatomy, faculty of medicine, Chulalongkorn University, Thailand

Inclusion criteria

- The cadavers are completely preserved in all processes, one eye from each cadaver will be included.

Exclusion criteria

- The cadavers who has orbital trauma which distort orbital anatomy

Sample size determination

From the pilot study of 10 eyes (1 left eye and 9 right eyes), the standard deviation of the distance between anterior edge of the ciliary ganglion and the scleral insertion of the lateral rectus muscle was 3.009 millimeter. This current study will used the sample size equation from the descriptive study and confidence interval set as 95%

$$n = \frac{Z_{\frac{\alpha}{2}}^{2}\,\sigma^{2}}{d^{2}}$$

When $Z_{\frac{\alpha}{2}}^{2} = Z_{\frac{0.05}{2}}^{2} = 1.96$(two tail)

σ^{2} = variance = $(SD)^{2}$ = 3.009

d^{2} = acceptable error = 1 mm

Therefore $$n = \frac{(1.96)^{2}(3.009)^{2}}{1^{2}}$$

n = 34

The calculated sample size is at least 34 eyes. Therefore, 40eyes of cadavers will be included in this current study.

Materials and Methods

Equiments

1. Dissection instruments i.e. blade, forceps, scissors, probe and clamps/wirer

2. Non-drying dough and clay

3. 3.5x magnifying surgical loupe

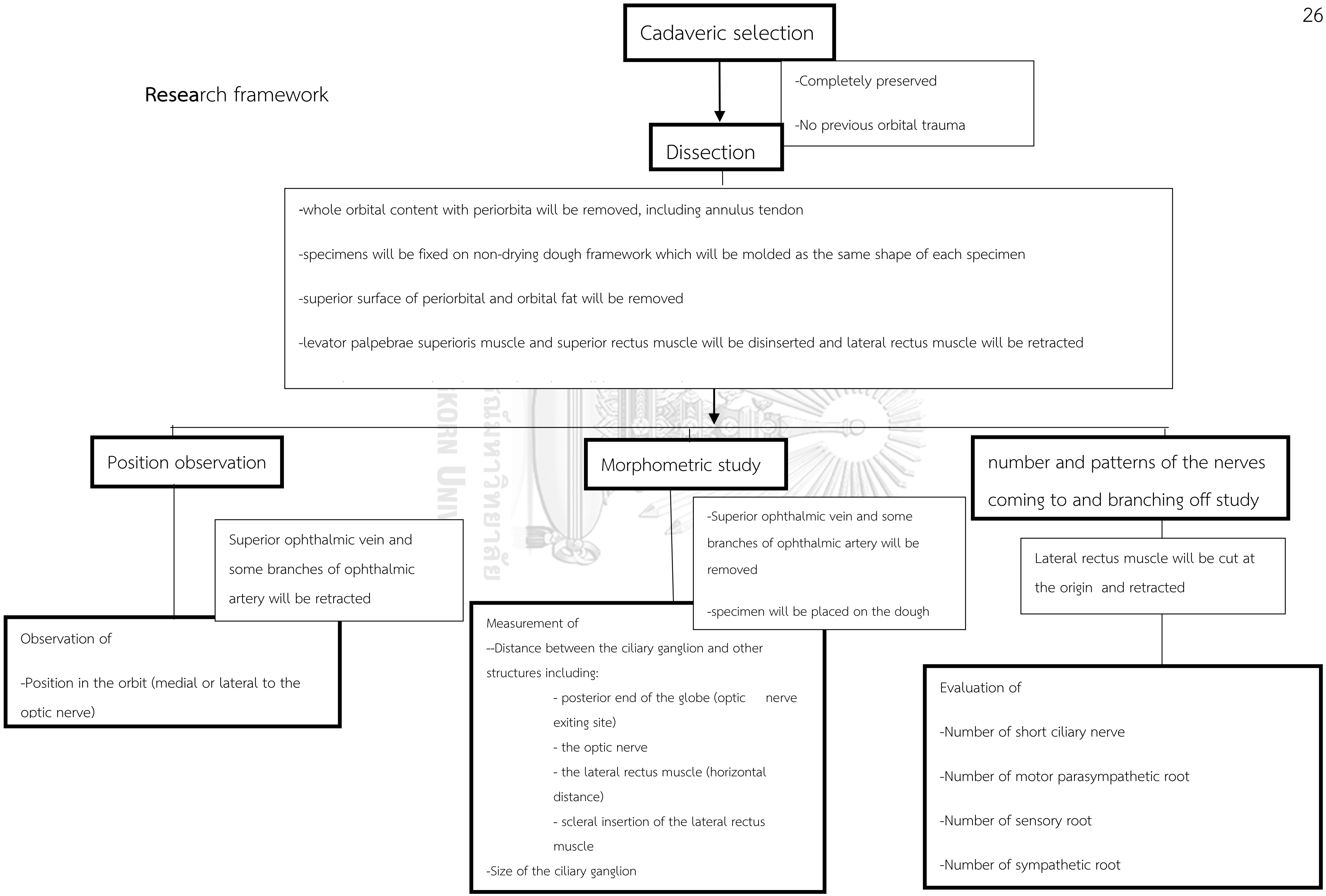
3. Digital vernier caliper (GuangLu ® 0-100 mm)

4. Pins

5. Scale

7. Digital camera

Research framework



Methods

Dissection

1. One globe with complete orbital content; either right or left side will be removed from all cadavers. All globes with orbital content will be gouged with absolute periorbita. (Fig. 8)

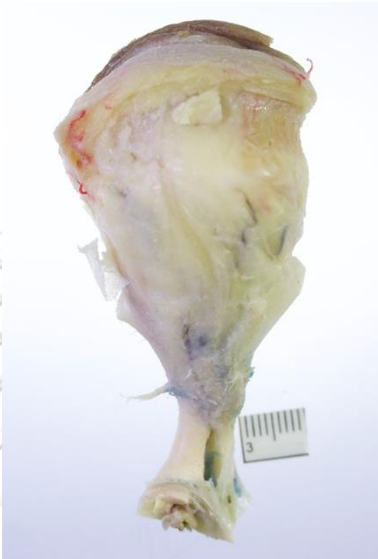


Figure 8. Globe with whole periorbita will be gauged from each cadaver.

2. Afterward, all specimens will be soaked in 10% formalin for more than a day for easier dissection. (Fig. 9)

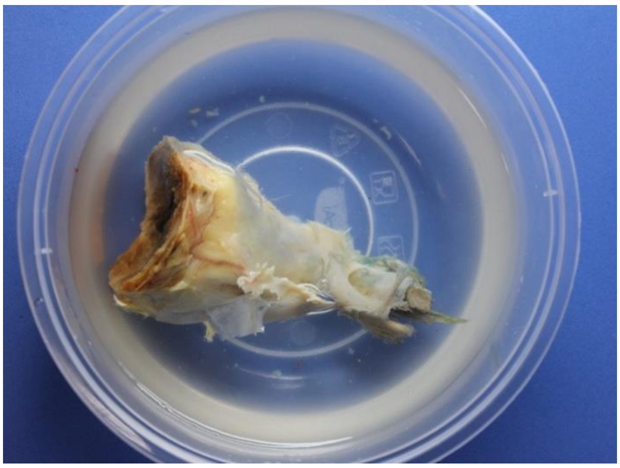


Figure 9. Preservation of each specimen in 10% formalin

3. Non-drying dough and clay will be molded as the shape of each specimen. The non-drying dough will be put aside, but the clay will be used to fix the specimens. (Fig. 10)

Figure 10. Molded non-drying dough of each specimen's shape

4. The superior side of the periorbita will be cut and removed, but medial and lateral side will not be disturbed so as to avoid error during measuring. (Fig. 11)

Figure 11. The distracted superior side of periorbita will be removed.

5. Frontal nerve and some orbital fat will be cut and removed. Then superior oblique muscle and levator palpebrae superioris will be clearly seen. (Fig. 12)

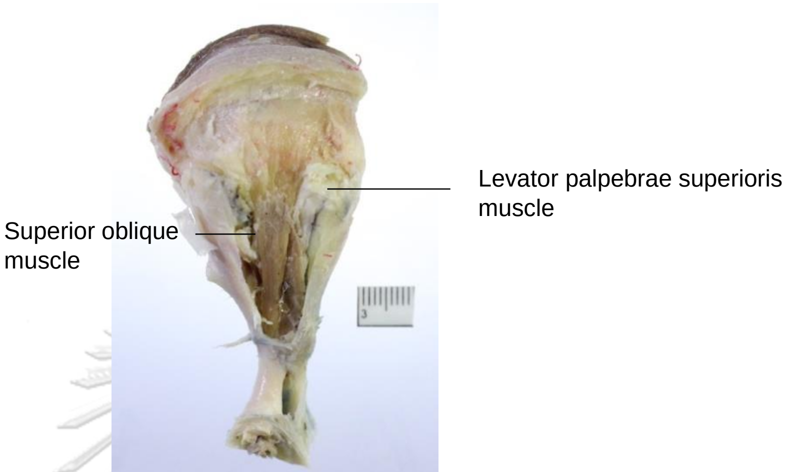


Figure 12. The frontal nerve and some orbital fat will be removed.

6. The levator palpebrae superioris will be carefully disinserted and retracted to posterior, then will be fixed with the pin. (Fig. 13)

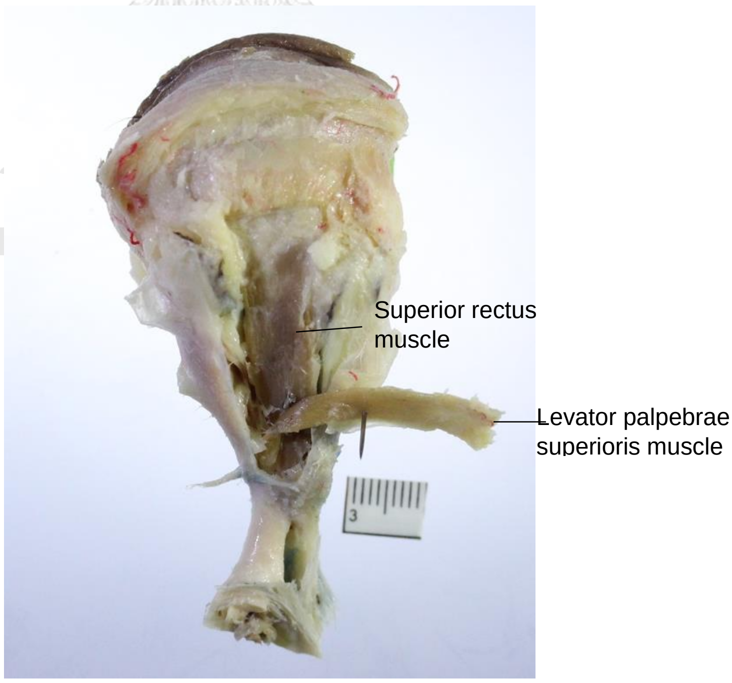


Figure 13. Disinsertion of levator palpabrae superioris muscle

7. The superior rectus muscle will be disinserted and retracted. Afterwards, nerve to levator palpebrae superioris and the superior rectus muscle will be seen and can be tracked to superior division of the oculomotor nerve. (Fig. 14)

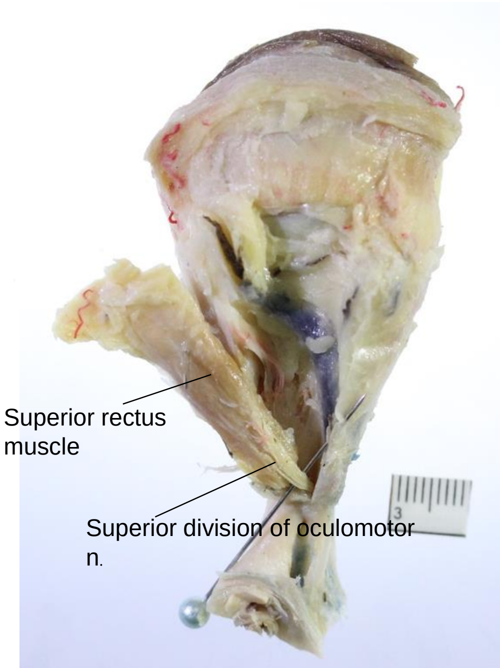


Figure 14. The superior rectus muscle will be disinsert and retracted.

8. Part of the superior rectus muscle and the levator palpebrae superioris muscle will be cut for convenient dissection. Trochlear nerve which lies above the superior oblique muscle will be cut and the superior oblique muscle will be disinserted and partially cut. (Fig. 15)

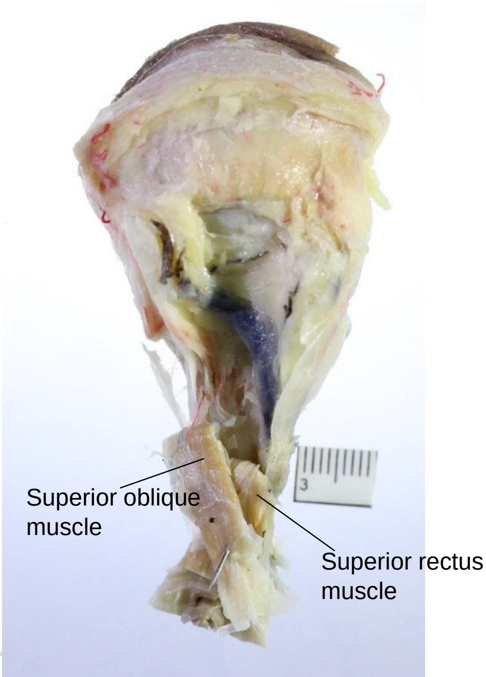


Figure 15. Trochlear nerve and superior oblique muscle will be disinserted.

9. The fat and branches of ophthalmic vein and artery under the superior oblique muscle, the levator palpebrae superioris muscle, and the superior rectus muscle which have already been cut will be removed. Then nasociliary nerve will be cleary seen. (Fig. 16)

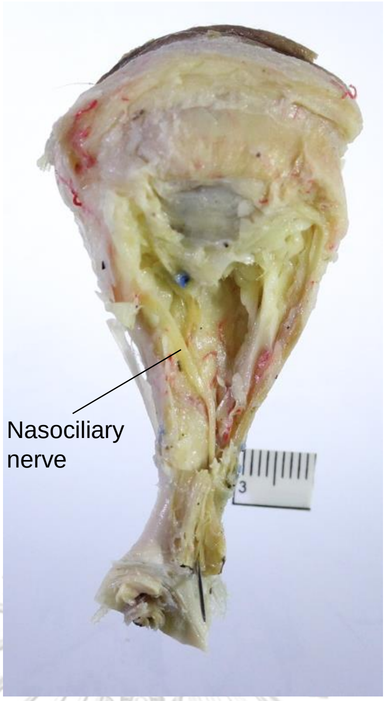


Figure 16. The fat and branches of ophthalmic vein and artery under the superior oblique muscle, the levator palpebrae superioris muscle, and the superior rectus muscle which have already been will be removed.

10. Follow the nasociliary nerve and the superior branch of the oculomotor nerve backward to find the inferior branch of the oculomotor nerve at just anterior to the annulus tendon. (Fig. 17)

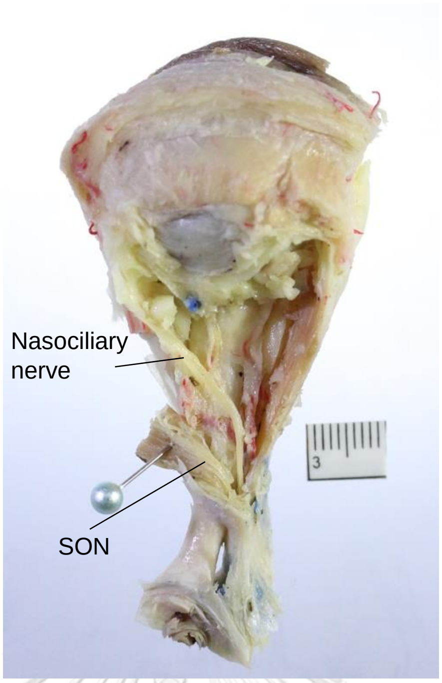


Figure 17. Tracking for inferior division of oculomotor nerve. SON=superior division of oculomotor nerve

11. After following nasociliary branch and the branch from inferior branch of the oculomotor nerve, the ciliary ganglion will be found lateral to the optic nerve.(Fig. 18)

12. The orbital fat between the ciliary ganglion and medial surface of the lateral rectus muscle will be detached for better exposure of the ciliary ganglion. (Fig. 18)

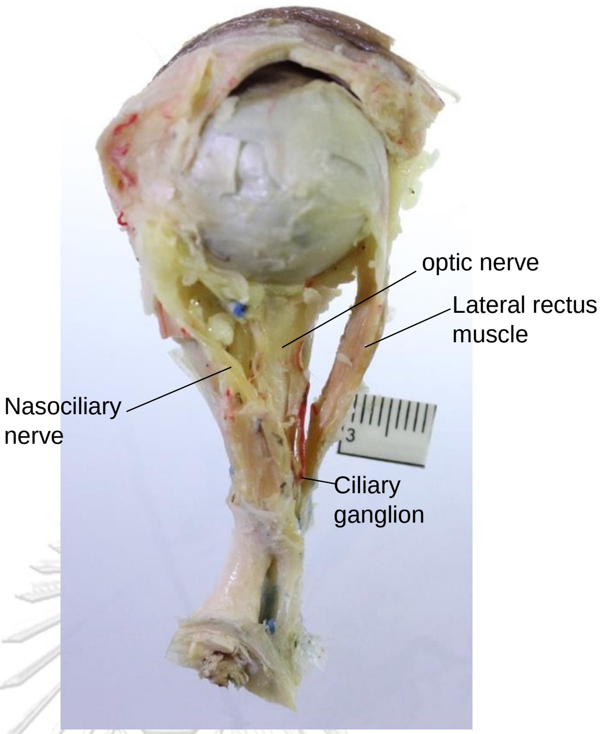


Figure 18. After tracking for ciliary ganglion, orbital fat between lateral rectus muscle and the ciliary ganglion will be removed.

13. The measurement between the ciliary ganglion and the lateral rectus muscle in horizontal direction, and optic nerve will be done. (Fig. 18)
14. The lateral rectus muscle will be cut near the annulus ring and retracted anteriorly. The fat around the ciliary ganglion will be removed with the 2.5Xmagnifying loupe.

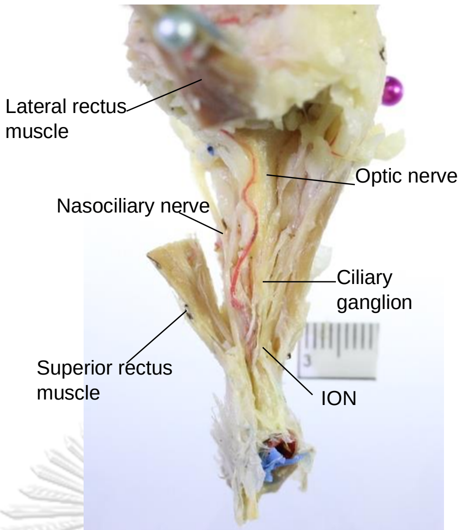


Figure 19. The lateral rectus muscle will be cut near the annulus ring and retracted anteriorly. ION=inferior division of oculomotor nerve

15. The scleral insertion of the lateral rectus muscle and posterior end of the globe, especially site of the optic nerve entering the globe will be thoroughly dissected.

(Fig. 20,21,22)

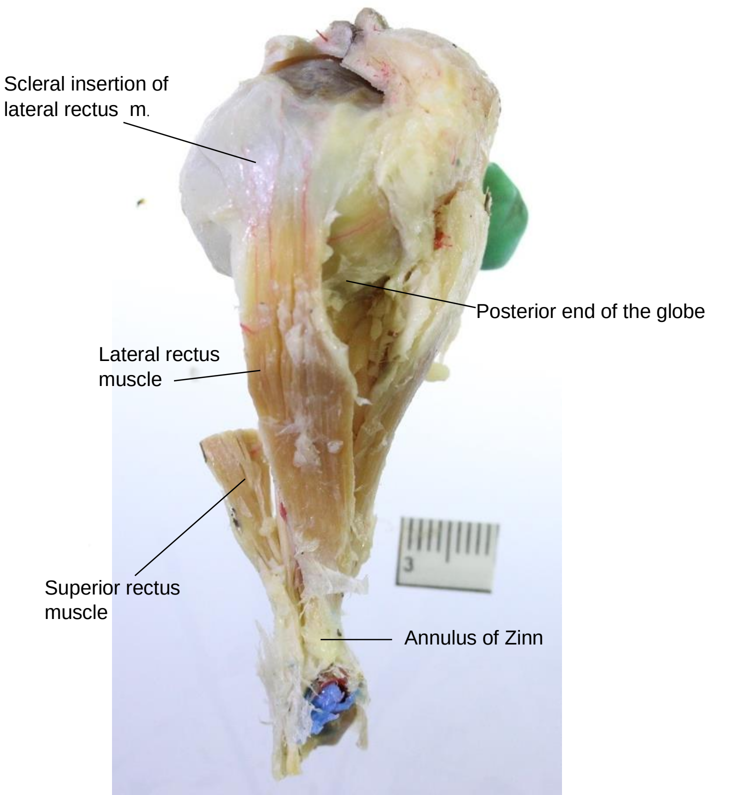


Figure 20. The scleral insertion and posterior end of the globe will be cleaned.

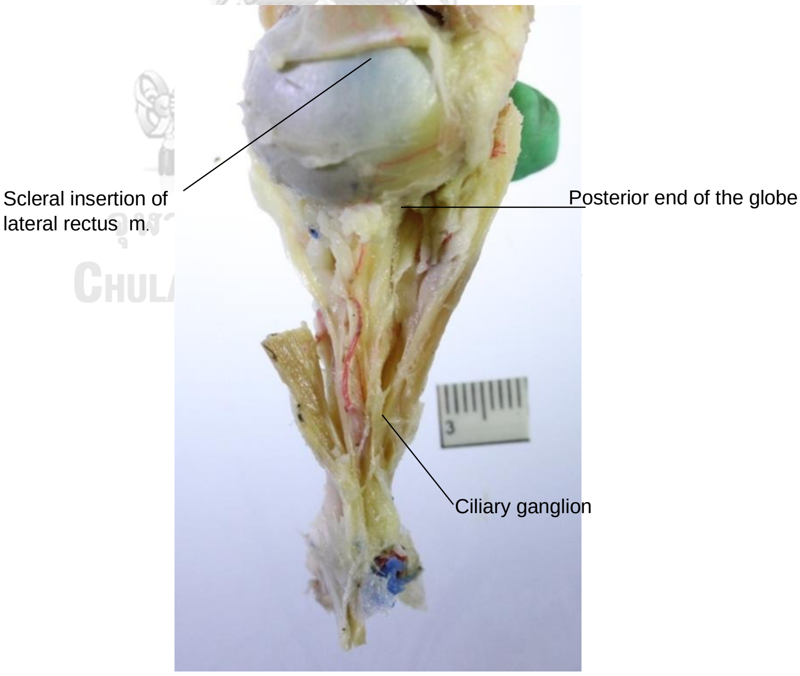


Figure 21. The lateral rectus muscle will be retracted anteriorly and the posterior end of the globe will be cleaned.

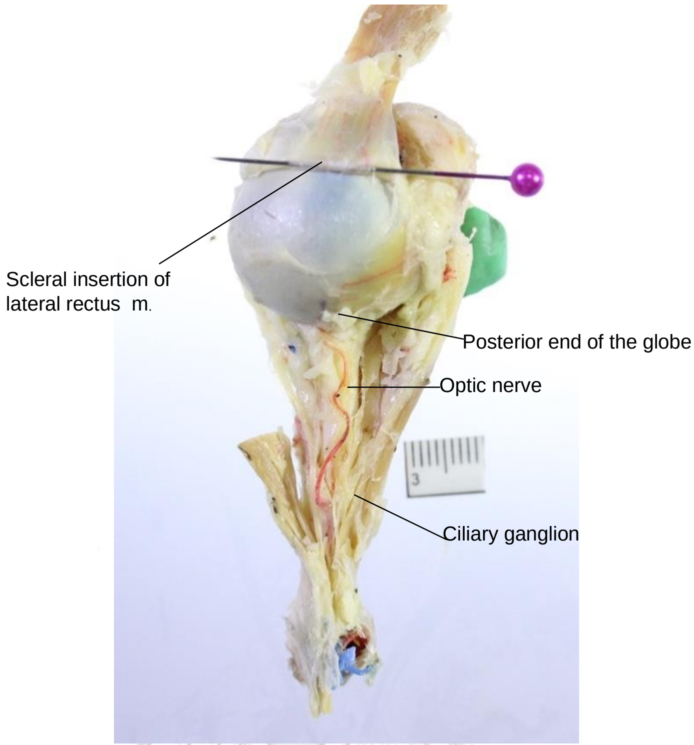


Figure 22. The pin will be point at the insertion to fix for measurement.

16. Short ciliary nerve and ciliary ganglion's roots were observed (Fig. 23)

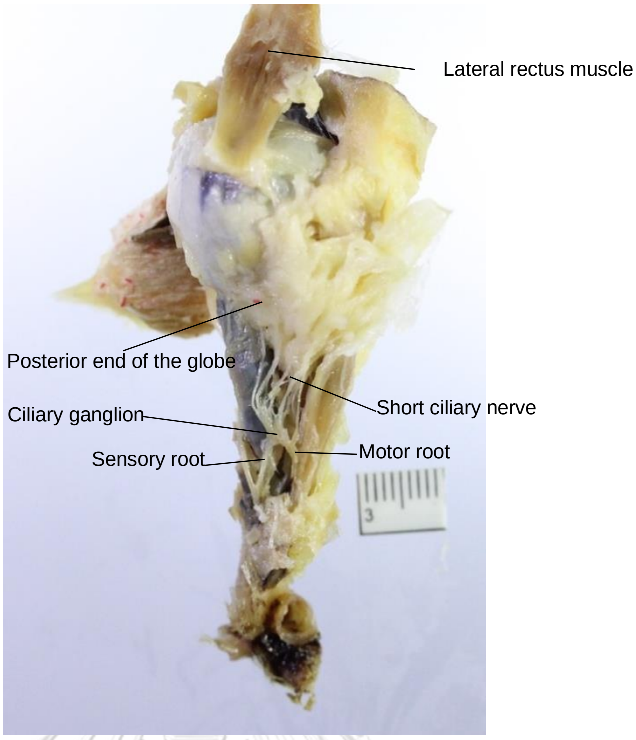


Figure 23. The dissection of lateral rectus muscle, posterior end of the globe, optic nerve and the ciliary ganglion.

Observation

1. Position of the ciliary ganglion in the orbit (medial or lateral to the optic nerve) will be observed to discover if there is any variation in position in Thai cadavers.
2. Number of short ciliary nerve will be counted after removing the lateral rectus muscle.
3. Number of motor parasympathetic root will be describing with their branching off pattern from inferior division of the oculomotor nerve.
4. Number of sensory root will be evaluated.
5. Number of sympathetic root will be described.

Measurements

The measurements will be taken by digital Vernier caliper (GuangLu ®0-100 mm). The parameters will be measured from 1 to 6 and will be repeated 3 times as an one day intervals.

1. Horizontal distance from the ciliary ganglion to the lateral rectus muscle in will be measured. Then the lateral rectus muscle will be disinserted and cut for better exposure of the ciliary ganglion.
2. Distance between the ciliary ganglion and the optic nerve will be measured.
3. Distance between the scleral insertion of the lateral rectus muscle and the ciliary ganglion will be measured.
4. Distance from posterior end of the globe (A, exit site of the optic nerve) to anterior edge of the ciliary ganglion (B), which is the length of the short ciliary nerve, will be measured.
5. Maximum width (D) of the ciliary ganglion which its axis is perpendicular to axis of the optic nerve will be measured.
6. Maximum distance from the anterior edge of the ciliary ganglion (B) to the posterior edge of it (C) will be measured. This distance is parallel to the optic nerve.

Data collection

All data will note in the Case record form

Case record form

Faculty of Medicine, Chulalongkorn University

Table NO. .... Sex:☐ Male☐ Female Cadaveric Code: .... Age: .... Years Side:

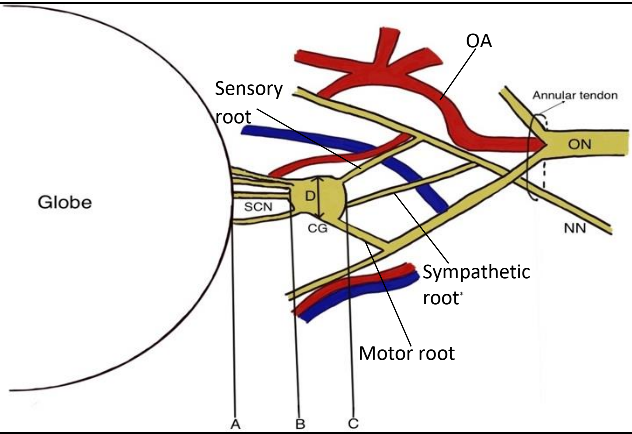
☐ Left ☐ Right

Ciliary ganglion

Position in orbit

☐Lateral to optic N

☐ Medial to optic N



A= posterior end of the globe, B=anterior edge of the ciliary ganglion, c=posterior edge of the ciliary ganglion, D= width of the ciliary ganglion, B-C=length of the ciliary ganglion, ON=oculomotor nerve, NN=nasociliary nerve, CG=ciliary ganglion, SCN=short ciliary nerve, *= always coming between the other 2 roots and not branching from NN and nerve from oculomotor nevre

Distance (mm)	1st	2nd	3rd	**Average**
A-B				
B-C				
D maximum				
Between CG to Optic N				

CG (anterior edge)to insertion point of lateral rectus M.					
CG to lateral rectus M. (horizontal distance)					
Root to CG	Number			Pattern	Average
	1st	2nd	3rd		
Motor root					
Sensory root					
Sympathetic root					
Number of SCN					

Data analysis

The statistical analysis will perform by SPSS software version 22.0 to calculate Mean with SD and calculate correlation coefficient to evaluate association between distance from ciliary ganglion to lateral rectus muscle (horizontal distance) and distance from end of posterior globe to ciliary ganglion. In addition, intraobserver variation will be also calculated for each parameter.

Ethical consideration

The human research ethics committee and the director of King Chulalongkorn Memorial hospital have to approve this current study.

Obstacles

1. The torn of branch of the ciliary ganglion by the dissector; therefore, the dissector should use 3.5X magnifying surgical loupe during dissecting and be meticulous in every steps of the dissection procedures.

2. The measurement error; therefore, the measurement process should be performed in the same measurer and repeated 3 times per parameter. Moreover, intra-observer variability will be calculated in every parameter and three of the lowest reliability will be shown.

3. The distortion of the lateral rectus muscle after dissection which will cause measurement errors; therefore, non-drying dough and clay are used to be a frame work which is molded as the shape of whole orbital content with complete periorbita before dissection. Moreover, dissection is not done on the medial and lateral side of the specimen but it is opened only from the top and same frame work will be used during measurement.

4. The origin of sympathetic root cannot be traced due to cutting sympathetic pathway during gauging the globe; therefore we will not observe the origin of sympathetic root but count the number of it.

Chapter IV Results

Baseline characteristic

Distance between the ciliary ganglion and surrounding structures were measured in 40 Thai cadavers which was fixed with 10% formalin. There were 24 (60%) male cadavers and 16 (40%) female cadavers. The mean age of these cadavers was 73.85 years old. In addition, the standard deviation of age was 12.48 years old. From 40 globes samples, there were 6 (15%) globes coming from left eyes and 34 (85%) globes coming from right eye (table 4).

Characteristics	N = 40
Gender, Number (%)	
Male	24 (60%)
Female	16 (40%)
Age (years)	
Mean (SD)	73.85 (12.48)
Minimum	52
Maximum	93

Table 4. Characteristics of cadaveric samples

Data from observation and measurement include distance between the ciliary ganglion and surrounding structures (table 8), any variations of the ciliary ganglion position in the orbit in Thai cadavers, size of the ciliary ganglion of Thai cadavers (table 5), characteristic of the ciliary ganglion roots (table 6,7), and number of short ciliary nerves given off the ciliary ganglion.

To track for the ciliary ganglion, primarily nasociliary nerve and inferior division of oculomotor nerve must be identify and then following their branch in the direction of lateral side to optic nerve. Then nerve to inferior oblique muscle which was a branch of inferior division of oculomotor nerve must be found, it was beneath the inferior border of lateral rectus muscle and always sent branch to ciliary ganglion as motor root. The important landmark of ciliary ganglion location was the point where ophthalmic artery crossed the optic nerve. Inferior division was identified and track for its distribution. The superior division and inferior division were found. The superior division passed medially above the optic nerve and innervated levator palpebrae superioris muscle and superior rectus muscle. The inferior division was found larger than superior division. It always gave three main branches including nerve to medial rectus muscle, nerve to inferior rectus muscle, and nerve to inferior oblique muscle. Moreover, nerve to medial rectus muscle was always discovered as the first branch and it came beneath the optic nerve whilst the others came laterally to the optic nerve.

Size of the ciliary ganglion in Thai cadavers

According to variation in shape of the ciliary ganglion from our observation, some specimens could not be categorized as any pattern. The width and length of the ciliary ganglion were concerned to be more important than pattern of shape and were recorded in this study.

The mean distance from anterior edge to posterior edge of the ciliary ganglion in axis parallel to the optic nerve was 3.50$\pm$0.73 mm. The mean distance between superior edge and inferior edge, which was perpendicular to the optic nerve axis was 2.24$\pm$0.57 mm (table 5).

Distance (Ciliary ganglion)	Mean(mm)	Maximum(mm)	Minimum(mm)	Std deviation(mm)
Anterior edge to posterior edge	3.50	5.21	1.70	0.73
Superior edge to inferior edge	2.24	3.95	1.39	0.57

Table 5. Size of the ciliary ganglion in Thai cadavers

Variation in position of the ciliary ganglion

According to our observation, all specimen (n=40) had no variation in position in the orbit. All of them located lateral to the optic nerve and medial to lateral rectus muscle.

Pattern and number of motor (parasympathetic) root, sensory root and sympathetic root reaching the ciliary ganglion **(table 3)**

Motor root (parasympathetic root)

25(62.5%) out of 40 specimens had 1 motor root (parasympathetic root). 3(7.5%) out of 40 specimens had 1 root coming from inferior division of oculomotor nerve that had already sent branch to medial rectus muscle (fig. 24). The other 22(55%) specimens had 1 root from branch of nerve to inferior oblique muscle (fig. 25).

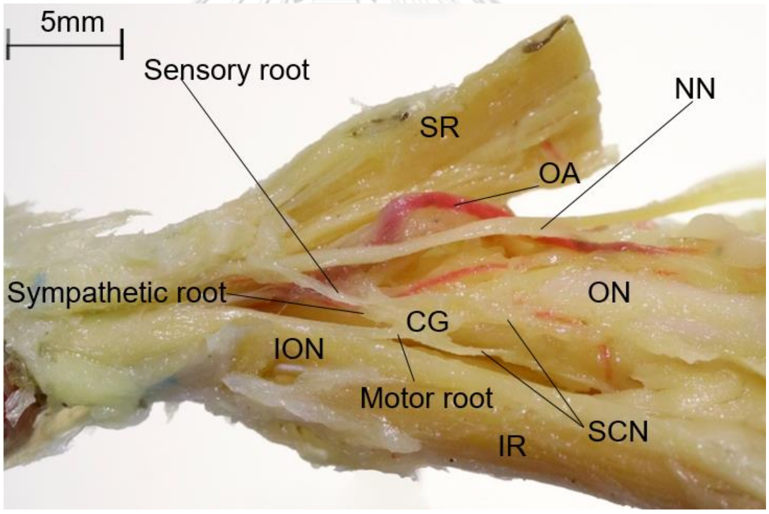


Figure 24. Cadaveric dissection showing 1 motor root (parasympathetic root) comes from inferior division of oculomotor nerve. The lateral rectus has been retracted and cut. CG=ciliary ganglion, ION=inferior division of oculomotor nerve, IR=inferior rectus muscle, NN=nasociliary nerve, OA=ophthalmic artery, ON=optic nerve, SCN=short ciliary nerve, SR=superior rectus muscle.

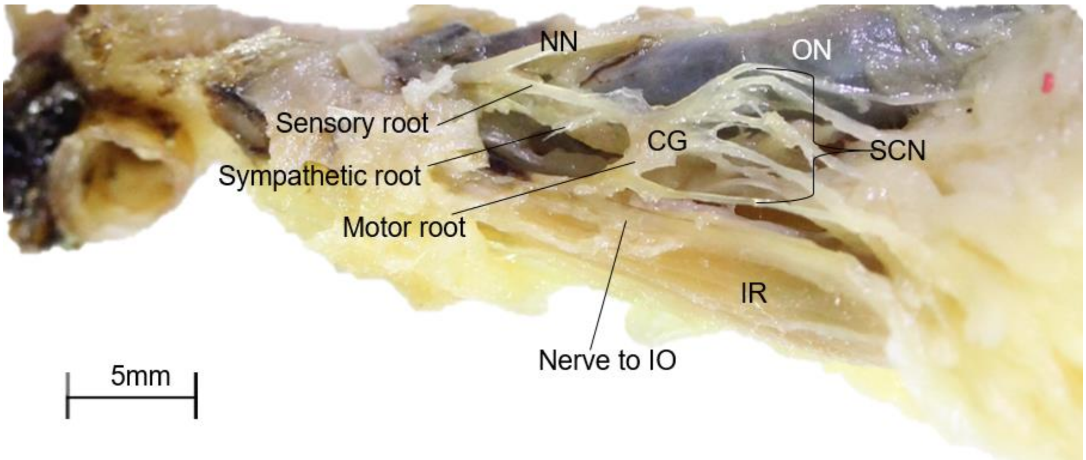


Figure 25. Cadaveric dissection showing 1 motor root (parasympathetic root) comes from nerve to inferior oblique muscle. The lateral rectus has been retracted and cut. CG=ciliary ganglion, IO=inferior oblique muslce, IR=inferior rectus muscle NN=nasociliary nerve, ON=optic nerve, SCN=short ciliary nerve.

7(17.5%) out of 40 specimens had 2 motor roots reaching the ciliary ganglion. 4(10%) out of 7 specimens had both of two motor roots branched out from nerve to inferior oblique muscle (fig. 26). The other 3(7.5%) out of 7 specimens had 1 motor root from nerve to inferior oblique muscle, and the other branched from inferior division of oculomotor nerve before giving off nerve to inferior oblique muscle (fig. 27).

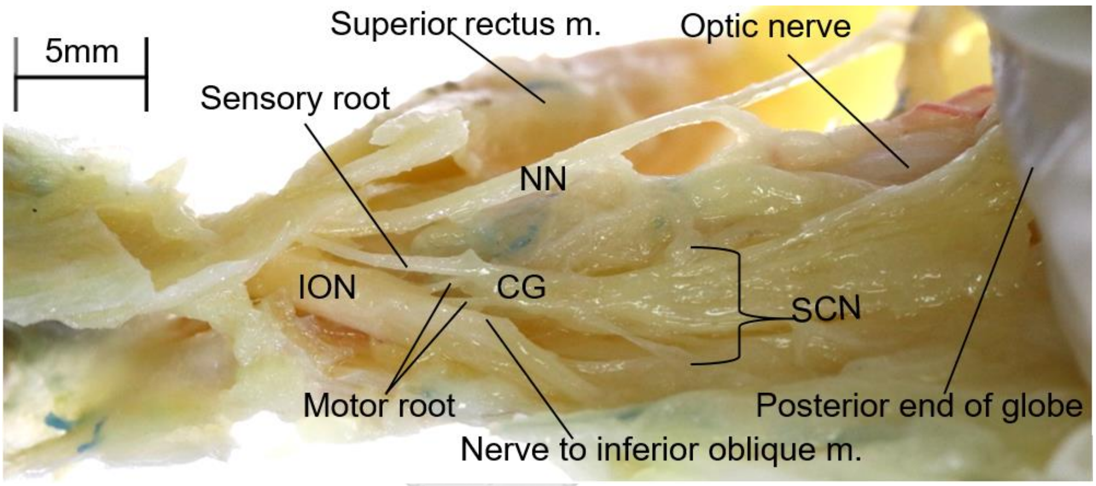


Figure 26. Cadaveric dissection representing 2 motor roots branches from nerve to inferior oblique muscle. The lateral rectus muscle and the superior rectus muscle have been cut. CG=ciliary ganglion, ION=inferior division of oculomotor nerve NN=nasociliary nerve, SCN=short ciliary nerve.

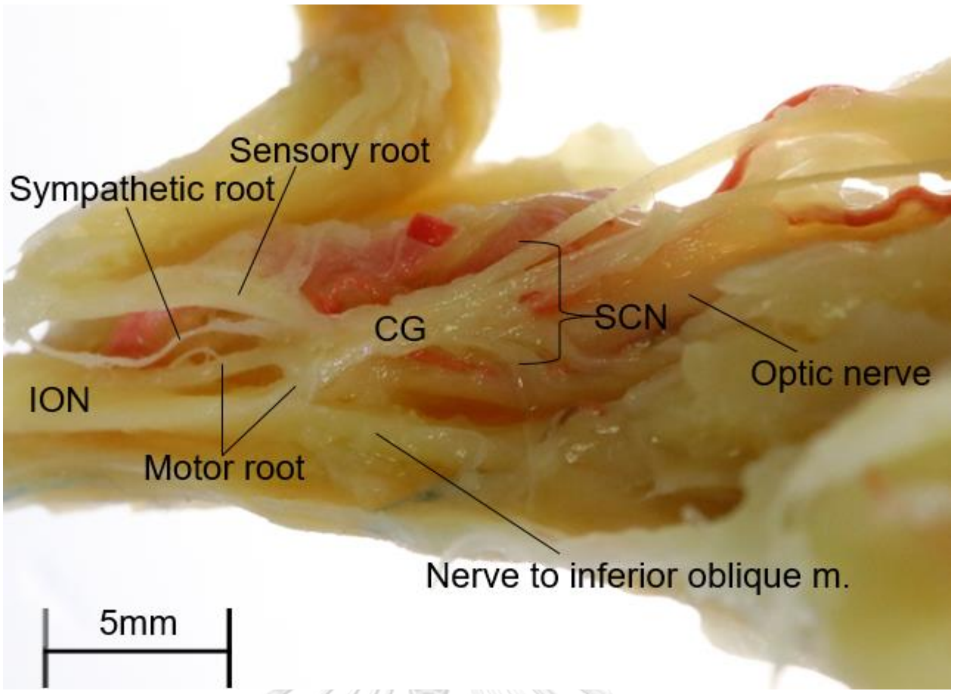


Figure 27. Cadaveric dissection representing 2 motor roots including 1 root branches from nerve to inferior oblique muscle and the other branches from inferior division of oculomotor nerve. The lateral rectus muscle and the superior rectus muscle have been cut. CG=ciliary ganglion, ION=inferior division of oculomotor nerve, SCN=short ciliary nerve.

1(2.5%) out of 40 specimens had 3 motor roots coming from nerve to inferior oblique muscle (fig. 28).

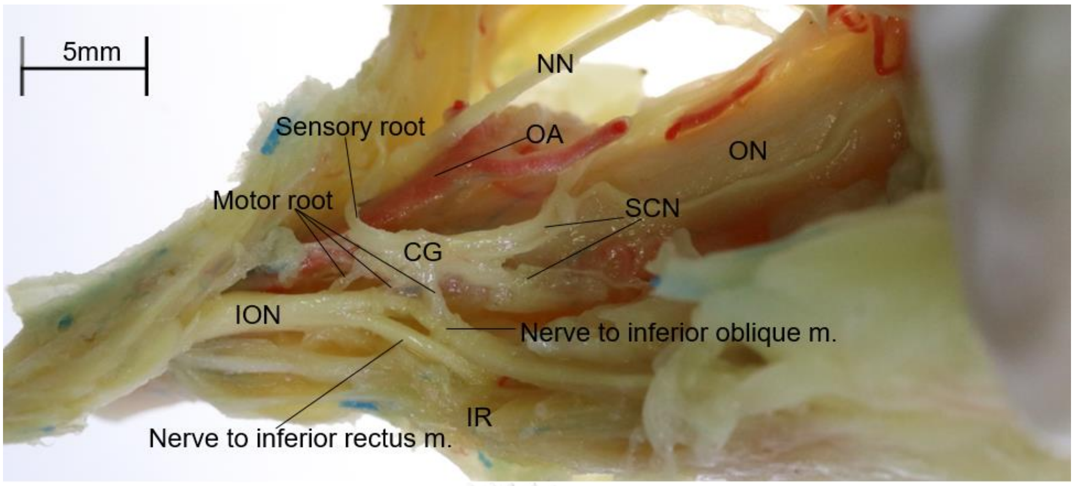


Figure 28. Cadaveric dissection represents 3 motor roots branching from nerve to inferior oblique muscle. The lateral rectus muscle and the superior rectus muscle have been cut. CG=ciliary ganglion, ION=inferior division of oculomotor nerve, IR=inferior rectus muscle, NN=nasociliary nerve, OA=ophthalmic artery, ON=optic nerve, SCN=short ciliary nerve.

7(17.5%) out of 40 specimens had no motor root, but ciliary ganglion lay on either nerve to inferior oblique muscle or inferior division of oculomotor nerve. 5(12.5%) out of 7 specimens had ciliary ganglion directly attached to nerve to inferior oblique muscle (fig. 29). The other 2(5%) specimens directly attached to inferior division of oculomotor nerve (fig. 30). Table 6 showed pattern and number of motor root.

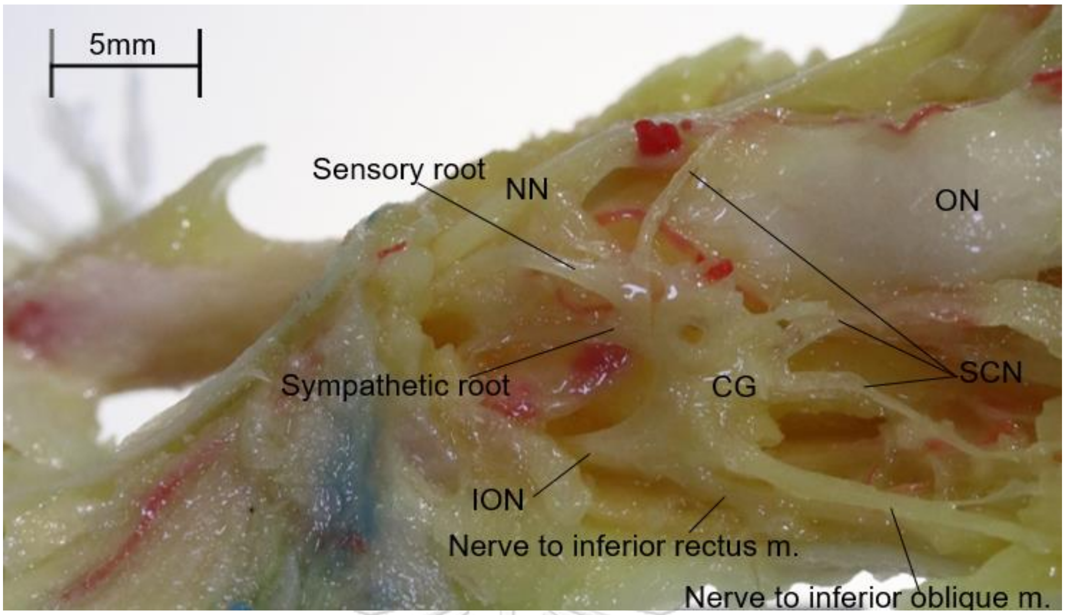


Figure 29. Cadaveric dissection shows the ciliary ganglion has no motor root. It lies on nerve to inferior oblique muscle. The lateral rectus muscle and the superior rectus muscle have been cut. CG=ciliary ganglion, ION=inferior division of oculomotor neve, NN=nasociliary nerve, ON=optic nerve, SCN=short ciliary nerve.

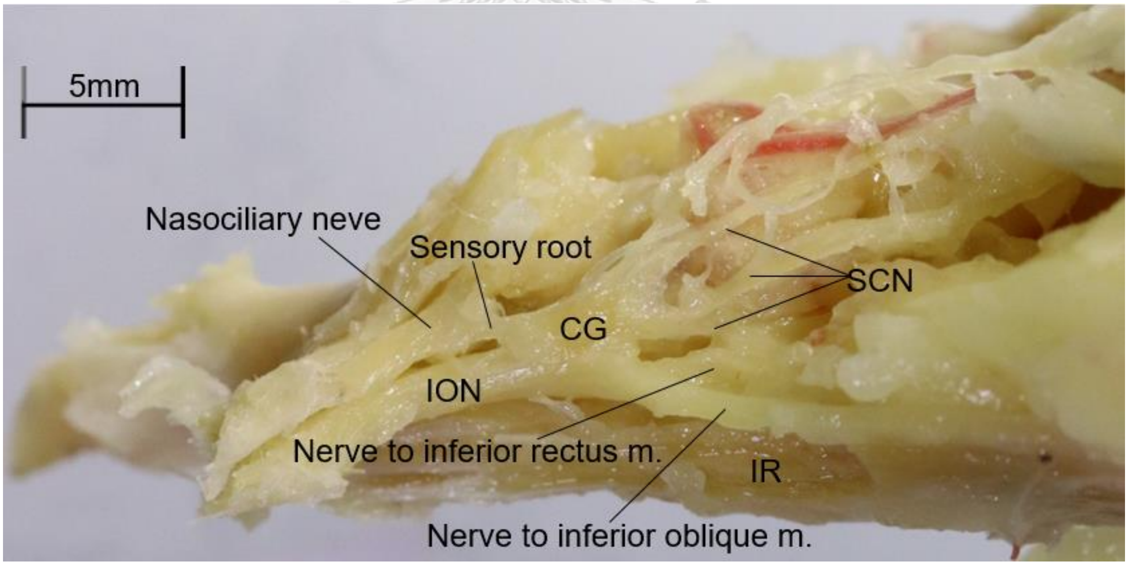


Figure 30. Cadaveric dissection depicts the ciliary ganglion had no motor root, but directly attaches to inferior division of oculomotor nerve. The lateral rectus muscle and the superior rectus muscle have been cut. CG=ciliary ganglion, ION=inferior division of oculomotor nerve, IR=inferior rectus muscle, SCN=short ciliary nerve.

Number of motor root	Branching out pattern	Number of specimens (%)
1	From nerve to inferior oblique m.	22(55%)
1	From inferior division of oculomotor n.	3(7.5%)
2	From nerve to inferior oblique m.	4(10%)
2	- 1 root from inferior division of oculomotor n. - The other 1 root from nerve to inferior oblique muscle	3(7.5%)
3	From nerve to inferior oblique muscle	1(2.5%)
0	Lying on nerve to inferior oblique muscle	5(12.5%)
0	Lying on inferior division of oculomotor n.	2(5%)
	Total	40 (100%)

Table 6. Number and pattern of motor (parasympathetic) root

Sympathetic root

4(10%) out of 40 specimens could not be identified sympathetic root as being shown in table 7. The other 36(90%) specimens had 1 sympathetic root and always approached ciliary ganglion between motor (parasympathetic) root and sensory root (table 7). Due to limitation of cadavers remained from student study, the origin of sympathetic nerve could not be tracked and identified.

Number of specimens	Number of sympathetic root
36(90%)	1
4(10%)	0

Table 7. Number of sympathetic root

Sensory root

All of the 40 specimens had only 1 sensory root. This root came from nasociliary nerve and approached to ciliary ganglion in postero-superior angle. This root was easy to identified because it located in the most superior location and branched out from nasociliary nerve which was large and prominent.

Number of short ciliary nerves branching from the ciliary ganglion

Some specimens had short ciliary nerve contributing into two bundle before dividing in numerous nerves, but some had no two bundle of short ciliary nerve. The mean number of short ciliary nerve with standard deviation of short ciliary nerve was 9± 2 nerves. The maximum in number from our study was 14 nerves, whereas the minimum was 6 nerves. The mode number of short ciliary nerve was 9 nerves which was found in 7(17.5%) samples (fig. 31). The number of short ciliary nerve and the number of samples was shown in figure 31.

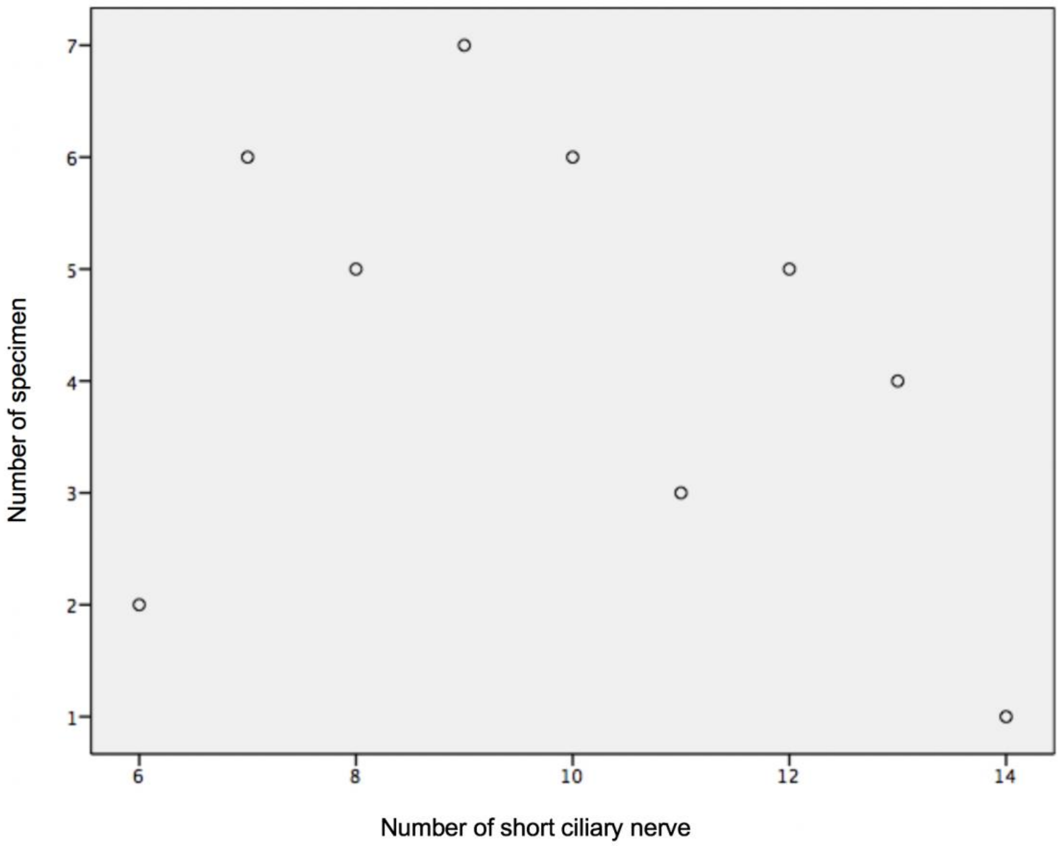


Figure 31. Scatter plot graph presents the number of samples in Y axis and the number of short ciliary nerve in X axis

Distance between the ciliary ganglion and surrounding structures

The mean distance between anterior edge of the ciliary ganglion and posterior end of the globe where optic nerve exit was 16.04±2.83 mm. In addition, measurement between the ciliary ganglion and lateral rectus muscle was done, including shortest distance from the ciliary ganglion to lateral rectus muscle in horizontal direction and distance from anterior edge of the ciliary ganglion to scleral insertion of the lateral rectus muscle. The mean distance from the ciliary ganglion to lateral rectus muscle in horizontal direction was 2.88±0.66 mm. Moreover, the mean distance from scleral insertion of lateral rectus muscle point to anterior edge of the ciliary ganglion was 31.53±3.67mm. The average distance between the ciliary ganglion and the optic nerve was also measured. It was 1.47±0.4 mm. Table 8 shows all data that was described above.

Distance	Mean(mm)	Maximum(mm)	Minimum(mm)	Std Deviation(mm)
CG to posterior end of globe	16.04	24.60	9.18	2.83
CG to LR (horizontal)	2.88	4.49	1.86	0.66
CG to LR's insertion on sclera	31.53	40.55	23.27	3.67
CG to optic nerve	1.47	2.44	0.81	0.4

Table 8. Distance between the ciliary ganglion and surrounding structures

*CG=ciliary ganglion, LR=lateral rectus muscle

Correlation between distance from anterior edge of ciliary ganglion to posterior end of globe and distance from ciliary ganglion to lateral rectus muscle in horizontal direction

Pearson correlation coefficient was used to calculate correlation between distance from anterior edge of the ciliary ganglion to posterior end of the globe and distance from the ciliary ganglion to lateral rectus muscle in horizontal direction. The correlation between these two parameters was negative linear correlation. Pearson correlation coefficient was -0.438 and it could be interpreted as moderate negative correlation. Table 9 represented correlation between these two parameters. Figure 32 displayed scatter plot graph for these data and also included trendline for showing negative correlation.

		AB_AVG	CG-LRM_AVG
AB_AVG	Pearson Correlation	1	-.438**
	Sig. (2-tailed)		.005
	N	40	40
CG-LRM_AVG	Pearson Correlation	-.438**	1
	Sig. (2-tailed)	.005	
	N	40	40

**. Correlation is significant at the 0.01 level (2-tailed).

Table 9. Correlation between the distance between anterior edge of the ciliary ganglion and posterior end of the globe and the distance from the ciliary ganglion to the lateral rectus muscle in horizontal direction. AB_AVG= the distance between anterior edge of the ciliary ganglion and posterior end of the globe, CG-LRM_AVG= the distance between the ciliary ganglion and the lateral rectus muscle.

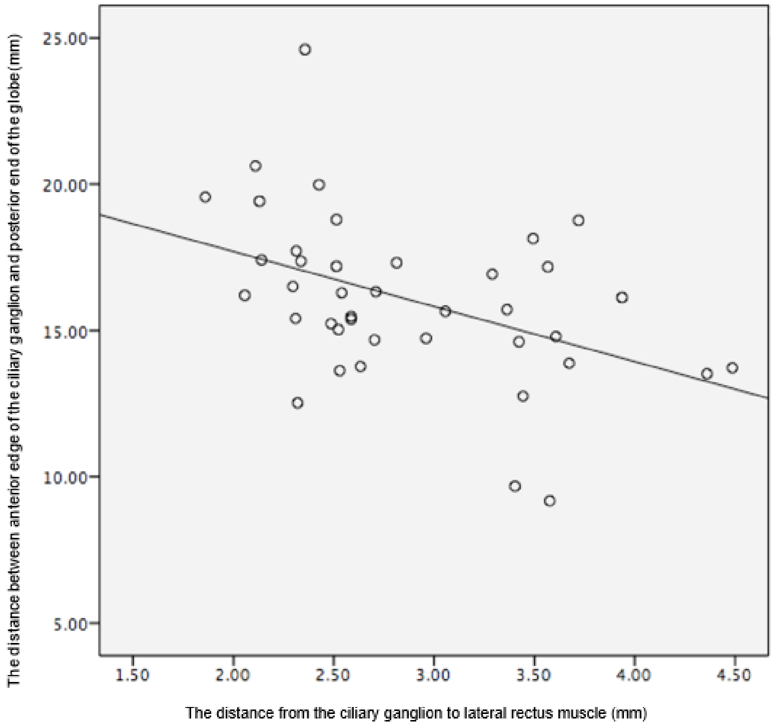


Figure 32. Scatter plot graph shows x axis as the distance from the ciliary ganglion to lateral rectus muscle in millimeter (mm) and Y axis as the distance between anterior edge of the ciliary ganglion and posterior end of the globe in millimeter (mm). The trend line represents the negative correlation is also shown.

Chapter V Discussion

Knowledge of the ciliary ganglion anatomy and morphometric study between surrounding structures is important for surgeons performing intraorbital procedures[7]. Schacher (1701) was the first person who described about the ciliary ganglion in the orbit[12].

After that, Winslow (1732) and Haller (1743) gave more detail about the ciliary ganglion, including its roots and short ciliary nerves[12]. Since then, there has been few studies about the ciliary ganglion especially morphometric study between it and its surrounding structures.

Since 1960, Grimes and Von Sallmann informed about variable size and shape of the ciliary ganglion[33]. Sinnreich and Nathan (1981), and Gonul and Izci (2006) also insisted that the shape of the ciliary ganglion was varied[1, 12]. The size of the ciliary ganglion has been depicted from Gonul and Izci (2006) study. The mean distance from anterior edge to posterior edge of the ciliary ganglion from their report was 5.25 mm (range 4.15-6.45 mm). Moreover, the mean width of the ciliary ganglion was 3.04 mm (range 2.75-3.40mm). Our study also reported about the size of the ciliary ganglion both from anterior edge to posterior edge and from superior edge to inferior edge. The mean size which was measured from anterior edge to posterior edge was 3.5 mm (range 1.70-5.21 mm). Whereas, the mean size measured from superior edge to inferior edge was found 2.24 mm (range 1.39-3.95 mm). The size of the ciliary ganglion was discovered smaller than Izci and Gonul (2006)'s report (table 12). The difference in race between two reports was believed to affect the size of the ciliary ganglion. The ciliary ganglion of Asian samples appeared to be smaller than European samples. The shape of the ciliary ganglion in our study was not been reported because it was found very varied and irregular. This finding came to agreement with the report that was mentioned earlier.

Inferior division of oculomotor nerve has been found three main branches including nerves to medial rectus muscle, inferior rectus muscle and inferior oblique muscle. Motor (parasympathetic root) of the ciliary ganglion derived from inferior division of oculomotor nerve. It approached the ciliary ganglion in postero-inferior angle. After parasympathetic fiber synapsed the ciliary ganglion, it would come with the short ciliary nerve to innervate the ciliary body and iris. Sinnreich and Nathan (1981) made observation about roots reaching the ciliary in 30 cadavers. Motor (parasympathetic) root in their study was depicted in one motor root, two motor roots and no motor root. Their study did not show the origin of the root in three, two, and one motor root(s), but they did in no motor root pattern. To elucidate, the ciliary ganglion that had no motor root directly located on either nerve to inferior oblique muscle or inferior division of oculomotor nerve[(12)]. Hamel et al (2012) studied about the afferent and efferent nerves of the ciliary ganglion[(34)]. They described motor root as one motor root, two motor roots and no motor root which was postulated that the absence of motor root might be due to the excess or default in the migration of neural crest cell along cranial nerve. They also did not observe where is the point that the motor root derived from, whereas they found the ciliary ganglion located on inferior division of oculomotor nerve. In our study, the motor root of the ciliary ganglion is discovered into four disposition, including three motor roots, two motor roots, one motor root and no motor root. The nerve where they came from was also observed. The finding of three motor roots has never described in any studies before. All three roots branched out from nerve to inferior oblique muscle. The origin of the two motor roots was varied. There were two dispositions. First disposition was that both of them came from nerve to inferior oblique muscle. The other disposition was that one of them came from nerve to inferior oblique muscle and the other came from inferior division of oculomotor nerve. The origin of one motor root was from either nerve to inferior oblique muscle or inferior division of oculomotor nerve. Moreover, the ciliary ganglion that had no motor root lay on either nerve to inferior oblique muscle or inferior division of oculomotor nerve. This finding got along with reports of Sinnreich and Nathan (1981) and Hamel et al (2012) as showed in table 10.

Number of motor root	Sinnreich and Nathan (1981)	Hamel et al (2012)	Our study
No motor root	Yes -Attach to inferior division of oculomotor nerve -Attach to nerve to inferior oblique muscle	Yes -Attach to inferior division of oculomotor nerve	Yes -Attach to inferior division of oculomotor nerve -Attach to nerve to inferior oblique muscle
1motor root	Yes -Branch from nerve to inferior oblique muscle	yes	Yes -Branch from nerve to inferior oblique muscle -Branch from inferior division of oculomotor nerve
2 motor roots	Yes	-	Yes -Branch from nerve to inferior oblique muscle -Branch from inferior division of oculomotor nerve
3 motor roots	-	-	Yes -Branch from nerve to inferior oblique muscle

Table 10. Comparison of motor (parasympathetic) root's number and different finding between each study

In addition, sensory root has been reported that it always comes from nasociliary nerve and is always one root[7, 34]. According to our study, the sensory root was identified in all specimens and found one root which came from nasociliary nerve constantly.

The sympathetic fibers are formed by post ganglionic fiber from neurons located at the superior cervical ganglion. The postganglionic fibers leave superior cervical ganglion via internal and external carotid nerve, then form the carotid plexus around internal carotid artery[15]. The sympathetic root reaching the ciliary ganglion could come from either directly from cavernous plexus in cavernous sinus and come to the orbit via superior orbital fissure, or from plexus around the ophthalmic artery which is already in the orbit[15]. There was a report fining it coming from both source but many studies could not identify the sympathetic root reaching the ciliary ganglion in some of their specimens[12, 16, 34, 35]. Johnston and Parkinston (1974) believed that the reason of unidentified sympathetic fiber was that it joined with the abducens nerve and were distributed with the branches of the ophthalmic nerve[35]. Moreover, Sinnreich and Nathan (1981) reported that sympathetic roots branched from either internal carotid plexus or plexus surrounding ophthalmic artery and some specimens could be found from both sources (table 11). In our report, 4 out of 40 specimens could not be found sympathetic root and every identified sympathetic root were found 1 root. Due to limitation of the specimens in this study, the origin of sympathetic root could not be observed.

Origin	Sinnreich and Nathan (1981)	Natori and Rhoton (1995)	Gonul and Izci (2006)	Hamel et al (2012)	Our study
	N=30	N=30	N=10	N=20	N=40
Internal carotid plexus	17	22	10	16	NA
Plexus around opthalmic artey and its branch	2	-	-	-	NA
Both	3	5	-	-	NA
No sympathetic root	8	3	-	4	4

Table 11. Comparison of sympathetic root's origin and different finding between each study.

Izci and Gonul (2006) was the first study that depicted morphometric study of the ciliary ganglion and its surrounding structures(1). Apart from the mean size of the ciliary ganglion that they reported. They also measured the distance from the ciliary ganglion and surrounding structures. The mean distance from anterior edge of the ciliary ganglion to posterior end of the globe was reported 12 mm (range 7.75-19.80 mm). In addition, the mean distance from the ciliary ganglion to optic nerved was found 2.90 mm (range 2.70-3.10 mm). The mean distance from the ciliary ganglion and lateral rectus muscle was also been reported in their study and it was 10.4 mm (range 9.20-11.20 mm). On the report of our study, we found the mean distance from the ciliary ganglion to posterior end of the globe was 16.04 mm (range 9.18-24.60 mm), from the ciliary ganglion to the lateral rectus muscle was 2.88 mm (range 1.86-4.99 mm) and from the ciliary ganglion to optic nerve was 1.47 mm (range 0.81-2.44 mm).

From both studies, it was shown that the ciliary ganglion was closer to optic nerve than to the lateral rectus muscle. The mean distance of the ciliary ganglion to posterior end of the globe in our study was longer than the mean distance of the previous study (table 11). On the contrary, the mean distance between the ciliary ganglion and the optic nerve and the mean distance between the ciliary ganglion and the lateral rectus muscle was lesser than the mean distance in the previous study. According to our study, we found correlation coefficient between the distance from the posterior end of the globe to the ciliary ganglion and the distance from the lateral rectus muscle to the ciliary ganglion in horizontal direction was -0.4. It could be conveyed that as the distance from the ciliary ganglion increased, the distance from the ciliary ganglion to the lateral rectus muscle decreased. The -0.4 correlation coefficient was moderate association. As a result, a greater distance from the posterior end of the globe to the anterior edge of the ciliary ganglion in Asian population as claimed by our report would cause the closer between the ciliary ganglion and the lateral rectus muscle. Besides, the difference value of the distance from the ciliary ganglion to the lateral rectus muscle between two studies was believed to be affected by different sample size, disparate ethnicities and the point on the lateral rectus muscle that was measured. Therefore, awareness of the closer distance of the ciliary ganglion-lateral rectus should be considered especially in Asian population during operation involved the lateral rectus muscle which would be explained beneath.

Measure		Gonul and Izci (2006)	Our study
From	To	Mean (mm.)	Mean(mm.)
Posterior end of the globe	Anterior edge of the CG	12	16.04
Anterior edge of the CG	Posterior edge of the CG	5.25	3.5

Superior edge of the CG	Inferior edge of the CG	3.04	2.24
CG	LRM	10.4	2.88
CG	ON	2.90	1.47

Table 12. Comparison of morphometric study between Gonul and Izci (2006)'s report and ours' report

*CG = ciliary ganglion, LRM = lateral rectus muscle, ON = optic nerve.

Besides, our study was the first which included the distance measured from the anterior edge of the ciliary ganglion to the lateral rectus muscle's scleral insertion. It was believed to be concerned in some procedures involving with manipulation of the lateral rectus muscle[5, 6, 8-10]. The mean distance between the ciliary ganglion and the lateral rectus muscle's scleral insertion was 31.53 mm (range 23.27-40.55 mm).

Short ciliary nerves were the efferent fiber from the ciliary ganglion and also functioned as sensory tract carrying sensory signal to the ciliary ganglion. After parasympathetic fiber (from motor root) synapsing the ciliary ganglion, it left the ciliary ganglion by means of short ciliary nerves to innervate the ciliary body for controlling accommodation and pupillary sphincter of iris allowing constriction of the pupil in response to light. The sympathetic fiber was transmitted from the ciliary ganglion to pupil dilator muscle by both short ciliary nerves and long ciliary nerve. Short ciliary nerves also conducted sensory fiber originated from eye ball, mainly cornea to the ciliary ganglion[12, 16, 19]. On one hand, Sinnreich and Nathan (1981) found short ciliary nerves leave the ciliary ganglion at anterior pole in three bundle and then give further 12-20 nerves[12]. On the other hand, Hamel et al (2012) reported the short ciliary nerves initially formed two bundle after leaving the ciliary ganglion. Then, each bundle gave off 5-8 nerves[34]. Moreover, Izci and Gonul (2006) described the mean number of the short ciliary nerves which was 7 nerves (range 6-10 nerves)[1] (table 13). From our observation, the short ciliary nerves were not always form bundle constantly. So, we focused on the number of nerve that the short ciliary nerve branched. The mean number of the short ciliary nerved was 9 nerves (range 6-14 nerves). The mode number of the short ciliary nerves according to our observation was 9 nerves which was found in 7 specimens (17.5%). It can be observed that the number of the short ciliary nerves of each report was hardly different.

SCN	Sinnreich and Nathan (1981)	Gonul and Izci (2006)	Hamel et al (2012)	Our study
Number	12-20	6-10	10-16	6-14

Table 13. Comparison of number of short ciliary nerve among studies

*SCN = short ciliary nerve

Girijavallabhan and Ramakrishna (2008) discovered the ciliary ganglion in the specimen of 62 years old south Indian right eye cadaver locating superomedial to optic nerve, beneath the superior rectus muscle and close contact to the ophthalmic artery[13]. This variation of the position of the ciliary ganglion was not found in our study. Every specimen had the ciliary ganglion locating lateral to the optic nerve.

Parasympathetic innervation of ocular structure came from neurons in the Edinger-Westphal preganglionic (EWpg) cell group locating at the rostral mesencephalon and preganglionic neurons in the superior salivatory nucleus (SSN) lying on the ventrolateral medulla. The preganglionic neuron from Edinger-Westphal nucleus transfer fibers by means of the oculomotor nerve (CNIII) to synapse postganglionic neuron in the ciliary ganglion, whereas the preganglionic neuron of superior salivatory nucleus branched fiber by way of the greater petrosal branch of the facial (VII) nerve to synapse postganglionic neuron in the pterygopalatine ganglion (also termed the sphenopalatine ganglion). The pterygopalatine ganglion took part in regulation of ocular blood flow and intraocular pressure (IOP). The parasympathetic fiber from the Edinger-Westphal nucleus played an important role in pupillary near response and pupillary light reflex. Some of parasympathetic fibers went through the short ciliary nerve to innervate the ciliary body for accommodation which was a part of pupillary near response and the remaining fibers innervate pupillary sphincter for constriction in response to light of pupillary light reflex[36]. Disruption of parasympathetic pathway including injury to the nerve to inferior oblique muscle, the ciliary ganglion and the short ciliary nerve resulted in mydriasis pupil and local typed tonic pupil. Tonic pupil was divided into three type composing of Adie tonic pupil, neuropathic tonic pupil and local tonic pupil[30]. The characteristics of tonic pupil are unilateral dilation of pupil; light near dissociation (LND) which is poor or absent response to light but response to near; segmental palsy of the iris sphincter; and denervation hypersensitivity to the dilute cholinergic agents[11].

Many surgical procedures involved in the ciliary ganglion injury were reported. Arai H et al (1996) described 1 out of 26 patient with intraorbital tumor who underwent lateral orbitotomy surgery, developed anisocoria as a postoperative complication[37]. Furthermore, Kapanoglu et al (2002) showed 1 out of 8 patient had tonic pupil as a complication after lateral orbitotomy[38]. Gonul and Timurkaynak (1998) explained the anatomical study of lateral approach of the orbit. Lateral orbitotomy which was adequate exposure for tumors located in superior, lateral or inferior to optic nerve, was approached laterally of the orbit. As claimed by their study, the ciliary ganglion was located posterolateral in the orbit, medial to the lateral rectus muscle and lateral to the optic nerve. As a consequence, retraction of the lateral rectus muscle during lateral orbitotomy would allow the ciliary ganglion comfortably be accessed which resulted in easily being injured[2]. Additionally, Inferolateral endoscopic orbital approach (IL-EOA) to the orbit as an alternative microsurgery of lateral orbitotomy were also involved in the ciliary ganglion injury owning to the fact that the lateral rectus muscle is disinserted and retracted posteriorly, then not blocks these structure[3]. Gonul at el (2003) studied about anatomy in the orbit during transmaxillary approach to the orbit which offered access to the inferomedial and inferolateral orbit and to the inferior aspect of the optic nerve. In spite of the fact that this technique as an alternative approach for orbital surgery was a less invasive extradural approach to the orbit with avoiding the use of craniotomy and brain retraction and was also cosmetically acceptable, there was still a risk of the ciliary ganglion and neurovascular injury, especially by way of lateral approach. As these neural structure including the inferior oblique muscle branch of the oculomotor nerve, the motor root to the ciliary ganglion, and the short ciliary nerves escaped observation within orbital fat(4).

There were a case reports about manipulation of inferior oblique muscle during medial orbital floor fracture reconstruction caused unilateral mydriasis because of interruption of parasympathetic pathway. It is low possibility that medial floor fracture involved with direct ciliary ganglion injury, but manipulation of the inferior oblique muscle was the cause of the ciliary ganglion injury. Since the inferior division of the oculomotor nerve which sent branch to synapse the ciliary ganglion lay on the inferior rectus muscle, manipulation of the inferior oblique muscle which joined the capsulopalpebral fascia with the inferior rectus muscle would disturb both the inferior rectus muscle and inferior division of oculomotor nerve(24, 25).

Hornblass also reported the association of posterior orbital floor fracture and unilateral mydriasis pupil(26). Moreover, during inferior oblique muscle surgery as a treatment of strabismus especially in denervation-extirpation, excessive traction on it can cause excessive traction on the ciliary ganglion. As a result, excessive traction of this muscle can cause injury to the ciliary ganglion directly(6)

Optic nerve sheath fenestration (ONSF) is most commonly indicated in for optic neuropathy in the setting of raised intracranial pressure, especially in patients with severe or progressive visual loss due to pseudotumor cerebri syndrome (PTSC)(28).There are many surgical approach techniques, for instance the lateral orbitotomy approach, the medial approach and anterior medial upper eyelid crease approach(29). The medial approach (transconjunctiva and under the medial rectus muscle) is more popular due to less complicated technique. There was a review about postoperative complication after optic nerve sheath fenestration in 15 recent studies (from 1985-2014). Many different approaches of optic nerve sheath fenestration were taken in including medial transconjunctival, lateral transconjunctival, combined transconjunctival and superomedial lid slit approaches. 9.7% of total 77 complications were anisocoria from tonic pupil. Almost all of the complication was transient[(39)]. The ciliary ganglion was easily injured mostly via lateral approach. Moreover, Blessing and Tse (2018) revealed a revised lateral approach for temporal optic nerve access of optic nerve sheath fenestration which avoided rectus muscle disinsertion, abstained orbitotomy and provided perpendicular view of the optic nerve resulting in being more direct view than oblique view from medial approach. Despite its less invasiveness, there was still a possibility of the ciliary ganglion injury from this technique[(40)].

Some ophthalmologists introduce botulinum toxin (BTX-A) injection into the antagonist muscle of the paretic muscle to decrease adduction tone of antagonist muscle as one of the treatment choices of strabismus. Moreover, BTX-A is used for treatment of blepharospasm and cosmetic purpose. Five cases of transient mydriasis from botulinum toxin (BTX-A)injection to extraocular muscles were reported in humans.[(8)] In these five cases, after botulinum toxin injection, mostly to the lateral rectus muscles, transient mydriasis was shown with tonic pupils. All of these cases, mydriasis were showed temporary and only for a few weeks.[(8)] Apart from injection to the lateral rectus muscle causing mydriasis, Christiansen et al (2016) reported 3 cases out of 27 participants developed left eye tonic pupil after they were performed BTX-A injection to medial rectus muscle as a treatment of esotropia[(9)]. Moreover, Akkaya et al, 2015 found unilateral transient mydriasis and ptosis after botulinum toxin injection for a cosmetic procedure in 36-year-old patient[(8)]. The suspected causes of occurred tonic pupil of botulinum toxin injection in these procedure was either from pharmacological blockage of the cholinergic activity of the iris by way of trans-sclera diffusion or by ciliary artery perfusion, if the injection was superficial to the muscle or from direct injury at the parasympathetic pathway neural structures including ciliary ganglion and short ciliary nerves in the event that injection was too deep[9].

As these mentioned procedures were involve with the ciliary ganglion injury, the distance between the ciliary ganglion and surrounding structures in this study which was the first study conducted in Asian cadavers should be concerned during operation involved with manipulation of the lateral rectus muscle when operating in Asian patients. Moreover, the novel parameter between the ciliary ganglion and scleral insertion of the lateral rectus muscle from this study could be applied in many surgeries associated with the lateral rectus muscle such as BTX-A injection, recession and retraction of the lateral rectus muscle.

The limitation of this study was the absence of reporting about origin and pathway of sympathetic root and also intraorbital vessels. For the reason that the specimens which were from cadavers for medical student study were limit to track for the origin and pathway of sympathetic root.

Chapter VI Conclusion

Anatomical knowledge of the ciliary ganglion and its surrounding structure was essential for surgeons to reduce the ciliary ganglion injury as postoperative complication.

In Asian population from this study, the width and length of CG were 2.24 and 3.50 mm, respectively and was located in orbital apex, posterolateral in the globe, lateral to optic nerve and medial to lateral rectus muscle. The size and position of CG did not differ from the literature. Regarding this study, the motor (parasympathetic) root of CG was discovered into four dispositions, including three motor roots, two motor roots, one motor root and no motor root. Moreover, CG with three motor roots has never been reported. All three roots branched out from nerve to inferior oblique muscle. The distance between CG and surrounding structures, which are considered useful during intraorbital procedures, were measured in Asian population in our study. Comparing with the study in Turkey which their material and methods were comparable to this study [(1)], distance from CG to lateral rectus muscle was shorter, but the distance between the posterior end of globe and anterior edge of CG was longer in our study. Therefore, the CG in Asians might locate very close to the lateral rectus and near the orbital apex more than the Turkish. These differences may be due to disparate ethnicities. This result can be used for estimating the location of CG in the orbital apex. Because of the location of CG was very close to lateral rectus in Asians, it could be easily injured from retraction of the lateral rectus muscle during operation of lateral orbitotomy[(2,3,4,37,38)]. Therefore, awareness of CG-lateral rectus and CG-posterior end of globe relationships should be considered especially in Asian population during these operations. Moreover, during operation involved retraction or recession of lateral rectus muscle, CG-lateral rectus muscle insertion which was firstly described here should be considered to avoid CG injury [(2,3,4,37,38)].

Botulinum toxin type A (BTX-A) injection into the antagonist muscle of the paretic muscle to decrease tone of antagonist muscle is used as one strabismus treatment. Moreover, BTX-A is used for treatment of blepharospasm and for cosmetic purposes. There are many studies that reported temporary mydriasis, tonic pupil and ptosis after BTX-A injection to periocular area and extraocular muscles, which commonly occur in lateral rectus muscle injection(8). Because injection BTX-A into the lateral rectus muscle might cause CG injury, the distance from lateral rectus muscle insertion to CG in this study should be realized.

Optic nerve sheath fenestration (ONSF) is commonly indicated in optic neuropathy in the setting of raised intracranial pressure, especially in patients with severe progressive visual loss due to idiopathic intracranial hypertension (IIH)(29). There was a review about postoperative complications after optic nerve sheath fenestration in 15 studies (from 1985-2014). Many different approaches of optic nerve sheath fenestration were included, but tonic pupil complication was often found in the lateral orbitotomy approach. CG injury was suspected to have an association with tonic pupil complication(5,39). As a result, the distance from optic nerve to CG and also the distance between CG and lateral rectus muscle should be considered during ONSF operation via lateral approach. These study results are useful and applicable in this operation in Asian population.

บรรณานุกรม

1. Izci Y, Gonul E. The microsurgical anatomy of the ciliary ganglion and its clinical importance in orbital traumas: an anatomic study. Minim Invasive Neurosurg 2006;49:156-60.

2. Gonul E, Timurkaynak E. Lateral approach to the orbit: an anatomical study. Neurosurg Rev 1998;21:111-6.

3. Duz B, Secer HI, Gonul E. Endoscopic approaches to the orbit: a cadaveric study. Minim Invasive Neurosurg 2009;52:107-13.

4. Gonul E, Erdogan E, Duz B, Timurkaynak E. Transmaxillary approach to the orbit: an anatomic study. Neurosurgery 2003;53:935-41; discussion 41-2.

5. Tse DT, Nerad JA, Anderson RL, Corbett JJ. Optic nerve sheath fenestration in pseudotumor cerebri. A lateral orbitotomy approach. Arch Ophthalmol 1988;106:1458-62.

6. Kushner BJ. How to perform superior surgery on the Inferior oblique and avoid inferior surgery on the superior oblique. In: Kushner BJ, editor. Strabismus: Practical pearls you won't find in textbooks Cham, Switzerland: Springer; 2017. p. 221-40.

7. Bodker FS, Cytryn AS, Putterman AM, Marschall MA. Postoperative mydriasis after repair of orbital floor fracture. Am J Ophthalmol 1993;115:372-5.

8. Akkaya S, Kokcen HK, Atakan T. Unilateral transient mydriasis and ptosis after botulinum toxin injection for a cosmetic procedure. Clin Ophthalmol 2015;9:313-5.

9. Christiansen SP, Chandler DL, Lee KA, Superstein R, de Alba Campomanes A, Bothun ED, et al. Tonic pupil after botulinum toxin-A injection for treatment of esotropia in children. J aapos 2016;20:78-81.

10. Hemmerdinger C, Srinivasan S, Marsh IB. Reversible pupillary dilation following botulinum toxin injection to the lateral rectus. Eye (Lond) 2006;20:1478-9.

11. McGee S. The pupils. In: Mcgee S, editor. Evidence-based physical diagnosis. 4 ed. Philadephia, PA: Elsveir; 2018. p. 161-83.

12. Sinnreich Z, Nathan H. The ciliary ganglion in man (anatomical observations). Anat Anz 1981;150:287-97.

13. Girijavallabhan V, Bhat KMR. Positional variation of the ciliary ganglion and its clinical relevance. Neuroanatomy 2008;7:38-40.

14. Zhang Y, Liu H, Liu EZ, Lin YZ, Zhao SG, Jing GH. Microsurgical anatomy of the ocular motor nerves. Surg Radiol Anat 2010;32:623-8.

15. Neuhuber W, Schrodl F. Autonomic control of the eye and the iris. Auton Neurosci 2011;165:67-79.

16. Natori Y, Rhoton AL, Jr. Microsurgical anatomy of the superior orbital fissure. Neurosurgery 1995;36:762-75.

17. Yeo MS, Al-Mousa R, Sundar G, Lim TC. Mydriasis during Orbital Floor Fracture Reconstruction: A Novel Diagnostic and Treatment Algorithm. Craniomaxillofac Trauma Reconstr 2010;3:209-16.

18. Apaydin N, Kendir S, Karahan ST. The Anatomical Relationships of the Ocular Motor Nerves with an Emphasis on Surgical Anatomy of the Orbit. Anat Rec (Hoboken) 2018.

19. Company V, Moreno-Bravo JA, Perez-Balaguer A, Puelles E. The Amniote Oculomotor Complex. Anat Rec (Hoboken) 2018.

20. Park HK, Rha HK, Lee KJ, Chough CK, Joo W. Microsurgical Anatomy of the Oculomotor Nerve. Clin Anat 2017;30:21-31.

21. Morard M, Tcherekayev V, de Tribolet N. The superior orbital fissure: a microanatomical study. Neurosurgery 1994;35:1087-93.

22. Gonul E, Timurkaynak E. Inferolateral microsurgical approach to the orbit: an anatomical study. Minim Invasive Neurosurg 1999;42:137-41.

23. Surej Kumar LK, Vinod MK, Menon PV. Lateral orbital approach: Gateway to intraorbital lesions. Natl J Maxillofac Surg 2014;5:217-20.

24. Lee KA. Anisocoria After Repair of Blowout Fracture. J Craniofac Surg 2017;28:1289-90.

25. Lee JI, Kang SJ, Jeon SP, Sun H. Transient Anisocoria during Medial Blowout Fracture Surgery. Arch Craniofac Surg 2016;17:154-7.

26. Hornblass A. Pupillary dilatation in fractures of the floor of the orbit. Ophthalmic Surg, 1979;10:44-6.

27. Stillwater LB, Levine PA. Anisocoria with orbital floor fractures: worry and wait. Otolaryngol Head Neck Surg 1981;89:882-5.

28. Hayreh SS. Pathogenesis of oedema of the optic disc. Doc Ophthalmol 1968;24:289-411.

29. Ko MW. Optic disc swelling: papilledema and other cause. In: Liu GT, Volpe NJ, SL G, editors. Neuro-opthalmology: diagnosis and management. 3 ed. china: elsveir; 2018. p. 197-235.

30. Thompson HS, Kardon RH. The Argyll Robertson pupil. J Neuroophthalmol 2006;26:134-8.

31. Kardon RH, Corbett JJ, Thompson HS. Segmental denervation and reinnervation of the iris sphincter as shown by infrared videographic transillumination. Ophthalmology 1998;105:313-21.

32. Loewenfeld IE. The Argyll Robertson pupil 1869-1969. A critical survey of the literature. Surv Ophthalmol 1969;14:199-299.

33. Grimes P, Von Sallmann L. Comparative anatomy of the ciliary nerves. Arch Ophthalmol 1960;64:81-91.

34. Hamel O, Corre P, Ploteau S, Armstrong O, Rogez JM, Robert R, et al. Ciliary ganglion afferents and efferents variations: a possible explanation of postganglionic mydriasis. Surg Radiol Anat 2012;34:897-902.

35. Johnston JA, Parkinson D. Intracranial sympathetic pathways associated with the sixth cranial nerve. J Neurosurg 1974;40:236-43.

36. McDougal DH, Gamlin PD. Autonomic control of the eye. Compr Physiol 2015;5:439-73.

37. Arai H, Sato K, Katsuta T, Rhoton AL, Jr. Lateral approach to intraorbital lesions: anatomic and surgical considerations. Neurosurgery 1996;39:1157-62; discussion 62-3.

38. Kaptanoglu E, Solaroglu I, Okutan O, Beskonakli E. lateral orbital approach to intraorbital lesions. journal of ankara medical school, 2002;24:171-82.

39. Gilbert AL, Chwalisz B, Mallery R. Complications of Optic Nerve Sheath Fenestration as a Treatment for Idiopathic Intracranial Hypertension. Semin Ophthalmol 2018;33:36-41.

40. Blessing NW, Tse DT. Optic nerve sheath fenestration: a revised lateral approach for nerve access. Orbit 2018:1-7.

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