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박 사 학 위 논 문

Cadaver Study Confirming the Location of Dye after Trigeminal Ganglion Rhizotomy

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Cadaver Study Confirming the Location of Dye after Trigeminal Ganglion Rhizotomy 이 수 현 2021년 2월

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Cadaver Study Confirming the Location of Dye after Trigeminal Ganglion Rhizotomy

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이 논문을 박사학위 논문으로 제출함

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2021년 2월

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1. Introduction

Among cranial neuralgia, idiopathic trigeminal neuralgia (TN) is the most common form of neuralgia. The main clinical feature of TN is paroxysmal lancinating and electrical shock-like pain of face confined within the distribution of trigeminal nerve (1,2). Although the reported incidence of TN is low ranging from 0.03% - 0.3% (3), severe pain of TN significantly impairs quality of life with resultant psychologic distress and may even lead to suicide (4).

As an initial treatment modality, carbamazepine medication shows an excellent pain relief for TN. However, 10% of TN patients shows minimal response to oral medication and severe side effects of carbamazepine hamper the popular use of such medication (5). Various effective treatments including microvascular decompression, radiofrequency thermal rhizotomy (RF-TR), glycerol rhizolysis and percutaneous balloon microcompression are useful options for such intractable cases. Among such procedures, RF-TR demonstrates excellent treatment outcome with a success rate of 80% to 97%, although it shows reoccurrence in some of TN patients (6-9). The main advantage of RF-TR is that it can be a good option for poor surgical candidates and its possibility of repeated procedure in the same patients. In addition, RF-TR can provide more selective destruction of trigeminal branch, which is essential for TN in a single nerve distribution (6-8,10,11).

Reported complications in cases of wrong trajectories with the electrode are intracranial hemorrhage, carotid artery injury, other cranial nerve or brain stem injury, and even blindness (6,12-14).

Considering serious complications above, accurate and correct positioning of electrode is the essential key for the safe and effective RF-TR. Previous work suggested that the triangular plexus as the best place to create more selective lesion (15). The sensory trigeminal system located in the Meckel's cave is segmented into two parts: the trigeminal ganglion and the triangular plexus. The triangular plexus has been defined as the portion of the trigeminal nerve from the posterior margin of the trigeminal ganglion to the path over the upper ridge of the petrous bone. The triangular plexus is immediate retrogasserian portion of the trigeminal root and it corresponds to the dorsal sensory rootlet. It makes a triangular shape with a plexual distribution (16). The anatomy of the triangular plexus has been relatively unrecognized contrary to the trigeminal ganglion with its three divisions. In spite of its importance, the anatomical study related to therapeutic procedure is scarce. It is valuable to pay special attention to the anatomy of this particular segment, as this may contribute to the accuracy and safety of therapeutic procedures of TN.

Most commonly, placement of electrode tip is controlled by fluoroscopic guidance, especially lateral cranial x-rays, combined with stimulation-induced paresthesia provocation in an awake patient. For locating the electrode tip into the desired triangular plexus, the lateral cranial view should confirm that the tip of the needle arrives at the petroclival junction (6,9). Conversely, other studies suggest that an electrode tip should be placed just behind the clival line to reach the triangular plexus (14,15).

Although the triangular plexus is suggested as the best place of lesioning during RF-TR, there is no anatomical study showing that the triangular plexus is targeted if an electrode is placed around the petroclival junction. The primary endpoint of this study is to confirm with gross and microscopic finding of trigeminal system if an electrode

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tip is placed into the petroclival junction in lateral cranial view, not beyond the clival line, it actually arrives at the triangular plexus or not. The secondary endpoint is to examine the triangular plexus with morphological and histological method.

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2. Materials and Methods

2.1. Cadavers

A total of 8 adult Asian cadavers (age range, 65-89 yr; mean age, 77.7 yr; 2 males, 6 females) were used in this study. Those cadavers were supplied from the department of anatomy of our institution for research and educational purposes. Our institutional ethics committees approved this study. Eight cadavers were fixed with a 10% formalin solution via the right femoral artery perfusion within 24 hr after death.

2.2. Percutaneous procedure

The same procedures of RF-TR which is performed for the trigeminal ganglion rhizotomy of TN were used in this study. All procedures were performed under C-arm guidance. Cadavers lay in the supine position with neck slightly extended and chin up. A 10 cm pillow was placed under the upper back to facilitate the position of neck extension. The C-arm was tilted caudally 30 to 35 degrees and rotated to right or left side 10 to 15 degrees obliquely to visualize the foramen ovale (Figure 1A). The skin entry was done at 2 - 3 cm lateral to the angle of the mouth. To make an equal situation of RF-TR performed during clinical practice, a RF cannula of 22 gauge, 10 cm, 2 mm active tip was used. After confirming the clear visualization of foramen ovale, the cannula was inserted in a coaxial manner to the fluoroscopic beam toward the foramen ovale. During the needle insertion until the entrance of foramen ovale, intermittent fluoroscopy of anteroposterior (AP) and lateral views

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was checked. When the cannula just arrived in front of the foramen ovale in lateral view, this cannula was advanced 2-5 mm further through the puncture of foramen ovale. After this procedure, cannula tip was confirmed to reach the junction of the petrous ridge of the temporal bone and the clivus on lateral (Figure 1B) and AP view (Figure 1C). After fluoroscopic confirming of the appropriate location of cannula tip, 0.2 mL of green tissue dye (Davidson® marking system, Bradley product, Inc., Minnesota, USA) was injected and RF-TR cannula was removed. Both sides of the trigeminal ganglion were punctured using the same technique.

2.3. Gross examination of trigeminal system

As a next step of percutaneous procedure, dissection of the trigeminal ganglion of both side was performed. Calvaria was removed using a power saw. During removal of calvaria, special attention was paid not to damage the inner structure. Brain except the pontine and trigeminal ganglion area was removed carefully. Dissection around the trigeminal ganglion was performed to include the triangular plexus and root which originates from pons. During a dissection, a course of ophthalmic (V1), maxillary (V2), and mandibular (V3) branch of trigeminal ganglion was identified. In addition, we tried to identify the morphologic difference and anatomical location of the triangular plexus and trigeminal ganglion. Before extraction of trigeminal specimens injected with green tissue dye, we measured the transverse and vertical diameter of triangular plexus. In each cadaver, right and left side of triangular plexus were measured respectively. Imaginary triangular line was drawn in the triangular plexus to measure the transverse and vertical diameter more precisely.

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The transverse diameter means the base of this triangle where facing the trigeminal ganglion. The vertical diameter was defined as the distance from the base to the apex of triangle. This aplex of triangle was placed on upper petrous ridge.

2.4. Confirmation of location of electrode tip

Confirmation of the location of electrode tip was determined according to the presence of the injected dye within trigeminal system. Grossly, if an injected green tissue dye was seen more widely in the triangular plexus than the trigeminal ganglion, it was considered that an electrode tip reached the triangular plexus. In cases of obscurity whether the injected dye was seen in the triangular plexus or trigeminal ganglion under gross finding, such cases were determined in the microscopic field.

2.5. Microscopic examination of trigeminal system

All specimens were fixed in 10% neutral-buffered formalin and processed routinely for paraffin embedded blocks. Conventional 4 sections were obtained from the paraffin blocks and incubated in an oven at 60 °C for an hour. Sections were then dewaxed in xylene for 10 minutes and rehydrated through graded alcohol to distilled water. These slides were stained with hematoxylin and eosin (H&E) dyes according to conventional method.

In the microscopic field, the presence of an injected dye was identified. This identification was performed by a pathologist with more than 10-year experience and pain physician who was not involved in the

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percutaneous procedure. If an injected green tissue dye was observed in the area of triangular plexus more widely than the trigeminal ganglion, it was considered that an electrode tip reached the triangular plexus. Conversely, more wide observation of an injected dye in the trigeminal ganglion than the triangular plexus, it was considered that an electrode tip reached the trigeminal ganglion. After finishing the confirmation of location of dye, diameter of every nerve bundle in the triangular plexus was measured using an imaging analysis system (Image scope, Leica biosystems imaging, Inc., California, USA). Measurement of the nerve bundle and identification of characteristic histologic finding of triangular plexus and trigeminal ganglion were performed by a pathologist.

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3. Results

3.1. Puncture of foramen ovale

Fifteen sides of foramen ovale of 8 adult cadavers were punctured successfully and confirmed with lateral and AP cranial view to arrive in petroclival junction, not beyond the clival line (Figure 1A-C). In spite of repeated attempts, one foramen ovale was impossible to be punctured. Overall, 15 trigeminal systems were evaluated.

3.2. Gross finding of trigeminal system

The V1, V2 and V3 branch of the trigeminal ganglion traversed the superior orbital fissure, the foramen rotundum, and the foramen ovale respectively, to enter the cavernous sinus region. Then they merged together to form the trigeminal ganglion. The nerve fibers from the trigeminal ganglion formed a plexiform distribution forming the triangular plexus. All specimens showed the triangular shape of triangular plexus with broadest margin facing trigeminal ganglion and its apex is formed around the upper petrous ridge. Beyond the upper petrous ridge, those fibers of triangular plexus turned into the root and coursed posteriorly to reach the pons (Figure 2A&B).

3.3. Determination of electrode tip location

Among 15 trigeminal systems of gross evaluation, 8 trigeminal systems could be identifiable the location of injected dye (Figure 3A).

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However, 7 trigeminal systems were uncertain whether the injected dye was in the triangular plexus or trigeminal ganglion. Therefore, final determination of the electrode tip location was performed depending on the location where green tissue dye was observed in the microscopic finding. Among 15 trigeminal systems, 8 showed dye appearance in the triangular plexus while 6 showed it in the trigeminal ganglion. In one trigeminal system, dye appearance was found neither gross nor microscopic evaluation. Overall, 53% of RF-TR could reach the triangular plexus when an electrode tip was place on the petroclival junction (Table 1).

3.4. Microscopic finding of trigeminal system

Trigeminal ganglion consisted of aggregates of ganglion cells with a characteristic round-shaped cell body. From the trigeminal ganglion, small nerve bundles extended to the triangular plexus region. Each of the nerve bundles in the triangular plexus were surrounded by meningothelial cells and radiated through loose connective tissue. These nerve bundles were transformed densely packed structure in the root region. The border where the ganglion cells of trigeminal ganglion converted to the cells of nerve bundle of triangular plexus was identifiable (Figure 3B, HE stain x 40).

3.5. Gross and microscopic measurement of triangular plexus

Gross and microscopic measurement of triangular plexus were

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performed in 15 trigeminal systems. Grossly measured average triangular plexus vertical and transverse diameter were 0.8 cm and 1.3 cm, respectively (Table 2, Figure 4A).

Average 33 regions of nerve bundle per 1 triangular plexus were measured. This region was made in order to include every bundle which was seen microscopically. Microscopically measured average triangular plexus bundle size was 188.04 μm (range from 134 μm to 242 μm) (Table 3, Figure 4B, HE stain x 10).

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Table 1. Location of Tissue Dye Appearance of Trigeminal System under Microscopic Evaluation

Cadaver	Sex	Age	Right side	Left side
1	M	88	None	Triangular Plexus
2	F	85	Trigeminal Ganglion	Triangular Plexus
3	M	71	Trigeminal Ganglion	Triangular Plexus
4	F	89	Trigeminal Ganglion	Trigeminal Ganglion
5	F	62	Triangular Plexus	Triangular Plexus
6	F	72	Triangular Plexus	Triangular Plexus
7	F	85	Trigeminal Ganglion	None
8	F	67	Trigeminal Ganglion	Triangular Plexus

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Table 2. Gross Size of Triangular Plexus

Cadaver	Sex	Age (yr)	Triangular Plexus (mean VD*, cm)	Triangular Plexus (mean TD**, cm)
1	M	88	0.7	1.3
2	F	85	0.8	1.2
3	M	71	0.8	1.5
4	F	89	0.8	1.1
5	F	62	0.7	1.2
6	F	72	0.8	1.7
7	F	85	0.8	1.3
8	F	67	0.9	1.4
Average		77.7	0.8	1.3

The vertical and transverse diameter of triangular plexus from cadaver 1 to 8 were measured at right and left side of trigeminal system respectively except cadaver 1 which showed only one foramen ovale puncture.

*VD: Vertical diameter; **TD: Transverse diameter.

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Table 3. Microscopic Size of Nerve Bundle in Triangular Plexus

Cadaver	Right side (μm)	Region*	Left side (μm)	Region*
1	None	None	165 ± 105	1 - 17
2	169 ± 86	1 - 30	175 ± 56	1 - 28
3	214 ± 56	1 - 36	203 ± 112.6	1 - 38
4	176 ± 81	1 - 41	134 ± 59	1 - 35
5	158 ± 95	1 - 28	175 ± 104	1 - 30
6	174 ± 91	1 - 35	139 ± 110	1 - 26
7	225 ± 110	1 - 50	242 ± 95	1 - 23
8	180 ± 91	1 - 67	184 ± 95	1 - 36
Average	191 ± 75		183 ± 75	

Values are mean ± standard deviation.

*Region: An area of TP where the size of nerve bundle was measured.

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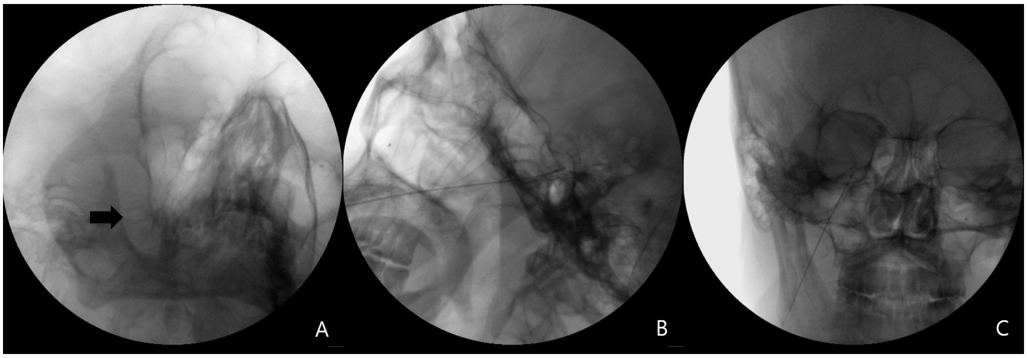

Figure 1. Anteroposterior oblique (A), lateral (B) and anteroposterior (C) view under fluoroscopy. The foramen ovale is indicated with black arrow (A). The needle tip is located in the petroclival line (B). The needle tip reached the junction of the petrous ridge of the temporal bone and the clivus (C).

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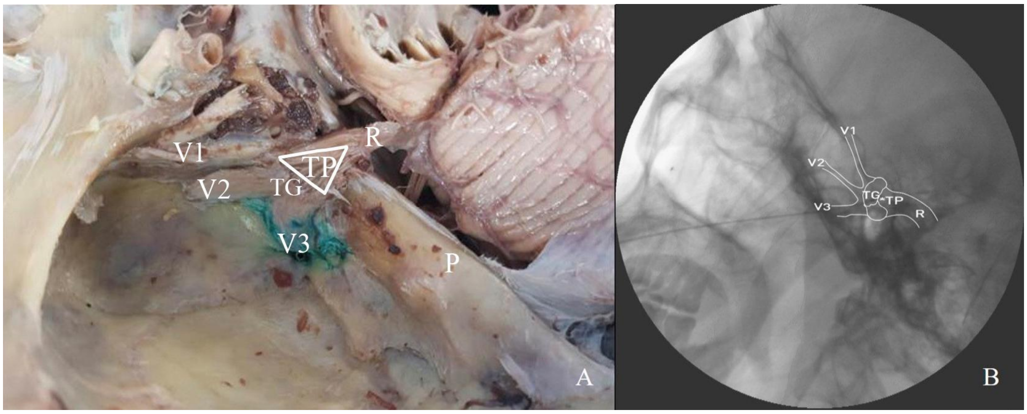

Figure 2. Trigeminal system (A) and its schematic illustration on lateral view (B). * indicates the distal part of the electrode. V1: ophthalmic branch; V2: maxillary branch; V3: mandibular branch; TG: trigeminal ganglion; TP: triangular plexus; R: root; P: petrous ridge.

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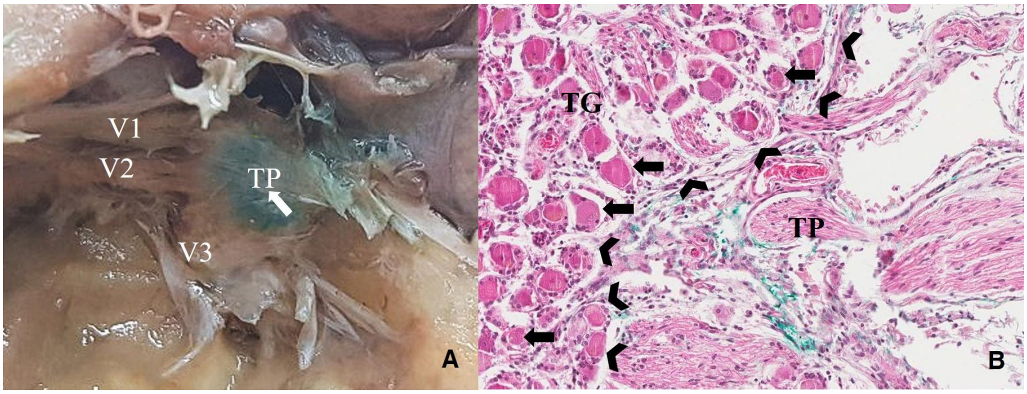

Figure 3. Trigeminal system showing injected green tissue dye (white arrow) in the triangular plexus (A). Injected green tissue dye was observed dominantly in the area of triangular plexus microscopically. Black arrow heads indicate the border between trigeminal ganglion and triangular plexus. Area of triangular plexus showed the nerve bundles with loose connective tissues. Within trigeminal ganglion, round shaped sensory cell bodies (black arrows) are seen (B, HE stain x 40). V1: ophthalmic branch; V2: maxillary branch; V3: mandibular branch; TG: trigeminal ganglion; TP: triangular plexus.

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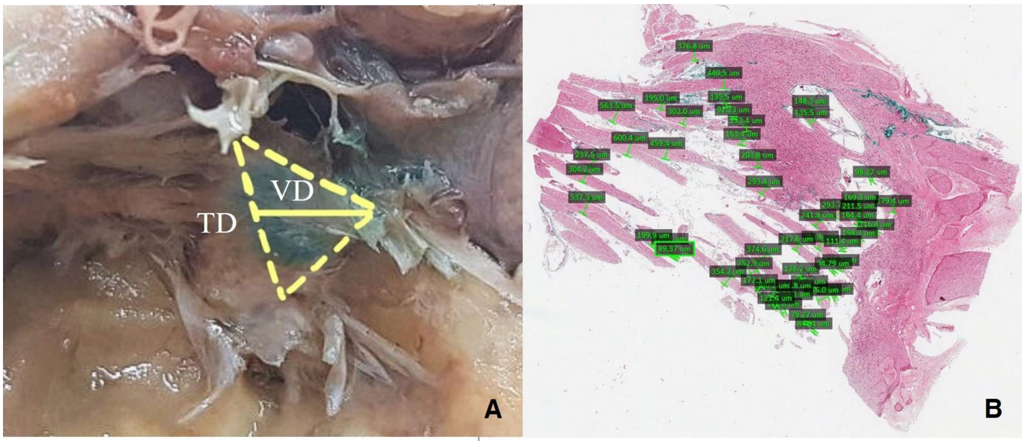

Figure 4. Dotted triangle showing measurement of gross size of triangular plexus (A). Green numerical number within the black rectangle indicates the region where microscopic measurement of the nerve bundle of triangular plexus was performed (B, HE stain x 10). V1: ophthalmic branch; V2: maxillary branch; V3: mandibular branch; TD: transverse diameter; VD: vertical diameter.

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4. Discussion

In this study, one foramen ovale was impossible to puncture. The anatomy and nearby structure of foramen ovale is critical for successful performance of RF-TR. The foramen ovale is located in the greater wing of the sphenoid bone which varies greatly in shape and size (17). Previous study showed that 6 distinctive shapes of foramen ovale and 5 anomalous variants from the anatomical view were found (18). Significant variability in the foramen ovale's shape and size might affect the successful cannulation. Also, poor visualization of foramen ovale due to old age of cadaver 1 (88 yr) during RF-TR might be one reason.

The triangular plexus demonstrated a plexual distribution (97.4%) with anastomoses (96.7%) and somatotopic distribution. At the triangular plexus level, somatotopy of sensory fibers is almost clear-cut as in the trigeminal ganglion. The shape of triangular plexus was characterized by a triangular form. The characteristic triangular blade of triangular plexus, like a hand in a glove, was formed due to abundant anastomosis(16).

In this study, we could confirm the triangular shape of triangular plexus with its base facing trigeminal ganglion and its apex being placed on the upper petrous ridge. The average vertical and transverse diameter of grossly measured triangular plexus was 0.8 cm and 1.3 cm, respectively. This size means that the triangular shape of the triangular plexus is a broad based triangle with a relatively short height. When placing an electrode on the triangular plexus, it is suggested that V1 and V3 branch should be in the most superior-medial and inferior-lateral part of the triangular plexus, respectively. In cases of V2 branch, it should be placed between V1 and V3 branch (19). Therefore,

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when placing an electrode on the triangular plexus, this shape of triangle should be considered. Essentially, this small area of triangle requires more sophisticated movement of an electrode within the triangular plexus under the guidance of an electrical stimulation.

Previous study showed that the triangular plexus contained bundles of nerve fibers of diameter up to 100 – 150 μm, especially located in the superficial part of triangular plexus (18,20). The diameter of nerve bundle measured in this study was larger than previous study.

The trigeminal ganglion forms a semilunar shape. Contrary to the triangular plexus, the trigeminal ganglion did not show any plexual distribution without anastomosis nor arachnoid sheet. However, it also showed clear somatotopic distribution like the triangular plexus (16).

Microscopically, we could confirm a definite difference between the trigeminal ganglion and triangular plexus. Trigeminal ganglion showed aggregates of ganglion cells with a characteristic round-shaped cell body whereas triangular plexus showed the nerve bundles with loose connective tissue. The border between different types of cells of triangular plexus and trigeminal ganglion could be identified. This is the reason why we tried to identify the location of an injected dye under microscopic examination. There is few study showing triangular plexus-trigeminal ganglion junction precisely.

This study demonstrated that 53% of RF-TR could reach the triangular plexus when an electrode tip was placed on the petroclival junction. Although controversies exist about the radiologic landmark to reach the triangular plexus (6,9,14,15), most pain physicians target the petroclival junction especially if a patient is suffering V2 TN. Previous case report showed a brain stem injury after RF-TR. In that report, lateral cranial X-ray demonstrated that an electrode tip was located far behind the clival line (14). Since a vital structure is located behind the

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clival line, how far away an electrode should be placed from the clival line is a matter of importance. Previous study of retrospective evaluation of an electrode tip location in RF-TR showed that 69% of RF-TR cases was in behind the clival line. Concretely, an electrode tip was located 1.57 – 3.05 mm behind the clival line. Only 7% of RF-TR cases showed that an electrode tip was located precisely on the posterior edge of the clivus (15).

In this study about half of RF-TR cases could not reach the triangular plexus. During percutaneous procedure of RF-TR, obtaining true lateral cranial view is essential to assess the final location of electrode tip. During percutaneous procedure, we could encounter some difficulties obtaining a true lateral cranial view. Two cadavers had distorted neck. Although we tried to obtain true lateral cranial view by rotating an oblique angle in such cases, this phenomenon might affect the decision of location of electrode tip.

This study includes several limitations. First, the procedure of RF-TR does not inject any material but the lesioning around the electrode shaft. Therefore, this study for identifying an electrode tip location through an injection of tissue dye might have a difference with an actual RF-TR in clinical situation. However, to minimize such difference, we injected a tissue dye as small as 0.2 mL. Usually 0.2 – 0.4 mL of glycerol is injected into the trigeminal ganglion to include the trigeminal system (21).

Second, to confirm the location of an electrode tip, only radiologic landmark was used in this study. However, in a clinical situation of RF-TR, final placement of an electrode should be determined under the guidance of electrical stimulation. Therefore, further study confirming the location of an electrode tip under the guidance of radiologic landmark and electrical stimulation is needed.

In conclusion, when an electrode tip was place on the petroclival junction, 53% of RF-TR could reach the triangular plexus. The triangular plexus showed a triangular shape with an average vertical and transverse diameter of 0.8 cm and 1.3 cm, respectively. Therefore, careful and delicate movement of an electrode within trigeminal system is required to prevent further damage of vital structure.

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5. Summary

The primary endpoint of this study is to confirm with gross and microscopic finding of trigeminal system if an electrode tip is placed into the petroclival junction in lateral cranial view. The secondary endpoint is to examine the triangular plexus with morphological and histological method. Eight adult Asian cadavers were used and all procedures were performed under C-arm guidance. After fluoroscopic confirmation of the appropriate location of cannula tip, green tissue dye was injected and gross and microscopic analysis were made. This study demonstrated that 53% of RF-TR could reach the triangular plexus when an electrode tip was placed on the petroclival junction. Microscopically, triangular plexus showed the nerve bundles with loose connective tissue. In this study, we could confirm the triangular shape of triangular plexus with broad based triangle with a relatively short height. Therefore, careful and delicate movement of an electrode within trigeminal system is required to prevent further damage of vital structure.

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Cadaver Study Confirming the Location of Dye after Trigeminal Ganglion Rhizotomy

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(Abstract)

Radiofrequency thermal rhizotomy (RF-TR) demonstrates an excellent treatment outcome with a high success rate among patients of intractable trigeminal neuralgia. The triangular plexus (TP) is suggested as the best place of lesioning during RF-TR. However, the anatomy of the TP has been relatively unrecognized and the anatomical study related to therapeutic procedure is scarce. The purpose of this study is to confirm with gross and microscopic finding of trigeminal system if an electrode tip is placed on the petroclival (PC) junction in lateral cranial view, it actually arrives at the TP or not. In relation to therapeutic procedure, we examined the TP with morphological and histological method. Percutaneous procedure of RF-TR under C-arm guidance was performed in 8 cadavers. Final target of an electrode tip

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was PC junction under true lateral cranial view. The location of an electrode tip was determined under observation of the presence of an injected dye. TP size was measured grossly and microscopically. Gross and microscopic evaluation of TP was performed. Among 15 trigeminal systems, 8 showed dye appearance in the TP while 6 showed it in the TG. Overall, 53% of RF-TR could reach the TP when an electrode tip was place on the PC junction. Grossly measured average TP vertical and transverse diameter were 0.8 cm and 1.3 cm, respectively.

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삼차신경통 환자에서 고주파 열 응고술 시행 시 전극 끝 위치에 관한 해부학적 연구

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(초록)

난치성 삼차신경통 환자에게 고주파 열 응고술을 시행한다면 높은 성공률로 우수한 치료 효과를 볼 수 있다. 고주파 열 응고술 시 삼각부가 가장 적합한 장소로 여겨지나, 삼각부에 대한 해부학적인 특성은 잘 알려진 바가 없고 치료적 시술과 관련된 해부학적 연구는 드물다. 따라서 이 연구를 통해 전극이 머리뼈 측면 영상에서 추체경사대 연접 부위에 도달했을 때 육안적, 현미경학적으로 전극의 끝이 삼각부에 도달하는지를 확인하는 것을 목표로 하였다. 치료적 시술과 관련하여 우리는 삼각부를 형태학적, 조직학적으로 관찰하였다. X선 투시 촬영장치를 통해 총 8구의 카데바에 경피적 고주파 열 응고술을 시행하였고 전극의 최종 위치는 머리뼈 측면 영상에서 추체경사대 연접 부위로 하였다. 전극을 통해 염색약을 주입해 전극 끝 위치를 확인하였고 삼각부의 크기를 육안적, 현미경학적으로 측정하였다. 총 15개의 삼차신경 시스템 중, 8개는 삼각부 부위에, 6개는 삼차신경절 부위

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에 염색약이 관찰되었다. 종합하면 고주파 열 응고술 시술 시 53%에서 전극의 끝이 삼각부에서 관찰되었다. 육안적으로 측정한 삼각부의 수직, 수평 직경은 각각 0.8 cm, 1.3 cm 이었다.

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