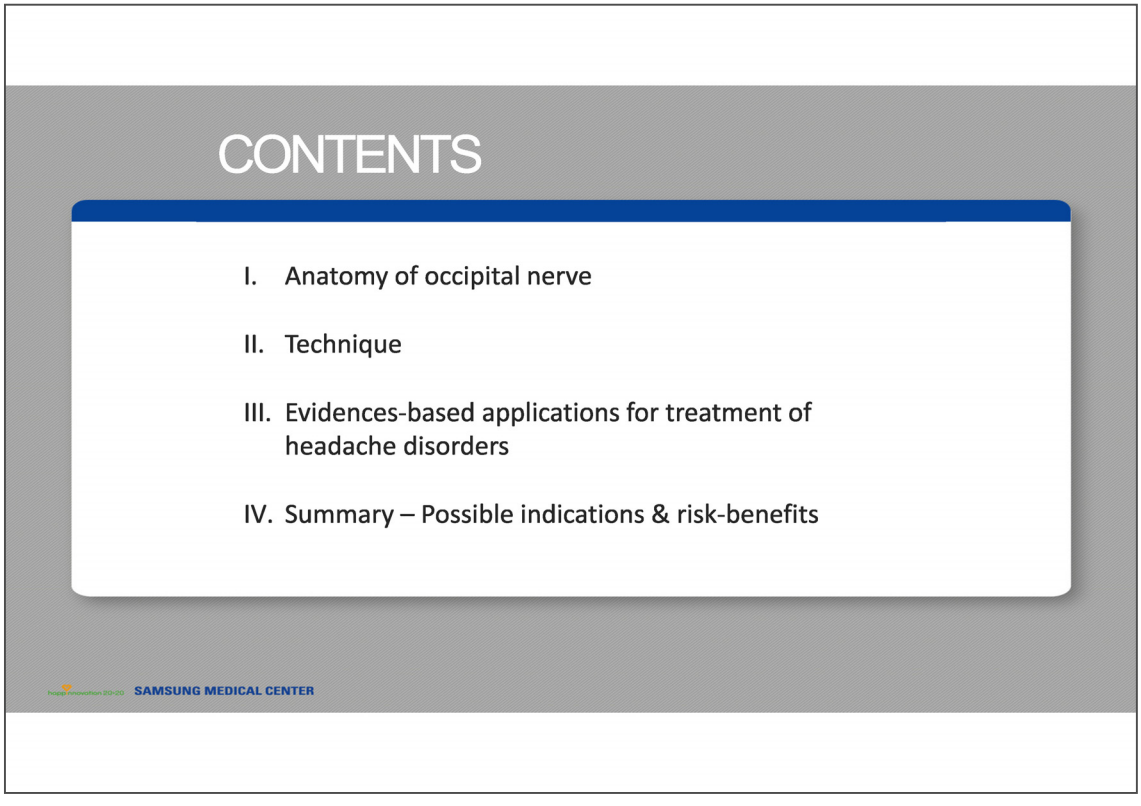
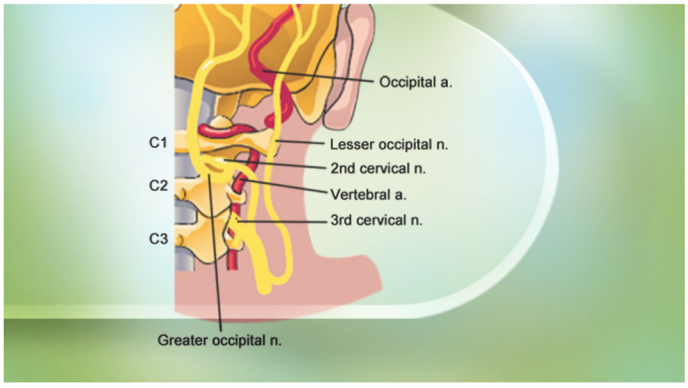
신경차단술, 보툴리눔독소 치료

이 미 지
삼성서울병원



Occipital Nerve

Anatomy



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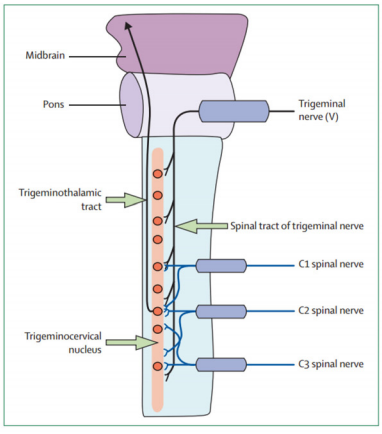
Occipital Nerve

Trigeminocervical complex



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Occipital Nerve

Effects on the trigeminal nerve

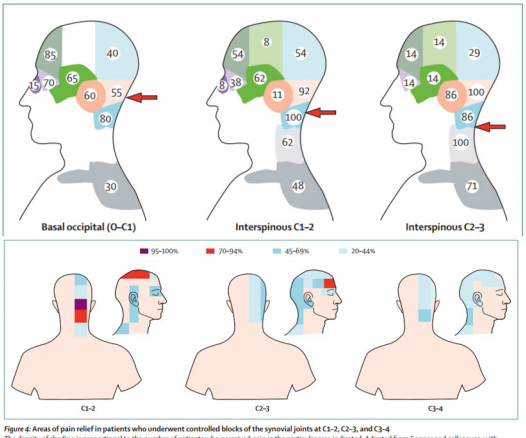
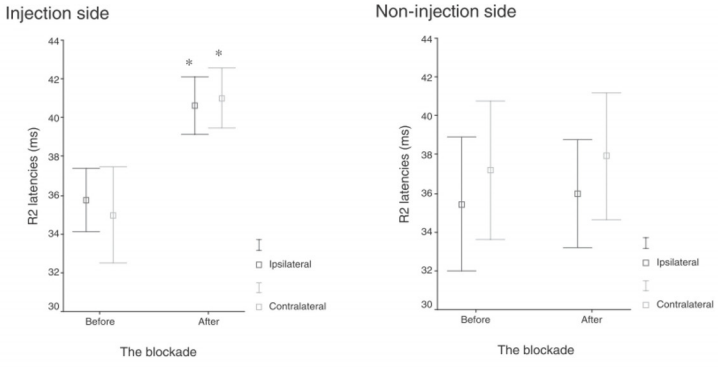


Figure 4: Areas of pain relief in patients who underwent controlled blocks of the synovial joints at C1–2, C2–3, and C3–4
The density of shading is proportional to the number of patients who perceived pain in the particular area indicated. Adapted from Cooper and colleagues, with permission from Blackwell Science.[18]

Occipital Nerve

Functional connectivity between occipital-trigeminal nerves



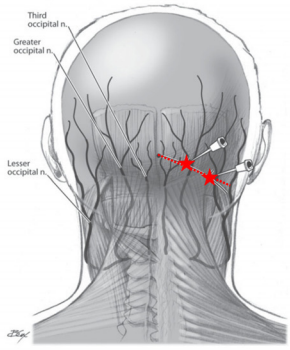
ONB leads to functional changes in the trigeminal nociception

Cephalalgia 2006; 26:50–55.

Greater Occipital Nerve Block

Technique (1) location

- Location of injection
  - Occipital protuberance와 mastoid process 잇는 선의 1/3 지점
  - Immediately medial to occipital artery
- Palpation of max tenderness
- Palpation of arterial pulsation



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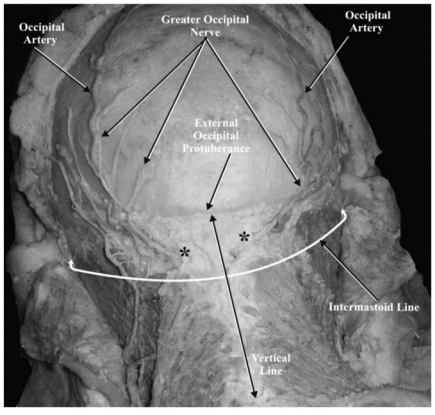
Greater Occipital Nerve Block

Technique (1) location



41% of intermastoid line
22% of inion-mastoid line
2cm lateral & 2cm inferior to Inion

Figure 1. The relationship of the right and left greater occipital nerves (*) at their exit point with the vertical and intermastoid lines.

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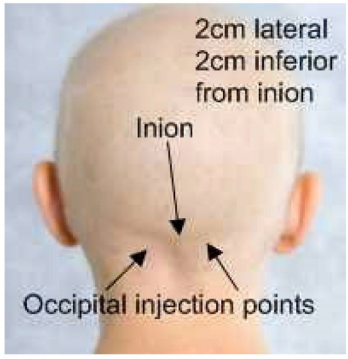
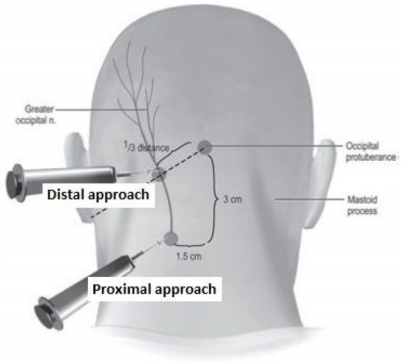
Greater Occipital Nerve Block

Technique (1) location





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Greater Occipital Nerve Block

Technique (2) injection

- 5mL syringe
- 26 or 30 gauge, 0.5 or 1 inch needle
- Insert to contact the periosteum,
  then slightly withdraw,
  pull the plunger,
  inject the solution
- Single injection or a fan-like distribution

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Greater Occipital Nerve Block

Technique (3) drugs to use

- Lidocaine 0.25 – 2% and/or bupivacaine 0.25 – 0.5 %
- Combination: L/B ratio 1:1 – 1:3
- Corticosteroids
  - For cluster headache
  - 다른 headache disorders 에서도 local anesthetics에 효과가 불충분하면 추가해볼 수
- Volume: 4 mL (1.5 – 3 mL) per site
- To minimize AE, <300mg lidocaine, <175mg Bupivacaine per treatment session

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Greater Occipital Nerve Block

Technique (3) drugs to use

- Steroids for GONB

	Equivalent to TA 1mg (mg)	Biologic Half-life (hours)	Dose range reported per individual GON block (mg)
Triamcinolone	1.0	18-36 (intermediate)	5 – 40
Methylprednisolone	1.0	18-36 (intermediate)	20 – 160
Betamethasone	0.15	36-54 (long)	18
Dexamethasone	0.19	36-54 (long)	4

- Onset of pain relief from steroid is slower than anesthetics
- Analgesic effect may not occur within the first 20 minutes of injections

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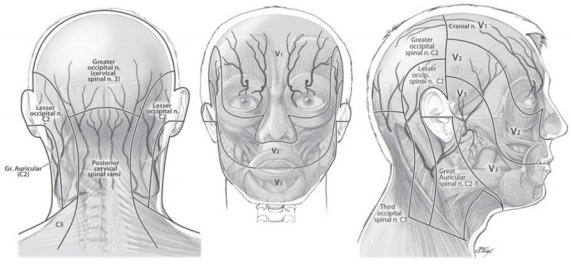
Greater Occipital Nerve Block

Technique (4) post-injection

- Numbness in the area of the GON dermatome
- Should occur within 5 minutes after lidocaine injection and within 10-15 minutes after bupivacaine injection



Greater Occipital Nerve Block

Adverse effect of GONB

- Frequent
  - Pain
  - Vasovagal syncope
  - Deterioration of symptoms
- Rare
  - Hitting the artery
  - Dysphagia (anterior cervical block)
  - Alopecia/cutaneous atrophy (Steroid)
  - Coma (in patients with cranial defect/craniotomy)

Greater Occipital Nerve Block

Adverse effect of local steroid injection

- Systemic AE
  - Cushing syndrome induced by serial (6 times/3mo) bilateral ONBs using triamcinolone 40mg per site
  - Caution in patients with DM, glaucoma
- Local AE
  - Alopecia, cutaneous atrophy
  - Should be avoided when performing the trigeminal nerve blockade

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Greater Occipital Nerve Block

Treatment plan

- Next injection?
  - As needed
  - Recommended frequency: once every 2 – 4 weeks
  - Depending on response of the individual patient
  - Steroid → >3 months-interval but less in patients with cluster headache
    (2-4 days apart in the study by Leroux et al.)

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Evidences for headache disorders

Summary of study results

- Migraine
  - RCT evidence for the transitional treatment of chronic migraine and/or medication-overuse headache
  - Case series evidences for acute treatment for migraine attack
  - Less robust evidence for preventive treatment for episodic migraine
- Cluster headache
  - Transitional treatment for CH (Level A recommendation)
    - Long-lasting steroid use is mandatory

Evidences for headache disorders

Summary of study results

- Occipital neuralgia
  - ONB is a part of diagnosis and treatment
- Cervicogenic headache
  - Possibly effective for cervicogenic headache
  - Comparable to C2/C3 root blocks
  - Repeated blocks may lead to complete HA freedom
  - Long-term remission possible – case report

Summary

- Easy
- Cost-effective
- Well-tolerated
- Takes <5 minutes
- Expert recommendation & Evidence-based treatment for many headache disorders

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Botulinum Toxin Injection for Treatment of Chronic Migraine

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Department of Neurology, Samsung Medical Center,
Sungkyunkwan University, Seoul, Korea

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Why Botulinum Toxin A?

History of investigation

- The beneficial effect of Botulinum Toxin A (BoNT-A) in migraine was first noted in patients who were treated for facial wrinkles (Binder et al., 1998)
- Several studies on the efficacy of BoNT-A in migraine and tension-type headache (1999 – 2011)
  - Inconsistent results, underpowered designs, mostly negative for episodic migraine and tension-type headache
- RCT for chronic migraine (2010)
  - PREEMPT-1 (2010) – negative
  - PREEMPT-2 (2010) – positive
- Currently, standard treatment option for chronic migraine

Why Botulinum Toxin A?

BoNT-A mechanism of action

- BoNT-A preferentially acts on cholinergic neurons (motor and sympathetic nerve terminals)
- Non-cholinergic action of BoNT-A
  - Blocks the Ca2+-evoked neuroexocytosis of neurotransmitters other than Ach
- Sympathetic sudomotor C nerve fiber terminals – co-localization of Ach and CGRP

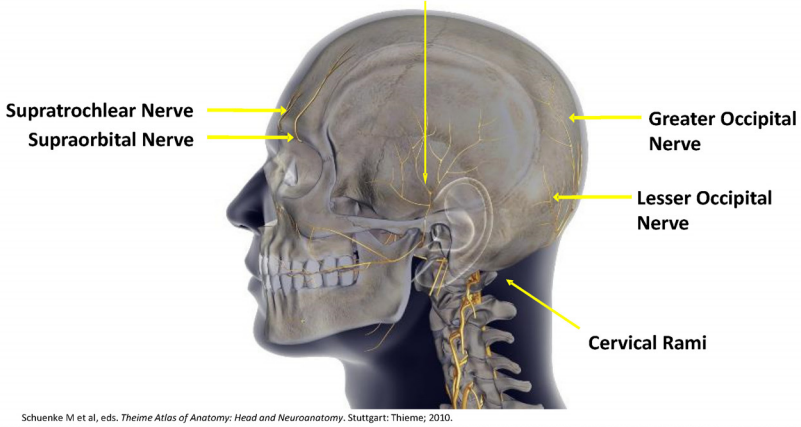
Why Botulinum Toxin A?

Proposed mechanism of antinociceptive action

- Preclinical findings
  - **Inhibit substance P release** in dorsal root ganglion neurons
  - **Reduce stimulated release of CGRP** from trigeminal ganglia neurons
  - In the experimental pain model, **BoNT-A inhibits activation of primary sensory neurons** (glutamate release; Fox expression in the spinal cord, and activation of wide dynamic range (WDR) neurons in the dorsal horn)
- Healthy volunteers
  - Did not show anti-nociceptive effects

Why Botulinum Toxin A?

Proposed mechanism of antinociceptive action



Schuenke M et al, eds. *Theime Atlas of Anatomy: Head and Neuroanatomy*. Stuttgart: Thieme; 2010.

What to expect from BoNT-A injection

PREEMPT-2 trial results

- Indication: adult patients with chronic migraine (with or without medication overuse)
- 2 sessions 12 week apart (total 24 weeks)
- Standardized injection: fixed dose (155 units), fixed sites (31 sites)
- Additional injection: follow-the-pain strategy

- Result: -9 headache days (vs. -6.7 days placebo) per 28 days relative to baseline

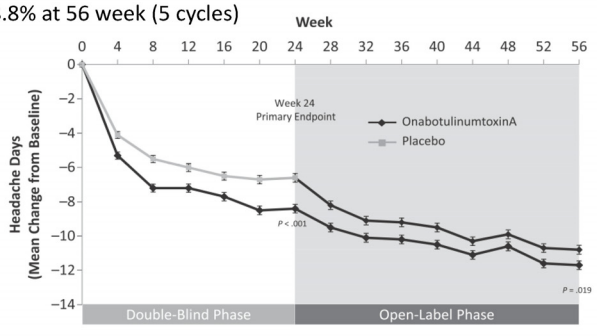
Diener et al. Cephalalgia 30(7) 804–814

What to expect from BoNT-A injection

PREEMPT-2 trial results

50% responder rate

- 47.1% at 24 week (2 cycles)
- 68.8% at 56 week (5 cycles)



Aurora et al. Headache 2011;51:1358-1373

What to expect from BoNT-A injection

Real-World Data

- Real-world data of 254 patients
  - Headache days: 27 days → 18 days (-7 days)
  - Migraine days: 15 days → 7 days (-6 days)
  - Crystal clear days: 3 days → 12 days (+7 days)
- It's important to set **a realistic goal** before treatment
- Non-responder at 1st cycle
  - **additional 10%** respond at 2nd cycle
  - **additional 10%** respond at 3rd cycle

Khalil et al. The Journal of Headache and Pain 2014;15:54
J Neurol Neurosurg Psychiatry 2015;86:996–1001.

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Preparation

Botulinum toxin A 100 IU (X2)

Normal Saline

2cc Syringe (X2)

1cc Insulin Syringe (X4)

or

1cc syringe & 30G needle

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Preparation

Reconstitution and Dilution

100U　　N/S 2cc　　50U per 1cc

5U per 0.1cc

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PREEMPT protocol

General Principle

MUSCLE AREA	RECOMMENDED DOSE/NUMBER OF SITES
Corrugator	10 Units divided between 2 sites
Procerus	5 Units in 1 site
Frontalis	20 Units divided between 4 sites
Temporalis	40 Units divided between 8 sites
Occipitalis	30 Units divided between 6 sites
Cervical paraspinal	20 Units divided between 4 sites
Trapezius	30 Units divided between 6 sites
TOTAL DOSE	155 Units† divided between 31 sites

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PREEMPT protocol

General Principle

- 0.1 mL (equivalent to 5 Units) for each injection
- Depth of the needle
  - Consider injecting in the most superficial aspect of the muscle
  - Not too superficially, not too deeply (to prevent injection into the dermis or periosteum)
- Direction of the needle
  - 45도 각도 (*예외: procerus, corrugator, trapezius – 90도)
  - With the bevel up
  - Not toward the muscles of frequent side-effects
- Injection
  - Ensure no blood regurgitation before the injection
  - Hold the hub of the needle

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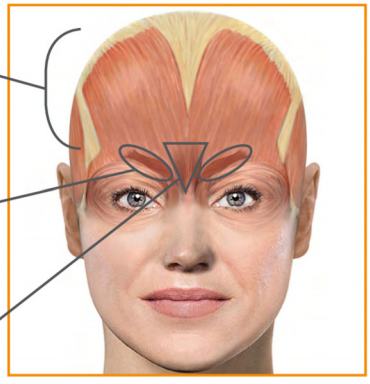
PREEMPT protocol

Anterior injection – Overview

Frontalis
Originates from the epicranial aponeurosis, and attaches distally to the skin of the forehead and eyebrow.[18]

Corrugator
Attaches to the nasal-frontal bone medially and the skin of the eyebrow laterally.[18,19]

Procerus
Originates from the aponeurotic fascia of the nose and inserts into the glabellar skin.[18]



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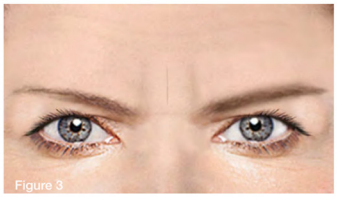
PREEMPT protocol

Anterior injection – Corrugator

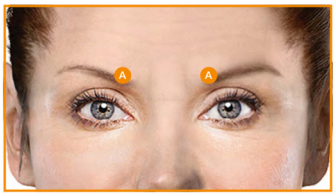
The **corrugator muscle** is a brow depressor, pulling the brow downward.[18] Weakening of this muscle may elevate the brow.

Activating the corrugator creates vertical lines between the brow (Figure 3).[18]



Injection site A
- About 1.5 cm (≈ 1 fingerbreadth) above the medial inferior edge of the superior orbital rim (bony landmark). This may vary based on individual anatomy

90도 각도로 시행



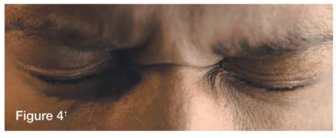
Corrugator injection sites[1]

PREEMPT protocol

Anterior injection – Procerus

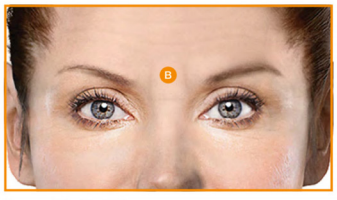
The **procerus muscle** draws down the medial aspect of the brow.[18]

Activating the procerus creates a transverse ridge over the nose (Figure 4).[18]



Injection site B
- The base of the procerus resides approximately midway between the 2 corrugator injections

90도 각도로 시행



Procerus injection site[1]

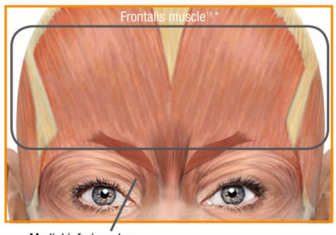
PREEMPT protocol

Anterior injection – Frontalis

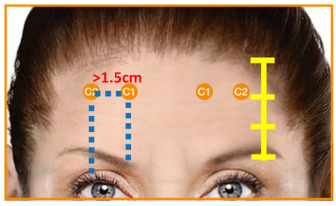
Dose[1]
- 5 Units (0.1 mL) in each site
- Total 20 Units divided into 4 sites

Medial injection site C1
- Visually, draw a vertical line up from the medial inferior edge of the superior orbital rim
- Medial injection is generally within the upper one-third of the forehead, and at least 1.5 cm (≈ 1 fingerbreadth) above the corrugator injection site. This may vary based on individual anatomy

Lateral injection site C2
- Lateral injections are parallel, lining up with the lateral limbus of the cornea, and at least 1.5 cm (≈ 1 fingerbreadth) lateral to the medial injection site (Figure 8). This may vary based on individual anatomy



Medial inferior edge of the superior orbital rim[18,*]

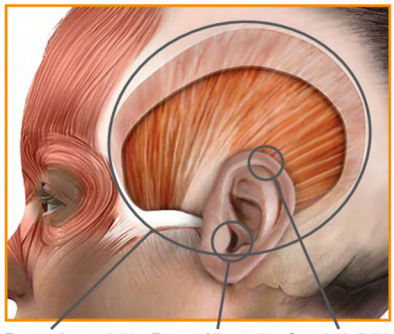


Frontalis injection sites[1]

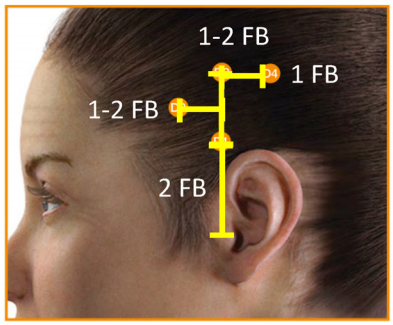
Forehead
Upper 1/3 이내

PREEMPT protocol

Temporalis injection



Temporalis muscle[18,*] Tragus of the ear[18,*] Superior helix[20,*]



Temporalis injection sites[1]

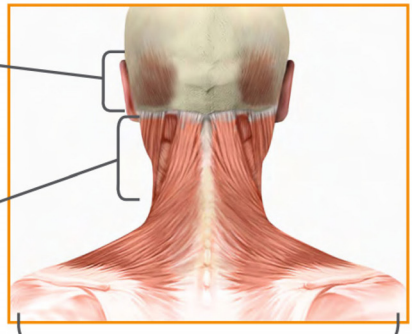
PREEMPT protocol

Posterior injection – overview

Occipitalis—Originates at the highest nuchal line and inserts into the epicranial aponeurosis, which is attached to the frontalis.[18]

Cervical paraspinal muscles should be considered a group (including the splenius capitis and semispinalis capitis) running deep alongside the cervical spine.[18]

Trapezius—A flat, triangular muscle situated over the back of the neck and upper thorax.[18]



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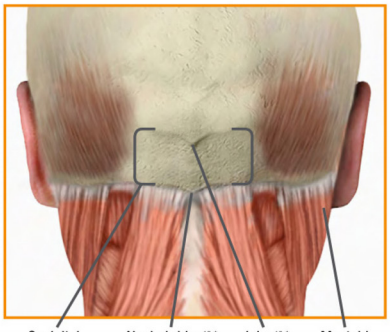
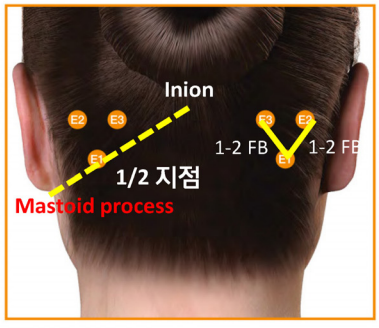
PREEMPT protocol

Posterior injection – occipitalis



Occipital protuberance[18,*] Nuchal ridge[18,*] Inion[18,*] Mastoid process[18,*]



Occipitalis injection sites[1]

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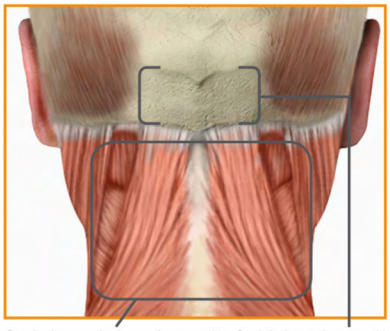
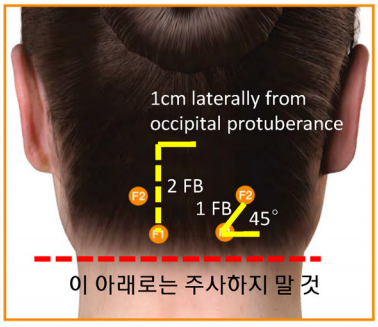
PREEMPT protocol

Posterior injection – cervical paraspinal



Cervical paraspinal muscle group[18,*] Occipital protuberance[18,*]



Cervical paraspinal injection sites[1]

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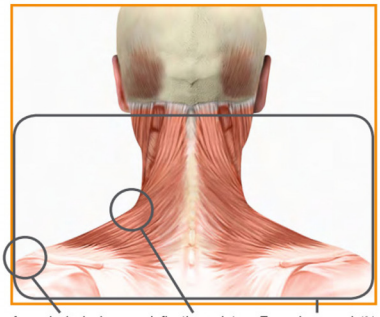
PREEMPT protocol

Posterior injection – trapezius



Acromioclavicular joint[18,20,*] Inflection point of neck (necklace line)* Trapezius muscle[18,*]

Trapezius injection sites[1]

1/2 지점

Inject superficially and horizontally to the muscle
(Needle을 거의 눕혀서 주사)

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Side effect

PREEMT study results

- The most frequently reported adverse reactions following injection of BoNT-A vs. placebo
  - Neck pain (9% vs 3%), headache (5% vs 3%), eyelid ptosis (4% vs < 1%), migraine (4% vs 3%), muscular weakness (4% vs < 1%), musculoskeletal stiffness (4% vs 1%), bronchitis (3% vs 2%), injection-site pain (3% vs 2%), musculoskeletal pain (3% vs 1%), myalgia (3% vs 1%), facial paresis (2% vs 0%), hypertension (2% vs 1%), and muscle spasms (2% vs 1%).
- No serious AEs reported

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Thank you for your kind attention

Questions?

Mailto: mijilee.md@gmail.com

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