

## Cadaver Study

## Currently Recommended TON Injectate Volumes Concomitantly Block the GON: Clinical Implications for Managing Cervicogenic Headache

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Disclaimer: There was no external funding in the preparation of this manuscript. Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 10-13-2015  
Revised manuscript received: 04-15-2016  
Accepted for publication: 04-28-2016

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**Background:** Headache (HA) is a significant cause of morbidity globally. Despite many available treatment options, HAs that are refractory to conservative management can be challenging to treat. Third occipital nerve (TON) and greater occipital nerve (GON) irritation are potential etiologic agents of primary and cervicogenic HAs that can be targeted using minimally invasive treatment options such as nerve blocks or radiofrequency ablation. However, a substantial number of patients that undergo radiofrequency ablation do not experience pain relief despite a positive diagnostic medial branch block (MBB).

**Objective:** In this study, we investigate the underlying cause for the high rate of false positives associated with MBBs by evaluating injectate spread in cadaveric subjects.

**Study Design:** Cadaveric study.

**Setting:** Academic medical center.

**Methods:** After obtaining exemption status from our Institutional Review Board, TON injections were performed on 5 preserved cadavers, a total of 10 TONs, using anatomic landmarks, partial dissection, and palpation to guide needle placement. Cadaveric dissections were performed to evaluate the location, vertical spread, and grossly observed injectate coating of the TON and GON for each quantity of methylene blue injectate, 0.3 mL and 0.5 mL, administered.

**Results:** The average distance between the TON and GON at their respective foraminal exit points was 1.81 cm. The average vertical spread for 0.3 mL and 0.5 mL of methylene blue injectate was 2.02 + 0.35 cm and 3.26 + 0.48 cm when performing a TON block. When using 0.3 mL injectate, both the TON and GON were simultaneously coated 60% of the time. After increasing the injectate volume to 0.5 mL, both the TON and GON were simultaneously coated 100% of the time.

**Limitations:** The cadaveric design of this study presents limitations when translating cadaveric findings to the clinical setting. Also, the small sample size limits its power and generalizability. Lastly, the potential for researcher bias exists as the investigators were not blinded.

**Conclusions:** This study demonstrates that currently recommended injectate volumes for TON blocks may result in concomitant coating of the GON. Conventional radiofrequency ablation (RFA) of these nerves may not lesion both the TON and GON given its restrictive circumferential lesioning diameter of 5 – 7 mm. As such, interventionalists should consider performing radiofrequency ablation to both the TON and GON after a positive TON block.

**Key Words:** Chronic pain, cervicogenic headache, third occipital nerve, greater occipital nerve, injectate spread, radiofrequency ablation

**Pain Physician 2016; 19:E1079-E1086**

**H**eadache (HA) has a profound impact on our ability to function optimally and affects 46% of individuals worldwide as concluded by Stovner et al. (1) As such, the World Health Organization has designated HA as one of the 10 most disabling conditions for both men and women globally (2).

There is a health care need toward the development of interventional techniques for treating HAs. Oral pharmacotherapy is the mainstay of care. However, medications alone are often ineffective at providing complete resolution of symptoms (3). Greater occipital nerve (GON) treatments may supplement, or in cases refractory to oral pharmacotherapy, replace medication management. Third occipital nerve (TON) as well as GON neuropathy are common anatomical triggers for primary and cervicogenic HAs (4-7). Medial branch blocks (MBB) of the TON can be performed along its proximal segment with the use of fluoroscopic, computed tomography (CT), and ultrasound guidance in order to identify a potential pain generator (8-12). Image-guided MBBs can be both diagnostic and therapeutic. Unfortunately, not all patients experience long-lasting pain relief from MBBs. If short-term pain relief is achieved from a MBB, patients are typically offered radiofrequency ablation for longer-lasting pain relief. However, up to 30% of patients undergoing radiofrequency ablation do not experience pain relief despite 2 positive diagnostic MBBs (13-16). In this study, we offer a possible explanation for this high false-positive rate through cadaveric evaluation of injectate spread to the TON and GON.

The TON lies deep to the semispinalis capitis muscle and is unique when compared to other cervical occipital nerves. The TON serves as the primary source of sensory innervation of the C2-C3 zygapophysial joint and is recognized as a source of occipital pain. It exists as a superficial medial branch of the C3 dorsal ramus, and, along its proximal segment, the TON lies in close proximity to the GON (8,14). Caudal to the TON, all subsequent cervical zygapophysial joints receive innervation from 2 medial branches. Each medial branch travels from the dorsal rami of 2 successive spinal nerve roots.

When performing a TON block, it is probable that the GON is inadvertently affected due to its close proximity to the TON (15). Distinguishing which occipital nerve is the irritating structure may not be possible using currently recommended techniques and injectate volumes. This is problematic when developing a treatment plan for patients suffering from primary or cervicogenic HAs. Historically, pain physicians have tar-

geted only the TON when performing radiofrequency ablation in response to a positive TON block. However, if both the GON and TON are concomitantly affected when performing a TON block, targeting both occipital nerves with radiofrequency ablation may help to improve the false-positive rate and result in better patient outcomes. No publications have verified this assumption. Here, we report the first study examining injectate spread when performing an isolated TON block and its effect on the GON.

## **METHODS**

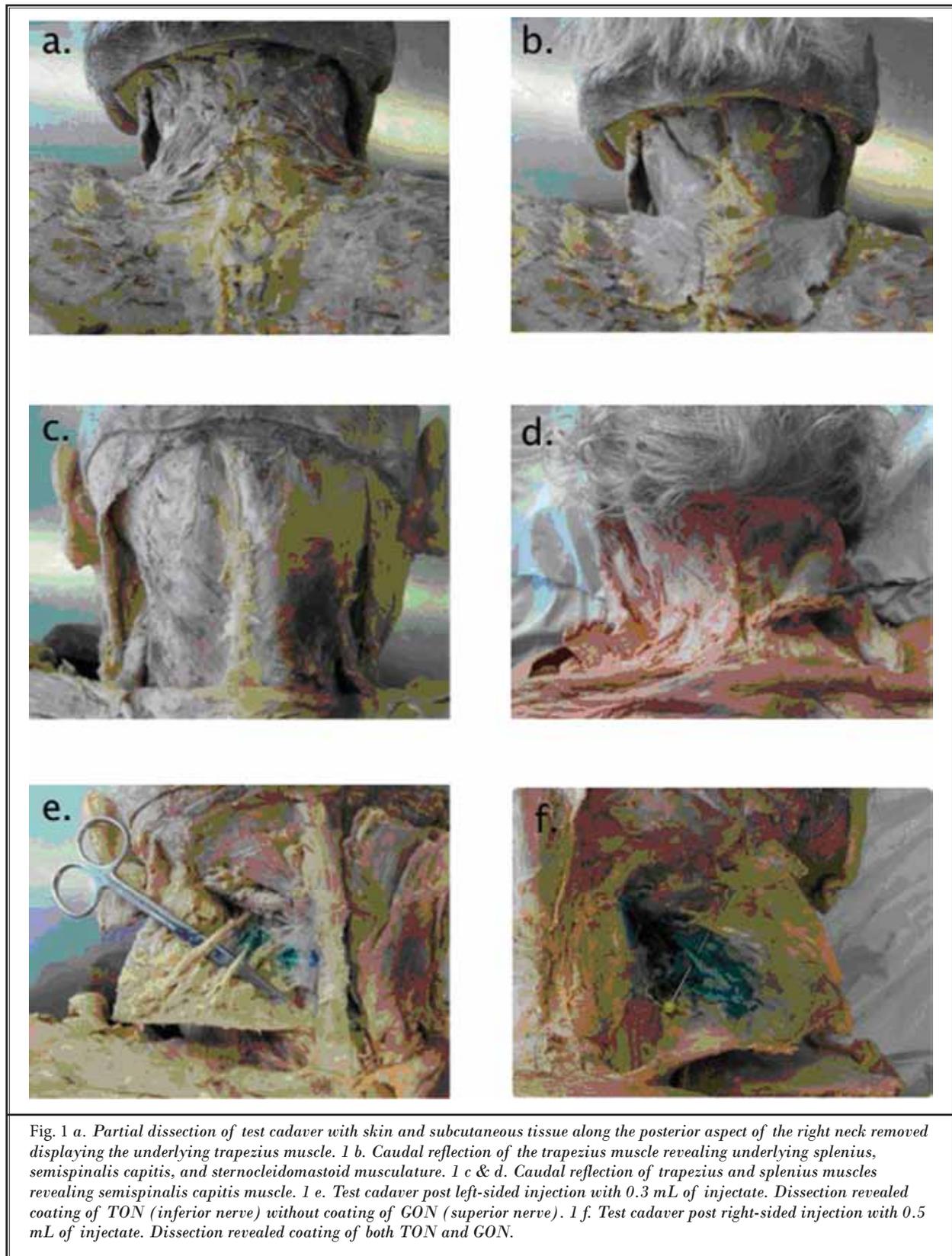
A request for exemption was approved by our Institutional Review Board. TON injections were performed on 5 preserved cadavers, a total of 10 TONs, using anatomic landmarks, partial dissection, and palpation to guide needle placement. Cadaveric dissections were performed to evaluate the location, vertical spread, and grossly observed injectate coating of the TON and GON for each quantity of methylene blue injectate, 0.3 mL and 0.5 mL, administered (Fig. 1 a-f).

### **Cadaveric Preparatory Dissection**

Initially, each cadaver was partially dissected to the level of the semispinalis capitis muscle. This allowed for confirmation of the needle placement at the level of the TON via direct palpation of the needle bevel in relation to palpable anatomic landmarks. Partial dissection was accomplished by using a scalpel to remove the skin and subcutaneous tissue along the cervical spine. The trapezius muscle was then carefully dissected along its fascial plane in order to avoid disruption of underlying tissue, and reflected laterally. Next, an incision was made through the medial attachment of the splenius capitis and cervicis muscles which were then dissected along their fascial plane and reflected laterally. This revealed the semispinalis capitis muscle (Fig. 1 a-d). The TON and GON are invested in the fascia which lies directly anterior to the semispinalis capitis muscle. These nerves were not dissected at this time.

### **Anatomic Landmarks**

After performing the partial dissection, bony anatomic landmarks were readily palpable. Two anatomic landmarks were used as coordinate points for needle placement: the tip of the mastoid process and the C3 spinous process. A distance of 2.5 cm was measured caudally from the tip of the mastoid process and marked with a surgical pen. This coordinate served as the entry point for the needle. The C3 spinous process



was identified by palpating the inferior border of the occiput along its midline until a step-off was appreciated. Palpating caudally from there, the first spinous process encountered was C2, followed by the spinous process of C3. The C3 spinous process served as the second coordinate point and was marked with a surgical pen. The 2 coordinates served as the respective start and end points of the needle, thus mapping out the needle trajectory.

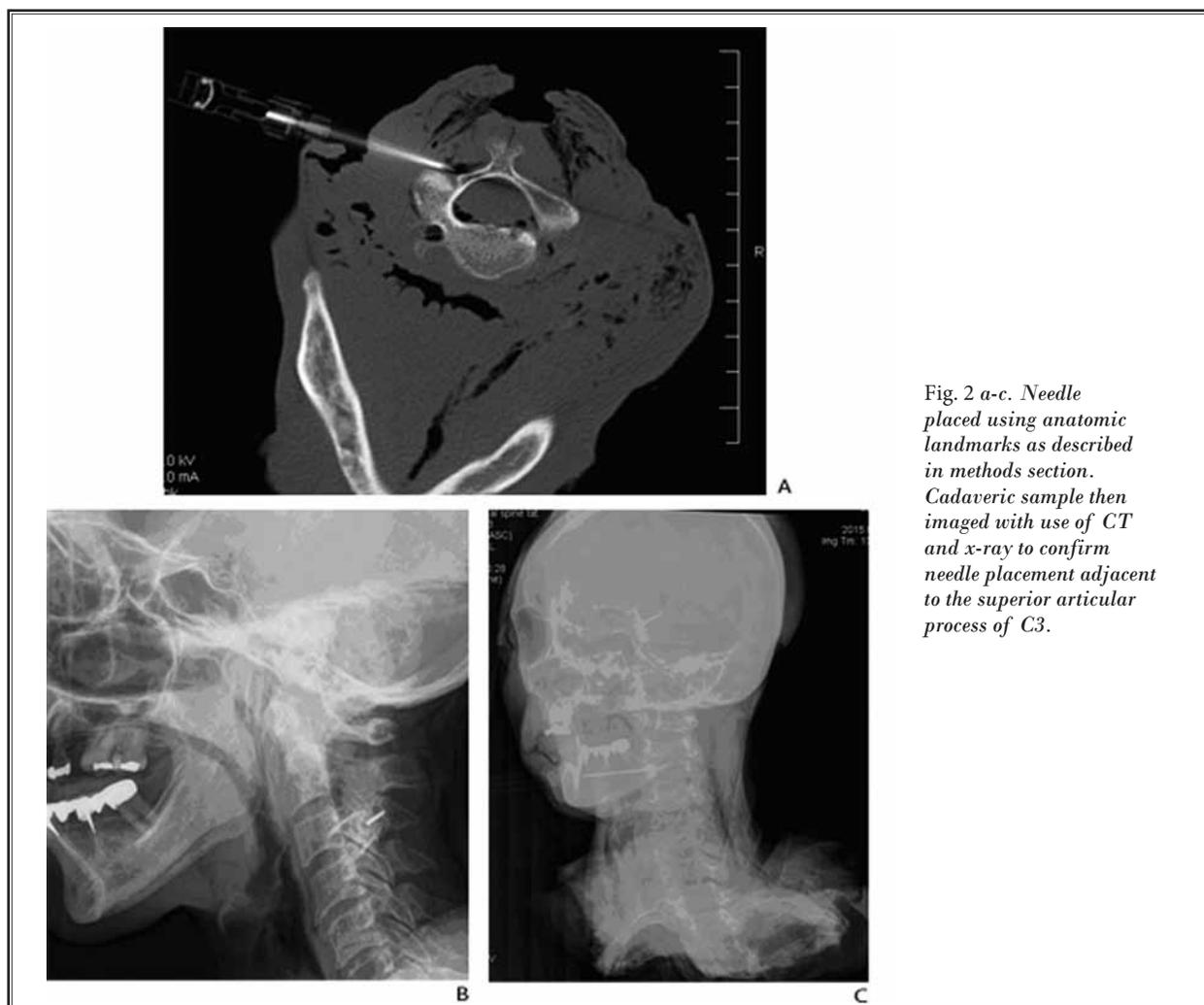
### Needle Positioning and Injection

A 1 inch, 25 gauge needle was placed at a 30 degree angle at the mastoid coordinate and advanced from an antero-lateral to postero-medial direction toward the C3 spinous process. The needle was advanced until the inferior border of the spinous process was reached. Once bone was encountered, the needle was retracted 1 cm. In order to confirm the location, we

then palpated for the needle bevel through the overlying semispinalis capitis muscle. If the bevel was not palpable between the spinous and transverse processes of the C3 vertebrae, it was re-directed.

Once in place, either 0.3 mL or 0.5 mL of methylene blue 0.01% concentrate was administered as the injectate. The left cervical spine of 5 cadavers received 0.3 mL of methylene blue, while 0.5 mL were administered on the right. Methylene blue was chosen because it shares a similar viscosity as that of the local anesthetic typically used for diagnostic cervical blocks.

To ensure that anatomic landmarks of the partial dissection injection were commensurate with the typical approach used by most interventional practitioners, CT and x-ray images were taken of one cadaver after needle placement (Fig. 2 a-c) (8,16). These images confirmed that the needle was placed adjacent to the superior articular process (SAP) of C3 where the TON is



*Fig. 2 a-c. Needle placed using anatomic landmarks as described in methods section. Cadaveric sample then imaged with use of CT and x-ray to confirm needle placement adjacent to the superior articular process of C3.*

known to traverse. Therefore, using partial dissection, anatomic landmarks, and direct palpation, we were able to accurately target the location of the TON.

### Completed Dissection and Evaluation of Injectate Spread

Cadaveric dissection to evaluate injectate spread was completed immediately after the injection. This was done by cutting the semispinalis capitis from its occipital attachment and dissecting along its anterior fascia to identify the TON and GON. Both nerves were evaluated grossly for coating with methylene blue injectate (Fig. 1 e-f). Each nerve was evaluated for blue

color change by 2 different researchers and recorded as “yes” if a color change was observed or “no” if no color change occurred (Tables 1 and 2). The vertical spread of the injectate was then measured where the greatest distance of spread was observed (Table 3).

Both the TON and GON were then dissected back to their foraminal exit points. The distance between exit points was measured and recorded. Points on each nerve 2 cm from the nerve exit point were then measured and labeled as points “A” and “B” for the TON and GON, respectively. The distance between points “A” and “B” were then measured and recorded (Table 4).

### RESULTS

Table 1. Number of TONs and GONs coated with 0.3 mL or 0.5 mL methylene blue injectate.

Cadaveric Subject	Quantity of Injectate (mL)	GON coated with injectate (Y/N)	TON coated with injectate (Y/N)
1L	0.3	Y	N
1R	0.5	Y	Y
2L	0.3	Y	N
2R	0.5	Y	Y
3L	0.3	Y	Y
3R	0.5	Y	Y
4L	0.3	Y	Y
4R	0.5	Y	Y
5L	0.3	Y	Y
5R	0.5	Y	Y

Table 2. Percentage of TONs and/or GONs coated with 0.3 mL or 0.5 mL methylene blue injectate.

Quantity of injectate (mL)	% TON subjects coated	% GON subjects coated	% of both TON & GON subjects coated with one injection
0.3	3/5 = 60%	5/5 = 100%	3/5 = 60%
0.5	5/5 = 100%	5/5 = 100%	5/5 = 100%
Total	8/10 = 80%	10/10 = 100%	8/10 = 80%

Table 3. Vertical spread of 0.3 mL and 0.5 mL methylene blue injectate in test and control cadavers.

	Average vertical spread (cm)	N
0.3 mL	2.02 + 0.35	5
0.5 mL	3.26 + 0.48	5

Table 4. Distance between TON and GON at foraminal exit point and 2 cm from the foraminal exit point.

Average distance between TON and GON at foraminal exit point (cm)	Average distance between TON and GON at 2 cm from foraminal exit point (cm)	N
1.81	1.71	5

The number of TONs and GONs coated with injectate were tabulated in Tables 1 and 2. When using 0.3 mL injectate, both the TON and GON were simultaneously coated 60% of the time. After increasing the injectate volume to 0.5 mL, both the TON and GON were simultaneously coated 100% of the time.

The average vertical spread for each injection was measured for 0.3 mL and 0.5 mL injectate volumes (Table 3). For 0.3 mL injectates, the average vertical spread was  $2.02 \pm 0.35$  cm. When 0.5 mL injectates were used, the average vertical spread was  $3.26 \pm 0.48$  cm.

The average distance between the TON and GON at their respective foraminal exit points was 1.81 cm (Table 4). At a distance of 2 cm from the foraminal exit points, the average distance between the TON and GON was 1.71 cm.

## Discussion

HA disorders cause individual and socioeconomic morbidity due to decreased productivity and absenteeism from work. A study examining the cost of tension type headaches across Europe revealed that the mean per-person annual cost was equivalent to \$346 (in U.S. dollars). In all 27 EU countries, the total annual cost of HA amongst adults was estimated at \$197 billion annually (17). Although many treatment options exist, including pharmacologic agents, physical therapy, and biofeedback, these methods may produce limited or temporary relief (18). Occipital nerve blocks and radiofrequency ablation are minimally invasive alternatives for treating HA disorders that are refractory to more conservative options.

Both the TON and GON are common sources of pain for primary and cervicogenic HA, and are located in close proximity to one another along their proximal segments. When treating HA, it is important for clinicians to identify an underlying etiologic agent. In this study we examined the implications of injectate spread when performing occipital nerve blocks along the proximal segments of the TON and GON. By gaining a better understanding of the anatomic relationship between these nerves, we can better understand the shortcomings of fluoroscopic TON blocks.

Image guidance has been used to perform diagnostic TON blocks for primary and cervicogenic headaches (8,11,19-21). The GON has also been targeted for HA management at its distal segment along the superior nuchal ridge, however the literature is lacking with respect to the GON at its proximal segment. The results from this study show that the average distance be-

tween the TON and GON at their respective foraminal exit points is 1.81 cm. At a distance of 2 cm distal to their foraminal exit points the TON and GON are 1.71 cm apart (Table 4). Given the close proximity of these 2 nerves, we decided to evaluate the quantity of injectate that is commonly used to perform TON blocks.

The recommended quantity of injectate for ultrasound-guided TON blocks ranges from 0.3 – 0.5 mL to as much as 0.9 mL (8,11). In our study, 2 injectate volumes were used, 0.3 and 0.5 mL. When using 0.3 mL of injectate, the average vertical distance of spread was  $2.02 \pm 0.35$  cm, while 0.5 mL of injectate had an average vertical spread of  $3.26 \pm 0.48$  cm (Table 3). The injectate spread for both volumes is therefore greater than that of the distance between the nerves as previously described (Tables 3 and 4). The results from our study suggest that a volume of 0.5 mL is not specific for TON-mediated pain. These findings are consistent with prior research by Cohen et al (14) that examined injectate spread with the use of CT imaging. Their study recommended decreasing injectate volume from 0.5 to 0.25 mL in order to improve specificity for cervical MBBs (14).

With the needle placed between the TON and GON there is the potential to coat both nerves simultaneously. Through the use of our technique, 60% of injections performed using 0.3 mL of injectate resulted in both nerves being coated simultaneously, while 100% were simultaneously coated when using 0.5 mL. This evidence supports the hypothesis that the TON cannot be distinguished from the GON as a pain source when performing a diagnostic block with injectate volumes of 0.5 mL. Using less volume, 0.3 mL, improved targeting specificity but still exhibited significant overflow to the adjacent GON. In order to improve specificity, the volume of injectate used should be less than 0.3 mL and needle placement should be confirmed with imaging (15).

Due to the variability in muscle bulk, soft tissue thickness, and cervical vertebrae size, TON blocks cannot be performed safely or reliably using anatomic landmarks alone. Image guidance must be used. In this study, injections were performed using anatomic landmarks in conjunction with partial dissection and palpation techniques to confirm needle placement. Since the needle bevel could not be directly visualized, CT and x-ray imaging were performed on one cadaveric subject to confirm that needle placement was commensurate with typical TON fluoroscopic landmarks (Fig. 2 a-c) (8,16). The results of this test revealed appropriate

needle placement adjacent to the superior articular process of C3 where the TON typically traverses. As such, the investigators believed that needle placement was reliably on target when following the previously stated injection technique on partially dissected cadavers and additional imaging was not performed on subsequent specimens.

The clinical significance of these findings is readily apparent when developing a treatment strategy based on the results of a diagnostic TON block. Typically patients with a positive diagnostic TON block are candidates for radiofrequency ablation (22-25). However, we have demonstrated that a positive clinical response to a TON block is not specific for outcome following radiofrequency ablation as the TON block may impact the GON as well. Traditional radiofrequency ablation needles have a 5–7 mm ablation diameter, roughly 1 to 1.5 times the diameter of the electrode, leading to the almost certain lack of lesioning of the GON (26). Cooled radiofrequency ablation can extend this circumferential diameter to 1.5 cm but this may lead to increased local tissue damage and also may not effectively ablate the GON with the typical TON radiofrequency ablation technique (25). In the absence of specific diagnostic information about pain generation from the TON vs GON, clinicians should consider performing radiofrequency ablation targeting the TON and GON independently.

### **Limitations**

There are several limitations that may have impacted the results of this study. Most notably, the cadaveric design presents limitations when translating cadaveric findings to the clinical setting. Cadaveric soft tissue composition and architecture may become distorted as a result of the embalming process and as a result of tissue dehydration over time. Also, the protocol included partial dissection of the cervical region prior to performing the injection of methylene blue. While this improved needle placement, it may have led to distortion of the soft tissues that impact measurements of

injectate spread.

The small sample size also limits the generalizability and overall power of the data, necessitating future large scale studies. This study is also limited in terms of researcher bias as both investigators evaluating the injectate distribution and nerve involvement were not blinded. Future randomized, blinded studies are needed to evaluate if lower volume TON diagnostic blocks result in more reliable outcomes in a clinical setting and, in cases where specific TON blockade does not resolve pain, if ablating both the TON and GON result in improved patient outcomes.

### **CONCLUSION**

This study highlights several important factors that should be considered when treating primary and cervicogenic headaches with fluoroscopically guided TON blocks. It is unlikely that one can distinguish pathology existing at the proximal segment of the TON from that of the GON by performing a diagnostic block with currently recommended injectate volumes. Given the close proximity of the TON to the GON in the region targeted for injection, the use of volumes less than 0.3 mL is recommended to improve specificity when performing diagnostic blocks. Additionally, it is recommended that practitioners utilize image guidance when performing such blocks. When using volumes > 0.3 mL, pain relief may occur by blockade of the GON as well as the TON. In these cases, both the TON and GON should be considered potential pain generators and both should be targeted when performing radiofrequency ablation as treatment for primary and cervicogenic headaches.

### **Acknowledgment**

The authors of this paper would like to express their appreciation to the individuals who made this research possible by so selflessly donating their bodies to science.

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