

## Role of Magnetic Resonance Imaging in Evaluation of Trigeminal Neuralgia with its Anatomical Correlation

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<http://dx.doi.org/10.13005/bpj/1640>

(Received: 17 July 2018; accepted: 07 January 2019)

Neuropathic Pain is caused by a primary lesion or dysfunction of the peripheral or central nervous system. Trigeminal neuralgia is one such disease which is characterized by episodes of unilateral, lancinating, shock-like pains and are also intermixed with pain free episodes. It has a primary or classic and secondary type. Primary TN is due to neurovascular compression whereas secondary TN is due to any tumor in the brain stem. Trigeminal nerve has a sensory and motor root arising from the pons and travels to the face where it ends as three branches namely ophthalmic, maxillary and mandibular. Magnetic resonance Imaging is a gold in identifying these lesions. However, it is not always prescribed due to lack of insight in using MRI as an evaluating tool. It results in over dosage of medication as the physician prescribes the drug without identifying whether the lesion is primary or secondary. This article give an insight on the various MRI sequences imaged various studies available and also throws light on other sequence which has to be explored in this disease.

**Keywords:** Trigeminal Neuralgia, Oraofacial pain, Magenetic Resonance Imaging, Carmazepine.

The International Association for the study of pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. IASP in November 2010 further extended to define neuropathic pain as "Pain initiated or caused by primary lesion or dysfunction of the peripheral or central nervous system<sup>1</sup>. This is a modification of the previous definition of neuropathic pain which was described as "pain initiated or caused by a primary lesion, dysfunction, or transitory perturbation of the peripheral or central nervous system"<sup>2</sup>. When compared to nociceptive pain, the persistence of neuropathic pain is longer, not quite responsive to pain medications, often debilitating and difficult to treat<sup>3</sup>. Neuropathic pain is frequent with other predisposing conditions like diabetes, carpal tunnel

syndrome, sciatica, Guillain-Barre syndrome, cancer, multiple sclerosis, kidney disorders, alcoholism, HIV etc. The prevalence and incidence of neuropathic pain is estimated between 1 and 10%, with few studies admitted that neuropathic component may be present in 35% of all painful syndromes<sup>4</sup>. Smith BH and co-workers stated that the estimate of prevalence tends to be lower (1-2%) than those based on classic symptoms reports<sup>5</sup>. Gustorff *et al.* from their prospective survey in 2008 showed that in Austria the occurrence of neuropathic pain was 3.3%, with an increase in prevalence (up to 26%) as the age increases<sup>6</sup>. Van Hecke *et al.* believed that due to lack of universal evidences and protocols, a range of incidence and prevalence rates has been identified. They also suggested that future epidemiological studies should take note of mentioned factors<sup>7</sup>.



**Trigeminal neuralgia (TN)**

Trigeminal neuralgia (Tic douloureux), is a chronic pain affecting the Trigeminal nerve. Burchiel KJ defined trigeminal neuropathic pain as constant unilateral facial pain that varies in intensity, is triggerable, and not curable<sup>8</sup>. This is characterized by episodes of unilateral, lancinating, shock-like pains and are also intermixed with pain free episodes.

**Clinical features for trigeminal neuralgia**

International Headache Society had recently proposed strict clinical criteria for trigeminal neuralgia diagnosis and according to this, diagnosis only can be made when there are at least three attacks of unilateral facial pain occur fulfilling the following criteria such as (1) occurring in one or more divisions of the trigeminal nerve, with no radiation beyond the trigeminal distribution and (2) pain with at least, recurring in paroxysmal attacks lasting from a fraction of second to 2 minutes or severe intensity or electric shock-like, shooting, stabbing, or sharp in quality or precipitated by innocuous stimuli to the affected side of the face<sup>9</sup>. Eller JL and co-workers, in their new classification differentiated TN into type 1 and type 2 which was earlier referred as classic or typical TN and secondary TN respectively. Type 1 is characterized by episodic pain whereas type 2 expresses as pain which more than 50% of the time is constant in nature<sup>10</sup>. It also has been theorized that in type 2, there is likelihood to detect a structural abnormality such as tumours or vascular malformations.

**Imaging modalities in evaluation of trigeminal neuralgia**

A wide variety of imaging modalities were used in past for image evaluation of the cranial nerves. Pneumocephalography was the first cross-sectional imaging study used to demonstrate cranial nerves. This technique involves introduction of air into subarachnoid space around cranial nerves in order to allow clear visualization of nerves within the basal cisterns<sup>11</sup>. Later, with advent of CT, the detail in visualizing the regions of cranial nerves has improved and further with injection of intrathecal contrast shows linear filling defects within subarachnoid space. But the visualization is limited to the cisternal or subarachnoid course of cranial nerves. But with advent of MRI, an imaging modality without using ionizing radiation

and acquisition of multiple plane images it became standard mode of imaging of cranial nerves<sup>12</sup>.

It is quite challenging to image of the cranial nerves as they are small with complex anatomy and cannot be easily distinguished from surrounding soft tissues<sup>13,14</sup>. Being the largest cranial nerve trigeminal nerve can be visualized better with various modern imaging techniques<sup>15</sup>. Computer Tomography gives better visibility of the foramina and the nerve exit but a right sequence of MRI is the preferable imaging for cranial nerves<sup>16</sup>. Advances in MRI plays a vital role in presurgical evaluation of the trigeminal nerve.

**Magnetic resonance imaging**

The primary imaging modality for evaluation of patients with trigeminal neuralgia is MRI<sup>13</sup>. It has been used as an adjunct for planning the management of trigeminal nerve pathologies<sup>17</sup>. The basic standardized procedure for those patients with symptoms of trigeminal neuralgia consists of T<sub>1</sub> weighted spin echo sequences (in axial plane) with a turbo STIR (short tau inversion recovery) sequence (in coronal plane)<sup>18</sup>. In order to visualize and analyse different segments of various cranial nerves, right sequences must be used. The choice of which is based on the tissue or fluid that is surrounding the nerve. T<sub>2</sub> weighted (T<sub>2</sub>W), proton-density and multi-echo fast field echo (m-FFE) gives better details of the cranial nerve nuclei and fascicular segment of cranial nerves. Heavy T<sub>2</sub> sequences were used to visualize cisternal segment of the nerve which is surrounded by cerebrospinal fluid (CSF)<sup>16</sup>. Various sequences which are heavily T<sub>2</sub>W 3D- sequences such as CISS, 3D-TSE, b-FEE, DRIVE, 3D-FSE, FIESTA etc. provides very high resolution images, but they tend to produce artefacts at periphery of the image and therefore must be carefully chosen<sup>18-22</sup>. High resolution contrast-enhanced Time-Of-Flight MRA images or high resolution 2D or 3D images shows better visualization of blood vessels around the nerve. Peripheral segments or terminal branches of cranial nerves which are surrounded by soft tissues are better visualized by T<sub>1</sub>W SE and TSE. Arterial spin labelling MRI is used to demonstrate the cerebral perfusion<sup>23</sup> in diseases like Migraine, Alzheimers, Cerebrovascular stroke but its not used in evaluating Trigeminal Neuralgia. Since a vascular component is involved in Trigeminal Neuralgia future studies using this sequence may

disclose undiscovered etiological or contributing factors in trigeminal neuralgia.

### **Anatomy of trigeminal nerve to identify lesions in MRI**

Trigeminal nerve is the largest cranial nerve. It emerges from anterior aspect of pons by two roots i.e. a sensory root that carries sensory information to brain from facial region and a motor root provides motor innervation to the muscles of mastication. There are four central brain stem nuclei that are (1) mesencephalic nucleus, mediating proprioception (2) main sensory nucleus, mediating tactile sensation (3) the motor nucleus provides motor innervation and (4) the spinal nucleus mediates pain and temperature sensation. They lie in tegmentum of lateral pons, along the anterolateral aspect of fourth ventricle and close to the root entry zone of trigeminal nerve (Figure 1). Both the roots (larger sensory and smaller motor) exit via the lateral pons as a common trunk. Sensory root becomes progressively flattened laterally and medially as it expands resulting in formation of ganglionic swelling i.e., the trigeminal ganglion. Compared to sensory root, the motor root is relatively smaller in size and is situated anterior and medial to the sensory root, and it exits via foramen ovale. After the afferent fibers converges from three main sensory roots of the nerve ( $V_1$ ,  $V_2$  and  $V_3$ ) the main trunk of trigeminal nerve enters through porus terminus, an opening into the dura mater while entering the Meckel's cave. From this point, the nerve carries its dural covering with it and the myelin sheath surrounding the nerve transitions from that derived from Schwann cells to that derived from oligodendrocytes, and this point of transition from peripheral to central myelin is referred as transition zone and the point where nerve enters pons is called as root entry point or zone (REZ)<sup>24</sup> (Figure 1). The nerve is usually compressed by the one of the neighboring arteries which can be superior cerebellar artery<sup>25</sup>, anterior inferior cerebellar artery<sup>26</sup>, basilar artery, vertebral artery, posterior inferior cerebellar artery and pontine artery<sup>27</sup>. Neurovascular compression is graded on MRI based on the extent of the compression of the nerve and vessel<sup>28</sup>. Grade I Mild contact between the nerve and blood vessel, Grade II Mild distortion /displacement of the nerve root by artery, Grade III Marked indentation of the nerve root by the vessel.

### **Demonstration of lesions at various levels in MRI**

MRI is often used as a work up of patients with TN. To assess anatomical characteristics and patterns of neurovascular compression, brain gray matter volume and cortical thickness (CT) and *diffusion imaging* (diffusion tensor images) to assess brain white matter and trigeminal nerve microstructure structural MRI for TN uses *high-resolution anatomical imaging* (variations of T1- and T2-weighted images)<sup>29</sup>. To image trigeminal neuropathy, high field units (1T to 3T) are required as they provide better spatial resolution, better signal-to-noise ratio and shorter examination time<sup>30</sup>. Table 1 is presented with details of various investigational studies on trigeminal neuralgia using Magnetic Resonance Imaging (MRI).

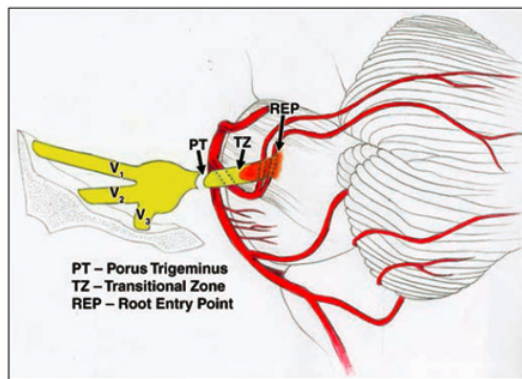
### **Brainstem**

Five distinct anatomical portions of trigeminal nuclear complex and nerve in the brain stem can be identified<sup>31</sup>. In MS plaques are hyper intense on T2W and hypo intense on T1W sequences. Sometimes, thin line of T1 hyperintensity can be seen attributing to free radicals and protein accumulations<sup>31</sup>. Approximately 25% of infarcts acute strokes occurs in brainstem and infarcts involving the posterior inferior cerebellar artery territory may affect the trigeminal nuclei i.e. dorsal nucleus resulting in cranial nerve V symptoms.

### **Cisternal segment**

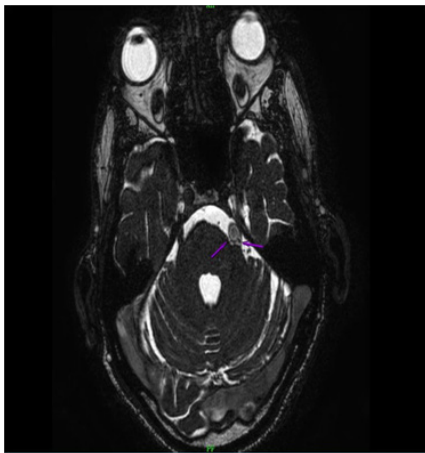
In this segment, the portion of trigeminal nerve corresponds to the transition between central nervous system myelin to peripheral nervous system myelin. Lesions or pathologies involving this segment typically present with trigeminal neuralgia. This relative thinness in myelin lining of the nerve in this nerve makes it vulnerable to extrinsic compression<sup>32</sup>. Compression of nerve by adjacent blood vessel (Neurovascular compression (NVC)) revealed focal demyelination in that region resulting in clinical features of TN<sup>33,34</sup> (Figure 2). Arteriovenous malformations, aneurysms, vascular loops, fistulas, vascular ectasias also exhibit symptoms of TN. Coronal or oblique sagittal T1- weighted MR images may demonstrate neurovascular contact with or without compression of cisternal segment of 5<sup>th</sup> cranial nerve. Structural MRI can be used to test whether NVC sufficiently explains TN aetiology. Satoh T and co-workers had categorized NVC into four categories based on

the proximity of nerve with the vessel as severe, moderate, simple and none. Also, they found that in affected nerves of patients this proximity is severe, whereas in unaffected nerves of patients or in healthy individuals it is mostly a simple contact form<sup>35</sup>. In MS- related TN, a plaque of demyelination at the region of REZ is seen, which results in gadolinium enhancement at MR imaging. In MR imaging of those with chronic inflammatory demyelinating polyneuropathy, enlargement of cranial nerves was seen at cisternal and peripheral extracranial segments. Schwannoma is common primary neoplasm that frequently affects cisternal

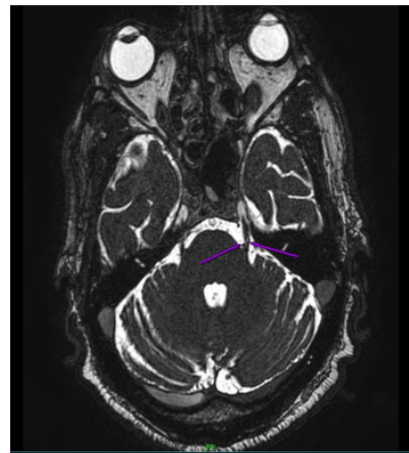


**Fig. 1.** Diagrammatic representation showing the convergence of three sensory branches of trigeminal nerve into Gasserian ganglion. Adapted from article of Hughes et al. (15)

**Fig. 2.** Shows the NVC at cisternal region by Superior Cerebellar Artery(2a) and Vertebral Artery(2b)



**Fig. 2a.** Indentation by SCA at the cisternal region of right trigeminal nerve



**Fig. 2b.** Close contact by vertebral artery at cisternal region of right trigeminal nerve

segment along with other portions. On MR imaging, these lesions grow along the side of the nerve and may be dumbbell or saddle- shaped<sup>36,37</sup>.

### **Meckel's cave and Cavernous sinus segments**

Giant aneurysms in cavernous portions of internal carotid artery may cause compression of cranial nerves and one-third of cases with unruptured aneurysms has reported trigeminal nerve involvement<sup>38</sup>. On MR imaging, narrowing of the cavernous portion of internal carotid artery is a common finding. Infrequently, inflammatory lesions effect the cavernous sinus and Meckel's cave is also seen. Symptoms of non-specific inflammation in these segments includes ophthalmoparesis, pupillary dysfunction, paraesthesia of forehead etc. Meckel's cave comprises of 0.5% of intracranial tumors and most common lesions seen at this site are schwannomas, meningiomas and malignant nerve sheath tumors. The nerve may also be impinged upon by both benign and malignant lesions involving the cerebellopontine angle cistern and skull base. And also, some meningiomas (e.g., petroclival) that are extending into the Meckel's cave exhibits TN symptoms.

### **Peripheral Segments**

The terminal branches of trigeminal nerve are most commonly involved in peri neural spread of malignancies of head and neck regions. Schwannomas involving the terminal branches are rare with common involvement of ophthalmic

Table 1. Investigational studies on Trigeminal neuralgia using MRI

S.no	Title of Publication	Author	Methodology	No. of patients	Inference
1.	Preoperative evaluation of neurovascular compression in patients with trigeminal neuralgia by use of three-dimensional reconstruction from two types of high-resolution magnetic resonance imaging	Akimoto H et al (2002)	Assessed the value of three-dimensional (3-D) images reconstructed from 3-D constructive interference in steady state (3-D-CISS) and 3-D fast inflow with steady-state precession (3-D-FISP) images for the visualization of neurovascular compression in patients with trigeminal neuralgia. The authors aimed to assess whether individuals without symptoms of trigeminal neuralgia exhibit vascular compression of the trigeminal nerve. This was investigated using ultra-high-field MR imaging.	24 consecutive patients with trigeminal neuralgia underwent preoperative 3-D-FISP and 3-D-CISS imaging	3-D reconstructions from two types of high-resolution magnetic resonance images (3-D-CISS and 3-D-FISP) are very useful for creating preoperative simulations and in deciding whether to perform surgery in patients with trigeminal neuralgia. It concluded that it was first study to have evaluated NVC of the trigeminal nerve in asymptomatic individuals using 3-T MR imaging. Their findings strongly suggest that vascular compression of the trigeminal nerve is not necessarily pathological. Combination of high resolution 3D T2-weighted with angio-MR-TOF is a reliable technique for detecting NVC and predicting the degree of compression in NVC.
2.	Vascular compression of the trigeminal nerve is a frequent finding in asymptomatic individuals: 3-T MR imaging of 200 trigeminal nerves using 3D CISS sequences.	Peker S, Dincer A, Necmettin PM (2009)	The authors aimed to assess whether individuals without symptoms of trigeminal neuralgia exhibit vascular compression of the trigeminal nerve. This was investigated using ultra-high-field MR imaging.	100 subjects were imaged using a 3-T magnet and high-spatial-resolution MR imaging with 3D constructive interference in steady-state sequences.	It concluded that it was first study to have evaluated NVC of the trigeminal nerve in asymptomatic individuals using 3-T MR imaging. Their findings strongly suggest that vascular compression of the trigeminal nerve is not necessarily pathological. Combination of high resolution 3D T2-weighted with angio-MR-TOF is a reliable technique for detecting NVC and predicting the degree of compression in NVC.
3.	MRI sequences for detection of neurovascular conflicts in patients with TN and predictive value for characterization of conflict (particularly degree of vascular compression)	Leal PR, Froment JC, Sindou M. (2010)	As pre-operative visualization of the neurovascular compression (NVC) by MRI is vital for therapeutic decision, they investigated the predictive value of MRI for detecting and assessing degree of vascular compression in trigeminal neuralgia. Prospective study and systemic review with meta-analysis was conducted to determine whether Micro Vascular Decompression (MVD) is safe and effective treatment in elderly patients with trigeminal neuralgia (TN). An MRI image of the brain was taken.	91 consecutive patients with a preoperative MRI using 3D T2-weighted and angio-MR-TOF.	Concluded that majority of elderly patients with TN can safely undergo MVD.
4.	Microvascular decompression for elderly patients with trigeminal neuralgia: a prospective study and systematic review with meta-analysis	Sekula RS et al. (2011)	Microvascular decompression (MVD) is safe and effective treatment in elderly patients with trigeminal neuralgia (TN). An MRI image of the brain was taken.	36 elderly patients (mean age 73.0 ± 5.9 years) and 53 nonelderly patients (mean age 52.9 ± 8.8 years)	Concluded that majority of elderly patients with TN can safely undergo MVD.
5.	Trigeminal neuralgia due to neurovascular compression: high-spatial-resolution diffusion-tensor imaging reveals microstructural neural changes	Lutz J et al. (2011)	A single-shot diffusion-tensor echo-planar sequence was used along 15 different diffusion directions, with a b value of 1000 sec/mm <sup>2</sup> and a section thickness of 2 mm. For anatomic correlation, 0.6-mm isotropic three-dimensional fast imaging employing steady-state images were acquired for coregistration with the functional diffusion-tensor maps.	20 patients with TN and evidence of neurovascular contact were examined	Diffusion-tensor imaging enables the identification and quantification of anisotropic changes between normal nerve tissue and TN-affected trigeminal nerves. Correlation with anatomic 3D fast imaging employs excellent delineation of cisternal segments of tn.
6.	Pre-operative MRI/MRA for microvascular decompression	Vergani F et al.	Presented a protocol for preoperative investigation of TN patients and	Out of 92 patients who had MVD for primary	Preoperative MRI has both good sensitivity and positive

in trigeminal neuralgia: consecutive series of 67 patients	(2011)	correlated the MR findings with surgical evidence of vascular compression, in order to calculate specificity and sensitivity of preoperative MRI and MRA	TN, 67 who underwent a preoperative MRI and MRA according to protocol were included	predictive value. Specificity and negative predictive values were limited in this series.
7. Pre-vascular demonstration of neurovascular relationship in trigeminal neuralgia by using 3D FIESTA sequence	Zhou Q et al. (2012)	Evaluated the value of high-resolution three-dimensional FIESTA imaging in the visualization of neurovascular relationship in patients with TN.	37 patients with unilateral typical TN.	Anatomical relationships defined by this method can be useful in surgical planning and predicting surgical findings as it enables accurate visualization of neurovascular contact in patients with TN. Concluded that trigeminal REZ NVC, as detected by MRI, is highly likely to be symptomatic when it is associated with anatomical nerve changes.
8. Magnetic resonance imaging contribution for diagnosing symptomatic neurovascular contact in classic trigeminal neuralgia: A blinded case-control study and meta-analysis	Antonini J et al. (2014)	To assess the accuracy of MRI in distinguishing symptomatic from asymptomatic trigeminal neurovascular contact (NVC). Examiners evaluated whether the trigeminal nerve displayed NVC in the REZ or non REZ, whether it was dislocated by 38 the vessel or displayed atrophy at the contact site.	24 classical TN patients and a similar number of age- matched healthy controls.	
9. Neurovascular study of the trigeminal nerve at 3 t MRI	Docampo J et al. 2015	Prospective study aimed to show a novel visualization method to investigate compression of trigeminal nerve using 3D FIESTA and 3D TOF MRA.	80 patients, 30 with unilateral TN and 50 without symptoms of TN (control group)	The use of combination of these sequences enables quick and efficient visualization and assessment of relation between trigeminal nerve and neighbouring vascular structures.
10. Preoperative MRI in neurovascular compression syndromes and its role in microsurgical considerations	Tanrikulu L et al. (2015)	To minimize the risk of recurrent TN, vascular structures in anatomical relation to trigeminal nerve root at lateral pontine aspect should be decompressed maximally. New MR techniques, their chances and potential impact were evaluated.	8 patients, in which 7 were with TN and one with vertigo	High resolution MR images provide reliable and detailed information on corresponding intraoperative anatomy. So application of these techniques can be an aid to indication, planning & teaching purposes.

division was seen. Direct spread or metastases from distant malignancies can cause trigeminal neuropathy due to compression of the peripheral branches<sup>38</sup>.

### Magnetic Resonance Neurography (MRN)

This method provides better visualization of peripheral nerves over MRI i.e., small nerves owing to their size, surrounding vessels and muscles. The sequences in this technique uses fat suppression, which further enables the assessment of specific nerve morphological features such as calibre, internal fascicular pattern and the amount of perineurial- endoneurial fluid<sup>39</sup>.

### CONCLUSION

The root entry zone at the brain stem is the most common site of the lesion followed by the cistern segment, Meckel's cave and the peripheral nerve. The nerve anatomy, site of the lesion in the course of the nerve and the vessel compressing the nerve is well appreciated in an MRI. But the vascularity and the contribution of the cerebral perfusion in that region towards Trigeminal Neuralgia is not well explored. To analyse and to confirm whether cerebral perfusion plays a role in the pathogenesis of the disease an arterial spin labelling MRI would be the imaging of choice. If cerebral perfusion has any contribution then the treatment protocol would vary else it will add more evidence towards the earlier demyelination hypothesis in etiopathogenesis of Trigeminal Neuralgia.

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