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Diagnostischer Wert des präoperativen MRT zur Erkennung einer neurovaskulären Kompression des Nervus Trigeminus bei Patienten mit Trigeminusneuralgie

Inaugural-Dissertation
zur
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vorgelegt von

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In cooperation with University Clinic Gießen and Marburg GmbH, Location Marburg

Diagnostic value of preoperative Magnetic Resonance Imaging in evaluation of vascular compression of trigeminal nerve in patients with trigeminal neuralgia

Inaugural-Dissertation
to
Acknowledgement of the PhD Degree in humane Medicine

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applied by

Mariana Gurschi (Țurcanu)
from Chişinău, Moldova

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Dedicated to my Parents
Aurora and Grigore Țurcanu

C O N T E N T

1. INTRODUCTION

Trigeminal neuralgia (TGN), or **tic douloureux**, is a severe chronic pain syndrome characterized by dramatic, brief stabbing or electric shock-like pain paroxysms felt in one or more divisions of the trigeminal distribution, either spontaneously or on gentle tactile stimulation of a trigger point on the face or in the oral cavity (Devor M. et al., 2002a). The pain produced by trigeminal neuralgia is excruciating, the most painful hemifacial pain syndrome, perhaps the worst pain known to human beings (Tavares M.P.,), painful to the extent of driving some suffers to the point of suicide. For four centuries, the pain of tic douloureux has been fascinating physicians. Perhaps the intense and disabling nature of the pain or its unprovoked and sporadic onset focuses scientists' attention. Investigators have searched continuously for clues to the pathophysiology of the disease process with the goal of identifying a universally effective cure (Jawahar A. et al., 2001; Majoie C.B. et al., 1998).

It can be a devastating disease interfering with the patients' professional and social life, depending on the frequency and intensity of the painful paroxysms and degree of pain control.

Many daily activities such as brushing the teeth, eating, shaving, or washing the face may provoke attacks and cause spasms of the facial muscles. This is why it is also called "Tic douloureux"(Waldman S.D., 1997). Multiple attacks can occur daily over weeks or months and in the beginning of stages spontaneously for weeks or months be suspended. The evolution is progressive as a rule. Twenty-nine percent (29%) of the patients have only one episode during their lives; twenty-eight percent (28%) have three or more episodes. During the first 5 years in about 21% of the patients repeated attacks occur (Katusic S. et al., 1991). The pain is characterized by paroxysms of electric shock-like pain lasting usually from several seconds to less than 2 min (Waldman S.D., 1997).

1.1. Incidence

Classical trigeminal neuralgia has an annual incidence of ~ 4.5 per 100 000.

It occurs in females 1,5 times more than in males, therefore the annual incidence is about 3.4/ 100 000 for men and 5.9/100 000 for women (Katusic S. et al., 1991; Yoshimasu F. et al., 1972).

It occurs most commonly in people over 50 years old (more than 70% of sufferers), at the time of atherosclerotic changes, which lead to increased tortuosity of the vessels, that may result in vascular compression of trigeminal nerve. This is why it is rarely seen prior to the age of 30 years. However young adults and children can also be affected (Childs A.M. et al., 2000; Mason W.E. et al., 1991; Resnick D.K. et al., 1998). If trigeminal neuralgia occurs in a younger patient, it almost always is associated with Multiple Sclerosis (MS). Katusic (Katusic S. et al., 1990) reported an age-specific incidence of 0.2 per 100 000 in the population up to 40 years old, as compared with 33.7 per 100 000 in the population 70 to 79 years old. Of 227 patients who underwent surgery, Klun (Klun B., 1992) operated on only 4 patients (1.8%) who were in their twenties. Loeser (Loeser J.D., 1985) estimated that the onset of symptoms occurs before the age of 20 years in approximately 1% of patients with trigeminal neuralgia.

To a certain extent, trigeminal neuralgia runs in families. About 5% of patients have a family history of it (Duff J.M. et al., 1999; Mason W.E. et al., 1991; Smyth P. et al., 2003). Family occurrence is common for Charcot-Marie-Tooth disease (Coffey R.J. et al., 1991).

The pain is unilateral in 97% of the cases. Bilateral trigeminal neuralgia can occur in 3-5%. If it is bilateral it occurs in the same division of the nerve and it is mostly common for MS. The second (18%) or third division (15%) of the nerve is affected in the majority of patients either separately or combined (36-40%), with the first division affected less than 5% of the time. The right side of the face is more commonly affected (in 57%) (Waldman S.D., 1997).

1.2. Historical aspects

The first known description of trigeminal neuralgia was written in the second century AD by Aretaeus of Cappadocia, a contemporary of Galen (Nurmikko T.J. et al., 2001). Also known for his descriptions of migraine, he mentions a pain in which “spasm and distortion of the countenance take place” (Rose F.C., 1999). Jujani, an Arab physician, in the 11th century, mentions unilateral facial pain causing spasms and anxiety in his writings. Interestingly, he suggests that the cause of the pain is “the proximity of the artery to the nerve” (Ameli N.O., 1965).

The first full account of TGN was published in 1773 when John Forthergill presented a report to the Medical Society of London. He described the typical features of the condition in detail, including paroxysms of unilateral facial pain, evoked by eating or speaking or touch, starting and ending abruptly, and associated with anxiety (Nurmikko T.J. et al., 2001; Rose F.C., 1999). Some time earlier, Nicolaus André had used the term “tic douloureux” to describe what he thought was a new clinical entity (Nurmikko T.J. et al., 2001; Rose F.C., 1999).

Sporadic observations later in the 18th and 19th century by Pujol, Chapman and Tiffany helped to complete the clinical picture and differentiate trigeminal neuralgia from common facial pain conditions such as toothache. In the early 20th century, Oppenheim alluded to an association between MS and trigeminal neuralgia and Patrick commented on its familial incidence (Fromm G.H. et al., 1990; Nurmikko T.J. et al., 2001).

The earliest surgical treatment of trigeminal neuralgia dates back to the 19th century when Sir Victor Horsley sectioned the preganglionic trigeminal roots from the middle cranial fossa (1891). Complete transsection of the nerve was later modified by Spiller and Frazier in 1901 to a partial sectioning using this same extradural approach (Elias W.J. et al., 2002).

A wide range of treatments was in use by the beginning of the last century. Modern neurosurgical treatment can be traced back to 1925 when the

concept of vascular compression was introduced (Dandy W.E., 1934). Walter Dandy pioneered the posterior fossa approach for the treatment of trigeminal neuralgia. He approached and sectioned the trigeminal nerve from the posterior fossa and was able to report the seminal observation regarding TGN: the trigeminal nerve was compressed or grooved by structures such as tumours, aneurysms, vascular malformations, or normal vessels. Despite this realization, Dandy persisted in partially sectioning the nerve (Elias W.J. et al., 2002). In 1934, Dandy outlined his theory that a blood vessel compressing cranial nerves can cause clinical syndromes, and pointed to the main problem with that theory, namely, that vascular contact occasionally occurs without the production of pain and may be absent when neuralgia is present.

Dandy identified the major compressing vessel as the anterior inferior cerebellar artery (Dandy W.E., 1934).

However, it took half a century before microvascular decompression (MVD) gained widespread acceptance as a treatment method. Gardner and Miklos promoted the theory and modified the technique further in the 1950s and 1960s and are credited for being first to decompress a trigeminal nerve as a treatment for trigeminal neuralgia (Gardner W.J. et al., 1959).

It was not until the large case series published in 1970s by Jannetta (Jannetta P.J., 1967) that a major shift in neurosurgical practice began to appear. Peter Jannetta was the first neurosurgeon to apply the operating microscope to the problem of trigeminal neuralgia. He observed the almost universal occurrence of vascular channels compressing the trigeminal nerve in patients with trigeminal neuralgia and devised a technique for non-destructive microvascular decompression of the nerve (Tavares M.P.,).

Neuroablative procedures kept evolving throughout the century, with attempts to balance adverse effects of neuronal injury with sufficient pain control. Radiosurgery is the latest innovation in this process (Nurmikko T.J. et al., 2001).

Pharmacotherapy had little success in this condition until Bergouignance's discovery in 1942 that phenytoin was effective in preventing pain paroxysms (Bergouignan M., 1942). Soon following the introduction of diphenylhydantoin

and carbamazepine for treatment of epilepsy, controlled trials were published showing its superiority over placebo in trigeminal neuralgia. Since then, anticonvulsants have remained the mainstay of pharmacological treatment, though controlled trials have been surprisingly rare (Nurmikko T.J. et al., 2001).

1.3. Definition of TGN

There is still a great deal of confusion regarding the terminology used for trigeminal nerve pathology. Trigeminal neuralgia and trigeminal neuropathy are often used interchangeably and primary and secondary trigeminal neuralgia is another terminology commonly encountered in the medical literature.

The absence of objective tests to validate the diagnosis of trigeminal neuralgia has led to the emergence of precise definitions and strict diagnostic criteria based upon clinical findings. These are mandatory to provide better understanding of the pathophysiology, adequate management and to assure that patients recruited for clinical trials all have the same condition (Borges A., 2005).

Trigeminal neuralgia is usually classified into two different categories (Borges A., 2005):

- **primary** or **idiopathic**, which include patients with a negative physical exam and otherwise normal sensory and motor functions where an organic cause for pain has been excluded;
- and **secondary**, including patients with associated physical findings related to organic lesions involving the course of the nerve, often the gasserian ganglion sensory root or root entry zone at the pons (Chavin J.M., 2003; Zakrzewska J.M., 2002). The increasing use of high resolution MRI in the evaluation of trigeminal neuralgia revealed a large number of patients with vascular compression of the nerve at the root entry zone (REZ) among the idiopathic group, and therefore neurovascular conflict is now the most commonly accepted pathophysiologic mechanism to explain the primary disease.

Both the International Association for the Study of Pain (IASP) and International Headache Society (IHS) have suggested their definitions and diagnostic criteria for trigeminal neuralgia (Merskey H., 1994) (http://www.i-h-s.org/). These are remarkably similar and highlight the

sudden, explosive nature of the pain. In further descriptions of the condition, both classifications allude to vascular compression, MS and tumours as known aetiological causes (Nurmikko T.J. et al., 2001). The IASP classification makes a distinction between trigeminal neuralgia (including MS) and secondary **neuralgia** (caused by structural lesions and injuries, but not including MS), while IHS separates idiopathic trigeminal neuralgia from the symptomatic form depending on the presence of a structural lesion; it is not quite clear if vascular compression qualifies as such. Neither approach includes reference to variant forms of trigeminal neuralgia, which satisfy the diagnostic criteria but display additional features as well (Nurmikko T.J. et al., 2001).

IASP definition (Merskey H., 1994): Sudden, usually unilateral, severe brief stabbing recurrent pains in the distribution of one or more branches of the 5th cranial nerve.

IHS definition (Bussone G. et al., 2004) (http://www.i-h-s.org/): Painful unilateral affliction of the face, characterized by brief electric shock like pain limited to the distribution of one or more divisions of the trigeminal nerve. Pain is commonly evoked by trivial stimuli including washing, shaving, smoking, talking, and brushing the teeth, but may also occur spontaneously. The pain is abrupt in onset and termination and may remit for varying periods.

The International Headache Society has suggested the following criteria for the diagnosis of trigeminal neuralgia:

1. Paroxysmal attacks of facial or frontal pain that last a few seconds to less than 2 minutes.
2. Pain has at least four of the following characteristics:
    - distribution along one or more divisions of the trigeminal nerve,
    - sudden, intense, sharp, superficial, stabbing, or burning in quality:
    - severe intensity,
    - precipitation from trigger areas or by certain daily activities such as eating, talking, washing the face, or cleaning the teeth,
    - the patient is entirely asymptomatic between paroxysms,

3. No neurological deficit.
4. Attacks are stereotyped in the individual patient.
5. Exclusion of other causes of facial pain by history, physical examination findings, and special investigation when necessary (Zakrzewska J.M., 2002).

The comparison of definitions of trigeminal neuralgia is given in the Tab. 1.

Table 1 *Comparison of definitions of TGN. (Nurmikko T.J. et al., 2001)*

	TGN (IASP and HIS definition)	Typical TGN (Liverpool criteria)	Atypical TGN (Liverpool criteria)	Trigeminal neuropathy (Liverpool criteria)
Site	Unilateral	Unilateral	Unilateral	Uni- or bilateral
Quality of pain	Sharp, stabbing, burning, superficial	Sharp, shooting, stabbing, lingering aftersensations	Sharp, shooting, stabbing, lingering aftersensations, burning, smarting	Dull or sharp, smarting, steady pain with shooting sensations superimposed
Duration of pain	Brief	A few seconds at most	Several seconds	Any duration, usually hours
Duration of paroxysms	2 minutes	Seconds to minutes	Seconds to minutes	Continuous with pain-free spells
Refractory period	Yes	Yes	Yes	No
Continuous pain	No	No	Yes, no severe	Dominant features
Allodynia	Limited trigger zone	Small trigger zone	Small trigger zone	Large allodynic areas
Associated features	Slight flush	Vasodilatation, swelling seen with severe pain	Vasodilatation, swelling seen with severe pain	Variable vasodilatation and swelling, may be constantly present
Radiation	None outside affected division	None outside affected division	None outside affected division	May extend outside trigeminal territory
Provoking factors	Eating, talking, washing face, brushing teeth, smoking	Touching, speaking, eating, drinking, cold, occasionally heat, movement	Touching, speaking, eating, drinking, cold, occasionally heat, movement	Same as atypical TGN
Variability of pain	Stereotyped	Some variation	Definite variation	Definite variation
Sensory loss	None	Not detectable with bedside test QST may be abnormal	May be detectable with bedside test QST usually abnormal	Prominent, easily detected with bedside tests, confirmed by QST
Pain behaviour	Not discussed	Aversion to touch guarded to speech	Aversion to touch guarded to speech	Tolerates touching speech not affected
Course of pain	Spontaneous remissions	Early remissions pre- TGN	Early remissions previously typical TGN	No remissions; slow progression

1.4. Anatomy of trigeminal nerve

The trigeminal nerve, or the 5th (V) cranial nerve as the largest of the cranial nerves, is a mixed, predominantly sensorial cranial nerve. Embryologically it is the first nerve of the branchial arch. After the differentiation of the branchial arch into the mandibular and mastication muscles, it supplies as the 5th cranial nerve with its bigger sensorial part face skin, the conjunctiva, as well as the mucosa of the face, partially of the mouth, teeth and most of the scalp. A smaller motoric part innervates the muscles of mastication (Bien S. et al., 1988). Both parts are successively described below in their topography from central to the periphery. Because a long course from the brainstem nuclei to the peripheral branches is seen, it is useful to subdivide the nerve in several segments and then tailor the imaging modality and the imaging study to that specific segment. This is particularly true in cases where topographic diagnosis can be used to locate a lesion in the course of these nerves (Borges A., 2005).

1.4.1. Brainstem

The central component of the trigeminal nerve is located in the brainstem and arises from one motor nucleus and three sensory nuclei: the principal or the major (Borges A., 2005), the mesencephalic and the spinal, which extend throughout most of the length of the brainstem (Fig 1+2).

The principal sensory nucleus is located in the lateral pontine tegmentum, anterior and lateral to the 4^{th} ventricle (lateral to the entering of the trigeminal root – Kamel H. et al., 2000 (Fig. 1+2) and carries facial tactile sensation of touch and pressure (Borges A., 2005).

The spinal trigeminal nucleus (tract) or *nucleus of the spinal tract*, is the caudal extension of the principal sensory nucleus, extends downward through the medulla into the upper cervical cord up to the level C2–C4 and emerges with the dorsal grey matter (Borges A., 2005; Kamel H.A. et al., 2001; Woolfall P. et al., 2001), (Fig.1+2).

The mesencephalic trigeminal nucleus, the superior extent of the major sensory nucleus, extends from upper pons into the midbrain and forms a slender cell column near the lateral margin of the central grey matter anterior to the upper fourth ventricle and aqueduct. Afferent fibers of the mesencephalic nucleus convey proprioception from teeth, hard palate, temporomandibular joint and masticator muscles (Fig. 1+2) (Kamel H.A. et al., 2001).

There is a single motor nucleus of the trigeminal nerve which is located in the midpons antero-medial to the principal sensory nucleus in the upper pons (Woolfall P. et al., 2001). It forms an oval column of cell responsible for innervation of the muscles of the first branchial arch, which include the muscles of mastication as well as the mylohyoid muscle, anterior belly of the digastric muscle, musculus tensor veli palatini and tensor tympani, (Borges A., 2005; Casselman J.W., 2004; Go J.L. et al., 2001; Kamel H.A. et al., 2001; Laine F.J. et al., 1998; Louryan S., 2004) (Fig.1+2).

Eventually all tracts from the principle sensory and spinal trigeminal nuclei project to the postero-medial nucleus of the thalamus, from which they track through the most posterior aspect of the posterior limb of the internal capsule and project to the postcentral gyrus (Kamel H.A. et al., 2001).

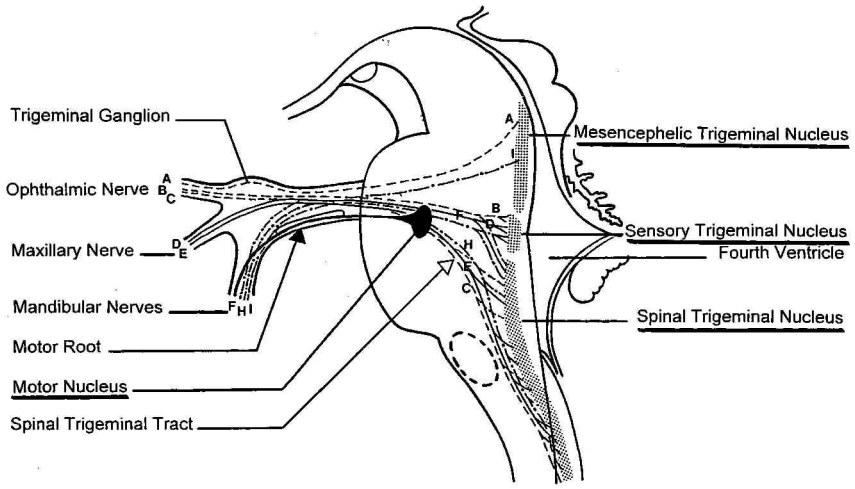


Fig. 1 *(Kamel H.A. et al., 2001). —Sagittal diagram shows three peripheral divisions of trigeminal nerve entering convexity and root bundles leaving concavity of sickle-shaped trigeminal ganglion. Motor root (solid arrowhead) bypasses ganglion and reunites with mandibular nerve in foramen ovale basis cranii. Open arrowhead indicates descending spinal trigeminal tract. Diagram also shows motor and sensory trigeminal nuclei (underline) in brainstem and cervical cord. A, B, and C track nuclear origin of fibers contributing to ophthalmic; D and E, the maxillary; and F, H, and I, mandibular divisions of trigeminal nerve.*

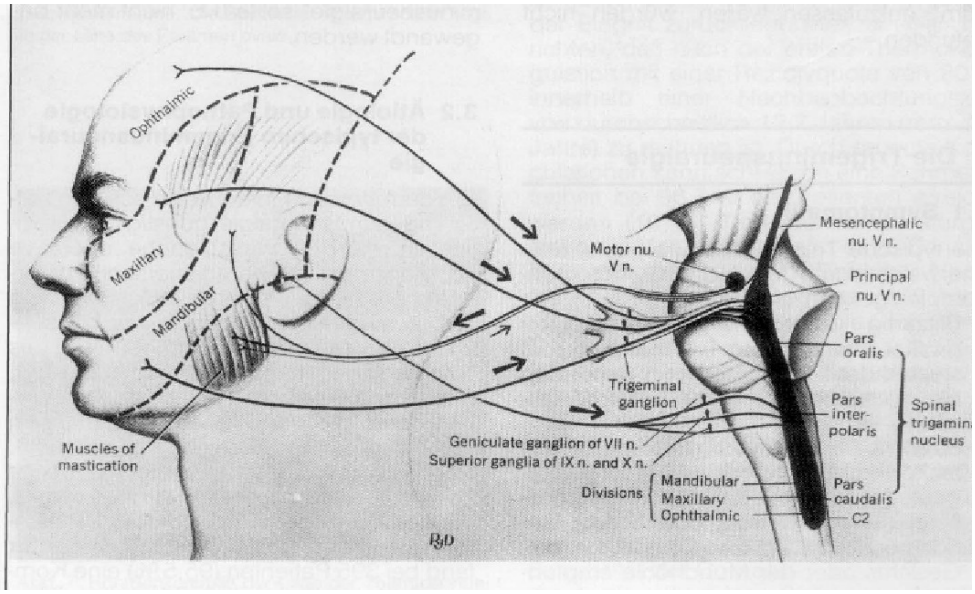


Fig. 2 *Innervation areas of the sensory Branches and of the motor part des trigeminal nerve (Noback, Ch. R. Et al.* ***The human nervous system. Basic principles of neurobiology, 1981,*** *from Bien S. et al., 1988)*

1.4.2. Trigeminal ganglion and preganglionic trigeminal nerve

1.4.2.1. Cisternal segment

The trigeminal nerve exits the ventro-lateral aspect of the midpons as a large sensory root and a much smaller motor root, where sensory root lies posterior and lateral to the motor root and traverses anteriorly and slightly lateral through the pre-pontine cistern (Fig. 1 + 2).

As it exits the pons, the point of change from central to peripheral myelin is known as the root entry zone (REZ). It is at this point that the nerve is thought to be most susceptible to compression by tortuous branches of the posterior circulation vessels, an important cause of trigeminal neuralgia (Woolfall P. et al., 2001). It is also called Obersteiner-Redlich (O-R) transitional zone (according to description of (Calvin W.H. et al., 1977) and is generally located 2 to 3 mm outside the zone of entry into the pons The dorsal REZ represents the junction between the peripheral and central myelins of Schwann cells and astrocytes. The central branches of the unipolar ganglion cells enter the pons through this transition zone on their course toward the brainstem and spinal nuclei. Any process at this level can potentially alter the function of the whole neurone (Nurmikko T.J. et al., 2001).

The nerve continues anteriorly along the medial wall of the apex of the petrous temporal bone. Here it enters the medial cranial fossa through a dural foramen, the “porus trigeminus”, leading to a dural compartment, Meckel’s cavity, a cerebrospinal fluid (CSF) containing arachnoidal space lying immediately postero-lateral to the cavernous sinus and protruding from the posterior cranial fossa. The nerve trunk then expands to form the trigeminal (or Gasserian, or semilunar) ganglion, located within trigeminal recess at the infero-medial wall of the petrous apex which trifurcates at its ventral aspect giving off three branches: ophthalmic or V1, maxillary or V2 and mandibular or V3 (Borges A., 2005; Kamel H.A. et al., 2001; Woolfall P. et al., 2001).

The motor root passes immediately beneath the ganglion, turns inferiorly exiting the skull base at the foramen ovale together, but without merging, with the mandibular division of the sensory root and enters the nasopharyngeal masticator space (Borges A., 2005; Kamel H.A. et al., 2001; Woolfall P. et al., 2001).

1.4.2.2. Cavernous segment

Medial to the ganglion in the Meckel's cavity is the internal carotid artery in the posterior portion of the cavernous sinus. Inferior is the motor root of the trigeminal nerve and the apex of the petrous temporal with the internal carotid artery in its bony canal (Kamel H.A. et al., 2001).

The ophthalmic and maxillary divisions of the sensory root continue further anteriorly within the lateral wall of the cavernous sinus, below cranial nerve IV and lateral to cranial nerve VI and cavernous carotid artery. The nerves travel from superomedial to inferolateral as they course anteriorly (Borges A., 2005; Casselman J.W., 2004; Go J.L. et al., 2001; Laine F.J. et al., 1998; Louryan S., 2004).

1.4.3. Peripheral division of the trigeminal nerve

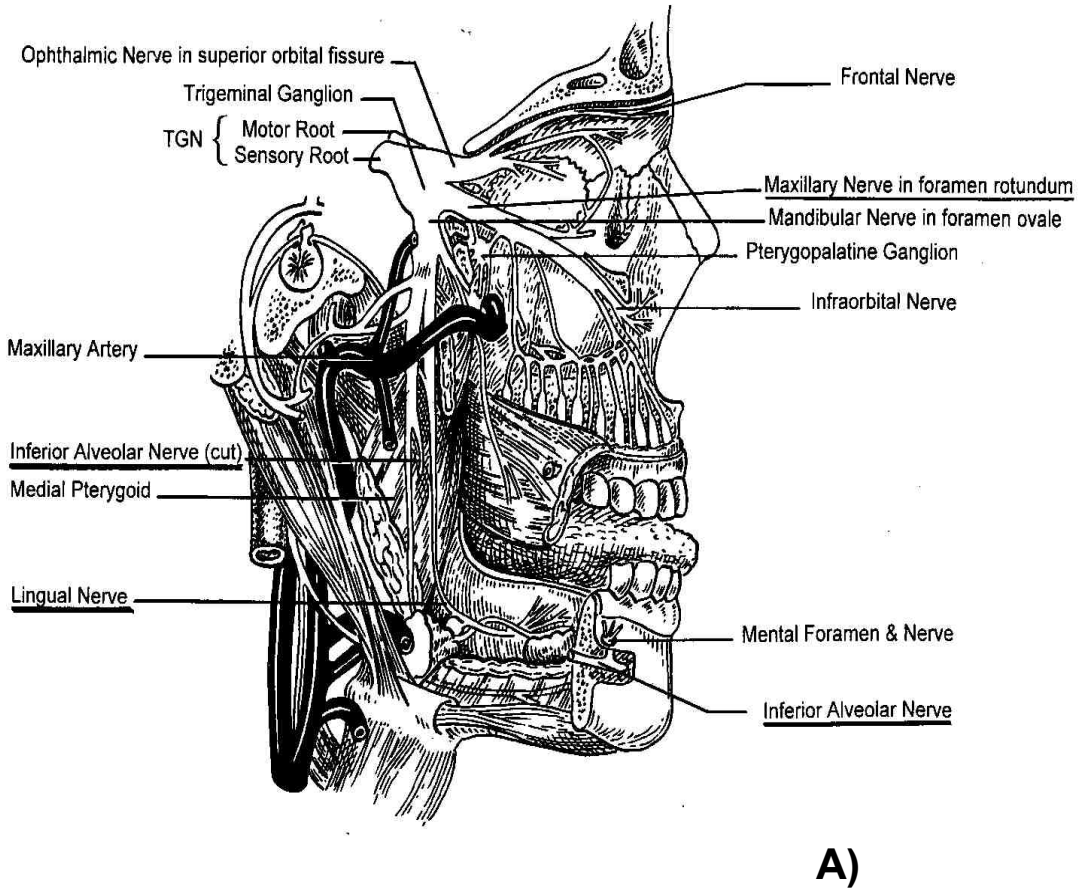
The trigeminal nerve trifurcates distaly to the trigeminal ganglion into ophthalmic, maxillary and mandibular nerves.

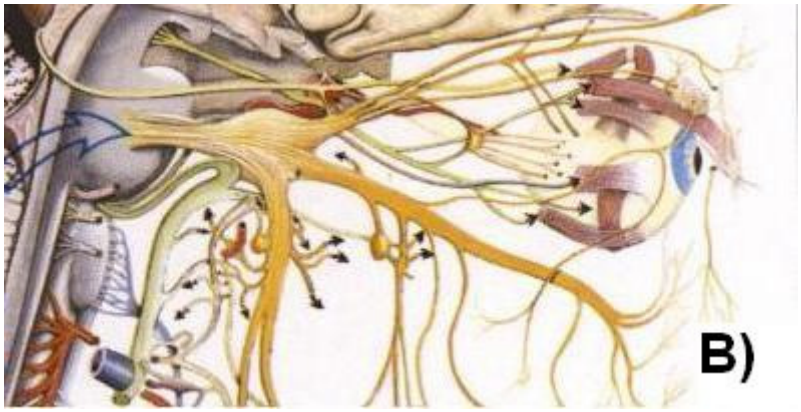
The ophthalmic nerve passes forward through the lateral wall of the cavernous sinus. It gains access into the orbit via the superior orbital fissure (Fig. 3abc). The ophthalmic nerve then gives off three major branches: **lacrimal**, **frontal** and **nasociliary** nerves that provide sensory information to the forehead, nose and globe. Its terminal branch, the supraorbital nerve, exits the orbit through the supra-orbital foramen and supplies sensory innervations to the upper third of the face (Borges A., 2005; Kamel H.A. et al., 2001).

The *maxillary nerve* has a shorter course exiting the skull base through the foramen rotundum ossis sphenoidalis inferolateral to the cavernous sinus (at

the most inferior part of the cavernous sinus). It then enters the pterygopalatine fossa where it gives off several branches: **meningeal**, **zygomatic**, **pterygopalatine** and **posterior superior alveolar** branches. Its main trunk continues anteriorly through the inferior orbital fissure in the orbital floor (Fig. 3abc) and emerges into the face as the infraorbital nerve. This terminal branch travels within the infraorbital canal, exits the orbit through the infraorbital foramen and supplies sensory information to the midface, cheek and maxillary teeth (Borges A., 2005; Kamel H.A. et al., 2001).

The mandibular nerve, the largest of the three, runs laterally along the skull base then exits the cranium by descending through the foramen ovale into the masticator space. The motor root of the trigeminal nerve bypasses the trigeminal ganglion and reunites with the mandibular nerve in the foramen ovale basis cranii (Fig. 3abc). As the mandibular nerve enters the nasopharyngeal masticators space, it divides into four sensory branches: **buccal**, **auriculotemporal**, **lingual** and **inferior alveolar nerves**. The terminal branch, inferior alveolar nerve, enters the mandibular foramen at the lingual aspect of the mandibular ramus and travels along the body of the mandible within the inferior alveolar canal. It exits the mandible at the parasymphyseal region at the mental foramen and ends as the mental nerve, receiving sensory information from the lower third of the face, tongue, floor of the mouth and jaw (Fig. 3abc). The motor root of the mandibular nerve divides into two major branches: the **masticator nerve** supplying motor innervation to the temporal, masseter, and pterygoid muscles, and the **mylohyoid branch** that supplies the mylohyoid and the anterior belly of the digastric muscle (Borges A., 2005; Kamel H.A. et al., 2001).


Ophthalmic Nerve in superior orbital fissure
Trigeminal Ganglion
TGN
Motor Root
Sensory Root
Frontal Nerve
Maxillary Nerve in foramen rotundum
Mandibular Nerve in foramen ovale
Pterygopalatine Ganglion
Infraorbital Nerve
Maxillary Artery
Inferior Alveolar Nerve (cut)
Medial Pterygoid
Lingual Nerve
Mental Foramen & Nerve
Inferior Alveolar Nerve
A)


B)

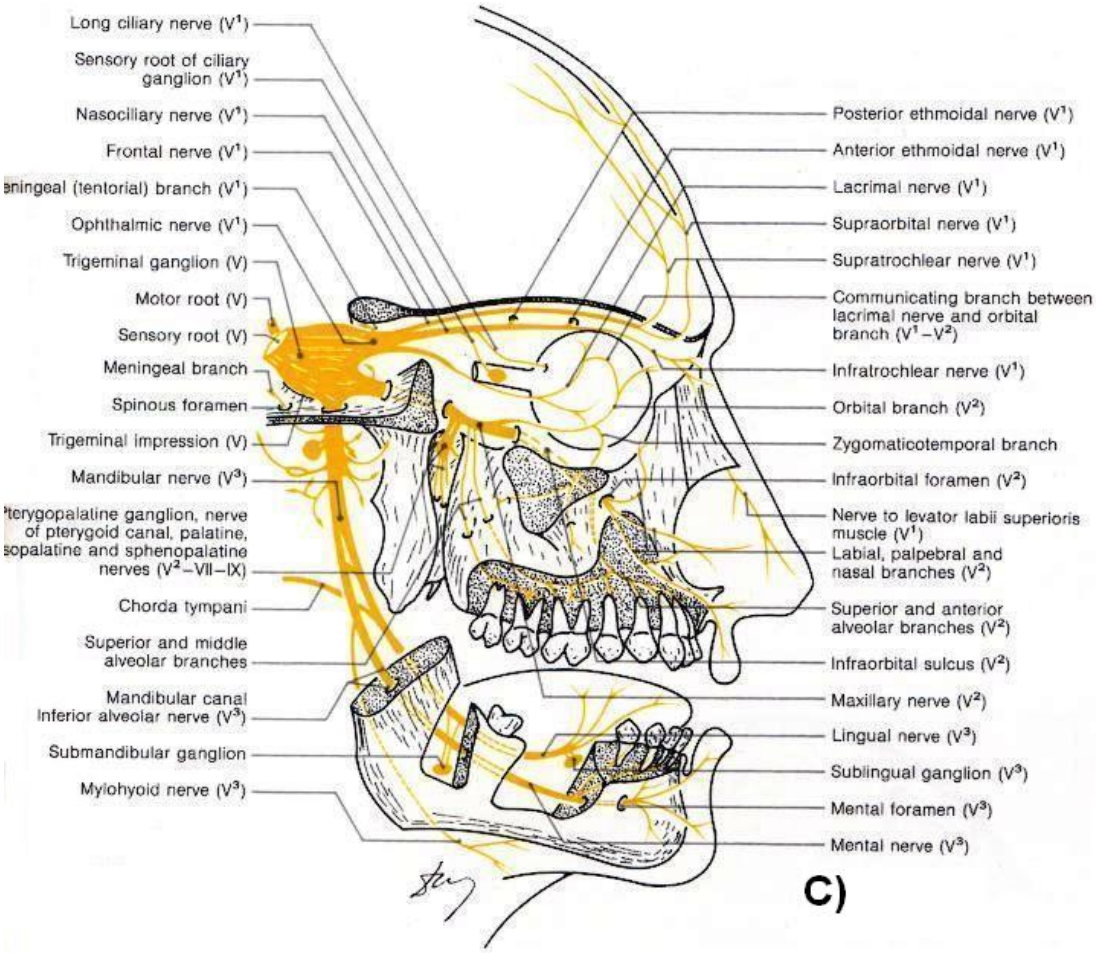


Fig. 3a *(Kamel H.A. et al., 2001);* ***3b, 3c*** *(Leblanc A., 1992).—Diagram shows trigeminal nerve, trigeminal ganglion, peripheral divisions and their branches. From foramen rotundum ossis sphenoidalis, maxillary nerve gains access to pterygopalatine fossa and continues in floor of orbit as infraorbital nerve. Inferior alveolar and lingual nerves are branches of mandibular nerve.*

The schematic description of the course in innervations areas is given in the table 2.

Table 2 *Divisions of the trigeminal nerve (Woolfall P. et al., 2001)*

Branch	Course	Function
Ophthalmic (V_1)	Anteriorly through cavernous sinus. Accompanied by III, IV, VI and V_2 cranial nerves. Exits skull through superior orbital fissure and enters orbit	Sensory to nose, paranasal sinuses and upper face
Maxillary (V_2)	Accompanies V_1 through cavernous sinus. Exits skull through foramen rotundum and enters pterygopalatine fossa	Sensory to middle third of face and upper teeth
Mandibular (V_3)	Immediately exits skull through foramen ovale	Sensory to lower face tongue, jaw and lower teeth. Motor to muscles of mastication, and mylohyoid and other small muscles

1.5. Aetiology of Trigeminal neuralgia

1.5.1. General considerations

It is obviously problematic to determine the aetiological causes for the pathological entity known as trigeminal neuralgia (Nurmikko T.J. et al., 2001). Trigeminal neuropathy is a generic term that includes a broad range of disease processes with different managements and treatment options. Any intrinsic or extrinsic lesion impinging upon the cisternal segment of cranial nerve V (CN V), involving the root entry zone, may lead to trigeminal neuralgia (Borges A., 2005).

Trigeminal neuralgia consists mainly from subjective pain rather than some hard signs or laboratory tests (Nurmikko T.J. et al., 2001). In the majority of patients, the trigeminal neuralgia is idiopathic. So there is no identifiable cause, however in up to 15% of patients an underlying cause was established and secondary or symptomatic TGN was diagnosed (Zakrzewska J.M., 2002). Often, these patients present other associated clinical manifestations besides pain, such as sensory and motor deficits and are labelled as secondary trigeminal neuralgia (Borges A., 2005).

Current theories cite both central and peripheral mechanisms for the development of pain in trigeminal neuralgia. Peripheral mechanism theories frequently invoke segmental demyelination as a trigger of ephaptic transmission or abnormal impulse generation. Central mechanism theories cite differentiation of the trigeminal nucleus as the cause of spontaneous neuronal hyperactivity and discharges that are perceived as pain (Jawahar A. et al., 2001).

The discovery 60 years ago that trigeminal neuralgia responds dramatically to certain anticonvulsant drugs gave rise to the widely held theory that pain paroxysms in trigeminal neuralgia result from seizures in brain stem trigeminal structures. However, the relation between the presence

of pain paroxysms and trigeminal root compression by various abnormalities led to the belief that trigeminal neuralgia is a form of peripheral neuropathy (Devor M. et al., 2002b).

Following the peripheral mechanism theory it could be pointed that most of trigeminal neuralgia are caused by compression of the trigeminal nerve root by an aberrant overlying blood vessel, most frequently artery - A. cerebelli superior, usually within a few millimetres of its entry into the pons, i.e. the root entry zone.

In some cases (2-4% of patients) trigeminal neuralgia is due to a primary demyelinating disorder, most frequently, MS (Love S. et al., 2001). Conversely, trigeminal neuralgia is diagnosed in 1-5% of patients with MS. In this case trigeminal neuralgia symptoms are the first manifestation of the disease. These patients are younger than the trigeminal neuralgia population, their neuralgia is more frequent bilateral and the first branch of trigeminal nerve is considerable more often affected (Nurmikko T.J. et al., 2001).

Other, rare cases include infiltration or compression of the nerve root, gasserian ganglion or nerve by a tumour of posterior fossa: meningeoma or neurinoma (2%), metastasis, cyst, aneurysm; arteriovenous malformation.

There are also described cases of infiltrative disorders, such as carcinomatous deposits within the nerve, nerve root, or gasserian ganglion (Chong V.F., 1996) and amyloidomas (Bornemann A. et al., 1993; Love S. et al., 1998).

Small numbers of patients have been reported in whom trigeminal neuralgia was associated with a small infarct (Golby A.J. et al., 1998; Nakamura K. et al., 1996) or angioma (Saito A. et al., 1989) in the brainstem.

1.5.2. Affection of the TN according to its anatomical parts

Following the entire route of the 5th nerve intracerebral from the pons to the Meckel's cavity and then after Gasserian ganglion trifurcation into ophthalmic, maxillary and mandibular parts the most common affecting lesions of the trigeminal nerve according its divisions could be noted (Table 3).

1.5.2.1. Brainstem

Multiple sclerosis (up to 4% of patients) or primary demyelination lesions, *glioma* and *infarction* are the most common brainstem and upper cervical cord lesions resulting in fifth cranial nerve symptom. Less common lesions include *metastasis* or others neoplasm (*hamartoma* in type I of *neurofibromatosis*), *cavernous hemangioma*, *haemorrhage* and *arteriovenous malformation*. Rarely, *rhomboencephalitis*, or other infection may develop as a result of retrograde extension of *herpes simplex virus* type 1 from trigeminal ganglion into the brainstem (Kamel H.A. et al., 2001). Syringobulbia may present with cranial neuropathies and is often secondary to previous trauma or pre-existing anomalies such as Arnold–Chiari malformation ((Woolfall P. et al., 2001).

It should always be kept in mind that any pathologic processes involving the upper spinal cord may lead to trigeminal neuropathy by affecting the dorsally located trigeminal tracts (Borges A., 2005).

1.5.2.2. Trigeminal ganglion and preganglionic trigeminal nerve (cisternal part and cavernous segment)

The Meckel's cave can be involved either by extrinsic or intrinsic disease.

Extrinsic lesions, usually *bony metastasis*, *chordoma*, or *chondrosarcoma*, destroy adjacent bone as they extend toward the Meckel's cavity. Intrinsic lesions simply expand the Meckel's cavity. When the tumour is large enough, the pressure exerted by its leads to erosion of the surrounding bone.

Tumours may also extend away from the Meckel's cavity with enlargement of the foramen ovale basis cranii, foramen rotundum ossis sphenoidalis, or the superior orbital fissure (Borges A., 2005; Kamel H.A. et al., 2001).

Intrinsic lesions include *primary tumours* of the Meckel's cave as well as *secondary neoplasms* from perineural spread of local tumours, leptomeningeal, or hematogenous metastasis. Primary tumours of the Meckel's cave include *trigeminal schwannoma*, *petroclival* or *paracellar meningioma* and *epidermoid* or *arachnoidal cysts* located at the cerebello-pontine angle. Trigeminal schwannomas are classified based upon their location along the course of the nerve which dictates both the clinical presentation and surgical approach: type I: arisen from the gasserian ganglion located in the middle cranial fossa; type II: limited to the posterior fossa and to the cisternal segment of the trigeminal nerve; type III: dumbbell-shaped tumours with a posterior fossa component in the prepontine cistern and a middle cranial fossa component in Meckel's cave, separated by a thin waist at the level of the porus trigeminus: type IV: comprise all extracranial tumours along the peripheral branches of the 5th cranial nerve with or without minimal intracranial extent (Borges A., 2005; Lufkin R.B. et al., 2000; Lufkin R.B. et al., 2001). Pituitary fossa and cavernous sinus lesions may extend to the Meckel's cavity or involve the cavernous portion of the trigeminal nerve divisions. As many as one third of patients with intracavernous carotid aneurysms have trigeminal nerve manifestations (Borges A., 2005; Kamel H.A. et al., 2001).

The root entry zone, as already in the anatomical description part mentioned, is the cisternal part of the trigeminal nerve just as it enters the pons. Lesions affecting the REZ include vascular compression, primary and secondary neoplasms and infection (Borges A., 2005; Kamel H.A. et al., 2001; Lufkin R.B. et al., 2000; Lufkin R.B. et al., 2001).

The trigeminal nerve is commonly involved by infectious/ inflammatory lesions of the petrous apex, known as petrous apicitis. Facial pain in the distribution of the trigeminal nerve together with 6th cranial nerve palsy and suppurative otitis media make up the triad that defines Gradenigo's syndrome (Larrier D. et al., 2003).

Vascular contact with the REZ is thought to represent the most common cause of idiopathic trigeminal neuralgia, up to 59% of the patients with trigeminal neuralgia symptoms. Other conditions leading to vascular compression include aneurysms, arteriovenous malformations, dural arteriovenous fistulas and vertebrobasilar ectasia.

Primary tumours involving the prepontine cistern include meningioma, trigeminal schwannoma, epidermoid cyst, vestibular schwannoma and lipoma. Secondary neoplasms affecting the REZ include perineural spread of tumours from head and neck malignancy, hematogenous metastasis and leptomeningeal spread of tumours.

Benign inflammatory or infectious conditions such as sarcoidosis, viral encephalitis, herpes neuritis and Lyme disease can also affect the REZ (Kamel H.A. et al., 2001).

Metastatic disease is the second most common lesion (after microvascular compression) to present as a cavernous sinus mass with trigeminal neuropathy (Kamel H.A. et al., 2001). Clival chordoma, osteocartilaginous tumours, invasive pituitary adenomas, plasmocytoma, lymphoma in cavernous sinus, all may lead to trigeminal nerve symptoms. Trigeminal neuropathy is also a feature of Tolosa–Hunt syndrome, a lymphocytic infiltration of the dura in the region of the orbital apex and cavernous sinus leading to painful ophthalmoplegia (Borges A., 2005).

1.5.2.3. Peripheral divisions

The most common lesion affecting the peripheral trigeminal nerve is perineural spread of head and neck malignancies. This occurs more commonly along the second division or maxillary division of the trigeminal nerve due to its extensive branching network, but may also occur along V1 and V3. Several head and neck neoplasms show this type of spread including, *adenoid cystic carcinoma, mucoepidermoid carcinoma, adenocarcinoma, lymphoma and melanoma,* just to mention the most common. Perineural spread can occur in both retrograde or anterograde direction, although retrograde spread is seen more often. Infections of the paranasal sinuses and of the masticator space are also to be mentioned.

Primary tumours of the peripheral branches are typically of nerve sheath origin and are uncommon. Around one-quarter are seen in the setting of neurofibromatosis. Another possible source of trigeminal neuropathy is neural compression at the bony foramina due to fibro-osseous conditions such as fibrous dysplasia and Paget's disease (Borges A., 2005; Kamel H.A. et al., 2001).

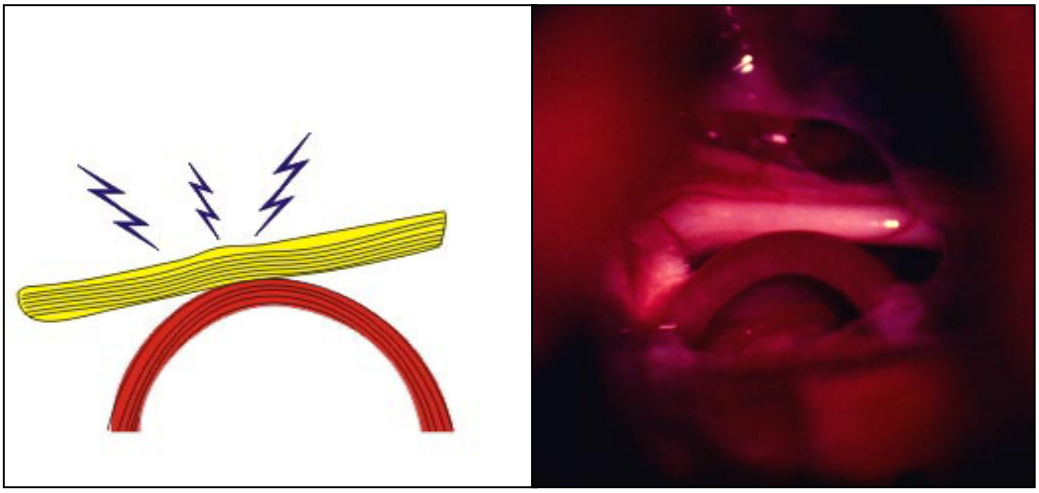
***Table 3**. Causes of trigeminal neuralgia: segmental approach (adapted from (De Marco J.K. et al., 1993)*

BRAINSTEM	Multiple sclerosis Brainstem neoplasm: glioma, hamartoma, metastasis Vascular lesion: infarct, AVM, cavernous angioma Syringohydrobulbia Rhombencephalitis
CISTERNAL SEGMENT	Neurovascular conflict: SCA, AICA, pontine perforators from basilar artery, VB dolichoectasia, petrosal vein, AVM, aneurysm Neoplasm: trigeminal schwannoma, meningioma, epidermoid, lipoma, lymphoma, acoustic schwannoma, hematogenous or perineural spread, CSF seeding Infection/inflammation: trigeminal neuritis (HZV, HSV, Ramsay-Hunt syndrome), basilar meningitis (fungal, TB, sarcoid), spread from contiguous petrous apicitis (Gradenigo's syndrome)
MECKEL'S CAVE	Neoplasm: trigeminal schwannoma, meningioma, epidermoid, hematogenous or perineural spread, CSF seeding, direct invasion from central skull base lesions (clival chordoma, chondrossarcoma, multiple myeloma, bony metastasis)
CAVERNOUS SINUS	Neoplasm: meningioma, trigeminal schwannoma, perineural spread, metastasis, spread from contiguous neoplasms (pituitary macroadenoma) Infectious/inflammatory: Tolosa-Hunt syndrome Vascular: cavernous carotid aneurysm
PERIPHERAL BRANCHES	Perineural spread of head and neck neoplasm (SCC, adenoid cystic carcinoma, mucoepidermoid carcinoma, adenocarcinoma, melanoma, sarcomas) Primary neoplasm: schwannoma, neurofibroma, malignant schwannoma Infection: sinonasal, masticator space

1.5.3. Vascular Compression

Focusing on the peripheral nervous system (PNS), ever since Dandy, it has been widely believed, as already mentioned, that stable or pulsatile microvascular compression of the trigeminal nerve root, close to its point of entry into the pons, by an aberrant loop of blood vessel demyelinates sensory axons in the trigeminal root and that this is the primary pathogenic process that causes trigeminal neuralgia (Fig. 4). This presumption was strongly supported by Jannetta and others, who not only documented vascular compression in a high proportion of trigeminal neuralgia patients, but also showed that prolonged pain relief can often be obtained by microvascular decompression (Devor M. et al., 2002a). So until now neurovascular compression is accepted as being the commonest cause of trigeminal neuralgia unresponsive to medical therapy.

Fig. 4 *Schematic and intraoperative representation of trigeminal neuralgia (with courtesy of Turel K.E., 2004)(Turel K.E., 2004)*



There is also an ongoing controversy regarding the possible offending vessel, with some authors considering both arteries and veins as possible culprits and others denying the role of veins in neurovascular conflicts, due to their plasticity, low pressure and absent pulsatility. Both these issues have not yet been solved by medicine based evidence, due to the lack of well designed prospective, blinded, controlled studies with an adequate number of

patients. However there are described cases even of the pontine vein going through the trigeminal nerve (Turel K.E., 2004).

According to some authors, in order to be clinically significant, the conflicting vessel must be an artery, must displace the normal course of the nerve, cross the nerve perpendicularly and the conflict must be at the level of the root entry zone (at a maximal distance of 6 mm from the emergence of the sensory root from the lateral pons) (Casselman J.W., 2004).

In spite of these strict criteria, there have been reports of neurovascular conflicts only from vessel contact and arising from venous structures isolated or in combination (Kuroiwa T. et al., 1996; Lee S.H. et al., 2000; Matsushima T. et al., 2004; Yoshino N. et al., 2003). Vascular lesions usually involved in neurovascular conflicts with the cisternal segment of the trigeminal nerve include, in decreasing order of frequency, vascular loops, vertebro-basilar dolichoectasia (Stone J.L. et al., 1993), arterio-venous malformations and dural arterio-venous fistulas. Vascular loops most commonly impinging upon the trigeminal nerve include branches of the:

- superior cerebellar artery (according to different authors 66.5 – 88%),
- anterior inferior cerebellar artery (5.7 – 25%),
- pontine branches of the basilar artery (1.1 – 23%),
- posterior inferior cerebellar artery (0 – 1.1%) and
- aberrant veins (5.5 – 16.6%) (Go J.L. et al., 2001; Linskey M.E. et al., 1994).

The below presented schematic pictures show the relationship of neurovascular conflict (Fig. 5) (Poeck K. et al., 2001).

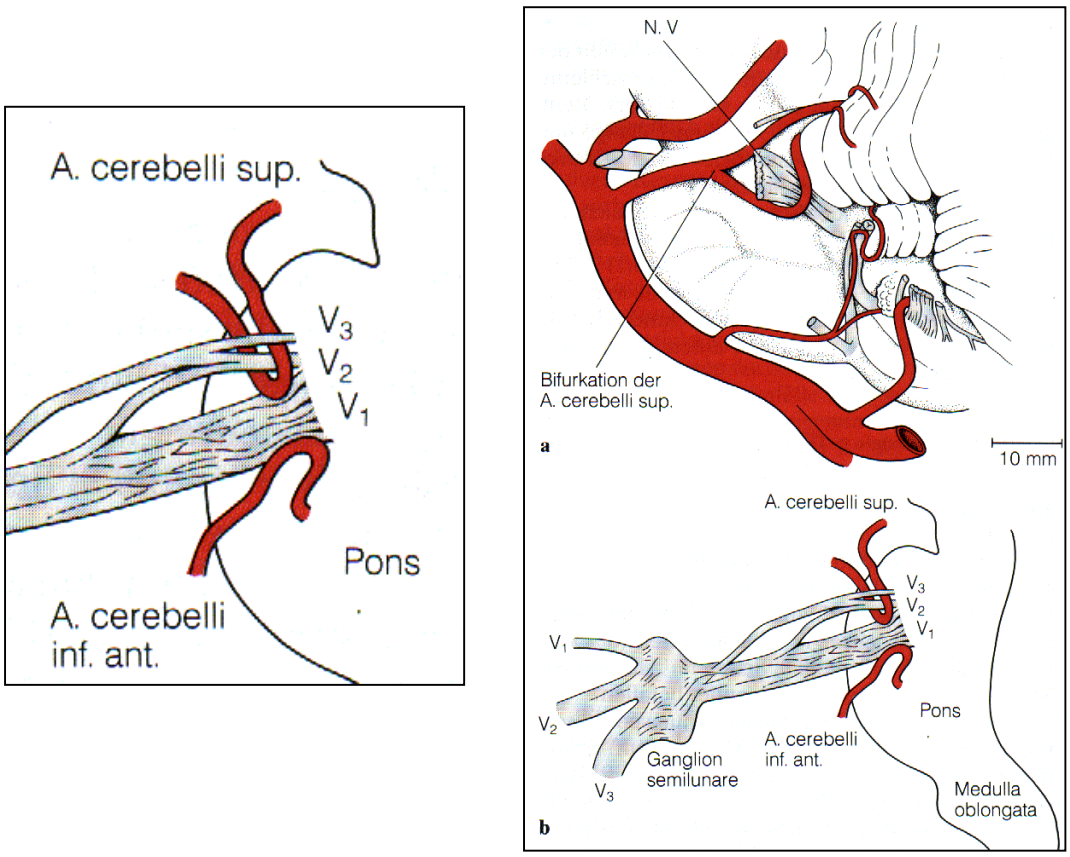


Fig. 5 *The relationship of neurovascular conflict, (Poeck K. et al., 2001).*

The exact correlation of affecting vessel according to different authors is given in the Table **4** (Sindou M. et al., 2002).

Table 4 *Conflicting Vessels found at operations in the most detailed series of MVD for TGN (Sindou M. et al., 2002)*

Authors	Total no. of patients	SCA		AICA		PICA		VBA		Vein only		Vein+ artery		Unspecified small artery		No conflict	
		No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Barker et al.	1204	909	75	116	10	8	1	28	23	151	13	671	56	189	15.2	0	0
Klun	215	115	66.5	13	7.5	0	0	2	1.1	13	7.5	11	6.3	19	11	42	19.5
Zorman & Wilson	118	75	83.3	14	15.5	1	1.1	1	1.1	15	16.6	?	?	0	0	28	23.7
Piatt& Wilkins	103	57	72.1	11	13.9	0	0	2	2.5	5	6.3	?	?	10	12.6	24	23.3
Kolluri & Heros	71	56	80	4	5.7	0	0	1	1.4	7	10	19	27.1	2	2.8	1	1.4
Sindou et al.	579	493	88	141	25	0	0	20	3.5	31	5.5	124	22.1	0	0	19	3.2

AICA – anterior inferior cerebellar artery; PICA – posterior inferior cerebellar artery; SCA – superior cerebellar artery; VBA – vertebro-basilar arteries; MVD – microvascular decompression; TGN – trigeminal neuralgia

Sindou M. et al (2002) communicate that during their posterior fossa exploration on patients with trigeminal neuralgia, which was resistant to prolonged and high doses of carbamazepine and other anticonvulsants, in 96.7% cases, one or several conflicting vessels were identified:

- superior cerebellar artery (alone or in association with other conflicting vessels) – 88% of the patients,
- anterior inferior cerebellar artery in 25.1%,
- a vein embedded in the nerve in 27.6%,
- basilar artery in 3.5%,
- several conflicting vessels were found in association in 37.8% of the patients.

In the remaining 3.3% of the patients with idiopathic trigeminal neuralgia, no vascular conflict was found, despite of the careful and complete exploration of the trigeminal root, from Porus of Meckel's cave to trigeminal REZ at the pons. These patients had no clinical peculiarities compared to the group with "conflicting" vessel. But anatomically in most cases the nerve was rather globally atrophic without any obvious identifiable cause for it (Sindou M. et al., 2002).

Illustration of the various types of conflicting vessels are given in fig. 6 (Sindou M. et al., 2002).

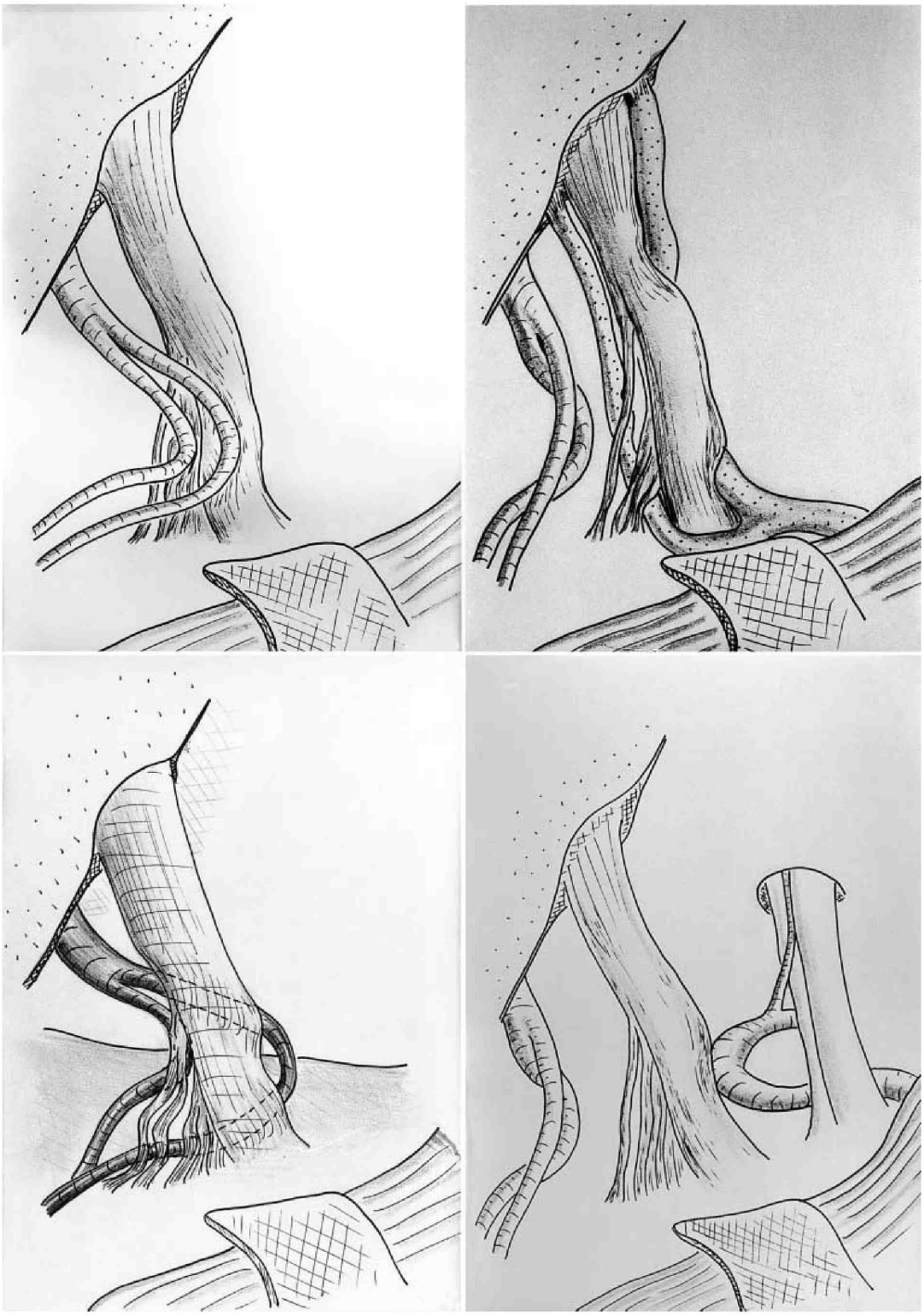


Fig. 6 *(Sindou M. et al., 2002): Examples of various types of Neuro-vascular conflicts (seen through posterior approach of right cerebello-pontine angle): superior cerebellar artery in supero-medial (upper left) or superolateral (upper right) position; anterior inferior cerebellar artery inferiorly compressing the Trigeminal Root Entry Zone at the pons (lower left); satellite trigeminal veins embedded in the trigeminal nerve tissue (lower right),*

Sindou M et al., 2002 also have described the anatomical changes and the site of the conflicts reported to the trigeminal nerve root in case of vascular compression during their microvascular decompression. These observations are classified as followed:

1.5.3.1. Site of the conflicts along the root (after Sindou M. et al., 2002)

In 52.3% of the patients the clearcut conflicts were located at the very Trigeminal Root Entry Zone (TREZ) – less than 7 mm from the entry into the pons (=**juxta-pontine segment** of the root), in 54.3% - at the midthird of the root (=**mid-cisternall segment**) and in 9.8% - at the exit of the root from Meckel's cave (=**juxta-petrous segment**). One or several types could be found in the same patient (Fig. 7).

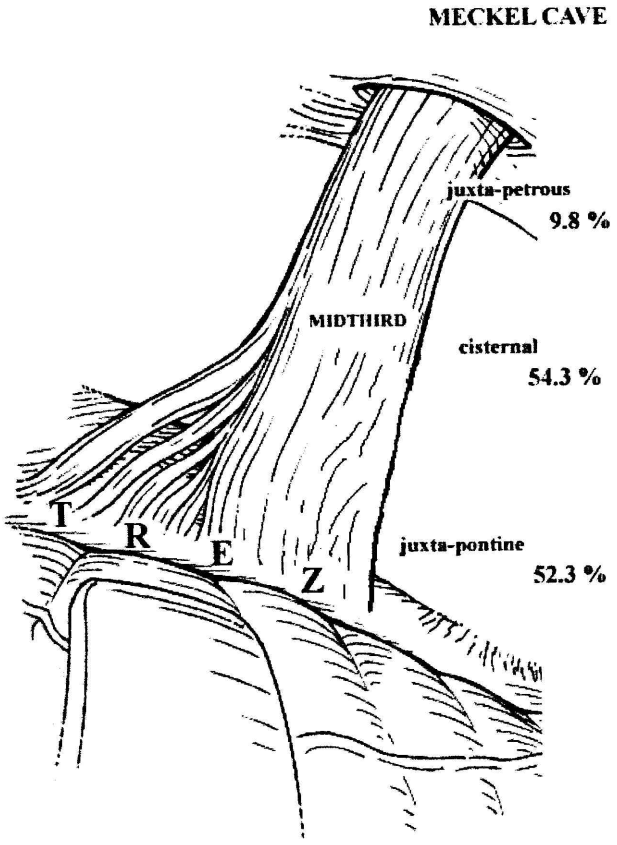


Fig. 7 *(Sindou M. et al., 2002): Site of the conflicts along the nerve (Sindou)*

1.5.3.2. Location of the neurovascular conflict around the circumference of the root (after Sindou M. et al., 2002)

Sindou M. and his colleagues described the following location of the neurovascular conflict around the circumference of the nerve root:

supero-medial to the root (SM) - 53.9%,

supero-lateral (SL) - 31.6%,

and inferior (INF) - 14.5% (Fig. 8).

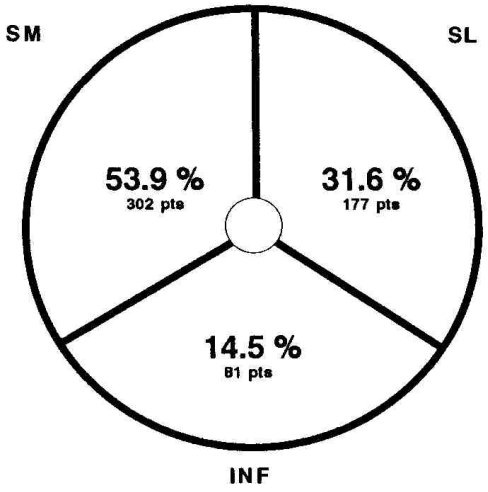


Fig. 8 *(Sindou M. et al., 2002): Relation of the conflicts to surface of the root (Sindou)*

In his turn, Norio Yoshino (2003) classified the position of the blood vessel compressing the nerve into one of the following four sites: cranial, caudal, medial, or lateral as in figure 9. When compression was detected in two or more sites, it was defined as a compression of two or more sites.

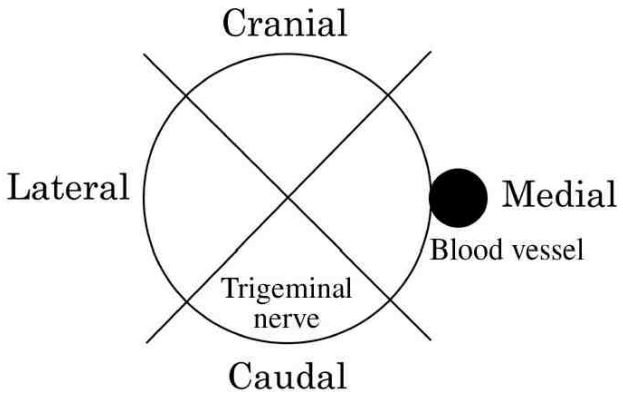


Fig. 9 *(Yoshino N. et al., 2003). Schematic demonstrates the classification of the position of a blood vessel that compresses the trigeminal nerve on its cross section. When the blood vessel has compressed the trigeminal nerve at the position shown in this schematic, it is classified as a medial site.*

1.5.3.3. Correlations between topography of pain and location of the neurovascular conflicts around the root

Sindou M. et al. (2002) made up a study, in which there was either one conflicting vessel or if several, a markedly dominant one and elaborated the correlation between topography of pain (according to the trigeminal branches) and location of the conflicting vessel in relation to the circumference of the root, i.e. supero-medial, supero-lateral or inferior. The results are:

- when the first division (V1) was affected – alone or in association with other division(s), the neurovascular conflict (NVC) was located superomedially in 74%, superolaterally in 20.5% and inferiorly in 5.5%;
- when the second division (V2) was involved – alone or in association, the NVC was located superomedially in 61%, superolaterally in 28% and inferiorly in 10%;
- when the third division (V3) was affected – alone or in association, the NVC was located superomedially in 53%, superolaterally in 30% and inferiorly in 17%.

Because there is a somatotopic distribution of the sensory fibers in the trigeminal root – the fibers from V1 being situated superiorly and medially, the ones from V3 inferiorly and laterally, and the one from V2 in an intermediate situation, there is a correlation between the trigeminal division(s) clinically involved and the various anatomical locations of the vascular conflicts. The data of Sindou M. et al., 2002 suggest that the higher the topography of facial pain is, the more frequently the superior location of the conflict.

Yoshino et al, 2003 also demonstrated a close relationship between the region of neuralgic manifestation, where a corresponding division of the trigeminal nerve is distributed, and the site of vascular compression in the trigeminal nerve. It has been reported that the first branch fibers of the trigeminal nerve at the REZ are distributed in one-third of the cranial area; the second branch fibers, in one-third of the middle area; and the third branch fibers, in one-third of the caudal area. As shown in Figure 10, the nerve fibers of the second branch are widely distributed medially and those of the third branch are widely distributed laterally.

Summarising, the higher the territory of trigeminal neuralgia, the most frequently the location of neurovascular compression at the supero-medial aspect of the nerve was, and the lower the neuralgia, the more often the inferior location of neurovascular compression was. More accurate, in patients with pain in V1 division the neurovascular conflict was always supero-medial. In patients with pain in V2 division the neurovascular conflict was supero-medial in 59.1%, supero-lateral in 30.7% and inferior in 10.2%. In patients with pain in V3 the neurovascular conflict was supero-medial in 46,8%, supero-lateral in 29% and inferior in 24.2% (Sindou M. et al., 2002).

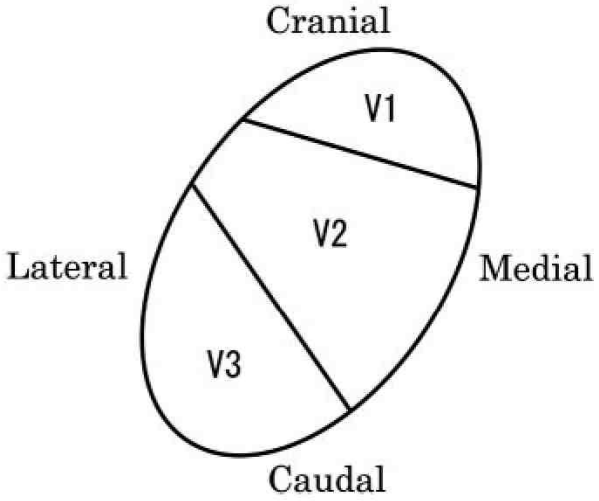


Fig. 10 *(Yoshino N. et al., 2003). Schematic of the trigeminal nerve fiber arrays at the REZ. The nerve fibers of the second branch (V2) are widely distributed medially, those of the third branch (V3) are widely distributed laterally, and those of the first branch (V1) are distributed cranially.*

1.5.3.4. Degree of severity of the conflicts (Sindou M. et al., 2002)

The following degrees of conflict severity are described in Sindou's study:

- **grade I**: the vessel is in contact with the root but without any visible indentation (17.6%);
- **grade II**: a displacement and/or a distortion of the root (49.2%);
- **grade III**: a clear-cut and marked indentation of the root (33.2%).

1.5.3.5. Root alterations and surrounding abnormalities

Besides eventual segmental indentations of the nerve at the side of the offending vessel(s), alterations of the whole trigeminal nerve root were frequently observed. In 46.5% the nerve had a significant degree of atrophy, i.e., caliber diminished by one third or more. In 17.5% the atrophy was more marked, with a caliber reduction of the order of two-thirds of the normal caliber together with a ribbon-shape and a greyish colour. In addition the following abnormalities were found by Sindou’s team: local thickening of the arachnoid with strong adhesions to the nerve (18.2%), an absence of, or a shallow, cisternal space around the nerve due to the small size of the

posterior fossa (3.9%) and a marked angulation of the root at its junction with the triangular plexus on crossing over the petrous ridge after exit from Meckel's cave (12.6%). Such an angulation frequently coexists with an elongated superior cerebellar artery in a superior position, strongly pushing down the nerve, making it flat and even sometimes hammock-shaped and markedly atrophic (Sindou M. et al., 2002).

1.5.3.6. Microvascular decompression the elective operative treatment in TGN caused by microvascular compression

It is well known that microvascular decompression at the trigeminal root entry zone is still the most effective and approved treatment for patients with trigeminal neuralgia in case of intraoperative presence of a causative vessel. It relieves neurovascular compression in cranial nerve V by dissecting and buffering the offending vessel. A Goretex® membrane or Teflon interponate is placed between nerve and vessel in order to get separation from each other and provide relief from constant trauma caused by pulsation of the offending vessel. In most of the patients (about 90%) elimination of the compression leads to long-term pain relief and patients can discontinue their medications (Barker F.G. et al., 1996; Barker F.G. et al., 1997; Javadpour M. et al., 2003; Kress B. et al., 2004; Nurmikko T.J. et al., 2001; Richter H.P. et al., 1984; Sun T. et al., 1994; Taarnhoj P., 1982).

Microvascular decompression (MVD) of the trigeminal nerve is now recognized as the sole medical and surgical management technique that directly addresses the presumed underlying pathology. Although the results of MVD have endured the longest regarding the preservation of facial sensation, surgeons have been cautious to accept this as the universal treatment for patients with TGN because posterior fossa surgery is traditionally associated with the risk of serious morbidity and no negligible mortality. However, contemporary microsurgical and anesthetic techniques have allowed neurosurgeons to operate in the posterior fossa with more confidence and safety. The preservation of trigeminal sensation and long-

term pain relief have become attractive endpoints for patients faced with the decision of treatment modality (Elias W.J. et al., 2002).

1.5.4. Other compressive lesions*:*

As prior mentioned, a wide range of other compressive lesions can cause trigeminal neuralgia. These include vestibular schwannomas (Matthies C. et al., 1997), meningeomas (Haddad F.S. et al., 1990; Ogasawara K. et al., 1995), epidermoid cysts (Jamjoom A.B. et al., 1996; Mohanty A. et al., 1997) and various other cysts and tumours (Jamjoom A.B. et al., 1996; Kato T. et al., 1995; Matsuura N. et al., 1996; Revuelta R. et al., 1995).

In some reported cases, the neuralgia was contralateral to the side of the compressing lesion (Haddad F.S. et al., 1990; Matsuura N. et al., 1996; Revuelta R. et al., 1995). It follows that trigeminal nerve root compression can be mediated not only by the tumour itself, or by an interposed blood vessel, but also by the distortion of the contents of the posterior fossa in case of tumour with displacement of the nerve root against a blood vessel or the skull base at the contralateral side (Love S. et al., 2001).

According to some studies, in a series of patients whose trigeminal neuralgia was associated with an extra-axial tumour in the posterior fossa, vascular compression of the trigeminal nerve root entry zone was found in all cases (Barker F.G. et al., 1996). This is one more evidence that the pathogenesis of the trigeminal neuralgia is primarily mediated by a neurovascular conflict.

Schwannomas arising from the trigeminal nerve may present with typical trigeminal neuralgia (McCormick P.C. et al., 1988).

There are also registered cases of recurrent trigeminal neuralgia caused by prosthetic material (Teflon or polyurethane sponge) used for microvascular decompression of the trigeminal nerve root (Fujimaki T. et al., 1996; Sun T. et al., 1994).

Rarely, trigeminal neuralgia results from bony compression of the nerve, due to an osteoma (Ruelle A. et al., 1994) or an osteogenesis imperfecta (Reilly M.M. et al., 1995).

1.5.5. Primary demyelinating disorders

Trigeminal neuralgia is a well-recognized complication of multiple sclerosis. Typically, a plaque of demyelination encompasses the root entry zone of the trigeminal nerve in the pons. Rarely, patients with peripheral nerve demyelination due to Charcot–Marie–Tooth disease develop trigeminal neuralgia (Coffey R.J. et al., 1991). Vascular compression of the trigeminal nerve root may contribute to trigeminal neuralgia even in patients with demyelinating disorders; compression of the root entry zone by a blood vessel has been demonstrated in a sizeable minority of patients with multiple sclerosis and trigeminal neuralgia and in an occasional patient with Charcot–Marie–Tooth disease. In many such cases, decompression of the nerve root leads to relief of symptoms (Coffey R.J. et al., 1991; Love S. et al., 2001).

1.6. Pathophysiology and pathogenesis of the TGN

The key feature of trigeminal neuralgia pain is its very dynamic nature, which is difficult to explain in purely anatomical terms (Nurmikko T.J. et al., 2001). The pathophysiology of trigeminal neuralgia has been much debated, the pain being ascribed variously to hyperactivity or abnormal discharges arising from the gasserian ganglion, the “injured” nerve root and the trigeminal nucleus within the brainstem (Burchiel K.J., 1993; Love S. et al., 2001; Moller A.R., 1999; Moulin D.E., 1998; Rappaport Z.H. et al., 1994).

It is still thought that none of the many existing theories fully explain all known characteristics of trigeminal neuralgia pain (Kitt C.A. et al., 2000; Tenser R.B., 1998). The most of current evidence points to the trigeminal nerve rather than the CNS as the site of generation of trigeminal neuralgia. Any credible explanation of the pathophysiology has to account for both the abnormal generation of sensory impulse and their spread from fibres subserving light touch to pathways involved in the perception of pain in non-congruous region of the face (Love S. et al., 2001).

As suggested by Rappaport and Devor (Rappaport Z.H. et al., 1994) the above “cross-excitation” may be at the root of the unique pain seen in trigeminal neuralgia and offers a logical explanation for the extraordinary initial responsiveness of pain in trigeminal neuralgia to almost any procedure aimed at the nerve. The last evidences show that it is unlikely that the generator of pain is located in the central nervous system but central sensitisation may well develop following prolonged barrage of nerve impulses which can explain the development of some features of atypical trigeminal neuralgia (Love S. et al., 2001; Nurmikko T.J. et al., 2001). Equally, continuous pain in the atypical form can result from the progressive damage to the central terminals of trigeminal afferents, which become the source of continuous ectopic discharges (Nurmikko T.J. et al., 2001).

These existing evidences show that a slowly evolving process, either a compression exerted on the nerve by the blood vessel or tumour or

affectation of the nerve by an MS plaque at the level of the root entry zone, leads to increased excitability in the trigeminal afferents and subsequently to typical trigeminal neuralgia. Sensory impairment in trigeminal neuralgia has been documented by several authors (Bowsher D. et al., 1997; Nurmikko T.J., 1991)using quantitative sensory testing and neurophysiological methods.

The trigeminal ganglion in trigeminal neuralgia is not normal but shows unique pathological changes, such as degenerative hypermyelination and formation of “microneuromata” (Kerr F.W., 1967). The ganglion cells themselves appear mostly intact. At the site of vascular compression of the trigeminal root, electron microscopic studies show demyelination and remyelination.

Vasodilatation is known to occur in trigeminal neuralgia and it normalises when pain is controlled (Nurmikko T.J. et al., 2001). There is a good experimental evidence that ectopic impulses can arise from demyelinated axons (Love S. et al., 2001; Rasminsky M., 1978; Smith K.J. et al., 1980b; Smith K.J. et al., 1982).

Smith and McDonald demonstrated that many experimentally demyelinated nerve fibres in the dorsal spinal white matter of the cat were spontaneously active, discharging either in small bursts or steadily at 15-45 impulses per second for many hours (Smith K.J. et al., 1980b; Smith K.J. et al., 1982). Small deformation of the spinal cord in the region of the demyelination not only increased the level of activity in fibres already discharging, but also transiently induced activity in fibres that had previously been electrically silent. In the context of vascular compression of the trigeminal nerve root, these observations raise the possibility that pulsatile compression of the demyelinated axons by an overlying blood vessel may be responsible for initiating the aberrant impulses in some patients (Love S. et al., 2001).

Insofar as the subsequent spread of impulses is concerned (Hilton D.A. et al., 1994; Love S. et al., 1998; Love S. et al., 2001) that the close apposition of demyelinated axons in region of vascular compression should facilitate the ephaptic transmission of nerve impulses, as has been demonstrated between immediately adjacent non-myelinated axons in experimental studies (Ramon F. et al., 1978; Rasminsky M. et al., 1978). Ephaptic “cross-talk” between fibres mediating light touch and those involved in the generation of pain may account for the precipitation of attacks of neuralgia by light tactile stimulation of facial trigger zones. The frequency of involvement of the trigeminal nerve root entry zone in multiple sclerosis patients with trigeminal neuralgia as well as in patients with vascular compression probably reflects the fact that fibres subserving light touch and those involved in the generation of pain are in closest proximity in this region (Love S. et al., 2001).

Early ultrastructural studies (Beaver D.L., 1967; Kerr F.W. et al., 1966) concentrated on the morphology of the trigeminal ganglion and nerve and described a range of abnormalities of myelin sheaths, including proliferative degenerative changes and myelin disintegration. These studies antedated the observations of Jannetta and others on the association of trigeminal neuralgia with vascular compression of the nerve root (Love S. et al., 2001).

The first detailed description of ultrastructural abnormalities in the nerve root in the region of vascular compression was by Hilton and colleagues (Hilton D.A. et al., 1994). The authors observed focal loss of myelin and close apposition of demyelinated axons. There were few residual oligodendrocytes and no inflammatory cells. Immunoelectron microscopy for glial fibrillary acid protein revealed that astrocyte processes were largely confined to the periphery of the lesion (Love S. et al., 2001).

On the further trigeminal rhizotomy specimens from patients with trigeminal neuralgia in the absence of detectable vascular compression of the nerve root, only partially from the patients with multiple sclerosis, showed demyelination, but in those cases astrocyte processes separated many of the demyelinated axons and the lesions contained perivascular clusters of

perivascular lymphocytes and scattered lipid-laden macrophages (Love S. et al., 2001).

The findings in relations to vascular compression of the nerve root were confirmed in a subsequent electron microscope study of trigeminal rhizotomy specimens from some further patients with medically intractable trigeminal neuralgia, in whom, because of the local vascular anatomy, the compressing artery or vein could not safely be repositioned (Love S. et al., 1998). In those specimens, examination revealed a circumscribed zone of chronic demyelination immediately beneath the region of indentation. The demyelination was restricted to proximal (CNS) tissue but occurred close to the junction of this part of the root with distal (PNS) tissue. Adjacent to the zone of demyelination were small numbers of thinly myelinated axons, reflecting either demyelination and remyelination, or partial demyelination of the affected fibres (Love S. et al., 2001).

Similar findings were described by Rappaport and colleagues (Rappaport Z.H. et al., 1997). Although Rappaport illustrated disrupted myelin in the proximal, CNS part of the trigeminal root, they also described (but did not illustrate) the presence of large numbers of collagen fibrils in the extracellular matrix, suggesting that the abnormalities in their cases also involved the distal part of the nerve root (Love S. et al., 1998).

According to the studies of Love and his colleagues in the trigeminal rhizotomy specimens (large enough to allow assessment of the size of the zone of demyelination) from patients with vascular compression of the nerve root, the zone of demyelination limited to the immediate vicinity of the point of vascular indentation, extends no more than ~2mm in any direction. Foci of apposition of demyelinated axons and a paucity of glial and inflammatory cells have been relatively consistent ultrastructural features in their biopsies (Love S. et al., 2001). It should be mentioned that in their study Love and his colleagues they have found the trigeminal rhizotomy specimen from a small number of patients with visible vascular compression of the nerve root on

neuroimaging or at craniotomy to be ultrastructurally normal, without demyelination.

However, as the region of demyelination has rarely been visible macroscopically in the cases of vascular compression and a typical rhizotomy specimen measures no more than a few millimetres in diameter, it seems likely that the lack of abnormality in a small proportion of specimens reflects sampling error rather than heterogeneity in the pathology and pathogenesis of the disorder (Love S. et al., 2001).

In some different studies Fish and Blakemore, (Fish C.J. et al., 1983), Clifford-Jones et al., (Clifford-Jones R.E. et al., 1985) commented on the occurrence of partial demyelination after chronic compression of white matter. The most persuasive evidence of this was the finding of variations in the thickness of the myelin sheath along individual internodes. In trigeminal rhizotomy specimens from patients with trigeminal neuralgia, the distribution and extent of charge are more variable than in the experimental animals and the thinly myelinated fibres, in particular, tend to be distributed quite unpredictably. This may reflect several differences between these experimental models and trigeminal neuralgia, including the greater chronicity of the compression in the human disorder and the fact that the compression is likely to be pulsatile in nature, particularly if an artery is involved rather than a vein (Love S. et al., 2001).

An objection that has been raised to a central role for demyelination in the development of trigeminal neuralgia relates to the rapid clinical and electrophysiological recovery that usually occurs after surgical decompression of the affected nerve root. Many patients experience complete relief of symptoms immediately after operation, and electrophysiological monitoring of conduction through the compressed nerve root has shown very substantial recovery of conduction almost immediately after microvascular decompression in many patients (Leandri M. et al., 1998). The explanation, we suggest, is that the clinical improvement and recovery of conduction reflect two distinct processes (Love S. et al., 2001).

1. The rapid relief of clinical symptoms probably reflects the cessation of the ectopic generation of impulses and of their ephaptic spread to adjust fibres. Experimental studies indicate that reversal of the focal indentation and distortion of demyelinated axons is likely to reduce spontaneous impulse activity within the region of demyelination (Smith K.J. et al., 1980b; Smith K.J. et al., 1982). Release from compression should also lead to the separation of demyelinated axons that were previously compacted together and this would be expected to prevent ephaptic cross-talk. Reperfusion through previously compressed endoneurial capillaries and venules and endoneurial oedema resulting from the trauma of surgical manipulation may further contribute to separation of the demyelinated fibres.

2. The recovery of conduction probably reflects rapid reversal of conduction block in relatively large-calibre, fast-conducting fibres that are not demyelinated. Reversible conduction block is a well-documented manifestation of nerve fibre compression. Although most extensively investigated in the PNS, several studies have demonstrated compression-induced conduction block within the CNS (Bennett M.H. et al., 1983; Sakatani K. et al., 1989; Shi R. et al., 1996). This is the most likely to occur during the conduction of high-frequency trains of impulses (Sakatani K. et al., 1989). In compression of low-to-moderate severity, large-calibre myelinated fibres seem to be more susceptible than smaller fibres to conduction block (Battista A.F. et al., 1983; Fern R. et al., 1991). Reversal of conduction block in these large fibres would account for the rapid fall in conduction latencies across the trigeminal nerve root as soon as it is decompressed. Compression-induced conduction block in a proportion of the larger myelinated fibres may also explained the mild reduction in the perception of light touch over a more extensive area of trigeminal innervation than could be attributed to the impairment of conduction across the relatively small zone of nerve root demyelination (Love S. et al., 2001).

The fact that clinical improvement appears to be dissociated from recovery of conduction in some patients after microvascular decompression support the concept that these are two distinct processes that are simply related by their common aetiology: nerve root compression (Love S. et al., 2001).

The pathogenesis of some phenomena related to trigeminal neuralgia remains unclear. These include the very occasional triggering of attacks by stimuli outside of the field of innervation of the trigeminal nerve, and even by bright lights or loud noises (Bowsher D. et al., 1997), which must involve central pathways. Another well-documented findings in some patients is the occurrence of a refractory period of second to minutes after an attack of trigeminal neuralgia, during which further attacks cannot be provoked (Kugelberg E. et al., 1959).

Experimental studies have shown the length of time for which nerve fibres are refractory to further excitation to be increased after demyelination in both the PNS (Smith K.J. et al., 1980a) and the CNS (Smith K.J. et al., 1981), but the duration of refractory period in this experimental studies is much shorter than that in patients with trigeminal neuralgia.

However, factors other than demyelination “per se” could conceivably delay the restoration of membrane potentials and excitability after an episode of trigeminal neuralgia. These include impaired mitocondrial generation of ATP in an environment of focal endoneurial ischaemia due to the nerve root compression, with resulting delay in the restoration of ionic gradients after a burst of discharges and the paucity of extracellular fluid and increased longitudinal resistance to ionic current between closely juxtaposed demyelinated axons (Love S. et al., 2001).

Following neuroablative procedures, the degree of sensory loss correlates positively with the duration of pain relief (Nurmikko T.J. et al., 2001; Taha J.M. et al., 1995). Microvascular decompression (MVD) relieves neurovascular compression in cranial nerve V by dissecting and buffering the

offending vessel (Leandri M. et al., 1998; Miles J.B. et al., 1997; Nurmikko T.J. et al., 2001).

The role, if any, of remyelination in initial symptomatic recovery after microvascular decompression is unclear. Clearly, remyelination cannot account for the immediate relief from neuralgia. In the longer term, however, it is possible that remyelination helps to ensure that relief of symptoms is sustained. Remyelination can also be responsible for spontaneous remission of trigeminal neuralgia in some patients. Failure of microvascular decompression to relief symptoms is most common in patients with very long-standing disease, in whom severe local depletion of oligodendrocytes and astrocytes may prevent effective remyelination after decompressive surgery.

A further possibility is that the aberrant remyelination that is occasionally seen in the compressed nerve root may, by preventing the separation of groups of apposed axons after decompression, contribute to the failure of this procedure in a few patients (Love S. et al., 2001).

Devor and his colleagues (Devor M. et al., 2002a) put also to discussions as a challenge some paradoxical observations. Even if trigeminal root compression is indeed the primary pathology in trigeminal neuralgia, demyelination alone does not provide a straightforward account of the disease's characteristic symptomatology. Activity in myelinated sensory axons is generally associated with touch and vibration sense, not pain. Furthermore, demyelination "per se" is expected to block impulse propagation, and hence yields patches of numbness rather than pain paroxysms.

Indeed, careful examination of trigeminal neuralgia patients between pain attacks often reveals minor sensory loss. Ephaptic contact between adjacent denuded axons has long been cited as a pain mechanism in trigeminal neuralgia, if without much specific evidence. Although ephapsis might amplify the sensation evoked by applied stimuli, generating hyperesthesia and even

pain, it does not explain why pain paroxysms in trigeminal neuralgia outlast the triggering stimulus and why their intensity bears no relation to the intensity of the stimulus (Devor M. et al., 2002a).

Marshall Devor (Devor M. et al., 2002a) described also some observations which are still to be explained: Scientific inference can be a powerful tool, and the existence of trigeminal neuralgia patients at least in principle provides a platform for critically testing hypothetical schemata. It is important, however, to define the specific signs and symptoms that need explanations. For example, although it is obvious that any successful theory must explain why a weak tactile stimulus at a trigger point evokes pain, not all investigators have considered the need to explain why the pain outlasts the stimulus or why it comes to an end after a characteristic period, usually measured in seconds or at most minutes.

1.7. Diagnosis of TGN

No specific tests exist for the diagnosis of trigeminal neuralgia (Nurmikko T.J. et al., 2001). Until recently, it has been impossible to demonstrate vascular compression at the root entry or exit zone of the trigeminal nerve in patients with trigeminal neuralgia preoperatively, although surgical findings have revealed apparent neurovascular compression and its correction has resulted in a good outcome in most cases (Fukuda H. et al., 2003).

Revealing the anatomic correlation between nerves and vessels at the REZ preoperatively would be useful to predict operative findings (Fukuda H. et al., 2003).

The most deciding factor to diagnose trigeminal neuralgia and to establish the operative indications is until nowadays the characteristic pain criteria. Trigeminal neuralgia remains a clinical diagnosis dependent on a history of sudden shooting or stabbing pain, coming as solitary sensation or paroxysms and separated by pain-free intervals (Nurmikko T.J. et al., 2001).

The accuracy of diagnosis depends on how carefully the history was taken and how thoroughly the pain characteristics were first ascertained (Zakrzewska J.M., 2002). It is important to estimate the frequency of each feature because these will determine reliability during diagnosis (e.g., 95-70% of patients will use words such as sharp, cutting, or shooting to describe trigeminal neuralgia and 73% will have pain-free intervals). In contrast only 1 to 2% of patients will report bilateral pain, hence, trigeminal neuralgia will not be considered in a patient reporting sharp but bilateral continuous (Zakrzewska J.M., 2002). Adding 95% confidence intervals provide improved validity. According the observations in literature (e.g., both (Katusic S. et al., 1990; Rasmussen P., 1990) there are reported low numbers of bilateral cases with confidence limits of 3.9-1.26 (Katusic) and 3.8-0.18 (Rasmussen).

Provoking factors are also strong predictors for the presence of trigeminal neuralgia (96%), whereas in idiopathic facial pains (60%) are likely to be

reported. The provoking factors most frequently reported are chewing and talking (76%), whereas in idiopathic facial pain the corresponding figures are lower (24%). Trigger areas are reported in 50% of patients with trigeminal neuralgia and in only 9% of patients with idiopathic facial pain (Zakrzewska J.M., 2002).

1.7.1. Differential diagnosis

The list of differential diagnoses is long and includes a number of pathological conditions affecting the sinuses, teeth, temporomandibular joints, eyes, nose, and the neck. Most of these are easily ruled out after the interview and brief clinical examination

Some patients have many features of trigeminal neuralgia, yet some aspects of their history do not agree with the typical manifestations of the condition. The surgical literature contains many references to atypical trigeminal neuralgia having specifically divided patients into classical and atypical trigeminal neuralgia groups. Not only are outcomes after surgery different for these groups of patients, but there may be underlying physiological reasons (e.g., increased neurological damage). Table 5 lists the features of classical and atypical trigeminal neuralgia (Zakrzewska J.M., 2002). These data are based on literature reviews and have not been validated by case control studies or consensus views.

Table 5 *Differential diagnosis of orofacial pains that present predominately as unilateral pains with no immediately identifiable cause (Zakrzewska J 2002)*

Condition	**Prevalence**	**Major location and radiation**	**Timing**	**Character/severity**	**Provoking factors**	**Associated factors**
Dental -Pulpal-exposed dentine due to caries, defective restoration, traumatic	Very common	Well localised to a tooth	Can last for 10-20 min after sugary stimulus	Sharp, stabbing, throbbing, dull, moderate to severe	Hot, cold, or sweet foods provoke it, rarely spontaneous	Immediate relief on removal of stimulus
Fractured or cracked tooth	Fairly common	Localised to one or two teeth, but may be poorly localised, difficult to visualize	Very short lasting, seconds, intermittent, hours	Sharp, moderate	Biting, never spontaneous, may be sensitive to heat	Rebound pain, worse after force removed, opposing natural tooth normally present
Pulpal–Chronic pulpitis	Common	Poorly localised intraorally	Intermittent, hours	Mild, dull, throbbing	Occasionally heat	Often large restoration
Periodontal-Chronic apical periodontitis	Common	Poorly localised intraoral	Intermittent, minutes to hours	Mild, dull, throbbing	Large restoration	Sinus may be visible, bad taste
Bony pain–osteomyelitis	Rare	Most often mandible, widespread	Continuous	Throbbing, severe	Biting on mobile tooth	Pyrexia, malaise, trismus, swelling, may be parasthesia, pus, mobile teeth, sequestra
Denture pain, pressure on mental nerve secondary TGN	Rare	Localized intraoral	Intermittent, daily	Aching, may be sharp if over mental nerve	Eating with denture	Often redness, ulceration in area of pressure
Neurological TGN (classical/typical)	Rare	Intraoral or extraoral in trigeminal region	Each episode of pain lasts for seconds to minutes, refractory periods and long periods of no pain	Sharp, shooting, moderate to very severe	Light-touch provoked (e.g., eating, washing, talking)	Discrete trigger zones

Table 5 *Differential diagnosis of orofacial pains that present predominately as unilateral pains with no immediately identifiable cause (Zakrzewska J 2002) continued*

Condition	**Prevalence**	**Major location and radiation**	**Timing**	**Character/severity**	**Provoking factors**	**Associated factors**
Atypical TGN	Rare	Intraoral or extraoral in trigeminal region	Sharp attacks lasting seconds to minutes, more continuous-type background pain, less likely to have complete pain remission	Sharp, shooting, moderate to severe but also dull, burning, continuous mild background pain	Light-touch provoked, but continuous-type pain not so clearly provoked	May have small trigger areas, variable pattern
Trigeminal neuropathy	Very rare	Trigeminal area, but may radiate beyond	Continuous	Dull with sharp exacerbation	Areas of allodynia, light touch	Sensory loss subjective/ objective, progressive, vasodilatation and swelling may occur
Glossofaryngeal neuralgia	Very rare	Intraoral in distribution of glossofaryngeal	Each episode lasts for seconds up to 2 min	Sharp, stabbing, burning, severe	Swallowing, chewing, talking	No neurological deficit
Postherpetic neuralgia	Rare	Most commonly first division of trigeminal	Continuous pain	Tingling, severity, varies	Tactile allodynia	More than 6/12 days after acute herpes zoster
Vascular Cluster headache, episodic pain-free periods, chronic, no remissions	Rare	Orbital, supraiorbital, temporal	15-180 min to several hours, from 1 every other day to 8 per day	Hot, searing, punctate, severe	Vasodilators (e.g., alcohol)	Conjunctival injection, lacrimation, nasal congestion, rhinorrhea,, sweating, miosis, ptosis, eyelid edema, restlessness
SUNCT[1]	Very rare	Ocular, periocular, but may radiate to frontotemporal area, upper jaw, and palate	Each episode last up to 2 minutes intermittent, several attacks per day and then may remit	Burning, electrical, stabbing, severe	Neck movements	Conjunctival injection, lacrimation, nasal stuffiness, rhinorrhea

Table 5 *Differential diagnosis of orofacial pains that present predominately as unilateral pains with no immediately identifiable cause (Zakrzewska J 2002) continued*

Condition	**Prevalence**	**Major location and radiation**	**Timing**	**Character/severity**	**Provoking factors**	**Associated factors**
Chronical paroxysmal hemicrania	Very rare	Eye, forehead	Pain lasts 2-45 min., 5-10 daily	Stabbing, throbbing, boring	Head movements, responds to indomethacin	Autonomic symptoms as for SUNCT
Giant cell arteritis	Rare	May be bilateral, mostly over temporal artery	Continuous	Aching, throbbing, boring, sharp	Chewing	Jaw claudication, neck pain, anorexia, visual symptoms, temporal artery biopsy is gold standard
Temporomandibular disorders, idiopathic orofacial pain, facial arthromyalgia	Relatively common	May be bilateral, periauricular, radiate to neck, temples	Intermittent, may last for hours, may have severe exacerbations	Throbbing, sharp, or dull aching	Clenching and grinding, opening wide, psychosocial factors, trauma	May be limitation in opening, tenderness of muscles of mustication, altered occlusion, respond to relaxation
Atypical facial pain	Relatively common	May be bilateral or unilateral, can radiate widely beyond trigeminal area, variable location	Intermittent or continuous, often long history of pain	Nagging, throbbing, aching, sharp (wide range of words used) and severity mild to moderate	Life events, stress, weather changes, movements	Dysesthesia, facial edema, headaches, depression
Atypical odontalgia/ phantom tooth	Rare	Intraoral in a tooth or teeth, gingival, moves to another area	Continuous, few minutes to hours	Dull, throbbing, may be sharp, mild to moderate	Life events, emotional, teeth hypersensitive to temperature and pressure	Often history of tooth extraction

[1]SUNCT - shorter lasting, unilateral neuralgiform, conjunctival injection and tearing.

Some patients have a definite sensory deficit noted during routine sensory testing described as trigeminal neuropathy, but these patients have not been well characterized. An entity of pre-TGN has also been described that with time becomes classical trigeminal neuralgia and others may be classified as having trigeminal neuropathy (Zakrzewska J.M., 2002).

Because trigeminal neuralgia is primarily a unilateral pain (only 3% of patients have bilateral symptoms), which in most cases is not active at the same time, the main differentials that need to be considered are those that result in unilateral orofacial pain. These can range from dental causes to atypical facial pain. Many of the differential causes of orofacial pain may also present with bilateral pain, but confusion can occur when the symptoms occur unilaterally.

Many patients often attribute their pain to dental causes and will seek dental therapy as a first line of treatment. Because dental pain is extremely common, this is a valid assumption; however, it is important that dentists are open to nondental causes of pain and do not attempt complex and irreversible procedures. Although neurosurgically the data frequently state that trigeminal neuralgia develops in up to 80% of patients after dental treatment, the first attack of trigeminal neuralgia is often sudden in onset and can mimic dental pain. trigeminal neuralgia may also present exclusively intraorally, which can be confusing for patients and clinicians (Zakrzewska J.M., 2002).

Table 5 lists some of the types of orofacial pain that need to be considered when there is no obvious immediate cause, such as an infection or trauma.

The list of differential diagnoses can be large and can vary in different settings. Patients presenting in the dental and oral-surgical environments are more likely to be considered to have dental pain than patients attending a neurologist or headache clinic.

Patient's perceptions of what they consider their pain to be caused by and what they concerns about diagnosis may be influence the referral. Patients attending a headache clinic are more likely to be concerned about having an intracranial tumour than patients attending the dentist, and will have pain outside the dental field. In these cases, rare causes of pain (e.g., cluster headaches; shorter lasting, unilateral neuralgiform, conjunctival injection and tearing; cranial arteritis; postherpetic neuralgia) need to be considered.

As shown in the Table 5, the prevalence of the conditions must also be taken into account when assessing other differentials (Zakrzewska J.M., 2002).

It is important to repeat neurological examinations at intervals because these abnormalities may become apparent with time, indicating that there is a secondary cause of trigeminal neuralgia (Zakrzewska J.M., 2002).

1.7.2. Investigations in Trigeminal neuralgia

Some form of pain measurement helps the clinician during diagnosis and treatment. The most common used measures are the verbal and visual analogue scales. The long and short forms of the McGill questionnaire are multidimensional in their measurement and provide added data that can be used to distinguish between trigeminal neuralgia and atypical facial pain. Other quality-of-live, psychosocial, or daily-activity measures are used to gain improved insight regarding the disability of the condition and to evaluate treatment outcomes (Zakrzewska J.M., 2002).

All patients undergoing the medical management of trigeminal neuralgia should also undergo baseline haematologic and biochemical investigations to evaluate whether side effects of therapy are related to biochemical or haematologic effects. Investigations should include haemoglobin levels with a full blood and erythrocyte count, folate and B12 estimation, urea and electrolyte evaluation and liver function tests (including γ-glutamyl transpeptidase) (Zakrzewska J.M., 2002).

In patients suspected of also having a dental cause of pain, intraoral radiographs and panoramic tomograms of the upper and lower jaws are needed and should be evaluated by a dentist or a dental radiologist. Occipito-mental and posterior anterior views of the skull are useful for investigating sinus disease, though other structural lesions can be discovered by computed tomography scans (Zakrzewska J.M., 2002).

Several groups have developed electrophysiological techniques for assessment of trigeminal nerve function in the clinic. There is insufficient evidence of their usefulness in either confirming or ruling out trigeminal neuralgia. However, abnormalities in tests for eye blink and jaw reflexes strongly point to trigeminal neuropathic pain or “atypical facial pain” (Nurmikko T.J. et al., 2001).

1.7.2.1. Imaging modalities in neurovascular compression

There are no specific clinical features allowing confident localisation of pathology affecting the pre-ganglionic trigeminal nerve (Zakrzewska J.M., 2002). It is very difficult to localize a lesion on the course of cranial nerve V, based solely on clinical examination. Because the trigeminal nerve has complex branching and anastomotic patterns, clinical topographic diagnosis is not possible. This means that clinical symptoms and signs cannot predict the exact location of a lesion. A patient may present with symptoms related to a particular division of the trigeminal nerve without a lesion in that particular branch or may have a pre-ganglionic lesion without clinical involvement of all distal branches (Borges A., 2005).

Therefore, the entire course of the nerve from its brainstem nuclei to the peripheral branches must be imaged in patients presenting with trigeminal neuropathy (Borges A., 2005).

For complete coverage of the trigeminal system, imaging studies must include the neuroaxis from the midbrain to the cervical spinal cord (C2–C4 level) and the suprahyoid head and neck compartment from the orbital roof to the mental foramen (Borges A., 2005).

Another point that should be taken into account is that trigeminal lesions may be clinically silent for long periods. Of utmost importance is the imaging diagnosis of perineural spread of head and neck malignancies during primary staging of neoplasm. This may occur both anterograde and retrograde, may have skipped areas of neural involvement and should be treated along with the primary tumour which means including the entire course of possibly involved nerve branches in the field of the imaging study, even in patients without cranial nerve symptoms or signs (Borges A., 2005).

The imaging modalities recommended for trigeminal nerve evaluation include CT (Jager L., 2003; Worthington C. et al., 2000) and MRI (Boecher-Schwarz H.G. et al., 1998; Chavez G.D. et al., 2005; Furuya Y. et al., 1992; Heine C. et al., 2002; Held P. et al., 2001; Kumon Y. et al., 1997; Kuroiwa T. et al., 1996; Magnaldi S. et al., 1992; Majoie C.B. et al., 1997; Masur H. et al., 1995; Tash R.R. et al., 1989) eventually used together to give a full picture of the bone and soft tissue changes, respectively. CT is particularly well suited to depict neurovascular foramina and canals as well as to provide a roadmap of skull base and facial bony anatomy required for planning surgical and radiosurgical procedures. Deformation, enlargement or destructive changes along the foramina or nerve canals are indirect signs of a lesion along the course of the corresponding nerve. An important sign of neural involvement to look for is the loss or replacement of the fat pads in close association with neurovascular foramina. This is nicely depicted using either CT or MRI due to the typical features of fat on both modalities: low density values (around –100 HU) on CT and high signal intensity on MR T1-w images that disappear on fat suppressed sequences (Borges A., 2005).

Contrast enhancement is mandatory. On CT, it increases lesion conspicuity in most cases, particularly when dealing with neoplasms, and determines the relationship between lesions and adjacent vascular structures. It is also mandatory when a neurovascular conflict is in question by depicting the offending vessel as an enhancing structure from the non-enhancing nerve. On MRI, gadolinium enhancement is the only imaging finding allowing the diagnosis of many infectious/ inflammatory and some

neoplastic conditions such as perineural spread of malignancies, lymphoma or even very small intrinsic tumours (Borges A., 2005).

1.7.2.1.1. CT-technique

Current standard of care for CT imaging the trigeminal nerve must include helical or volume acquisition scans from the orbital roof to the mandibular symphysis after intravenous administration of iodinated contrast material, reconstructed in the axial, coronal and sagittal planes, on both soft tissue and bony algorithms. Slice thickness should be kept to a minimum, preferably below 3 mm, without interslice gap. CT angiography of the posterior circulation has been increasingly used for the diagnosis of neurovascular conflicts, particularly in patients with contraindications for MR imaging (Borges A., 2005). However, the CT scan offers poor visualisation of the posterior fossa because of the high interference of the bone component. The trigeminal nerve is not visualized in the CT image; it can be inferred from its relationship with the petrous ridge, at the site where the trigeminal nerve crosses to Meckel's cavity. In the past, it was used for radiosurgery targeting, with poor results in pain control (Chavez G.D. et al., 2005).

1.7.2.1.2. MRI technique

1.7.2.1.2.1. MR Sequences

The introduction of MRI, especially with contrast medium administration (Gd-DTPA) permitted better visualisation of the trigeminal complex, and it is the method of choice for evaluating the trigeminal nerve (Chavez G.D. et al., 2005; Sevick R.J. et al., 1991; Williams L.S. et al., 2003).

As already described the trigeminal nerve is often involved in generalized neurological conditions such as cerebrovascular disease and primary demyelination, which are multifocal in nature. It is therefore essential to ensure that all significant pathology is demonstrated through a standardized brain MRI protocol (Woolfall P. et al., 2001), which can contain following sequences:

T2-weighted fast-spin echo sequence or turbo-spin echo (T2-w FSE or T2-w TSE);

T1-weighted spin-echo sequence (T1-w SE) native and eventually with contrast agent;

FLAIR (fluid attenuated inversion recovery) sequence

acquired in the axial plane.

The MRI can determine whether benign or malignant lesions or plaques of multiple sclerosis are present and are being increasingly used at an early stage in the diagnosis. The axial MRI T2-weighted fast-spin echo sequences are used routinely to assess head and neck pathology and will identify structural lesions such as tumours and multiple sclerosis. Enhanced T1-weighted gadolinium enhanced sequences will give improved sensitivity for small tumours and meningeal disease (Zakrzewska J.M., 2002). In her turn Alexandra Borges (Borges A., 2005) recommend following MR-techniques to detect various lesions that cause trigeminal neuralgia symptoms: MR imaging should include T2-w FSE images of the brainstem and upper cervical cord to evaluate the nuclei and fascicular segment of the nerve, pre- and post-gadolinium thin section, conventional SE (spin-echo) T1-w images in the axial and coronal planes, with fat-suppressed contrast enhanced images

when perineural spread of tumour is suspected followed eventually by specials acquisitions for depicting neurovascular compression.

Although the concept of neurovascular compression in the aetiology of trigeminal neuralgia has already been generally accepted, neurovascular relationships until recently have not been demonstrated preoperatively by neuroraiological examinations such as computed tomography (CT), magnetic resonance imaging (MRI), or cerebral angiography. That's why recently preoperative detection of offending vessels has been tried using high-resolution MRI (Fukuda H. et al., 2003). Non-invasive diagnosis of the neurovascular compression by MRI/ MRA may improve patients' selection and operative planning for microvascular decompression (Bakshi R. et al., 2001; Yang J. et al., 1996).

Since the introduction of MR imaging, neurovascular relationships have been examined using several modalities including T2- and T1- weighted sequences, MRT-angiography, combination of different imaging sequences within a protocol and different orientation. However, although visualisation of vascular compression has been demonstrated by use of conventional high-resolution MRI scans, consistent findings of vascular compression using only T1-weighted images is very difficult. In addition, it is very difficult to identify the divisions of the trigeminal nerve and the related vasculature by use of these methods (Chavez G.D. et al., 2005).

1.7.2.1.2.2. High-resolution MR for evaluation of microvascular compression

Patients with trigeminal neuralgia should be extra imaged with high-resolution (HR) MR with special 3D-sequences (Woolfall P. et al., 2001). Improvements in MR technology and progress in developing new 3D-MR imaging protocols provide sufficiently high resolution below 1mm, even between consecutive slices. These kinds of new 3D-MR acquisitions are:

- **3D heavily** (or **strongly**) **T2-w gradient echo (GE)** sequence, although there are some acquisitions with fast-spin echo (FSE):
  - **3D-FIESTA:** three-dimensional fast imaging employing steady-state acquisition (in General Electric Scanners), or
  - **3D-CISS:** three-dimensional constructive interference in steady state (in Siemens Scanners), or
  - **3D-CE-FAST**: three-dimensional contrast enhanced Fourier acquired steady state, or
  - **3D- DRIVE** (in Philips Scanners), or
    eventually other similar sequence according to different MR-Scanners;

- Multiplanar (**3D or 2D**) gradient echo (**GE**) T1-w sequence native and after contrast medium administration:
  - **3D-FSPGR**: three-dimensional fast spoiled gradient echo (in GE Scanners), or
  - **3DFT-MPRAGE**: three-dimensional Fourier transform magnetization prepared rapid gradient echo (in Siemens Scanners), or
  - **3D-GRASS**: three-dimensional gradient recalled acquisition in the steady state (in General Electric Scanners), or
  - **FFE T1-w**: fast field echo **T1-w** (in Philips Scanners)

- And High resolution **TOF** (time of flight)- and contrast enhanced-**MRTA**:
  - **3DFT-FISP** three-dimensional Fourier transform fast inflow with steady-state precession (in Siemens Scanners), or
  - **3DFT-FLASH MRA** three-dimensional Fourier transform fast low angle shot **MRA** (in Siemens Scanners), or
  - **2D FLASH GE** bi-dimensional fast low angle shot gradient echo **T1-w**.

These are special high resolution sequences to detect neurovascular compression in patients with trigeminal neuralgia symptoms, although the last two sequences (3D T1-w GE and MRA or MRTA) seems to have similar

characteristics and imaging criteria as well as spatial resolution between nerves, vessels and CSF as I could conclude after analysing the current literature dedicated to this subject and are used electively (in addition to 3D-T2-w FSE or GE sequence either a 3D T1-w GE with or without contrast agent or TOF MRA) (Akimoto H. et al., 2002; Borges A., 2005; Elias W.J. et al., 2002; Fukuda H. et al., 2003; Jawahar A. et al., 2001; Patel N.K. et al., 2003; Umehara F. et al., 1995; Woolfall P. et al., 2001; Yoshino N. et al., 2003).

Elias, W. Jeffrey et al. (Elias W.J. et al., 2002) performed in their study all of these three MRI acquisitions, thus they could compare them: three-dimensional time-of-flight sequenced MR angiography (3D TOF MRA) shows arteries well but the nerves poorly, better observation of the nerve is obtained with three-dimensional spin-gradient (gradient-echo) sequences (3D T1-w GE), T2-weighted fast-spin echo sequences (T2 FSE) are sensitive but may not distinguish the nerve, artery, or vein, Gadolinium-enhanced three-dimensional spin-gradient sequencing (3D T1-w GE + CM) shows veins in addition to arteries, and its combination with three-dimensional time-of-flight sequenced MR angiography is necessary to accurately differentiate the veins and arteries.

The 3D heavily T2-w GE sequence has a high special resolution and excellent contrast between structures (Yoshino N. et al., 2003). These imaging data demonstrate improved contrast between neighbouring structures, allowing us to differentiate cranial nerves and vessels as having a low intensity within the high-intensity CSF space at the surface of the brainstem (Naraghi R. et al., 2004), but it is not able to differentiate these structures: nerves from vessels. This high-resolution, heavily T2-weighted image is capable of contrasting both vascular structures and nerves from cerebrospinal fluid. Some authors (Chavez G.D. et al., 2005) describe that a such high contrast resolution as 3D-FIESTA sequence in their study allowed visualisation of the divisions of the trigeminal nerve (V1, V2, V3) inside Meckel's cavity or near the gasserian ganglion, which correlated precisely with the anatomic specimens.

With this sequence, Yousry et al., (Yousry I. et al., 2000) demonstrated the trigeminal nerve in 100% of the patients, Held et al. (Held P. et al., 2001)

determined that the detectability of the trigeminal nerve at its apparent origin at the brainstem and near Meckel's cavity, as well as the gasserian ganglion, is best when this sequence is used, Yoshino et al. (Yoshino N. et al., 2003) demonstrated not only the trigeminal nerve and the artery but also the veins to be related in all the patients studied. It is necessary to add a 3D-FIESTA or 3-D CISS sequence to the routine MRI studies in patients with trigeminal neuralgia, not only to localize the nerve for radiosurgery but also to depict the cause that might be responsible for the neuralgia, especially in microvascular compression (Yamakami I. et al., 2000). Because the FIESTA sequence has demonstrated its usefulness for showing the trigeminal nerve rootlets, it may be used for radiosurgical treatment of dermatomal trigeminal neuralgia (Chavez G.D. et al., 2005).

Unlike heavily T2-w images, in 3D T1-w GE vessels appear as high-signal intensity areas, nerves are displayed as intermediate signal intensity and CSF has low signal intensity. Thus 3D T1-w GE has a good differentiation between vessels and nerves and when contrastated by a double dose of contrast medium there is a good contrast between nerves and arteries or veins, which have more chance to be contrastated as without gadolinium. But the trigeminal nerve is not as clearly displayed (does not have such a good spatial resolution) as in 3D- heavily T2-w images.

The 3D heavily T2-w images provide an efficient contrast for identification of the trigeminal nerve and brainstem, and the 3D T1-w GE images provide efficient contrast for the causative vessels. Therefore is reasonable to scan both images from the same position in all patients in order to diagnose neurovascular compression.

A combination of both high-resolution imaging techniques is more likely to detect the causative vessel in patients suffering from trigeminal neuralgia if the investigator knows which side exhibits the symptoms (Nurmikko T.J. et al., 2001).

Between others, also Meaney and colleagues (Meaney J.F. et al., 1994) developed a special technique to optimally image the relationship of the nerve and the blood vessels in its vicinity. Essentially, by choosing specific scanning parameters to visualize blood vessels as high signal intensity

structures and using thin slices they were able to perform reconstructions around the nerve in any orientations. While arteries were easily identifiable, veins could be properly visualized only after enhancement with intravenous Gadolinium-DTPA. They obtained through their technique a sensitivity of 100% and specificity of 96% (Nurmikko T.J. et al., 2001).

Although every clinic uses its own protocols in order to diagnose the potential microvascular compression, they are likely to have common or similar sequences. A typical MR-protocol with sequences and parameters used in the evaluation of the trigeminal gives us (Jager L. et al., 2001) (Table 6).

Table 6 *MR imaging sequences and parameters used in the evaluation of the trigeminal nerve (adapted from (Jager L. et al., 2001)*

Sequence	SE T1W pre- and post-gad	TSE T2W (brainstem)	3DFT-MPRAGE	3DFT-CISS	3DFT-FISP turbo MRA
TR	684	4000	11.6	12.25	35
TE	20	99	4.9	5.9	6.4
FA	90°	180°	12°	70°	15°
Acq. time	5 min, 31 s	3 min	10 min, 51 s	7 min, 14 s	4 min, 8 s
Thickness	2 mm	4 mm	1 mm	0.7 mm	0.75 mm
Matrix	160×256	242×512	192×256	192×256	320×512
FOV	230	300	240	95	200
Pixel size	0.90×0.90	0.62×0.59	0.94×0.94	0.49×0.37	0.94×0.39
Weighting	T1	T2	T1	T2	T1

Although heavily T2-weighted MR images as well as T1 GE MR Sequences and time of flight MR angiography produce 3D imaging data, it is important to point out the principal difference between 3D imaging data and 3D visualisation. A number of studies apply 3D MR sequences and they are interpreted like to be 3D illustrations or visualisations. But in terms of computer graphics, 3D visualisation comprises all methods of volume rendering, which allow to extract and to show 3D representations of 3D imaging data. Complete 3D images or illustrations proved to have a higher sensitivity and specificity as just plain 3D MR imaging data or sequences (Naraghi R. et al., 2004).

2. PURPOSE OF THE STUDY

Microvascular decompression (MVD) remains the only treatment of trigeminal neuralgia that directly addresses the presumed pathogenesis. It is a proven therapy, associated with the longest duration of pain relief while preserving facial sensation (Elias W.J. et al., 2002). Surgical treatment of trigeminal neuralgia may be also helpful for refractory cases of conservative treatment.

A preoperative determination of microvascular compression in terms of exact localization of the compressing vessel, direction of the vessel and relationship between root entry zone (REZ) and vasculature could be of great value for the neurosurgeon. There are in the literature only a few radiological reports dealing with preoperative evaluation of the relationship between clinical symptoms related to the trigeminal branches and those related to the site of compression at the root entry zone of the nerve (Yoshino N. et al., 2003).

Non-invasive diagnosis of the neurovascular compressions by MRI/ MRA may improve patient selection and operative planning for neurovascular decompression. The preoperative evaluation of the relation between clinical symptoms and the site of compression of the nerve is important for both a more accurate microvascular decompression procedure and the selective rhizotomy of the trigeminal nerve in patients with trigeminal neuralgia as alternative operative treatment. An early MVD is demanding because the disease's natural progression, in the absence of treatment, is toward the development of more atypical features that are refractory to treatment, signifying ongoing neuropathic injury.

In an effort to more successfully select candidates for MVD, a high-resolution magnetic resonance imaging as preoperative algorithm is necessary, since it has proven to demonstrate neurovascular relations at the trigeminal nerve complex according to the pertinent literature (Akimoto H. et al., 2002; Chang J.W. et al., 2000; Elias W.J. et al., 2002; Fukuda H. et al., 2003; Hastreiter P. et al., 2003; Kakizawa Y. et al., 2003; Patel N.K. et al., 2003; Yoshino N. et al., 2003).

High-resolution magnetic resonance imaging (HR-MRI) is used in preoperative evaluation of neurovascular compression in patients with trigeminal neuralgia. Advancement of HR-MRI, namely 3D-FSPGR and 3D-FIESTA allowed various imaging sequence and projections to be used.

Our objectives were:

- To asses whether vascular compression of the trigeminal nerve could be reliably demonstrated by preoperative HR-MRI examination of patients with trigeminal neuralgia symptoms and how high is the correspondence among the MRI results and intraoperative findings in a single-blinded study;
- To establish which imaging possibilities and limits have both used HR–MR sequences 3D-FSPGR with double dose of contrast media and 3D-FIESTA;
- To find the shortcomings of chosen protocols of preoperative MR - examination in patients with trigeminal neuralgia;
- Which additional technical modalities are to be further performed in routine examinations in order to improve the results of detection the causative vessel of neurovascular compression.

3. PATIENTS AND METHODS

3.1. Patients' characteristics

Between March 1998 and April 2005, **30** (thirty) patients with trigeminal neuralgia symptoms were preoperatively examined in the Department of Neuroradiology, and then underwent operative intervention of neurovascular decompression in the Department of Neurosurgery of the Philipps-University of Marburg.

The mean age of the patients constituted 61.4. The youngest patient was 29 years old and the oldest 76 years. The female sex prevailed with 56.67 % (17 women and 13 men), thus the female prevalence reached 1.3.

The exact age distribution is represented in the table 7

***Table 7**: Age distribution of the patients (n=30 patients)*

Age group	Patients, n	%
20 –40 years	1	3,33
41 – 60 years	11	36,67
61 – 80 years	18	60.0
Total	**30**	100

Patients with tumour compression at the trigeminal root were excluded.

3.2. Neuroimaging MR techniques

Preoperative High-Resolution MRI was performed at a 1.5 Tesla scanner with a head coil (Signa Horizon, GE Medical Systems, Milwaukee, Wis., USA).

All of the patients were examined using a 3D-FSPGR (three-dimensional fast spoiled gradient-recalled) sequence with TR 8.6 milliseconds, TE 1.7 milliseconds, matrix 256×256 and 3 NEXs. To increase the signal of vascular structures, a double dose of Gadolinium-DTPA (Magnevist® - Schering) - 30 ml was intravenously injected. One half of the contrast medium - 15 ml was given at the beginning of the examination (those not before starting the standard protocol including T1-weighted native sequence) and the other half when starting the 3D-FSPGR sequence.

In 13 patients we also performed an additional 3D-FIESTA (three dimensional fast imaging employing steady-state acquisition) sequence (a heavily T2-weighted sequence, equal to 3D-CISS at Siemens unit) with the following parameters: TR 5000 milliseconds, TE 455 milliseconds, matrix 512×256 and 1 NEX.

For differential diagnosis to exclude various lesions that could lead to a secondary trigeminal neuropathy a standard protocol with T2-, T1-w SE and FLAIR sequences was performed.

Table 8 illustrates the exact protocol of MR parameters used as standard examination for the patients with trigeminal neuralgia.

Table 8 *Protocol of MR parameters and values for applied MR Sequences[*] (according to "MR 1.5 Signa® EXCITE™ 11.0 Learning and Reference Guide, 2384192-100 Rev. 2 (01/04),* ***2004 General Electric Company")*** *(General Electric Company, 2004)*

Parameters	**Imaging Modality**					
	T_2-weighted	**T_1-w (native and + CM)**	**T_1-w**	**FLAIR**	**3D-FSPGR**	**3D-FIESTA**
Orientation	axial	axial	coronal	axial FLAIR	axial 3D-block with parallel and perpendicular to the course of TN reconstr.	axial 3D-block with parallel and perpendicular to the course of TN reconstr.
TR (msec)	6200	460	460	9002	8.9	5000
TE (msec)	92.6	14	14	149	2.0	455
Slice thickness (mm)	6.0	6.0	6.0	6.0	3D slab	3D slab
No. of slice	20	20	20	20	-	-
Distance factor (%)	10 (0.6mm)	10	10	10	-	-
Field of view (mm)	240x180	240x180	240x180	240x240	180x180	220x220
NEX	2	2	2	1	3	4
Flip angle (°)	180	75	75	180	25	55 - 65
Matrix	512x224	320x224	320x224	256x192	256x256	384x256
Voxel size (mm)	0,5x0,8x6,0	0,8x0,8x6,0	0,8x0,8x6,0	0,9x1,3x6,0	0,7x0,7x	0,6x0,9x
SNR	1.00	1.00	1.00	1.00	1.00	1.00

[*]FLAIR = fluid- attenuated inversion-recovery; SNR = signal/noise ratio, CM=contrast media, TN= trigeminal nerve

The figures 11 show the representation of trigeminal nerve in T2-w and T1-w sequence and corresponding anatomical section as well as schematical image in this position (Kretschmann H.-J. et al., 2002; Leblanc A., 1992)

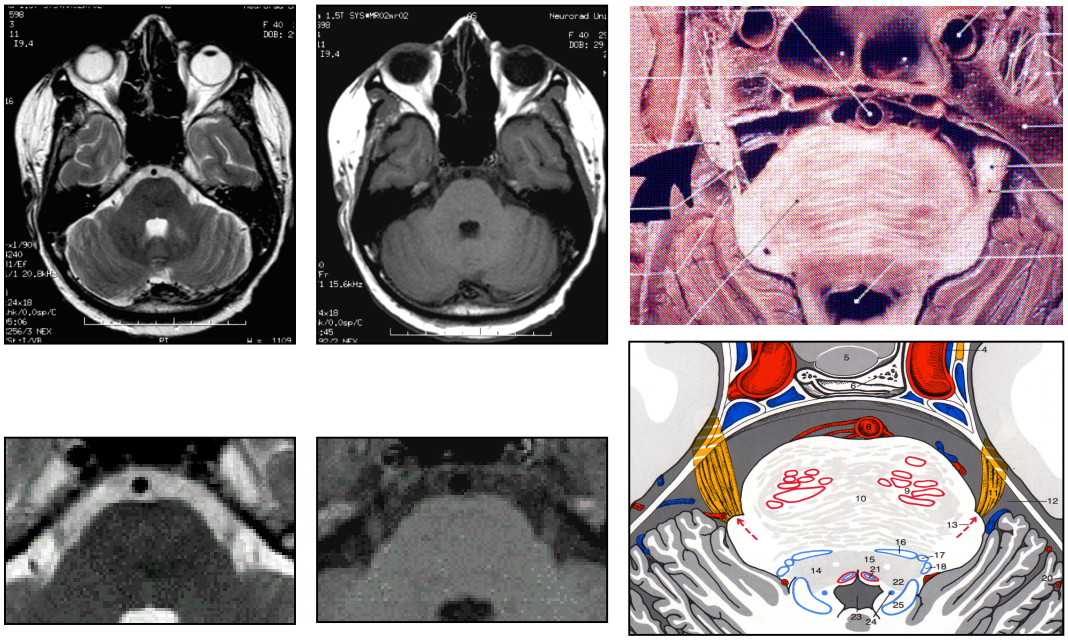


Fig. 11a *Trigeminal nerve: T2-w, T1-w images with corresponding anatomical section and schematical image (axial projection)(Kretschmann H.-J. et al., 2002; Leblanc A., 1992)*

3.2.1. Postprocessing of the row data

Postprocessing was done at a separate SUN-workstation (Sun Microsystems, Palo Alto, Calif., USA; Advantage Windows 3.1, GE Medical Systems, Milwaukee, USA). We obtained multiplanar reconstruction (MPR) images from both sequences with slices parallel to each trigeminal nerve and also coronal planes perpendicular to the nerve from REZ and along the whole cisternal segment in Cavum Meckeli with 0.5 mm thickness and 0.8 mm gap. For image analysis we used the axial original images as well as these MPR coronal and sagittal reformatted images for both axial 3D-FSPGR and 3D-FIESTA sequences.

Examples of each kind of sequence and its sagittal and coronal reconstructions are shown bellow in Figure 12.

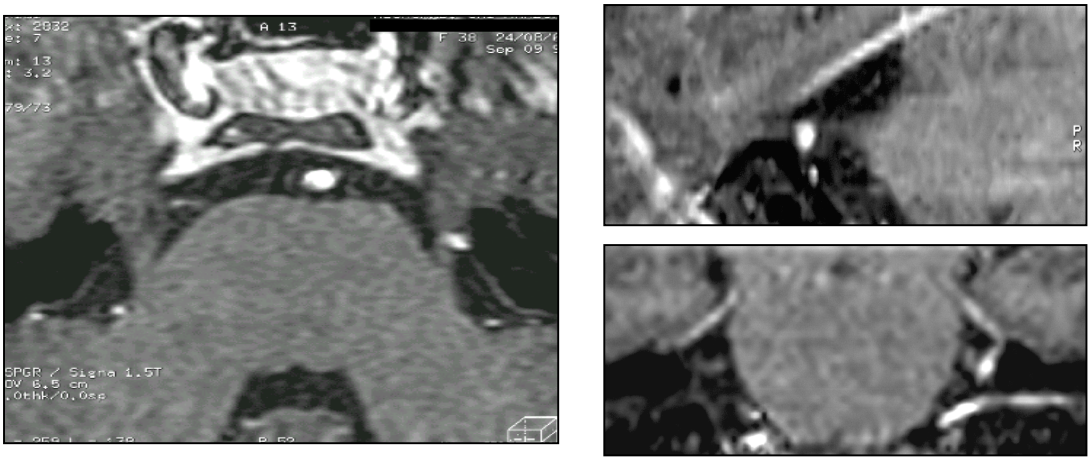


Fig. 12a *3D-FSPGR sequence axial with sagittal and coronal reconstructions (small vessel compressing the left TN).*

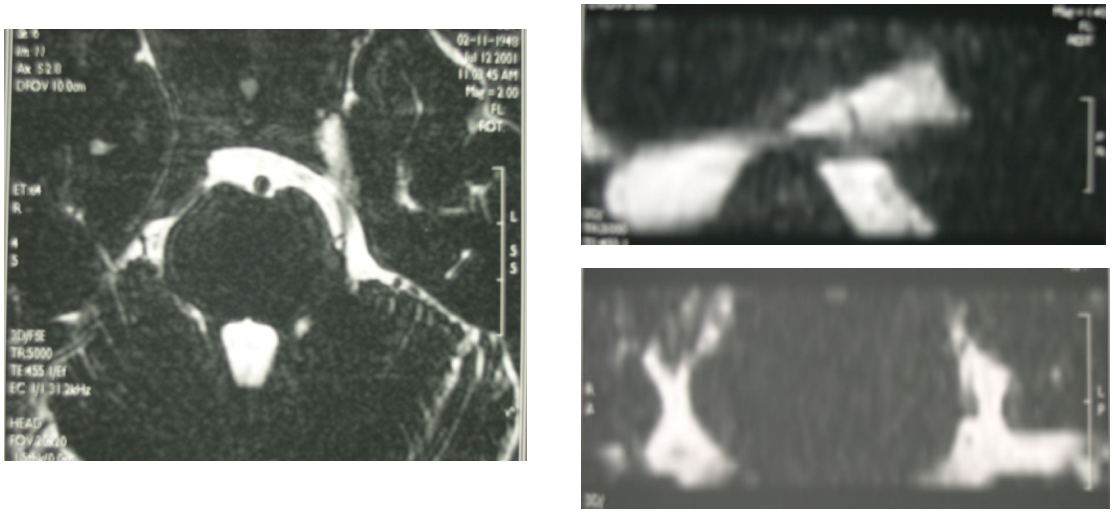


Fig. 12b *3D-FIESTA sequence axial with sagittal and coronal reconstructions (small vessel compressing the left TN)*

3.3. Neuroimaging criteria – image analysis:

To avoid prejudice and to exclude the possibility of subjective estimation of imaging, the clinical evident side of neuralgia was remained unknown to the neuroradiologists who analysed images, thus they were blinded to the clinical findings. Both nerves were studied. The trigeminal nerve was identified on the basis of its course from the pons to the Meckel's cavity. The following parameters were rated:

a. presentation of the trigeminal nerve itself;
b. trigeminal nerve/ blood vessel relationship at the root entry zone;
c. trigeminal nerve/ blood vessel relationship at the peripheral segment of nerve.

We did not identify the arteries specifically because our scan bloc was not wide enough for tracing the vessels to their origin in the basilar artery. Neither was any attempt made to differentiate artery from vein.

Both sequences (3D-FSPGR and 3D-FIESTA if available) were estimated separately and the suspicious side of neurovascular compression was noted. Compression was radiologically diagnosed when a close contact (or touch) of the blood vessel and the nerve at the REZ and at the peripheral segment was clearly identified in two or more slices of the transverse slices as well as on the coronal and sagittal reconstructed images. The vessels, which were near but not touching the nerve, have not been considered. An evaluation scale was used for evaluation of the structure in question:

1. evident vascular contact,
2. probable vascular contact,
3. doubtful and
4. no vascular contact.

The following working protocol was used (table 9):

Table 9 *Working protocol during blind analysing of HR –MR images (3D-FSPGR 3D-FIESTA)*

Name of the patient, date of birth	**3D-FSPGR**		**3D-FIESTA**	
	Right	**Left**	**Right**	**Left**
Presentation of the TN				
Good				
Middle				
Bad				
Root entry zone				
Evident vascular contact				
Probable vascular contact				
Doubtful vascular contact				
No vascular contact				
Peripheral, prepontine segment				
Evident vascular contact				
Probable vascular contact				
Doubtful vascular contact				
No vascular contact				
Remarks	**Presumed side**			
OP- Situs – date (Right / Left)	Intraoperative findings			

3.4. Intraoperative video-observations:

Every surgical procedure was documented by videotaping. Retrospectively the same neurosurgeon analysed these recordings and intraoperative findings. The intraoperative observations were compared with the MRI-evaluations.

3.5. Retrospective analysis

After revealing the side of symptomatology and the intraoperative situs of each patient, the same MR-images were analysed second time. It was of special interest to see if our results would have been different already knowing the intraoperative findings and if we could recognize the real pathomorphology retrospectively in those cases we failed.

4. RESULTS

4.1 Blind analysis of images

In all 30 cases the trigeminal nerve could be seen clearly in the 3D-FSPGR sequence. The MPR with parallel and coronal plane to the fifth cranial nerve provided very good images to evaluate the trigeminal nerve. By injection of Gadolinium – DTPA even small vessels showed a good enhancement to distinguish them from the surroundings.

The 3D – FIESTA sequence that was performed additionally in 13 (43.3%) patients, was also able to show excellent spatial relationship between the structures, however this modality as in the literature described was not able to distinguish between nerves and vessels.

In case of motion artefacts because of gross head movement (in 3 patients – 10%) these images could not be analysed sufficiently. In these patients the double-dose contrast enhanced 3D- FSPGR sequence could show a better contrast of vessels to neighbourhood to allow an analysis of the neurovascular situation of trigeminal nerve.

The results of blind analysis of HR-MR images are illustrated in the table 10.

Table 10 *Results of blind analysis of HR-MR images*

	3D-FSPGR (T1w)										
	Representation			Root entry zone (vascular contact)				Periphere, prepontine zone			
	Good	Midle	Bad	evident	probable	doubtfull	no	evident	probable	doubtfull	no
1. F/76	1+0			0							x
2. F/58	1+0				0		1		0		1
3. M/61	1+0			1	0					1	0
4. F/73	1+0			1		0			1	0	
5. M/76	1+0						x		1		0
6. M/60	0	1			1	0			0		1
7. F/41	1+0					0	1		1		0
8. F/66	1+0			1		0					x
9. M/54	1+0				1		0				x
10. M/63	1+0			1			0				x
11. M/66	1+0			0			1				x
12. F/66	1	0			1		0				x
13. F/59	1+0			1		0					x
14. F/61	1+0				0		1			1	0
15. F/69	0	1			0		1				x
16. F/71	1+0						x	0			1
17. M/55	1+0				0		1			1	0
18. F/60	1+0						x			0	1
19. F/65	1+0			0			1				x
20. M/74	0		1				0				0
21. F/62	1+0			0		1				0	1
22. M/60	1+0				0	1					x
23. F/29	1+0				1		0				x
24. M/45	1+0						x			1+0	
25. F/60	1+0						x				x
26. M/61	0	1			1+0						x
27. F/67	1+0			0			1			0	1
28. F/54	1	0			1		0			1	0
29. F/70	1+0			0			1				x
30. M/61	1+0			0		1				x	

0 – left; 1 – right; x – none

Table 10 *(continued) Results of blind analysis of HR-MR images*

No	**3D-FIESTA (T2w)**											Neuro-radiologicaly suspicious side
	Representation			Root entry zone (vascular contact)				Periphere, prepontine zone				
	Good	Midle	Bad	evident	probable	doubtfull	no	evident	probable	doubtfull	no	
1.	1+0				0						x	0
2.												0
3.												1
4.	0		1				0				0	1
5.												1
6.			1+0									1
7.	1+0						x			1	0	1
8.	1+0											1
9.	1+0					1	0			1	0	1
10.	1+0					1	0				x	1
11.												0
12.			1+0									1
13.		1+0					x			1	0	1
14.												0
15.												0
16.												0
17.												0
18.												0
19.												0
20.												x
21.	1+0				0	1				0	1	0
22.												0
23.												1
24.												x
25.												x
26.												1+0
27.	1+0				0	1					x	0
28.		1+0			1	0					x	1
29.	1+0			0			1				x	0
30.												0

0 – left; 1 – right; x – none

4.2. Comparison of the 3D HR-MR images and intraoperative observations

The symptoms of TGN were found on the right side in 63.3% (n=19) and in 36.7% (n=11) on the left side.

The following dermatomes combinations were affected: first division of the trigeminal nerve in combination with the second branch; second division of the nerve; third division and a combination of the second and third division. No patient had symptoms of the V1 dermatome alone.

All patients underwent later on microvascular decompression. The intraoperative found causative vessel for neurovascular compression was:

- Superior cerebellar artery (SCA) in 63.33% (n=19), or
- Anterior inferior cerebellar artery (AICA) in 10.0% (n=3).
- Teflon interposition in 6.67% (n=2), and
- Venous compression (petrosal vein) in 6.67% (n=2), was likely to be responsible for the symptoms of the individuals.
- In 2 patients (6.67%) termocoagulation was performed.
- In 1 patient (10%) (female, 29 years old patient) the intraoperative result turned out to be demyelination lesion.

In 13 of 30 patients - **43.33%** preoperative HR-MRI demonstrated the neurovascular compression in good agreement with the intraoperative findings. The noted suspicious side of pathology and also the affected region of trigeminal nerve (REZ or peripheral zone) were in accordance with the intraoperative findings in 12 of 13 cases.

In one patient (nr. 10) we saw an affecting vessel at the root entry zone, whereas the operative situs showed neurovascular compression by a convolute of SCA and a petrosal vein more in the peripheral part of the nerve.

The assessment of preoperative HR-MRI concerning the side of neurovascular compression failed in 8 of 30 cases **- 26.67%**. There was no accordance with the intraoperative situs.

In 2 of 9 remaining patients (no. 19, 20) surgery revealed a trigeminal compression caused by an interposed body of a previous MVD (Teflon interponate). Preoperative MRI had shown no neurovascular affection at the concerning side, whereas the other side demonstrated a close spatial relationship between nerve and vessel.

Neither preoperative HR-MRI on the affected side, nor intraoperative observations demonstrated neurovascular compression in patients no. 21 and 22 with evident TGN, so termocoagulation was performed.

Preoperative MRI of patient no. 23 demonstrated a close spatial relationship of right trigeminal nerve and vessel. Intraoperative situs showed no artery adjacent to the nerve. There was only a vein to be found intraoperatively close to the fifth cranial nerve but without compressing effect. Later on in biopsy it proved to be a demyelination lesion.

No neurovascular affection at either side could be seen in MRI examination in patient no. 24 with a clear trigeminal neuralgia left. The neurosurgeon however found two nerve affecting loops of the superior cerebellar artery and a definite impression at trigeminal nerve.

No clear vascular affection of trigeminal nerve was seen in case nr. 25 in MRI, and also surgery showed no evident vascular compression. The surgeon documented however in his report that the symptomatology presumably was caused by two arterial loops at the pontine surface.

Very close spatial neurovascular relationship at both sides showed preoperative MRI in case no. 26, so that the suspicious side could not be specified. Surgery revealed a loop of superior cerebellar artery (SCA) compressing the nerve at the side of symptomatology (left).

A vascular compression at the REZ of the right trigeminal nerve has been seen in patient no. 28. The symptomatology was been manifested on the contralateral side, so the neurosurgeons operated on the left side, but without finding a causative compressing vessel and isolating the nerve from all surrounding (but not compressing) vessels.

Overall, preoperative HR-MRI presented a reliable neurovascular situation in patients no. 19-22 as well in 26 and 28 whereas in cases no. 23 - 25 the imaging modality failed.

So in total preoperative HR-MRI demonstrated the neurovascular condition in good accordance with the intraoperative observations in 19 of 30 patients (**63.33%**). MRI failed in 11 of 30 cases (**36.67%**).

In the subgroup with 13 patients where additionally 3D-FIESTA was available, neurovascular situation was in agreement with the intraoperative findings in 9 cases (69.23%). In the group with 8 incorrect evaluated cases in HR-MRI only 2 have got 3D-FIESTA sequence, out of them, in one the presentation of trigeminal nerve was appreciated as bad, so no conclusion concerning affected side could be done.

The comparison data are summarized in table 11.

Table 11 *Clinical data/ MRI results/ retrospective analysis (F female; M male; V1, V2, V3 first, second and third branch divisions of the trigeminal nerve; SCA superior cerebellar artery; AICA anterior inferior cerebellar artery)*

First group – accordance

Patient no.	Gender / age	Clinical findings	Suspicious side in MRI / 3D – FIESTA available	Intraoperative finding	Retrospective analysis
1.	F/76	Left	Left/yes	Left AICA	Accordance
2.	F/58	Left V1+2	Left/no	Left SCA	Accordance
3.	M/61	Right V2+3	Right/no	Right AICA	Accordance
4.	F/73	Right V2+3	Right/yes	Right SCA	Accordance
5.	M/76	Right/V1+2	Right/no	Right SCA	Accordance
6.	M/60	Right V3	Right/yes	Right AICA	Accordance
7.	F/41	Right V2	Right/yes	Right SCA	Accordance
8.	F/66	Right V2	Right/yes	Right SCA	Accordance
9.	M/54	Right V2	Right/yes	Right petrosal vein	Accordance
10.	M/63	Right V1+2	Right/yes	Right SCA + petrosal vein	See above in the text
27	M/67	Left V2+V3	Left/yes	Left SCA	Accordance
29.	F/70	Left V1	Left/yes	Left SCA	Accordance
30.	M/61	Left V2	Left/no	Left SCA	Accordance

Second group – wrong MRI side

Patient no.	Gender / age	Clinical findings	Suspicious side in MRI / 3D – FIESTA available	Intraoperative finding	Retrospective analysis
11.	M/66	Right	Left/no	Right SCA	The vessel on the right side clearly detectable
12	F/66	Left V2	Right/yes	Left SCA	Not detectable
13.	F/59	Left V2	Right/yes	Left SCA	The vessel on the left side clearly detectable
14.	F/61	Right V2	Left/no	Right SCA	Not detectable
15.	F/69	Right V3	Left/no	Right SCA	The vessel on the right side clearly detectable
16.	F/71	Right/V1+2	Left/no	Right SCA	Not detectable
17.	M/55	Right V2+3	Left/no	Right SCA	Not detectable
18.	F/60	Right/V3	Left/no	Right SCA	Not detectable

Third group – miscellaneous

Patient no.	**Gender / age**	**Clinical findings**	**Suspicious side in MRI / 3D – FIESTA available**	**Intraoperative finding**	**Retrospective analysis**
19.	F/65	Right V3	Left/no	Right Teflon	No vascul contact on the right side - **accordance**
20.	M/74	Right V2+3	No compression/no	Right Teflon	**Accordance**
21.	F/62	Right	Left/yes	No vascular compression (Termocoagulation)	No vascul contact on the right side - **accordance**
22.	M/60	Right V3	Left/no	No vascular compression (Termocoagulation)	No vascul contact on the right side - **accordance**
23.	F/29	Right V2+3	Right/no	Demyelination (Biopsy)	Vascular contact right – **wrong** result
24.	M/45	Left V3	No compression/no	Left SCA	No vessel detectable **wrong** result
25.	F/60	Left V3	No compression/no	Left pontine branches	No vessel detectable **wrong** result
26	M/61	Left V2	Both sides/no	Left SCA	Also both sides vasc contact – **accordance** for the left side
28.	F/54	Left V1+V2	Right/yes	No distinct vessel found	No vessel detectable **accordance** on the left side

4.3. Retrospective analysis

Retrospective analysis of images revealed incorrect evaluation of preoperative MRI in **3** (three) cases. Knowing the intraoperative side the neurovascular compression could be seen definitely in the majority of cases. The other, not affected side however showed also a close spatial neurovascular relationship. In all other patients retrospective appraisal did not change our first evaluation.

However in **5** (five) patients the causative factor of presumed trigeminal neuralgia was different as vascular compression of trigeminal nerve, e.g. Teflon interponate from previous surgery, demyelinating (unknown) lesions or no compressive vessels so termocoagulation was performed.

5. DISCUSSIONS

5.1 Dilemma: "vascular compression" as a major cause of TGN or not;
REZ or the whole course of the 5th nerve

In the last three decades evidence has been raising that in a large proportion of cases, vascular compression of the trigeminal nerve root or near the dorsal root entry zone by a blood vessel is a major causative or contributing factor of trigeminal neuralgia and is now thought by the majority of authors to account for 80-90-% of cases (Bowsher D. et al., 1997; Haines S.J. et al., 1980; Hamlyn P.J., 1997; Jannetta P.J., 1980; McLaughlin M.R. et al., 1999; Meaney J.F. et al., 1995; Richards P. et al., 1983). There are several evidences that support this view. First, novel imaging modalities such as MRI and the visualisations during posterior fossa surgery for TGN have consistently shown a blood vessel in contact with the nerve root. Second, elimination of the compression leads to long-term pain relief in most patients (Barba D. et al., 1984; Cutbush K. et al., 1994; Kolluri S. et al., 1984). Third, intra-operative recordings show immediate improvement in nerve conduction following decompression. Fourth, sensory functions recover as well following decompression (Nurmikko T.J. et al., 2001).

Several hypotheses regarding the development of cranial nerve compression syndromes have been published. Jannetta suggested that vascular compression develops when blood vessels elongate, leading to formation of vascular loops, an increased risk for vascular compression of one or more cranial nerves. He assumed that the mechanical effect of a pulsating blood vessel was the cause of the disease. He further hypothesized that the compression must be at the Root Entry Zone (REZ) of the cranial nerve to cause symptoms (De Ridder D. et al., 2002; Jannetta P.J., 1979).

Classically the REZ is considered the site of the pathology, as it is the locus of the transition from central to the peripheral myelin, being so a more

vulnerable part of the nerve (Gardner W.J., 1962; Jannetta P.J., 1979; van Loveren H. et al., 1982). This Obersteiner-Redlich (O-R) transitional zone is generally located 2 to 3 mm outside the zone of entry into the pons. An offending vessel at this point seems to be the most logic etiological mechanism responsible for TGN (Calvin W.H. et al., 1977). Even more, according to Kondo's Japanese group, if nerve compression by a blood vessel occurs at a site remote from the REZ, no symptoms develop (Kondo A., 1997; Sindou M. et al., 2002). However, Leclercq et al. (Leclercq T.A. et al., 1980) and Møller AR (Moller A.R., 1999) suggested that the compression can occur at any point along the cranial nerve, at the CNS segment also, and not only at the root entry zone. Also in the experience of Sindou's group (Sindou M. et al., 2002) a vascular contact or compression along the midthird portion of the nerve was found in 54.3% and at the exit of the nerve from Meckel's cave in 9.8% of the patients, versus 52.3% at the very site of the REZ. In addition to the fact that there is a great variation in the location of the OR (Obersteiner-Redlich) transitional zone in different individuals (Latchaw J.P., Jr. et al., 1983), there is a mechanism, at least indirectly, at the OR transitional zone. When a neurovascular compression remote to the REZ was found, it often exerted an important traction on the trigeminal REZ at the pons, especially when the offending vessel is an elongated superior cerebellar artery in a superior position pushing down the midthird of the root (Sindou M. et al., 2002).

The part of the nerve root that is usually compressed (the root entry zone) is actually within CNS tissue, which extends several millimetres along the root, so that the junction between CNS and PNS is well away from the surface of the pons (Love S. et al., 2001).

There is considerable evidence meantime that any vascular contact (artery or vein) can cause symptomatic (Moller A.R., 1999). But, vascular contact with a cranial nerve is common (Ouaknine G.E. et al., 1980; Schwaber M.K. et al., 1992)8, however, symptoms of vascular compression are rare (Adams C.B., 1989; Auger R.G. et al., 1990; Katusic S. et al., 1990). Adams in his work "Microvascular compression: an alternative view and hypothesis", 1989

and Sweet (Sweet W.H., 1990) have affirmed that microvascular contact with trigeminal roots is a normal ageing change and that root compression is not a specific cause of trigeminal neuralgia. They strongly deny the responsibility of a vascular agent as the main cause of the trigeminal neuralgia and consequently do not agree with the fact that microvascular decompression procedure is a justified surgical treatment. The alternative to this suggestion is that microvascular compression, distinct from mere (simple) vascular contact, appears to be common in trigeminal neuralgia and rare in persons without TGN symptoms (Hamlyn P.J. et al., 1992). The degree of pathological change within the nerve was turned to grad with the degree of present compression, moreover, severe changes were restricted to the quadrant of the root that directly abutted the vessel (Devor M. et al., 2002b). Besides of that, microvascular decompression surgery provides pain relief. Therefore is considered that damage caused by trigeminal root compression is a sufficient condition to induce symptoms of trigeminal neuralgia, though it is not a necessary condition (Devor M. et al., 2002a).

This discrepancy has been explained also by the assumption that a second factor, such as previous minor injury, is necessary for creating symptoms such as trigeminal neuralgia (Moller M.B. et al., 1993).

All described in the pathophysiology chapter changes normalise following successful microvascular decompression (Leandri M. et al., 1998; Miles J.B. et al., 1997; Nurmikko T.J. et al., 2001). If it would be assumed that the dynamic pain of trigeminal neuralgia reflects a state of hyperexcitability in the trigeminal afferents rather than a fixed anatomical aberration constantly driving the pain mediating fibres, then either permanent destruction of the relevant fibres or complete restoration of their normal function (e.g. following decompression) will only achieve sustained pain relief (Nurmikko T.J. et al., 2001).

5.2 Reliability of the HR-MR sequences to detect the causative vessel of microvascular compression in trigeminal neuralgia

The pertinent literature includes meantime a growing number of reports pointing out the accuracy of high resolution MRI in predicting compression on the trigeminal root (Akimoto H. et al., 2002; Chang J.W. et al., 2000; Elias W.J. et al., 2002; Fukuda H. et al., 2003; Hastreiter P. et al., 2003; Kakizawa Y. et al., 2003; Patel N.K. et al., 2003; Yoshino N. et al., 2003). Recent developments in HR-MR sequences as (3D heavily T2-w and 3D T1 GE) had led to their increased value of vascular imaging. The high resolution gradient-echo sequences (T1-weighted or TOF) as also in our case 3D-FSPGR depict fast-flowing blood as high signal intensity and provide thin-slice images that can be processed for multiplanar reconstruction parallel and coronal to the trigeminal nerve to gain information of possible vascular compression. The contrast resolution of 3D-FSPGR sequence, between cerebrospinal fluid and the trigeminal nerve is not so satisfactory as for 3D-FIESTA sequence. This high-resolution, heavily T2-weighted image is capable of contrasting both vascular structures and nerves from cerebrospinal fluid. A combination of both high-resolution imaging techniques is more likely to detect the causative vessel in patients suffering from trigeminal neuralgia if the investigator knows which side exhibits the symptoms, in our case neurosurgeon. To overcome prejudice we analysed the accuracy of high-resolution imaging for microvascular compression by withholding the patients' clinical details during neuroradiological interpretation of the images.

As we could, in almost all cases, depict the vessel in close relationship to the trigeminal nerve or REZ, the difficulty was to decide whether this is the causative vessel for the patients' complaints. Perhaps HR-MRI is more likely to reveal larger vessels than those vessels that may be observed intraoperatively.

Our data demonstrate that high-resolution magnetic resonance imaging (HR-MRI) using double-dose contrast-enhanced 3D-FSPGR (n=30) and 3D-FIESTA (n=13) sequences in patients with trigeminal neuralgia is presently may be not sufficient enough for an accurate detection and assessment of

neurovascular compression when the neuroradiologist is blind to the affected side. Although 3D imaging provided high resolution between the cerebrospinal fluid and the trigeminal nerve, neurovascular compression could be predicted in 60.71% of the individuals, in accordance with the intraoperative finding in our study. In 13 patients where, additionally, 3D-FIESTA sequences were applied the accordance inclined to 69.23%. This detail conveys the impression that better spatial resolution of nerve, vessel and cerebrospinal fluid improves the diagnostic value of HR-MRI.

Therefore, 3D-FIESTA sequence, which contrasts liquid and solid structures, is a very helpful tool to determine whether there is cerebrospinal fluid between the vessels and nerve.

Also stereoscopic views and fly-through movie-style images are helpful tools for studying the surrounding anatomy.

The additional use of complementary time-of-flight (TOF) MR angiography sequences with and without contrast media as obtained by Yousry (Yousry I. et al., 2004), or Elias (Elias W.J. et al., 2002), or Akimoto (Akimoto H. et al., 2002) provides a reasonable tool to assess the neurovascular relationships between all branches of the trigeminal nerve. This complementary technique might have improved our results in terms of causative vessel detection.

Also the possibility to obtain real three-dimensional images (we obtained only 3D data) for visualisation could improve our results. The 2D slice-images require extensive experience from the observer part to achieve a correct assessment, which may be incomprehensible to others observers. In many cases this modality does not give a satisfactory overview of the underlying complex anatomy in the posterior fossa. The importance of 3D visualisation was proved in their studies by Naraghi R. and his colleagues (Naraghi R. et al., 2004). There are many reports of the use of 3-D images as time-of-flight sequences or 3D heavily T2-weighted sequences in the evaluation of patients with trigeminal neuralgia (Akimoto H. et al., 2002; Boecher-Schwarz H.G. et al., 1998; Casselman J.W. et al., 1993; Furuya Y. et al., 1992; Hermans R. et al., 1997; Korogi Y. et al., 1995; Meaney J.F. et al., 1995; Nagaseki Y. et al., 1992). Although heavily T2-weighted MR images as well as T1 GE MR sequences and time of flight MR angiography produce 3D

imaging data, it is important to point out the principal difference between 3D imaging data and 3D visualisation. A number of studies apply 3D MR sequences and they are interpreted like to be 3D illustrations or visualisations. But in terms of computer graphics, 3D visualisation comprises all methods of volume rendering, which allow to extract and to show 3D representations of 3D imaging data. Complete 3D images or illustrations are likely to have a higher sensitivity and specificity as just plain 3D MR imaging data or sequences (Naraghi R. et al., 2004).

Another problem of 3D-MRI imaging is the difficulty in examining and recognizing smaller arterial branches, or even veins. Small causative vessels can fail to be noticed by MRI due to overlap with the vertebro-basilar arteries or other dominant large arteries. Our results reveal that the specificity and accuracy of these methods and mainly the use of 3D-FSPGR MRI sequence and reconstructions are relatively low in term to detect small causative vessel.

The problem of image resolution might have influenced our results, while detecting the causative vessel for trigeminal neuralgia in this single-blind setting. Using only 3D-FSPGR sequences the investigator always had the difficulty of deciding whether visualized vessels were causative or not. These results, therefore, are contrary to some data presented in the literature, where up to 93% (Meaney J.F. et al., 1995; Patel N.K. et al., 2003) – 90.5%; (Yoshino N. et al., 2003) of the vascular compression was identified by MR angiography, or 95% (Akimoto H. et al., 2002) after 3D reconstructed images of 3D-FISP and 3D-CISS sequences had been observed. To overcome these shortcomings we must achieve higher resolution MR images to gain better discrimination of different vessel types compressing the trigeminal nerve and its entry zone and we must perform both sequences concomitantly from the same position in all patients.

We could not establish in our images the location of the neurovascular conflict around the nerve and along the trigeminal root to make the evaluations of which trigeminal branch(-es) were affected clinically (V1, V2,

or V3). We found it to speculative to make these clinical judgment based on images, were already to determine the causative vessel between many of them, always present around the nerve, was a challenge. Differentiation between artery and vein was not attempted, as this factor was not thought to influence the treatment management and we did not find it completely reliable in this respect. We did no attempt to name the vessel, not only would this not change management, it turned to be difficult. And we couldn't also identify the degree of compression of the trigeminal nerve root.

Nurmiko T.J. and Eldridge P.R. in their publication "Trigeminal neuralgia – pathophysiology, diagnosis and current treatment, 2001" made their observations towards the blinded studies: Because to date there are no prospective studies comparing different facial pain groups and healthy controls, evaluated by radiologists blinded to the conditions and side, the accuracy of MRTA in differentiating TGN from other painful trigeminal neuropathies remains uncertain. And also Sindou M. and colleagues in their study "Anatomical observations during microvascular decompression for idiopathic trigeminal neuralgia (with correlations between topography of pain and site of the neurovascular conflict). Prospective study in a series of 579 patients, 2002" conclude that their experience does not confirm MRI examination reliable enough to affirm the presence or the absence of neurovascular compression. Therefore, MRTA cannot be used to diagnose trigeminal neuralgia (according to Sindou M. et al., 2002). The current practice of Nurmiko and Eldridge is to use MRTA to help in determining the likelihood that, at operation, a significant vessel contact would be found.

So, our initially prospective blinded to neuroradiologists study and subsequently with a retrospective after deblinding analyse is one of the few in the current literatures blinded studies concerning trigeminal neuralgia (Patel N.K. et al., 2003): "How accurate is magnetic resonance angiography in predicting neurovascular compression in patients with trigeminal neuralgia? A prospective, single-blinded comparative study"; (Yoshino N. et al., 2003): "Trigeminal neuralgia: Evaluation of Neuralgic Manifestation and Site of Neurovascular Compression with 3D CISS MR Imaging and MR Angiography").

Neurosurgeons will also gain information about the presence or absence of vessels in contact with the trigeminal nerve, which will help to determine how to explore the area. Most neurosurgeons perform an MRI with special HR-MR for microvascular compression before performing a microvascular decompression.

Although operative indications should be based on clinical symptoms, vascular contact at the trigeminal nerve seen neuroradiologicaly on the symptomatic side provides support for operation. HR-MRI with its special sequences for microvascular compression is considered useful diagnostic tool in that it enables us to predict operative findings in advance: for example, compression by dolichoectatic artery of the vertebro-basilar system or by two or more vessels makes the operation more difficult than usual. That is why the neurosurgeons require preoperative HR-MRI imaging for vascular compression representation with a competent report of an experienced neuroradiologist.

5.3 Retrospective analysis

While analysing our results after deblinding we could conclude that our first look was almost not different from the second. We could change our results only in three cases (10%). For the rest of the cases we could further affirm that we saw our causative vessel same as before. Knowing the intraoperative situs the neurovascular compression could be proved clearly. In these cases however the other unaffected side showed a close spatial neurovascular relationship as well. This could have provoked a distraction, thus the observer preferred the false side.

This conclusion gives us the persuasion that the first prospective analysis is not subjective and doesn't depend on the observers (in-)competence, attention, or other subjective factors. It is likely our insufficient accuracy of the HR-MR results are based on the technique unsatisfactory factors: either still not performant enough for such demanding microvascular contact or it is too laborious to be used in daily practice.

5.4. Conclusion

We proved in our study, particularly by retrospective analysis that the high-resolution magnetic resonance imaging with double-dose contrast-enhanced 3D-FSPGR and 3D-FIESTA sequences could be objective, especially when clinical data are not blind to neuroradiologists. In order to get more precise results, the usage of both high-resolution MR sequences should be a condition. Our study revealed that the improving of technique modalities as described in “Discussion” chapter is to be introduced routinely.

In spite of neurosurgeons’ conclusion that the high-resolution magnetic resonance imaging with double-dose contrast-enhanced 3D-FSPGR and 3D-FIESTA sequences are not reliable enough to demonstrate the neurovascular compression, they still prefer to have preoperatively the 3D-FSPGR and 3D-FIESTA images, thus knowing clinically the affected side we are able to improve preoperative preparations and intraoperative expectations.

The surgical decision in order to perform microsurgical decompression in patients with trigeminal neuralgia should still be, and is made by clinical consideration. Our results show that HR-MRI should presently not be regarded as a decision-making tool for routine clinical work until its image quality is improved by higher image resolution for the trigeminal nerve, veins and arteries.

We should next perform both 3D-FIESTA and 3D-FSPGR in all patients in the same position. We should gain for both sequences real three-dimensional images for a satisfactory overview of the small vessels around the trigeminal nerve. It would be of a great importance the use of such additional tools as TOF Angiography and 3D visualisation (not 3D data) (Naraghi R. et al., 2004; Yousry I. et al., 2004). Additionally such modalities as volumetry and cisternoscopy to analyse the root alterations and surrounding abnormalities as described in the pertinent literature could be over great usage to detect the affected side in neurovascular compression of trigeminal nerve (el Gammal T. et al., 1994; Heine C. et al., 2002; Kress B. et al., 2004; Sindou M. et al., 2002).

6. Summary

Introduction: Neurovascular compression of the trigeminal nerve by an overlying vessel, mostly at the root entry zone is considered to be the major cause of trigeminal neuralgia (TGN).

The most prevalently used operation technique in patients with trigeminal neuralgia is the microvascular decompression (MVD). Peter Jannetta was the first neurosurgeon to apply the operating microscope to the problem of TGN and devised a technique for nondestructive MVD of the nerve. Decompression of the nerve root produces a rapid and long-term relief of symptoms in most patients (80-90%) with vessel-associated TGN.

High-Resolution Magnetic Resonance Imaging (HR-MRI) with special sequences: 3D-FSPGR und 3D-FIESTA is used in preoperative evaluation of neurovascular compression in patients with TGN.

Purpose: To assess whether vascular compression of trigeminal nerve in patients with trigeminal neuralgia could be demonstrated reliably by preoperative HR-MRI and how high is the correspondence among MRI results and intraoperative findings in a single blinded study with retrospective analysis after deblinding.

Patients and methods: We examined preoperatively thirty (30) patients with TGN with HR-MRI using 3D-FIESTA (three-dimensional fast imaging employing steady-state acquisition) and double-dose contrast enhanced 3D-FSPGR (three-dimensional fast spoiled gradient-recalled) sequences. These images and postprocessed multiplanar reconstruction (MPR) images were analyzed and later compared with intraoperative videoobservations. Afterwards these results were evaluated in a retrospective analysis of the same MR-images.

Results: In all 30 cases the trigeminal nerve could be seen clearly in the 3D-FSPGR sequence. The MPR provided very good images to evaluate the fifth cranial nerve. By injection of double dose of Gadolinium-DTPA even

small vessels showed a good enhancement to distinguish them from the surroundings.

The 3D-FIESTA sequence, additionally performed in 13 patients, was also able to show the spatial relationships between the structures brilliantly.

In 13 of 30 patients (43.33%) preoperative HR-MRI demonstrated the neurovascular compression in good agreement with the intraoperative findings. The noted suspicious side of pathology and also the affected region of trigeminal nerve were in accordance with the intraoperative findings in 12 of 13 cases.

The assessment of preoperative HR-MRI concerning the side of neurovascular compression failed in 8 of 30 cases (26.67%).

In 9 remaining patients the postoperative results turned out to be different as neurovascular compression: demyelination lesion, Teflon® interponate from previous operation, or neither preoperative MRI on the affected side, nor intraoperative observations demonstrated neurovascular compression with evident TGN, so termocoagulation was performed.

So in total preoperative HR-MRI demonstrated the neurovascular condition in good accordance with the intraoperative observations in 19 of 30 patients **(63.33%)**. MRI failed in 11 of 30 cases **(36.67%)**.

Conclusion: The HR-MRI with special sequences could be objective, especially when clinical data are not blind to neuroradiologists. In order to get more precise results, the usage of both high-resolution MR sequences should be a condition.

Although the HR-MRI is not absolutely reliably in order to show neurovascular compression, the neurosurgeons still prefer to have preoperatively the 3D-FSPGR and 3D-FIESTA images, thus knowing clinically the affected side they are able to improve preoperative preparations and intraoperative expectations.

Zusammenfassung

Diagnostischer Wert des präoperativen MRT zur Erkennung einer neurovaskulären Kompression des Nervus Trigeminus bei Patienten mit Trigeminusneuralgie.

Einleitung: Die neurovaskuläre Kompression des Nervus Trigeminus durch eine Gefäßschlinge, meist an der Austrittstelle des Nerven aus dem Hirnstamm, an der so genannten „Root Entry Zone“, wird als Hauptursache der Trigeminusneuralgie angesehen.

Die am häufigsten durchgeführte Operationstechnik bei Patienten mit Trigeminusneuralgie (TGN) ist die microvaskuläre Dekompression (MVD). Peter Jannetta war der erste Neurochirurg, der bei der Behandlung einer TGN, das Operationsmikroskop einsetzte und die Technik einer nicht destruktiven MVD des Trigeminus entwickelte. Die Dekompression der Nervenwurzel führt bei den meisten Patienten mit vaskulärer Kompression des Nervus Trigeminus zu einer schnellen und langfristigen Schmerzfreiheit.

Zur präoperativen Darstellung der neurovaskulären Kompression bei Patienten mit Trigeminusneuralgie wird heute die hoch auflösende Magnetresonanztomografie (HR-MRT) mit speziellen Sequenzen (3D-FSPGR und 3D-FIESTA) angewendet.

Ziel dieser Arbeit: Die Beurteilung der Zuverlässigkeit der präoperativen Darstellung der neurovasculären Kompression im HR-MRT bei Patienten mit Trigeminusneuralgie bzw. die Frage wie hoch die Übereinstimmung der MRT- Befunde mit dem intraoperativen Situs ist.

Patienten und Methoden: Dreißig (30) Patienten mit TGN wurden präoperativ kernspintomografisch mit speziellen Sequenzen – 3D-FIESTA (three-dimensional fast imaging employing steady-state acquisition) und 3D-FSPGR (three-dimensional fast spoiled gradient-recalled) mit doppelter Dosis Kontrastmittel untersucht. Diese Aufnahmen sowie die nachberechneten multiplanaren Rekonstruktionen (MPR) wurden blind, ohne die klinische betroffene Seite im Kenntnis zu haben, beurteilt und anschließend mit dem intraoperativen Videomaterial verglichen. Nach Entblindung wurden die gleichen MR-Aufnahmen nochmals retrospektiv analysiert.

Ergebnisse: Bei allen Patienten konnte der Nervus Trigeminus insbesondere in der 3D-FSPGR Sequenz klar dargestellt werden. Die MPR lieferte sehr gute Bilder zur Beurteilung des fünften Hirnnervens. Durch Injektion einer doppelten Dosis von Gadolinium-DTPA konnten auch die kleinen Gefäße kontrastiert und von der Umgebung gut differenziert werden.

Bei 13 Patienten wurde zusätzlich eine 3D-FIESTA Sequenz durchgeführt. Sie lieferte ebenfalls eine ausgezeichnete Hochauflösung zwischen den unterschiedlichen Strukturen.
Bei 13 von 30 Patienten (43,33%) zeigte sich eine gute Korrelation zwischen HR-MRT und intraoperativem Befund, bzw. die neurovaskuläre Kompression. Die kernspintomografisch verdächtigte Seite sowie die tatsächliche betroffene Region stimmten in 12 von 13 Fällen mit dem intraoperativen Befund überein.
In 8 von 30 Fällen (26,67%) gab es keine Übereinstimmung des MRT-Befundes mit dem intraoperativen Situs.
Bei den 9 verbleibenden Patienten offenbarte die Operation andere Gründe für die TGN: demyelinisierende Läsionen, Teflon®-Interponat von Voroperationen. In manchen Fällen fand sich weder im MRT noch operativ eine neurovaskuläre Kompression.
Insgesamt fanden wir bei 19 von 30 Patienten **(63,33%)** eine Übereinstimmung des präoperativen HR-MRT mit den intraoperativen Ergebnissen.

Schlussfolgerung: Das HR-MRT mit speziellen Sequenzen kann zuverlässige Ergebnisse bezüglich einer neurovaskulären Kompression liefern, insbesondere wenn klinische Angaben für Neuroradiologen bekannt sind.
Dabei sind beide hochauflösende Sequenzen erforderlich und ergänzen sich. Trotz nicht hundertprozentiger Aussagekraft des HR-MRT bezüglich der neurovaskulären Kompression ist die präoperative Bildgebung von Seiten der Neurochirurgie erwünscht, da sie so die intraoperativen Erwartungen besser einschätzen können.

Rezumat

Valoarea diagnostică a imagisticii preoperatorii prin rezonanță magnetică în evaluarea compresiei vasculare a nervului trigemen la pacienții cu neuralgie de trigemen

Introducere: Compresiunea neurovasculară a nervului trigemen de către un vas sangvin, în majoritatea cazurilor în zona de ieşire a nervului din trunchiul cerebral, aşa numita „root entry zone" este considerată cauza majoră a neuralgiei de trigemen.

Tehnica operatorie efectuată cu predilecție la pacienții cu neuralgie de trigemen (TGN) este decompresia microvasculară (MVD). Peter Jannetta a fost primul neurochirurg care a utilizat microscopul în problema TGN şi a dezvoltat o tehnică pentru MVD a nervului. Decompresia nervului produce eliberarea rapida şi de durată de simptome la majoritatea pacienților (80-90%) cu TGN vasculară.

Imagistica prin rezonanță magnetică (IRM) cu rezoluție înaltă (HR-MRI) cu secvențe speciale: 3D-FSPGR şi 3D-FIESTA) este utilizată în evaluarea preoperatorie a compresiei neurovasculare la pacienții cu TGN.

Scopul lucrării a fost de a aprecia dacă compresia vasculară a nervului trigemen la pacienții cu neuralgie de trigemen poate fi demonstrată cu fermitate prin HR-MRI şi care e concordanța între rezultatele IRM şi constatările intraoperatorii într-un studiu orb simplu cu analiză retrospectivă după divulgarea datelor clinice.

Pacienți şi metode: Am examinat preoperativ treizeci (30) pacienți cu TGN prin HR-MRI utilizând secvențele 3D-FIESTA (three-dimensional fast imaging employing steady-state acquisition) şi 3D-FSPGR (three-dimensional fast spoiled gradient-recalled) cu doză dubla de remediu de contrast. Aceste imagini şi imaginile postprocesate după reconstrucție multiplanară (MPR) au fost analizate şi apoi comparate cu observările video intraoperatorii. Ulterior aceste rezultate au fost evaluate retrospectiv în baza aceloraşi imagini.

Rezultate: În toate 30 de cazuri nervul trigemen a putut fi clar vizualizat in secvența 3D-FSPGR. Cu ajutorul MPR au putut fi realizate imagini bune în vederea evaluării nervului cranial cinci. Prin injectarea dozei duble de Gadolinium-DTPA până şi vasele sangvine mici se contrastează aşa încât se pot diferenția excelent de structurile înconjurătoare.

Secvența 3D-FIESTA efectuată adăugător la 13 pacienți a furnizat imagini cu rezoluție spațială înaltă între structurile anatomice.

La 13 din 30 pacienți (43,33%) HR-MRI preoparativ a demonstrat compresia vasculară în coincidență completă cu rezultatele intraoperatorii. Atât partea patologică suspectă notată, cât şi regiunea afectată a nervului trigemen a coincis cu situația intraoperatorie în 12 din 13 cazuri.

Evaluarea preoperativă prin HR-MRI privitor la partea afectată prin compresie neurovasculară a eşuat în 8 din 30 cazuri (26,67%).

La cei 9 pacienți rămaşi rezulatatele postoperatorii s-au dovedit a fi deosebite decât compresia neurovasculară: leziuni demielinizante, interponat Teflon® de la operațiile anterioare, sau nici IRM preoperativ referitor la partea afectată, nici intraoperator nu s-a demonstrat compresie neurovasculară, astfel încât s-a efectuat termocoagularea nervului.

În total, HR-MRI a demonstrat compresia neurovasculară în coincidență cu situația intraoperatorie la 19 din 30 pacienți **(63,33%)**.

Concluzii: HR-MRI cu secvențele speciale poate demonstra cu fermitate compresia neurovasculară preoperativ, mai ales când datele clinice le sunt cunoscute neuroradiologilor. Pentru a obține rezultate mai precise, e necesar de a efectua ambele secvențe de IRM cu rezoluție înaltă.

În pofida sensibilității secvențelor speciale de IRM ce nu atinge nivelul maximal întru demonstrarea compresiei neurovasculare, imagistica preoperatorie este favorizată de către neurochirurgi, întrucât ei pot avea aşteptări mai sigure intraoperatorii şi pot cu o mai pare precizie planifica intervenția chirurgicală.

7. Reference List

1. Adams C.B.: **Microvascular compression: an alternative view and hypothesis**, *J.Neurosurg.* 1989; 70 (1): 1-12.

2. Akimoto H., Nagaoka T., Nariai T., Takada Y., Ohno K., Yoshino N.: **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**, *Neurosurgery* 2002; 51 (4): 956-961.

3. Ameli N.O.: **Avicenna and trigeminal neuralgia**, *J.Neurol.Sci.* 1965; 2 (2): 105-107.

4. Auger R.G., McManis P.G.: **Trigeminal sensory neuropathy associated with decreased oral sensation and impairment of the masseter inhibitory reflex**, *Neurology* 1990; 40 (5): 759-763.

5. Bakshi R., Lerner A., Fritz J.V., Sambuchi G.D.: **Vascular compression in trigeminal neuralgia shown by magnetic resonance imaging and magnetic resonance angiography image registration**, *Arch Neurol.* 2001; 58 (8): 1290-1291.

6. Barba D., Alksne J.F.: **Success of microvascular decompression with and without prior surgical therapy for trigeminal neuralgia**, *J.Neurosurg.* 1984; 60 (1): 104-107.

7. Barker F.G., Jannetta P.J., Babu R.P., Pomonis S., Bissonette D.J., Jho H.D.: **Long-term outcome after operation for trigeminal neuralgia in patients with posterior fossa tumors**, *J.Neurosurg.* 1996; 84 (5): 818-825.

8. Barker F.G., Jannetta P.J., Bissonette D.J., Jho H.D.: **Trigeminal numbness and tic relief after microvascular decompression for typical trigeminal neuralgia**, *Neurosurgery* 1997; 40 (1): 39-45.

9. Battista A.F., Alban E.: **Effect of graded ligature compression on nerve conduction**, *Exp.Neurol.* 1983; 80 (1): 186-194.

10. Beaver D.L.: **Electron microscopy of the gasserian ganglion in trigeminal neuralgia**, *J.Neurosurg.* 1967; 26 (1): Suppl-50.

11. Bennett M.H., Jannetta P.J.: **Evoked potentials in trigeminal neuralgia**, *Neurosurgery* 1983; 13 (3): 242-247.

12. Bergouignan M.: **Cures heureuses de nevralgies facialis essentielles par le diphennyl-hydantoinate de soude**, *Laryngol Otol Rhinol (Bord)* 1942; 63 34-41.

13. Bien S., Richter H.P., Schafer M., Klein H.J.: **[Pathophysiology, differential diagnosis and therapy of trigeminal neuralgia]**, *ZWR.* 1988; 97 (11): 950-963.

14. Boecher-Schwarz H.G., Bruehl K., Kessel G., Guenthner M., Perneczky A., Stoeter P.: **Sensitivity and specificity of MRA in the diagnosis of neurovascular compression in patients with trigeminal neuralgia. A correlation of MRA and surgical findings**, *Neuroradiology* 1998; 40 (2): 88-95.

15. Borges A.: **Trigeminal neuralgia and facial nerve paralysis**, *Eur.Radiol.* 2005; 15 (3): 511-533.

16. Bornemann A., Bohl J., Hey O., Storkel S., Gamm H., Muller-Forell W., Perneczky A., Goebel H.H.: **Amyloidoma of the gasserian ganglion as a cause of symptomatic neuralgia of the trigeminal nerve: report of three cases**, *J.Neurol.* 1993; 241 (1): 10-14.

17. Bowsher D., Miles J., Haggett C.E., Eldridge P.: **Trigeminal neuralgia: a quantitative sensory perception threshold study in patients who had not undergone previous invasive procedures**, *J Neurosurg* 1997; 86 190-192.

18. Burchiel K.J.: **Trigeminal neuropathic pain**, *Acta Neurochir.Suppl (Wien.)* 1993; 58 145-149.

19. Bussone G., Usai S.: **Trigeminal autonomic cephalalgias: from pathophysiology to clinical aspects**, *Neurol.Sci.* 2004; 25 Suppl 3 S74-S76.

20. Calvin W.H., Loeser J.D., Howe J.F.: **A neurophysiological theory for the pain mechanism of tic douloureux**, *Pain* 1977; 3 (2): 147-154.

21. Casselman J.W.: **The upper and lower cranial nerves**, 2004;

22. Casselman J.W., Kuhweide R., Deimling M., Ampe W., Dehaene I., Meeus L.: **Constructive interference in stedy state: 3DFT MR imaging of the inner ear and cerebellopontine angle**, *AJNR Am.J.Neuroradiol.* 1993; 14 47-57.

23. Chang J.W., Chang J.H., Park Y.G., Chung S.S.: **Microvascular decompression in trigeminal neuralgia: a correlation of three-**

dimensional time-of-flight magnetic resonance angiography and surgical findings, *Stereotact.Funct.Neurosurg.* 2000; 74 (3-4): 167-174.

24. Chavez G.D., De Salles A.A., Solberg T.D., Pedroso A., Espinoza D., Villablanca P.: **Three-dimensional fast imaging employing steady-state acquisition magnetic resonance imaging for stereotactic radiosurgery of trigeminal neuralgia**, *Neurosurgery* 2005; 56 (3): E628-

25. Chavin J.M.: **Cranial neuralgias and headaches associated with cranial vascular disorders**, *Otolaryngol.Clin.North Am.* 2003; 36 (6): 1079-93, vi.

26. Childs A.M., Meaney J.F., Ferrie C.D., Holland P.C.: **Neurovascular compression of the trigeminal and glossopharyngeal nerve: three case reports**, *Arch Dis.Child* 2000; 82 (4): 311-315.

27. Chong V.F.: **Trigeminal neuralgia in nasopharyngeal carcinoma**, *J.Laryngol.Otol.* 1996; 110 (4): 394-396.

28. Clifford-Jones R.E., McDonald W.I., Landon D.N.: **Chronic optic nerve compression. An experimental study**, *Brain* 1985; 108 (Pt 1) 241-262.

29. Coffey R.J., Fromm G.H.: **Familial trigeminal neuralgia and Charcot-Marie-Tooth neuropathy. Report of two families and review**, *Surg Neurol.* 1991; 35 (1): 49-53.

30. Cutbush K., Atkinson R.L.: **Treatment of trigeminal neuralgia by posterior fossa microvascular decompression**, *Aust.N.Z.J.Surg* 1994; 64 (3): 173-176.

31. Dandy W.E.: **Concerning the coause of the trigeminal neuralgia**, *Am J Surg* 1934; 24 447-455.

32. De Marco J.K., Hesselink J.R.: **Trigeminal neuropathy**, *Neuroimaging Clin.N.Am.* 1993; 3 117-

33. De Ridder D., Moller A., Verlooy J., Cornelissen M., De Ridder L.: **Is the root entry/exit zone important in microvascular compression syndromes?**, *Neurosurgery* 2002; 51 (2): 427-433.

34. Devor M., Amir R., Rappaport Z.H.: **Pathophysiology of trigeminal neuralgia: the ignition hypothesis**, *Clin.J.Pain* 2002a; 18 (1): 4-13.

35. Devor M., Govrin-Lippmann R., Rappaport Z.H.: **Mechanism of trigeminal neuralgia: an ultrastructural analysis of trigeminal root specimens obtained during microvascular decompression surgery**, *J.Neurosurg.* 2002b; 96 (3): 532-543.

36. Duff J.M., Spinner R.J., Lindor N.M., Dodick D.W., Atkinson J.L.: **Familial trigeminal neuralgia and contralateral hemifacial spasm**, *Neurology* 1999; 53 216-218.

37. el Gammal T., Brooks B.S.: **MR cisternography: initial experience in 41 cases**, *AJNR Am.J.Neuroradiol.* 1994; 15 (9): 1647-1656.

38. Elias W.J., Burchiel K.J.: **Microvascular decompression**, *Clin.J.Pain* 2002; 18 (1): 35-41.

39. Fern R., Harrison P.J.: **The effects of compression upon conduction in myelinated axons of the isolated frog sciatic nerve**, *J.Physiol* 1991; 432 111-122.

40. Fish C.J., Blakemore W.F.: **A model of chronic spinal cord compression in the cat**, *Neuropathol.Appl.Neurobiol.* 1983; 9 (2): 109-119.

41. Fromm G.H., Graff-Radford S.B., Terrence C.F., Sweet W.H.: **Pre-trigeminal neuralgia**, *Neurology* 1990; 40 (10): 1493-1495.

42. Fujimaki T., Hoya K., Sasaki T., Kirino T.: **Recurrent trigeminal neuralgia caused by an inserted prosthesis: report of two cases**, *Acta Neurochir.(Wien.)* 1996; 138 (11): 1307-1309.

43. Fukuda H., Ishikawa M., Okumura R.: **Demonstration of neurovascular compression in trigeminal neuralgia and hemifacial spasm with magnetic resonance imaging: comparison with surgical findings in 60 consecutive cases**, *Surg Neurol.* 2003; 59 (2): 93-99.

44. Furuya Y., Ryu H., Uemura K., Sugiyama K., Isoda H., Hasegawa S., Takahashi M., Kaneko M.: **MRI of intracranial neurovascular compression**, *J.Comput.Assist.Tomogr.* 1992; 16 (4): 503-505.

45. Gardner W.J.: **Concerning the mechanism of trigeminal neuralgia and hemifacial spasm**, *J.Neurosurg.* 1962; 19 947-958.

46. Gardner W.J., Miclos M.V.: **Response of trigeminal neuralgia to decompression of sensory root; discussion of cause of trigeminal neuralgia**, *J.Am.Med.Assoc.* 1959; 170 (15): 1773-1776.

47. General Electric Company: **MR 1.5 Signa® EXCITE™ 11.0 Learning and Reference Guide**, 2004; *2384192-100 Rev. 2 (01/04)*

48. Go J.L., Kim P.E., Zee C.S.: **The trigeminal nerve**, *Semin.Ultrasound CT MR* 2001; 22 (6): 502-520.

49. Golby A.J., Norbash A., Silverberg G.D.: **Trigeminal neuralgia resulting from infarction of the root entry zone of the trigeminal nerve: case report**, *Neurosurgery* 1998; 43 (3): 620-622.

50. Haddad F.S., Taha J.M.: **An unusual cause for trigeminal neuralgia: contralateral meningioma of the posterior fossa**, *Neurosurgery* 1990; 26 (6): 1033-1038.

51. Haines S.J., Jannetta P.J., Zorub D.S.: **Microvascular relations of the trigeminal nerve. An anatomical study with clinical correlation**, *J.Neurosurg.* 1980; 52 (3): 381-386.

52. Hamlyn P.J.: **Neurovascular relationships in the posterior cranial fossa, with special reference to trigeminal neuralgia. 2. Neurovascular compression of the trigeminal nerve in cadaveric controls and patients with trigeminal neuralgia: quantification and influence of method**, *Clin.Anat.* 1997; 10 (6): 380-388.

53. Hamlyn P.J., King T.T.: **Neurovascular compression in trigeminal neuralgia: a clinical and anatomical study**, *J.Neurosurg.* 1992; 76 (6): 948-954.

54. Hastreiter P., Naraghi R., Tomandl B., Bonk A., Fahlbusch R.: **Analysis and 3-dimensional visualization of neurovascular compression syndromes**, *Acad.Radiol.* 2003; 10 (12): 1369-1379.

55. Heine C., Klingebiel R., Lehmann R.: **Three-dimensional MR visualization of the intracisternal course of the cranial nerves V-VIII by virtual cisternoscopy**, *Acta Radiol.* 2002; 43 (3): 242-248.

56. Held P., Frund R., Seitz J., Nitz W., Haffke T., Hees H.: **Comparison of 2-D turbo spin echo and 3-D gradient echo sequences for the detection of the trigeminal nerve and branches anatomy**, *Eur.J.Radiol.* 2001; 37 (1): 18-25.

57. Hermans R., Van der G.A., De Foer B., Baert A.L.: **MRI screening for acoustic neuroma without gadolinium: value of 3DFT-CISS sequence**, *Neuroradiology* 1997; 39 (8): 593-598.

58. Hilton D.A., Love S., Gradidge T., Coakham H.B.: **Pathological findings associated with trigeminal neuralgia caused by vascular compression**, *Neurosurgery* 1994; 35 (2): 299-303.

59. Jager L.: **Temporal bone imaging with multislice CT**, 2003;

60. Jager L., Reiser M.: **CT and MR imaging of the normal and pathologic conditions of the facial nerve**, *Eur.J.Radiol.* 2001; 40 (2): 133-146.

61. Jamjoom A.B., Jamjoom Z.A., al Fehaily M., el Watidy S., al Moallem M., Nain U.R.: **Trigeminal neuralgia related to cerebellopontine angle tumors**, *Neurosurg.Rev.* 1996; 19 (4): 237-241.

62. Jannetta P.J.: **Arterial compression of the trigeminal nerve at the pons in patients with trigeminal neuralgia**, *J.Neurosurg.* 1967; 26 (1): Suppl-62.

63. Jannetta P.J.: **Microsurgery of cranial nerve cross-compression**, *Clin.Neurosurg.* 1979; 26 607-615.

64. Jannetta P.J.: **Neurovascular compression in cranial nerve and systemic disease**, *Ann.Surg* 1980; 192 (4): 518-525.

65. Javadpour M., Eldridge P.R., Varma T.R., Miles J.B., Nurmikko T.J.: **Microvascular decompression for trigeminal neuralgia in patients over 70 years of age**, *Neurology* 2003; 60 (3): 520-

66. Jawahar A., Kondziolka D., Kanal E., Bissonette D.J., Lunsford L.D.: **Imaging the trigeminal nerve and pons before and after surgical intervention for trigeminal neuralgia**, *Neurosurgery* 2001; 48 (1): 101-106.

67. Kakizawa Y., Hongo K., Takasawa H., Miyairi Y., Sato A., Tanaka Y., Kobayashi S.: **"Real" three-dimensional constructive interference in steady-state imaging to discern microneurosurgical anatomy. Technical note**, *J.Neurosurg.* 2003; 98 (3): 625-630.

68. Kamel H.A., Toland J.: **Trigeminal nerve anatomy: illustrated using examples of abnormalities**, *AJR Am.J.Roentgenol.* 2001; 176 (1): 247-251.

69. Kato T., Sawamura Y., Abe H.: **Trigeminal neuralgia caused by a cerebellopontine-angle lipoma: case report**, *Surg Neurol.* 1995; 44 (1): 33-35.

70. Katusic S., Beard C.M., Bergstralh E., Kurland L.T.: **Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945-1984**, *Ann.Neurol.* 1990; 27 (1): 89-95.

71. Katusic S., Williams D.B., Beard C.M., Bergstralh E.J., Kurland L.T.: **Epidemiology and clinical features of idiopathic trigeminal neuralgia and glossopharyngeal neuralgia: similarities and differences, Rochester, Minnesota, 1945-1984**, *Neuroepidemiology* 1991; 10 (5-6): 276-281.

72. Kerr F.W.: **Evidence for a peripheral etiology of trigeminal neuralgia**, *J.Neurosurg.* 1967; 26 (1): Suppl-74.

73. Kerr F.W., Miller R.H.: **The pathology of trigeminal neuralgia. Electron microscopic studies**, *Arch Neurol.* 1966; 15 308-319.

74. Kitt C.A., Gruber K., Davis M., Woolf C.J., Levine J.D.: **Trigeminal neuralgia: opportunities for research and treatment**, *Pain* 2000; 85 (1-2): 3-7.

75. Klun B.: **Microvascular decompression and partial sensory rhizotomy in the treatment of trigeminal neuralgia: personal experience with 220 patients**, *Neurosurgery* 1992; 30 (1): 49-52.

76. Kolluri S., Heros R.C.: **Microvascular decompression for trigeminal neuralgia. A five-year follow-up study**, *Surg Neurol.* 1984; 22 (3): 235-240.

77. Kondo A.: **Follow-up results of microvascular decompression in trigeminal neuralgia and hemifacial spasm**, *Neurosurgery* 1997; 40 (1): 46-51.

78. Korogi Y., Nagahiro S., Du C., Sakamoto Y., Takada A., Ushio Y., Ikushima I., Takahashi M.: **Evaluation of vascular compression in trigeminal neuralgia by 3D time-of-flight MRA**, *J.Comput.Assist.Tomogr.* 1995; 19 (6): 879-884.

79. Kress B., Griesbeck F., Stippich C., Bahren W., Sartor K.: **[Quantitative analysis of MRI intensity in of the major petrosal nerve in patients with idiopathic facial paralysis]**, *Nervenarzt* 2004; 75 (2): 124-127.

80. Kretschmann H.-J., Weinrich W.: **Klinische Neuroanatomie und kranielle Bilddiagnostik**, 2002; 3.

81. Kugelberg E., Lindblom U.: **The mechanism of the pain in trigeminal neuralgia**, *J.Neurochem.* 1959; 22 (1): 36-43.

82. Kumon Y., Sakaki S., Kohno K., Ohta S., Ohue S., Miki H.: **Three-dimensional imaging for presentation of the causative vessels in patients with hemifacial spasm and trigeminal neuralgia**, *Surg Neurol.* 1997; 47 (2): 178-184.

83. Kuroiwa T., Matsumoto S., Kato A., Harano K., Totoki T., Tabuchi K., Kudo S.: **MR imaging of idiopathic trigeminal neuralgia: correlation with non-surgical therapy**, *Radiat.Med.* 1996; 14 (5): 235-239.

84. Laine F.J., Smoker W.R.: **Anatomy of the cranial nerves**, *Neuroimaging Clin.N.Am.* 1998; 8 (1): 69-100.

85. Larrier D., Lee A.: **Anatomy of headache and facial pain**, *Otolaryngol.Clin.North Am.* 2003; 36 (6): 1041-53, v.

86. Latchaw J.P., Jr., Hardy R.W., Jr., Forsythe S.B., Cook A.F.: **Trigeminal neuralgia treated by radiofrequency coagulation**, *J.Neurosurg.* 1983; 59 (3): 479-484.

87. Leandri M., Eldridge P., Miles J.: **Recovery of nerve conduction following microvascular decompression for trigeminal neuralgia**, *Neurology* 1998; 51 (6): 1641-1646.

88. Leblanc A.: **Anatomy and Imaging of the Cranial Nerves**, 1992;

89. Leclercq T.A., Hill C.L., Grisoli F.: **Retromastoid microsurgical approach to vascular compression of the eighth cranial nerve**, *Laryngoscope* 1980; 90 (6 Pt 1): 1011-1017.

90. Lee S.H., Levy E.I., Scarrow A.M., Kassam A., Jannetta P.J.: **Recurrent trigeminal neuralgia attributable to veins after microvascular decompression**, *Neurosurgery* 2000; 46 (2): 356-361.

91. Linskey M.E., Jho H.D., Jannetta P.J.: **Microvascular decompression for trigeminal neuralgia caused by vertebrobasilar compression**, *J.Neurosurg.* 1994; 81 (1): 1-9.

92. Loeser J.D.: **Tic douloureux and atypical facial pain.**, *J.Can.Dent.Assoc.* 1985; 51 917-923.

93. Louryan S.: **Anatomy of the cranial nerves**, 2004;

94. Love S., Coakham H.B.: **Trigeminal neuralgia: pathology and pathogenesis**, *Brain* 2001; 124 (Pt 12): 2347-2360.

95. Love S., Hilton D.A., Coakham H.B.: **Central demyelination of the Vth nerve root in trigeminal neuralgia associated with vascular compression**, *Brain Pathol.* 1998; 8 (1): 1-11.

96. Lufkin R.B., Borges A., Nguyen K., Anzai Y.: **MRI of the head and neck**, 2001; 2nd

97. Lufkin R.B., Borges A., Villablanca P.: **Teaching atlas of head and neck imaging**, 2000; 1st

98. Magnaldi S., Cecconi P., Skrap M., Ricci C., Cova M.A., Pozzi-Mucelli R.S.: **[Magnetic resonance in trigeminal neuralgia]**, *Radiol.Med.(Torino)* 1992; 83 (6): 700-705.

99. Majoie C.B., Hulsmans F.J., Castelijns J.A., Verbeeten B., Jr., Tiren D., van Beek E.J., Valk J., Bosch D.A.: **Symptoms and signs related to the trigeminal nerve: diagnostic yield of MR imaging**, *Radiology* 1998; 209 (2): 557-562.

100. Majoie C.B., Hulsmans F.J., Verbeeten B., Jr., Castelijns J.A., van Beek E.J., Valk J., Bosch D.A.: **Trigeminal neuralgia: comparison of two MR imaging techniques in the demonstration of neurovascular contact**, *Radiology* 1997; 204 (2): 455-460.

101. Mason W.E., Kollros P., Jannetta P.J.: **Trigeminal neuralgia and its treatment in a 13-month-old child: a review and case report**, *J.Craniomandib.Disord.* 1991; 5 (3): 213-216.

102. Masur H., Papke K., Bongartz G., Vollbrecht K.: **The significance of three-dimensional MR-defined neurovascular compression for the pathogenesis of trigeminal neuralgia**, *J.Neurol.* 1995; 242 (2): 93-98.

103. Matsushima T., Huynh-Le P., Miyazono M.: **Trigeminal neuralgia caused by venous compression**, *Neurosurgery* 2004; 55 (2): 334-337.

104. Matsuura N., Kondo A.: **Trigeminal neuralgia and hemifacial spasm as false localizing signs in patients with a contralateral mass of the posterior cranial fossa. Report of three cases**, *J.Neurosurg.* 1996; 84 (6): 1067-1071.

105. Matthies C., Samii M.: **Management of 1000 vestibular schwannomas (acoustic neuromas): clinical presentation**, *Neurosurgery* 1997; 40 (1): 1-9.

106. McCormick P.C., Bello J.A., Post K.D.: **Trigeminal schwannoma. Surgical series of 14 cases with review of the literature**, *J.Neurosurg.* 1988; 69 (6): 850-860.

107. McLaughlin M.R., Jannetta P.J., Clyde B.L., Subach B.R., Comey C.H., Resnick D.K.: **Microvascular decompression of cranial nerves: lessons learned after 4400 operations**, *J.Neurosurg.* 1999; 90 (1): 1-8.

108. Meaney J.F., Eldridge P.R., Dunn L.T., Nixon T.E., Whitehouse G.H., Miles J.B.: **Demonstration of neurovascular compression in trigeminal neuralgia with magnetic resonance imaging. Comparison with surgical findings in 52 consecutive operative cases**, *J.Neurosurg.* 1995; 83 (5): 799-805.

109. Meaney J.F., Miles J.B., Nixon T.E., Whitehouse G.H., Ballantyne E.S., Eldridge P.R.: **Vascular contact with the fifth cranial nerve at the pons in patients with trigeminal neuralgia: detection with 3D FISP imaging**, *AJR Am.J.Roentgenol.* 1994; 163 (6): 1447-1452.

110. Merskey H.: **Logic, truth and language in concepts of pain**, *Qual.Life Res.* 1994; 3 Suppl 1 S69-S76.

111. Miles J.B., Eldridge P.R., Haggett C.E., Bowsher D.: **Sensory effects of microvascular decompression in trigeminal neuralgia**, *J.Neurosurg.* 1997; 86 (2): 193-196.

112. Mohanty A., Venkatrama S.K., Roa B.R., Chandramouli B.A., Jayakumar P.N., Das B.S.: **Experience with cerebellopontine angle epidermoids**, *Neurosurgery* 1997; 40 24-29.

113. Moller A.R.: **Vascular compression of cranial nerves: II: pathophysiology**, *Neurol.Res.* 1999; 21 (5): 439-443.

114. Moller M.B., Moller A.R., Jannetta P.J., Jho H.D.: **Vascular decompression surgery for severe tinnitus: selection criteria and results**, *Laryngoscope* 1993; 103 (4 Pt 1): 421-427.

115. Moulin D.E.: **Pain in central and peripheral demyelinating disorders**, *Neurol.Clin.* 1998; 16 (4): 889-898.

116. Nagaseki Y., Horikoshi T., Omata T., Ueno T., Uchida M., Nukui H., Tsuji R., Sasaki H.: **Oblique sagittal magnetic resonance imaging visualizing vascular compression of the trigeminal or facial nerve**, *J.Neurosurg.* 1992; 77 (3): 379-386.

117. Nakamura K., Yamamoto T., Zamashita M.: **Small medullary infarction presenting as painful trigeminal sensory neuropathy**, *J Neurol Neurosurg Psychiatry* 1996; 61 138-

118. Naraghi R., Hastreiter P., Tomandl B., Bonk A., Huk W., Fahlbusch R.: **Three-dimensional visualization of neurovascular relationships in the posterior fossa: technique and clinical application**, *J.Neurosurg.* 2004; 100 (6): 1025-1035.

119. Nurmikko T.J.: **Altered cutaneous sensation in trigeminal neuralgia**, *Arch Neurol.* 1991; 48 (5): 523-527.

120. Nurmikko T.J., Eldridge P.R.: **Trigeminal neuralgia--pathophysiology, diagnosis and current treatment**, *Br.J.Anaesth.* 2001; 87 (1): 117-132.

121. Ogasawara K., Koshu K., Nagamine Y., Fujiwara S., Mizoi K., Yoshimoto T.: **[Surgical decompression for massive cerebellar infarction]**, *No Shinkei Geka* 1995; 23 (1): 43-48.

122. Ouaknine G.E., Robert F., Molina-Negro P., Hardy J.: **Geniculate neuralgia and audiovestibular disturbances due to compression of the intermediate and eighth nerves by the postero-inferior cerebellar artery**, *Surg Neurol.* 1980; 13 147-150.

123. Patel N.K., Aquilina K., Clarke Y., Renowden S.A., Coakham H.B.: **How accurate is magnetic resonance angiography in predicting neurovascular compression in patients with trigeminal neuralgia? A prospective, single-blinded comparative study**, *Br.J.Neurosurg.* 2003; 17 (1): 60-64.

124. Poeck K., Hacke W.: **Neurologie**, 2001; 12.

125. Ramon F., Moore J.W.: **Ephaptic transmission in squid giant axons**, *Am.J.Physiol* 1978; 234 (5): C162-C169.

126. Rappaport Z.H., Devor M.: **Trigeminal neuralgia: the role of self-sustaining discharge in the trigeminal ganglion**, *Pain* 1994; 56 (2): 127-138.

127. Rappaport Z.H., Govrin-Lippmann R., Devor M.: **An electron-microscopic analysis of biopsy samples of the trigeminal root taken during microvascular decompressive surgery**, *Stereotact.Funct.Neurosurg.* 1997; 68 (1-4 Pt 1): 182-186.

128. Rasminsky M.: **Ectopic generation of impulses and cross-talk in spinal nerve roots of "dystrophic" mice**, *Ann.Neurol.* 1978; 3 (4): 351-357.

129. Rasminsky M., Kearney R.E., Aguayo A.J., Bray G.M.: **Conduction of nervous impulses in spinal roots and peripheral nerves of dystrophic mice**, *Brain Res.* 1978; 143 (1): 71-85.

130. Rasmussen P.: **Facial pain. II. A prospective survey of 1052 patients with a view of: character of the attacks, onset, course, and character of pain**, *Acta Neurochir.(Wien.)* 1990; 107 (3-4): 121-128.

131. Reilly M.M., Valentine A.R., Ginsberg L.: **Trigeminal neuralgia associated with osteogenesis imperfecta**, *J.Neurol.Neurosurg.Psychiatry* 1995; 58 (6): 665-

132. Resnick D.K., Levy E.I., Jannetta P.J.: **Microvascular decompression for pediatric onset trigeminal neuralgia**, *Neurosurgery* 1998; 43 (4): 804-807.

133. Revuelta R., Juambelz P., Balderrama J., Teixeira F.: **Contralateral trigeminal neuralgia: a new clinical manifestation of neurocysticercosis: case report**, *Neurosurgery* 1995; 37 (1): 138-139.

134. Richards P., Shawdon H., Illingworth R.: **Operative findings on microsurgical exploration of the cerebello-pontine angle in trigeminal neuralgia**, *J.Neurol.Neurosurg.Psychiatry* 1983; 46 (12): 1098-1101.

135. Richter H.P., Bien S., Schafer M., Klein H.J.: **[Microvascular decompression of the trigeminal nerve - a causal therapy of trigeminal neuralgia?]**, *Fortschr.Med.* 1984; 102 (1-2): 41-45.

136. Rose F.C.: **Trigeminal neuralgia**, *Arch Neurol.* 1999; 56 (9): 1163-1164.

137. Ruelle A., Datti R., Andrioli G.: **Cerebellopontine angle osteoma causing trigeminal neuralgia: case report**, *Neurosurgery* 1994; 35 (6): 1135-1137.

138. Saito A., Nakazawa T., Matsuda M., Handa J.: **[Comparison of computed tomographic scanning and magnetic resonance imaging in the diagnosis of trigeminal schwannoma. Report of four cases]**, *Neurol.Med.Chir (Tokyo)* 1989; 29 (12): 1101-1106.

139. Sakatani K., Ohta T., Yamagata Y., Shimo-Oku M.: **Effects of spinal cord compression on repetitive impulse conduction of the ascending fibers of the dorsal column**, *Neurosurg Rev* 1989; 12 (1): 575-581.

140. Schwaber M.K., Hall J.W.: **Cochleovestibular nerve compression syndrome. I. Clinical features and audiovestibular findings**, *Laryngoscope* 1992; 102 (9): 1020-1029.

141. Sevick R.J., Dillon W.P., Engstrom J., Bergman W.G., Harnsberger H.R.: **Trigeminal neuropathy: Gd-DTPA enhanced MR imaging**, *J.Comput.Assist.Tomogr.* 1991; 15 (4): 605-611.

142. Shi R., Blight A.R.: **Compression injury of mammalian spinal cord in vitro and the dynamics of action potential conduction failure**, *J.Neurophysiol.* 1996; 76 (3): 1572-1580.

143. Sindou M., Howeidy T., Acevedo G.: **Anatomical observations during microvascular decompression for idiopathic trigeminal neuralgia (with correlations between topography of pain and site of the neurovascular conflict). Prospective study in a series of 579 patients**, *Acta Neurochir.(Wien.)* 2002; 144 (1): 1-12.

144. Smith K.J., Blakemore W.F., McDonald W.I.: **The restoration of conduction by central remyelination**, *Brain* 1981; 104 383-404.

145. Smith K.J., Hall S.M.: **Nerve conduction during peripheral demyelination and remyelination**, *J.Neurol.Sci.* 1980a; 48 (2): 201-219.

146. Smith K.J., McDonald W.I.: **Spontaneous and mechanically evoked activity due to central demyelinating lesion**, *Nature* 1980b; 286 (5769): 154-155.

147. Smith K.J., McDonald W.I.: **Spontaneous and evoked electrical discharges from a central demyelinating lesion**, *J.Neurol.Sci.* 1982; 55 (1): 39-47.

148. Smyth P., Greenough G., Stommel E.: **Familial trigeminal neuralgia: case reports and review of the literature**, *Headache* 2003; 43 (8): 910-915.

149. Stone J.L., Lichtor T., Crowell R.M.: **Microvascular sling decompression for trigeminal neuralgia secondary to ectatic vertebrobasilar compression. Case report**, *J.Neurosurg.* 1993; 79 (6): 943-945.

150. Sun T., Saito S., Nakai O., Ando T.: **Long-term results of microvascular decompression for trigeminal neuralgia with reference to probability of recurrence**, *Acta Neurochir.(Wien.)* 1994; 126 (2-4): 144-148.

151. Sweet W.H.: **Complications of treating trigeminal neuralgia; an analysis of the literature and response to questionnaire. Evidence from manipulations anterior to the porus trigemini against the hypothesis that extrinsic compression of the trigeminal root near the pons is the most common cause of trigeminal neuralgia.**, 1990; 251-279.

152. Taarnhoj P.: **Decompression of the posterior trigeminal root in trigeminal neuralgia. A 30-year follow-up review**, *J.Neurosurg.* 1982; 57 (1): 14-17.

153. Taha J.M., Tew J.M., Jr., van Loveren H.R., Keller J.T., el Kalliny M.: **Comparison of conventional and skull base surgical approaches for the excision of trigeminal neurinomas**, *J.Neurosurg.* 1995; 82 (5): 719-725.

154. Tash R.R., Sze G., Leslie D.R.: **Trigeminal neuralgia: MR imaging features**, *Radiology* 1989; 172 (3): 767-770.

155. Tavares M.P.: **Trigeminal Neuralgia - Microvascular Decompression**,

156. Tenser R.B.: **Trigeminal neuralgia: mechanisms of treatment**, *Neurology* 1998; 51 (1): 17-19.

157. Turel K.E.: **Microvascular Decompression (MVD) for Trigeminal Neuralgia**, 2004;

158. Umehara F., Kamishima K., Kashio N., Yamaguchi K., Sakimoto T., Osame M.: **Magnetic resonance tomographic angiography: diagnostic value in trigeminal neuralgia**, *Neuroradiology* 1995; 37 (5): 353-355.

159. van Loveren H., Tew J.M., Jr., Keller J.T., Nurre M.A.: **a 10-year experience in the treatment of trigeminal neuralgia. Comparison of percutaneous stereotaxic rhizotomy and posterior fossa exploration**, *J.Neurosurg.* 1982; 57 (6): 757-764.

160. Waldman S.D.: **Trigeminal Neuralgia Evaluation & Treatment**, *Pain Digest* 1997; 7 (1): 21-24.

161. Williams L.S., Schmalfuss I.M., Sistrom C.L., Inoue T., Tanaka R., Seoane E.R., Mancuso A.A.: **MR imaging of the trigeminal ganglion, nerve, and the perineural vascular plexus: normal appearance and variants with correlation to cadaver specimens**, *AJNR Am.J.Neuroradiol.* 2003; 24 (7): 1317-1323.

162. Woolfall P., Coulthard A.: **Pictorial review: Trigeminal nerve: anatomy and pathology**, *Br.J.Radiol.* 2001; 74 (881): 458-467.

163. Worthington C., Hutson K., Boulware R., Neglia W., Gibbons J.P., Clark R., Rand J.: **Computerized tomography cisternography of the trigeminal nerve for stereotactic radiosurgery. Case report**, *J.Neurosurg.* 2000; 93 Suppl 3 169-171.

164. Yamakami I., Kobayashi E., Hirai S., Yamaura A.: **Preoperative assessment of trigeminal neuralgia and hemifacial spasm using constructive interference in steady state-three-dimensional Fourier transformation magnetic resonance imaging**, *Neurol.Med.Chir (Tokyo)* 2000; 40 (11): 545-555.

165. Yang J., Simonson T.M., Ruprecht A., Meng D., Vincent S.D., Yuh W.T.: **Magnetic resonance imaging used to assess patients with trigeminal neuralgia**, *Oral Surg Oral Med.Oral Pathol.Oral Radiol.Endod.* 1996; 81 (3): 343-350.

166. Yoshimasu F., Kurland L.T., Elveback L.R.: **Tic douloureux in Rochester, Minnesota, 1945-1969**, *Neurology* 1972; 22 (9): 952-956.

167. Yoshino N., Akimoto H., Yamada I., Nagaoka T., Tetsumura A., Kurabayashi T., Honda E., Nakamura S., Sasaki T.: **Trigeminal neuralgia: evaluation of neuralgic manifestation and site of neurovascular compression with 3D CISS MR imaging and MR angiography**, *Radiology* 2003; 228 (2): 539-545.

168. Yousry I., Camelio S., Schmid U.D., Horsfield M.A., Wiesmann M., Bruckmann H., Yousry T.A.: **Visualization of cranial nerves I-XII: value of 3D CISS and T2-weighted FSE sequences**, *Eur.Radiol.* 2000; 10 (7): 1061-1067.

169. Yousry I., Moriggl B., Holtmannspoetter M., Schmid U.D., Naidich T.P., Yousry T.A.: **Detailed anatomy of the motor and sensory roots of the trigeminal nerve and their neurovascular relationships: a magnetic resonance imaging study**, *J.Neurosurg.* 2004; 101 (3): 427-434.

170. Zakrzewska J.M.: **Diagnosis and differential diagnosis of trigeminal neuralgia**, *Clin.J.Pain* 2002; 18 (1): 14-21.

8. Annex

Abreviations

2D FLASH GE	bi-dimensional fast low angle shot gradient echo T1-w
3D (2D)-MR	three-dimensional (bi-dimensional) magnetic resonance
3D-CE-FAST	three-dimensional contrast enhanced Fourier acquired steady state
3D-CISS	three-dimensional constructive interference in steady state
3D-FIESTA	three-dimensional fast imaging employing steady-state acquisition
3D-FSPGR	three-dimensional fast spoiled gradient echo
3DFT-FISP	three-dimensional Fourier transforms fast inflow with steady-state precession
3DFT-FLASH MRA	three-dimensional Fourier transform fast low angle shot MRA
3DFT-MPRAGE	three-dimensional Fourier transform magnetization prepared rapid gradient echo
3D-GRASS	three-dimensional gradient recalled acquisition in the steady state
AICA	anterior inferior cerebellar artery
CM	contrast medium
CN	cranial nerve
CNS	central nervous system
CSF	cerebrospinal fluid
CT	computed tomography
FFE T1-w	fast field echo T1-weighted
FLAIR	fluid attenuated inversion recovery sequence
FSE	fast spin-echo
Gd-DTPA	Gadolinium – Diethylenetriamine Pentaacetic Acid
GE	General Electrics

GE	gradient-echo
HIS	International Headache Society
HR-MRI	high-resolution magnetic resonance imaging
HU	Hounsfield units
IASP	International Association for the Study of Pain
MPR	multiplanar reconstruction
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MRTA	magnetic resonance tomographic angiography
MS	multiple sclerosis
MVD	microvascular decompression
NEX	number of excitations
NVC	neurovascular compression
O-R transitional zone	Obersteiner-Redlich transitional zone
PNS	peripheral nervous system
REZ	root entry zone
SCA	superior cerebellar artery
SE	spin-echo
SNR	signal/ noise ratio
SUNCT	shorter lasting, unilateral neuralgiform, conjunctival injection and tearing
T1 (T2)-w	T1 (T2)-weighted (MR) sequence
TGN	trigeminal neuralgia
TN	trigeminal nerve
TOF	time of flight
TREZ	trigeminal root entry zone
V nerve	trigeminal (5^{th}) cranial nerve
V1	ophthalmic division of the trigeminal nerve
V2	maxillary division of the trigeminal nerve
V3	mandibular division of the trigeminal nerve
VBA	vertebro-basilar arteries

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