

# **The diagnostic value of magnetic resonance imaging in post-traumatic trigeminal neuropathy**

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## **Conflict of Interest Statement**

The authors declare that there are no conflicts of interest or financial disclosures with regards to the conduction and reporting of the data of the trial presented in this manuscript.

**Abstract:**

Introduction: MRI has the potential to become a strong diagnostic tool for patients with post-traumatic trigeminal neuropathy (PTTN), but it is strongly depending on the used sequences. The aim of this study is to evaluate the diagnostic value of current commonly used sequences in the context of PTTN and to compare this with results of MRIs taken for classical or secondary trigeminal neuralgia.

Methods: This study retrospectively analysed all protocols of MRIs that were performed between 01/02/2012 and 20/06/2018 commissioned by the Department of Oral and Maxillofacial surgery, University Hospitals Leuven. A total of 132 MRIs in the context of trigeminal pain could be linked to 128 different patients. Demographic, clinical and radiological data were extracted from the records of these patients.

Results: The sensitivity and negative predictive value of MRI in the PTTN subgroup was respectively 0,18 and 0,77 which was lower than in the two other subgroups. Artefacts interfered the visualisation of a possible cause of the trigeminal pain in 24,4% of MRIs for PTTN compared to 6-7% for classical or secondary trigeminal neuralgia. An MRI resulted only once (2,4%) in a changed policy for patients with PTTN compared to 25-30% in classical or secondary trigeminal neuralgia.

Conclusion: the diagnostic value of the most commonly used MRI sequences for PTTN is low and has little impact on the clinical management of these patients. Consequently, there is a need for dedicated sequences with high resolution and low artefact susceptibility.

## 1. Introduction

Despite the fact that neuropathic pain has an incidence of 8.2 per 1000 person-years it is often considered as one of the most difficult pain syndromes to diagnose and manage <sup>1</sup>. Trigeminal pain is one of those neuropathic pains with a considerable incidence and impact on the quality of life <sup>2</sup>. Melek et al. proved that patients with classical trigeminal neuralgia or post-traumatic trigeminal neuropathy showed signs of depression in respectively 54% and 36% of the cases <sup>3</sup>. Trigeminal pain can be caused by a wide variety of trauma, infections, neurovascular conflicts or iatrogenic injuries. Onset and characteristics of these pain syndromes in the trigeminal nerve area vary significantly, independent of the cause. Trigeminal neuropathy is the collective term for all clinical disorders caused by injury or disease affecting the trigeminal nerve <sup>4</sup>. Because of the wide variety of causes and clinical presentations, the International Headache Society published a classification for “pain attributed to a lesion or disease of the trigeminal nerve” <sup>5</sup>. If the trigeminal pain is caused by a neurovascular compression or an underlying disease, it is respectively called a *classical trigeminal neuralgia* or a *secondary trigeminal neuralgia*. With a history of major or minor trauma, chemical or thermal aggression or radiation of the trigeminal nerve which causes the orofacial pain it is called a *painful post-traumatic trigeminal neuropathy* (PPTTN) <sup>5</sup>. However, it is important to know that a significant part of the patients will consult with only numbness, hypoesthesia or altered feelings in the dermatome of the injured branch of the trigeminal nerve without pain, which does not exclude damage to the neurons <sup>6</sup>.

The diagnosis of neuropathic pain in general and post-traumatic trigeminal neuropathy (PTTN) specifically poses a great challenge due to the complex trigeminal nerve system and the variety in clinical symptoms and causes. Therefore, disorders of the trigeminal nerve are often misdiagnosed, which can lead to unnecessary and invasive diagnostic or therapeutic interventions <sup>7</sup>. The diagnostic process for orofacial pain starts with a comprehensive history with special attention for the clinical history and the specific neurological symptoms.

Subsequently, a physical examination with a neurological and sensory evaluation of the trigeminal area could provide the diagnosis of a trigeminal sensory or motor deficit, but the cause remains often unknown<sup>4</sup>. Already in 1990, Hutchins et al. settled that magnetic resonance imaging (MRI) can provide important information about causes of trigeminal pain<sup>8</sup>. While Cone Beam CT as well as Multislice CT are used for the 3D evaluation of the bony structures, MRI is preferred for soft tissue and neurovascular visualisation. Therefore, these techniques are often routinely used in the diagnostic process of trigeminal pathologies<sup>9</sup>. Considering the rapid development of MRI-techniques a strong correlation between MRI results and neurosurgical findings has already been identified for symptomatic patients with a classical trigeminal neuralgia caused by a neurovascular compression. The same is true for secondary trigeminal neuralgia caused by inflammation or infections, which can be increasingly diagnosed on MRI<sup>10,11</sup>. Chhabra et al. showed that magnetic resonance neurography (MRN), an MRI sequence adjusted for the imaging of peripheral nerves, can have an important impact on the management of patients with a peripheral neuropathy<sup>12</sup>. It can even be an added value in the diagnosis and pre-surgical planning of peripheral trigeminal neuropathy<sup>13</sup>. Considering these results, MRI has the potential to be a strong diagnostic tool for patients with PTTN. However, the visualisation capability of the MRI is strongly depending on the chosen sequence<sup>14</sup>. For diagnosis of classical trigeminal neuralgia, caused by a neurovascular conflict in the cisternal part of the trigeminal nerve, a combination of a high-resolution T1 pre- and post-gadolinium sequence, a 3D heavily T2 weighted sequence and a Magnetic Resonance Angiography (MRA) is recommended<sup>15</sup>. Since traumatic injuries of the trigeminal nerve most often occur in the peripheral part, there is a need for a combination of CT and MRI in the evaluation of PTTN<sup>15</sup>. Zuniga et al. showed that an MRN using sparse imaging or 3D reverse-echo gradient-echo (PSIF) allows for diagnosing nerve injuries causing post-traumatic trigeminal neuropathy<sup>16</sup>.

The aim of this retrospective study is to evaluate the diagnostic value of the most commonly used MRI sequences for patients who consult with a post-traumatic trigeminal neuropathy and to compare these results with the sensitivity and specificity of MRIs taken in the context of classical or secondary trigeminal neuralgia.

## **2. Methods**

This study was approved by the Ethics Committee of the University Hospitals Leuven (S62823) and conducted in compliance with Good Clinical Practice standards and the Declaration of Helsinki. We retrospectively analysed all protocols of MRI scans that were performed between 01/02/2012 and 20/06/2018 commissioned by the Department of Oral and Maxillofacial surgery of the University Hospitals Leuven. Out of the 533 MRIs performed during this period, 132 could be linked to 128 different patients for the indication of trigeminal pain (figure 1). The other 401 were excluded because they were in the context of non-trigeminal pathologies. The medical records of the 128 patients with trigeminal pain were evaluated for demographic, clinical and radiological characteristics. The following demographic and clinical data were collected: age, sex, clinical background of the trigeminal pain, indication (classical trigeminal neuralgia, secondary trigeminal neuralgia or post-traumatic trigeminal neuropathy (PTTN)), changed policy by MRI, which policy was chosen if changed due to the MRI, which branch of the trigeminal nerve was affected, the clinical opinion about the nerve damage. This opinion was defined as the diagnosis based on other radiological modalities or surgical exploration. The following MRI statistics were extracted from the radiological reports: which MRI sequence was used, the use of contrast agents, was the total nerve of interest visualised on MRI, was the most plausible cause of the trigeminal pain visualised on MRI, additional radiological procedures, the presence of artefacts on the MRI which limited the reporting of a possible lesion of the trigeminal nerve and the type of artefact.

Statistical analysis was conducted in GraphPad Prism 8® (GraphPad Software, Inc., La Jolla, USA). The age of the patients in the total trigeminal pain group and the different subgroups were evaluated on normality with the D'Agostino-Pearson test. Considering parametric age distribution in all subgroups, the unpaired parametric t-test was used for the intergroup comparison.

### **3. Results**

#### ***3.1 Patient characteristics***

Of the 128 patients with an MRI for trigeminal pain 83 were female (64,8%) and 45 were male. Their mean age was  $52,83 \pm 16,21$  years with a range between 4 and 85 years (table 1). The patients with post-traumatic trigeminal neuropathy were significantly younger than the two other two subgroups ( $P < 0,01$ ). More than half of all patients consulted the maxillofacial surgery department with symptoms without a known cause. Yet, within the group of post-traumatic trigeminal neuropathy the majority of patients had a possible cause in the medical history, most frequently being tooth extraction or orthognathic surgery. In the diagnostic work-up a dental panoramic radiography was almost always added to the MRI and in the group of post-traumatic trigeminal neuropathy a Cone-Beam CT was commonly added as well. In 31,3% of the MRIs, an evaluation of the total trigeminal nerve was asked, especially for classical trigeminal neuralgia this was the most evaluated nerve.

#### ***3.2 Contingency tables***

The contingency table of total trigeminal pain shows high values for positive predictive value (PPV), negative predictive value (NPV) and specificity (spec) and a lower value for sensitivity (sens) (table 2). A comparison of the contingency tables of classical trigeminal neuralgia (table 3) and the PTTN (table 4) shows that there is a significant difference, from 0,86 to 0,18 in the

sensitivity of the MRI. For classical trigeminal neuralgia the sensitivity is comparably high with the specificity, NPV and PPV of the MRI, but for PTTN the sensitivity (0,18) is significantly lower than the other values. Not only the sensitivity of MRI is lower for PTTN, but also the negative predictive value goes from 0,94 for classical trigeminal neuralgia to 0,77 for PTTN. Because of the low numbers in the secondary trigeminal neuralgia subgroup, there was no contingency table made for this group.

### ***3.3 MRI sequences and artefacts***

All 132 MRIs were taken on an Ingenia 3T scanner (Philips Healthcare, Best, Netherlands). A total of 19 different MRI sequences were used in the 132 MRIs of patients with trigeminal pain. The most commonly used MRI sequences for patients with classical trigeminal neuralgia were a balanced dual excitation sequence (CISS), a T2-weighted sequence and a T1-Turbo Spin Echo sequence (T1-TSE) (figure 2). The combination of these 3 sequences was used in 61% of all MRIs in the context of classical trigeminal neuralgia. The same combination was respectively used in 29% and 24% of the MRIs for patients with secondary trigeminal neuralgia or PTTN. This combination was commonly supplemented with other sequences in the group of secondary trigeminal neuralgia. The sequences used in the context of secondary trigeminal neuralgia and PTTN showed a similar distribution with a T1-turbo spin echo as most commonly used sequence. A gadolinium-based contrast agent was used in MRIs taken in the context of PTTN and secondary trigeminal neuralgia in respectively 95% and 94%, whereas this was only 80% for classical trigeminal neuralgia.

An artefact which limited the visualisation of a possible cause of the trigeminal pain was present in 12,5% of the MRIs (table 1). The percentage of MRIs with an artefact was higher in the PTTN category compared with the two other groups and this was due to the larger amount of

metal artefacts in this group. In the classical trigeminal neuralgia group only 1 out of 5 artefacts was caused by metal whereas this was 9 out of 10 in the PTTN group.

The nerve of interest could be clearly visualised on MRI in respectively 96% and 100% for classical and secondary trigeminal neuralgia while this was only possible in 73% of the MRIs in the context of PTTN.

### ***3.4 Changed policy***

The management of the trigeminal pain after the MRI was evaluated based on the medical records of the consultations following the MRI. For classical trigeminal neuralgia and secondary trigeminal neuralgia an MRI resulted in a changed policy for 25-30% of the patients (figure 3). Mostly, their medication schedule or follow-up changed, or, in the case of classical trigeminal neuralgia, a surgical procedure was done to resolve the neurovascular compression. On the other hand, an MRI resulted only once (2,4%) in a changed policy for PTTN patients.

## **4. Discussion**

This study provides a comparison of the diagnostic value of MRI in the context of classical trigeminal neuralgia and PTTN. The demographic results, age and sex ratio, for total trigeminal pain and subgroups were in line with the findings of other articles on the same subject<sup>16-19</sup>. The mean age of patients with PTTN was significantly lower than the other two subgroups and the most evaluated nerves were the lingual nerve (31,7%) and the inferior alveolar nerve (26,8%). This is linked to the large proportion of patients with iatrogenic trigeminal nerve damage in this subgroup. Renton et al. already showed that those two branches of the trigeminal nerve are the most commonly injured during an invasive orofacial procedure and that the mean age of those patients is 38,4 years for lingual nerve injury and 44,0 years for an inferior alveolar nerve injury



The most plausible cause of the trigeminal pain could only be visualised on MRI in 20% of all patients. Studies by Devine et al. and Ögütçen-Toller et al. showed higher numbers, but this is probably due to other patient inclusion criteria <sup>17,19</sup>. The present study excluded patients with a space-occupying lesion or other non-trigeminal injury pathologies, whereas the previous studies included all patients with an MRI in the context of orofacial pain.

In the guidelines of the European Academy of Neurology (EAN) on trigeminal neuralgia, published in 2019, an MRI is strongly recommended for patients with trigeminal pain to exclude secondary causes <sup>21</sup>. In this study 5 MRIs showed a secondary cause of the trigeminal pain and this always resulted in a changed policy. The EAN also suggest that an MRI can be an important aid to detect neurovascular compression and consequently diagnose classical trigeminal neuralgia <sup>21</sup>. Leal et al. previously stated that MRI has a very good sensitivity and specificity for classical trigeminal neuralgia and this was proved again in the present study <sup>18,22</sup>. Therefore, an MRI can have an important effect on the management of trigeminal pain by excluding or proving an underlying disease and by detecting a neurovascular compression.

Although MRI has good results for the diagnosis of classical and secondary trigeminal neuralgia, it's even included in the guidelines for these two pathologies, it remains a question if it can be an asset in the diagnosis of post-traumatic trigeminal neuropathy. Currently, the systematic use of MRI comes often late in the diagnostic work-up of these patients and is only indicated in select cases where severe damage is suspected, and surgical intervention or reintervention is considered. On the other hand, Bagheri et al. showed that it's important to diagnose a trigeminal nerve injury as soon as possible to allow a successful nerve repair since the odds of improvement decreases by 6% for lingual nerve and 11% for inferior alveolar nerve damage with each month that passes <sup>23,24</sup>. Therefore, the most appropriate time period for this repair remains a controversial topic, but the systematic review of Kushnerev et al. shows that 6 months is a frequently chosen cut-off before which the nerve repair had to be done to achieve

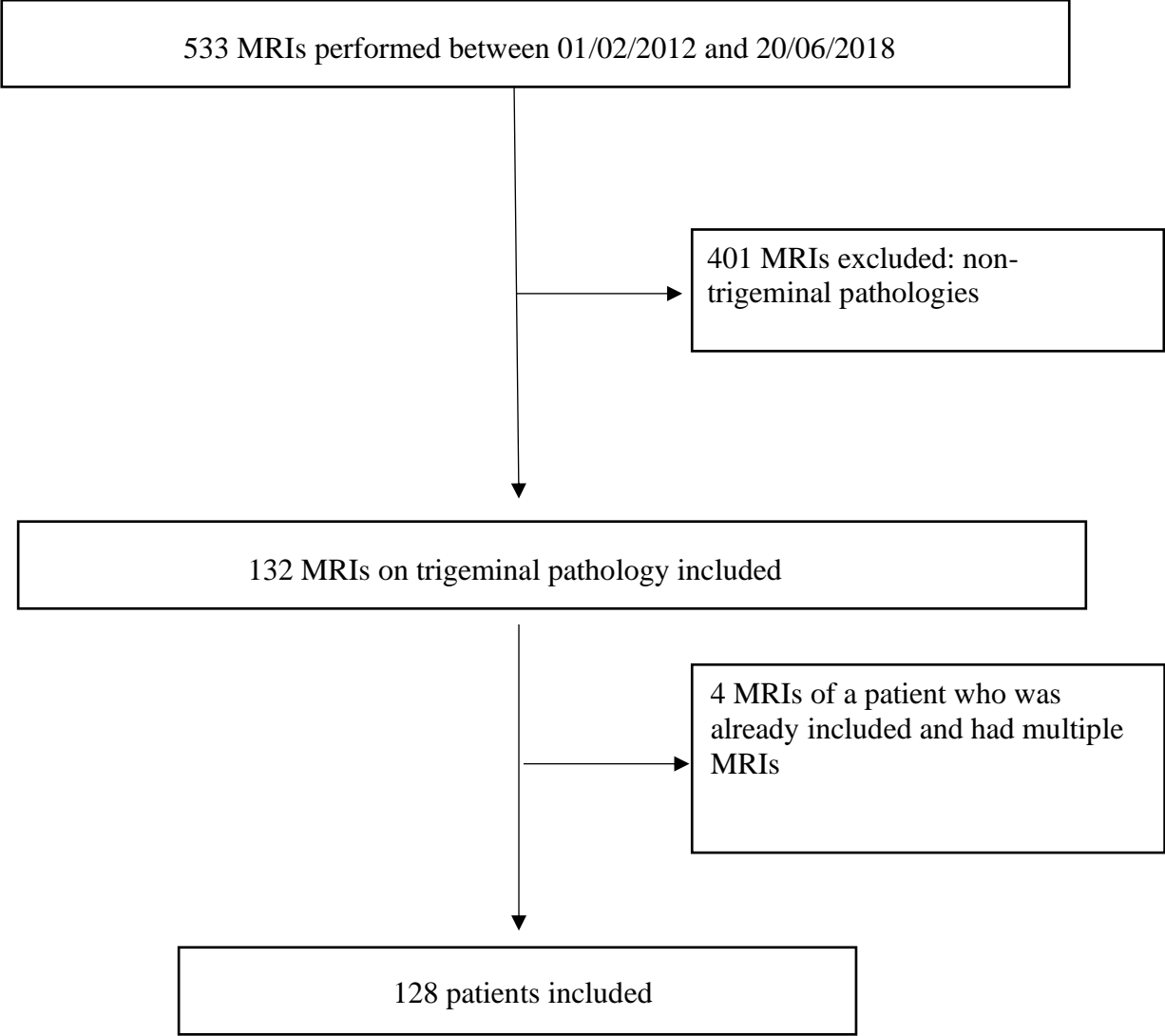
good results<sup>25</sup>. Both elements are making the decision about the timing of an MRI for patients with PTTN very difficult. However, this is not the only reason why an MRI is not part of the standard diagnostic protocol for PTTN. This study shows that the sensitivity and NPV of MRI for PTTN is respectively 0,18 and 0,77. This means that an MRI examination with the current sequences is not designated to diagnose post-traumatic trigeminal injuries, otherwise too much false negative results will be obtained. In contrast to the peripheral trigeminal nerve branches, MRI with a combination of a T1-TSE, a T2-TSE and a short tau inversion recovery (STIR) sequence has already been used with success to diagnose traumatic brachial plexopathy and increasingly influences the management of this post-traumatic neuropathic pain<sup>26-28</sup>. A possible explanation for the low diagnostic value of the current MRI sequences for PTTN is the frequent presence of an artefact which limits the visualisation of a possible lesion. In this study, there was an artefact in 10 out the 41 MRIs for PTTN. This resulted in 4 patients where the lesion could not be seen on MRI but was surgically visualised later in the therapeutic process. In 9/10 MRIs the artefact was caused by a metal object placed during the surgery that caused the nerve damage (eg. orthognathic surgery) or a surgery immediately after a trauma that caused the damage.

More important in the clinical practice is the influence of MRI on the management of patients with trigeminal pain. MRI resulted in a changed policy for respectively 26% and 29% of patients with classical and secondary trigeminal neuralgia. On the other hand, MRI resulted only once (2%) in a changed policy in the group of PTTN. This was a patient with neuropathic trigeminal pain immediately after a third molar extraction and where the nerve damage could be visualised on MRI with a T1-turbo spin echo (T1-TSE), a T2-turbo spin echo (T2-TSE), a T1-turbo spin echo sensitivity encoding (T1-TSE-SENSE) and a balanced dual excitation sequence (CISS). Therefore, a surgery was performed to re-establish the damaged inferior alveolar nerve. A possible explanation for the difference in changed policy between the PTTN

group and the two other trigeminal pain groups is the difference in treatment options. Treatment of classical trigeminal neuralgia consists of carbamazepine as medical treatment and a microvascular decompression as second line surgical treatment<sup>29</sup>. This surgical procedure is frequently performed whereas there is no surgical standard of care for PTTN.

In conclusion, this study confirmed the place of MRI in the diagnostic work-up of patients with classical and secondary trigeminal neuralgia. Otherwise, the diagnostic value of the most commonly used MRI sequences for PTTN patients is low and has little impact on the clinical management of these patients. Consequently, there is a need for dedicated MRI sequences with high resolution and low artefact susceptibility for visualising the post-traumatic injuries of the trigeminal branches in the maxillofacial area.

**Tables & figures**



**Figure 1:** Flowchart of the inclusion procedure of MRIs for this study.

	<b>Classical Trigeminal Neuralgia</b>	<b>Secondary Trigeminal Neuralgia</b>	<b>Post-Traumatic Trigeminal Neuropathy</b>	<b>Total Trigeminal pain</b>
<b>Number of MRI (n)</b>	70	17	41	128
<i>mean age</i>	57,53 y	58,18 y	42,59 y	52,83 y
<i>Most evaluated nerve (n)</i>	Total trigeminal nerve (44,3%)	Total mandibular nerve (29,4%)	Lingual nerve (31,7%)	Total trigeminal nerve (31,3%)
<i>Clinical context</i>	Symptoms (88,6%)	Symptoms (52,9%)	Extraction (46,3%)	Symptoms (56,3%)
<i>Most used additional imaging</i>	PANO (87,1%)	PANO (94,1%)	PANO (85,4%)	PANO (87,5%)
<i>Artefacts on MRI</i>	5 (7,1%)	1 (5,9%)	10 (24,4%)	16 (12,5%)

**Table 1:** Comparison of the patient characteristics between the three groups of trigeminal pain and the total trigeminal pain group.

PANO: dental panoramic radiography

	<b>Clinical +</b>	<b>Clinical -</b>	<b>Total</b>	
<b>MRI +</b>	26	0	26	<b>PPV= 1</b>
<b>MRI -</b>	12	90	102	<b>NPV= 0,88</b>
<b>Total</b>	38	90	128	
	<b>Sens= 0,68</b>	<b>Spec= 1</b>		

**Table 2:** Contingency table of total trigeminal pain. A positive MRI (MRI +) means that the most plausible cause of the trigeminal pain could be visualised on MRI. The clinical opinion was defined as the diagnosis based on other radiological modalities or surgical exploration and was positive when the most plausible cause of the trigeminal pain could be demonstrated.

Sens: Sensitivity; Spec: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value

	<b>Clinical +</b>	<b>Clinical -</b>	<b>Total</b>	
<b>MRI +</b>	19	0	19	<b>PPV= 1</b>
<b>MRI –</b>	3	48	51	<b>NPV= 0,94</b>
<b>Total</b>	22	48	70	
	<b>Sens= 0,86</b>	<b>Spec= 1</b>		

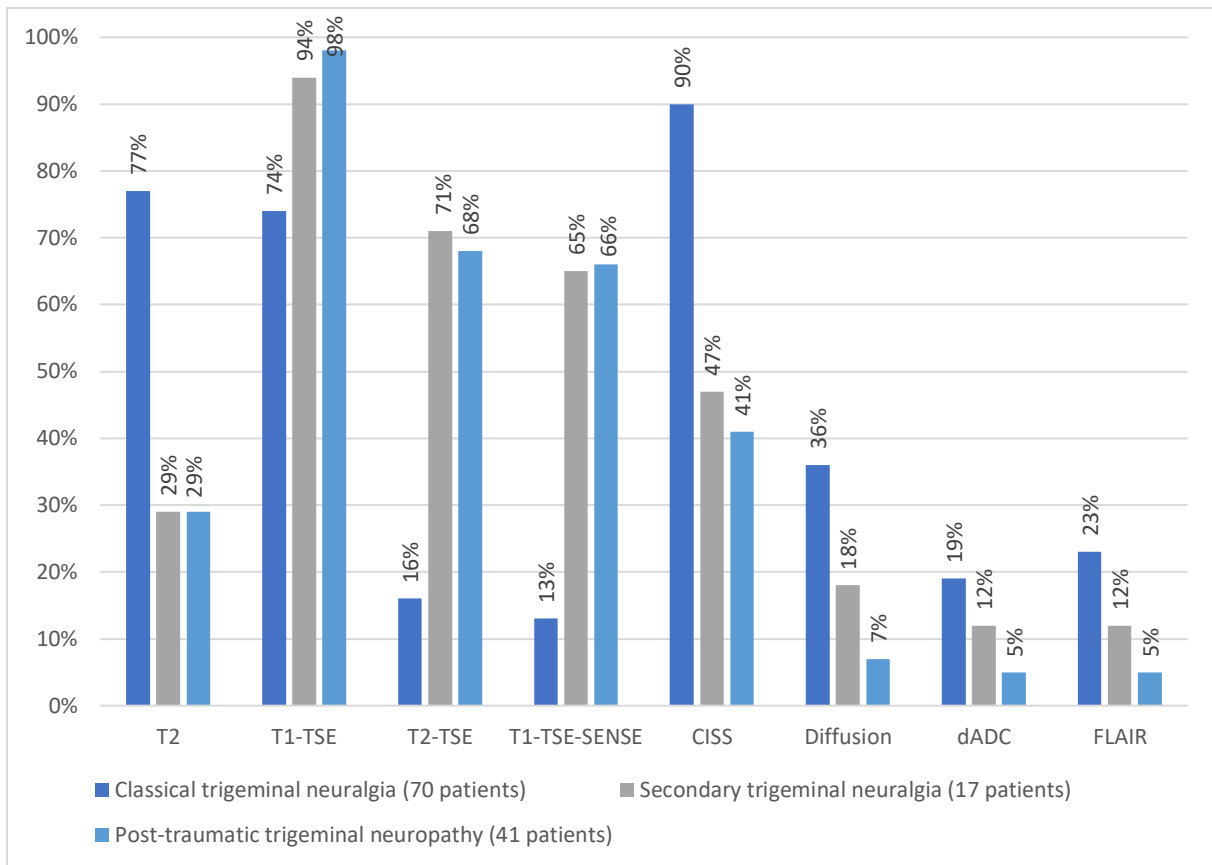
**Table 3:** Contingency table of Classical Trigeminal Neuralgia. A positive MRI (MRI +) means that the most plausible cause of the trigeminal pain could be visualised on MRI. The clinical opinion was defined as the diagnosis based on other radiological modalities or surgical exploration and was positive when the most plausible cause of the trigeminal pain could be demonstrated.

Sens: Sensitivity; Spec: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value

	<b>Clinical +</b>	<b>Clinical -</b>	<b>Total</b>	
<b>MRI +</b>	2	0	2	<b>PPV= 1</b>
<b>MRI –</b>	9	30	39	<b>NPV= 0,77</b>
<b>Total</b>	11	30	41	
	<b>Sens= 0,18</b>	<b>Spec= 1</b>		

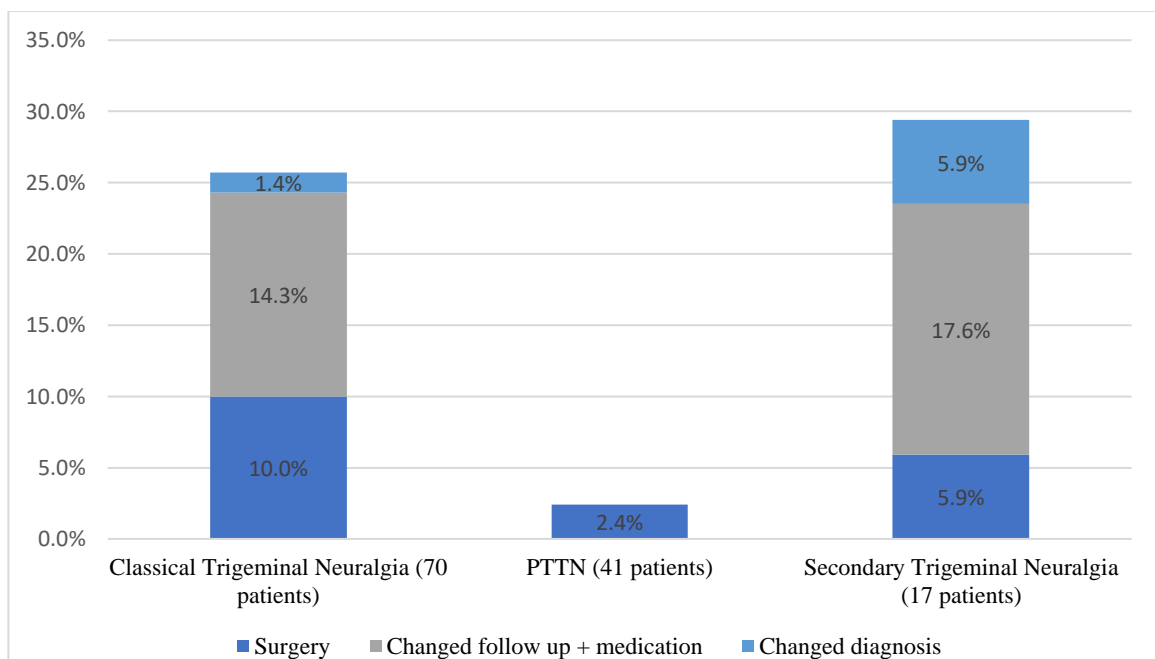
**Table 4:** Contingency table of PTTN. A positive MRI (MRI +) means that the most plausible cause of the trigeminal pain could be visualised on MRI. The clinical opinion was defined as the diagnosis based on other radiological modalities or surgical exploration and was positive when the most plausible cause of the trigeminal pain could be demonstrated.

Sens: Sensitivity; Spec: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value



**Figure 2:** Used MRI sequences in MRIs taken in the context of trigeminal pain. In total, 19 different MRI sequences were used in 128 patients. Only the MRI sequences used in  $\geq 5\%$  of a subgroup were shown in this figure.

T2: T2 weighted sequence; T1-TSE: T1 weighted Turbo Spin Echo; T2-TSE: T2 weighted Turbo Spin Echo; T1-TSE-SENSE: T1 weighted Turbo Spin Echo Sensitivity Encoding;



**Figure 3:** The proportion of changed policies in the three subgroups of trigeminal pain and a subdivision of these changed policies. In the classical and secondary trigeminal neuralgia subgroups, an MRI resulted in a changed policy for 25-30% of the patients, whereas this was 2,4% in the PTTN subgroup.

PTTN: Post-Traumatic Trigeminal Neuropathy

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