NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of stereotactic radiosurgery for trigeminal neuralgia

Typical trigeminal neuralgia is sudden and severe facial pain, usually affecting one side of the face and lasting for a few seconds to about 2 minutes. Some people have a more continuous aching, throbbing or burning sensation. It can be caused by pressure on the trigeminal nerve, which carries sensations from the face to the brain. In this procedure, radiation is focused at the place where the trigeminal nerve enters the brain. The aim is to relieve pain.

Contents

Abbreviations

Word or phrase	Abbreviation
Barrow Neurological Institute	BNI
Confidence interval	CI
Gray	Gy
Interquartile range	IQR
Linear accelerator	LINAC
Modified Marseille Scale	MMS
Multiple sclerosis	MS

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in April 2021.

Procedure name

- Stereotactic radiosurgery for trigeminal neuralgia.

Professional societies

- Association of British Neurologists
- Society of British Neurological Surgeons
- British Society for Stereotactic and Functional Neurosurgery
- Royal College of Radiologists.

Description of the procedure

Indications and current treatment

Trigeminal neuralgia is a chronic pain condition that affects the trigeminal (fifth) cranial nerve, one of the most widely distributed nerves in the head. The pain occurs in the areas supplied by the trigeminal nerve: the cheeks, jaw, teeth, gums, lips and around the eye or forehead. The typical form, type 1, causes sudden and severe facial pain, usually affecting 1 side of the face and lasting for a few seconds or minutes. It may be triggered by touch, talking, eating or brushing teeth. Atypical trigeminal neuralgia (type 2) is characterised by constant aching, burning, or stabbing pain of lower intensity than type 1. Some people have both types.

Trigeminal neuralgia can be idiopathic or may be caused by pressure on the trigeminal nerve from an artery or a vein (primary trigeminal neuralgia). It can also result from a medical condition such as a tumour, MS or previous injury (secondary trigeminal neuralgia).

Medication is the first line treatment for trigeminal neuralgia. Other treatment options are considered for people who experience severe pain despite medication, or who have side effects from medication. Percutaneous treatments include glycerol injection, radiofrequency lesioning (applying short bursts of radiofrequency to the nerve through a needle), and balloon microcompression, (inflating a balloon near the nerve). These procedures typically have high recurrence rates.

Microvascular decompression is a more invasive procedure involving opening the skull, to relieve the pressure on the trigeminal nerve. This can provide longer lasting relief but carries a risk of potentially serious complications, such as facial numbness, hearing loss, stroke and death.

What the procedure involves

Stereotactic radiosurgery for trigeminal neuralgia uses precisely focused multiple beams aimed at the trigeminal nerve where it enters the brainstem, to deliver a high dose of ionising radiation in a single treatment session. It does not require open surgery, needle insertion or general anaesthesia. The aim is to damage the trigeminal nerve and stop the transmission of pain signals.

There are different systems available for stereotactic radiosurgery and details of the techniques vary.

In one system, a metal frame is attached to the patient's head with 4 pins inserted through the scalp under local anaesthetic. An imaging procedure (usually MRI) is used to accurately locate the target area for treatment. The patient lies with their head in a treatment machine for 20 minutes to 2 hours while the radiation is given. The frame and pins are removed before the patient goes home. In another system, a thermoplastic mask that covers the face is made for each patient. CT and MRI scans are used to locate the target. The radiosurgery is done using a robotic arm positioned over the patient, and takes about 40 to 50 minutes.

It can take a few weeks or months for the patient to notice any change after stereotactic radiosurgery.

Outcome measures

BNI Pain Intensity Scale

- 1 - complete pain relief without medication
- 2 - occasional pain not requiring medication
- 3 - some pain but adequately controlled with medication
    - 3a - no pain, continued medication
    - 3b - persistent pain, controlled with medication
- 4 - some pain inadequately controlled with medication
- 5 - continued severe pain or no pain relief.

Efficacy summary

Pain relief

In a systematic review of 6,461 patients with classical idiopathic trigeminal neuralgia (65 studies), the mean proportion of patients with freedom from pain with or without medication was 85% for Gamma Knife studies, 87% for LINAC studies and 79% for Cyberknife studies. For freedom from pain without medication, the rates were 53%, 49% and 56% respectively. The time to pain relief ranged from 0 to 480 days (Tuleasca 2019).

In a systematic review of 646 patients (12 studies) with secondary trigeminal neuralgia related to MS, the pooled proportion of patients who had an initial response to treatment was 83% (95% CI 74 to 90%; I^2=76%). The cumulative proportion of successful treatments at the end of the study was 47% (95% CI 33 to 60%; I^2=90%) (Spina 2021).

In a systematic review of 13,805 patients (58 studies) with trigeminal neuralgia who had stereotactic radiosurgery or microvascular decompression, initial success rates were 71% and 87% respectively (p<0.0001). At 2 years, the success rates were 78% and 91% (p=0.0002) and at 5 years, the success rates were 64% and 84% respectively (p=0.0361) (Gubian 2017).

In a systematic review of 1,462 patients (14 studies) with trigeminal neuralgia, increasing radiation dose was associated with improved outcomes across all doses (p<0.001). The mean proportion of patients with good pain control was 52% for doses of 70 to 75 Gy, 65% for 80 Gy, 71% for 85 Gy and 82% for 90 Gy (Wilson 2020).

In a randomised controlled trial of 441 patients with primary trigeminal neuralgia who had stereotactic radiosurgery or microvascular decompression, 1% (3/221) and 86% (189/220) of patients, respectively, had complete pain relief within the first postoperative week. At 2-year follow up, 25% (55/221) of patients who had radiosurgery and 83% (183/220) of patients who had microvascular decompression had a BNI score of 1 (p<0.05). For BNI scores of 1 or 2, the rates were similar between the 2 groups (73% [161/221] and 85% [188/220] respectively; p=not significant) (Zeng 2018).

In a case series of 343 patients with drug-resistant trigeminal neuralgia, the proportion of patients with pain relief at 6, 12, 24, and 36 months after stereotactic radiotherapy was 92%, 87%, 82% and 76% respectively. Overall, 78% of patients were completely pain free (BNI score 1 or 2) after 1 year (Romanelli 2019).

In a case series of 870 patients with trigeminal neuralgia, 86% (747/870) of patients had improvement in pain. At the last follow up (median 36.5 months) 62% (539/870) of patients reported excellent pain control and 19% (162/870) reported good pain control. The proportion of patients with good to excellent pain relief at 4 years was statistically significantly higher for those who had a higher dose (79% for 82 Gy or lower, 82% for 83 to 86 Gy and 92% for 90 Gy or higher, p=0.0019) (Kotecha 2016).

In a cohort study of 700 patients, 91% of patients who only had stereotactic radiosurgery (n=658) and 80% of patients who had stereotactic radiosurgery after microvascular decompression (n=42) had pain relief at 12 months (Wang 2018).

Recurrence

In the systematic review of 6,461 patients with classical idiopathic trigeminal neuralgia, the mean recurrence rate was 25% (range 0 to 52%) for Gamma Knife studies, 32% (range 19 to 63%) for LINAC studies and 26% (range 16 to 33%) for Cyberknife studies. The mean time to recurrence was 9 months in

1 Cyberknife study and ranged from 6 to 48 months for Gamma Knife studies and 7.5 to 20.4 months for LINAC studies (Tuleasca 2019).

In the systematic review of 13,805 patients with trigeminal neuralgia who had stereotactic radiosurgery or microvascular decompression, the median recurrence rates at median follow up of 36 months were 25% and 11%, respectively (p=0.0015). The mean recurrence-free periods were 30.6 months and 30.4 months, respectively (p=0.987) (Gubian 2017).

In the randomised controlled trial of 441 patients with primary trigeminal neuralgia who had stereotactic radiosurgery or microvascular decompression, there was no statistically significant difference between the groups in the recurrence rate at 2 years (0.9% compared with 0.5%) (Zeng 2018).

In the case series of 343 patients with drug-resistant trigeminal neuralgia, 16% (55/343) of patients who initially had pain relief had recurrent pain within 3 years of the procedure (Romanelli 2019). In the cohort study of 700 patients, 24% of patients who only had stereotactic radiosurgery and 19% of patients who had stereotactic radiosurgery after microvascular decompression had recurrence at 3 years. At 10 years, the recurrence rates were 44% and 49%, respectively (p=0.84) (Wang 2018).

Patient satisfaction

In the cohort study of 700 patients, 82% (537/658) of patients who only had stereotactic radiosurgery did not regret choosing the procedure and 10% (64/658) of patients had no opinion. In the group of patients who had stereotactic radiosurgery after microvascular decompression, the rates of ‘no regret’, ‘no opinion’ and ‘regret’ were 69% (29/42), 26% (11/42) and 5% (2/42), respectively (Wang 2018).

Safety summary

Hypaesthesia or dysaesthesia

Bothersome or very bothersome hypaesthesia was reported in 14% of patients in 1 LINAC study and the mean rate was 3% in Gamma Knife studies and 9% in Cyberknife studies in the systematic review of 6,461 patients with classical idiopathic trigeminal neuralgia (Tuleasca 2019). The rate of facial hypaesthesia after stereotactic radiosurgery ranged from 0% to 71% of patients in the systematic review of 646 patients with secondary trigeminal neuralgia related to MS (Spina 2021). Dysaesthesia was reported in 28% of patients after stereotactic radiosurgery and 2% of patients after microvascular decompression (p=0.02) in the systematic review of 13,805 patients (Gubian 2017). The mean rates of bothersome numbness were 1% (95% CI 0 to 4%) for patients who had a dose of

70 to 75 Gy, 1% (95% CI 0 to 2%) for patients who had 80 Gy, 2% (95% CI 1 to 5%) for patients who had 85 Gy and 5% (95% CI 2 to 8%) for patients who had 90 Gy (Wilson 2020). Facial numbness was reported in 5% (11/221) of patients who had stereotactic radiosurgery and <1% (1/220) of patients who had microvascular decompression in the randomised controlled trial of 441 patients (Zeng 2018). Facial numbness associated with bothering dysaesthesia (BNI numbness class 3 or 4) was reported in 6% (21/343) of patients at 36 months in the case series of 343 patients; 3 were after first treatments and 18 were after retreatments (Romanelli 2019). A BNI facial numbness score of 3 or 4 was reported by 29% (253/870) of patients during follow up in the case series of 870 patients; at last follow up (median 36.5 months), 13% (112/870) of patients had class 3 numbness and 5% (45/870) had class 4 numbness (Kotecha 2016).

Cranial nerve palsy (excluding the trigeminal nerve)

Cranial nerve palsy (excluding the trigeminal nerve) was reported in 3% of patients after stereotactic radiosurgery and 1% of patients after microvascular decompression (p=0.01) in the systematic review of 13,805 patients (Gubian 2017).

Facial paralysis or palsy

Facial paralysis was reported in 1 patient who had stereotactic radiosurgery and facial palsy and facial nerve palsy were each reported in 1 patient who had microvascular decompression in the randomised controlled trial of 441 patients (Zeng 2018).

Anaesthesia dolorosa

Anaesthesia dolorosa was reported in <1% of patients after stereotactic radiosurgery in the systematic review of 13,805 patients (Gubian 2017) and in 1% (9/870) of patients in the case series of 870 patients (Kotecha 2016). It was reported in 10% (4/42) of patients who had stereotactic radiosurgery after a previous microvascular decompression (Wang 2018).

Hearing loss

Hearing loss was reported in 1% of patients after stereotactic radiosurgery and 2% of patients after microvascular decompression (p=0.02) in the systematic review of 13,805 patients (Gubian 2017). Hearing impairment was reported in 1 out of 221 patients who had stereotactic radiosurgery in the randomised controlled trial of 441 patients (Zeng 2018).

Tinnitus

Tinnitus was reported in <1% of patients after stereotactic radiosurgery (n=5,540) in the systematic review of 13,805 patients (Gubian 2017).

Loss of corneal reflex

Loss of corneal reflex was reported in 6% (13/221) of patients who had stereotactic radiosurgery in the randomised controlled trial of 441 patients (Zeng 2018). Abnormal corneal reflex was reported in 1 out of 42 patients who had stereotactic radiosurgery after a previous microvascular decompression (Wang 2018).

Dry eye was reported as a complication in the systematic review of 6,461 patients with classical idiopathic trigeminal neuralgia (Tuleasca 2019).

Diplopia

Diplopia was reported in 1 out of 221 patients who had stereotactic radiosurgery and 1 out of 220 patients who had microvascular decompression in the randomised controlled trial of 441 patients (Zeng 2018).

Vertigo

Vertigo was reported in 2% of patients after stereotactic radiosurgery and 4% of patients after microvascular decompression (p=0.001) in the systematic review of 13,805 patients (Gubian 2017).

Keratitis

Keratitis was reported in 3% of patients after stereotactic radiosurgery (n=5,540) in the systematic review of 13,805 patients (Gubian 2017).

Brainstem oedema

Brainstem oedema was reported in <1% of patients after stereotactic radiosurgery (n=5,540) in the systematic review of 13,805 patients (Gubian 2017).

Chronic fatigue

Chronic fatigue was reported in <1% of patients after stereotactic radiosurgery (n=5,540) in the systematic review of 13,805 patients (Gubian 2017).

Chronic headache

Chronic headache was reported in <1% of patients after stereotactic radiosurgery and <1% of patients after microvascular decompression in the systematic review of 13,805 patients (Gubian 2017).

Infection

Infection was reported in <1% of patients after stereotactic radiosurgery and about 2% of patients after microvascular decompression in the systematic review of 13,805 patients (Gubian 2017).

Other

Necrotising Teflon granuloma after microvascular decompression and stereotactic radiosurgery and radiation necrosis after repeated stereotactic radiosurgery were each described in case reports (Bigder 2017; Wang 2020). Invasive keratinising squamous cell carcinoma in the left posterior mandibular oral mucosa after 2 radiosurgery treatments for trigeminal neuralgia is also described in a case report (Berti 2018). Other case reports of adverse events after stereotactic radiosurgery included aneurysm (Chen 2017), ruptured aneurysm (Dominguez 2020), neurological deficit from late onset MS (Kemp 2016), atheromatous plaque formation (Li 2015), vision loss (Naseri 2004), pseudoaneurysm (Pak 2018), first bite syndrome (Redon 2018) and oral mucositis (Peddada 2011).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened).

For this procedure, no responses were received.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to stereotactic radiosurgery for trigeminal neuralgia. The following databases were searched, covering the period from their start to 16 April 2021: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with trigeminal neuralgia.
Intervention/test	Stereotactic radiosurgery.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on more than 10,000 patients who had stereotactic radiosurgery from 4 systematic reviews, 1 randomised controlled trial, 2 case series, 1 cohort study and 11 case reports (Tuleasca 2019; Spina 2021; Gubian 2017; Wilson 2020; Zeng 2018; Romanelli 2019; Kotecha 2016; Wang 2018; Berti 2018; Bigder 2017; Chen 2017; Dominguez 2020; Kemp 2016; Li 2015; Naseri 2004; Pak 2018; Redon 2018; Wang 2020; Peddada 2011).

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on stereotactic radiosurgery for trigeminal neuralgia

Study 1 Tuleasca C (2019)

Study details

Study type	Systematic review
Country	Not reported for individual studies

Recruitment period	Search date: December 2015
Study population and number	n=6,461 (65 studies) Patients with classical idiopathic trigeminal neuralgia
Age and sex	Mean age ranged from 56 to 78 years
Patient selection criteria	Inclusion criteria: English language articles reporting on outcomes specific to external beam radiosurgical treatments of classical idiopathic trigeminal neuralgia, the first radiosurgical treatment, MRI-based targeting (CT-based targeting reported separately to exclude potential bias), and clear outcomes obtained using validated instruments. Classical trigeminal neuralgia refers to all cases without an established aetiology (idiopathic), including those with potential vascular compression. Exclusion criteria: studies that did not report specific outcomes for idiopathic trigeminal neuralgia and those reporting on repeat radiosurgery or radiosurgery in the treatment of trigeminal surgery associated with MS or other secondary causes.
Technique	45 studies used Gamma Knife (n=5,687), 11 used LINAC (n=511), and 9 used CyberKnife (n=263). The mean maximal doses ranged from 71.1 to 90.1 Gy for the Gamma Knife studies, from 70 to 90 Gy for LINAC studies, and from 64.3 to 80.5 Gy for CyberKnife studies. The ranges of maximal doses were: 60 to 97 Gy (most were 60 to 90 Gy) for Gamma Knife, 50 to 90 Gy for LINAC, and 66 to 90 Gy for CyberKnife. Most of the studies targeted the root entry zone.
Follow up	The mean follow up periods ranged from 7.1 to 92 months for Gamma Knife studies, from 18 to 56.5 months for LINAC studies, and 8 to 20.4 months for CyberKnife studies.
Conflict of interest/source of funding	1 author has been a consultant for Elekta AB, 1 author has been a consultant for Medtronic and has received support from Elekta for non–study-related clinical or research effort, 1 author has received honoraria for past educational seminars from Medtronic, Elekta AB, Accuray Inc., and Varian Medical Systems and research grants from Elekta AB and belongs to the Elekta MR LINAC Research Consortium.

Analysis

Follow up issues: completeness of follow up for the individual studies is not discussed in the paper.

Study design issues: All except 1 of the studies were retrospective. Most of the studies reported outcomes using the BNI Pain Intensity Scale or a variation. The generic inverse variance method and fixed effects model in Review Manager were used to pool data. The outcome measures used the log hazard ratio (lnHR) and its variance, which were estimated using the hazard ratio meta-analysis toolbox.

In addition to the 65 studies included in the systematic review, there were a further 55 papers that the authors reviewed and discussed separately. These dealt with specific aspects of the procedure, such as target, timing and dose.

Study population issues: Some studies included patients with atypical pain and did not always describe it separately. There is some overlap with the systematic review by Gubian et al., 2017.

Key efficacy findings

Number of patients analysed: 6,461

Freedom from pain response, with or without medication adjustment

- Gamma Knife studies=mean 84.8%, median 85.6% (range 66.6% to 100%)
- LINAC studies=mean 87.3%, median 88.5% (range 75% to 100%)
- CyberKnife studies=mean 79.3%, median 79% (range 50% to 100%)

The differences between Gamma Knife and LINAC or CyberKnife were not statistically significant.

Freedom from pain response without medication

- Gamma Knife studies=mean 53.1%, median 52.1% (range 28.6% to 100%)
- LINAC studies=mean 49.3%, median 43.2% (range 17.3% to 76%)
- CyberKnife studies=mean 56.3%, median 58% (range 40% to 72%)

The differences between Gamma Knife and LINAC or CyberKnife were not statistically significant.

Time to pain relief

- All studies=range 0 to 480 days
- Gamma Knife studies=mean ranged from 15 to 78 days, median ranged from 10 to 90 days
- LINAC studies=mean ranged from 28 to 81 days, median ranged from 8.5 to 60 days
- CyberKnife studies=mean and median not reported

Recurrence rate

- Gamma Knife studies=mean 24.6%, median 23% (range 0% to 52.2%)
- LINAC studies=mean 32.2%, median 29% (range 19% to 63%)
- CyberKnife studies=mean 25.8%, median 27.2% (range 15.8% to 33%)

Time to recurrence

- Gamma Knife studies=mean ranged from 6 to 48 months (crude interval 1 to 150.1 months)
- LINAC studies=mean ranged from 7.5 to 20.4 months (crude interval 3 to 47 months)
- CyberKnife (1 study)=mean 9 months (crude interval 1 to 43 months)

Two Gamma Knife studies reported 30% and 45.3% of patients who were pain free without medication at 10 years.

Key safety findings

Hypaesthesia onset (all BNI scores, crude rates)

- Gamma Knife studies=mean 21.7%, median 19% (range 0% to 68.8%)
- LINAC studies=mean 27.6%, median 28.5% (range 11.4% to 49.7%)
- CyberKnife studies=mean 29.1%, median 18.7% (range 11.8% to 51.2%)

The follow up periods for LINAC and CyberKnife were more limited in time than in the Gamma Knife studies.

The mean time to hypaesthesia onset in the Gamma Knife group ranged from 6 to 36 months, and the time varied from 1 to 94 months.

Bothersome or very bothersome hypaesthesia onset (BNI scores 3 and 4)

- Gamma Knife studies=mean 3.1%, median 0% (range 0% to 17.3%)
- LINAC (1 study)=13.6%
- CyberKnife studies=mean 9.3%, median 10% (range 5.9% to 12%)

Other complications

- Deafferentation pain
- Dry eye
- Dysaesthesia
- Keratitis
- Paraesthesia

Study 2 Spina A (2021)

Study details

Study type	Systematic review
Country	Not reported for individual studies
Recruitment period	Search date: 2019
Study population and number	n=646 (12 studies) Adult patients with secondary trigeminal neuralgia related to MS
Age and sex	Mean 56 years (range 51 to 63); sex not reported
Patient selection criteria	Inclusion criteria were English-language publications reporting stereotactic radiosurgery treatment. Articles referring to other treatments, non-English articles, and abstracts or case reports were excluded from the final analysis. The population of interest was patients with MS who had Gamma Knife radiosurgery for the treatment of trigeminal neuralgia either as first invasive treatment after medical therapy failure or as secondary treatment after other surgical procedures.
Technique	Gamma Knife stereotactic radiosurgery. The median dose was 80.76 Gy (range 72.5 to 90; median 80).
Follow up	Median 44.6 months (range 17 to 104)
Conflict of interest/source of funding	Not reported

Analysis

Follow up issues: The follow up period was not reported for 1 study.

Study design issues: Systematic review of evidence on Gamma Knife treatment for trigeminal neuralgia associated with MS. Outcomes of interest were the number of patients who had improved pain after Gamma Knife radiosurgery defined as initial responders and those who had pain control at the end of the follow-up, defined as cumulative proportion of successful treatments at the end of the study. In both cases, a successful outcome was defined as a BNI score 1 to 3b. Data analyses were done using R software. Heterogeneity was assessed through visual inspection of forest plots and using formal tests. The I^2 statistic was used to quantify heterogeneity with thresholds of 25%, 50%, and 75% indicating low, medium, and high heterogeneity, respectively. Visual inspection of the funnel plot and Egger's regression confirmed the absence of publication bias (p=0.892).

Study population issues: The mean duration of trigeminal neuralgia symptoms was 108.6 months (range 82.5 to 117; median 96).

Key efficacy findings

Number of patients analysed: 646

Initial response

Pooled proportion of patients who had an initial response to treatment was 83% (95% CI 74 to 90%; I^2=75.7%).

Successful treatment

The cumulative proportion of successful treatments at the end of the study was 47% (95% CI 33 to 60%; I^2=89.6%).

The only explanatory variable of the heterogeneity found in the proportion of successful treatments was the length of the follow up.

Key safety findings

The most frequently reported adverse reaction after Gamma Knife radiosurgery was facial hypaesthesia: the reported rate ranged from 0 to 71.4%

Study 3 Gubian A (2017)

Study details

Study type	Systematic review
Country	Not reported for individual studies
Recruitment period	Search period: 2005 to 2015
Study population and number	n=13,805 (5,540 radiosurgery and 8,265 microvascular decompression); 58 studies Patients with trigeminal neuralgia
Age and sex	Mean 63.7 years (65.3 for radiosurgery and 59.8 for microvascular decompression); 56% female
Patient selection criteria	Inclusion criteria for studies: human study, case control study or cohort study or randomised clinical trial, studies providing data of outcome of pain control or complications of treatment or both, study is focused on idiopathic trigeminal neuralgia, study was published in the last 10 years. Exclusion criteria: animal study, review or case report, studies not providing outcome of pain or complications of treatment, studies focused exclusively on secondary treatment of trigeminal neuralgia, studies focused exclusively on trigeminal neuralgia secondary to an underlying pathology (such as MS or a tumour), studies focused on management option other than microvascular decompression, radiosurgery and thermocoagulation. The studies included in the review had to match a level of evidence higher than 2b or exceed a score of 6 on the Newcastle-Ottawa Scale.
Technique	Radiosurgery or microvascular decompression.
Follow up	Mean 44 months
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: Completeness of follow up for the individual studies is not discussed.

Study design issues: Systematic review, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The primary outcome was pain relief, defined as a decrease in intensity and frequency of the paroxysmal crisis and its evolution over time. The secondary outcome was the assessment of the side effects. The BNI pain assessment scale was used to evaluate the outcome of pain response. Recurrences were defined as being the reappearance of pain in patients who were initially pain free. Therapeutic success was defined as a BNI score of 1 to 3. Therapeutic failure corresponded to a BNI score of 4 and 5. Differences in outcome after treatment were analysed using t tests and weighted averages.

Of the 58 studies, 12 were prospective and 46 were retrospective; 5 studies were comparative. There were no randomised controlled trials. The mean number of patients included per study was 238 (range 17 to 3,273). There is some overlap with the systematic review by Tuleasca et al., 2019.

Key efficacy findings

Number of patients analysed: 13,805 (5,540 radiosurgery and 8,265 microvascular decompression)

Initial success rate

- Radiosurgery=71.1%
- Microvascular decompression=86.9%, p<0.0001

Success rate at 2 years

- Radiosurgery=77.8%
- Microvascular decompression=91.4%, p=0.0002

Success rate between 2 and 5 years

- Radiosurgery=63.1%
- Microvascular decompression=80.6%, p=0.0098

Success rate at 5 years

- Radiosurgery=63.8%
- Microvascular decompression=84%, p=0.0361

Median recurrence rate at median follow up of 36 months

- Radiosurgery=25%
- Microvascular decompression=11%, p=0.0015

Mean recurrence-free period

- Radiosurgery=30.6 months
- Microvascular decompression=30.4 months, p=0.987

Key safety findings

Of 58 studies, 46 reported side effects for radiosurgery (5,196 patients) and 17 reported side effects for microvascular decompression (5,351 patients).

Comparison of the incidence of common complications

Complication	Radiosurgery	Microvascular decompression	p value
Dysaesthesia	28.1%	2.3%	0.02
Hearing loss	0.7%	1.5%	0.02
Vertigo	1.8%	3.5%	0.001
Cranial nerve palsy (excluding trigeminal nerve)	3.3%	0.7%	0.01

Other complications reported after radiosurgery

- Keratitis=2.5%
- Anaesthesia dolorosa=0.04%
- Tinnitus=0.2%
- Brainstem oedema=0.06%
- Chronic fatigue=0.8%
- Chronic headache≈0.4% (estimated from graph)
- Infection≈0.1% (estimated from graph)

Other complications reported after microvascular decompression

- Perioperative mortality=0.3%
- Cerebrospinal leak=2.7%
- Combined cerebrovascular, cardiological, pneumological, or thromboembolic events=3.9%
- Infection≈2.1% (estimated from graph)
- Chronic headache≈0.2% (estimated from graph)

Study 4 Wilson T (2020)

Study details

Study type	Systematic review
Country	Not reported for individual studies
Recruitment period	Search date: 2019
Study population and number	n=1,462 (14 studies) for dose analysis; n=2,092 (27 studies) for target analysis Patients with trigeminal neuralgia
Age and sex	Not reported for whole patient population
Patient selection criteria	Non-English studies, case reports, editorials and commentaries, review articles, systematic reviews, and nonhuman studies were excluded. Studies with fewer than 10 patients in a treatment arm and those with median follow-up less than 12 months were excluded. In addition, studies not relevant to the topic (such as studies that evaluated radiosurgical treatment of atypical facial pain, postherpetic neuralgia, or tumour associated neuralgia) were excluded. Studies that grouped more than 1 dose together or did not distinguish between radiation doses in their results were excluded. Studies that did not differentiate between target locations in their results or treated multiple isocentres along the nerve were excluded. Studies that reported only initial pain response, were unclear about last follow-up, or used actuarial rates for pain scores over time were excluded.
Technique	Devices: Gamma Knife (Elekta, Sweden), CyberKnife (Accuray, US), or linear accelerator (LINAC). The radiosurgery doses analysed were 70 Gy, 75 Gy, 80 Gy, 85 Gy, and 90 Gy. The anatomic targets analysed were the root entry zone and distal trigeminal nerve locations, typically described as cisternal or retrogasserian treatment targets.
Follow up	In the dose meta-analysis, median follow up ranged from 12 to 59 months. In the target meta-analysis, median follow up ranged from 9 to 92 months.
Conflict of interest/source of funding	None

Analysis

Study design issues: Systematic review with meta-analysis was done in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol guidelines, to investigate the association of prescription dose and anatomic target on outcomes in patients with typical trigeminal neuralgia. The primary outcome was pain score at last follow-up. Most studies used the BNI scale or the MMS to report pain outcomes. Based on procedure success, pain outcomes were consolidated into good (BNI grade 1 to 3; MMS grade 1 to 4) or poor (BNI grade 4 to 5; MMS grade 5 to 6) to allow comparison. The few studies reporting fair outcomes were included with poor outcomes. Subgroups for radiosurgery dose were 70 to 75 Gy, 80 Gy, 85 Gy, and 90 Gy. Subgroups for anatomic target were the root entry zone and distal locations. Forest plots with the percentage of outcomes for each individual study and the pooled proportion for each subgroup with the accompanying 95% CI were created for both radiosurgery dose and anatomic target. Subgroups were compared via pooled proportions and 95% CIs with nonoverlap suggestive of statistically significant differences between subgroups. Meta-regression was used to investigate the relationship of the radiosurgery dose and target subgroups with each outcome variable. Most of the included studies were retrospective. No publication bias was identified. The authors noted that the heterogeneity in treatment variables, outcome measures, and study design limited comparability across studies. To reduce variability, they used stricter inclusion criteria with fewer studies.

Key efficacy and safety findings

Number of patients analysed: 1,462 for dose meta-analysis and 2,092 for target meta-analysis

Outcomes based on radiation dose

Variable	70 to 75 Gy (n=114)	80 Gy (n=280)	85 Gy (n=81)	90 Gy (n=987)
Median age, years (IQR)	69 (69 to 69)	65 (65 to 71)	60 (60 to 71)	68 (68 to 69)
Median follow up, months (IQR)	26 (26 to 26)	47 (33 to 49)	29 (29 to 30)	55 (30 to 55)
Good pain control, %, mean (95% CI)	51.8 (42.7 to 61.0)	65.0 (59.4 to 70.5)	71.2 (56.8 to 85.7)	81.6 (79.2 to 84.0)
Bothersome numbness, %, mean (95% CI)	1.4 (0.0 to 3.5)	0.8 (0.2 to 1.8)	1.9 (1.4 to 5.2)	4.9 (1.9 to 8.3)

Increasing radiation dose was associated with improved outcomes across all doses (p<0.001).

Increasing radiation dose was not associated with higher percentages of bothersome numbness (p=0.183). Although there was a slight trend toward increased bothersome numbness in the 90 Gy group, most of this pooled percentage comes from a single outlier study, which reported bothersome numbness in 32% of patients compared with 12% or less in all other studies. When excluding the outlier study, there are similar percentages of bothersome numbness across all doses and the trend disappears (p=0.406).

For radiosurgery dose, the I^2 for heterogeneity within each subgroup was low, except pain control in the 85 Gy subgroup and bothersome numbness in the 90 Gy subgroup. Because of the high heterogeneity, a leave-one-out analysis was done on the 90 Gy subgroup for bothersome numbness. When the outlier study was excluded, the I^2 for heterogeneity decreased to 25.2%.

Outcomes based on target location

Variable	Root entry zone (n=980)	Distal target (n=1,112)
Median age, years (IQR)	67 (64 to 70)	68 (66 to 68)
Median follow up, months (IQR)	29 (18 to 49)	33 (21 to 54)
Dose, Gy, median (IQR)	80 (80 to 83)	85 (85 to 90)
Good pain control, %, mean (95% CI)	70.6 (67.7 to 73.4)	81.0 (77.0 to 85.0)
Bothersome numbness, %, mean (95% CI)	2.8 (1.4 to 4.3)	1.5 (0.3 to 2.7)

Patients treated at the distal target had higher rates of good pain control compared with those treated at the root entry zone target (81.0% compared with 70.6%; p<0.001). When considering target and radiation dose, both distal target (<0.001) and increased dose (p=0.022) were independently associated with higher rates of good pain control.

There was no difference in rates of bothersome numbness between the radiation targets (p=0.369). In the regression model, neither target (p=0.202) nor radiation dose (p=0.498) was associated with development of bothersome numbness.

For the anatomic targets, the heterogeneity was low to moderate within subgroups for both pain control and bothersome numbness.

Study 5 Zeng Y (2018)

Study details

Study type	Randomised controlled trial
Country	China
Recruitment period	2015 to 2016
Study population and number	n=441 (221 stereotactic radiosurgery, 220 microvascular decompression) Patients with primary trigeminal neuralgia
Age and sex	Mean 61 years (radiosurgery) and 56 years (microvascular decompression); 58% (254/441) female
Patient selection criteria	Patients with a diagnosis of primary trigeminal neuralgia according to the International Classification of Diseases, Tenth Revision, were included. The exclusion criteria included secondary trigeminal neuralgia caused by a tumour, arachnoid cyst, Chiari malformation, or MS; poor surgical candidacy because of severe systemic illness; patient history of brain surgery or injury; bilateral trigeminal neuralgia; or the presence of psychoses.
Technique	Radiosurgery was done using Gamma Knife. The radiation dose was set to 80 to 90 Gy at the lesion centre and 42 to 45 Gy around it. For microvascular decompression, a Teflon prosthesis was placed between the trigeminal nerve and the responsible vessel.
Follow up	2 years
Conflict of interest/source of funding	None

Analysis

Follow-up issues: An additional 22 patients were randomised but did not complete the follow up, so were excluded from the study. All patients were followed up at 1, 3, 6, 12, 18, and 24 months in the outpatient clinic.

Study design issues: Single centre randomised controlled trial, comparing Gamma Knife surgery with microvascular decompression. Randomisation was done by a statistician not otherwise involved in the study using a computer-generated random number list. The extent of pain relief was assessed at each time point by an independent neurologist using the BNI pain intensity scale.

Study population issues: The sex and age distributions, pain duration from disease onset, affected side, and involved nerve branches were similar between the treatment groups. The mean duration from disease onset was 5.0 years (range 0.1 to 30) in the radiosurgery group and 5.5 years (range 0.1 to 30) in the microvascular decompression group. In the radiosurgery group, vascular compression was observed in 105 (47%) patients during target zone localisation; 116 (53%) patients had no obvious compression. In the microvascular decompression group, the pretreatment incidence of vascular compression detected by MRI was 56% (n=124). Overall, 191 (87%) patients in this group had compression confirmed by MRI or intraoperatively.

Key efficacy findings

Number of patients analysed: 441 (221 radiosurgery, 220 microvascular decompression)

Pain relief immediately after procedure

- Radiosurgery: 3 (1%) patients had complete pain relief within the first postoperative week.
- Microvascular decompression: 189 (86%) patients had immediate and complete postoperative pain relief.

Pain relief at 2-year follow up

At the 2-year follow-up, patient pain had statistically significantly decreased relative to pretreatment levels, in both treatment groups ($p<0.01$).

Distribution of BNI scores before and after surgery at 2-year follow up

BNI scores	Radiosurgery Before surgery, n (%)	Radiosurgery Follow up, n (%)	Microvascular decompression Before surgery, n (%)	Microvascular decompression Follow up, n (%)
1	0 (0)	55 (24.9)	0 (0)	183 (83.2)
2	0 (0)	106 (48.0)	0 (0)	5 (2.3)
3	27 (12.2)	23 (10.4)	25 (11.4)	12 (5.5)
4 to 5	194 (87.8)	37 (16.7)	195 (88.6)	20 (9.1)

The rate of complete pain relief (BNI 1) was statistically significantly higher in the microvascular decompression group than in the radiosurgery group ($p<0.05$). However, there was no statistically significant difference in the number of patients with effective relief (BNI 1 and BNI 2) between the 2 groups. Duration of disease (more than 5 years compared with less than 5 years) was the only statistically significant factor associated with lack of pain relief at 2 years in both groups (other factors that were considered were age, sex, affected side, and involved branches).

Recurrence rate

There was no statistically significant difference in the recurrence rate at 2 years (0.9% compared with 0.45%).

Key safety findings

Postoperative complications in radiosurgery group

- Loss of corneal reflex=5.9% (13/221)
- Facial numbness=5.0% (11/221)
- Facial paralysis=0.4% (1/221)
- Diplopia=0.4% (1/221)
- Hearing impairment=0.4% (1/221)

Postoperative complications in microvascular decompression group

- Intracranial bleeding=1.4% (3/220)
- Encephaledema=0.9% (1/220)
- Intracranial infection=1.8% (4/220)
- Chemical meningitis=6.4% (14/220); patients presented with headache and fever but had normal cerebrospinal fluid results. All patients recovered within 1 to 2 weeks.
- Cerebrospinal fluid leakage=0.5% (1/220)
- Facial palsy=0.5% (1/220)
- Facial numbness=0.5% (1/220)
- Vertigo=0.5% (1/220)
- Diplopia=0.5% (1/220)
- Facial nerve palsy=0.5% (1/220)

There were no deaths in either group.

Study 6 Romanelli P (2019)

Study details

Study type	Case series
Country	Italy
Recruitment period	2009 to 2018
Study population and number	n=343 (387 treatments) Patients with drug-resistant trigeminal neuralgia
Age and sex	Mean 63.7 years; sex not reported
Patient selection criteria	The procedure was offered to patients with drug-resistant trigeminal neuralgia, after the failure of other treatments or refusal of invasive procedures. A second treatment was offered to patients with a poor response after the first treatment or with recurrent pain.
Technique	Frameless image-guided robotic radiosurgery (a CyberKnife G3 [Accuray Inc., US] was used until October 2011 and a Cyberknife VSI [Accuray Inc., US] was used from October 2011 onwards). Treatment protocol required the non-isocentric delivery of 60 Gy prescribed to the 80% isodose to a 6 mm retrogasserian segment of the affected trigeminal nerve. Retreatments typically used 45 Gy, prescribed to the 80% isodose. The final plan used CT imaging and was developed accordingly to individual anatomy and dose distribution over the trigeminal nerve, gasserian ganglion, and brainstem. The radiosurgery treatment was done the day after imaging and planning and took about 50 minutes.
Follow up	36 months
Conflict of interest/source of funding	Two authors declared personal fees from Accuray Inc.

Analysis

Follow-up issues: Patients with a minimum follow up of 36 months were included. An additional 184 patients were treated during the study period but were excluded from the analysis because they had a shorter follow up period.

Study design issues: Single centre, retrospective case series. Clinical and treatment data were collected in a digital archive. Follow up information was retrospectively obtained by outpatient clinical evaluation at defined time intervals. The endpoints analysed were: effects on pain scores, effects on medication, occurrence of sensory disturbance, onset and intensity of recurrent pain. Pain level was scored using the BNI scale. For hypaesthesia evaluation, the BNI facial hypaesthesia scale was used (class 1: no facial numbness; 2: mild facial numbness, not bothersome; 3: facial numbness, somewhat bothersome; 4: facial numbness, very bothersome). The pain response was defined as sufficient if the patients reported BNI pain scores 1 to 3b. A clinically insignificant numbness was defined as BNI grades 1 to 2.

Study population issues: Preoperatively, all patients had severe pain with a numerical rating scale score above 7 (median score 9) and were in BNI class 4 (33%) or 5 (67%). All patients had taken medications for an average of 4.3 years (range 11 months to 17 years) before treatment. Of the 527 patients treated during the study period, 5% had MS, 17% had had previous procedures, including microvascular decompression, glycerol injection, thermal ablation or balloon compression, and a neurovascular conflict was identified in 59% of patients.

Key efficacy findings

Number of patients analysed: 343

Pain relief by follow up period

- 6 months=92%
- 12 months=87%
- 18 months=87%
- 24 months=82%
- 30 months=78%
- 36 months=76%

After a median time of 3 weeks, significant pain relief (a decrease in visual analogue scale score of more than 5) was reported in 67% of patients. At 6 months, the rate of patients free of pain without medication (BNI pain class 1) was 61%, rising to 72% after 1 year. Overall 78% were completely pain-free (BNI classes 1 and 2) after 1 year. 8% (28/343) of patients did not report any benefit after the procedure.

Recurrence

16% (55/343) of patients who initially had pain relief had recurrent pain within 3 years of the procedure.

Repeat treatment

12.8% (44/343) of patients had a second treatment during the study period (20 who did not have pain control after a minimum of 6 months and 24 who had recurrent pain within 3 years). All 44 patients had good pain control (BNI pain scores 1 to 3) at the last follow-up.

Key safety findings

- Facial numbness associated with bothering dysaesthesia (BNI numbness class 3 or 4) at 36 months = 6.1% (21/343); 3 were after first treatments and 18 were after retreatments.
- Mild, non-bothersome sensory disturbances (BNI class 2) = 14.0% (48/343)
- Salivary drooling=1.2% (4/343) (associated with BNI class 2 to 3 numbness)

On average, sensory complications developed after 16.4 ±8.7 months.

No further complications, such as temporal lobe radionecrosis, anaesthesia dolorosa, lockjaw, weakness of the mandible, diplopia, dry-eye syndrome, keratitis, or hearing loss, were reported.

Study 7 Kotecha R (2016)

Study details

Study type	Case series
Country	US (2 centres)
Recruitment period	1997 to 2014
Study population and number	n=870 Patients with trigeminal neuralgia
Age and sex	Median 71 years (range 25 to 98); 61% (533/870) female
Patient selection criteria	Patients who had stereotactic radiosurgery for trigeminal neuralgia during the study period were included.
Technique	Device: Gamma Knife (Elekta Instruments, Sweden). Before 2007, a 201-source 60Co system was used. After this date, a 192-source unit (Perfexion) was used at both hospitals. A single 4-mm isocentre was typically positioned at the emergence of the trigeminal nerve (dorsal root entry zone); 47 patients were treated with concentrically aimed and equally weighted 4- and 8-mm isocentres. The doses varied over this period from 70 to 95 Gy prescribed to the 100% isodose line.
Follow-up	Median 36.5 months (range 0 to 207.9 months).
Conflict of interest/source of funding	One author has received research support from Varian Medical Systems, and reimbursement from Elekta for travel expenses, 1 has consulted for Elekta, 1 has ownership interest in Autonomic Technologies Inc., Cardionomics, and Enspire, and a consultant relationship with Functional Neuromodulation and Spinal Modulation, and 1 has received an honorarium from Varian Medical Systems.

Analysis

Follow-up issues: Of the 870 patients, 69 patients (8%) did not have a pain response recorded at follow-up, and these patients were excluded from the analysis for pain response, although other variables and outcomes may have been collected. Follow-up records for the assessment of facial numbness were available for 802 patients (92%). The median follow up for patients treated with 83 to 86 Gy was shorter (6.6 months) than for patients treated with ≤82 Gy (22.4 months) or ≥90 Gy (48.7 months).

Study design issues: Retrospective review of databases held at 2 centres. Patients were categorised into 3 dose groups: ≤82 Gy (n=352), 83 to 86 Gy (n=85), and ≥90 Gy (n=433). Outcome measures were pain response and facial numbness. Pain response was assessed using the BNI scale and also coded into a simplified 4-group categorical scoring system (excellent, good, fair, poor). Excellent was scored if the patient was pain-free and off medications, good if they had rare pain or were pain-free on doses of medications not producing side effects, fair if they had persistent pain but less severe than before treatment, or poor if they had no significant response to therapy. The BNI facial numbness scale was used to assess treatment-related facial numbness. For both pain failure and numbness, patients without the respective endpoint were censored at time of last follow up.

Study population issues: Most patients had typical trigeminal neuralgia (827 patients, 95%); 78 patients (9%) had MS. The median age at first onset of symptoms was 63 years (range 11 to 96 years). The median time from first pain episode to stereotactic radiosurgery treatment was 48.7 months (range 0 to 610 months). Stereotactic radiosurgery was the primary treatment for 637 patients (73%).

Key efficacy findings

Number of patients analysed: 870

Pain relief

- Improvement in pain=85.9% (747/870) of all patients; 93.3% (747/801) of patients with follow up data on pain response.
- 4-year rate of excellent to good pain relief=86.7% (95% CI 83.6% to 89.8%).
- At last follow-up, 539 patients (62%) reported excellent and 162 patients (19%) reported good pain control.
- Patients treated with ≥90 Gy had longer times to pain failure compared with those treated with ≤82 Gy (p=0.0019).

Proportion of patients with excellent to good pain relief at 4 years by dose

- ≤82 Gy=79.0% (95% CI 73.1% to 85.0%)
- 83 to 86 Gy=81.6% (95% CI 63.4% to 99.9%)
- ≥90 Gy=92.0% (95% CI 88.7% to 95.4%), p=0.0019

Proportion of patients with MS or atypical trigeminal neuralgia with excellent to good pain relief at 4 years by dose

- ≤82 Gy=71.6% (95% CI 56.4% to 86.8%)
- ≥90 Gy=85.3% (95% CI 72.0% to 98.7%), p=0.21

Univariate analysis showed that dose, age at time of procedure, and a history of prior procedures were predictors of pain failure after stereotactic radiosurgery. Patients treated with lower doses (≤82 Gy) were at higher risk of a having a recurrence of their pain (hazard ratio 2.0, 95% CI 1.3 to 3.0) compared with patients treated with ≥90 Gy (p=0.0007).

Multivariate analysis confirmed that prescribed dose influenced pain control outcomes (p=0.008), and an increasing number of procedures before stereotactic radiosurgery was also significantly associated with an increased risk of pain failure after stereotactic radiosurgery (p=0.033)

Key safety findings

Worst facial numbness score during follow up

- Class 1=43.6% (379/870)
- Class 2=19.5% (170/870)
- Class 3=20.1% (175/870)
- Class 4=9.0% (78/870)
- 5-year rate of freedom from class 3 or 4 facial numbness=58.4% (95% CI 53.9% to 62.8%)

4-year rates of freedom from class 3 or 4 facial numbness by dose

- ≤82 Gy=74.9% (95% CI 68.8% to 80.9%)
- 83 to 86 Gy=50.7% (95% CI 20.7% to 80.8%)
- ≥90 Gy=59.7% (95% CI 54.3% to 65.2%), p=0.0056

On univariate analysis, patients treated with doses ≥90 Gy were at higher risk of developing a class 3 or 4 facial numbness (hazard ratio 1.53, 95% CI 1.16 to 2.04) compared with patients treated with the lowest doses (≤82 Gy, p=0.0028). Gender, age at time of stereotactic radiosurgery, MS, or history of a previous surgical procedure did not relate to risk of treatment-related facial numbness.

Facial numbness score at last follow up

- Class 1=58.7% (511/870)
- Class 2=14.9% (130/870)
- Class 3=12.9% (112/870)
- Class 4=5.2% (45/870)

- Anaesthesia dolorosa=1.0% (9/870) (all 9 patients were treated with doses ≤86 Gy)

Study 8 Wang Y (2018)

Study details

Study type	Cohort study
Country	China
Recruitment period	2008 to 2015
Study population and number	n=700 (658 patients had radiosurgery as their only surgical treatment and 42 patients had radiosurgery for recurrent trigeminal neuralgia after microvascular decompression) Patients with trigeminal neuralgia
Age and sex	Mean 48 years (exclusive radiosurgery) and 54 years (radiosurgery after microvascular decompression); range 27 to 81 years; 53% (374/700) female
Patient selection criteria	The diagnosis of trigeminal pain agreed with the International Headache Society. Trigeminal pain was classified as idiopathic trigeminal neuralgia type 1 or type 2. The patients who had previous microvascular decompression fulfilled the diagnostic criteria of trigeminal neuralgia type 1 and had explicit vascular compression on imaging. Patients with a history of multiple sclerosis or megadolichobasilar artery compression were excluded.
Technique	Gamma Knife surgery. All treatments used the Leksell Knife Model C (Elekta AB) with a single 4-mm isocentre. The target was located at the cisternal portion of the trigeminal nerve. The median distance from the target centre to the anterior portion of where the nerve emerged was 7.4 mm (range 4.1 to 10.6 mm). The median maximum prescription dose was 85 Gy (range 70 to 90 Gy). The radiation dose received by the brainstem was also calculated and was limited to 15 Gy by scaling down the dose and applying the plug technology.
Follow-up	Median 6.2 years (range 1.1 to 10 years).
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were followed up at 1 month, 3 months, 6 months, and 12 months and yearly thereafter until the patient was lost to follow up. The initial follow up assessment was done as an outpatient, and long-term follow-up assessments was by telephone review and other means.

Study design issues: Retrospective single-centre cohort study. The main aim was to evaluate efficacy and safety of stereotactic radiosurgery for patients with recurrent trigeminal neuralgia after previous microvascular decompression. Efficacy was evaluated using the BNI scale (grades 1 to 3a were defined as successful). Patients with recurrence went from BNI grades 1 to 3a to a lower grade. Hypaesthesia was assessed using the BNI scale. Patient satisfaction was classified on 3 levels: no regret, no opinion, and regret.

Key efficacy findings

Number of patients analysed: 700

Proportion of patients with pain relief by follow up period

Follow up	Stereotactic radiosurgery only (n=658)	Stereotactic radiosurgery after microvascular decompression (n=42)
1 month	74.8%	56.8%
2 months	79.0%	68.2%
3 months	81.6%	Not reported
4 months	85.1%	Not reported
5 months	87.0%	72.7%
12 months	90.5%	79.5%

Kaplan-Meier survival analysis indicated that the initial rate of pain relief in patients who had previous microvascular decompression was lower than in patients who had not (p=0.01, hazard ratio=1.64)

Recurrence rate by follow up period

Follow up	Stereotactic radiosurgery only (n=658)	Stereotactic radiosurgery after microvascular decompression (n=42)	p value
1 year	10.0%	4.8%	Not reported
2 years	19.2%	19.0%	Not reported
3 years	23.8%	19.0%	Not reported
4 years	37.4%	40.6%	0.76
5 years	41.1%	Not reported	Not reported
10 years	43.7%	49.1%	0.84

Patient satisfaction

In the stereotactic radiosurgery only group, 537 (81.6%) patients did not regret choosing the procedure, and 64 (9.7%) patients had no opinion. The reasons for patients regretting it included the following: waiting to be pain-free for an extended period (41 patients), inability to tolerate the pain during the time frame of the treatment (11 patients) and claustrophobia (5 patients).

In the stereotactic radiosurgery with previous microvascular decompression group, the rate of no regret, no opinion, and regret was 69.0% (29 patients), 26.2% (11 patients), and 4.8% (2 patients).

Key safety findings

In the stereotactic radiosurgery only group, the long-term complication rate was 11.0%. The complication rate at 1 and 2 years was 4.10% and 9.90%, respectively.

In the stereotactic radiosurgery with previous microvascular decompression group, all complications manifested within 1 year (9.5%) and were unchanged until the end of the study. Complications included abnormal corneal reflex (n=1), dysaesthesia (n=5), paraesthesia (n=2), anaesthesia dolorosa (n=4).

Study 9 Berti A (2018)

Study details

Study type	Case report
Country	US
Recruitment period	First stereotactic radiosurgery treatment was in 2001
Study population and number	n=1 Patient with invasive keratinising squamous cell carcinoma in the left posterior mandibular oral mucosa after 2 radiosurgery treatments for trigeminal neuralgia
Age and sex	96 year old male
Patient selection criteria	Not applicable
Technique	First treatment (2001): Gamma Knife (Elekta, Sweden) using 80 Gy targeting 4 mm of the left retrogasserian trigeminal nerve. The brainstem dose was 98 cGy at the left trigeminal root entry zone. Second treatment (2012): CyberKnife (Accuray Inc, US) with 6,550 cGy using 1 5.0 mm collimator with a total of 104 beams employed to the same left trigeminal nerve. The brainstem dose was 84 cGy. The combined total dose with both treatments was 145.5 Gy.
Follow up	15 years from initial radiosurgery
Conflict of interest/source of funding	None

Key safety findings

A healthy, active, 96 year old patient, was diagnosed with invasive keratinising squamous cell carcinoma in the left posterior mandibular oral mucosa 4 years after a second stereotactic radiosurgery treatment for recurrent trigeminal neuralgia. The initial radiosurgery treatment was done 11 years before the repeat treatment. The patient had no history of smoking or human papillomavirus infection. It was postulated that the cancer developed secondary to the long-term radiation effect with a very localised area being exposed twice to a focused, cumulative, high-dose radiation.

The oral carcinoma was treated with intensity modulated radiation therapy. Follow up has shown resolution of the cancerous area in the oral mucosa.

Study 10 Bigder M (2017)

Study details

Study type	Case report
Country	Canada
Recruitment period	Stereotactic radiosurgery treatment was in 2007
Study population and number	n=1 Patient with necrotising Teflon granuloma after microvascular decompression and stereotactic radiosurgery
Age and sex	77 year old female
Patient selection criteria	Not applicable
Technique	Device: Gamma Knife (80-Gy dose was prescribed to the proximal trigeminal nerve root)
Follow up	8 years after stereotactic radiosurgery
Conflict of interest/source of funding	None

Key safety findings

In 2006, the patient had a microvascular decompression for trigeminal neuralgia. A shredded Teflon felt implant was placed between the superior cerebellar artery and the underlying trigeminal nerve root. She had limited pain relief and had a Gamma Knife procedure in 2007. She had minimal, delayed pain relief, and continued with medical management until having radiofrequency rhizotomy in 2009, which provided minimal pain relief. This also resulted in corneal anaesthesia and 80% preservation of sensation in V1 and V2 distributions and full preservation of V3. Over the following years, she developed a progressive full sensory loss of all 3 trigeminal nerve distributions, temporalis and masseter muscle atrophy, accompanied by alleviation of her neuralgia. In 2015, she developed a progressive gait ataxia and MRI showed a lobulated, enhancing mass in the region of the previously inserted Teflon implant along with significant oedema involving adjacent brain.

A posterior fossa exploration was done through a retrosigmoid craniectomy. The lesion had a firm capsule surrounding the inner contents of the tumour, consisting of soft white material intermixed with the Teflon implants. After internal debulking and dissection of the tumour from the neurovascular structures, a thin rim of residual tumour was left adherent to the nerve and superior cerebellar artery. At 6-month follow up, the patient reported a mild improvement of her gait instability. Based on the absence of microorganisms, it was concluded that granulomatous inflammation was associated with the Teflon implant. The authors speculated that radiosurgery, in conjunction with presence of a foreign body, may have contributed to a heightened inflammatory response and resultant granuloma formation in this patient.

Study 11 Chen J (2017)

Study details

Study type	Case report
Country	US
Recruitment period	Stereotactic radiosurgery treatment was in 2003
Study population and number	n=1 Patient with an aneurysm after stereotactic radiosurgery for trigeminal neuralgia
Age and sex	90 year old male (age 79 at the time of radiosurgery)
Patient selection criteria	Not applicable
Technique	Linear accelerator radiosurgery; a dose of 90 Gy was delivered via a 4 mm conical collimator to the proximal cisternal extent of the trigeminal nerve.
Follow up	11 years
Conflict of interest/source of funding	Not reported

Key safety findings

In 2003, the patient had stereotactic radiosurgery treatment for medically refractory left sided trigeminal neuralgia. The patient had an excellent pain free result and was able to discontinue his medical therapy. Good relief occurred within 24 hours of the treatment. 18 months after his treatment, the patient presented to the clinic for routine follow-up with complaint of new mild hypaesthesia in the V1 and V2 distribution. He maintained excellent relief of pain. 32 months after treatment, the patient presented again to the clinic for routine follow-up with continued pain-free result. The hypaesthesia had improved. The patient was lost to follow-up until 2012, 9 years after treatment, when he had decline of right sided (contralateral) hearing. An MRI of the internal auditory canals was unremarkable. There were no visible abnormalities in the vicinity of the left trigeminal nerve. In 2014, 11 years after treatment, at the age of 90 years, the patient presented with a 2-month course of worsening numbness involving the entire left side of the face. The MRI showed a left sided mass at the trigeminal root entry zone. Magnetic resonance angiography showed an 8 mm aneurysm of the superior cerebellar artery, which was successfully treated with coil embolisation.

Study 12 Dominguez L (2020)

Study details

Study type	Case report
Country	US
Recruitment period	First stereotactic radiosurgery treatment was in 2001
Study population and number	n=1 Patient with fatal ruptured aneurysm after 2 stereotactic radiosurgery treatments for trigeminal neuralgia.
Age and sex	77 year old female
Patient selection criteria	Not applicable
Technique	Gamma Knife stereotactic radiosurgery
Follow up	Not reported
Conflict of interest/source of funding	None

Key safety findings

The patient had stereotactic radiosurgery for refractory, right-sided trigeminal neuralgia in 2001 and 2006. She presented to the emergency department with sudden-onset severe headache, vomiting, right eye vision loss, left-sided facial droop, and left-sided hemiparesis. She had no history of hypertension or smoking. Initial head CT scan showed an intraparenchymal haemorrhage centred in the right middle cerebellar peduncle with subarachnoid haemorrhage in the basal cisterns and extension into the fourth ventricle causing early hydrocephalus. Head CT angiography showed a distal right superior cerebellar artery aneurysm adjacent to the haemorrhage. The patient's mental status deteriorated into coma after suspected re-rupture needing immediate intubation, external ventricular drain placement, and emergent cerebral angiogram with coil embolisation. Despite surgical and medical management, the patient did not improve neurologically and care was ultimately withdrawn.

Study 13 Kemp S (2016)

Study details

Study type	Case report
Country	Australia
Recruitment period	Not reported
Study population and number	n=1 Patient with neurological deficit from late onset MS, after stereotactic radiosurgery for trigeminal neuralgia
Age and sex	65 year old woman
Patient selection criteria	Not applicable
Technique	A Novalis Tx LINAC device (BrainLAB AG, Germany) was used with a 90 Gy point dose delivered to the root entry zone and the 50% isodose line tangential to the pons. The treatment used 7 non-coplanar arcs delivered with the 4 mm collimator using a frameless radiosurgery setup.
Follow up	3 years
Conflict of interest/source of funding	None

Key safety findings

The patient initially had microvascular decompression for right-sided typical trigeminal neuralgia and had complete remission of pain for 14 months. The symptoms then recurred, and she had stereotactic radiosurgery. She was pain free within 21 days and gabapentin was weaned. At 3 months, the patient remained pain free but had right-sided facial numbness. Two weeks after the onset of facial numbness the patient experienced left-sided upper and lower limb paraesthesia and ataxic gait. Repeat MRI showed irregular enhancement of the brainstem at the level of the right trigeminal root entry zone. In contrast, no changes in the root entry zone had been seen on 3 separate MRIs done within the 2 years before surgery, nor on 2 MRIs done between surgery and radiosurgery. A presumptive diagnosis of radiation-induced neurotoxicity was made and pulsed intravenous methylprednisolone was administered. Over the next few months the patient's gait normalised and she remained pain free. At 10 months after radiosurgery, following a viral upper respiratory tract infection, the patient developed left lower limb weakness and recurrent gait ataxia. Repeat MRI showed persistent T2 signal change at the right trigeminal root entry zone, multiple non-enhancing cerebral white matter lesions and a lesion in the cervical spinal cord consistent with demyelination. A diagnosis of relapsing MS was made, and methylprednisolone and disease-modifying therapy started. Six months later the patient had largely returned to baseline but continued to have a mild persistent gait disturbance. On most recent review, 3 years after radiosurgery, she had recurrence of her right-sided trigeminal neuralgia which she managed with pregabalin. The authors hypothesised that breakdown of the blood brain barrier at the site of the radiosurgery facilitated a vigorous inflammatory response. In retrospect, it is likely that occult MS pathology at this site predated stereotactic radiosurgery and was responsible for the patient's initial presentation of trigeminal neuralgia.

Study 14 Li C (2015)

Study details

Study type	Case report
Country	Taiwan
Recruitment period	Not reported
Study population and number	n=1 Patient with atheromatous plaque formation after stereotactic radiosurgery for trigeminal neuralgia
Age and sex	39 year old male
Patient selection criteria	Not applicable
Technique	Gamma Knife (Elekta, Sweden) radiosurgery. A single 4-mm isocentre of radiation was used to target the root entry zone of the trigeminal nerve. The maximum radiation dose was 80 Gy.
Follow up	11 months
Conflict of interest/source of funding	Not reported

Key safety findings

The patient had a history of hypertension for 3 years without regular medication control. His weight was 107 kg and height was 177 cm. He had high-density lipoprotein cholesterol 24 mg/dL, low-density lipoprotein cholesterol 169 mg/dL, total cholesterol 256 mg/dL, and triglycerides 278 mg/dL. His plasma glucose after overnight fasting was normal. Enhanced magnetic resonance angiography showed an ectatic and tortuous vertebrobasilar artery in the left cerebellopontine angle close to the trigeminal nerve. He had Gamma Knife radiosurgery for left-sided typical trigeminal neuralgia. There was some pain relief but he continued to need high doses of carbamazepine. He began to have more frequent attacks of severe pain at levels that he had never had before and chose to have microvascular decompression 11 months after the radiosurgery. Focal atheromatous changes to the parent vessel remote from the root entry zone of the trigeminal nerve were discovered during the surgery. The authors suggest that younger male patients with hyperlipidemia who have stereotactic radiosurgery for trigeminal neuralgia may be at an increased risk of postradiation atheromatous formation.

The authors noted that, to their knowledge, this is the fourth patient worldwide to be reported to have such focal atheromatous changes.

Study 15 Naseri A (2004)

Study details

Study type	Case report
Country	US
Recruitment period	2003
Study population and number	n=1 Patient with vision loss after stereotactic radiosurgery for trigeminal neuralgia
Age and sex	68 year old man
Patient selection criteria	Not applicable
Technique	Gamma knife radiosurgery (Leksell Gamma Knife, Elekta Inc, US). The dose matrix grid was 0.6 mm and the right trigeminal root entry zone was targeted tangential to the brainstem. The prescription dose was 40 Gy to the 50% isodose line. A single run with a single shot (treatment time 29 minutes) used a 4 mm collimator.
Follow up	9 months
Conflict of interest/source of funding	Not reported

Key safety findings

The patient presented in September 2003 with 3 weeks of fluctuating blurred vision in the right eye. The blurring was preceded by complete numbness of the right side of his face for 1 week. The patient's medical history was remarkable for right sided trigeminal neuralgia that began in 1998, predominantly involving the V2 dermatome. He had stereotactic radiosurgery in December 2002 and was pain free without medication. He also had a history of chronic renal failure needing dialysis 3 times weekly, hypertension, a myeloproliferative disorder, prostate cancer, and hyperlipidaemia. In 1998, he had resection of a left frontal lobe meningioma. His ocular history included bilateral cataract surgery but no history of herpes zoster or herpes simplex.

On initial examination, his vision measured 20/25 right eye and 20/25 left eye. Slit lamp examination of the right cornea revealed a fine punctate epitheliopathy. Corneal sensation was absent both subjectively and by blink reflex. The patient's vision gradually declined despite treatment with artificial tears and a punctal plug placed in the right lower lid. Ten weeks after presentation, his vision measured 20/200 right eye and 20/25 left eye. Slit lamp examination revealed severe epithelial keratopathy in the right eye. Fourteen months after radiosurgery, MRI showed increased signal intensity in the anterior aspect of the right fifth nerve. A punctal plug was placed in the right upper lid. During the next 6 weeks, the corneal surface improved, and at last follow up the patient's vision was 20/60.

Study 16 Pak S (2018)

Study details

Study type	Case report
Country	US
Recruitment period	Not reported
Study population and number	n=1 Patient with pseudoaneurysm after stereotactic radiosurgery for trigeminal neuralgia
Age and sex	81 year old male
Patient selection criteria	Not applicable
Technique	Gamma Knife stereotactic radiosurgery
Follow up	8 years
Conflict of interest/source of funding	None

Key safety findings

The patient presented with sudden-onset numbness and tingling in his right arm associated with profound right-sided weakness, 8 years after Gamma Knife radiosurgery for trigeminal neuralgia. On examination, he had a right-sided facial nerve palsy and severe left-sided sensory deficits. CT of the brain showed an acute thalamic infarct and a hyperdense mass lesion at the cerebellopontine angle on the right side. The patient was treated with tissue plasminogen activator which resolved the symptoms and neurological deficits. At this time, the mass-lesion detected on the CT scan was thought to be a malignant lesion. About 1 month later, the patient had a syncopal episode which lasted for about 5 min without any prodromal symptoms. He also described progressively worsening headaches and ataxia over the last month. His blood pressure was 107/76 mmHg, heart rate was 79/min, respiration rate was 17/min, and oxygen saturation was 95% on room air. Physical examination showed a mild facial nerve palsy and sensory deficits in the V1 and V2 distribution on the right side and profound ataxia. A repeat CT scan of the head showed a right cerebellopontine angle mass lesion, which had increased in size. Neuroangiography showed a large fusiform pseudoaneurysm on the superior cerebellar artery. Endovascular coil embolisation of the pseudoaneurysm and its parent artery was done to prevent further enlargement of the pseudoaneurysm. One month after the procedure, the patient reported significant improvement in his headache and ataxia.

Study 17 Redon S (2018)

Study details

Study type	Case report
Country	France
Recruitment period	Not reported
Study population and number	n=1 Patient with first bite syndrome after stereotactic radiosurgery for trigeminal neuralgia
Age and sex	41 year old woman
Patient selection criteria	Not applicable
Technique	Gamma Knife radiosurgery (85 Gy)
Follow up	10 months
Conflict of interest/source of funding	Not reported

Key safety findings

The patient was diagnosed with MS at the age of 28 and developed trigeminal neuralgia a year later. Symptoms were controlled by medication until she reached 40, when she had Gamma Knife radiosurgery. Ten months after the radiosurgery, she reported attacks of cramp and tension in the right parotid region, sometimes associated with a moderate pain, irradiating to the ear. The attacks were only triggered by the first bite at each meal. The intensity of the attacks diminished over the next 6 months.

The authors stated that the delay of 10 months before the first bite syndrome was compatible with a trigeminal denervation induced by the Gamma Knife radiosurgery.

Study 18 Wang A (2020)

Study details

Study type	Case report
Country	Canada
Recruitment period	The first stereotactic radiosurgery treatment was in 2013
Study population and number	n=1 Patient with radiation necrosis after repeated stereotactic radiosurgery treatments for trigeminal neuralgia
Age and sex	85 year old male
Patient selection criteria	Not applicable
Technique	CyberKnife radiosurgery (60 Gy). The radiation was predominantly delivered to the right preganglionic trigeminal nerve, with 14 Gy targeted to the Gasserian ganglion. The patient had an additional 50 Gy of irradiation to the right Gasserian ganglion 2 years later.
Follow up	16 months
Conflict of interest/source of funding	None

Key safety findings

The patient had stereotactic radiosurgery in 2013 and again in 2015 for trigeminal neuralgia. In April 2017, he presented with dysarthria and right sided weakness and acute ischemic stroke was diagnosed. MRI incidentally showed a right temporal fluid attenuated inversion recovery hyperintensity. A follow-up MRI 10 months later in March 2018 showed a new ring-enhancing lesion within this area. The patient was diagnosed with presumed high grade glioma. At this time, his symptoms included constant right sided facial pain, right hemifacial numbness in V1-3, and a mild facial droop. Several months after this diagnosis, the patient presented to the emergency room with myocardial infarction. Repeat MRI showed marginal interval decrease in the peripheral enhancement and vasogenic oedema of the temporal lesion. The possibility of radiation necrosis rather than high-grade glioma was considered. The patient refused all interventions, including a stereotactic biopsy for tissue diagnosis, so a non-invasive approach was used (magnetic resonance spectroscopy) to characterise the lesion. The results favoured a diagnosis of radiation necrosis over high-grade glioma.

At 2-month follow up, the patient remained well with no new symptoms or examination findings suggestive of progression of his neurological disease. At 7-month follow up, he had discontinued dexamethasone and had no further symptoms.

Study 19 Peddada A (2011)

Study details

Study type	Case report
Country	US
Recruitment period	Not reported
Study population and number	n=1 Patient with oral mucositis after stereotactic radiosurgery for trigeminal neuralgia
Age and sex	74 year old male
Patient selection criteria	Not applicable
Technique	Device: Cyberknife G4 robotic system (Accuray Inc.) The source to treatment distance was reduced from the normal 80 cm to 65 cm to increase the dose rate (reducing the treatment time), and reduce the effective size of the smallest collimated beam from 5 mm to 4 mm. The single session of treatment lasted 35 minutes. In the treatment planning process, the maximum monitor units per beam was set to a relatively high value (300 MU) and the maximum number per node was not constrained. This allowed multiple beams from 1 node to enter the patient through the mouth. Typically, the maximum monitor unit per beam would be set at 150 to 180 MU and the maximum monitor unit per node is limited to 4 times the beam monitor unit.
Follow up	2 weeks
Conflict of interest/source of funding	Two authors have ownership in Colorado Springs CK Leasing, LLC.

Key safety findings

The patient presented with a 4-month history of debilitating right-sided facial pain. MRI did not show any obvious pathology. He was diagnosed with idiopathic trigeminal neuralgia with a BNI score of 4. Medical management was unsuitable for the patient and he chose to have stereotactic radiosurgery. Two weeks after the procedure, the patient reported that his original symptoms had gone but he had new pain in his oral cavity and lip that were somewhat bothersome. On examination, he was found to have oral mucositis involving the upper lip, hard palate and tongue. He was offered a topical anaesthetic and local wound care to the lip. The symptoms resolved within 2 weeks.

The authors noted that an error occurred because the usual dose constraints were not imposed at the treatment planning stage. They highlight the importance of implementing a site-specific checklist and peer review before approving a treatment plan, to avoid such errors.

Validity and generalisability of the studies

- There are several recent systematic reviews and meta-analyses, which include different patient populations.
- There was a large randomised controlled trial that compared stereotactic radiosurgery with microvascular decompression, with a 2-year follow up. This study only included patients with primary trigeminal neuralgia (Zeng 2018).
- There are different devices used and different treatment regimens.
- Although most studies used the BNI score to assess pain relief after the procedure, success was defined in different ways.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Transcranial MRI-guided focused ultrasound thalamotomy for neuropathic pain. Interventional procedures guidance 632 (2018). Available from http://www.nice.org.uk/guidance/IPG632
- Percutaneous electrical nerve stimulation for refractory neuropathic pain. Interventional procedures guidance 450 (2013). Available from http://www.nice.org.uk/guidance/IPG450

NICE guidelines

- Neuropathic pain in adults: pharmacological management in non-specialist settings. Clinical guideline 173. Published November 2013, Last updated: July 2019. Available from http://www.nice.org.uk/guidance/CG173

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

No Professional expert questionnaires were submitted.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 2 companies who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- Ongoing trial: A Personalised Radiosurgery Procedure for People With Trigeminal Neuralgia to Improve Pain, Quality of Life and Reduce Complications (NCT04117035); RCT; UK; n=40; estimated study completion date January 2021.
- A Clinical Commissioning Policy on 'Stereotactic Radiosurgery for Trigeminal Neuralgia' was prepared by the NHS Commissioning Board Clinical Reference Group for Stereotactic Radiosurgery and published in 2013. The policy states that patients meeting all the following criteria will be routinely funded for SRS:

‘Patient meets the diagnostic criteria for trigeminal neuralgia (TN) as described by the International Headache Society and have typical TN (type 1) OR Trigeminal Neuralgia Syndrome associated with known neuromedical predisposing conditions AND

Patient is unable to tolerate drug therapy, or has had intractable pain despite medication normally expected for a minimum period of at least six months AND

Patient has been reviewed by a neurosurgeon who has assessed the patient as requiring surgery AND

Other treatment modalities (microvascular decompression and ablative techniques) are deemed inappropriate for the patient.’

References

1. Tuleasca C, Regis J, Sahgal A et al. (2019) Stereotactic radiosurgery for trigeminal neuralgia: a systematic review. Journal of Neurosurgery 130: 733–57
2. Spina A, Nocera G, Boari N et al. (2021) Efficacy of Gamma Knife radiosurgery in the management of multiple sclerosis-related trigeminal neuralgia: a systematic review and meta-analysis. Neurosurgical Review https://doi.org/10.1007/s10143-021-01507-3
3. Gubian A, Rosahl SK (2017) Meta-analysis on safety and efficacy of microsurgical and radiosurgical treatment of trigeminal neuralgia. World Neurosurgery 103: 757–67
4. Wilson TA, Karlsson B, Huang L et al. (2020) Optimizing radiosurgery for trigeminal neuralgia: impact of radiation dose and anatomic target on patient outcomes. World Neurosurgery 143: e482–91
5. Zeng YJ, Zhang H, Yu S et al. (2018) Efficacy and safety of microvascular decompression and gamma knife surgery treatments for patients with primary trigeminal neuralgia: a prospective study. World Neurosurgery 116: e113–17
6. Romanelli P, Conti A, Redaelli I et al. (2019) Cyberknife radiosurgery for trigeminal neuralgia. Cureus 11: e6014
7. Kotecha R, Kotecha R, Modugula S et al. (2016) Trigeminal neuralgia treated with stereotactic radiosurgery: the effect of dose escalation on pain control and treatment outcomes. International Journal of Radiation Oncology, Biology, Physics 96: 142–8
8. Wang DD, Raygor KP, Cage TA et al. (2018) Prospective comparison of long-term pain relief rates after first-time microvascular decompression and stereotactic radiosurgery for trigeminal neuralgia. Journal of Neurosurgery 128: 68–77
9. Berti A, Granville M, Jacobson RE (2018) Oral squamous cell carcinoma found inline with the fields of repeat stereotactic radiosurgery for recurrent trigeminal neuralgia. Cureus 10: e2054
10. Bigder M, Matsuda K, Kaufmann A (2017) Necrotizing Teflon granuloma after microvascular decompression and gamma knife. The Canadian Journal of Neurological Sciences 44: 757–58
11. Chen JCT, Chao K, Rahimian J (2017) De novo superior cerebellar artery aneurysm following radiosurgery for trigeminal neuralgia. Journal of Clinical Neuroscience 38: 87–90
12. Dominguez L, Saway B, Benko MJ et al. (2020) Ruptured distal superior cerebellar artery aneurysm after gamma knife radiosurgery for trigeminal

neuralgia: a case report and review of the literature. World Neurosurgery 135: 2–6

13. Kemp S, Allan RS, Patanjali N et al. (2016) Neurological deficit following stereotactic radiosurgery for trigeminal neuralgia. Journal of Clinical Neuroscience 34: 229–31
14. Li, C.-S.; Liu, J.-T.; Chang, C.-S.; et al. (2015) Atheromatous plaque formation in a man with high-risk atherosclerosis after Gamma Knife stereotactic radiosurgery for trigeminal neuralgia. Tzu Chi Medical Journal 27: 181–3
15. Naseri A, Patel NP (2004) Vision loss as a complication of gamma knife radiosurgery for trigeminal neuralgia. The British Journal of Ophthalmology 88: 1225–6
16. Pak S, Cha D, Valencia D et al. (2018) Pseudoaneurysm as a late complication of gamma knife surgery for trigeminal neuralgia. Neurology India 66: 514–5
17. Redon S, Graillon N, Regis J et al. (2018) First bite syndrome after trigeminal radiosurgery: case report and pathophysiology. Headache 58: 1680–1
18. Wang AP, Suryavanshi T, Marcucci M et al. (2020) Radiation necrosis following stereotactic radiosurgery for trigeminal neuralgia. Canadian Journal of Neurological Sciences 47: 425–7
19. Peddada AV, Sceats DJ, White GA et al. (2011) CyberKnife radiosurgery for trigeminal neuralgia: unanticipated iatrogenic effect following successful treatment. Journal of Neurosurgery 115: 940–4

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	16/04/2021	Issue 4 of 12, April 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	16/04/2021	Issue 4 of 12, April 2021
International HTA database (INAHTA)	16/04/2021	-
MEDLINE (Ovid)	16/04/2021	1946 to April 15, 2021
MEDLINE In-Process (Ovid)	16/04/2021	1946 to April 15, 2021
MEDLINE Epubs ahead of print (Ovid)	16/04/2021	April 15, 2021
EMBASE (Ovid)	16/04/2021	1974 to 2021 April 15

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Literature search strategy

Number	Search term
1	exp Trigeminal Nerve Diseases/
2	Trigeminal Nerve/
3	((epileptiform? or trifacial or trigemin* or idiopathic) adj4 (neuralgia* or neuropath*)).tw.
4	(trigemin* adj4 nerv* adj4 (disease* or pals* or neuropath* or pressure* or compression or avulsion* or contusion* or injur* or trauma or transection* or disorder*)).tw.
5	(tic doulo?reux or prosopalgia or suicide disease* or Fothergill* disease*).tw
6	((v or vs or 5th or fifth* or five) adj2 cranial adj2 nerv*).tw.
7	Facial Neuralgia/
8	Facial Pain/
9	Fac* pain*.tw.
10	Fac* neuralgia*.tw.
11	or/1-10

12	exp Radiotherapy/
13	(radiosurger* or radiation* or radiotherap*).tw.
14	(stereotactic adj4 (radi* or therap* or surger*)).tw.
15	(cobalt radioisotope? or cobalt 60).tw.
16	((linear accelerator or LINAC) adj4 radi*).tw.
17	gamma knife.tw.
18	cyberknife.tw.
19	Truebeam.tw.
20	ZAP-X.tw.
21	Relivion.tw.
22	or/12-21
23	11 and 22
24	animals/ not humans/
25	23 not 24
26	limit 25 to english language

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Case series with fewer than 100 patients have been excluded.

Additional papers identified

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Alahmadi H, Zadeh G, Laperriere N et al. (2012) Trigeminal nerve integrated dose and pain outcome after gamma knife radiosurgery for trigeminal neuralgia. Journal of Radiosurgery and SBRT 1: 295–301	Case series n=145 FU=mean 24 months	33% of patients were pain free with no medications, and 33% were pain free maintained on medications. 19% of patients had significant reduction in their pain severity. 15% of patients did not have any significant pain reduction. 30% of patients developed facial numbness. Recurrence=35% Numbness after treatment was a predictor of good treatment response (odds ratio 2.72, CI 1.19 to 6.20, p=0.017). Higher integrated dose was a predictor of poor pain response to radiosurgery (odds ratio 0.73, CI 0.57 to 0.94, p=0.015). Longer pain duration before treatment was the only independent predictor of increased recurrence risk (HR 1.04, 95% CI 1.00 to 1.08; p=0.041).	Studies with more patients or longer follow up are included.
Alvarez-Pinzon AM, Wolf AL, Swedberg HN et al. (2017)	Non-randomised	Immediate pain relief occurred in 87% of patients who had balloon	Retrospective non-randomised

Comparison of percutaneous retrogasserian balloon compression and Gamma Knife radiosurgery for the treatment of trigeminal neuralgia in multiple sclerosis. World Neurosurgery 97: 590–4	comparative study n=202 FU=minimum 24 months	compression and in 23% of patients who had stereotactic radiosurgery. The 50% recurrence rate was at 12 months for the balloon compression group and 18 months for the radiosurgery group. Complication (excluding numbness) rates were 3% for radiosurgery and 21% for balloon compression (p=0.03).	comparative study.
Amutio Gutierrez S, Soto-Gonzalez M (2016) Effectiveness of gamma knife treatment in patients affected by idiopathic recurrent trigeminal neuralgia. Neurologia 31: 482–90	Review 16 articles	Only retrospective studies were identified. Gamma knife treatment is a non-invasive, safe, and effective technique for treating classic trigeminal neuralgia that is refractory to medication and surgery.	A more recent systematic review is included.
Barzaghi LR, Albano L, Scudieri C et al. (2020) Gamma Knife radiosurgery for trigeminal neuralgia: role of trigeminal length and pontotrigeminal angle on target definition and on clinical effects. World Neurosurgery 142: e140–50	Case series n=112	The pontotrigeminal angle and the shot-emergence distance should be considered during Gamma Knife radiosurgery planning: the first as a potential risk factor for hypaesthesia, and the second should not exceed 8 mm.	Studies with more patients or longer follow up are included.
Barzaghi LR, Albano L, Scudieri C et al. (2021) Factors affecting long-lasting pain relief after Gamma Knife radiosurgery for trigeminal neuralgia: a single institutional analysis and literature review. Neurosurgical Review	Case series n=112 FU=mean 61.5 months	Factors related to poor long-term pain relief were prescription dose <80 Gy (p=0.038), calibration dose rate <2.5 Gy/min (p=0.018), and distance between isocentre and trigeminal nerve emergence >8 mm (p<0.001).	Studies with more patients or longer follow up are included.
Baschnagel AM, Cartier JL, Dreyer J et	Case series	92% of patients had a BNI score 1 to 3 after	Studies with more patients

al. (2014) Trigeminal neuralgia pain relief after gamma knife stereotactic radiosurgery. Clinical Neurology and Neurosurgery 117: 107–11	n=149 FU=median 27 months	radiosurgery. Of those who had pain relief, 32% developed pain recurrence defined as a BNI score of 4 or 5. The actuarial rate of freedom from pain recurrence at 1, 2 and 3-years was 76%, 69% and 60%, respectively. The rate of pain relief of 27 patients who had a repeat procedure was 70% and 62% at 1 and 2 years, respectively. 25% of patients had new or worsening post-treatment numbness.	or longer follow up are included.
Bir SC, Ward T, Bollam P et al. (2015) First 1,000 cases of gamma knife surgery for various intracranial disorders in LSU Health-Shreveport: Radiological and Clinical Outcome. The Journal of the Louisiana State Medical Society 167: 54–65	Case series n=911 (169 trigeminal neuralgia)	The complete and partial relief of pain in patients with trigeminal neuralgia was 56% and 22% respectively.	Mixed indications.
Boling W, Song M, Shih W et al. (2019) Gamma knife radiosurgery for trigeminal neuralgia: A comparison of dose protocols. Brain Sciences 9: 134	Cohort study (comparing 2 doses) n=63	The 85 Gy dose provided a more durable pain relief compared to 80 Gy without a significantly elevated occurrence of facial sensory disturbance.	Studies with more patients or longer follow up are included.
Brisman R (2007) Microvascular decompression vs. gamma knife radiosurgery for typical trigeminal neuralgia: preliminary findings. Stereotactic and Functional	Non-randomised comparative study n=85	Complete pain relief (no pain no medicines) occurred at 12 and 18 months in 68 and 68% of patients treated with microvascular decompression and 58 and 24% with gamma knife radiosurgery (p=0.089), and 90% or greater pain	Studies with more patients or longer follow up are included.

Neurosurgery 85: 94–8		relief (with or without medicine) at 12 and 18 months in 90 and 78% with microvascular decompression and 75 and 48% with radiosurgery (p=0.171). There were no permanent complications.	
Brisman R (2004) Gamma knife surgery with a dose of 75 to 76.8 Gray for trigeminal neuralgia. Journal of Neurosurgery 100: 848–54	Case series n=293 FU=median 1.9 years	Gamma knife surgery is a safe and effective way to relieve trigeminal neuralgia. Patients who have between 75 and 89% pain relief are more likely to describe this outcome as good or excellent than those who have between 50 and 74% pain relief.	Studies with more patients or longer follow up are included.
Brisman R, Khandji AG, Mooij RBM (2002) Trigeminal nerve-blood vessel relationship as revealed by high-resolution magnetic resonance imaging and its effect on pain relief after Gamma Knife radiosurgery for trigeminal neuralgia. Neurosurgery 50: 1261–7	Case series n=179	In patients who have not had previous surgery for trigeminal neuralgia, blood vessel-cranial nerve V contact revealed by high-resolution magnetic resonance imaging may indicate a particularly favourable response to Gamma Knife radiosurgery.	Study focuses on effects of relationship between blood vessel and nerve.
Brisman R (2000) Gamma knife radiosurgery for primary management for trigeminal neuralgia. Journal of Neurosurgery 93: 159–61	Cohort study n=172 FU=6 to 12 months	Patients with trigeminal neuralgia who are treated with Gamma Knife radiosurgery as primary management have better pain relief than those treated with it as secondary management. Patients are more likely to have pain relief if they do not have MS.	Studies with more patients or longer follow up are included.
Chang C-S, Huang C-W, Chou H-H et al. (2018) Outcome of Gamma Knife radiosurgery for	Case series n=130 FU=4 to 14 years	Neurovascular compression did not affect pain outcome for trigeminal neuralgia patients who had gamma knife radiosurgery.	Study focuses on effect of neurovascular compression.

trigeminal neuralgia associated with neurovascular compression. Journal of Clinical Neuroscience 47: 174–7			
Chen C-J, Paisan G, Buell TJ et al. (2017) Stereotactic radiosurgery for type 1 versus type 2 trigeminal neuralgias. World Neurosurgery 108: 581–88	Cohort study n=112 FU=up to 48 months	Stereotactic radiosurgery offers similar rates of initial pain relief, pain score distribution, pain recurrence, and time to pain recurrence between patients with type 1 and type 2 trigeminal neuralgia. The time to initial pain relief was longer for patients with type 2 trigeminal neuralgia.	Studies with more patients or longer follow up are included.
Chung MH, Wang P-W, Wu Y-C et al. (2020) Unusual cerebral aneurysm after stereotactic radiosurgery to treat trigeminal neuralgia. Stereotactic and Functional Neurosurgery 2020	Case report n=1	**Cerebral aneurysm** The patient had stereotactic radiosurgery with 66 Gy for trigeminal neuralgia. During a 9-year follow-up exam, dizziness with a spinning sensation was reported and a right superior cerebellar thrombosed aneurysm was diagnosed. He had transarterial embolisation with coiling of the aneurysm and reported no subsequent complications.	Another case report of aneurysm is included.
Cohen J, Mousavi SH, Faraji AH et al. (2017) Stereotactic radiosurgery as initial surgical management for elderly patients with trigeminal neuralgia. Stereotactic and Functional Neurosurgery 95: 158–65	Case series n=127	Initial pain control was achieved in 91% of patients after 1 treatment. Complete pain relief (BNI score 1) developed in 75 patients (59%) and was maintained in 59, 39, and 22% of patients at 1, 3, and 5 years. After repeat treatment, the rate of complete pain relief was 79, 55, and 41% at 1, 3, and 5 years. The incidence of trigeminal sensory loss was 17% after initial	Studies with more patients or longer follow up are included.

		treatment but increased to 39% after repeat treatment.	
Conti A, Acker G, Pontoriero A et al. (2020) Factors affecting outcome in frameless non-isocentric stereotactic radiosurgery for trigeminal neuralgia: A multicentric cohort study. Radiation Oncology 15: 115	Case series n=262 FU=median 38 months	Pain control rate (BNI 1 to 3) at 6, 12, 24, 36, 48, and 60 months were 97, 91, 84, 81, 74, and 71%, respectively. Overall, 18% of patients developed sensory disturbances. Patients with volume ≥30 mm^3 were more likely to maintain pain relief (p=0.03), and low integral dose (<1.4 mJ) tended to be associated with more pain recurrence than intermediate (1.4 to 2.7 mJ) or high integral dose (>2.7 mJ). MS, integral dose, and mean dose were the factors associated with pain recurrence, while re-irradiation and MS were predictors for sensory disturbance in the multivariate analysis.	Studies with more patients or longer follow up are included.
Dai Z-F, Huang Q-L, Liu H-P et al. (2016) Efficacy of stereotactic gamma knife surgery and microvascular decompression in the treatment of primary trigeminal neuralgia: A retrospective study of 220 cases from a single center. Journal of Pain Research 9: 535–42	Non-randomised comparative study n=202 FU=2 years	Both Gamma Knife radiosurgery and microvascular decompression are safe and effective first-line and adjunctive treatment options for patients with trigeminal neuralgia. The clinical outcomes of pain relief and reduction of pain recurrence were better with microvascular decompression. For Gamma Knife radiosurgery, this study showed that the optimal radiation therapeutic dose range was 70 to 90 Gy, but brainstem radiation protection is recommended.	Studies with more patients or longer follow up are included.
Debono B, Lotterie J-A, Sol J-C et al.	Case series n=301	91% (273/301) of patients were initially pain free, and	Included in systematic

(2019) Dedicated linear accelerator radiosurgery for classic trigeminal neuralgia: a single-center experience with long-term follow-up. World Neurosurgery 121: e775–85	FU=mean 54.6 months	28 patients (9%) were unchanged. The actuarial probabilities of maintaining pain relief with or without medication (BNI 1 to 3a) at 0.5, 1, 2, 4, 5, and 10 years were 89%, 85%, 76%, 69%, 66%, and 48%, respectively. Hypaesthesia was present in 26% of patients (very bothersome, 0.3%). No anaesthesia dolorosa was reported. The actuarial probabilities of maintaining pain relief without further surgery at 0.5, 1, 2, 4, and 5 years were 99%, 98%, 96%, 91%, and 90%, respectively. Among all treated patients, 87% were satisfied by the procedure and would have stereotactic radiosurgery again.	review by Wilson et al. (2020).
Dhople AA, Adams JR, Maggio WW et al. (2009) Long-term outcomes of Gamma Knife radiosurgery for classic trigeminal neuralgia: implications of treatment and critical review of the literature. Clinical article. Journal of Neurosurgery 111: 351–8	Case series n=112 FU=median 5.6 years	After radiosurgery, 64% of patients reported a BNI score of 1, 5% had BNI 2, 12% had BNI 3, and 19% had a score of 4 or 5. The median time to response was 2 weeks (range 0 to 12 weeks) and the median response duration was 32 months (range 0 to 112 months). 81% of patients reported initial pain relief, and actuarial rates of freedom from treatment failure at 1, 3, 5, and 7 years were 60, 41, 34, and 22%, respectively. New bothersome facial numbness was reported in 6% of patients.	Studies with more patients or longer follow up are included.
Diana C, Kumar RD, Bodh R et al. (2021) Does the surgical	Systematic review	Microvascular decompression had a higher rate of initial pain-	All relevant studies are already

intervention for trigeminal neuralgia refractory to pharmacotherapy improve quality-of-life? - A systematic review. Journal of Oral and Maxillofacial surgery https://doi.org/10.1016/j.joms.2021.03.003	n=11,154 (10 studies)	free outcomes (97%) followed by Gamma knife radiosurgery (96%), cryotherapy (95%), percutaneous balloon compression (87%), percutaneous glycerol rhizotomy (85%) and the lowest rate of cohorts who were never pain-free (2%). Quality of life was improved to 100% as a result of pain relief which was evaluated in only 2 studies. Overall the recurrence rate was 0.45 to 52%.	included, either in the key evidence or appendix.
Elaimy AL, Lamm AF, Demakas JJ et al. (2013) Gamma knife radiosurgery for typical trigeminal neuralgia: An institutional review of 108 patients. Surgical Neurology International 4: 92	Case series n=108 FU=median 15 months	After the first Gamma Knife procedure, 71% of patients were grouped into BNI class 1 to 3b and the median duration of pain relief was 11.8 months. New facial numbness was reported in 19% of patients and new facial paraesthesias were reported in 7% of patients. 19 repeat procedures were done. After the second procedure, 73% of patients were grouped into BNI class 1 to 3b and the median duration of pain relief was 4.9 months. For repeat procedures, new facial numbness was reported in 22% of patients and new facial paraesthesias were reported in 6% of patients.	Studies with more patients or longer follow up are included.
Flickinger JC Jr, Kim H, Kano H et al. (2012) Do carbamazepine, gabapentin, or other anticonvulsants exert sufficient radioprotective effects	Case series n=200 FU=minimum 6 months	The use of carbamazepine or gabapentin at the time of radiosurgery does not decrease the rates of obtaining partial or complete pain relief after radiosurgery, but gabapentin may reduce the	Study focuses on effect of anti-convulsants on radiosurgery.

to alter responses from trigeminal neuralgia radiosurgery? International Journal of Radiation Oncology, Biology, Physics 83: e501–6		risks of developing post-radiosurgery trigeminal neuropathy.	
Flickinger JC, Pollock BE, Kondziolka D et al. (2001) Does increased nerve length within the treatment volume improve trigeminal neuralgia radiosurgery? A prospective double-blind, randomized study. International Journal of Radiation Oncology, Biology, Physics 51: 449–54	Randomised controlled trial (comparing 1 and 2 isocentres) n=87 FU=median 26 months	Increasing the treatment volume to include a longer nerve length for trigeminal neuralgia radiosurgery does not significantly improve pain relief but may increase complications.	Small trial comparing 1 and 2 isocentres.
Fountas KN, Smith JR, Lee GP et al. (2007) Gamma Knife stereotactic radiosurgical treatment of idiopathic trigeminal neuralgia: long-term outcome and complications. Neurosurgical Focus 23: e8	Case series n=106 FU=mean 34 months	The initial response rate in patients with no history of previous surgery was 93%; in those who had had previous surgery, the initial response rate was 86%. At 1-year follow up, an excellent outcome was achieved in 83% of patients who had not had previous surgery, and in 69% of those who had. The respective outcome rates for 2-year follow up were 78% and 64%, respectively. The most common complication was persistent paraesthesia (16%).	Studies with more patients or longer follow up are included.
Gagliardi F, Spina A, Bailo M et al. (2018) Effectiveness of gamma knife radiosurgery in	Case series n=166 FU=mean 64.7 months	Gamma knife radiosurgery statistically significantly improves quality of life and functional and psychosocial performance of patients	Studies with more patients or longer follow up are included.

improving psychophysical performance and patient's quality of life in idiopathic trigeminal neuralgia. World Neurosurgery 110: e776-85		with idiopathic trigeminal neuralgia. A trend was observed toward a more favourable outcome in patients with typical trigeminal neuralgia, compared with patients with atypical trigeminal neuralgia, without reaching a statistically significant distinction.	
Gorgulho A, Agazaryan N, Selch M et al. (2019) Immediate pain relief elicited after radiosurgery for classical and symptomatic trigeminal neuralgia. Cureus 11: e4777	Case series n=150 FU=48 hours	25 (20%) patients had immediate pain relief, defined as pain cessation within 48 hours of radiosurgery. Kaplan-Meier analysis showed that good or excellent pain outcomes were sustained and statistically significantly better in the immediate pain relief group (p=0.006) compared with those who did not have immediate relief.	Studies with more patients or longer follow up are included.
Hayashi M, Chernov M, Tamura Noriko et al. (2011) Stereotactic radiosurgery of essential trigeminal neuralgia using Leksell Gamma Knife model C with automatic positioning system: technical nuances and evaluation of outcome in 130 patients with at least 2 years follow-up after treatment. Neurosurgical Review 34: 497–508	Case series n=130 FU=minimum 2 years	Radiosurgery of essential trigeminal neuralgia results in a high rate of initial pain relief, but pain recurrences and associated complications are not uncommon. The outcome may be influenced by various technical nuances; therefore, treatment should be preferably done in specialised clinical centres with sufficient expertise in the management of this disorder.	Studies with more patients or longer follow up are included.
Hayashi M (2009) Trigeminal neuralgia. Progress in Neurological Surgery 22: 182–90	Case series n=150 FU=minimum 2 years	Initial pain reduction=97% (146/150); complete pain relief=77% (116/150). True recurrence=10% (15/146); delayed recurrence was detected at	Studies with more patients or longer follow up are included.

		6 to 9 (mean 8) months. Complications (hypaesthesia and dysaesthesia) = 28% (42/150)	
Helis CA, Lucas JT Jr, Bourland JD et al. (2015) Repeat radiosurgery for trigeminal neuralgia. Neurosurgery 77: 755–61	Case series n=125 FU=median 56.9 months	Repeat radiosurgery is an effective method of treating recurrent trigeminal neuralgia. Patients who have facial numbness after the first treatment and a positive pain response to the first treatment are more likely to respond well to the second treatment.	Study focuses on repeat treatment. Studies with more patients or longer follow up are included.
Henson CF, Goldman HW, Rosenwasser RH et al. (2005) Glycerol rhizotomy versus gamma knife radiosurgery for the treatment of trigeminal neuralgia: an analysis of patients treated at one institution. International Journal of Radiation Oncology, Biology, Physics 63: 82–90	Non-randomised comparative study n=188 (99 were evaluated) FU=median 29 months (for radiosurgery)	Despite greater facial numbness morbidity and a higher failure rate, glycerol rhizotomy provided more immediate pain relief than gamma knife. Glycerol rhizotomy should be considered in patients with disabling trigeminal pain who need urgent pain relief. For all other patients, gamma knife provides better long-term pain relief with less treatment-related morbidity and should be considered the preferred treatment for patients with medically refractory trigeminal neuralgia for whom microvascular nerve decompression is not suitable.	Retrospective non-randomised comparison of glycerol rhizotomy and radiosurgery.
Hitchon PW, Holland M, Noeller J et al. (2016) Options in treating trigeminal neuralgia: Experience with 195 patients. Clinical Neurology and Neurosurgery 149: 166–70	Non-randomised comparative study n=195 FU=32 months	Microvascular decompression is the treatment least likely to fail or need additional treatment. The highest rate of recurrence was in patients who had radiofrequency (64%). Facial numbness was least likely to occur with microvascular	Studies with more patients or longer follow up are included.

		decompression (16%) compared radiofrequency and stereotactic radiosurgery (50% and 36% respectively).	
Hung Y-C, Lee C-C, Liu K-D et al. (2014) Radiosurgery target location and individual anatomical variation in trigeminal nerves. Journal of Neurosurgery 121: 203–9	Case series n=106	The rate of pain relief did not differ according to anatomical nerve variations. However, the frequency of facial hypaesthesia was higher among patients in whom the nerve was longer (>11 mm) or the targeting ratio was lower (<36%).	The study focuses on anatomical variations and target locations.
Inoue T, Hirai H, Shima A et al. (2017) Long-term outcomes of microvascular decompression and Gamma Knife surgery for trigeminal neuralgia: a retrospective comparison study. Acta Neurochirurgica 159: 2127–35	Case series n=231 FU=minimum 1 year	BNI pain intensity and facial numbness scores at the final visit were statistically significantly lower in the microvascular decompression group than in the radiosurgery group (p<0.001, p=0.04, respectively). Following treatment, there were initially high rates of pain-free status without medication: 97% in the microvascular decompression group and 96% in the GKS group. However, 6% and 52%, respectively fell into a "with medication" state within median periods of 1.83 and 3.92 years, respectively (p<0.001).	Studies with more patients or longer follow up are included.
Kanner AA, Neyman G, Suh JH et al. (2004) Gamma knife radiosurgery for trigeminal neuralgia: comparing the use of a 4-mm versus concentric 4- and 8 mm collimators. Stereotactic and Functional	Non-randomised comparative study n=101	The use of a combined concentric 4- and 8-mm collimator treatment for medically refractory TN at a maximum dose of 75 Gy does not improve outcome as compared with a single 4-mm collimator with an equivalent maximum dose.	Study focuses on the use of combined collimators.

Neurosurgery 82: 49–57			
Kano H, Kondziolka D, Yang H-C et al. (2010) Outcome predictors after gamma knife radiosurgery for recurrent trigeminal neuralgia. Neurosurgery 67: 1637–45	Case series n=193	After gamma knife radiosurgery, 85% of patients had pain relief or improvement (BNI 1 to 3b). Pain recurred in 43% (73/168) of patients after 6 to 144 months (median 6 years). Factors associated with better long-term pain relief included no relief from the surgical procedure preceding radiosurgery, pain in a single branch, typical trigeminal neuralgia, and a single previous failed surgical procedure. 18 (9%) patients developed new or increased trigeminal sensory dysfunction, and 1 developed deafferentation pain. Patients who developed sensory loss had better long-term pain control (BNI 1 to 3b: 86% at 5 years).	Study focuses on patients with trigeminal neuralgia that recurred after surgery. Studies with more patients or longer follow up are included.
Kikuchi J, Takeuchi Y, Sugi K et al. (2019) Gamma knife surgery-induced aneurysm rupture associated with tissue plasminogen activator injection: A case report and literature review. Surgical Neurology International 10: 150	Case report n=1	**Gamma knife surgery-induced aneurysm rupture associated with tissue plasminogen activator injection** 18 years after Gamma Knife surgery for trigeminal neuralgia, the patient had middle cerebral artery occlusion with consciousness disturbance and right hemiparesis. She had an injection of tissue plasminogen activator and mechanical thrombectomy. A CT scan revealed subarachnoid haemorrhage with a haematoma in the left cerebellar hemisphere. Cerebral angiography revealed a small irregular-	Another case report of aneurysm rupture is included.

		shaped aneurysm at the branching site of the left circumflex branch at the distal position of the anterior inferior cerebellar artery, which was not detected on initial imaging. Coil embolisation was done. She was transferred to a rehabilitation hospital 1 month later, with a modified Rankin Scale score of 5.	
Kim YH, Kim DG, Kim JW et al. (2010) Is it effective to raise the irradiation dose from 80 to 85 Gy in gamma knife radiosurgery for trigeminal neuralgia? Stereotactic and Functional Neurosurgery 88: 169–76	Case series n=104 FU=3 years	Actuarial rates of a favourable pain control outcome at 1 and 3 years were 75% and 61% for 80 Gy and 66% and 60% for 85 Gy. Facial sensory loss developed in 21%. Time to maximal pain relief was shorter in the 85 Gy group. Protracted morbidity before radiosurgery was a favourable prognostic factor of pain control in a multivariate analysis.	Study focuses on different doses. Studies with more patients or longer follow up are included.
Kondziolka D, Zorro O, Lobato-Polo J et al. (2010) Gamma Knife stereotactic radiosurgery for idiopathic trigeminal neuralgia. Journal of Neurosurgery 112: 758–65	Case series n=503 FU=median 2 years	89% of patients had initial pain relief that was adequate or better, with or without medications (BNI Scores 1 to 3b). Significant pain relief (BNI Scores 1 to 3a) was achieved in 73% at 1 year, 65% at 2 years, and 41% at 5 years. A BNI score of 1 to 3b was found in 80% at 1 year, 71% at 3 years, 46% at 5 years, and 30% at 10 years. 10.5% (53/503) of patients had new or increased subjective facial paraesthesias or numbness and 1 had deafferentation pain; these symptoms resolved in 17 patients. Those who developed sensory loss had better	Included in the systematic review by Tuleasca et al. (2019).

		long-term pain control (78% at 5 years).	
Kondziolka D, Perez B, Flickinger JC et al. (1998) Gamma knife radiosurgery for trigeminal neuralgia: results and expectations. Archives of Neurology 55: 1524–29	Case series n=106 FU=median 18 months	Gamma Knife radiosurgery is associated with a low risk of facial paraesthesias, an approximate 80% rate of significant pain relief, and a low recurrence rate in patients who initially attain complete relief.	Study is included in systematic review by Tuleasca et al. (2019)
Lee C-C, Chen C-J, Chong ST et al. (2018) Early stereotactic radiosurgery for medically refractory trigeminal neuralgia. World Neurosurgery 112: e569–75	Case series n=108 FU=median 17 months	Gamma knife radiosurgery achieves a high rate of pain relief among patients with medically refractory idiopathic trigeminal neuralgia. Pain history of 5 years or less is a reliable predictor of pain relief and appears to be associated with shorter latency to pain relief.	Studies with more patients or longer follow up are included.
Lee JYK, Sandhu S, Miller D et al. (2015) Higher dose rate Gamma Knife radiosurgery may provide earlier and longer-lasting pain relief for patients with trigeminal neuralgia. Journal of Neurosurgery 123: 961–8	Case series n=133 FU=mean 1.3 months	Radiosurgery with a higher dose rate results in more pain relief at the early follow-up evaluation, and it may result in a lower recurrence rate at later follow-up.	Studies with more patients or longer follow up are included.
Li L, Seaman SC, Bathla G et al. (2020) Microvascular decompression versus stereotactic radiosurgery for trigeminal neuralgia: a single-institution experience. World Neurosurgery 143: e400–8	Non-randomised comparative study n=214	Factoring in patients' age and gender, both microvascular decompression and stereotactic radiosurgery can achieve a favourable outcome for medically refractory trigeminal neuralgia, although BNI scores of 4 and 5 were more common with radiosurgery.	Studies with more patients or longer follow up are included.

Li, P; Wang, W et al. (2013) A preliminary result of the prospective control study of gamma knife radiosurgery for trigeminal neuralgia with one or two isocenters. Stereotactic and Functional Neurosurgery 91: 55	Randomised controlled trial n=54 FU=mean 26.6 months	There is not enough evidence for the benefit with two isocentres based on the initial result of this study. A central radiation dose of 90 Gy might increase the risk of radiation induced brain injury. More cases and longer follow-up are needed.	Small randomised controlled trial comparing 1 and 2 isocentres.
Li P, Wang W, Liu Y et al. (2012) Clinical outcomes of 114 patients who underwent gamma-knife radiosurgery for medically refractory idiopathic trigeminal neuralgia. Journal of Clinical Neuroscience 19: 71–4	Case series n=114 FU=mean 29.6 months	Gamma Knife radiosurgery treatment for medically refractory idiopathic trigeminal neuralgia with 2 isocentres resulted in an initial pain improvement in 96% of patients. The early response to the treatment might suggest a good outcome but, given the high incidence of nerve deficits, Gamma Knife surgery for trigeminal neuralgia with 2 isocentres is not recommended as a routine treatment protocol.	Study focuses on the effect of treating 2 isocentres.
Linskey ME, Ratanatharathorn V, Penagaricano J (2008) A prospective cohort study of microvascular decompression and Gamma Knife surgery in patients with trigeminal neuralgia. Journal of Neurosurgery 109:160–72	Cohort study n=80 FU=mean 3.4 years	In this non-randomised prospective cohort trial of selected patients with potentially relevant intergroup differences, microvascular decompression was significantly superior to Gamma Knife surgery in achieving and maintaining a pain-free status in those with trigeminal neuralgia and provided similar early and superior longer-term patient satisfaction rates. The complications of wound cerebrospinal fluid leakage, hearing loss, and persistent diplopia were only seen after	Studies with more patients or longer follow up are included.

		microvascular decompression.	
Little AS, Shetter AG, Shetter ME et al. (2008) Long-term pain response and quality of life in patients with typical trigeminal neuralgia treated with gamma knife stereotactic radiosurgery. Neurosurgery 63: 915–24	Case series n=185 FU=minimum 4 years	Gamma Knife radiosurgery is a reasonable long-term treatment option for patients with typical trigeminal neuralgia. It yields durable pain control in most patients, as well as improved quality of life with limited complications and it does not significantly affect the efficacy of other surgical treatments, should they be needed.	Studies with more patients or longer follow up are included.
Longhi M, Rizzo P, Nicolato A et al. (2007) Gamma knife radiosurgery for trigeminal neuralgia: results and potentially predictive parameters--part I: Idiopathic trigeminal neuralgia. Neurosurgery 61: 1254–61	Case series n=160 FU=mean 37.4 months	Gamma knife radiosurgery represents a reliable second-line therapeutic approach for trigeminal neuralgia after pharmacological failure. Favourable prognostic factors include "primary gamma knife radiosurgery" and maximal dose between 80 and 90 Gy.	Included in the systematic review by Tuleasca et al. (2019).
Lopez BC, Hamlyn PJ, Zakrzewska JM (2004) Stereotactic radiosurgery for primary trigeminal neuralgia: state of the evidence and recommendations for future reports. Journal of Neurology, Neurosurgery, and Psychiatry 75: 1019–24	Systematic review 38 studies	Outcomes after stereotactic radiosurgery appear in line with other ablative techniques. Results are better when it is used as primary treatment in patients with typical symptoms. Current data are largely observational and the quality is generally poor. This technique should be evaluated in a randomised, controlled trial with universal outcome measures, actuarial methodology, and validated measures of patient satisfaction and quality of life.	More recent systematic reviews are included.
Lopez BC, Hamlyn PJ, Zakrzewska JM (2004) Systematic	Systematic review	In mixed series, radiofrequency thermocoagulation offered	More recent systematic

review of ablative neurosurgical techniques for the treatment of trigeminal neuralgia. Neurosurgery 54: 973–83	175 studies (9 used for pain outcomes and 22 for adverse events)	higher rates of complete pain relief, compared with glycerol rhizolysis and stereotactic radiosurgery, although it demonstrated the greatest number of complications.	reviews are included.
Lu VM, Duvall JB, Phan K et al. (2018) First treatment and retreatment of medically refractive trigeminal neuralgia by stereotactic radiosurgery versus microvascular decompression: a systematic review and Meta-analysis. British Journal of Neurosurgery 32: 355–64	Systematic review n=1,353 (13 studies)	Both stereotactic radiosurgery and microvascular decompression alleviate pain in medically refractive trigeminal neuralgia patients. Microvascular decompression had superior rates of short- and long-term pain relief, facial numbness and dysaesthesia control, and less recurrence amongst those in whom pain freedom was achieved, at the cost of greater postoperative complications when compared to stereotactic radiosurgery.	A similar systematic review with a more recent search is included.
Lucas JT Jr, Nida AM, Isom S et al. (2014) Predictive nomogram for the durability of pain relief from gamma knife radiation surgery in the treatment of trigeminal neuralgia. International Journal of Radiation Oncology, Biology, Physics 89: 120–6	Case series n=446 FU=median 21.2 months	Rates of freedom from BNI 4-5 failure at 1, 3, and 5 years were 85%, 70%, and 47%, respectively. Pain relief (BNI 1 to 3) at 1, 3, and 5 years was 86%, 74%, and 51% in patients with type 1 trigeminal neuralgia, 79%, 46%, and 29% in patients with type 2 trigeminal neuralgia; and 63%, 50%, and 25% in patients with atypical facial pain. 42% of patients developed post-Gamma Knife radiation surgery trigeminal dysfunction.	Included in systematic reviews by Tuleasca et al. (2019) and Gubian et al. (2017).
Lucas JT Jr, Huang AJ, Bourland JD et al. (2016) Predictors of trigeminal nerve	Case series n=446 FU=median 25 months (for	Trigeminal nerve dysfunction was observed in 45% of patients and was similar across facial pain	The same patients are included in a study that is

dysfunction following stereotactic radiosurgery for trigeminal neuralgia. Journal of Radiosurgery and SBRT 4: 117–23	patients with trigeminal nerve dysfunction)	types. It was associated with prolonged time to pain relapse. Multivariate analysis identified sharp pain at diagnosis (odds ratio 0.59; 95% CI 0.38 to 0.91), and dorsal root entry zone maximum dose (odds ratio 1.02; 95% CI 1.00 to 1.04) as predictors of trigeminal nerve dysfunction.	in the systematic reviews by Tuleasca et al. (2019) and Gubian et al. (2017).
Maesawa S, Salame C, Flickinger JC, et al. (2001) Clinical outcomes after stereotactic radiosurgery for idiopathic trigeminal neuralgia. Journal of Neurosurgery 94:14–20	Case series n=220 FU=median 2 years	135 patients (61%) had previously had surgery and 80 (36%) had some degree of sensory disturbance related to the earlier surgery. Complete or partial relief was achieved in 86% of patients at 1 year. Complete pain relief was achieved in 65% of patients at 6 months, 70% at 1 year, and 75% at 33 months. Patients with an atypical pain component had a lower rate of pain relief (p=0.025). Because of recurrences, only 56% of patients had complete or partial pain relief at 5 years. The absence of preoperative sensory disturbance (p=0.02) or previous surgery (p=0.01) correlated with an increased proportion of patients who experienced complete or partial pain relief over time. 30 patients (14%) reported pain recurrence 2 to 58 months after initial relief (median 15.4 months). 17 patients (10% at 2 years) developed new or increased subjective facial paraesthesia or numbness,	Studies with more patients or longer follow up are included. Study is included in systematic review by Tuleasca et al. (2019).

		including 1 who developed deafferentation pain.	
Maher CO, Pollock BE (2000) Radiation induced vascular injury after stereotactic radiosurgery for trigeminal neuralgia: case report. Surgical Neurology 54: 189–93	Case report n=1	**Focal atheromatous disease** A 69 year old man with trigeminal neuralgia had stereotactic radiosurgery after a failed balloon compression procedure. The radiosurgery also failed to provide the patient with any significant pain relief, and microvascular decompression of the trigeminal nerve was done 10 months later. At operation, 2 adjacent veins and the superior cerebellar artery had focal changes consistent with atheromatous disease.	Case report of an adverse event that is already described.
Marshall K, Chan MD, McCoy TP et al. (2012) Predictive variables for the successful treatment of trigeminal neuralgia with gamma knife radiosurgery. Neurosurgery 70: 566–73	Case series n=448 FU=median 20.9 months	At 3 months, 86% of patients had BNI pain scores 1 to 3, and 43% had a score of 1. 26% of patients reported post-treatment facial numbness; 28% of patients had a repeat procedure for relapsed pain, and median time to next procedure was 4.4 years. Multivariate analysis revealed that the development of postsurgical numbness (odds ratio 2.76; p=0.006) was the dominant factor predictive of efficacy.	Included in the systematic review by Tuleasca et al. (2019).
Martinez Moreno NE, Gutierrez-Sarraga J, Rey-Portoles G et al. (2016) Long-term outcomes in the treatment of classical trigeminal neuralgia by gamma knife radiosurgery: a retrospective study in	Case series n=117 FU=mean 66 months	Complete response at last follow-up was 81%, with an excellent response while off medication in 52%. Pain-free rates without medication were 85% at 3 years (CI 78% to 94%, 81% at 5 years (CI 72% to 91%), and 76% at 7 years (CI 65% to 90%). Complete	Studies with more patients or longer follow up are included.

patients with minimum 2-year follow-up. Neurosurgery 79: 879–88		response rates were 91% at 3 years (CI 86% to 97%), 86% at 5 years (CI 79% to 93%), and 82% at 7 years (CI 72% to 93%). New or worsening facial numbness was reported in 32.5% (30% score 2 and 2.5% score 3). No anaesthesia dolorosa was reported. Permanent recurrence pain rate was 12%.	
Massager N, Murata N, Tamura M et al. (2007) Influence of nerve radiation dose in the incidence of trigeminal dysfunction after trigeminal neuralgia radiosurgery. Neurosurgery 60: 681–8	Case series n=358	Using a similar target, the incidence of trigeminal dysfunction and the pain relief rate can vary according to the radiation energy received by the retrogasserian part of the trigeminal nerve root. The prescription dose and the use of beam channel blocking modify the integrated dose delivered to the nerve and may contribute to the different rates of trigeminal numbness and pain outcome. The radiobiological effect of gamma knife radiosurgery may be related to the energy delivered to nerve root volume, rather than to the maximal dose delivered.	Study compares different dosimetric strategies at 2 different centres.
Massager N, Nissim O, Murata N et al. (2006) Effect of beam channel plugging on the outcome of gamma knife radiosurgery for trigeminal neuralgia. International Journal of Radiation Oncology, Biology, Physics 65: 1200–5	Case series n=109	The use of plugs to protect the brainstem during gamma knife radiosurgery treatment for trigeminal neuralgia increases the dose of irradiation delivered to the intracisternal trigeminal nerve root and is associated with an important increase in the incidence of trigeminal nerve dysfunction.	Study focuses on the effect of using plugs for brainstem protection.

Matsuda S, Nagano O, Serizawa T et al. (2010) Trigeminal nerve dysfunction after Gamma Knife surgery for trigeminal neuralgia: a detailed analysis. Journal of Neurosurgery 113: 184–90	Case series n=104 FU=median 37 months	At the final clinical visit, 68% of patients were still pain-free. The incidence of trigeminal nerve dysfunction was 49%. The severity of the dysfunction improved in one-third of the affected patients, at long-term follow-up.	Included in systematic review by Gubian et al. (2017).
Matsuda S, Serizawa T, Nagano O et al. (2008) Comparison of the results of 2 targeting methods in Gamma Knife surgery for trigeminal neuralgia. Journal of Neurosurgery 109: 185–89	Case series n=100 FU=median 30 months	The posterior targeting group had better pain control and a lower complication rate. The authors recommend the posterior targeting method and use of 80 Gy for treatment of trigeminal neuralgia with Gamma Knife surgery.	Studies with more patients or longer follow up are included.
Mendelson ZS, Velagala JR, Kohli G et al. (2018) Pain-free outcomes and durability of surgical intervention for trigeminal neuralgia: a comparison of gamma knife and microvascular decompression. World Neurosurgery 112: e732–46	Systematic review n=5,496 (43 studies)	Microvascular decompression may be a more effective intervention than gamma knife surgery owing to higher rates of initial pain-free outcomes and long-term pain-free outcomes. There is a need for more consistent data reporting of outcomes for treatment of trigeminal neuralgia.	A similar review with a more recent search period is included.
Mohammad-Mohammadi A, Recinos PF, Lee JH et al. (2013) Surgical outcomes of trigeminal neuralgia in patients with multiple sclerosis. Neurosurgery 73: 941–50	Non-randomised comparative study n=96 FU=median 5.7 years	Recurrence rate=66% As an initial procedure, balloon compression had the highest initial pain-free response (95%; p=0.006) and median pain-free interval (28 months; p=0.05), followed by percutaneous retrogasserian glycerol rhizotomy.	Studies with more patients or longer follow up are included.

Montano N, Papacci F, Cioni B et al. (2013) What is the best treatment of drug-resistant trigeminal neuralgia in patients affected by multiple sclerosis? A literature analysis of surgical procedures. Clinical Neurology and Neurosurgery 115: 567–72	Review	There were no statistically significant differences in the short-term results among different procedures for trigeminal neuralgia in MS patients. Each technique has advantages and limitations in terms of long-term pain, recurrence rate and complication rate. Each patient should be informed on pros and cons of each procedure to be involved in the most appropriate choice.	More recent studies are included.
Mousavi SH, Niranjan A, Akpinar B et al. (2018) A proposed plan for personalized radiosurgery in patients with trigeminal neuralgia. Journal of Neurosurgery 128: 452–59	Case series n=155 FU=median 71 months	With current dose selection methods, nerve volume affects long-term clinical outcomes in patients with trigeminal neuralgia who have had stereotactic radiosurgery. This study suggests that the prescribed radiosurgery dose should be customised for each patient based on the nerve volume.	Studies with more patients or longer follow up are included.
Mousavi SH, Niranjan A, Huang MJ et al. (2015) Early radiosurgery provides superior pain relief for trigeminal neuralgia patients. Neurology 85: 2159–65	Case series n=121 FU=median 36 months	Pain relief (BNI score 1 to 3a) was achieved in 107 (88%) patients at a median time of 1 month. Patients who had earlier radiosurgery (within 3 years of pain onset) had a shorter interval until pain relief (1 week, p<0.001), had a longer interval of pain relief off medication (p<0.001), and had a longer duration of adequate pain control (p<0.001). Median pain-free intervals for patients who had radiosurgery at 1, 2, 3, and more than 3 years after trigeminal neuralgia diagnosis were 68, 37, 36, and 10 months, respectively. Patients who	Studies with more patients or longer follow up are included.

		responded within the first 3 weeks had a longer duration of complete pain relief compared to those with longer response times (p=0.001). 15 (12%) patients reported new sensory dysfunction after radiosurgery.	
Mureb M, Golub D, Benjamin C et al. (2020) Earlier radiosurgery leads to better pain relief and less medication usage for trigeminal neuralgia patients: an international multicenter study. Journal of Neurosurgery 1–8	Case series n=404 FU=mean 32 months	Patients with trigeminal neuralgia who had stereotactic radiosurgery within 4 years of diagnosis experienced a shorter interval to pain relief with low risk. There were significant decreases in adjunct medication usage. Radiosurgery should be considered earlier in the course of treatment for trigeminal neuralgia.	Studies with more patients or longer follow up are included.
Niranjan A, Lunsford L D et al. (2016) Radiosurgery for the management of refractory trigeminal neuralgia. Neurology India 64: 624–9	Case series n=503 FU=1 year	89% (449/503) of patients had initial pain relief at a median latency of 1 month. At 1 year, 73% patients were pain free (with or without medications) and 80% had pain control. Repeat radiosurgery was done for 193 patients (43%). At 1 year, 26% of these patients were completely pain free and 78% were pain free with or without medications.	Studies with longer follow up are included.
Oh IH, Choi SK, Park BJ et al. (2008) The treatment outcome of elderly patients with idiopathic trigeminal neuralgia: Micro-vascular decompression versus Gamma knife radiosurgery. Journal of Korean	Non-randomised comparative study n=45 FU=mean 33 months (for radiosurgery)	For trigeminal neuralgia patients with advanced age, microvascular decompression showed advantages in immediately relieving the pain. However, Gamma Knife radiosurgery was preferable overall, despite the delayed pain relief, because of the lower rate	Small study that focuses on elderly patients. Study is included in systematic review by Gubian et al., 2017.

Neurosurgical Society 44: 199–204		of surgical complications that arise.	
Pagni CA, Fariselli L, Zeme S (2008) Trigeminal neuralgia. Non-invasive techniques versus microvascular decompression. It is really available any further improvement? Acta Neurochirurgica. Supplement 101: 27–33	Non-randomised comparative study n=847 (46 radiosurgery) FU=1 to 32 years	Microvascular decompression gives the best results in term of long-term pain relief without collateral effects in drug-resistant trigeminal neuralgia. Percutaneous techniques are indicated in patients either without neurovascular conflict or with excessive surgical risk. Stereotactic radiosurgery and cyberknife radiosurgery might be considered an improvement of percutaneous and surgical techniques, but the rate of complete pain relief at long term is lower. In spite of the risks it entails, microvascular decompression remains the choice treatment for typical trigeminal neuralgia.	More recent studies are included.
Park HH, Kim WH, Jung H-H et al. (2020) Radiosurgery vs. microsurgery for newly diagnosed, small petroclival meningiomas with trigeminal neuralgia. Neurosurgical Review 43: 1631–40	Non-randomised comparative study n=70 FU=mean 50.5 months	Microsurgery could be more effective than Gamma Knife surgery in providing prompt, medication-free pain relief from trigeminal neuralgia for small petroclival meningiomas.	Studies with more patients or longer follow up are included.
Park K-J, Kondziolka D, Berkowitz O et al. (2012) Repeat gamma knife radiosurgery for trigeminal neuralgia. Neurosurgery 70: 295–305	Case series n=119 FU=median 48 months	Repeat gamma knife radiosurgery provides a similar rate of pain relief as the first procedure. The best responses were observed in patients who had good pain control after the first procedure and those who developed new sensory dysfunction in the	Studies with more patients or longer follow up are included.

		affected trigeminal distribution.	
Patra DP, Savardekar AR, Dossani RH et al. (2019) Repeat Gamma Knife radiosurgery versus microvascular decompression following failure of GKRS in trigeminal neuralgia: A systematic review and meta-analysis. Journal of Neurosurgery 131: 1197–206	Systematic review and meta-analysis n=787 (22 studies)	Repeat Gamma Knife radiosurgery and microvascular decompression are both valid treatment options for patients after failure of prior Gamma Knife radiosurgery. The current meta-analysis failed to identify any superiority of 1 treatment over the other, showing comparable outcomes in terms of adequate pain relief, postoperative facial numbness, and retreatment rates. However, microvascular decompression provided a better chance of complete pain relief than repeat Gamma Knife radiosurgery.	Review focuses on treatment of recurrent trigeminal neuralgia.
Peciu-Florianu I, Regis J, Levivier M et al. (2020) Trigeminal neuralgia secondary to meningiomas and vestibular schwannoma is improved after stereotactic radiosurgery: A systematic review and meta-analysis. Stereotactic and Functional Neurosurgery 99: 6–16	Systematic review and meta-analysis 13 studies	Pain relief: BNI score 1 was reported in 51% (range 36 to 65%) of patients and BNI score 1 to 3b in 84% (range 78 to 90%). There was no significant difference in series discussing outcomes for tumour targeting versus tumour and nerve targeting. There was heterogeneity among reports and targeting approaches.	Most studies targeted treatment at the tumour rather than the nerve.
Petit JH, Herman JM, Nagda S et al. (2003) Radiosurgical treatment of trigeminal neuralgia: evaluating quality of life and treatment outcomes. International Journal of Radiation	Case series n=112 FU=median 30 months	Gamma Knife radiosurgery provides significant pain relief and improves quality of life in the majority of patients treated for trigeminal neuralgia, with few bothersome side effects. Patients with both temporary and sustained	Studies with more patients or longer follow up are included.

Oncology, Biology, Physics 56: 1147–53		responses to treatment had improved quality of life and considered their treatment successful.	
Pollock BE, Schoeberl KA (2010) Prospective comparison of posterior fossa exploration and stereotactic radiosurgery dorsal root entry zone target as primary surgery for patients with idiopathic trigeminal neuralgia. Neurosurgery 67: 633–9	Non-randomised comparative study n=140 FU=median 38 months	Patients who had posterior fossa exploration more commonly were pain free off medications (84% at 1 year, 77% at 4 years) compared with those who had stereotactic radiosurgery (66% at 1 year, 56% at 4 years; hazard ratio = 2.5; 95% CI 1.4 to 4.6; p=0.003). Additional surgery for persistent or recurrent face pain was done in 15% of patients after posterior fossa exploration compared with 35% of patients after stereotactic radiosurgery (p=0.009). Non-bothersome facial numbness was more common in the radiosurgery group (33% compared with 18%; p=0.04). Other complications after posterior fossa exploration were dysaesthetic facial pain, n=3; cerebrospinal fluid leakage, n=3; hearing loss, n=2; wound infection, n=1; pneumonia, n=1; deep vein thrombosis, n=1). Dysaesthetic facial pain was reported in 4 patients after radiosurgery.	Studies with more patients or longer follow up are included.
Pollock BE (2005) Comparison of posterior fossa exploration and stereotactic radiosurgery in patients with previously nonsurgically treated	Non-randomised comparative study n=83 FU=mean 25.5 months	The results support posterior fossa exploration as a more effective primary surgery than stereotactic radiosurgery in patients with idiopathic trigeminal neuralgia. Moreover, injury to the trigeminal nerve during posterior fossa	Studies with more patients or longer follow up are included.

idiopathic trigeminal neuralgia. Neurosurgical Focus 18: e6		exploration is not required to achieve excellent facial pain outcomes.	
Pollock BE, Phuong LK, Gorman DA et al. (2002) Stereotactic radiosurgery for idiopathic trigeminal neuralgia. Journal of Neurosurgery 97: 347–53	Case series n=117 FU=median 26 months	The actuarial rate of achieving and maintaining an excellent outcome was 57% and 55% at 1 and 3 years, respectively, after radiosurgery. New persistent trigeminal dysfunction was noted in 43 patients (37%). Tolerable numbness or paraesthesias occurred in 29 patients (25%), whereas bothersome dysaesthesias developed in 14 patients (12%). Only a radiation dose of 90 Gy correlated with new trigeminal deficits or dysaesthesias.	Studies with more patients or longer follow up are included.
Rahman M, Neal D, Baruch W et al. (2014) The risk of malignancy anywhere in the body after linear accelerator (LINAC) stereotactic radiosurgery. Stereotactic and Functional Neurosurgery 92: 323–33	Cohort study n=627 (meningiomas, intracranial schwannomas, arteriovenous malformations, trigeminal neuralgia, pituitary adenomas, cavernous angiomas)	In a large population of stereotactic radiosurgery-treated patients, there was no increased risk of malignancy compared to the general population.	Mixed indications.
Raygor KP, Lee AT, Nichols N et al. (2020) Long-term pain outcomes in elderly patients with trigeminal neuralgia: comparison of first-time microvascular decompression and stereotactic radiosurgery. Neurosurgical Focus 49: e23	Non-randomised comparative study n=193 FU=minimum 1 year	Patients who had microvascular decompression had a statistically significantly longer duration of pain freedom than those who had microvascular decompression with partial sensory rhizotomy or stereotactic radiosurgery as their first procedure. Fewer adverse events were seen after radiosurgery. Overall,	Studies with more patients or longer follow up were included.

		the results suggest that both treatments are effective options for the elderly, despite their advanced age.	
Regis J, Tuleasca C, Resseguier N et al. (2016) The very long-term outcome of radiosurgery for classical trigeminal neuralgia. Stereotactic and Functional Neurosurgery 94: 24–32	Case series n=130 FU=median 9.9 years	94% (122/130) of patients became pain free (median delay 15 days) after the radiosurgery procedure (BNI class 1 to 3a). The probability of remaining pain free without medication at 3, 5, 7 and 10 years was 78, 74, 68 and 52%, respectively. 56 patients (46%) who were initially pain free had recurrent pain (median delay 73 months). At 10 years of the initial 130 patients, 68% were free of any recurrence needing new surgery. The new hypaesthesia rate was 21% (median delay of onset 12 months), and 1 patient reported very bothersome hypaesthesia.	Studies with more patients are included.
Regis J, Tuleasca C, Resseguier N et al. (2016) Long-term safety and efficacy of Gamma Knife surgery in classical trigeminal neuralgia: a 497-patient historical cohort study. Journal of Neurosurgery 124: 1079–87	Case series n=497 FU=median 43.8 months	92% (456/497) of patients were initially pain free in a median time of 10 days (range 1 to 180 days). Their actuarial probabilities of remaining pain free without medication at 3, 5, 7, and 10 years were 72%, 65%, 60%, and 45%, respectively. 157 patients (34%) who were initially pain free had at least 1 recurrence, with a median delay of onset of 24 months (range 0.6 to 150.1 months). The actuarial rate of maintaining pain relief without further surgery was 68% at 10 years. The hypaesthesia actuarial rate	Included in systematic review by Tuleasca et al. (2019).

		at 5 years was 20% and at 7 years reached 21% but remained stable until 14 years with a median delay of onset of 12 months (range 1 to 65 months). Very bothersome facial hypesthesia was reported in 3 patients (0.6%).	
Regis J, Metellus P, Hayashi M et al. (2006) Prospective controlled trial of gamma knife surgery for essential trigeminal neuralgia. Journal of Neurosurgery 104: 913–24	Case series (prospective) n=100 FU=minimum 12 months	At the last visit 83% of patients were reported to be pain free. 58 of these 83 patients had stopped taking medication during the study. All quality-of-life parameters were improved (p<0.001). 6 patients reported facial paraesthesia, and 4 reported hypaesthesia. These symptoms were classified as mild.	Included in systematic reviews by Tuleasca et al. (2019) and Gubian et al. (2017).
Romanelli P, Conti A, Bianchi L et al. (2018) Image-guided robotic radiosurgery for trigeminal neuralgia. Neurosurgery 83: 1023–30	Case series n=138 FU=median 52.4 months	Actuarial pain control rate (BNI class 1 to 3a) at 6, 12, 24, and 36 months were 94%, 86%, 80%, and 76%, respectively. Overall, 33 patients (24%) needed a second treatment. Overall, 18% developed sensory disturbances after 16.4 ± 8.7 months. One patient developed BNI grade 4 dysfunction; 6 (4%) developed BNI grade 3 (somewhat bothersome) hypaesthesia after retreatment; BNI grade 2 (not bothersome) hypaesthesia was reported by 18 patients (11 after retreatment).	Studies with more patients or longer follow up are included.
Sharma R, Phalak M, Katiyar V et al. (2018) Microvascular decompression versus stereotactic radiosurgery as	Systematic review n=720 (5 studies)	The initial success rate in the pooled data with microvascular decompression was 96% (95% CI 93% to 99%) as compared to gamma knife	A similar systematic review that also included retrospective studies is

primary treatment modality for trigeminal neuralgia: A systematic review and meta-analysis of prospective comparative trials. Neurology India 66: 688–94		which was 72% (95% CI 65% to 79%) with the ratio of 1.31 (95% CI 1.22 to 1.41; p<0.001). This superiority was sustained till the last follow up available in all the studies. Out of the complications common to both procedures, microvascular decompression had a lower rate of facial numbness, with a risk ratio of 0.48 (95% CI 0.30 to 0.78); and dysaesthetic pain, with a risk ratio of 0.47 (95% CI 0.17 to 1.29).	included (Gubian et al., 2017).
Sheehan JP, Ray DK, Monteith S et al. (2010) Gamma Knife radiosurgery for trigeminal neuralgia: the impact of magnetic resonance imaging-detected vascular impingement of the affected nerve. Journal of Neurosurgery 113: 53–8	Case series n=106 FU=median 31 months	Vascular impingement of the affected nerve was seen in the majority of patients with trigeminal neuralgia. Overall pain relief following GKRS was comparable in those with and without evidence of vascular compression on MR imaging.	Studies with more patients or longer follow up are included.
Sheehan J, Pan H-C, Stroila M et al. (2005) Gamma knife surgery for trigeminal neuralgia: outcomes and prognostic factors. Journal of Neurosurgery 102: 434–41	Case series n=136 FU=median 19 months	At the last follow up, gamma knife surgery effected pain relief in 44% of patients. Some degree of pain improvement at 3 years was noted in 70% of patients. Although less effective than microvascular decompression, gamma knife surgery remains a reasonable treatment option for those unwilling or unable to undergo more invasive surgical approaches and offers a low risk of side effects.	Included in systematic reviews by Tuleasca et al. (2019) and Gubian et al. (2017)

Singh R, Davis J, Sharma S (2016) Stereotactic radiosurgery for trigeminal neuralgia: a retrospective multi-institutional examination of treatment outcomes. Cureus 8: e554	Case series n=163 FU=2 years	Most patients (87%) had initial pain relief after Cyberknife radiosurgery. About 18% of patients with type 1 trigeminal neuralgia and 11% of patients with type 2 trigeminal neuralgia, experienced acute toxicities, with the most common being sensory neuropathy, generalised pain, and nausea.	Studies with more patients or longer follow up are included.
Smith ZA, Gorgulho AA, Bezrukiy N et al. (2011) Dedicated linear accelerator radiosurgery for trigeminal neuralgia: a single-center experience in 179 patients with varied dose prescriptions and treatment plans. International Journal of Radiation Oncology, Biology, Physics 81: 225–31	Case series n=169 FU=mean 28.8 months	Increased radiation dose and volume of brainstem irradiation may improve clinical outcomes with the trade-off of trigeminal dysfunction. Further study of the implications of dose and target are needed to optimise outcomes and to minimise complications.	Included in systematic review by Gubian et al. (2017)
Taich ZJ, Goetsch SJ, Monaco E et al. (2016) Stereotactic radiosurgery treatment of trigeminal neuralgia: clinical outcomes and prognostic factors. World Neurosurgery 90: 604-612e11	Case series n=263 FU=minimum 6 months	Excellent pain relief was achieved with the delivery of 85 Gy in a single-shot, 4-mm isocentre stereotactic radiosurgery targeting the dorsal root entry zone. Patients with classical trigeminal neuralgia, with age older than 70 years, or who underwent previous percutaneous procedures were more likely to benefit. Stereotactic radiosurgery is efficacious in patients with classical trigeminal neuralgia despite concurrent diagnosis of MS.	Studies with more patients or longer follow up are included.
Tripathi M, Sadashiva N, Gupta A et al. (2021) Please spare	Case series n=187	About 71% of patients were satisfied with their Gamma	Study focuses on dental procedures

my teeth! Dental procedures and trigeminal neuralgia. Surgical Neurology International 11: ni7292020	FU=median 49 months	Knife radiosurgery for trigeminal neuralgia.	that were done before trigeminal neuralgia was correctly diagnosed.
Tuleasca C, Paddick I, Hopewell JW et al. (2020) Establishment of a therapeutic ratio for Gamma Knife radiosurgery of trigeminal neuralgia: the critical importance of biologically effective dose versus physical dose. World Neurosurgery 134: e204–13	Case series n=408 FU=2 years	A clear relationship was found between the biologically effective dose and the incidence of hypaesthesia. Efficacy, in terms of freedom from pain, was about 90%, irrespective of the biologically effective dose at 1 and 2 years. The data suggested that "pain free" status developed more slowly at lower biologically effective dose values.	Studies with longer follow up are included.
Tuleasca C, Carron R, Resseguier N et al. (2014) Repeat Gamma Knife surgery for recurrent trigeminal neuralgia: long-term outcomes and systematic review. Journal of Neurosurgery 121: 210–21	Case series and systematic review n=626 (20 studies)	The rates of initial pain cessation and recurrence after repeat treatment seem comparable to, or even better than, those of the first stereotactic radiosurgery according to different studies, but toxicity is much higher.	Review focuses on repeat treatment.
Tuleasca C, Carron R, Resseguier N et al. (2012) Patterns of pain-free response in 497 cases of classic trigeminal neuralgia treated with Gamma Knife surgery and followed up for least 1 year. Journal of Neurosurgery 117: 181–8	Case series n=497 FU=median 43.75 months	91% (454/497) of patients were initially pain free within a median time of 10 days (range 1 to 459 days) and 37% of these (169/454) were pain free within the first 48 hours. The rate of hypaesthesia was higher in patients who became pain free more than 30 days after stereotactic radiosurgery, with a statistically significant difference between patient groups (p=0.014).	Included in systematic review by Tuleasca (2019).

Uchikawa H, Nishi T, Kaku Y et al. (2017) Delayed development of aneurysms following gamma knife surgery for trigeminal neuralgia: report of 2 Cases. World Neurosurgery 99: 813e13–19	Case reports n=2	**Intracranial aneurysm** 1. 77-year-old man had Gamma Knife surgery to treat recurrent trigeminal neuralgia after microvascular decompression surgery. At 13 years after the radiosurgery, he had a subarachnoid haemorrhage from a ruptured left anterior inferior cerebellar artery in close vicinity to the left trigeminal nerve. He died before intervention could be instituted. 2. 72-year-old woman had a subarachnoid haemorrhage 9 years after Gamma Knife surgery for trigeminal neuralgia. A ruptured left superior cerebellar artery aneurysm was treated successfully with endovascular occlusion of the parent artery. She recovered well after the surgery, and was discharged to the rehabilitation hospital with a modified Rankin Scale score of 2.	Another case report of aneurysm is included.
Urgosik D, Liscak R, Novotny J Jr et al. (2005) Treatment of essential trigeminal neuralgia with gamma knife surgery. Journal of Neurosurgery 102: 29–33	Case series n=107 FU=median 60 months	Initial successful results were achieved in 96% of patients, with complete pain relief in 80%. Relief was achieved after a median latency of 3 months (range 1 day to 13 months). Gamma knife surgery failed in 4% of patients. Pain recurred in 25% of patients after a median latent interval of 36 months (6 to 94 months). The initial success rate after a second procedure was 89% and 58% of patients were pain	Studies with more patients or longer follow up are included.

		free. Pain relapse occurred in 1 patient in this group. Hypaesthesia was observed in 20% of patients after the first procedure and in 32% after the second procedure. The median interval to hypaesthesia was 35 months (range 3 to 94 months) after 1 treatment and 21 months (range 1 to 72 months) after a second treatment.	
Vachhrajani S, Fawaz C, Mathieu D et al. (2008) Complications of Gamma Knife surgery: an early report from 2 Canadian centers. Journal of Neurosurgery 109: 2–7	Case series n=973 (270 with trigeminal neuralgia)	During the radiosurgical procedure, 19 patients (2%) had anxiety or syncopal episodes, and 2 patients had acute coronary events. Treatments were incompletely administered in 12 patients (1%). Severe pain was a delayed complication: 8 patients had unexpected headaches, and 9 patients had severe facial pain. New motor deficits developed in 11 patients, including oedema-induced ataxia in 4 and 1 facial weakness after treatment of a vestibular schwannoma. Four patients needed shunt placement for symptomatic hydrocephalus, and 16 patients had delayed seizures.	Mixed indications, including benign and malignant brain tumours.
Varela-Lema L, Lopez-Garcia M, Maceira-Rozas M et al. (2015) Linear accelerator stereotactic radiosurgery for trigeminal neuralgia.	Systematic review 11 studies	Satisfactory pain relief was achieved in 75% to 96% of patients. The mean time to relief from pain ranged from 8.5 days to 3.8 months. Recurrence rates after 1 year of follow up ranged from 5% to 29%. Facial swelling or hypaesthesia,	A more recent systematic review is included.

Pain Physician 18: 15– 27		mostly of a mild to moderate grade appeared in 8% to 52% of patients. Complete anaesthesia dolorosa was registered in 1 study (5%). Isolated cases of hearing loss (3%), brainstem oedema (6%), and neurotrophic keratoplasty (4%) were reported.	
Verheul JB, Hanssens PEJ, Lie ST et al. (2010) Gamma Knife surgery for trigeminal neuralgia: a review of 450 consecutive cases. Journal of neurosurgery 113: 160–7	Case series n=365 FU=median 28 months	In the idiopathic group, rates of adequate pain relief, defined as BNI Pain Scores 1 to 3b, were 75%, 60%, and 58% at 1, 3, and 5 years, respectively. In the MS-related group the rates of adequate pain relief were 56%, 30%, and 20% at 1, 3, and 5 years, respectively. Repeated treatment showed rates of adequate pain relief of 75% at 5 years in the idiopathic group and 46% in the MS-related group. Somewhat bothersome numbness was reported by 6% of patients after the first treatment and by 24% after repeat treatment. Very bothersome numbness was reported in 0.5% and 2% of patients after the first and second treatment, respectively.	Study is included in systematic review by Gubian et al. (2017)
Wang DD, Raygor KP, Cage TA et al. (2018) Prospective comparison of long-term pain relief rates after first-time microvascular decompression and stereotactic radiosurgery for trigeminal neuralgia.	Non-randomised comparative study (prospective) n=322 FU=mean 59 months	Immediate or short-term postoperative pain-free rates (BNI 1) were 96% for microvascular decompression and 75% for stereotactic radiosurgery. Percentages of patients with BNI score of 1 at 1, 5, and 10 years after microvascular decompression were 83%,	A similar randomised controlled trial is included.

Journal of Neurosurgery 128: 68–77		61%, and 44%, and the corresponding percentages after radiosurgery were 71%, 47%, and 27%, respectively. The median time to pain recurrence was 94 months and 53 months respectively (p=0.006).	
Wilson TA, Karlsson B, Huang L et al. (2020) Optimizing radiosurgery for trigeminal neuralgia: impact of radiation dose and anatomic target on patient outcomes. World Neurosurgery 143: e482–91	Meta-analysis	Higher radiation dose was associated with superior pain control without increasing bothersome numbness. Independent of dose, the distal target was also associated with improved pain control. Bothersome numbness was not related to dose or target.	Study was focused on the impact of dose and target on outcomes.
Wolf A, Naylor K, Tam M et al. (2019) Risk of radiation-associated intracranial malignancy after stereotactic radiosurgery: a retrospective, multicentre, cohort study. The Lancet. Oncology 20: 159–64	Cohort study n=4,905 (565 trigeminal neuralgia) FU=median 8 years	Overall incidence of radiosurgery-associated malignancy was 6.80 per 100 000 patients-years (95% CI 1.73 to 18.50), or a cumulative incidence of 0.00045% over 10 years (95% CI 0.00 to 0.0034). This is similar to the risk of developing a malignant central nervous system tumour in the general population of the USA and some European countries.	Mixed indications.
Xu Z, Mathieu D, Heroux F et al. (2019) Stereotactic radiosurgery for trigeminal neuralgia in patients with multiple sclerosis: a multicenter study. Neurosurgery 84: 499–505	Case series n=263	Reasonable pain control (BNI pain scores 1 to 3b) = 88% (232/263) The median maintenance period was 14 months. The actuarial reasonable pain control maintenance rates at 1, 2 and 4 years were 54%, 35%, and 24%, respectively. The median recurrence-free rate was 36 months and 12 months for BNI-1 and BNI >1, respectively (p=0.046). Among 210	Studies with more patients or longer follow up are included.

		patients with known status of complications, the rate of new-onset facial numbness was 10%.	
Young B, Shivazad A, Kryscio RJ et al. (2013) Long-term outcome of high-dose gamma knife surgery in treatment of trigeminal neuralgia. Journal of Neurosurgery 119: 1166–75	Case series n=250 FU=mean 69 months	Gamma Knife surgery using a maximum dose of 90 Gy to the trigeminal nerve provides satisfactory long-term pain control, reduces the use of medication, and improves quality of life. Physicians must be aware that higher doses may be associated with an increase in bothersome sensory complications. The benefits and risks of higher dose selection must be carefully discussed with patients, since facial numbness, even if bothersome, may be an acceptable trade-off for patients with severe pain.	Studies with more patients or longer follow up are included.
Young RF, Vermulen S, Posewitz A (1998) Gamma knife radiosurgery for the treatment of trigeminal neuralgia. Stereotactic and Functional Neurosurgery 70: 192–9	Case series n=110 FU=mean 19.8 months	Initial pain relief was achieved in 96% of patients with typical trigeminal neuralgia symptoms, who had not had prior surgical intervention, and 3% of these patients experienced recurrent pain during the follow-up period. Patients with atypical features to their pains or who had prior unsuccessful surgical attempts to relieve their pains achieved initial and long-term pain relief in 88 and 69%, respectively. 3 patients (3%) developed delayed loss of facial sensation following treatment, but no other complications were noted.	Studies with more patients or longer follow up are included.
Yu R, Wang C, Qu C et al. (2019) Study on	Non-randomised	Microvascular decompression should be	Studies with more patients

the therapeutic effects of trigeminal neuralgia with microvascular decompression and stereotactic gamma knife surgery in the elderly. The Journal of Craniofacial Surgery 30: e77-e80	comparative study n=193	done more prudently in elderly patients, and the indications for partial sensory rhizotomy should be relatively relaxed. Gamma knife treatment of trigeminal neuralgia had high safety, less complications, and positive curative effect, especially suitable for patients older than 80 years.	or longer follow up are included.
Zakrzewska JM, Akram H (2011) Neurosurgical interventions for the treatment of classical trigeminal neuralgia. The Cochrane database of systematic reviews no. 9: cd007312	Systematic review n=496 (11 studies)	There is very low quality evidence for the efficacy of most neurosurgical procedures for trigeminal neuralgia because of the poor quality of the trials. All procedures produced variable pain relief, but many resulted in sensory side effects.	Only included 1 RCT on stereotactic radiosurgery, comparing 1 and 2 isocentres to deliver radiation to the trigeminal nerve.
Zakrzewska JM, Linskey ME (2009) Trigeminal neuralgia. BMJ clinical evidence 2009	Systematic review n=14 systematic reviews, randomised controlled trials, or observational studies	There was no randomised controlled trial evidence assessing stereotactic radiosurgery. There was some observational data suggesting that radiofrequency thermocoagulation may offer higher rates of complete pain relief than glycerol rhizolysis and stereotactic radiosurgery, but is associated with the highest rate of complications. Typically, pain relief with radiosurgery is not immediate.	More recent systematic reviews are included.
Zhao H, Shen Y, Yao D et al. (2018) Outcomes of two-isocenter gamma knife radiosurgery for patients with typical trigeminal neuralgia: pain response and	Case series n=247 FU=median 49.7 months	Initial pain relief=88% Recurrence=4% (9/217) New facial numbness=32% (4% very bothersome) Dry eyes=13% Patients with a shorter history of trigeminal	Studies with more patients or longer follow up are included.

quality of life. World Neurosurgery 109: e531–38		neuralgia and patients without preoperative surgery had earlier initial pain relief.	