

Linac-based stereotactic radiosurgery for trigeminal neuralgia

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CASE SUMMARY

A 70-year-old male patient was referred to the CDD Unit of Radiotherapy and Radiosurgery Abreu Clinics in Santo Domingo, Dominican Republic, with a history of lower left jaw pain that evolved over 10 years into severe left hemifacial pain and dysphagia. He was treated unsuccessfully for many years with pregabalin and carbamazepine, until maximum doses eventually caused liver toxicity.

A cerebral MRI with contrast revealed a vascular image: a superior cerebellar artery (SUCA) contacting the upper surface of the left V cranial nerve, near its apparent origin.

After confirming a diagnosis of trigeminal neuralgia (TN), we treated the patient with intracranial stereotactic radiosurgery (SRS). Twenty-four hours

after treatment, the patient was completely asymptomatic. At the 25-month follow-up, our patient remained pain-free, had no swallowing disorders, and did not require pain medication.

IMAGING FINDINGS

We performed a brain MRI with contrast and cranial computed tomography (CT), with subsequent image fusion and stereotactic frame placement. We used the Brainlab system (iPlan; Munich, Germany) for treatment planning, and performed SRS using the Clinac 21iX linear accelerator (Varian Medical Systems, Palo Alto, California), conforming the cisternal target with 1 isocenter, 31 semi-arches and 7 arcs, all noncoplanar conformed with a 4-mm conical collimator. The prescription dose was 73 Gy to 90% isodose line, in 1 session (Figures 1 and 2).

DIAGNOSIS

Trigeminal neuralgia (TN)

DISCUSSION

In 1756, Nicolas André described TN as a “painful tic of the face;” it was also known as Trousseau’s neuralgia, and later epileptiform neuralgia. TN is a facial pain disorder occurring in 4 out

of 100,000 people. It typically affects patients older than 50, and is more common in women than men (1.5:1 to 2:1, respectively). TN is associated with a decreased quality of life and impaired daily function, affects employment in 34% of patients with depressive symptoms, and can be severely disabling with high morbidity.¹⁻³

Initial treatment is typically oral carbamazepine, producing complete or acceptable relief in 69% of cases.² With prolonged use, the therapeutic response drops to 50%, despite a progressive increase in dose. Traditionally, treatment has involved additional invasive neurosurgical procedures, including microvascular decompression of the affected nerve, and various procedures to interrupt pain transmission using heat, osmotic intervention or mechanical compression.²⁻⁴ TN was first treated with SRS by Lars Leksell in 1951. More recently, SRS has been established as a less invasive alternative to surgical procedures for patients who are refractory to medical treatment, cannot tolerate medical or surgical treatment, or who have recurrent pain.

TN is one of the fastest growing indications for SRS. From its initial use by Leksell to treat idiopathic TN, SRS has evolved as an accepted tool

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FIGURE 1. Target and OARs delimitation.

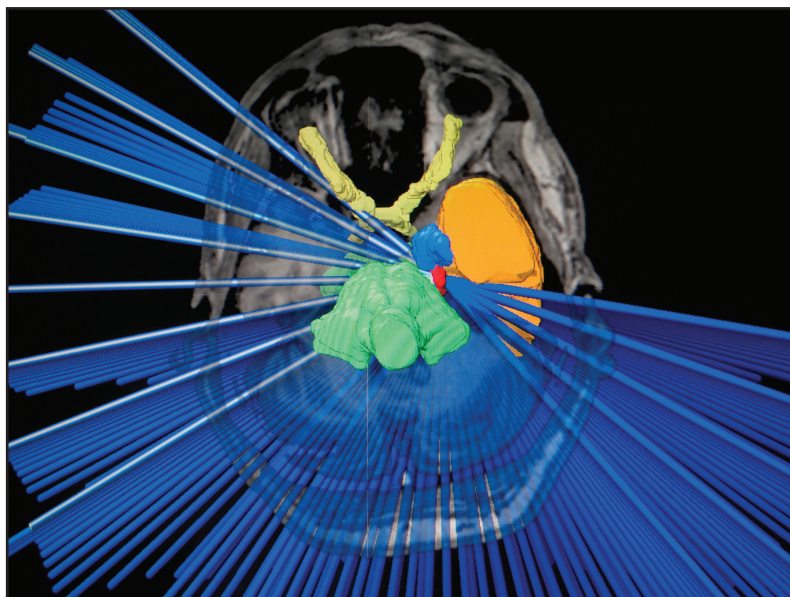


FIGURE 2. SRS planning, caudal view, 3-dimensional reconstruction.

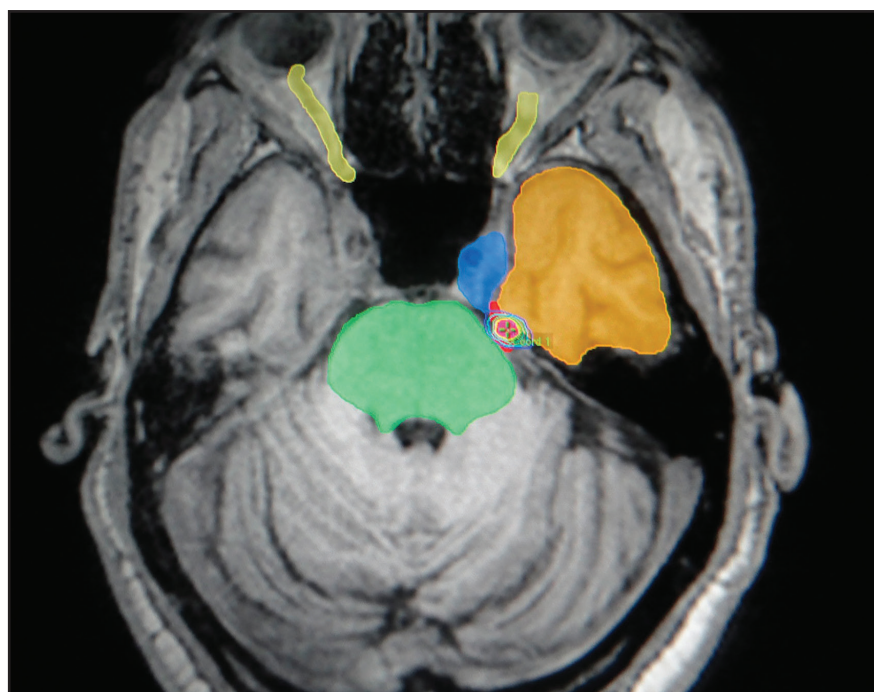


FIGURE 3. SRS planning dosimetry.

for functional neurosurgery. For TN, SRS is a safe, highly effective noninvasive treatment that provides initial pain relief in 75% to 89% of patients. Of note, radiosurgical studies excluding patients who previously underwent surgery demonstrated complete pain relief in 74% to 90% of patients —

similar to results achieved with conventional surgery.⁵

At present, there is no data suggesting any benefit from giving a dose > 70 Gy with linear accelerator-based SRS, or to increase the length of the nerve irradiated (increase irradiated volume).⁶⁻⁸ In fact, the only data

available comparing patients treated with higher doses (90 Gy) vs. typical doses (70-80 Gy) showed a significant increase in patient morbidity, and no benefit in treatment response (Figures 2 and 3). Increasing treatment volume to include a longer nerve length does not significantly improve pain relief, and may increase complications such as numbness and paresthesia.

Another controversy surrounding radiosurgery for TN involves position of the target (posterior or anterior).⁹ Massager et al reported excellent pain relief in 68% of patients, and satisfactory pain improvement in 83%.¹⁰ These authors demonstrated that using an anterior target (retrogasserian - cisternal) results in fewer complications compared with a posterior target (dorsal nerve input) with the same radiation dose. As such, the target should be 5 mm to 8 mm from the brainstem to achieve an optimal balance between pain control and complications of nerve dysfunction. Whether to deliver anterior or posterior irradiation to the nerve remains unclear and is the subject of phase III studies.^{9,10} The reason for comparing the anterior (distal) and proximal (more posterior) targets

Table 1. Main series of the literature, comparing published studies between Gamma Knife and linear accelerator

Study	Year	# Patients	Device%	Max Doses (Gy)			Median F/U (months)	% Patients			
				<70	70-80	>80		without pain	>90%	side effects	recurrence
Loeschner et al	2012	72	GK	0	100	0		39	71	31	-
Dos Santos et al	2011	52	LINAC	46.2	53.8	0	26.6	17.3	53.8	36	28.8
Kondziolka et al	2010	503	GK	1.6	94.9	3.4		89	89	10.5	42.9
Pusztaszeri et al	2007	17	LINAC	17	0	0	12 (2-60)	35	90	5.8	29.4
Régis et al	2006	110	GK	0	85 (70-90)		>12	83	97	10	17
Richards et al	2005	28	LINAC	0	100	0	49 (12-70)	46	61	52	23
Massager et al	2004	47	GK	0	0	100	12 (1-40)	57	75	14.2	46
Chen et al	2004	32	LINAC	37	0	67	14.1 (3-31)	40	70	17.5	17
Cheuk et al	2004	112	GK	75	0	0	8	78	87	0-9.3	-
Frighetto et al	2004	22	LINAC	70-85	17		-	80.2	89.6	5.2-10.4	-
Gross et al	2003	25	LINAC	0	0	25	18 (8-52)	76	100	32	0-44
Kannan et al	1999	6	GK	0	100	0	10 (5-16)	66	100	0	0

is to achieve better pain control and lower complication rates. Kondziolka et al considered the proximal trigeminal nerve and root entry zone an appropriate anatomical target, identified as the dorsal root entry zone (DREZ).^{14,15} Marshall et al considered the concept that better pain relief occurs when the isocenter is placed closer to the brainstem. This placement results in greater denervation in the zone where peripheral myelin formed by Schwann cells transforms to central myelin formed by oligodendroglia. Meanwhile, Régis et al considered the retrogasserian zone (RGZ) an adequate target, reporting

87% pain relief in 57 patients, with maximum doses of 75 to 90 Gy.^{16,17}

In a recent study of 169 essential TN patients treated with linear accelerator-based SRS, > 88% achieved significant relief, similar to reports of SRS using the Gamma Knife (Elekta, Stockholm, Sweden).^{8,11,12} Of patients who received SRS as initial treatment, > 90% experienced complete pain relief. Previous treatment has been a negative prognostic indicator in other studies; our patient only received drug treatment, and had no previous surgery.

Patients usually achieve maximum pain relief 1 month after treatment.

The disappearance of activation areas or frank pain relief occurs within 24 hours of treatment in up to one-third of patients, as reported in our case. Complete pain relief within 1 week of treatment has been reported in > 40% of patients. In addition, > 75% of patients with partial and complete response have responded within 3 months of treatment, and > 90% of complete responses are seen after 6 months.^{5,13} No deaths, systemic complications, or induced malignancy have been reported after treating TN with SRS (Table 1).

After a 25-month follow-up, our patient remains asymptomatic. Some

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reviewed studies with follow-up times of 8 to 49 months show that side effects could vary between 0% and 52%, with facial numbness as one of the most common. Improvement in pain relief, side effects and recurrence rates should not be attributed to equipment used for radiosurgery (Gamma Knife, linear accelerator, CyberKnife [Accuray, Sunnyvale, California]). Rather, a very short-term follow-up in final analysis, a diagnosis of multiple sclerosis, and previous surgical treatment of TN on the same side have been linked to a lower rate of pain control, shorter nerve, younger age, hypertension, etc. Regarding the procedure, physicians should consider the dose rate, maximum dose, location of the shot, and integrated dose to the nerve. High doses have allowed for pain relief of 90% to 95%, a relapse rate of 10% to 35%, and long-term pain relief of 70%. However, depending on shot location, loss of sensation could be 58.3%; major hypoesthesia, 19.4%; and subjective sensation of dry eye and decreased corneal reflex, 30.5%.^{18,19}

CONCLUSION

SRS is currently the less invasive treatment for TN. Initial results regarding recurrence rates and pain control seem to be in line with other surgical ablation techniques. For TN, SRS holds a unique place as a safe, noninvasive and effective treatment, providing initial

relief in 75% to 89% of patients. At present, no published data suggest any benefit of > 70 Gy dose, or to increase the length of the irradiated nerve. Patients without previous surgical procedures and typical symptoms are associated with better outcomes.

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