

# Dosimetric analysis of trigeminal nerve, brain stem doses in CyberKnife radiosurgery of trigeminal neuralgia

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## ABSTRACT

CyberKnife radiosurgery treatment of Trigeminal neuralgia (TN) is performed as a non-invasive image guided procedure. The prescription dose for TN is very high. The brainstem is the adjacent critical organ at risk (OAR) which is prone to receive the very high target dose of TN. The present study is to analyze the dose distribution inside the tiny trigeminal nerve target and also to analyze the dose fall off in the brain stem. Seven TN cases treated between November 2010 and January 2012 were taken for this study retrospectively. The treatment plans were analyzed for target dose conformity, homogeneity and dose coverage. In the brainstem the volume doses  $D_{1\%}$ ,  $D_{2\%}$  were taken for analyzing the higher doses in the brain stem. The dose fall off was analyzed in terms of  $D_{5\%}$  and  $D_{10\%}$ . The mean value of maximum dose within the trigeminal nerve target was  $73.5 \pm 2.1$  Gy ( $P=0.0007$ ) and the minimum dose was  $50.0 \pm 4.1$  Gy ( $P=0.1315$ ). The mean conformity index was 2.19 and the probable reason could be the smallest CyberKnife collimator of 5mm used in the treatment plan. The mean  $D_{5\%}$  of the brainstem was  $10.5 \pm 2.1$  Gy ( $P=0.5316$ ) and the mean value of the maximum point dose within the brainstem was  $35.6 \pm 3.8$  Gy. This shows the degree of dose fall off within the brainstem. Though the results of the present study are showing superior sparing of brain stem and reasonable of target coverage, it is necessary to execute the treatment plan with greater accuracy in CyberKnife as the immobilization is noninvasive and frameless.

**Key words:** Brainstem dose; cyberknife; stereotactic radiosurgery; trigeminal neuralgia

## Introduction

Trigeminal neuralgia (TN) is a trigeminal nerve disorder which causes an agonizing facial pain in the affected patients. TN is also called as "suicide disease"<sup>[1]</sup> and this terminology explains the extent of pain in patients. The cause for TN is the focal demyelination of trigeminal

nerve root by vascular compression.<sup>[2]</sup> Generally, TN occurs unilaterally; however, occasionally may be bilateral.<sup>[3]</sup> There are three main treatment modalities for TN: medical treatments through drugs, surgical treatment and radiosurgery treatment.<sup>[4-7]</sup> Micro-vascular decompression (MVD) is a well-known surgical treatment for TN.<sup>[8,9]</sup> Radiosurgery for TN has been performed either as a frame based or as a frameless radiosurgery. Frame based is an invasive method while frameless is a noninvasive method. Leksell Gamma Knife (Elekta Instruments, Norcross, GA)<sup>[10,11]</sup> radiosurgery is a frame based procedure, while CyberKnife (Accuray, Sunnyvale, USA)<sup>[12,13]</sup> is an image guided frameless procedures. In the BrainLAB Novalis (BrainLAB A.G., Heimstetten, Germany)<sup>[14,15]</sup> radiosurgery system, both the frame based and frameless procedures are being performed. The radiation dose required to treat TN is very large when compared with all other radiosurgical procedures performed in the cranium.

The dose in Gamma Knife is often prescribed to a 50% isodose, and the prescription dose is between 35 Gy to 40 Gy.<sup>[16]</sup> A maximum of 70 Gy to 90 Gy is delivered to the trigeminal nerve in Gamma Knife.<sup>[17]</sup> Similarly in

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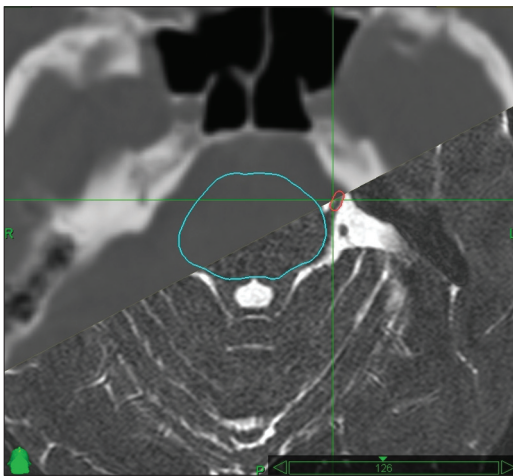
CyberKnife, the dose is prescribed to 75% to 85% isodose and the prescription dose is 60 Gy.<sup>[13]</sup> This very high dose prescription to the very tiny trigeminal nerve necessitates very precise targeting. Especially, the organs at risk (OAR) doses should be restricted to their tolerance limit. Brain stem is the critically closer OAR to the trigeminal nerve in the treatment of TN. Treatment planning plays a crucial role in restricting the dose to the brain stem. In CyberKnife, the treatment planning is performed in a dedicated planning system called Multiplan (Accuray, Sunnyvale, USA). There are many numbers of studies on the clinical outcomes of the radiosurgical treatment of TN. However, there are only a limited number of studies available on the dose distribution in and around the trigeminal nerve in the radiosurgery of TN, especially in the cyberknife radiosurgery. The present study aims to analyze the dose distribution in the trigeminal nerve and in the brain stem in cases treated with CyberKnife stereotactic radiosurgery system.

## Materials and Methods

Seven TN cases treated between November 2010 and January 2012 were taken retrospectively for this study. Out of these seven cases, four were cases of TN in the left side, and three were of TN in the right side. Four of them were males and three were female patients. The median age and the mean age were 61 and 57.2 years, respectively.

### Target and organs at risk delineation

Visualization of the trigeminal nerve is an important task in TN treatment. The Computed Tomography (CT) images of the cranium were acquired in 1 mm slice thickness. These CT images were fused accurately with a special T2 weighted Drive sequence magnetic resonance (MR) images [Figure 1]. With the help of these T2 Drive MR images, the trigeminal nerve and the OARs were drawn on the fused CT images. The target was drawn in such a way that the target segment of the trigeminal nerve starts from 2 to 3 mm away



**Figure 1:** The trigeminal nerve target in the Computed Tomography and T2 weighted Drive sequence Magnetic Resonance image fusion in a sample case

from the root entry zone (REZ). The length of the target segment in the trigeminal nerve was delineated for about 6 mm in 3 CT slices of 1 mm thickness.

### Treatment planning

CyberKnife plans are associated with site specific paths which give the information about the beam orientation. A dedicated trigeminal path is also provided for the treatment of TN. The smallest 5 mm fixed type collimator was taken for treating TN. The goal dose to the trigeminal nerve target was set as 60 Gy. The dose gradient around the target was set as a goal in the treatment planning. The 60 Gy dose was limited within a shell of 0.5 mm around the target. Similarly 55 Gy to 2 mm shell, 48 Gy to 5 mm shell and 28 Gy was set to 10 mm shell. The dose constraint for the brainstem was kept as 40 Gy. The maximum dose in the target was taken as the normalizing dose. The plans were made and evaluated.

### Treatment plan evaluation

The target volume doses  $D_{98\%}$ ,  $D_{90\%}$ ,  $D_{50\%}$ ,  $D_{30\%}$ , and  $D_{10\%}$  were evaluated from the dose volume histogram (DVH). The amount of trigeminal nerve target volume receiving 100% of the prescribed dose,  $V_{100\%}$ , was also evaluated in percentage. The dose conformity index and homogeneity index of the TN target were also analyzed. The formulae used to calculate the conformity index and the homogeneity index are given as follows.

$$\text{Conformity Index (CI)} = (V_{\text{RI}} \times \text{TV}) / (\text{TV}_{\text{RI}})^2 \quad \dots(1)$$

Where  $V_{\text{RI}}$  is the overall volume including the target volume, receiving the prescription isodose or more, TV is the volume of the trigeminal nerve target, and  $\text{TV}_{\text{RI}}$  is the volume of the target which receives the prescription isodose or more. This conformity index was initially proposed in an inverse way by Paddick<sup>[18]</sup> and modified in the current form by Nakamura *et al.*<sup>[19]</sup>

$$\text{Homogeneity index (HI)} = D_{\text{max}} / D_{\text{RI}} \quad \dots(2)$$

Where  $D_{\text{max}}$  is the maximum dose in the nerve target and  $D_{\text{RI}}$  is the reference / prescription isodose. Brainstem doses were evaluated in terms of  $D_{1\%}$ ,  $D_{2\%}$ ,  $D_{5\%}$  and  $D_{10\%}$ . This low percentage volume doses are representing the higher doses in the brain stem. Along with this, the maximum point doses and the mean doses in the target as well as in the brainstem were also estimated for analysis. The p-values were calculated using two tailed Student's T-test and tabulated in appropriate tables.

## Results

The mean volume of the trigeminal nerve target was  $37.9 \pm 2.5 \text{ mm}^3$ . The minimum volume was  $35.4 \text{ mm}^3$  and the maximum volume was  $42.3 \text{ mm}^3$ . The mean volume of

**Table 1: Target dose distribution analysis in terms of volume doses**

Study number	Target volume (mm <sup>3</sup> )	Volume doses of the trigeminal nerve target (Gy)				
		D <sub>98%</sub>	D <sub>90%</sub>	D <sub>50%</sub>	D <sub>30%</sub>	D <sub>10%</sub>
Case 1	37.8	53.3	54.8	64.5	67.5	72.0
Case 2	40.3	52.9	57.2	63.5	66.4	67.1
Case 3	42.3	49.5	51.8	65.3	69.8	74.3
Case 4	36.6	56.5	58.6	64.2	66.4	68.5
Case 5	36.6	45.0	53.3	63.8	66.8	72.0
Case 6	35.4	53.3	54.8	63.0	65.3	71.3
Case 7	36.6	52.0	56.3	63.7	66.6	70.2
Mean ± Standard deviation	37.9 ± 2.5	51.8 ± 3.6	55.3 ± 2.3	64.0 ± 0.7	66.9 ± 1.4	70.8 ± 2.4
P value	0.0665	0.0863	0.0092	0.0000	0.0001	0.0025

**Table 2: Target dose distribution analysis in terms of mean dose, minimum and maximum point doses**

Study number	Trigeminal nerve target doses (Gy)		
	Minimum	Maximum	Mean
Case 1	52.5	75.0	63.9
Case 2	52.4	70.6	63.3
Case 3	48.8	75.0	64.2
Case 4	55.5	70.6	64.0
Case 5	42.7	75.0	62.9
Case 6	48.7	75.0	63.0
Case 7	49.5	73.2	63.2
Mean ± Standard deviation	50 ± 4.1	73.5 ± 2.1	63.5 ± 0.5
P value	0.1315	0.0007	<0.0001

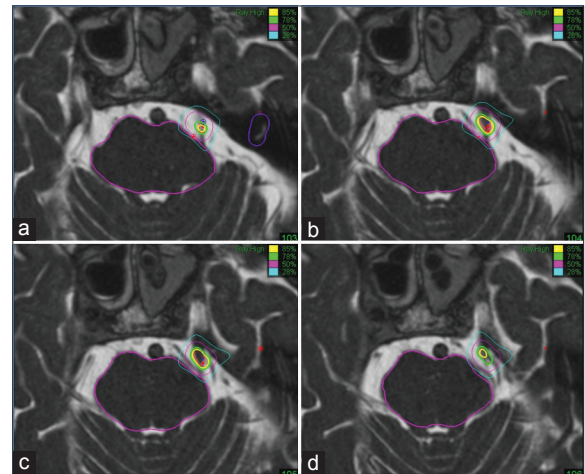


Figure 2: Dose distribution in the axial plane in a sample case

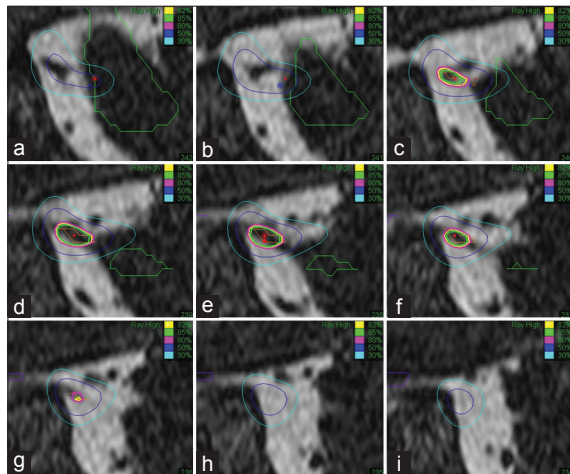


Figure 3: Dose distribution in the sagittal plane in a sample case

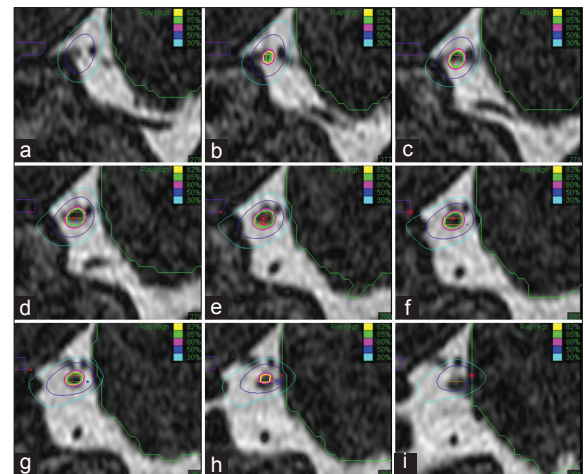


Figure 4: Dose distribution in the coronal plane in a sample case

the brainstem was  $22 \pm 4.7 \text{ cm}^3$ . The dose distributions in the axial, sagittal and coronal sections in the MR images are shown in Figure 2, Figure 3 and Figure 4 respectively.

**Analysis of the trigeminal nerve target dose**

The D<sub>98%</sub>, D<sub>90%</sub>, D<sub>50%</sub>, D<sub>30%</sub> and D<sub>10%</sub> values of the trigeminal nerve target are shown in Table 1. D<sub>98%</sub> is a measure of the minimum dose within the trigeminal nerve target. The

mean value of D<sub>98%</sub> was  $51.8 \pm 3.6 \text{ Gy}$ . The maximum and the minimum values of D<sub>98%</sub> were 56.5 Gy and 45.0 Gy, respectively. Similarly, D<sub>10%</sub> is the measure of maximum dose within the trigeminal target. D<sub>10%</sub> was ranging between 67.1 Gy and 74.3 Gy. The mean value was  $70.8 \pm 2.4 \text{ Gy}$ . The percentage volume of the trigeminal nerve target receiving 100% of the prescribed dose, V<sub>100%</sub>, was

75.8 ± 4.6%. The mean values of CI and the HI were 2.19 ± 0.32 and 1.2 ± 0.03, respectively. The mean value of the prescribing isodose was 81.7 ± 2.4%. The conformity and homogeneity indices, the prescribing isodose and  $V_{100\%}$  are shown in Table 2. Minimum, maximum point doses and the mean doses in the target are shown in Table 3. The mean maximum dose was 73.5 ± 2.1 Gy, and this maximum point dose was varying between 70.6 Gy and 75 Gy. Similarly the mean value of the minimum point dose was 50.0 ± 4.1 Gy and range of the minimum point dose in the trigeminal nerve target was from 42.7 Gy to 55.5 Gy.

### Analysis of the brainstem dose

The  $D_{1\%}$ ,  $D_{2\%}$ ,  $D_{5\%}$  and  $D_{10\%}$  values of the OAR brainstem are shown in Table 4. The mean brainstem dose and the maximum point dose in the brainstem are also shown in Table 4. The volume doses  $D_{1\%}$  and  $D_{2\%}$  are representing the maximum doses in the brainstem, while  $D_{5\%}$  and  $D_{10\%}$  are representing the degree of dose fall off in the brainstem. The mean values of  $D_{1\%}$ ,  $D_{2\%}$ ,  $D_{5\%}$  and  $D_{10\%}$  were 10.5 ± 2.1 Gy, 7.9 ± 1.8 Gy, 5.1 ± 1.7 Gy and 3.3 ± 1.3 Gy respectively. The maximum point dose was varying between 29.4 Gy and 40.0 Gy and the mean value was 35.6 ± 3.8 Gy.

### Discussion

The maximum dose to the target segment of the trigeminal nerve is a matter of concern in the radiosurgical treatment of TN. In Gamma Knife radiosurgery of TN, the maximum

dose often crosses 85 Gy.<sup>[16,21,22]</sup> However in CyberKnife radiosurgery for TN, the reported maximum doses are well within 80 Gy. Adler *et al.*<sup>[23]</sup> is reporting a maximum trigeminal nerve target dose in CyberKnife radiosurgery as 73.5 Gy which matches with the present study. The mean value of the maximum dose in the present CyberKnife study is 73.5 ± 2.1 Gy. Study by Villavicencio *et al.*<sup>[24]</sup> shows a median maximal dose to the trigeminal nerve of 78Gy. Though there is a difference in the maximum dose between the Gamma Knife radiosurgery and CyberKnife radiosurgery the clinical correlations are showing appreciable success rate in both the cases.<sup>[21-25]</sup>

The mean prescribing isodose line in the present study is 81.7% and the mean coverage is 75.8%. This shows that about 24% of the tiny trigeminal target is receiving dose lesser than 60 Gy. But the mean minimum dose of the target is 50.01 ± 4.06 Gy. Hence the trigeminal nerve target is in the range of ~50 Gy to ~73.5 Gy. However the mean conformity index is 2.19. This shows that there is an equal volume of normal tissue surrounding the target equal to the volume of the target is receiving the prescribing dose. This is mainly because of the size of the target and this TN target is possibly the smallest target among all the targets treated in radiosurgery. Also the minimum size of the collimator available in CyberKnife is 5 mm. The width of the TN nerve target in any of CT slice containing the target is about 2 mm only. These are the possible reason for the higher value of conformity index in radiosurgery treatment of TN. The mean value of the homogeneity index is 1.23 which

**Table 3: Target dose conformity, homogeneity analysis**

Study number	Conformity index	Homogeneity index	Prescribing isodose (%)	$V_{100\%}$ (%)
Case 1	2.08	1.25	80	72.6
Case 2	2.15	1.18	85	72.7
Case 3	2.01	1.25	80	75.8
Case 4	2.55	1.18	85	81.7
Case 5	1.87	1.25	80	70.0
Case 6	2.73	1.25	80	75.9
Case 7	2.00	1.22	82	82.0
Mean ± Standard deviation	2.19 ± 0.32	1.23 ± 0.03	81.7 ± 2.4	75.8 ± 4.6
P value	0.3795	0.0005	0.0008	0.0517

**Table 4: Brainstem dose analysis**

Serial number	Brainstem volume (cc)	Brainstem doses (Gy)					
		$D_{1\%}$	$D_{2\%}$	$D_{5\%}$	$D_{10\%}$	Maximum	Mean
Case 1	24.01	7.50	6.00	3.75	3.00	35.06	1.42
Case 2	26.24	12.71	9.88	6.35	4.24	29.37	2.01
Case 3	16.65	12.75	9.75	6.75	4.50	32.42	2.50
Case 4	28.69	9.88	7.76	5.65	3.53	37.51	1.93
Case 5	18.77	9.00	6.00	2.25	0.75	35.65	6.85
Case 6	16.86	9.00	6.75	4.50	3.00	39.52	1.50
Case 7	22.87	12.44	9.51	6.59	4.39	39.99	1.75
Mean ± Standard deviation	22.0 ± 4.7	10.5 ± 2.1	7.95 ± 1.75	5.12 ± 1.69	3.34 ± 1.31	35.65 ± 3.81	2.57 ± 1.92
P value	0.5488	0.5316	0.5611	0.6960	0.7412	0.2426	0.8631

shows that the dose variation within the target is about 23% and the mean value of the mean target dose is 63.5 Gy.

The target dose coverage usually lowered because of the dose restriction to the brain stem. The mean value of the  $D_{1\%}$  in the brainstem is 10Gy while the mean maximum point dose in brain stem is 35.6 Gy. The mean value of 1% volume of brainstem is  $0.22 \pm 0.05 \text{ cm}^3$ . This shows that the 50% of the prescribed 60 Gy dose (30 Gy) is falling well within this  $0.22 \text{ cm}^3$  volume of the brain stem which is closer to the trigeminal nerve REZ. The brainstem dose gradient analysis by  $D_{2\%}$ ,  $D_{5\%}$  and  $D_{10\%}$  are showing a better dose fall off of dose within the brainstem.

## Conclusion

The target segment of the trigeminal nerve should be irradiated with an adequate dose to reduce the pain due to TN. The present study shows that the point dose maximum in CyberKnife radiosurgery of TN is about 75 Gy. The study also shows that the dose distribution in the tiny target is not limited within the target. The minimal collimator of 5 mm could be the possible reason for this. Though there is a spillage of dose outside the target, it is not towards the critical OAR brainstem. According to the present study, the maximum brainstem point dose is less than 50% of the maximum point dose in the target. Though the results of the present study are showing superior sparing of brain stem and reasonable of target coverage, it is necessary to correlate the dose distribution with the clinical outcomes through follow ups. The effectiveness of the treatment plan exists in the proper execution with greatest accuracy, as the CyberKnife radiosurgery is executed with a noninvasive immobilization.

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