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CLINICAL STUDY – PATIENT STUDY

Dosimetric comparison of Linac-based (BrainLAB®) and robotic radiosurgery (CyberKnife®) stereotactic system plans for acoustic schwannoma

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Abstract A dosimetric comparison of linear accelerator (LA)-based (BrainLAB) and robotic radiosurgery (RS) (CyberKnife) systems for acoustic schwannoma (Acoustic neuroma, AN) was carried out. Seven patients with radiologically confirmed unilateral AN were planned with both an LA-based (BrainLAB) and robotic RS (CyberKnife) system using the same computed tomography (CT) dataset and contours. Gross tumour volume (GTV) was contoured on post-contrast magnetic resonance imaging (MRI) scan [planning target volume (PTV) margin 2 mm]. Planning and calculation were done with appropriate calculation algorithms. The prescribed isodose in both systems was considered adequate to cover at least 95% of the contoured target. Plan evaluations were done by examining the target coverage by the prescribed isodose line, and high- and low-dose volumes. Isodose plans and dose volume histograms generated by the two systems were compared. There was no statistically significant difference between the contoured volumes between the systems. Tumour volumes ranged from 380 to 3,100 mm^3. Dose prescription was 13–15 Gy in single fraction (median prescribed isodose 85%). There were no significant differences in conformity index (CI) (0.53 versus 0.58; $P = 0.225$), maximum brainstem dose (4.9 versus 4.7 Gy; $P = 0.935$), 2.5-Gy volume (39.9 versus 52.3 cc; $P = 0.238$) or 5-Gy volume (11.8 versus 16.8 cc; $P = 0.129$) between BrainLAB and CyberKnife system plans. There were statistically significant differences in organs at risk (OAR) doses, such as mean cochlear dose (6.9 versus 5.4 Gy; $P = 0.001$), mean mesial temporal dose (2.6 versus 1.7 Gy; $P = 0.07$) and high-dose (10 Gy) volume (3.2 versus 5.2 cc; $P = 0.017$). AN patients planned with the CyberKnife system had superior OAR (cochlea and mesial temporal lobe) sparing compared with those planned with the Linac-based system. Further evaluation of these findings in prospective studies with clinical correlation will provide actual clinical benefit from the dosimetric superiority of CyberKnife.

Keywords Acoustic schwannoma · Stereotactic radiosurgery · Robotic radiosurgery · Linear accelerator-based radiosurgery

Introduction

Acoustic schwannoma (Acoustic neuroma, AN) is a benign tumour of the vestibular nerve, and patients usually present with progressive sensory neural hearing loss, tinnitus or vertigo [1, 2]. A proportion of AN patients are young adults, and some of them are associated with neurofibromatosis (NF1). Patients with large AN (size >2.5 cm), with gross impairment of or no hearing function and patients with brainstem compression are treated with surgical resection [3]. On the other hand, small ANs (less than 2.5–3 cm) with relatively preserved hearing function are preferably treated with function-preserving approach such as radiosurgery (RS) [4–8]. Large prospective studies with long-term follow-up data and matched-pair analysis have shown equivalent loco-regional control with RS and microsurgery

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[7–11]. The RS patient cohort had equivalent local control to the microsurgery arm, but patients with microsurgery had higher facial nerve paresis and hearing function impairment [10–14].

GammaKnife is the gold standard for RS treatment and has been used to treat AN of less than 3 cm diameter for more than 40 years (first reported case way back in 1969) with usually 12–18 Gy in single fraction and control rate as high as 95% at 10-year follow-up [10–12]. In the last few decades, linear accelerator (LA)-based systems such as BrainLAB (introduced in 1998) and other systems have been used for RS. In 2001, the Food and Drug Administration (FDA) approved robotic RS (CyberKnife) as a treatment modality, and it has been introduced, with all the features of GammaKnife plus a few more advantages [15]. LA-based systems such as BrainLAB are isocentric forward planning systems, whereas the CyberKnife system is a non-isocentric inverse planning system [15].

Local control of possible treatment options (radiotherapy, RS, microsurgery) are similar, hence the optimal management option depends upon the toxicity profile. Apart from preservation of hearing function, another important end-point considered is preservation of neurocognitive function [16]. A recent publication by the present corresponding author correlated the dose to temporal lobe and decline in intelligent quotient (IQ) in paediatric and young adult patients treated with stereotactic radiation therapy [17]. AN is a benign disease, and higher dose to critical structures such as temporal lobe and cochlea will have detrimental effect on both IQ and hearing function [18, 19]. In the present study, we compared the dose parameters between BrainLAB and CyberKnife which may have clinically useful end-points such as effect on hearing and neurocognitive function.

Materials and methods

Seven patients (median age 23 years; 5 male, 2 female; 6 right sided) with radiologically confirmed unilateral AN with volume not more than 2.5 cm^3 with progressive hearing loss and at least partially preserved sensory neuronal hearing function on audiometry evaluation were planned with two different RS systems (BrainLAB and CyberKnife).

Linear accelerator-based (BrainLAB) RS plan

All seven patients had undergone planning contrast-enhanced CT scan and MRI scan according to the planning specification [1 mm slice thickness; MRI scan by three-dimensional fast spoiled gradient-recalled (3DFSPGR) sequence]. Planning CT and MRI scans were fused using a manual fusion algorithm. Contouring of target (CTV) and critical structures were done in the BrainLAB RS system. Mesial temporal lobe (limbic system) was contoured using MRI scan according to the standard guideline by Chera et al. [20] ("A radiation oncologist's guide to contouring the hippocampus"). Cochlea was contoured in CT scan. Primary disease showing contrast enhancement on MRI scan was contoured as GTV. PTV margin given was 2 mm. Forward planning was done in the BrainLAB system with multiple non-coplanar arcs and single isocentre. The number of arcs ranged from one to four. The dose prescription was 12–15 Gy at usually 95% isodose line (Fig. 1). The dose calculation algorithm used was 'convolution superimposition'. Plan evaluation was done considering target coverage and OAR constraints. The prescribed isodose in both systems was considered adequate to cover at least 95% of the contoured target. Plan evaluations were done by examining high- and low-dose volumes ($V_{2.5Gy}$, V_{5Gy} and V_{10Gy}), maximum dose to brainstem, ipsilateral cochlea and mean dose to ipsilateral mesial temporal lobe.

CyberKnife plan

CT scan with contours (target and OARs) data of these seven patients were transferred to the CyberKnife. No change was done in either contours (both target and OARs) or dose prescription. Planning was done with inverse planning using pencil-beam algorithm and multiple isocentres. Optimization was done using the 'pencil beam algorithm', and dose calculation was done using the 'convolution superimposition' method. The number of beamlets used was 80–150 (median 110). Dose parameters were collected from dose volume histograms (DVHs).

The prescribed isodose in both systems was considered adequate to cover at least 95% of the contoured target. Comparison between the plans generated with BrainLAB and CyberKnife was done for target coverage, OAR (mesial temporal lobe and cochlea) dose, and low- and high-dose volumes.

All data were collected and analyzed using SPSS version 15. Dosimetric data of PTV were collected from DVHs, and standard distribution data were analyzed. Comparisons of dosimetric data between the two system plans were done using independent *t* tests (Fig. 2).

Results

Dosimetric parameters of patients planned with BrainLAB and CyberKnife

The dosimetric parameters of seven patients planned with both BrainLAB and CyberKnife are presented in Table 1.

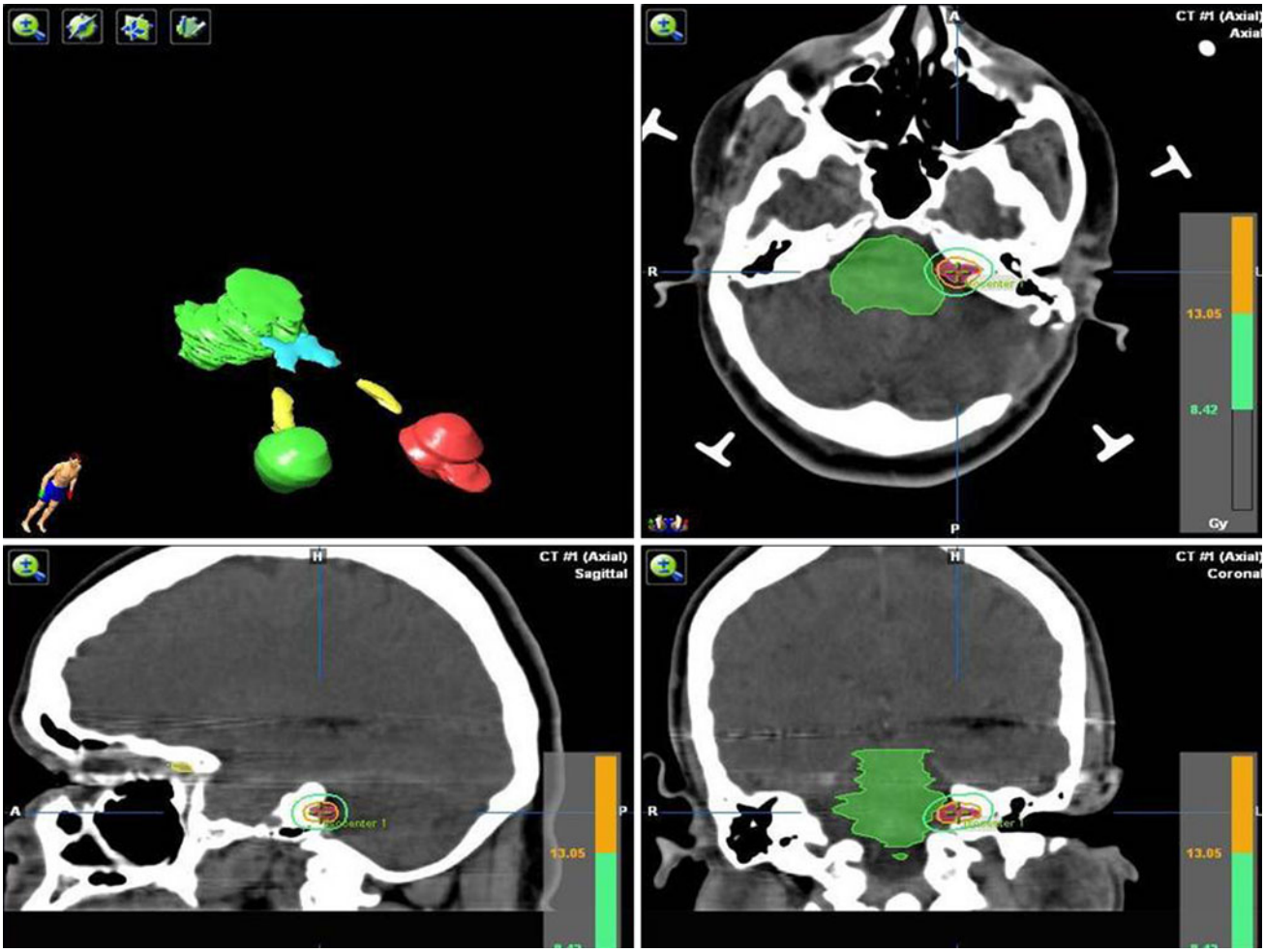

Fig. 1 CT scan images showing dose distribution of AN patient planned with LA-based system (BrainLAB)

Tumour volume (CTV) ranged from 0.4 to 2.1 cc, and prescribed dose between 13 and 15 Gy in single fraction. The isodose line at which dose was prescribed was 77–85% in the BrainLAB system and 85–90% in the CyberKnife system. The conformity index was 0.45–0.67 and 0.45–0.62 with the BrainLAB and CyberKnife system, respectively. The range of mean dose to cochlea was 6–8.1 Gy and 4.8–6.2 Gy in BrainLAB and CyberKnife, respectively. The range of mean dose to mesial temporal lobe was 0.6–3.1 Gy and 2–3.6 Gy in BrainLAB and CyberKnife, respectively.

Comparison between BrainLAB and CyberKnife

Comparison of the dose distribution in AN patients planned with the BrainLAB and CyberKnife systems is presented in Table 2. There were no significant differences in conformity index (0.53 versus 0.58; $P = 0.225$), maximum brainstem dose (4.9 versus 4.7 Gy; $P = 0.935$), 2.5-Gy volume (39.9 versus 52.3 cc; $P = 0.238$) or 5-Gy volume (11.8 versus 16.8 cc; $P = 0.129$) between BrainLAB and CyberKnife system plans. However, there were statistically significant differences in OAR doses, such as mean cochlear dose (6.9 versus 5.4 Gy; $P = 0.001$), mean mesial temporal dose (2.6 versus 1.7 Gy; $P = 0.07$) and high-dose (10 Gy) volume (3.2 versus 5.2 cc; $P = 0.017$). These results suggest that conformity index and low-volume doses were similar in the two planning systems. However, doses to OARs (cochlea and mesial temporal lobe) were significantly lower with the CyberKnife planning system.

Discussion

Long-term results of RS treatment in AN are encouraging. At 20-year follow-up, the clinico-radiological control rate was more than 90% and more than 70% of patients had stable or improved hearing function [4–7, 18, 19]. Apart from hearing function preservation, it is imperative to preserve neurocognitive function, especially in young patients with AN. Radiotherapy treatment is thought to

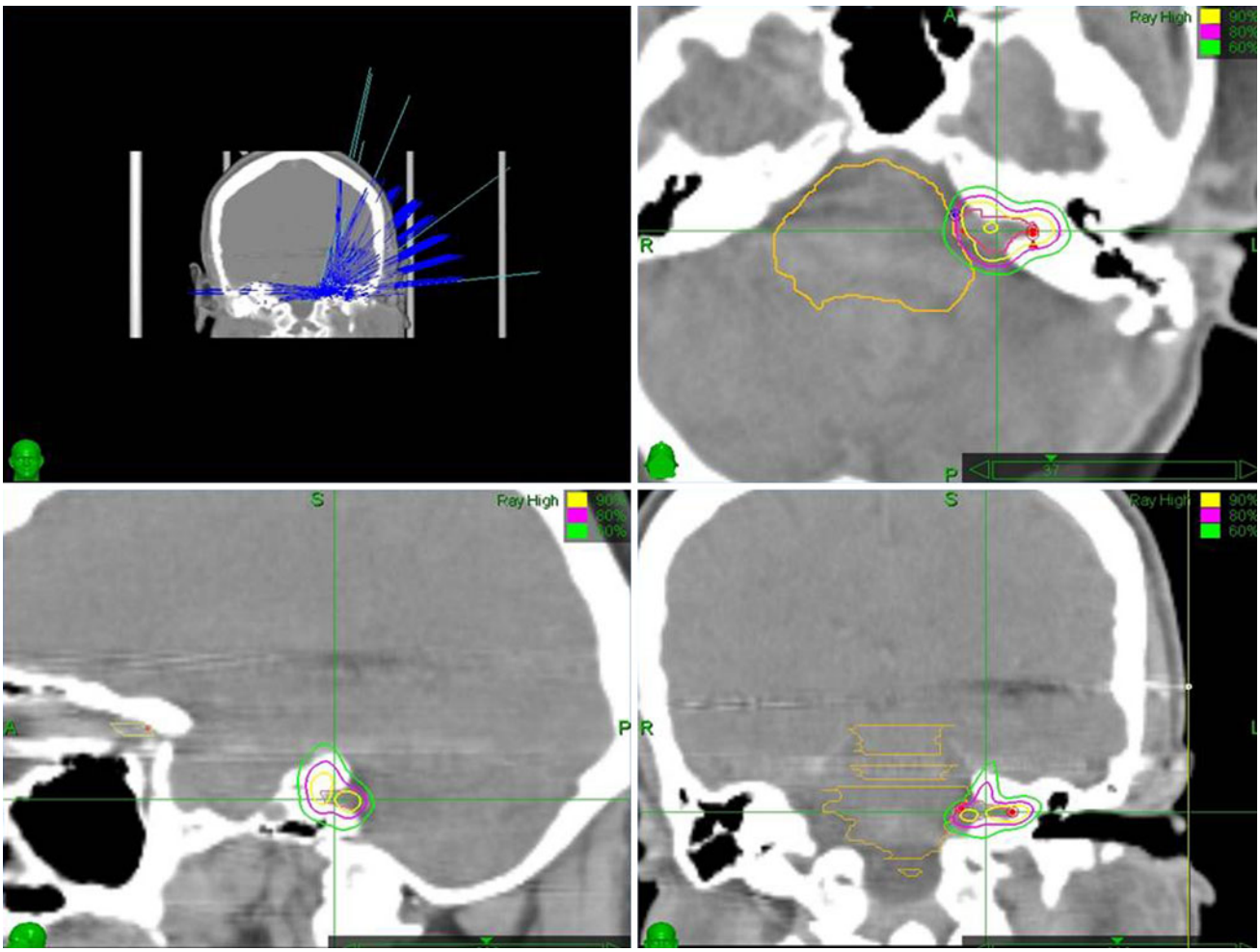

Fig. 2 CT scan images showing dose distribution of AN patient planned Robotic radiosurgery (CyberKnife) system

Table 1 Dosimetric parameters of AN patients treated with both LA-based (BrainLAB) and robotic RS system (CyberKnife) ($n = 7$)

Pt. sr. no.			Prescribed isodose (%)		Conformity index (CI)		Mean dose to cochlea (Gy)		Mean dose to mesial temporal lobe (Gy)	
	CTV (cc)	Dose prescribed (Gy)	LA based	Robotic	Robotic	LA based	Robotic	LA based	Robotic	LA based
1	0.78	14	77	88	0.6	0.62	6.2	8.1	1.8	2.6
2	1.7	13.5	80	85	0.45	0.47	5.8	7.1	2.8	3.6
3	3.1	13.5	80	85	0.62	0.52	5.2	6.8	3.1	3.6
4	0.4	14.5	80	85	0.64	0.53	5.1	6.5	0.6	2
5	0.74	13.5	80	88	0.67	0.62	4.8	6.2	1.5	2.8
6	2.1	13	85	85	0.58	0.50	5.9	7.5	1.3	3
7	0.3	15	82	90	0.5	0.45	4.8	6	0.6	1.1

Pt patient, *CTV* clinical target volume (cc), *TV* treated volume, *PTV* planning target volume, *CI* TV/PTV, *LA based* BrainLAB system, *Robotic* CyberKnife system

cause impairment of neurocognitive function [16]. However, in literature, neurocognitive function evaluation is not appropriately described in patients treated with RS. Recent prospective study in benign and low-grade brain tumour patients treated with stereotactic radiotherapy showed correlation between dose to left temporal lobe and

Table 2 Dosimetric comparison of LA-based and robotic RS system (mean ± standard deviation, SD)

	LA-based system	Robotic radiosurgery system	*P*-value[a]
CI	0.53 ± 0.06	0.58 ± 0.07	0.225
10-Gy volume (cc)	5.2 ± 1.6	3.2 ± 1.1	0.017
5-Gy volume (cc)	11.8 ± 4.9	16.8 ± 6.2	0.129
2.5-Gy volume (cc)	39.9 ± 17.2	52.3 ± 19.8	0.238
Max. dose brainstem (Gy)	4.9 ± 3.1	4.7 ± 2.6	0.935
Mean cochlea dose (Gy)	6.9 ± 0.7	5.4 ± 0.6	0.001
Mean mesial temporal lobe dose (Gy)	2.6 ± 0.9	1.7 ± 0.9	0.07

LA-based system BrainLAB, *Robotic system* CyberKnife

[a] Unpaired *t*-test

Table 3 Comparison between LA-based and robotic RS system

	LA-based system	Robotic radiosurgery
Beams	Usually 5–9	Usually >100
High-dose region	Spillage	Sharp dose gradient
Low-dose region	Spillage	Spillage
Treatment time	30 min	30 min
PTV margin	2 mm	0–1 mm
Conformity	Lesser	Higher
Planning method	Forward planning	Inverse planning
Treatment delivery accuracy	–	Higher
Intra-fraction movement correction	Not possible	Possible
Immobilization device	Rigid frame	Thermoplastic mask
Cost	Less	More

LA-based system BrainLAB, *Robotic system* CyberKnife

significant IQ function deterioration [17]. This study showed that patients receiving more than 43 Gy dose (2 Gy per fraction) to more than 50% volume of left temporal lobe had significant (more than 10% decline) IQ function deterioration at post-radiation-therapy 2-year follow-up evaluation. The age of patients in this study was below 25 years. A large proportion of AN patients are adolescent or young adults (below 25 years), and similar IQ function parameters are applicable. Nevertheless, there is no such prospective study for RS treatment correlating dose to temporal lobe and IQ function deterioration. It seems that RS treatment with mean dose of more than 6 Gy to left temporal lobe has detrimental effect on neurocognitive function [21–23]. It is now assumed that the hippocampus/mesial temporal lobe region is the critical structure for maintenance of neurocognitive function [21]. Hence, sparing of mesial temporal lobe may preserve long-term neurocognitive function.

GammaKnife is the gold-standard RS system [8, 9]. In the last few decades, LA-based RS systems such as BrainLAB have been used [24]. The LA-based RS system (BrainLAB) uses X-rays, a single isocentre, micro-multileaf collimators (MLCs) and forward planning, and is a more patient-friendly treatment approach [24]. Fractionated RS is also possible in larger tumours with use of a relocatable frame. However, the LA-based RS system usually requires a 1–2 mm PTV margin for isocentric inaccuracy determined by Ltuz test [25]. The CyberKnife system is a unique modern RS system with precise spatial definition of the target, steep fall-off of absorbed dose at the edges of the target volume owing to multiple non-coplanar pencil beam arrangements, no PTV margin, 'dose painting' and multiple isocentres [26]. CyberKnife does not require use of a rigid frame; nevertheless, treatment delivery accuracy is comparable to GammaKnife (Table 3).

In our dosimetric study, the conformity index was similar with both the BrainLAB and CyberKnife RS systems. Our plan evaluation criteria proposed to keep the target coverage similar (95% of the target required to be covered with prescribed isodose line). Keeping the same target coverage, the dose to critical structures was evaluated. Cochlear dose was significantly lower with CyberKnife. Permanent damage of cochlear hair cells (cells responsible for hearing) is radiation dose dependent, hence lesser dose to cochlea will increase the probability of hearing function preservation [18, 19]. Mean dose to mesial temporal lobe is significantly lower with robotic RS. This suggests that treatment with CyberKnife will deliver lower dose to both cochlea and mesial temporal lobe, hence with higher possibility of preserving both hearing and neurocognitive function. The present study is unique in this aspect of postulated reduction in toxicities after treatment with robotic RS. Nevertheless, dosimetric superiority of CyberKnife should ideally be evaluated in prospective randomized clinical settings with long-term follow-up. In the present study, PTV margin (2 mm) was given during planning in both systems. The CyberKnife system has higher accuracy, and such a large PTV margin is not mandated in actual treatment. (In CyberKnife treatment, PTV margin is usually 0–1 mm.) In smaller target volume, owing to the lack of PTV margin, the benefit of CyberKnife will be multiplied many fold [26].

AN is an uncommon benign tumour, mainly occurring in adolescents and with high cure rate; hence, the implications of neurocognitive function preservation are of paramount importance. However, it is unlikely that in the near future any prospective clinical study will be conducted in view of

the low patient numbers, requirement for long-term follow-up (at least 10 years) for any conclusive outcome and robustness of conducting a comprehensive prospective neurocognitive function evaluation study [16, 27]. We need to be speculative in this aspect, and dosimetric studies with supportive evidence from prospective studies will decide future treatment paradigm.

In summary, AN patients planned with the CyberKnife system had better sparing of OARs (cochlea and mesial temporal lobe) compared with those planned with the BrainLAB system. Lower dose to these OARs may preserve better hearing and neurocognitive function. However, evaluation of dosimetric superiority of CyberKnife system should be substantiated with prospective long-term clinical studies.

Conflict of interest None.

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