Acta Neurochir
DOI 10.1007/s00701-011-0962-0

CASE REPORT

Deep brain stimulation and frameless stereotactic radiosurgery in the treatment of bilateral parkinsonian tremor: target selection and case report of two patients

Angelo Franzini · Marcello Marchetti · Lorenzo Brait · Ida Milanesi · Giuseppe Messina · Elisabetta Forapani · Giovanni Broggi · Laura Fariselli

Received: 4 November 2010 / Accepted: 31 January 2011

Abstract Considerable positive experience in functional radiosurgery has been reported since Leksell's first experience in 1951, but the development of frameless radiosurgery was been limited because of the difficulty of identifying invisible functional targets. In this paper we report on two cases of bilateral parkinsonian tremor successfully treated with DBS on one side and with frameless radiosurgery on the contralateral side. We focus on the methodology developed to define the three-dimensional target coordinates for frameless radiosurgery. Two patients suffering from a disabling upper-limb parkinsonian tremor underwent frameless radiosurgical thalamotomy. To accurately identify the treatment target the CT gantry was treated as a stereotactic frame; a rototranslation between the origin of the screen and the origin of the stereotactic atlas allowed us to obtain atlas-registered 3D coordinates of each point on the CT axial brain slices. Both patients achieved complete bilateral tremor control by unilateral radiosurgery and contralateral DBS. We developed a method for determining the 3D coordinates of a known functional target to treat with frameless radiosurgery. Based on the initial experiences, frameless radiosurgery appears to be an alternative treatment for Parkinsonian upper limb tremor in the presence of increased surgical risks for DBS placement.

Keywords Deep brain stimulation · Parkinson's disease · Stereotactics radiosurgery · Tremor · Cyberknife

A. Franzini · M. Marchetti · G. Messina (✉) · E. Forapani · G. Broggi
Department of Neurosurgery,
Fondazione IRCCS Istituto Neurologico C. Besta,
Via Celoria 11,
20133 Milan, Italy
e-mail: giusmex@gmail.com

M. Marchetti · I. Milanesi · L. Fariselli
Division of Radiotherapy,
Fondazione IRCCS Istituto Neurologico C. Besta,
Milan, Italy

L. Brait · G. Broggi · L. Fariselli
CyberKnife Center, Centro Diagnostico Italiano,
Milan, Italy

Introduction

Stereotactic lesioning of the thalamus and basal ganglia for treatment of tremor is a well-known procedure that, prior to the introduction of deep brain stimulation, or DBS, was usually achieved using stereotactic surgical procedures [16]. Considerable positive experience in functional radiosurgery using the gamma knife or linear accelerators has been reported since Leksell's first report in 1951 [4, 8, 11, 13, 14, 17–19, 21, 24–27].

The CyberKnife (CK, Accuray Inc., Sunnyvale, CA) allows effective frameless stereotactic radiosurgery of visible intracranial targets such as arteriovenous malformations, tumours, and trigeminal neuralgia [1–3, 7, 9, 23].

Radiosurgery on invisible targets to treat movement disorders and intractable pain is still the domain of frame-based procedures because of the need for a solid reference system registered to the anterior commissure-posterior commissure (AC-PC) line, which allows the use of stereotactic atlases. In this report we describe a mathematical method that uses atlas-derived stereotactic coordinates to perform radiosurgery of invisible targets with the frameless CyberKnife methodology. The methodology and long-term results in two consecutive patients are reported with particular regard to the future applications of frameless radiosurgical treatment of upper limb and hand tremor in elderly patients. No similar cases have been reported in the literature.

Methods

Two patients who had previously undergone successful DBS for parkinsonian tremor on one side developed a severe tremor on the contralateral, untreated side. Both patients had contraindications or considerable risk factors for a second DBS surgery on the side contralateral to the previous DBS implant. Their cases are detailed below.

CyberKnife radiosurgical procedure

The CK is a stereotactic, frameless, image-guided radiosurgery system capable of delivering non-isocentric radiation distributions to a target with submillimetric precision [1, 2, 6, 27].

It consists of a miniaturized, lightweight 6-MV LINAC coupled with a six-degree-of-freedom robotic arm. The robotic arm provides a large number of non-coplanar beam trajectories (over 1,200 trajectories for the G3 version). Image guidance is based on the match between digitally reconstructed radiographs (DRRs) of the skull and real-time digital radiographs acquired during the treatment. A CT center is defined in order to establish a stereotactic coordinate system. Two x-ray imaging devices positioned on either side of the patients and two corresponding amorphous silicon sensors provide an accurate 3D reconstruction of the cranial volume. The system dynamically and automatically adjusts the LINAC position in order to keep the skull position aligned to the treatment planning.

Target definition and stereotactic atlas registration of the CT images

During CT scanning it is critical that the patient's head remains in a fixed position in order to avoid movement artefacts. For the patients reported here, high-quality images were obtained by restraining the patient's head using a standard thermoplastic mask and acquiring the images very rapidly, always taking less than 40 s, with the CT equipment in our possession (Light Speed Ultra, General Electric, Fairfield, CT). Mild sedation may be necessary for some patients with head tremor. In more severe cases, in which body and/or head movements could prevent an optimal image acquisition, administration of a low dosage of Midazolam under anaesthesiological control is mandatory. If the head is immobile the CT gantry behaves like a solid reference system with fixed relationships to the brain structures. In other words the CT screen may be seen as a bidimensional stereotactic frame, and each pixel of the CT screen represents a discrete part of the brain identified by X lateral and Y anteroposterior coordinates in relation to the screen origin. The slice containing the anterior commissure (AC) is arbitrarily assigned to depth=0 (Z coordinate); the depth of each slice is calculated relative to this point (the slices are 1.25 mm thick). In this system we can calculate the AC X, Y, and Z coordinates (Z=0) and the coordinates of the posterior commissure (PC) where Z is the distance in mm from slice zero. In cases in which the AC and PC lie on the same slice, AC and PC Z coordinates are both equal to zero, and the calculations are easier. Finally, the values in pixels are converted into millimetres based on the matrix/FOV ratio of the CT screen. In other words the X and Y values of each pixel of the brain image on the CT screen are obtained, and Z is derived as the depth of the slice measured as the vertical distance from slice 0. Finally, we calculate the coordinates of the AC-PC midpoint, which is the origin of the stereotactic atlas, and a simple rototranslation between the origin of the screen and the origin of the stereotactic atlas allows us to obtain atlas-registered X, Y, and Z coordinates in millimetres of each point on the CT axial brain slices (Fig. 1).

Target coordinates of the Voa/Vop complex (X=+/−12 mm , Y=2 mm , Z=2 mm) derived from the stereotactic atlases registered to the midcommissural point are easily transposed onto the corresponding CT slice, and the target is drawn on the treatment planning system (Multiplan, Accuray Inc.). In other words, the roto-translation of the axes between the CT screen and the commissural system of the patient allows the use of atlas-derived stereotactic coordinates to make the invisible functional target visible. The CT images may be fused with MRI to obtain more details about the anatomical structures surrounding the estimated target.

High quality control of CT couch movements is of course mandatory for the above-described procedure, and possible undesired movements of the CT couch during the examination could affect the precision of the Z coordinate; even if the Voa/Vop complex is relatively close (slice+2 mm) to the slice containing the anterior commissure (slice 0), possible errors must be taken into account.

Dose definition

The aim of this procedure is to cause a lesion confined to the estimated target. The first patient was treated with a dose of 70 Gy to the 100% isodose line. Due to the lack of side effects and considering the small size of the obtained lesion, in the second case the dose was escalated to 90 Gy to the 100% isodose line.

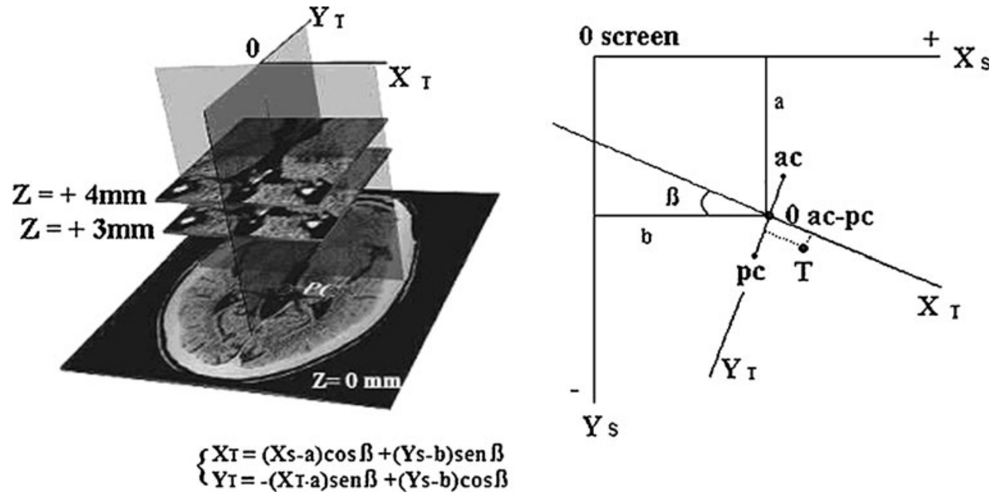

Fig. 1 Right: Schematic drawing of the CT slice sequences: the CT containing the AC-PC plane is considered Z=0 mm as in the stereotactic atlases. The origin of the bidimensional coordinate system (Xt, Yt) of each CT slice is the ac-pc midpoint (0). Left: Rototranslation between the CT screen coordinate system (Xs, Ys) and the ac-pc registered coordinate system of the patients (Xt, Yt) where the commissural line midpoint is the origin (0 ac-pc); beta represents the angle between the ac-pc line and the screen when the patient's head is rotated within the CT gantry. The algorithms that allow us to transform the screen coordinates (Xs, Ys) into stereotactic coordinates registered to the commissural system and vice versa (Xt, Yt) are seen at the bottom of the figure. The obtained coordinates are converted from pixels to millimetres and each point of the CT may be transposed to stereotactic atlases, and thus becomes visible. Conversely, any target may be transposed from the stereotactic atlas to the patient CT and utilised for CyberKnife lesioning

Case 1

The first patient is a 71-year-old man. Parkinsonian signs started at the age of 69, with rest and postural tremor of the right upper limb and subsequent major motor impairment of the right hand. He began levodopa treatment [levodopa equivalent daily dosage (LED) up to 400 mg] with improvement in akinesia but without a significant benefit for tremor control. One year later he began to complain of worsening of rest and postural tremor with further impairment of his capacity to manipulate common objects and severe difficulty in carrying out his daily living activities.

He came to our attention in September 2005. Upon observation, the patient had a typical tremorigenous parkinsonian picture with prevalence on the right hand side, four limb rigidity, and gait disturbance with a limited response of the tremor to dopaminergic treatment. The Unified Parkinson's Disease Rating Scale (UPDRS) motor score was 45 (see Table 1 for tremor items) [20, 21].

After neurological and neuroradiological investigations the patient underwent bilateral implantation of DBS electrodes within the VOA-VOP complex connected to two subclavicular implantable pulse generators (IPGs; Soletra Medtronic Inc., Minneapolis, MN). The patient showed a consistent improvement in tremor in both upper arms, maintained by high-frequency stimulation (185 Hz; 60 μs; 1.5 V). Unfortunately, because of a subgaleal infection, removal of the system became necessary on the left side, and tremor on the right side reappeared with the same intensity and characteristics as before the DBS implant. To restore the control of tremor on the right side, in January 2006 the patient, after signing an ad hoc informed consent, underwent CyberKnife radiosurgery for a left VOA-VOP thalamotomy using the target identification methodology described above. The

Table 1 Pre-/post-treatment scale scores (UPDRS, FTMTRS) and LED

Patient 1	Pre-cyberknife		Post-cyberknife		Patient 2	Pre-DBS STN sx		Pre- cyberknife		Post-cyberknife	
UPDRS motor score	45		34			33		26		18	
Tremor items	Dx	Sx	Dx	Sx		Dx	Sx	Dx	Sx	Dx	Sx
Trem. rest up. Limb	4	2	1	1		3	2	2	1	1	0
Trem. rest low. limb	1	1	1	1		2	1	1	2	0	1
Action trem.	3	2	1	1		3	2	0	1	0	1
LED	400		400			1,490		1,380		1180–1,500	
FTMTRS	94		27			69		–		12	

total dose was 70 Gy to the 100% isodose line. The treatment volume was 22.5 mm³, and a 5-mm collimator was used.

One month after treatment excellent tremor control was achieved on the right side. At 41 months' follow-up, tremor control was still preserved and the patient's independence maintained. Because the major source of this patient's disability was tremor, we administered the Fahn, Tolosa, Marin Tremor Rating Scale (FTMTRS) before and after the radiosurgical procedure to evaluate clinical and functional changes in the patient's life. This scale assesses specifically and accurately the severity, loss of function, and disability related to tremor [21]. Tremor items measured with the FTMTRS decreased from 94 preoperatively to 27 postoperatively (percentage reduction 71.3%). LED intake was left unchanged (400 mg) to control the non-tremor Parkinsonian symptoms.

A few days after CyberKnife treatment a brain MRI (performed with a 0.5-T apparatus because of the presence of a contralateral DBS electrode) revealed a hypointense spot on T2-weighted images (nearly matching the imaging expression of the removed electrode). Three months later, an MRI control showed a new small hyperintense volume on T2-weighted images within the thalamus. We believe this to be the correlate on MRI of the efficacy of radiosurgery treatment. The last available MRI, at 1-year follow-up, confirmed the presence of this hyperintense volume without further evolution.

Case 2

The second patient first came to our attention in 2005 when he was 73 years old. He had suffered from Parkinson's disease since 1998. Initially, the patient presented a typical tremorigenous parkinsonian picture, mainly affecting the right arm. The UPDRS motor score at the time of the first presentation was 33, and the total sum of tremor items was 15 (see Table 1). The LED was 1,490 mg. Medical therapy failed to control his symptoms, so in July 2005 the patient underwent implantation of a DBS electrode within the VOA-VOP complex. Postoperatively the patient improved both in tremor and akinesia. His UPDRS motor score was 26, the total sum of tremor items was 7, and the LED was reduced to 1,380 mg.

In September 2007 the patient returned to our attention because of worsening of the tremor on the untreated side. He had become a poor surgical candidate because of a chronic vascular disease, and so a radiosurgical approach was considered. In January 2008 a radiosurgical lesioning of the right VOA-VOP was planned. The total dose was 90 Gy to the 100% isodose line administered in a single fraction with a 5-mm collimator. The treatment volume was 12 mm³.

Immediately after the treatment the patient reported a significant improvement in his left upper limb tremor. Eighteen months after radiosurgery he showed very good tremor control of the left limbs. His UPDRS motor score was 18, the total sum of tremor items was 3, and the LED was 1,180 mg. He regained independence in most of his daily living activities, as shown by the variation in FTMTRS scores (pre-treatment 69 vs. post-treatment 12, a reduction of 82.6%).

Two months later the patient had a moderate clinical worsening as his non-tremorigenous symptoms advanced. This required a therapy adjustment (LED 1,500 mg), while the tremor control persisted. No side effects were observed. At 6 months' follow-up, no lesion was detected on MRI, but at 19 months, MRI showed the appearance of a consistent lesion in the irradiated area (Fig. 2). The lesion was characterised by central necrosis, peripheral-edge contrast enhancement, and perilesional oedema. Fusion of the treatment planning images with this postoperative MRI confirmed the correct localisation of the lesion. The lesion was still evident 2 months later, morphologically and dimensionally unchanged, and did not show any clinical correlate.

Discussion

The methodology we used to plan CyberKnife procedures on "invisible" functional targets is based on the concept that the CT gantry can be viewed as a stereotactic frame and the mathematical roto-translation (manually performed or embedded in software programs) allows the transfer of targets from any stereotactic atlases that locate structures relative to the commissural system (e.g., the Talairach, Schaltenbrand, and May atlases all have this property). An absolute requirement for stereotactic accuracy is that the head must be immobile during the CT acquisition, which on our CT scan equipment took less than 40 s.

In this preliminary experience we chose a safe target for the radiosurgical lesion; the VOA is anterior and medial to the posterior limb of the internal capsule (Fig. 3). The capsule itself can be transposed from the stereotactic atlas to the CyberKnife CT plan according to its known relationships to the commissural reference system. The choice of VOA (12 mm lateral to the midline, 2 mm anterior to the midcommissural point, and 2 mm superior to the commissural plane) was intended to lessen the risk of anatomical variability in these patients. In fact, this target is relatively far from the motor fibres running in the posterior limb of the internal capsule and far from other "eloquent" nuclei.

The lack of intraoperative neurophysiological confirmation of the target (e.g., microrecording, microstimulation, and macrostimulation) is the main limitation of the described procedure. In fact, nowadays, this procedure cannot be applied when the functional target is affected by individual anatomic variability (i.e., subthalamic nucleus, STN). Image fusion between CT (with the marked target)

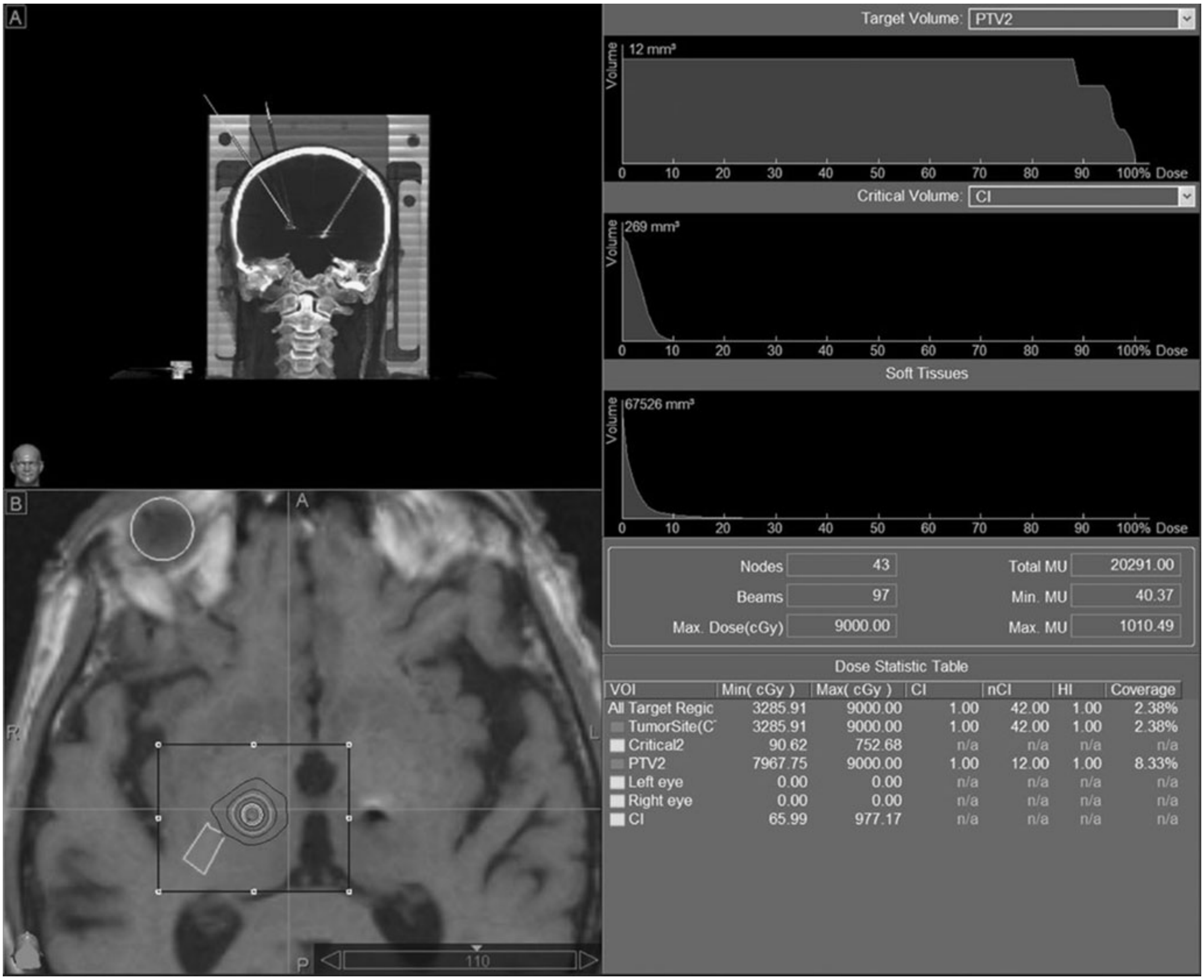

Fig. 2 Patient's MRI merged with the planned treatment. The 18-month post-treatment MRI shows a lesion surrounded by oedema overlapping the 10% isodose line

and MRI may be utilised to refine the targeting procedures with more anatomic individual details. In the cases reported here, however, MRI image fusion did not modify the original CT plans.

This procedure resulted in tremor control in the two cases presented, with significant improvement in daily living activities and quality of life, thus restoring or maintaining the patients' independence. From a clinical point of view this report describes an unconventional therapeutic option, the combination of DBS with radiosurgical lesioning to treat bilateral parkinsonian tremor in fragile patients in whom double or staged DBS implantation carries a double surgical risk [5, 12, 22]. We observed that neither patient complained of speech impairment after the procedure. Of course, two patients are not enough to state that the risk of speech impairment is lower with this "hybrid" procedure versus bilateral DBS, but because successful bilateral thalamic lesions often cause speech difficulty, the absence of speech impairment observed here is encouraging.

If compared to frame-based radiosurgery, frameless radiosurgery is a pain-free procedure that offers the advantage of better patient compliance, avoiding local anaesthesia and the discomfort of wearing the frame for what can be a long time period.

Moreover, the reported patients were over 70 years old, and the risks of DBS including skin erosion and recurrent infections cannot be underemphasised in aged patients.

Anyway, the aim of this report is not to demonstrate that frameless is preferable to frame-based radiosurgery , but instead to demonstrate the safety and the feasibility of frameless functional radiosurgery in the treatment of drug-refractory tremor.

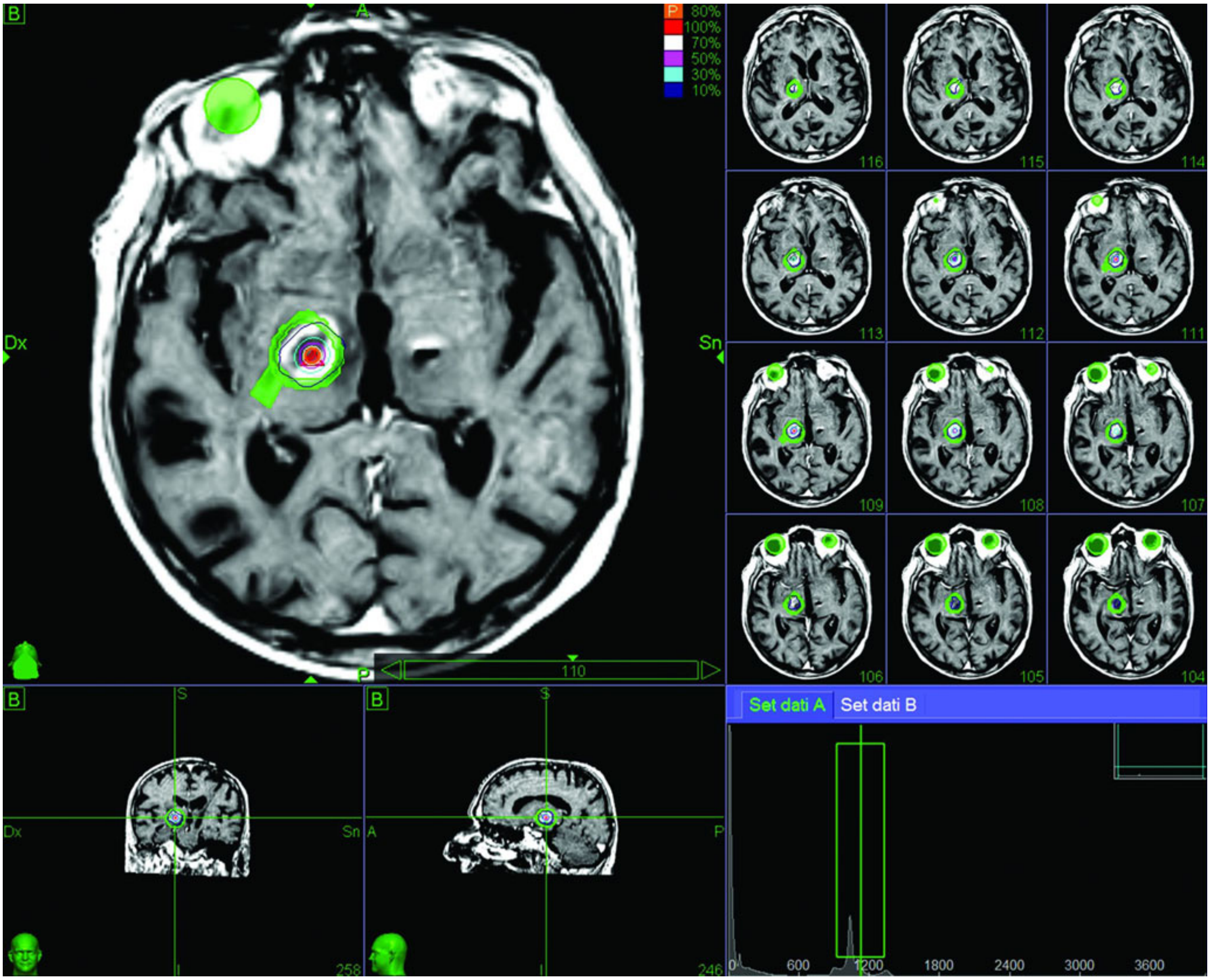

Fig. 3 Patient 2 treatment planning with the relative dose volume histograms. In our preliminary experience we chose a safe target for radiosurgical thalamotomy (VOA is anterior and medial to the posterior limb of the internal capsule). The capsule itself is contoured; it can be transposed from a stereotactic atlas

With just two patients treated, we can only speculate on the appropriate radiation dose for this procedure. The literature on functional radiosurgery shows that a mean dosage of 140 Gy has been used, but we used lower doses in both patients (70 and 90 Gy) [8, 10, 15, 25].

Both patients showed long-term control of tremor, but postoperative MRI and CT only showed minimal changes at the target in the 70-Gy case and a consistent lesion for the 90-Gy case. CyberKnife radiosurgery has been shown to be effective for trigeminal neuralgia when a maximum dose of about 75 Gy is delivered to the fifth nerve, so we can argue that this dosage is not ineffective on nervous tissue [3].

The absence of complications in the first patient, treated with up to 70 Gy, and the high doses found in published reports encouraged us to deliver a somewhat higher dose (90 Gy) to the second patient. A large lesion appeared at 19 months post-treatment at the estimated target, with surrounding oedema. Even if this lesion was clinically uneventful (mostly because of the target location), it suggests that lower doses should be delivered in elderly patients, particularly in the presence of neurovascular diffuse changes.

In our opinion, the size of the expected radiosurgical lesion cannot be accurately predicted, expecially in aged parkinsonian patients where locoregional vascular factors play a major role in the mechanisms and phenomenology of the actual size but, as was the case for trigeminal neuralgia, a standard dose needs to be determined statistically on a larger series of patients.

Long-term control of parkinsonian tremor in these patients was obtained. This may suggest that radiosensitivity is greater in patients of advanced age, but it is also possible that DBS and the radiosurgery lesion interacted. There may have been reciprocal strengthening between VOA DBS and VOA lesion. In fact, turning off the IPG resulted in recurrence of tremor on both sides, and tremor on the side contralateral to DBS reappeared earlier and was much more intense. Turning on the IPG restored the control of tremor on both sides in few minutes.

Conclusions

The interest in radiosurgical procedures for functional disorders may be renewed in light of the frameless, one-stage procedure reported here. At this point the procedure should be limited to elderly patients with a previous DBS implant who are at increased risk for undergoing a contralateral implant because of previous infection or age. In the future, if dosage issues have been resolved, this application may result in a new non-invasive tool to treat other diseases such as cancer pain (CM thalamotomy), tremor in multiple sclerosis patients (VOA-VOP thalamotomy), or spasticity (dentatotomy).

Aknowledgements The authors wish to thank Dr. David W. Schaal, Accuray Incorporated, for technical and editorial assistance.

Disclosure The authors have no financial interest in the instruments presented in this manuscript.

Conflicts of interest None.

Reference

1. Adler JR Jr, Chang SD, Murphy MJ, Doty J, Jeis P, Hancock SL (1997) The Cyberknife: a frameless robotic system for radiosurgery. Stereotact Funct Neurosurg 69:124–128
2. Adler JR Jr, Murphy MJ, Chang SD, Hancock SL (1999) Image guided robotic radiosurgery. Neurosurgery 44:1299–1307
3. Adler JR Jr, Bower R, Gupta G, Lim M, Efron A, Gibbs IC, Chang SD, Soltys SG (2009) Nonisocentric radiosurgical rhizotomy for trigeminal neuralgia. Neurosurgery 64(2 Suppl):A84–A90
4. Alvarez L, Macias R, Lopez G, Alvarez E, Pavon N, Rodriguez-Oroz MC, Juncos JL, Maragoto C, Guridi J, Litvan I, Tolosa ES, Koller W, Vitek J, DeLong MR, Obeso JA (2005) Bilateral subthalamotomy in Parkinson's disease: initial and long-term response. Brain 128(Pt 3):570–583
5. Benabid AL, Chabardes S, Mitrofanis J, Pollak P (2009) Deep brain stimulation of the subthalamic nucleus for the treatment of Parkinson's disease. Lancet Neurol 8(1):67–81
6. Chang SD, Main W, Martin DP, Gibbs IC, Heilbrun MP (2003) An analysis of the accuracy of the Cyberknife: a robotic frameless stereotactic radiosurgery system. Neurosurgery 52:140–147
7. Colombo F, Cavedon C, Casentini L, Francescon P, Causin F, Pinnna V (2009) Early results of CyberKnife radiosurgery for arteriovenous malformations. J Neurosurg 111:807–819
8. Duma CM, Jaques DB, Kopyov OV, Mark R, Copcutt B, Farokhi H (1998) Gamma knife radiosurgery for thalamotomy in parkinsonian tremor: a five years experience. J Neurosurg 88:1044–1049
9. Fariselli L, Marras C, De Santis M, Marchetti M, Milanesi I, Broggi G (2009) CyberKnife radiosurgery as a first treatment for idiopathic trigeminal neuralgia. Neurosurgery 64(2 Suppl):A96–A101
10. Friedman DP, Goldman HW, Flanders AE, Gollomp SM, Curran WJ Jr (1999) Stereotactic radiosurgical pallidotomy and thalamotomy with the gamma knife: MR imaging findings with clinical correlation–preliminary experience. Radiology 212(1):143–150
11. Frighetto L, De Salles A, Wallace R, Ford J, Selch M, Cabatan-Awang C, Solberg T (2004) Linear accelerator thalamotomy. Surg Neurol 62 (2):106–113, discussion 113-4
12. Hariz MI, Rehncrona S, Quinn NP et al. (2008) Multicentre advanced Parkinson's disease deep brain stimulation group. Multicenter study on deep brain stimulation in Parkinson's disease: an independent assessment of reported adverse events at 4 years. Mov Disord 23(3):416–21
13. Leksell L (1951) The stereotaxic method and radiosurgery of the brain. Acta Chir Scand 102(4):316–319
14. Lindquist C, Kihlstrom L, Hellstrand E (1991) Functional neurosurgery–a future for the gamma knife? Stereotact Funct Neurosurg 57(1–2):72–81
15. Mathieu D, Kondziolka D, Niranjan A, Flickinger J, Lunsford LD (2007) Gamma knife thalamotomy for multiple sclerosis tremor. Surg Neurol 68(4):394–399
16. Oh MY, Hodaie M, Kim SH, Alkhani A, Lang AE, Lozano AM (2001) Deep brain stimulator electrodes used for lesioning: proof of principle. Neurosurgery 49(2):363–367
17. Ohye C (2006) From selective thalamotomy with microrecording to gamma thalamotomy for movement disorders. Stereotact Funct Neurosurg 84(4):155–161
18. Ohye C, Shibazaki T, Ishihara J, Zhang J (2000) Evaluation of gamma thalamotomy for parkinsonian and other tremors: survival of neurons adjacent to the thalamic lesion after gamma thalamotomy. J Neurosurg 93(Suppl 3):120–127
19. Ohye C, Shibazaki T, Sato S (2005) Gamma knife thalamotomy for movement disorders: evaluation of the thalamic lesion and clinical results. J Neurosurg 102(Suppl):234–240
20. Stacy MA, Elble RJ, Ondo WG, Wu SC, Hulihan J (2007) Assessment of interrater and intrarater reliability of the Fahn-Tolosa-Marin Tremor Rating Scale in essential tremor. Mov Disord 22(6):833–838
21. Svennilson E, Torvik A, Lowe R, Leksell L (1960) Treatment of parkinsonism by stereotactic thermolesions in the pallidal region. A clinical evaluation of 81 cases. Acta Psychiatr Scand 35:358–377
22. Tripoliti E, Zrinzo L, Martinez-Torres I, Tisch S, Frost E, Borrell E, Hariz MI, Limousin P (2008) Effects of contact location and voltage amplitude on speech and movement in bilateral subthalamic nucleus deep brain stimulation. Mov Disord 23(16):2377–2383
23. Villavicencio AT, Lim M, Burneikiene S, Romanelli P, Adler JR, McNeely L, Chang SD, Fariselli L, McIntyre M, Bower R, Broggi G, Thramann JJ (2008) Cyberknife radiosurgery for trigeminal neuralgia treatment: a preliminary multicenter experience. Neurosurgery 62 (3):647–655
24. Young RF, Vermeulen SS, Grimm P, Posewitz AE, Jacques DB, Rand RW, Copcutt BG (1995) Gamma Knife thalamotomy for the treatment of persistent pain. Stereotact Funct Neurosurg 64(Suppl 1):172–181
25. Young RF, Shumway-Cook A, Vermeulen SS, Grimm P, Blasko J, Posewitz A, Burkhart WA, Goiney RC (1998) Gamma knife radiosurgery as a lesioning technique in movement disorder surgery. J Neurosurg 89(2):183–193
26. Young RF, Jacques S, Mark R, Kopyov O, Copcutt B, Posewitz A, Li F (2000) Gamma knife thalamotomy for treatment of tremor: long-term results. J Neurosurg 93(Suppl 3):128–135
27. Yu C, Main W, Taylor D, Kuduvalli G, Apuzzo LJ, Adler JR, Wang MY (2004) An anthropomorphic phantom study of the accuracy of cyberknife radiosurgery. Neurosurgery 55(5):1138–1149