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ORIGINAL ARTICLE - NEUROSURGICAL TECHNIQUE EVALUATION

Impact of the skull contour definition on Leksell Gamma Knife® Icon™ radiosurgery treatment planning

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Abstract

Introduction The Gamma Knife® planning software (TMR 10, Elekta Instruments, AB, Sweden) affords two ways of defining the skull volume, the "historical" one using manual measurements (still perform in some centers) and the new one using image-based skull contours. Our objective was to assess the potential variation of the dose delivery calculation using consecutively in the same patients the two above-mentioned techniques.

Materials and methods We included in this self-case-control study, 50 patients, treated with GKRS between July 2016 and January 2017 in Lausanne University Hospital, Switzerland, distributed among four groups: convexity targets ($n = 18$), deep-seated targets ($n = 13$), vestibular schwannomas ($n = 11$), and trigeminal neuralgias ($n = 8$). Each planning was performed consecutively with the 2 skull definition techniques. For each treatment, we recorded the beam-on time (min), target volume coverage (%), prescription isodose volume (cm^3), and maximal dose (Gy) to the nearest organ at risk if relevant, according to each of the 2 skull definition techniques. The image-based contours were performed using CT scan segmentation, based upon a standardized windowing for all patients.

Results The median difference in beam-on time between manual measures and image-based contouring was + 0.45 min (IQR; 0.2–0.6) and was statistically significant ($p < 0.0001$), corresponding to an increase of 1.28% beam-on time per treatment, when using image-based contouring. The target location was not associated with beam-on time variation ($p = 0.15$). Regarding target volume coverage ($p = 0.13$), prescription isodose volume ($p = 0.2$), and maximal dose to organs at risk ($p = 0.85$), no statistical difference was reported between the two skull contour definition techniques.

Conclusion The beam-on time significantly increased using image-based contouring, resulting in an increase of the total dose delivery per treatment with the new TMR 10 algorithm. Other dosimetric parameters did not differ significantly. This raises the question of other potential impacts. One is potential dose modulation that should be performed as an adjustment to new techniques developments. The second is how this changes the biologically equivalent dose per case, as related to an increased beam on time, delivered dose, etc., and how this potentially changes the radiobiological effects of GKRS in an individual patient.

Keywords Gamma Knife® Icon™ · Skull definition · Manual skull scaling · Image-based contours · Dosimetry · Radiosurgery · Single fraction

This article is part of the Topical Collection on *Neurosurgical technique evaluation*

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Introduction

Stereotactic radiosurgery (SRS) with Leksell Gamma Knife® (LGK, Elekta Instruments, AB, Sweden) is now part of the neurosurgical armamentarium for more than five decades [4, 5]. Through this time frame, technical advances, including the common use of high-resolution MRI and CT scan, improved target definition and accuracy of LGK treatment planning [7]. Technical developments, including the advanced automatized procedure since LGK Perfexion™, have also decreased the morbidity of several procedures, such as, for example, in the case of benign tumors, like vestibular schwannomas, where the risk of facial palsy virtually became zero [9].

Skull contour definition is one of the crucial steps of the dosimetry planning, as it is used by the algorithm to calculate beam attenuation when passing from outside to inside the patient's head.

The Gamma Knife planning software (TMR 10, Elekta Instruments, AB, Sweden) afford two ways of defining the skull volume, the "historical" one using manual measurements (still perform in some centers) and the new one using image-based skull contours. Our objective was to compare the potential variation of the treatment parameters between the two above-mentioned techniques.

The new algorithm allowing image-based skull contour definition has been introduced in the last available workflow of the treatment planning. The former was developed as an alternative to manual skull contour definition, which uses a dedicated plastic spherical skull scaling instrument to be placed on the stereotactic frame, and a ruler to define the skull contour in an individual patient. As the skull contour definition using image-based contours is supposed to be more accurate, we assumed it should be preferred for dosimetry planning [13]. However, little data is available related to this topic and more precisely on how this change in skull definition may affect the dose delivered and its further radiobiological consequences. Indeed, as clinical data gathered for more than 40 years are based on dose delivery calculated using the manual skull scaling instrument, switching to the image-based technique could potentially impact the delivered radiation dose, while eventually affecting both the tumor control and the related morbidity after SRS [1].

The present study evaluated the impact of the two possible skull volume definitions on the final dosimetry while using LGK Icon™ and the last TMR 10 algorithm. This is the first attempt to evaluate treatment beam on time with further eventual radiobiological implications after a period of more than 40 years constantly using the manual measurements. In this context, one could assume that the dose plan would be identical between manual and CT-based measurements. Here, our main research focus was a potential difference in beam on time, in the light of the recently published studies on this parameter using GKRS [10, 11].

Methods

Study design and radiosurgical planning workflow

Fifty LGK radiosurgical treatments were included in this prospective, self-controlled, case series, performed between July 2016 and January 2017 at Lausanne University Hospital. As a radiological and radiosurgical file review, with no specific patient's identification details, no prior approval from the ethical committee was needed.

All treatments were performed using the Leksell G Frame (Elekta AB, Stockholm, Sweden), as the fixation system. The patients benefited from a brain CT scan and 1.5T MRI (both Siemens AG, Erlangen, Germany). The treated targets were consecutive cases from four groups of patients to assess potential dosimetry delivery variations: convexity targets (n = 18), parenchymal deep-seated targets (n = 13), vestibular schwannomas (n = 11), and trigeminal neuralgias (n = 8); other indications or locations treated during the same period of time were not included in the study. Of note, the first three groups represent targets with volume delineation, while the fourth is a functional procedure, with the dose being prescribed to one point.

For each treatment, we recorded the beam-on time (min), target volume coverage (TVC, in mm^3), prescription isodose volume (PIV, in mm^3), the matrix (called "target" in the latest versions of Leksell GammaPlan®) width (in mm), and the maximal dose (in Gy) to the nearest organ at risk (OAR) if relevant (e.g., cochlea in vestibular schwannoma), according to each of the two skull contour definition techniques. Table 1 depicts the type of treated indications and the main characteristics of the radiosurgical planning. The manual measurements were performed using the dedicated plastic skull scaling instrument (24 measures), as standardly performed in the LGK user community (Fig. 1). In the last TMR 10 algorithm, it has been newly made available another skull measurement methodology. The former uses skull contours by direct CT scan segmentation, based upon a standardized windowing for all patients (Fig. 2). The dose plan of each patient was performed consecutively with both skull contour methods. Each patient was his own case-control. The image-based skull contour method was eventually the basis for GKRS treatment.

The treatments were planned with Leksell GammaPlan® 11.0.3 and the dose calculation algorithm TMR 10 (Elekta Instruments, AB, Sweden). The delivery unit was a LGK Icon™, calibrated in June 2016, with a mean dose rate of 3.71 Gy/min during the study period [12].

Of note, the radiosurgical dose planning remained identical while comparing the former manual skull measurements versus the newly available CT-based measurements, for the individual patient.

Table 1 Targets treated and the respective dosimetry parameters

Pathologies (number treated)	Target Volume (mean, mm^3)	Prescribed dose (mean, Gy)	Peripheral isodose (mean, %)	Number of shots	Matrix Width (mean, mm)
Meningioma (13)	2426	13.9	50	13	39
Vestibular Schwannoma (11, Koos grade: I:1, II:5, III:5)	2075	12	50	9.8	35
Metastasis (10)	4150	20	50	10	34
Trigeminal neuralgia (8)	–	88	100	1	33
Glioma (3)	748	18	50	6	34.5
AVM (2)	1604	22	55	7.5	43.5
Paraganglioma (1)	2371	16	50	15	31
Hemangioblastoma (1)	808	16	50	15	31
Schwannoma of V (1)	169	12	50	4	24

Eighteen targets were in the convexity group, and 13 in the deep-seated group. Vestibular schwannoma and trigeminal neuralgia constituted two independent groups

Statistical analyses

Quantitative variables were expressed as the median (interquartile range), and categorical variables were expressed as numbers (percentage). Intra-patients' comparisons according to the two skull definition techniques (manual scaling vs. image-based surfacing) were performed using Wilcoxon's signed-rank tests. Difference in beam-on time between the two skull definition techniques (beam-on time variation) was compared between the four groups using the Kruskal-Wallis test. Association of beam-on time variation with prescribed dose, target volume, and matrix width were studied by calculating the Spearman's rank correlation coefficients. Statistical testing was performed at the two-tailed α level of 0.05. Data were analyzed using the SAS software version 9.4 (SAS Institute, Cary, NC).

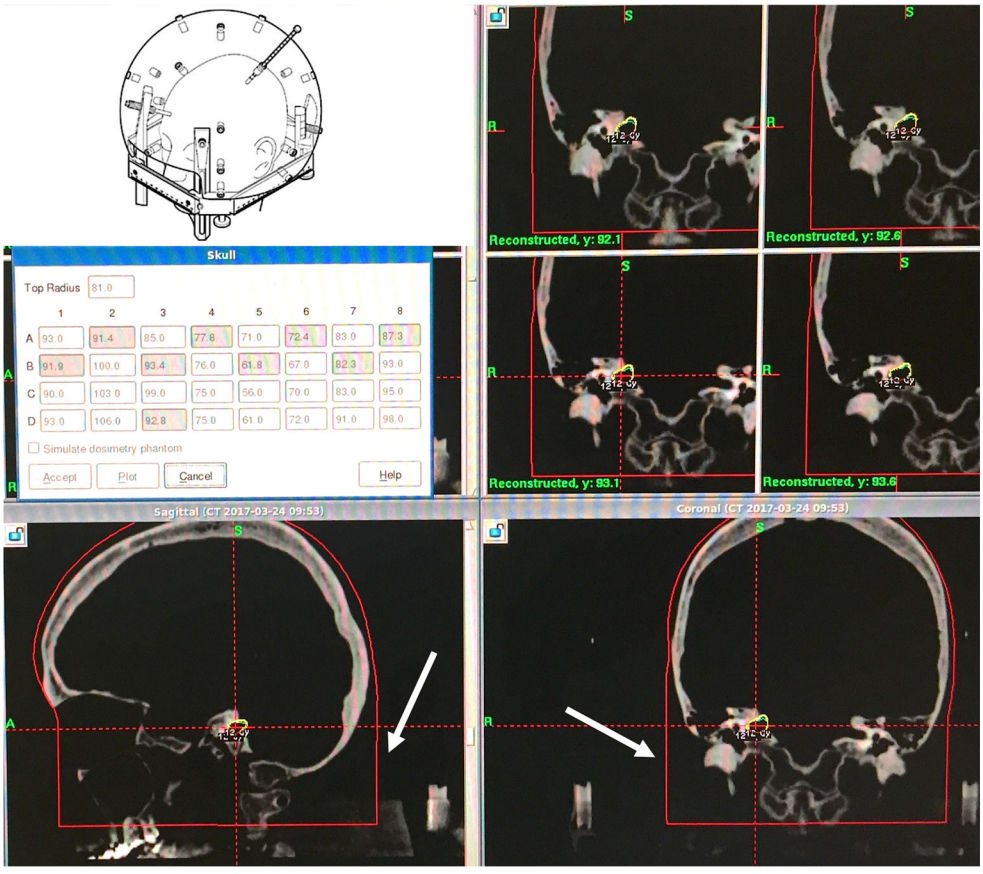

Fig. 1 Treatment of a right vestibular schwannoma, using manual skull contour definition. On the upper left, the skull scaling instrument is used for manual measurements. Then the user fills the table with the respective values in the software which ultimately generate the skull volume. The white arrows point to the inferior extrapolation of the skull contour definition

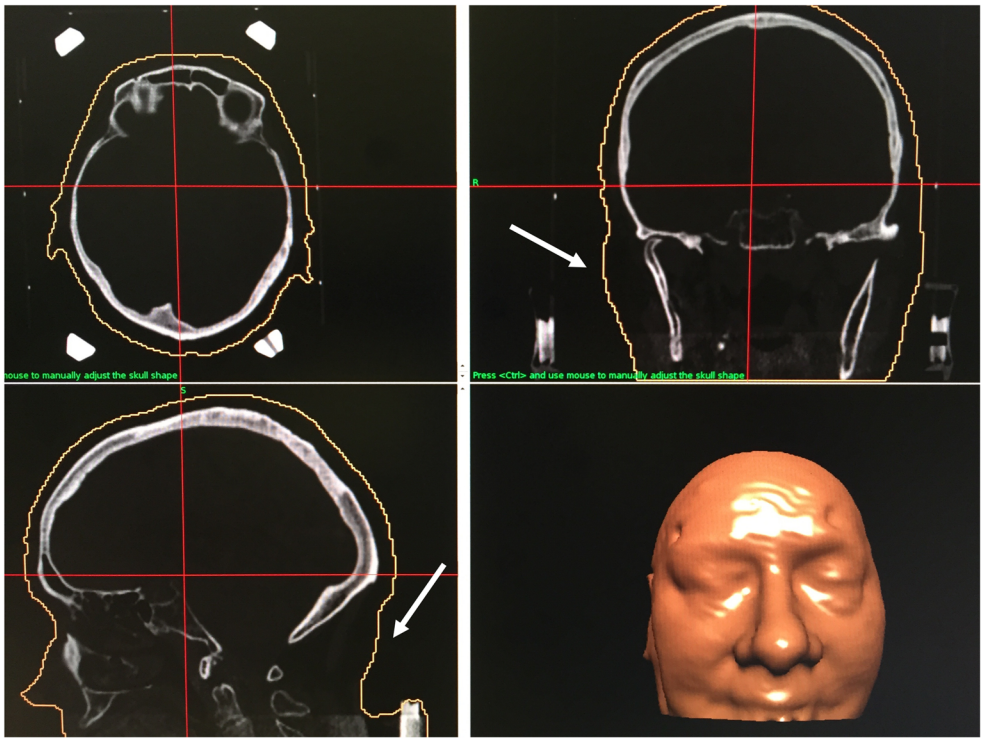

Fig. 2 Same patient as in Fig. 1. CT-scan segmentation was used to obtain the skull contour definition. In this process, no measurement is needed. The user is just asked if he agree with the generated volume from the CT scan of the patient. The white arrows point the inferior part of the skull contour definition, which fits with the soft tissue limits

Results

Beam-on time

The median difference of the beam-on time between manual scaling and image-based skull contouring was a statistically significant increase of + 0.45 min (IQR; 0.2–0.6) ($p < 0.0001$). The beam-on time increased 1.28% using image-based skull contouring. Table 2 summarizes all beam-on-time variations according to the type of target, its location, and the prescribed dose. During the study period, the mean dose rate was of 3.71 Gy/min. For example, for a trigeminal neuralgia case treated with 90 Gy at the 100% isodose delivered in one shot using a 4-mm collimator, the increase in beam-on time corresponded to an extra dose of 1.38 Gy. No statistical difference was reported concerning the beam-on time variation depending on the target location according to the four predefined groups (convexity targets, deep-seated targets, vestibular schwannomas, and trigeminal neuralgias) ($p = 0.15$). No correlation was noted between the prescribed dose ($p = 0.3$), the target volume ($p = 0.39$) or the matrix width ($p = 0.89$), and the beam-on time variation.

Target volume coverage

The median variation of TVC depending on the skull contour definition technique was 0 mm^3 (IQR, 0–0), with no statistical difference ($p = 0.13$). The range of TVC variation was − 7 to + 3 mm^3. The TVC decreased of 0.04% (corresponding to 0.6 mm^3) using image-based contouring. Seventeen patients harbored strictly no difference.

Prescription isodose volume

The median variation of the PIV was 0 mm^3 (IQR, 0–0), (range, − 213 mm^3; + 30 mm^3), with no statistical difference ($p = 0.2$). The extreme variation of 213 mm^3 was reported in convexity lesions. With image-based skull contour definition, the PIV decreased of 0.07% (corresponding to 12 mm^3).

Organs at risk

Twenty-three patients harbored a target close to an OAR. The distribution of the targets was as follow: 2 convexity, 3 deep-seated, 10 vestibular schwannoma, and 8 trigeminal neuralgia, respectively. The median difference of the maximal dose to the OAR depending on the skull contour definition technique was 0 Gy (IQR; − 0.1, + 0.1), (range, − 0.5 to + 0.9), with no statistical difference ($p = 0.85$). The extreme ranges were reported in posterior fossa targets (trigeminal neuralgia and vestibular schwannoma).

Table 2 Variation of the beam on time (BOT) according to the target type and location

Location	Target volume (cm3)	Dose (Gy)	BOT manual (min)	BOT CT contour (min)	Absolute variation (min)	Relative variation (%)
Convexity						
	1.216	20	35	35.5	0.5	1.43
	1.395	18	22.2	22.1	− 0.1	− 0.45
	0.339	14	25.5	25.5	0	0,00
	0.247	14	/	/	/	/
	0.137	24	14.7	14.6	−0.1	− 0.68
	0.483	18	70	70.2	0.2	0.29
	2.033	18	/	/	/	/
	4.177	20	114.5	115.9	1.4	1.22
	7.687	20	/	/	/	/
	22.17	18	41.7	41.7	0	0.00
	1.201	18	/	/	/	/
	3.706	14	33.4	33.6	0.2	0.60
	0.436	14	29.4	30	0.6	2.04
	1.389	14	/	/	/	/
	1.087	14	32.2	32.4	0.2	0.62
	3.757	14	39.1	39.5	0.4	1.02
	2.211	14	43.2	43.7	0.5	1.16
	1.046	14	/	/	/	/
Deep-seated						
	0.041	20	63.8	64.1	0.3	0.47
	0.346	20	/	/	/	/
	3.416	14	39.2	39.6	0.4	1.02
	0.673	18	35.2	35.3	0.1	0.28
	3.072	20	58.8	59.9	1.1	1.87
	0.555	20	32.4	33	0.6	1.85
	2.371	16	33.7	34.5	0.8	2.37
	0.222	24	9.8	10	0.2	2.04
	4.82	13	26.4	26.6	0.2	0.76
	0.958	14	33.7	34.1	0.4	1.19
	3.533	14	59.8	60.6	0.8	1.34
	0.808	16	49.8	50.7	0.9	1.81
	0.169	12	17	17.3	0.3	1.76
Vestibular schwannoma						
	NA	12	20.3	20.9	0.6	2.96
	2.195	12	31.8	32	0.2	0.63
	1.213	12	38.6	39.2	0.6	1.55
	0.215	12	22.6	23	0.4	1.77
	0.263	12	22.4	22.8	0.4	1.79
	1.489	12	38.5	38.6	0.1	0.26
	1.629	12	36.7	36.9	0.2	0.54
	1.145	12	25.6	26.1	0.5	1.95
	0.766	12	27.7	28.5	0.8	2.89
	0.364	12	22.8	23.1	0.3	1.32
	0.096	12	15.2	15.6	0.4	2.63
Trigeminal neuralgia						
		90	31.9	32.4	0.5	1.57
		90	32.9	33.4	0.5	1.52
		90	31.5	32	0.5	1.59
		75	57.1	58.5	1.4	2.45
		90	33.3	33.8	0.5	1.50
		90	33.5	33.9	0.4	1.19
		90	34.3	34.7	0.4	1.17
		90	34.7	35.3	0.6	1.73

/, signifies that the corresponding parameters are similar to the upper adjacent line (two targets treated in the same patient). NA, not available

Discussion

Beam-on time increase

In our present series, the only one evaluating such dosimetric parameters using the latest LGK Icon™ and GammaPlan® 11, the way of defining the skull contour significantly impacted the beam-on time. Using the newly available image-based skull contour definition, the median beam-on time significantly increased by 0.45 min, corresponding for a median treatment prolongation of 1.28%. This has been acknowledged without any change in the patient's dose planning, which remained identical for the comparison between both measurement techniques. We attribute this significant increase of the beam-on time to a systematic difference and not to a user-dependent variation. Indeed, the way of defining the skull with image-based contours does not imply the user input (excepted for the choice of reference images, CT or MRI)

whereas manual measurements do so. With the manual technique, a blunt probe is used to touch the scalp in order to provide the measurement. It would take only a little extra pressure against the scalp to measure it to be thinner. This would give a smaller outline, thus requiring shorter beam-on time to deliver a certain radiation dose compared with the CT scan-informed measurements which (without this artificial indentation) will make the scalp outline larger. The difference between the two techniques will be larger in cases where the scalp is thick and non-existent in, e.g., an elderly patient with thinned scalp particularly if they are bald.

Former studies using LGK Perfexion™ and 4C™ devices, such as Xu et al. study, reported the same range of discrepancy (2.5%) between the two skull contour definition techniques [14], as did the team of Kobayashi et al. (2%) [6]. Rojas-Villabona et al. also reported an increase of BOT of 1.45% with head contours derived from the CT scan [8]. As we used TMR 10, one could assume that the beam-on time increase was only due to the head's different skull measurement methodology. The TMR 10 algorithm considers that the whole skull volume is composed of the same density as water, since it is a water-based algorithm. If the skull volume is higher, the algorithm computes a longer beam-on time to consider the radiation attenuation between the skull surface and the targeted point to treat.

Consequently, one might assume that the "extra" beam-on time with the newly available image-based contouring might increase the total irradiation dose in comparison with manual skull measurements [13]. More importantly, a change in beam on time could potentially influence the desired radiobiological effect, as stipulated by Jones and Hopewell [3]. In the present study, we found that for a patient treated for an idiopathic trigeminal neuralgia receiving 90 Gy at the 100% isodose with one 4-mm shot, the treatment time is increased by 0.6 min, corresponding to an additional dose of 2 Gy, despite keeping the same dose planning while using two different skull measurement definition. This represents an increase of the maximal dose to the brainstem of 0.2 Gy. In another example, a patient treated for a vestibular schwannoma Koos III with serviceable hearing received 12 Gy at the 50% isodose with 14 shots (Fig. 3). As his treatment time increased by 0.8 min, this further corresponds to an additional irradiation of 0.3 Gy. With treatment time increase, one would assume a potential change in the biologically effective dose (BED), with further therapeutic implications. The mean dose to the cochlea did not differ.

However, at this stage, no short-term clinical event during the follow-up could be associated with this higher irradiation doses. The long-term effects of such changes remain to be established. As a beam on time increase could reflect also in a change of the BED, the exact potential radiobiological changes have to be evaluated [2]. Furthermore, while this calculation would be feasible for TN patients, for others, such as tumors, this remains more complex. Of note, one could also consider that dose rate varies tremendously in different regions, and further depends on how many isocenters were used, the collimator size, etc. Current planning software does not, however, provide such information.

Originally, we hypothesized that the beam-on time variation would be more significant with a lower location of the lesion in the skull volume. Indeed, when performing manual measuring with the plastic skull scaling instrument and the ruler, a linear extrapolation of the measures is done by the software at the inferior part of the skull volume (Fig. 1) which cannot be reached by the measuring tool, whereas the image-based skull volume definition seems to be more accurate in the lower zone (e.g., for cranial definition of the posterior fossa) (Fig. 2). However, according to our results, for the same dose planning inside the same patient, no correlation was reported between the target location and the beam-on time variation.

The beam-on time increase was not correlated to other dosimetry parameter variations, such as the prescribed dose, the target volume coverage, and even the matrix width.

Other dosimetry parameters

Regarding the TVC, no significant difference was reported between the two skull contouring techniques, using identical dose planning. The maximal variation of the TVC was of 7 mm^3 in a case of an occipital glioma (convexity lesion). For the PIV, the range of variation was higher, but still not reaching a statistical significance. The most important variation was of 213 mm^3, in a case of parietal metastasis (convexity lesion). In our series, the convexity lesions were more impacted by the skull definition technique than deep-seated lesions. Thus, we could not ascertain that these slight differences could impact the patient outcomes. Concerning the dose to OAR, the most important variation was of + 0.9 Gy to the brainstem in a case of trigeminal neuralgia treatment. The other variations > 0.5 Gy were also noted in trigeminal neuralgia patients. Although these results did not reach statistical significance, they were in line with our previous assumption that posterior fossa lesion dosimetry was more impacted by the skull definition technique.

Limitations

Performing manual measurements understand a range of inter-individual variability. That could explain, at least partially, the variation of the skull volume definition using manual skull contour. However, in the present study, the same practitioner carried out all manual measurements in order to reduce the bias of inter-individual variability.

The software used in this study, TMR 10, does not level out uneven thickness of the skull. Another algorithm is now

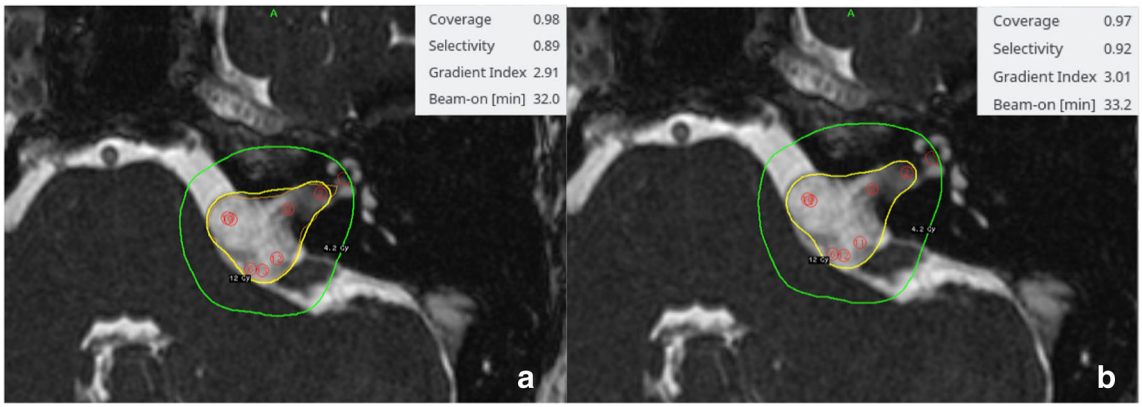

Fig. 3 Screenshots during treatment planning of a left vestibular schwannoma Koos grade III, with serviceable hearing. **a** manual skull contouring and **b** CT scan contouring. The treatment indexes slightly vary, but the dose to the cochlea does not change

evaluated in clinical practice (convolution algorithm) which takes into account the tissue interfaces (bone, air, brain tissue) to adjust the dosimetry. Further studies using convolution algorithm should be of interest.

The clinical effect of the variations in the beam-on time and the corresponding BED remains to be established in further studies. An open question is that of a potential dose modulation that should be performed as an adjustment to new techniques developments and, in particular, a change of the beam on time. Another is how it changes BED per case, as related to an increased beam on time, and how this further implies changes in radiobiological effects in an individual patient, for the same dose planning. However, calculating the exact BED was beyond the purpose of this study.

While on short-term basis, no adverse radiation effect was observed, and more data is needed to evaluate the changes in individual patients, if such exist. Moreover, this should be discussed for the specific treated pathology. For example, in the case of a Koos III vestibular schwannoma, an increase in dose of 0.3 Gy would not eventually create a major issue, while prescribing a standard and lower dose of 12 Gy in our series. However, in trigeminal neuralgia, one could eventually expect an eventual increase in toxicity, while for a 75 Gy at the 100% isodose line, treatment time increased with 1.4 min, corresponding to an additional dose of 1.8 Gy. However, these former aspects should be evaluated by further studies.

Here, we compared two different skull measurements techniques, both inside the same patient (intrapersonally) but also interpersonally (i.e., different group of pathologies). However, it was beyond our purpose to assess only the impact of the new TMR 10 algorithm on a given dose to a given point inside the skull. Our purpose, as clinicians, was to evaluate a dose planning and not only a specific dose to a specific point. This further aspect deserves a separate and dedicated research protocol.

A last aspect is related to the sensitivity and specificity between the two techniques. Nevertheless, here we analyzed the same dose planning for the same patient or between different groups of pathologies. In this sense, the results obtained using multiple measurements for an identical dose planning remains the same, with no possibility to provide a ROC curve, which is beyond the purpose of this study.

Conclusion

This present dosimetry study evaluating LGK Icon™ while using the recent algorithm based on image contouring of the skull reports a statistically significant difference in terms of beam on time for the same dose planning between this new method and the former one (i.e., manual skull contour definition). Additional multicentric studies should be performed to consolidate our results. Beam-on time is a relevant dosimetric parameter, which significantly increased using the CT scan-based skull contour, which further resulted in an increase of the total dose delivery per treatment. The clinical impact of such variation on short-term basis was not significant. However, long-term follow-up is needed for further evaluation. Evaluating the exact BED in these patients is also relevant, as this parameter (BED) depends on beam on time, and future developments should incorporate this in the Leksell GammaPlan® software. Regarding other dosimetry parameters, especially the TVC, the PIV, and the OAR irradiation, convexity lesions and trigeminal neuralgia treatments were more impacted by the skull definition technique, without reaching statistical significance. In the particular case of functional procedures, the clinical impact warrants further investigations.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study formal consent is not required.

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