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Adaptive hybrid surgery analysis (AHSA) for adjuvant gamma knife radiosurgery treatment of vestibular schwannoma residuals

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ABSTRACT

Objectives: Adaptive Hybrid Surgery Analysis (AHSA, Brainlab, Munich, Germany) is a software application generating in real-time conceptual dose plans for tumor residuals but has so far not been assessed for usability in a Gamma Knife (Elekta, Stockholm, Sweden) radiosurgery practice. We aimed to compare AHSA stereotactic radiosurgery dose plans with Leksell Gamma Plan (LGP, Elekta, Stockholm, Sweden) plans for adjuvant radiosurgical treatment of Vestibular Schwannoma (VS) residuals.

Patients and Methods: In this retrospective comparative study, we compared the automatically calculated AHSA dose plans with clinical LGP treatment plans in 13 patients radiosurgically treated for VS residuals. We first created an LGP template based on our specific constraints to organs at risk (OAR), and a tumor prescription volume coverage of minimum 98%. As most proximal anatomy at risk is not manually contoured in our practice, OARs (i.e. brainstem, optic apparatus and cochlea) in the planning images were automatically segmented in Elements Anatomical Mapping and imported into the AHSA software for re-planning and comparison with the LGP dose plans.

Results: There was no significant difference in tumor coverage and conformity index between the LGP and AHSA dose planning data, with the mean and maximal dose to the brainstem slightly higher in the latter.

Conclusion: The AHSA dose plans for adjuvant radiosurgical treatment of VS residuals were comparable to those of LGP used in our Gamma Knife practice, confirming the usability of AHSA in the management of Vestibular Schwannoma in a Gamma Knife practice.

1. Introduction

Planned subtotal tumor resection (STR) followed by stereotactic radiosurgery (SRS) is often referred to as Adaptive Hybrid Surgery (AHS). In the case of Vestibular Schwannoma (VS), combining open microsurgery with SRS aims at assuring tumor control while preserving the facial nerve function [1,2] Nevertheless, combining these techniques can be technically challenging and requires a good understanding of the two treatment modalities - something that might be difficult to master by the operating surgeon.

Abbreviations: AHS, Adaptive Hybrid Surgery; AHSA, Adaptive Hybrid Surgery Analysis; SRS, Stereotactic Radiosurgery; LGP, Leksell GammaPlan; GKRS, Gamma Knife radiosurgery; STR, Sub Total Resection; CI, Conformity Index; VS, Vestibular Schwannoma

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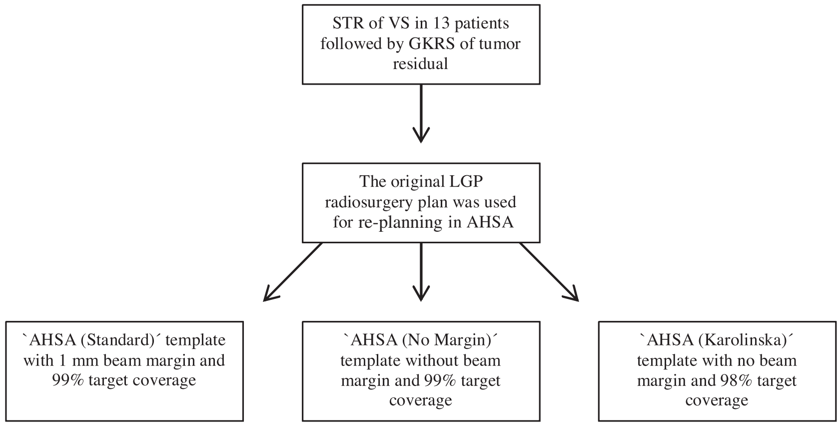

Fig. 1. Schematic depiction of our workflow process for re-planning the GKRS plans in AHSA.

Adaptive Hybrid Surgery Analysis (AHSA, Brainlab, Munich, Germany) is a novel software application for the Brainlab neuronavigational system (Brainlab, Munich, Germany), designed for intra-operative use to generate in real-time conceptual dose plans for tumor residuals. The software utilizes direct surgeon input via navigated brush technology to automatically render theoretical radiosurgery dose plans meant for Novalis Radiosurgery platforms, but has so far not been assessed for usability in a Gamma Knife (Elekta, Stockholm, Sweden) radiosurgery practice. The technique allows the neurosurgeon to evaluate in real time an ideal crossing point between surgical resection and adjuvant radiation treatment [3], as illustrated in Fig. 2.

Most tumor volumes can be treated with conventional fractionation, whereas single-fraction stereotactic radiosurgery (SRS) becomes available when tumor volume is sufficiently reduced so that SRS can be delivered while restraining radiation doses to organs at risk. In AHSA, adjuvant radiation plans are presented in a simplified visualization for the operating neurosurgeon, where necessary quality parameters for radiation treatments, including radiation toxicities for risk organs are displayed, and correlated to prescription templates. Instruments connected to the navigation system can be used to acquire real-time calculation of the residual tumor volume from which new dose plans are calculated, thus updating the conceptual radiosurgery plans in real time (Fig. 2).

Currently, intensity modulated radiation therapy (IMRT) technique is used to calculate the conceptual radiation plans for AHSA. IMRT uses linear accelerators (LINAC) to deliver the radiation treatment, whereas Gamma Knife (Elekta, Stockholm, Sweden) is a radiosurgical platform that utilizes cobalt-60 sources placed in a hemispheric array to achieve convergent radiosurgery plans. While the Gamma Knife platform is dedicated to radiosurgery, most LINACs are built for conventional fractionated radiotherapy and require additional technology and expertise to become dedicated radiosurgical tools [4,5].

The aim of this study was to evaluate to which extent conceptual dose plans generated by AHSA correspond to treatment plans generated by Leksell GammaPlan (LGP, Elekta, Stockholm, Sweden) in Vestibular Schwannoma (VS) patients.

2. Materials and methods

Thirteen VS patients planned for subtotal resection (STR) were consecutively included, all treated with a combination of STR followed by Gamma Knife radiosurgery (GKRS) for the tumor residual. The AHSA software can be used with various software features (e.g. Elements, Brainlab, Munich, Germany). Elements Anatomical Mapping 1.0.0 was used for automatic segmentation of critical structures (i.e. brainstem, optic apparatus and cochlea) in the MRI datasets, where these had not already been manually delineated in the original LGP plan. The segmented critical structures together with the original radiosurgery target structure for GKRS were exported to AHSA (Adaptive Hybrid Surgery Analysis 1.0.2, Brainlab, Munich, Germany) for re-planning of the radiosurgical treatment plans.

The AHSA template files contain input values for the dose calculation, such as dose prescriptions and toxicity constraints, for different risk organs. This can be visualized by the intra-operative display and can thus be adjusted for a particular clinical practice. The default AHSA template, from here on referred to as 'AHSA (Standard)', uses a 1 mm beam margin for an IMRT delivery technique and was customized in a new template, 'AHSA (No margin)', based on our local practice using GKRS without a beam margin. The two aforementioned templates (i.e. AHSA 'Standard' and 'No margin') were kept at default coverage prescription (99%) of the target. A third template,' AHSA (Karolinska)', represented the actual GKRS treatment coverage for every residual at their individual coverage down to a minimum of 98%. In addition to having no beam margin, the latter template also included hard constraints for the maximal dose to the brainstem and the mean dose to the ipsilateral cochlea, to better represent our local GKRS practice. The template' AHSA (Karolinska)' was thereby customized to meet our toxicity criteria as well as the conformity for the radiosurgery treatment planning data results at our institution; in our case, 12–13 Gy up to 98% coverage prescription, with Conformity Index (CI) < 1.5 at the prescription isodose line. The index used here for the evaluation of the conformity of the radiosurgical plans is the CI proposed by Paddick [6].

For re-planning processes and platform comparisons, current DICOM limitations may prevent advanced exchange of RT Structures and RT Dose matrices between different planning systems. Within AHSA, adaptive grids are used for both dose and volume definitions. Calculations performed at isomorphic grids, however, may interpolate small volumes requiring sub-millimetric control points. Therefore, the LGP plans were exported with smallest (1 mm) resolution and in addition to reading target coverage and CI values from the actual LGP application, the values were also read in an independent software, Elements Dose Review 1.0.0, which can display the LGP dose plan using finer resolution for smaller objects. A Wilcoxon rank sum test in MATLAB (MathWorks, Natick, MA, USA) was used for statistical analysis with a significance level of 0.05. A schematic overview of our re-planning process is depicted in Fig. 1.

3. Results

3.1. Patient material

We included 13 patients (6 males) and 7 females, with a median age of 51 (range, 35–80) at the time of the Gamma Knife treatment. The median VS size was median 25 mm in diameter (range, 9–40) at the time of resection, and median 16 mm in diameter (range, 4–26) at the time of the Gamma Knife treatment. The median radiological follow-up

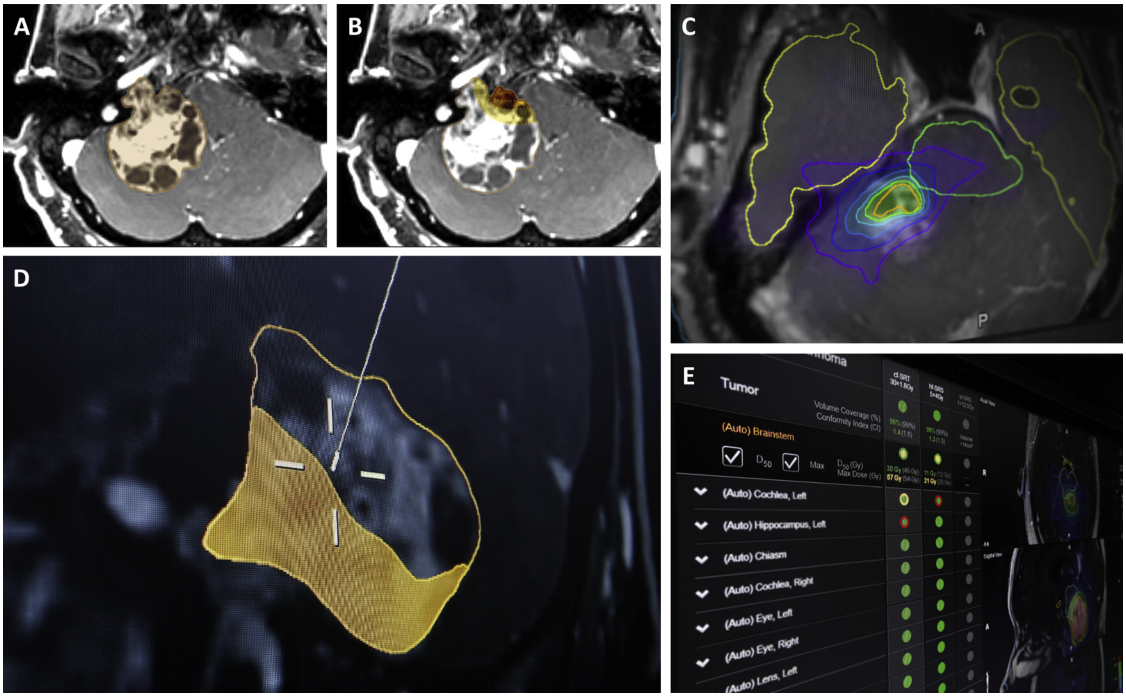

Fig. 2. Adaptive Hybrid Surgery Software (reprinted with permission from Brainlab) work-flow; T1WI MRI showing a large right vestibular schwannoma (A), STR is planned (B), simulation and optimization of residual tumor for radiosurgery (C), intraoperative update option for adjuvant radiosurgery plan (D), visualization of critical dose constraints (E). For additional details please visit https://www.brainlab.com/radiosurgery-products/brain/adaptive-hybrid-surgery/.

Table 1
Demographic data including patient age, VS size at time of surgery- and gamma knife treatment, years of follow-up and VS size at follow-up.

Patient no.	Age at Gamma Knife intervention (Gender)	VS size at surgery (mm)	VS size at Gamma Knife (mm)	Years of radiological follow-up	Size (decreased/ unchanged/ increased)
1.	35 (M)	33	16	4	Unchanged
2.	47 (F)	17	13	5	Decreased
3.	37 (M)	9	4	10	Unchanged
4.	69 (F)	12	12	5	Unchanged
5.	51 (M)	25	18	6	Unchanged
6.	70 (M)	39	22	4	Unchanged
7.	70 (M)	30	26	10	Decreased
8.	36 (M)	33	24	5	Decreased
9.	53 (F)	40	8	5	Unchanged
10.	44 (F)	28	10	6	Unchanged
11.	50 (F)	20	17	7	Increased
12.	70 (F)	18	21	5	Decreased
13.	80 (F)	20	10	4	Unchanged

was 5 years (range, 4–10) after the Gamma Knife treatment without any tumor growth observed in any of the patients. Please see Table 1 for further details.

3.2. Target coverage

Initially, we compared the average target coverage for the three different AHSA templates compared to target coverage in LGP (Elements Dose Review). A statistically significant difference ($p < 0.05$) according to Wilcoxon rank sum test was observed for 'AHSA (Standard)', 'AHSA (No margin)', and 'AHSA (Karolinska)' respectively, as is depicted in Fig. 3.

3.3. Conformity index

In terms of CI, 'AHSA (Karolinska)' template achieved similar values, compared to the original LGP (Elements Dose Review), without any statistical difference ($p = 0.78$) (Fig. 4).

3.4. Maximal and mean dose to Brainstem

On average, we observed a higher maximal dose to the brainstem for 'AHSA (Karolinska)', compared to LGP (Elements Dose Review) as depicted in Fig. 5, but this did not reach statistical significance ($p = 0.88$). The mean dose to the brainstem was higher in AHSA (Standard), but when the dose margin was abolished, no significant difference could be detected between AHSA (No margin) compared to LGP (Elements Dose Review) (Fig. 6), $p = 0.59$ and $p = 0.96$, respectively. The 'AHSA (Karolinska)' template can be considered representative of our local GKRS practice, as we would be able to achieve the same or slightly lower maximal dose to the brainstem in the final post-operative LGP plan, compared to the conceptual value given by ASHA.

3.5. Maximal and mean dose to the ipsilateral Cochlea

For the maximal and mean dose to the ipsilateral cochlea in Figs. 7 and 8, slight observed deviations between LGP (Elements Dose Review) and 'AHSA (Karolinska)' did not reach statistical significance ($p = 0.74$ and $p = 0.54$, respectively).

4. Discussion

In this comparative study, conceptual AHSA plans for thirteen patients undergoing planned STR of VS followed by GKRS of the residual tumor were compared with the actual LGP treatment plans. We demonstrated that if the AHSA template is adjusted in terms of prescription, target coverage, and hard constraints for organs at risk, the conceptual AHSA plans are applicable for a GKRS practice.

4.1. Current trend in VS surgery

Complete resection of large (> 3 cm) VS is associated with high risk

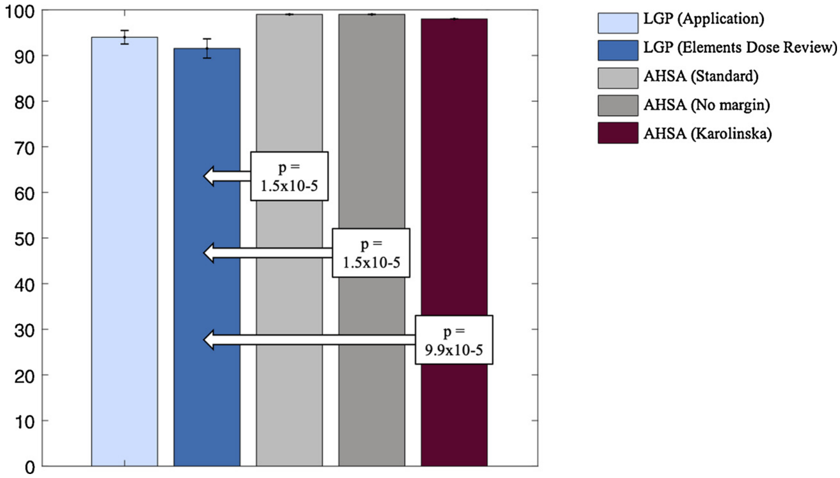

Fig. 3. Average target coverage [%] at prescription isodose line (12–13 Gy). The bar for LGP (Elements Dose Review) represents the LGP plan displayed in an independent software. Therefore, a deviation was observed between LGP (Application) and LGP (Elements Dose Review). Statistically significant differences were observed for' AHSA (Standard)',' AHSA (No margin)', and' AHSA (Karolinska)' respectively, according to Wilcoxon rank sum test ($p < 0.05$).

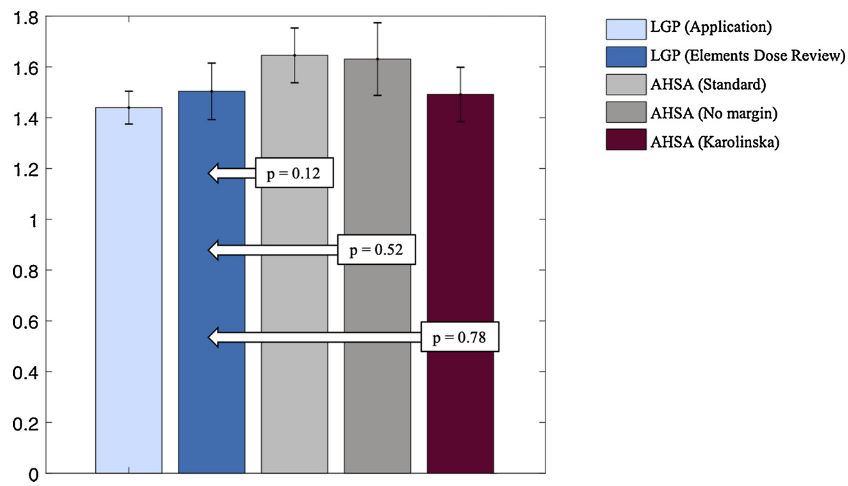

Fig. 4. Average Conformity Index (CI) using Inverse Paddick [3]. The LGP and' AHSA (Karolinska)' template corresponded with similar values. No statistically significant difference was observed ($p = 0.78$).

of peroperative morbidity, such as hearing loss [7–10]and facial nerve palsy [11–17]. To minimize the risk of neurological deterioration, neurosurgeons nowadays tend to advocate a planned partial resection of VS, leaving behind a portion of the VS, along the seventh nerve and eighth nerve. Using this combined approach for the management of large VS, a tumor control rate of up to 79–100% can be achieved. Further, accumulating data now suggests that microsurgery, also for large VS, can be performed with the risk of facial nerve palsy in the order of 5–14.3 % [1,2,18–23], and preserved functional hearing can in the short term follow up be preserved in up to 76.9% [24]. For the

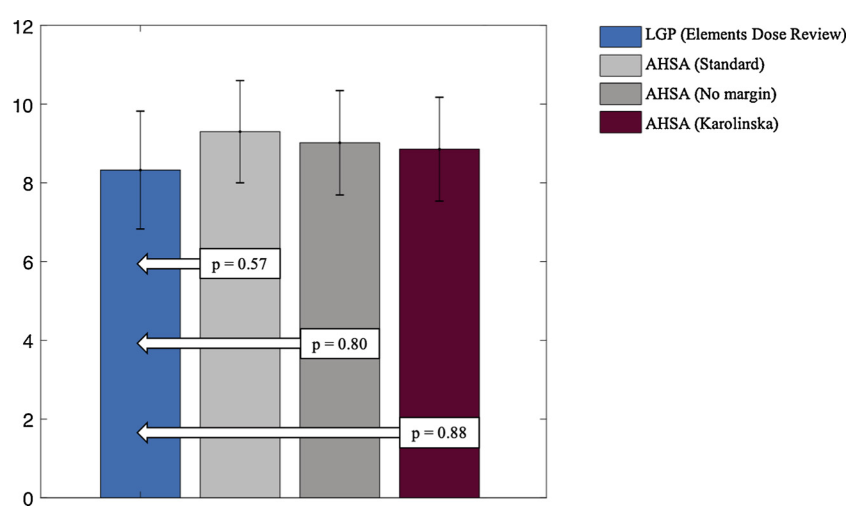

Fig. 5. Brainstem maximal dose [Gy]. On average, AHSA (Karolinska) observed a higher maximal dose to the brainstem, but this did not reach significance ($p = 0.88$). Therefore, using the 'AHSA (Karolinska)' template, we can achieve the same or better maximal dose to the brainstem with adjuvant GKRS.

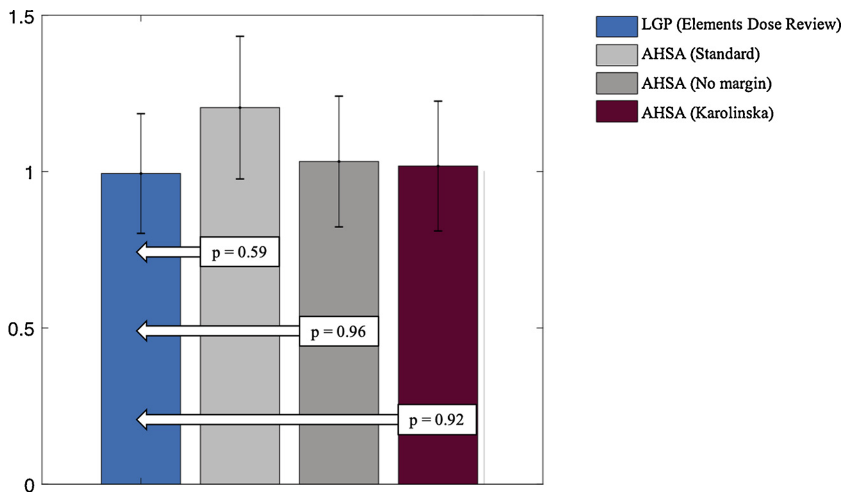

Fig. 6. Brainstem mean dose [Gy]. On average, the AHSA (Karolinska) template was representative of our clinical practice, without any significant difference (p = 0.92).

operating neurosurgeon, it can sometimes be difficult to estimate the extent of resection. Further, neurosurgeons not dedicated to radiosurgical practice may find it difficult to estimate the volume of the remaining tumor and the proximity to organs at risk during surgery, and thereby, to evaluate if a radiosurgical procedure is possible. For determining the residual tumor volume and location, an intraoperative MRI would be the preferred technique. However, also in neurosurgical centers equipped with intraoperative MRI, surgeons tend to find them cumbersome to use and repeating MRI scans would significantly disrupt the natural flow of the operation. Another option would be intraoperative CT co-registered with pre-operative MRI data; however, neither intraoperative imaging modality provides toxicity profiles for risk organs for an actual residual to evaluate the feasibility of complementary radiosurgery. The AHS system allows an update of the residual tumor volume without performing perioperative radiological procedure in real-time, while at the same time giving atomized doseplans for an adjuvant radiosurgical treatment [5].

4.2. Dosimetric comparison of AHSA automated dose plans and LGP dose plans

The automated dose plans generated for the residual tumor by the AHSA system is designed for a Novalis, LINAC-based Radiosurgery delivery platform. However, many neurosurgical centers use single fraction GKRS as the first choice of adjuvant radiosurgery for residual tumors after incomplete neurosurgical tumor resections [25–28]. For this reason, it was important to reassure that the automated doseplans also could also be applied in a neurosurgical center dedicated to GKRS.

Conformity Index (CI) is a measurement of how accurate the dose plan prescription dose mimics the delineated tumor volume. In this case, we used the inverse paddick index for CI. Importantly, we found no significant difference between the CI for the LGP dose plans compared to the automated AHSA dose plans. Moreover, we found that the AHSA dose plans could be further improved when customizing the restrains in accordance with the GKRS practice. When measuring and comparing the doses to risk organs (mean and maximal dose to brainstem and ipsilateral cochlea), no significant difference was detected. In the LGP, risk organs are delineated by hand and a significant interindividual discrepancy can here be seen between dose planners. The Brainlab Elements system is equipped with an anatomical mapping function that automatically delineate organs at risk, which allows a more consistent measurement of mean doses to the organ at risk, such as the brainstem and the optic apparatus.

The comparison of maximal dose to the brainstem revealed a nonsignificant tendency for higher maximal doses to the brainstem, for the AHSA generated dose plans compared to the LGP dose plans. The

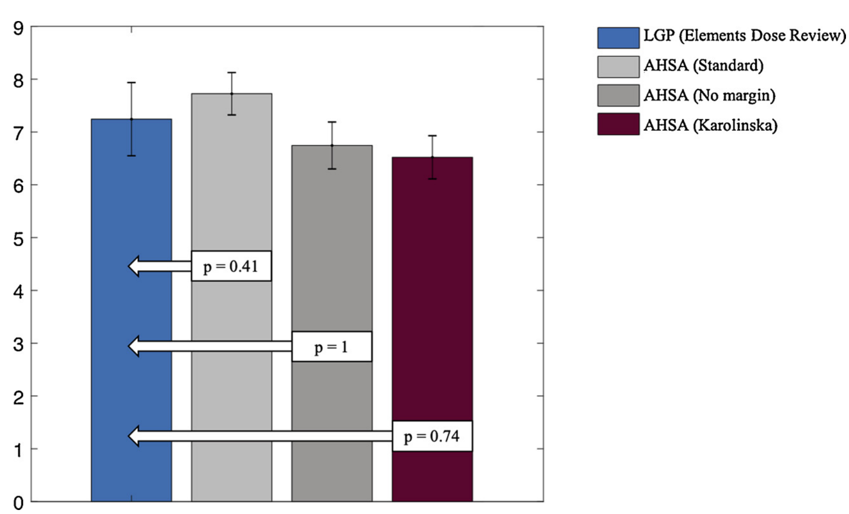

Fig. 7. Ipsilateral cochlea maximal dose [Gy]. On average, the maximal dose to the ipsilateral cochlea was observed to be slightly lower for AHSA (Karolinska), but this did not reach significance (p = 0.74).

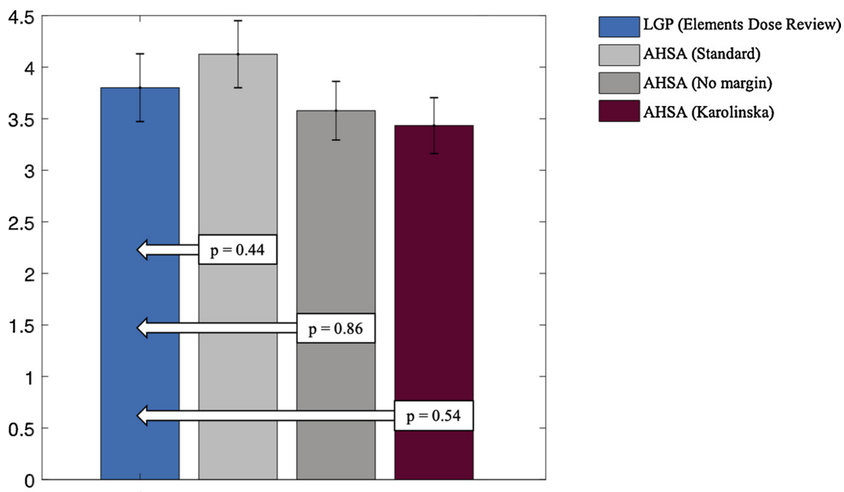

Fig. 8. Ipsilateral cochlea mean dose [Gy]. A slight reduction of the mean dose was observed on average for 'AHSA (Karolinska)', but this did not reach statistical significance (p = 0.54).

implication of this is that the 'AHSA (Karolinska)' slightly overestimate the maximal and mean dose to the brainstem, compared to the final post-operative LGP plan.

For an opposite scenario, where we would not be able to meet the constraints for the maximal dose to the brainstem in the final post-operative GP plan, it may not be feasible to deliver the treatment in a single fraction using GKRS unless the patient would undergo further resection and thus, a fractionated radiation regimen would be the remaining treatment option.

Dose to the cochlea has in many studies been recognized as a determining factor of preserved hearing [29]. In this comparison, no significance in max- or mean dose to the cochlea was detected, once again indicating the accuracy of the automated dose plans generated in the AHSA system, and its applicability also when a GKRS procedure is planned.

4.3. Limitations of the comparison

To reassure an external validity of the study, we used 13 clinical cases for comparison, where the patients had undergone STR followed by GKRS for the residual tumor. Individual dose planning was performed by different neurosurgeons, taken into account, patient age, growth rate of the VS residual, and history of transient facial nerve palsy after surgery. For this reason, prescription dose coverage for these patients was lower (mean 92%) than customary, when performing GKRS. This was most likely due to some neurosurgeon's tendency to lower the dose to the probable location of the facial nerve. For the automated AHSA dose plans, VS coverage was set to 98%, regardless of facial nerve location. To perform the comparison of CI and doses to risk organs, LGP (Elements dose review) dose plans were set to the same coverage (98%). Thus, slightly changing the original LGP dose plans.

Further the comparison was technically complicated due to the fact that LGP and AHSA dose planning system use different minimal grid size for the analysis of the DICOM files. LGP use 1 mm grid, while AHSA system is able to use submillimeter grid size for smaller volumes. This explains the difference seen in target volume coverage between LGP (application) and LGP (Elements Dose Review) in (Fig. 3).

5. Conclusion

In this comparative study, we demonstrate that AHSA, customized in terms of prescription dose and restraining doses to the organs at risk, matches our GKRS practice dose planning used for residual Vestibular Schwannomas after planned STR.

Data availability statement

Data supporting the results and findings in this paper can be obtained by request from the corresponding author.

Ethics statement

The study has been approved by the regional ethics board in Sweden (Dnr.2017/1760-31/1)

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Disclosures

This study was performed under a research agreement from Brainlab AG. Jiri Bartek Jr is a consultant for Brainlab AG. Hamza Benmaklouf is a consultant for Elekta. Nevertheless, there are no conflict of interest to report concerning the materials or methods used in this study, or the findings specified in this paper.

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