Clinical and Translational Radiation Oncology 23 (2020) 66–71

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.elsevier.com/locate/ctro

Short Communication

Dosimetric and volumetric outcomes of combining cyst puncture through an Ommaya reservoir with index-optimized hypofractionated stereotactic radiotherapy in the treatment of craniopharyngioma

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A R T I C L E I N F O

Article history:
Received 15 December 2019
Revised 5 May 2020
Accepted 6 May 2020
Available online 11 May 2020

A B S T R A C T

Large cystic craniopharyngioma management combining cyst puncture through an Ommaya reservoir with hypofractionated stereotactic radiotherapy was evaluated. The planning optimization was focused on the gradient and selectivity. Punctured and filled cyst treatment plans were compared with a retrospective analysis of volumetric and functional outcomes.

1. Introduction

Craniopharyngioma accounts for 2–5% of brain tumors and 4.7–7.9% of intracranial tumors in Europe [1]. Today's treatment approaches can be combined, with the objective of limiting morbidities. Total resection is associated with a risk of sequelae due to damage to nearby critical structures. An approach that combines partial resection with radiotherapy is safe [2,3], spares surrounding organs and reduces surgical morbidity. In case of large cystic tumors or mixed (liquid and solid) tumors which account for 84–99% of all cases [4], this approach still exposes to the risks of an invasive surgical procedure with large irradiated target volume.

Hypofractionated stereotactic radiosurgery is an effective treatment for craniopharyngioma, with a 4-years tumor control rate of 80–100% [5–9].In cases of cystic craniopharyngioma, the liquid contained in the cyst accounts for most of the tumor's volume and is probably the least radiosensitive part. A large cyst could impinge on surrounding structures and may be associated with higher morbidity. Radiotherapy of the cyst region is associated with a volume increase of 9 to 20% [9].

A smaller cyst volume tends to be associated with better tumor control, [5] and may limit the radiation target volume and thus potentially improve tolerance. Lastly, cysts can be repeatedly punctured through an Ommaya reservoir in case of cyst enlargement [10].

We retrospectively report volumetric, functional and dosimetric outcomes of six patients treated with combining cyst puncture through Ommaya and hypofractionated stereotactic radiotherapy based on gradient and selectivity optimization. The hypothesis is combined treatment is feasible and its association with index optimization could have a dosimetric advantage.

2. Materials and methods

2.1. Patient selection

All adult patients with a high cyst volume (>2 cm^3) mixed craniopharyngioma were included in our institution (Amiens University Medical Center, Amiens, France) between 2016 and 2019. Patients having undergone previous brain radiotherapy, compromise radiotherapy immobilization and patients presenting contraindications to neurosurgery were not included. Resection of craniopharyngioma was an exclusion criteria.

2.2. Placement of the Ommaya reservoir, and cyst puncture

An Ommaya reservoir was joined to the cystic part of the craniophayngioma. It was first implanted under general anesthesia with stereotactic robotic assistance (ROSA®, Medtech, Montpellier, France). As described previously [11], the ROSA® device has a robotic arm and a laser system for precise frameless registration of several thousand points. Using landmarks, the surgeon positioned the arm along the catheter placement trajectory and used it as an instrument holder. The cyst was punctured at the time of Ommaya reservoir placement and again at the time of the planning MRI scan.

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https://doi.org/10.1016/j.ctro.2020.05.003
2405-6308/

2.3. Treatment planning and dose prescription

Treatment was performed using a dedicated stereotactic radiosurgery Cyberknife® M6, Accuray Inc., Sunnyvale, CA linear accelerator mounted on a robotic arm. Image-guidance was based on 6D-Skull tracking (two orthogonal X-ray images compared with digitally reconstructed radiographs in turn adjusting arm position) with an individualized face mask used for immobilization and a ten-second image acquisition interval.

In the planning step, patients underwent a CT scan (slice thickness: 0.625 mm) and a gadolinium contrast-enhanced MRI scan (slice thickness: 1 mm) a week before the first radiation therapy session.

The target volume and organs at risk were defined precisely using contrast-enhanced three-dimensional (3D) T1 and Fast Imaging Employing Steady-state Acquisition (FIESTA) MRI sequences. No margin was applied between the CTV (Clinical target volume) and the PTV (Planning target volume). Given that the planning system is based on the CT data, guided image fusion was required. Inverse treatment planning was applied with a ray-tracing algorithm.

The goal of the optimization step was to find the best compromise between the dose delivered to two surrounding structures (the optic chiasm and the brainstem) on one hand and two dosimetric quality indexes (gradient, as defined in the International Commission on Radiation Units and Measurements (ICRU) Report 91, [12] and selectivity (ratio of the target volume treated to the prescription isodose volume) on the other. This last one is representative of normal tissue spared around the target. The intention was to reduce the dose delivered to the optic chiasm and the brainstem, achieve a gradient index between 2 and 3, and obtain a selectivity value as close to 100% as possible. The planning complied with the constraints from the American Association of Physicists in Medicine's Task Group 101 (TG101) report [13].

2.4. Volume measurements and functional outcomes

Cystic and solid parts of the craniopharyngioma were measured on the diagnostic, planning, and follow-up MRI datasets to set a volumetric evolution curve for each patient.

The patients' functional outcomes were estimated on reported symptoms and adverse events in medical notes.

2.5. Dosimetric comparisons

Treatment plans after cyst puncture (denoted as the "reference plan") and a "fictitious plan" as if the craniopharyngioma cyst had remained full of liquid were compared. When a patient had undergone several MRI scans before placement of the Ommaya reservoir, the scan with the largest observed cystic volume was considered to be the baseline value. The craniopharyngioma had not been treated between the time of the baseline MRI scan and the placement of the Ommaya reservoir. Segmentation of the fictitious plan was based on the baseline MRI merged with the CT of reference for planning. The same planning objectives, algorithm, and dose constraints were applied. The ICRU 91 dosimetric indexes were noted for each treatment plan. For each patient, the optic chiasm Dmax, Dmean, Dmin, and D0.2 cm^3 and Brainstem Dmax, Dmean, Dmin, and D0.03 cm^3 values on the reference and fictitious plans were compared.

3. Results

An illustrative example of the treatment process for Patient #2 is given in Fig. 1.

Main results are presented on Table 1.

A case was previously described [14].

3.1. Characteristics of the study population

Six patients (two men and four women) were treated for large cystic mixed craniopharyngioma at Amiens University Medical Center between December 2016 and July 2019 and included in the study.

Prior to the combined treatment, two patients (#4 and #5) had undergone ventriculoperitoneal shunts performed 5 years and 9 months before placement of the Ommaya reservoir respectively.

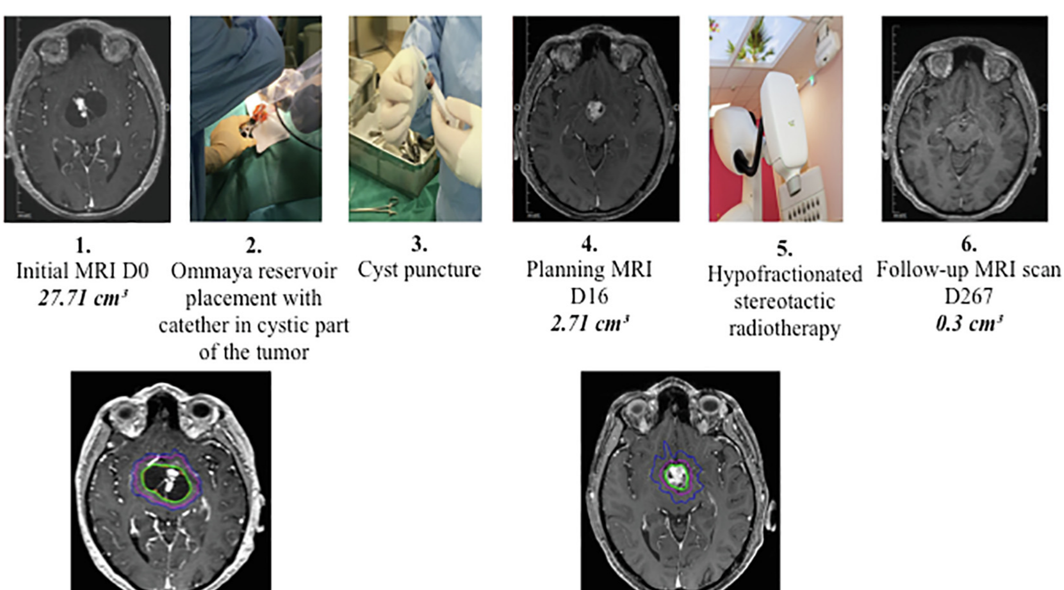

Fig. 1. The treatment process, and a tumor volume comparison (Patient #2). The fictitious and reference plans are shown below. The gross tumor volume and the 20% and 50% isodose volumes are shown in green, magenta and blue, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Main results of the combined approach.

	Mean	Median	Range
Age (year)	38.8	33	(19–68)
Delay Ommaya reservoir placement and planning imaging (days)	39.5	38	(5–80)
Follow-up (months)	12.83	12.5	(3–25)
Prescribed dose	25 Gy for 5 patients, 23 Gy for 1 patient		
Isodose for reference treatement plan	71.8	76.8	(51.9–84.9)
Volume before cyst puncture (cm3)	21.43	21.13	(2.63–37.95)
Volume at the time of planning MRI scan (cm3)	4.81	3.83	(2.62–10.79)
Isodose for fictitious treatement plan (%)	55.3	54.8%	(51.3–61.3)
Volume at the end of follow-up (cm3)	2.27	0.85	(0.2–4.95)

3.2. Volume measurements

The changes over time in tumor volume for each patient are reported in Fig. 2.

Three patients (#1, #2, and #6) presented a significant (>85%) tumor volume reduction between the baseline and the first follow-up MRI. Two patients (#3 and #6) showed transient enlargement of the cyst (2.13- and 3.75-fold, respectively) at the time of the planning MRI (2 months and 6 months after placement of the Ommaya reservoir for Patient #3 and Patient #6 respectively). At the end of the follow-up period, the volume reductions for patients #3 and #6 (after a new cyst puncture) were 62% and 91.5%, respectively. All other patients performed only two cyst punctures one after reservoir placement, one before the planning imaging. No patient had had tumor resection at the end of the follow-up.

3.3. Dosimetric comparisons

Dose-volume histograms are reported on Fig. 3. Comparative dosimetry data box plot are reported on Fig. 4.

The dose reduction in the optic chiasm Dmean was greatest for patients #1, #2 and #4, who presented large cysts (37.95 cm^3, 27.16 cm^3 and 37.57 cm^3, respectively).

3.4. Functional outcomes

After radiotherapy, the visual impairments had receded in patients #2, #3 and #6. Patients #2 and #3 developed endocrine deficiencies after radiotherapy balanced following prescription of replacement therapy. No neurological disorders were observed after radiotherapy.

4. Discussion

The combined approach described is intended to (I) treat large cystic or mixed craniopharyngioma while reducing and maintaining the size of the target volume, (II) using selectivity and gradient to optimize radiation doses to the target, (III) reducing the exposure of neighboring structures especially optic chiasm keeping high dose thanks to hypofractionation.

In Winkfield et al.'s pediatric series, substantial cyst size variations were reported during proton radiotherapy in 6 of the 17 children and prompted changes in treatment planning [15]. One patient in the series underwent cyst drainage to avoid enlargement of the treatment fields. In a study of 98 patients, Kobayashi et al. reported that a cystic/mixed tumor was a poor prognostic factor after gamma knife radiosurgery [16]. Chung et al. treated 31 patients with 12.2 Gy marginal dose gamma knife radiosurgery [17]. Cyst aspiration was performed in three cases, and led to satisfactory results. Smaller tumors (<4.2 cm^3) and single-component tumors were associated with a better prognosis. The puncture process might mitigate the poor prognosis associated with large cystic tumors and counteract further cyst enlargement.

Placement of an Ommaya reservoir enabled repeated cyst drainage until local control is obtained by radiotherapy. In an analysis of 11 adult patients with cystic craniopharyngioma, Frio et al. concluded that use of the Ommaya reservoir could reduce surgery-related morbidity [18]. After aspiration, visual function was improved. In the present study, three patients (#2, #3, and #6)

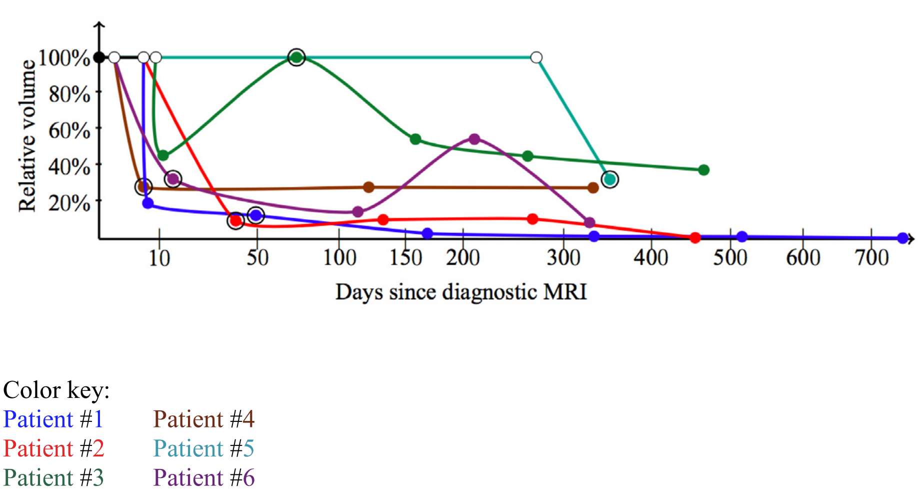

Fig. 2. Relative changes over time in the craniopharyngioma volume. A nonlinear time axis was chosen, so that the first time points could be seen more clearly. The black point is the craniopharyngioma volume at baseline (set to 100%). The Ommaya reservoir placement time is indicated by a white point. The planning MRI time points are indicated by a double circle. The later time points followed the radiotherapy.

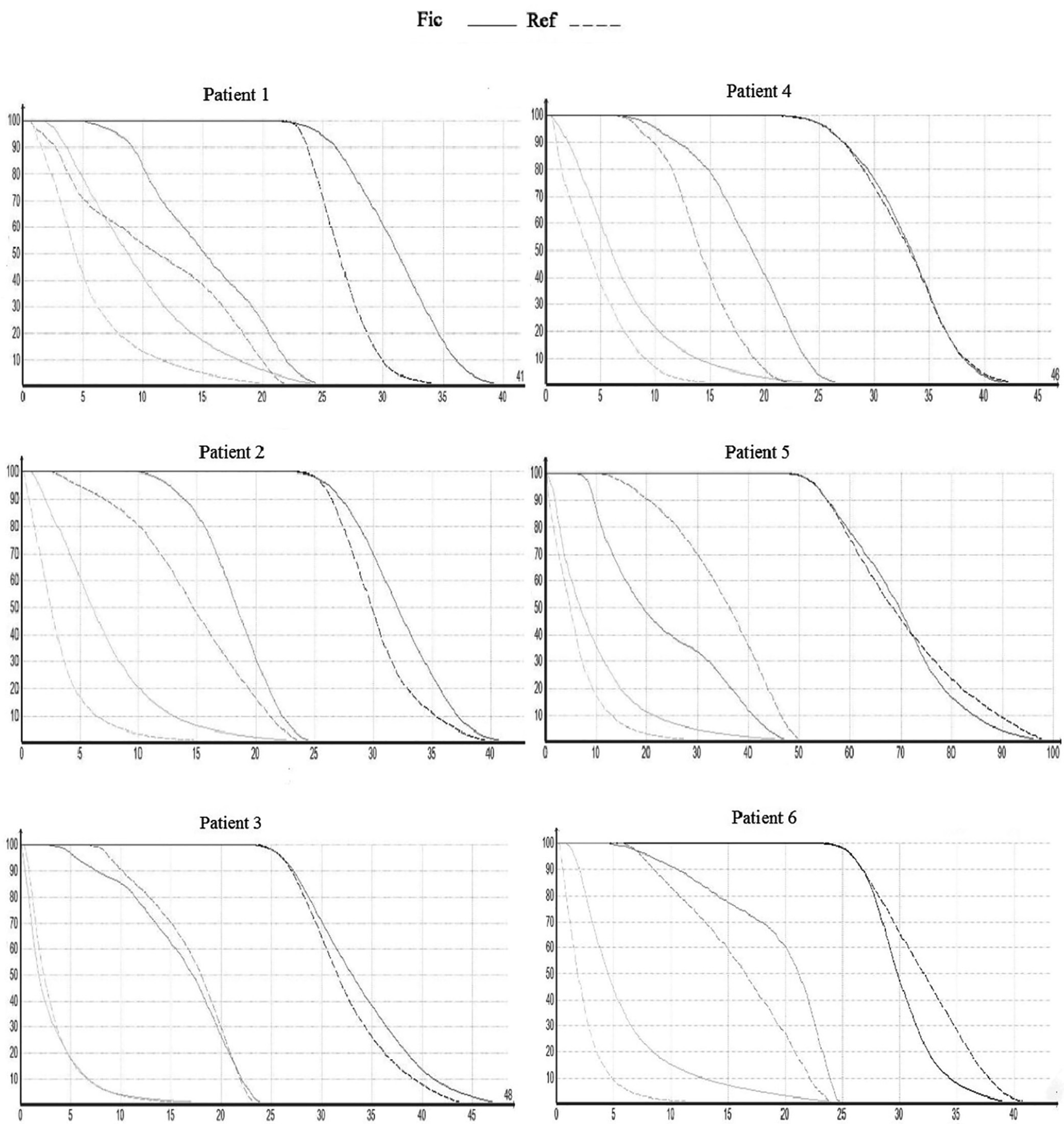

Fig. 3. Dose-volume curves. The target volume dose drop-offs are shown for the reference plan (the dotted black curve) and the fictitious plan (solid black curves). Dose-volume curves for the optic chiasm and the brainstem are shown in mid-grey and light grey, respectively. Fic: Fictitious plan, Ref: Reference plan.

experienced a reduction in visual symptoms after radiosurgery. The catheter conveniently placed for a trained team, was precise and safe thanks to the robotic assistance. Reservoir wound disunion was observed for one patient in our series, resolved two weeks later. Liu et al. evaluated the efficacy of aspiration and gamma knife radiosurgery in 77 patients with cystic tumors (including 9 craniopharyngiomas). Only reported adverse events were hemorrhage and transient nausea. Puncture provided rapid symptom relief, decreased the tumor volume, and minimizing radiation induced side effects [19].

The main advantages of stereotactic radiation are 3D positioning accuracy (enabling a reduction in target volume margins) and the multiple front beams (enabling a dose drop-off around the target). Hypofractionated radiosurgery enables to deliver higher doses to the target compared with the gamma knife while respecting constraints unattainable in a single dose [20].

Our treatment plans were optimized with regard to the gradient index from the ICRU 91 report and selectivity, rather than a prescription isodose. This might have affected the dose coverage, although dose fall-off may be a major concern for patients with a

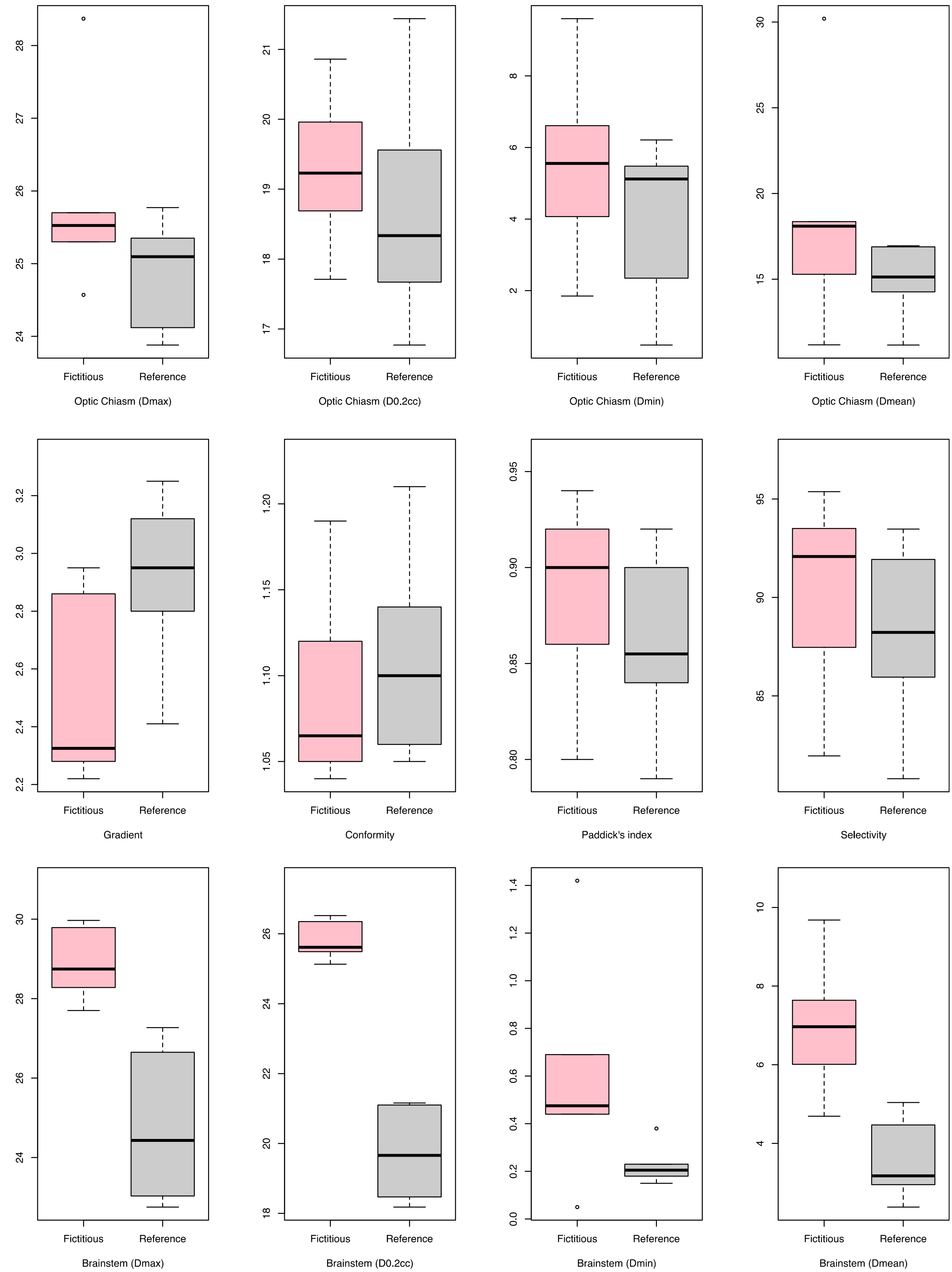

Fig. 4. Comparative dosimetric data. All brainstem Dmax and D0.03 cm^3 values were lower on the reference plan. The Optic chiasm Dmax values were lower for the reference plan with the exception of two patients.

benign tumor close to optic chiasm with a long life expectancy. Thanks to this optimization mean, most of the reference plans had a steeper dose fall-off for the target volume than the fictitious plans did. The observed indexes testified to the feasibility of the two treatment plans.

In all cases, the optic chiasm was relatively close to the target volume. We used 3D FIESTA sequences because the latter are known to define precisely optic chiasm and help to predict visual impairment [21]. High-quality imaging and cyst puncture improves the segmentation of organs at risk.

Hiniker et al. built a probit dose–response model to study visual pathway tolerance of perioptic tumors (including craniopharyngiomas) treated with hypofractionated stereotactic radiosurgery [22]. Based on the optic pathway constraints from TG101, a 25 Gy Dmax limit for 5 fractions is associated with a risk of radiation-induced optic neuropathy of less than 1%. For five fractions with a 20 to 30 Gy optic nerve Dmax was associated with a rise in the estimated risk of visual complications. The delivery of a dose of more than 10 Gy to the D0.2 cm^3 optic nerve could increase the likelihood of complications. The Dmax delivered to the optic pathway was considered to be the best predictor of toxicity. Except for Patient #2, all Dmax were lower for the reference plane in our dosimetry comparison. In contrast to the visual deterioration found to be associated with fractionated stereotactic radiosurgery in several studies [23–26], the visual impairment had improved after treatment for three of our six patients.

This technique could fit with large cystic tumors too close to structures to be spared for which a complete resection would be too morbid.

The small number of study participants prevented us from performing a statistical analysis. The retrospective aspect of the study prevented to obtain reliable toxicity and Ommaya tolerance data. Two patients in our series developed new-onset endocrine deficiencies after treatment, which is consistent with some published studies [6,24]. However, as a late-onset side effect, radiation-induced endocrinopathy and optic neuropathy can occur several years after treatment [27].

5. Conclusions

The combination of cyst puncture through an Ommaya reservoir with gradient and selectivity optimized hypofractionated radiotherapy appears to be feasible for large cystic craniopharyngiomas in adults. A longer follow-up period is needed to confirm a significant dosimetric advantage and to investigate late side effects.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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