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CLINICAL STUDY

Clinical outcomes of perioptic tumors treated with hypofractionated stereotactic radiotherapy using CyberKnife® stereotactic radiosurgery

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Abstract

Introduction Stereotactic radiation technique is widely reported as an effective treatment for various types of benign intracranial tumors. However, single fraction radiosurgery (SRS) is not recommended for tumors located close to the optic apparatus due to the restricted radiation tolerance dose of the optic pathway. Recent advances in radiotherapy include advanced frameless radiosurgery using hypofractionated stereotactic radiotherapy (HSRT), and this has become an attractive treatment option for perioptic tumors within 2–3 mm of the optic pathway. Accordingly, the aim of this study was to investigate the clinical outcomes of perioptic tumors treated with HSRT using CyberKnife® (CK) robotic radiosurgery system relative to tumor control, vision preservation and toxicity.

Methods This retrospective analysis of prospectively collected data included consecutive 100 patients that were diagnosed with and treated for perioptic tumor at the Radiosurgery center, Ramathibodi Hospital during the January 2009 to December 2012 study period.

Results The median tumor volume was 6.81 cm^3 (range 0.37–51.6), and the median prescribed dose was 25 Gy (range 20–35) in 5 fractions (range 3–5). After the median follow-up time of 37.5 months (range 21–103), two patients developed tumor progression at 6 and 34 months post-HSRT. The 5-year overall survival was 97%, and the 5-year local control was 97.5%. At the last follow-up, no vision deterioration or newly developed hypopituitarism was detected in our study.

Conclusions Although a longer follow-up is needed, HSRT yields a high level of local control and vision preservation, and should be considered a treatment of choice for perioptic tumor located close to the optic apparatus.

Keywords Clinical outcomes · Perioptic tumors · Hypofractionated stereotactic radiotherapy · CyberKnife® stereotactic radiosurgery

Introduction

Benign intracranial tumors originating from the pituitary fossa, tuberculum sella, cavernous sinus, sphenoid wing, orbital apex, or the optic nerve sheath can compromise the anterior visual pathways, and are, therefore, collectively referred to as perioptic tumors. Microsurgical technique is the treatment of choice, particularly in tumors that directly compress the optic apparatus. However, complete removal of a perioptic tumor may increase the risk of postoperative morbidity and mortality due to the complexity of the tumor and the nearby critical structures. Combination surgery and radiation therapy has been shown to be an effective method for managing complex perioptic tumors. Stereotactic radiation technique, including single-fraction radiosurgery (SRS) and conventional fractionated stereotactic radiotherapy (FSRT), is widely reported as an effective treatment in both adjuvant and primary settings for various types of benign intracranial tumors. However, SRS is excluded as a treatment option in benign perioptic tumors located within a few millimeters of the visual pathway, given the low radiation

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tolerance of the optic apparatus. As such, SRS is commonly recommended for benign perioptic tumor after surgery, and in tumors located an acceptable distance from the optic apparatus. FSRT is generally considered the radiation therapy of choice in tumors located adjacent or very close to the optic apparatus. The major disadvantage of this treatment choice is the prolonged treatment time (4–5 weeks). Recent advances in radiotherapy include advanced frameless radiosurgery using hypofractionated stereotactic radiotherapy (HSRT). The advantage of this treatment option is that perioptic tumors can be treated according to a fractionated schedule, which is considered to be safer for the optic apparatus than single large-dose radiosurgery, without compromising the tumor control rate. Moreover, the 2–5 fractions required for HSRT is significantly more convenient for the patient than the 25–30 fractions required for FSRT.

The first frameless robotic whole body radiosurgery system in Thailand was installed at our center in 2009; specifically, a CyberKnife® (CK) system. In an attempt to improve treatment outcome and patient satisfaction while maintaining a low rate of optic neuropathy, we began providing protocol-based HSRT for perioptic tumors using the CK system.

The aim of this study was to investigate the clinical outcomes of perioptic tumors treated with HSRT using CK relative to tumor control, vision preservation and toxicity.

Materials and methods

Patients

This retrospective analysis of prospectively collected data included consecutive patients that were diagnosed with and treated for perioptic tumor at the Radiosurgery center, Department of Radiology, Ramathibodi Hospital during the January 2009 to December 2012 study period. The inclusion criteria for HSRT protocol were, as follows: (1) benign intracranial perioptic tumor located within 2 mm of the optic apparatus, as determined by magnetic resonance imaging (MRI); (2) recurrent or residual tumor after maximum resection; (3) surgically or medically inoperable; and/or, (4) patient preference. All patients were counseled regarding the treatment protocol, and all cases were approved by our radiosurgery board before starting treatment. The protocol for this study was approved by the Ramathibodi Institutional Review Board, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. This study complied with all of the principles set forth in the Declaration of Helsinki (1964) and all of its subsequent amendments.

HSRT by CyberKnife® system

CyberKnife® (CK) model G4 (Accuray, Inc., Sunnyvale, CA, USA) uses a 6-MV light-weight linear accelerator that is mounted on an articulated robotic arm. Multiplan Treatment Planning Software (Accuray, Inc.) was used for inverse radiation treatment planning and real-time 6D skull tracking for image-guidance to visualize and engage the intracranial lesion. A thermoplastic facemask was individually constructed for patients to wear while lying in the supine position. A CT simulation, with or without contrast with the mask applied, was generated with 1.25 mm slice thickness. The set of CT simulation images, with or without gadolinium-enhanced MRI, was transferred to the treatment planning workstation. Gross tumor volume (GTV) and critical structure were delineated in each consecutive slice of CT and MRI. No additional margin was added to the GTV to obtain the clinical target volume (CTV) and the planning target volume (PTV).

HSRT was delivered in 3–5 fractions, with a total dose of 20–25 Gray (Gy). Radiation dose was prescribed to the periphery of the lesion. Prescribed isodoses were selected individually for each patient, ideally to cover > 95% of the target volume. Selection of total tumor dose, number of fractions, and prescribed isodose varied from patient to patient according to tumor subtype, size and shape of tumor, tumor location, and individual physician preference. For example, physicians at our center normally prefer a higher radiation dose in functioning pituitary adenoma compared to other benign tumors. As such, a higher total tumor dose might be prescribed. In instances where the maximal point dose delivered to the optic apparatus exceeded the tolerance dose of 5 Gy per fraction, the prescribed dose was reduced. Radiation treatment was given once a day, for a consecutively 3–5 days within a 1-week period. Treatment planning (Fig. 1) was determined and finalized by a radiosurgery team consisting of neurosurgeons, radiation oncologists, and medical physicists.

Assessment of response and toxicity

An integration of the neuro-ophthalmologic examination and MRI was regular performed to assess the overall outcome. Ophthalmologic outcome was measured by ophthalmologists before HSRT, every 3–6 months for the first 2 years after HSRT, and then annually thereafter. Visual acuity (VA) and visual field (VF) was evaluated by using the Snellen visual acuity test and the formal Goldman visual field with Swedish interactive thresholding algorithms (SITA) respectively. The improvement or impairment of VA was defined when reading ability increased

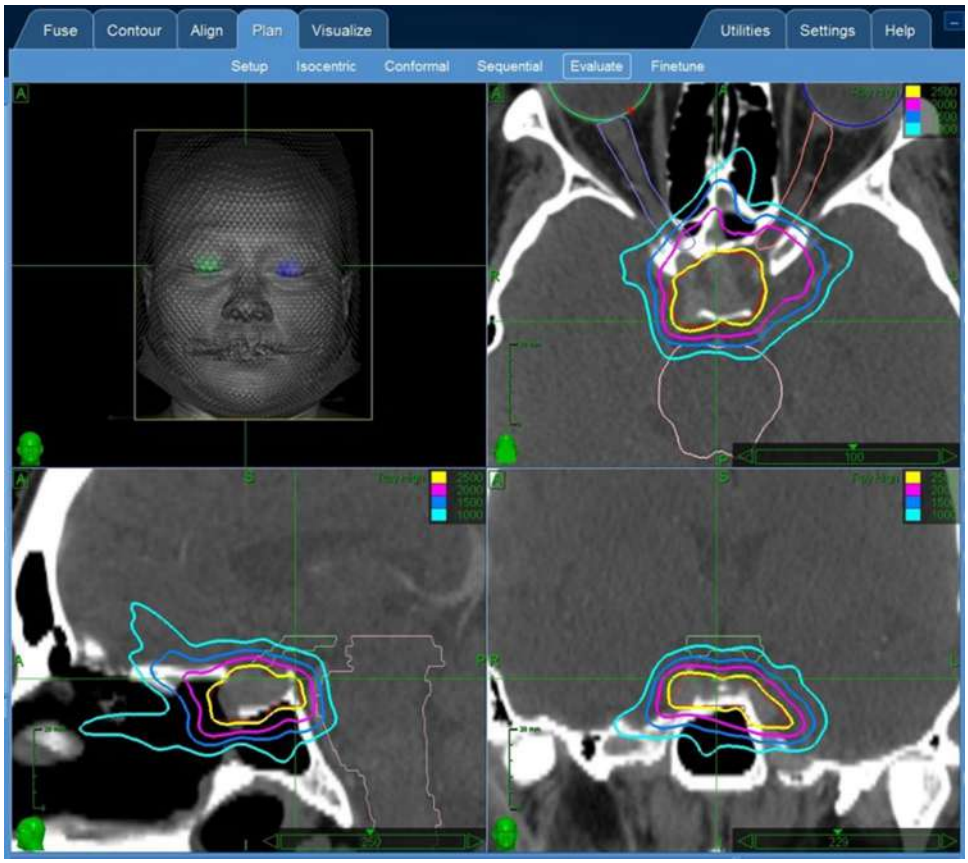

Fig. 1 Screen capture from CyberKnife® plan showing isodose lines covering the tumors and critical organs

or decreased by two lines or more. VF was considered better or worse when the VF mean deviation increased or decreased by 2 decibel or more, respectively.

MRI was performed annually or biannually for the first 5 years, and then every 2–3 years thereafter. Radiologic response was reported according to the standard RECIST criteria [1]. Complete response (CR) was defined as complete disappearance of lesion. Partial response (PR) was defined as more than 30% decrease in diameter compared to baseline. Progression disease (PD) was defined as more than 20% increase in diameter. Stable disease was defined as any response that not meet criteria for CR, PR, or PD. Tumor control was defined as the absence of radiologic tumor progression. Temporary increase in tumor size was also considered tumor control. Endocrine assessment with serum and/or urine tests was conducted by endocrinologists. The criteria for complete remission of functioning pituitary adenomas were, as follows (1) fasting growth hormone (GH) levels < 2.5 ng/ml and normal insulin-like growth factor 1 (IGF-1) level in acromegaly; (2) normalized ACTH, cortisol, and urinary free cortisol levels in Cushing disease; and, (3) prolactin levels < 20 ng/ml in prolactinoma.

Statistical analysis

All data analyses were performed using SPSS Statistics version 18 (SPSS, Inc., Chicago, IL, USA). Categorical data are presented as frequency and percentage, and continuous data are shown as median and range. Local tumor control (LC) and overall survival were calculated using Kaplan–Meier method.

Results

One hundred consecutive perioptic tumor patients treated with HSRT by CK were included. The gender proportion breakdown was 26 (26%) male and 74 (74%) female, with a median age of 49.5 years (range 15–76). 77 (77%) patients had previously undergone surgery, and 3 (3%) previously received radiation therapy by 2D or 3D conventional radiation technique (total dose: 50–54 Gy). 38 (38%) cases experienced visual deficit prior to HSRT, and 33 (33%) had previously received hormone supplement for treatment of hypopituitarism. The median prescribed dose of 25 Gy (range 20–35) in 5 fractions (range 3–5) was used. The

median prescribed isodose was 72% (range 65–85). The median prescribed and maximum biological effective dose (BED) Gy_2 of the tumor was 87.5 Gy (range 60–157.5) and 128.9 Gy (range 60–200), respectively. The median tumor volume was 6.81 cm^3 (range 0.37–51.6). The median maximum BED Gy_2 of the right optic nerve, left optic nerve and optic chiasm was 50.4, 39.7 and 54.6 Gy, respectively. The baseline demographic, clinical, and treatment characteristics of included perioptic tumor patients are summarized in Table 1.

Overall survival and tumor control

The median follow-up time was 37.5 months (range 21–103). Two patients developed tumor progression after HSRT. The first patient was a 35-year-old woman with prolactinoma. Tumor enlargement with uncontrolled prolactin level was detected at 6 months after HSRT. She was subsequently treated with tumor removal and was still alive without tumor progression at the last follow-up. The second case was a 65-year-old meningioma patient who developed tumor progression that was identified at 34-months post-HSRT. That patient succumbed to his disease. A patient who had pituitary adenoma died from acute brain hemorrhage without evidence of tumor progression at 16-months post-HSRT. In this study, the 5-year overall survival rate was 97%, and the 5-year local control rate was 97.5% (Fig. 2).

Imaging control

The imaging response included stable size (74%), partial response (24%) (Fig. 3), and progression disease (2%). There were few patients that their tumors initially progressed and then eventually became stable (Fig. 4).

Vision preservation

Thirty-eight (38%) of 100 patients experienced visual deficit before HSRT, and 4 of those (10.5%) reported vision improvement after HSRT. One pituitary adenoma patient developed transient slight visual impairment at 17 months post-HSRT without evidence of tumor progression. That patient's condition resolved a few months after start of symptomatic treatment. At the last follow-up, no newly reported post-HSRT permanent visual impairment was observed or reported.

Hormonal control

Of the 40 pituitary adenoma patients treated with HSRT, 13 functioning pituitary adenomas consisting of GH-producing (n = 7), prolactin-producing (n = 5), and ACTH-producing (n = 1) adenomas were followed for hormonal evaluation. Hormonal control to HSRT in the setting of concurrent medical therapy was analyzed. At the last follow-up, 7 of 13 functioning pituitary adenoma patients

Table 1 Baseline demographic, clinical, and and treatment characteristics of 100 perioptic tumor patients

Gender, n (%)	
Male	26 (26%)
Female	74 (74%)
Age (years), median (range)	49.5 (15–76)
Follow-up time (months), median (range)	37.5 (21–103)
Treatment setting, n (%)	
Previous surgery	77 (77%)
Radiation alone	23 (23%)
Previous radiation, n (%)	3 (3%)
Pre-CK visual deficit, n (%)	38 (38%)
Pre-CK hypopituitarism, n (%)	33 (33%)
Type of tumor	
Meningioma	57 (57%)
Pituitary adenoma	40 (40%)
Schwannoma	2 (2%)
Craniopharyngioma	1 (1%)
Location	
Pituitary fossa	41 (41%)
Cavernous sinus	38 (38%)
Sphenoid wing	15 (15%)
Anterior clinoid	2 (2%)
Petroclival	2 (2%)
Optic canal	2 (2%)
Target volume (cm^3), median (range)	6.81 (0.37–51.6)
Prescribed dose (Gy), median (range)	25 (20–35)
Prescribed BED Gy_2, median (range)	87.5 (60–157.5)
Maximum BED Gy_2, median (range)	128.9 (60–200)
Prescribed isodose, % (range)	72% (65–85%)
Total prescribed dose × no. of fractions, n (%)	
24 Gy × 3 (BED Gy_2 = 120)	4 (4%)
20 Gy × 4 (BED Gy_2 = 70)	1 (1%)
20–25 Gy × 5 (BED Gy_2 = 60–87.5)	94 (94%)
35 Gy × 5 (BED Gy_2 = 157.5)	1 (1%)
Conformality index, median (range)	1.32 (1.11–1.78)
Modified conformality index, median (range)	1.38 (1.14–1.87)
Heterogeneity index, median (range)	1.39 (1.18–1.91)
Median coverage, % (range)	95.05% (69.87–99.96%)
Maximum BED Gy_2 of optic nerve/chiasm, median (range)	
Right optic nerve	50.4 (3–126)
Left optic nerve	39.7 (6.3–117.2)
Optic chiasm	54.6 (3.9–134)

Pre-CK pre-CyberKnife® stereotactic radiosurgery, *BED* biologically effective dose, *Gy* gray

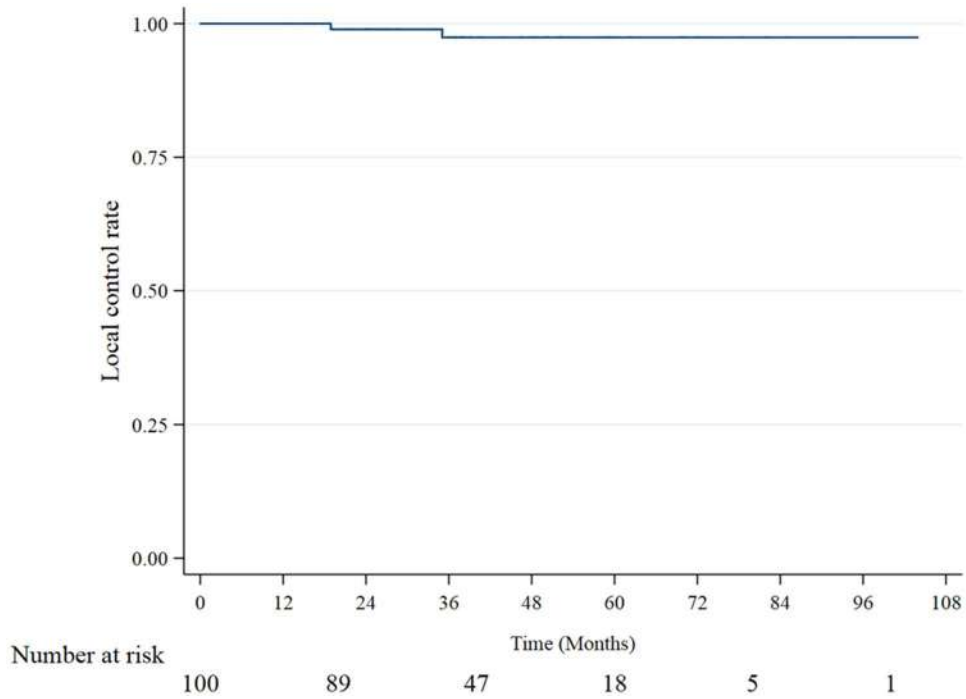

Fig. 2 Kaplan–Meier curve showing the local control rate

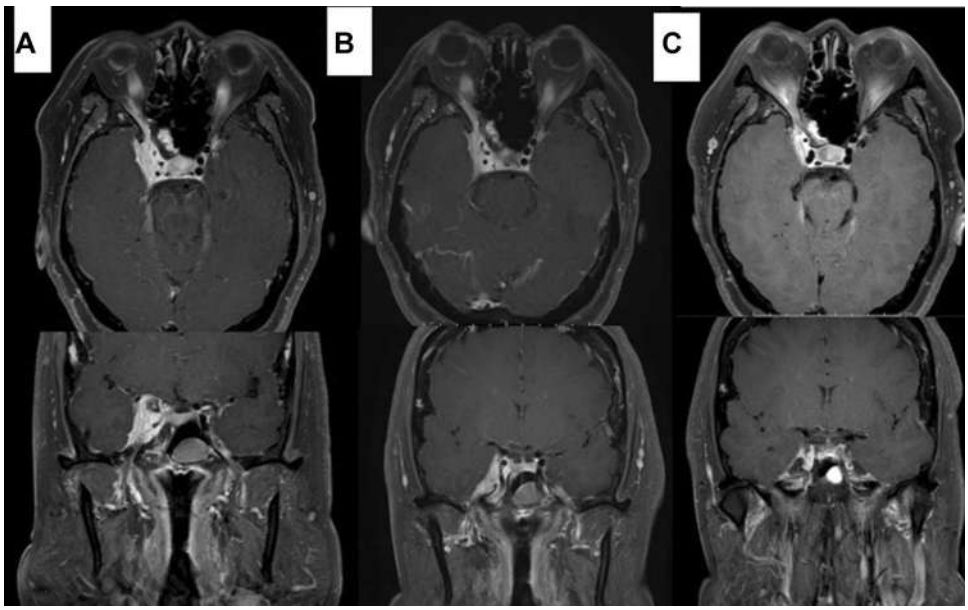

Fig. 3 Axial and coronal MRI showing residual pituitary adenoma in right cavernous sinus adhering to the right optic nerve and optic chiasm after tumor resection: **a** 1- and 3-year follow-up MRI; **b, c** tumor shrinkage is observed after hypofractionated stereotactic radiotherapy (HSRT) (25 Gy in 5 fractions)

(54%) had complete hormone normalization. The median time to hormone normalization was 28 months (range 24–71). The complete hormonal remission rate in GH-producing, prolactin-producing, and ACTH-producing adenoma was 57, 40, and 100%, respectively. One prolactinoma patient who had a significant increase in prolactin level and simultaneous enlargement of tumor in the HSRT field underwent salvage tumor removal. After repeat surgery, both the tumor and the hormone level were controlled at the last follow-up.

Complications

HSRT by CK was well-tolerated. No newly developed hypopituitarism or other significant morbidities were observed in any patient at the last follow-up.

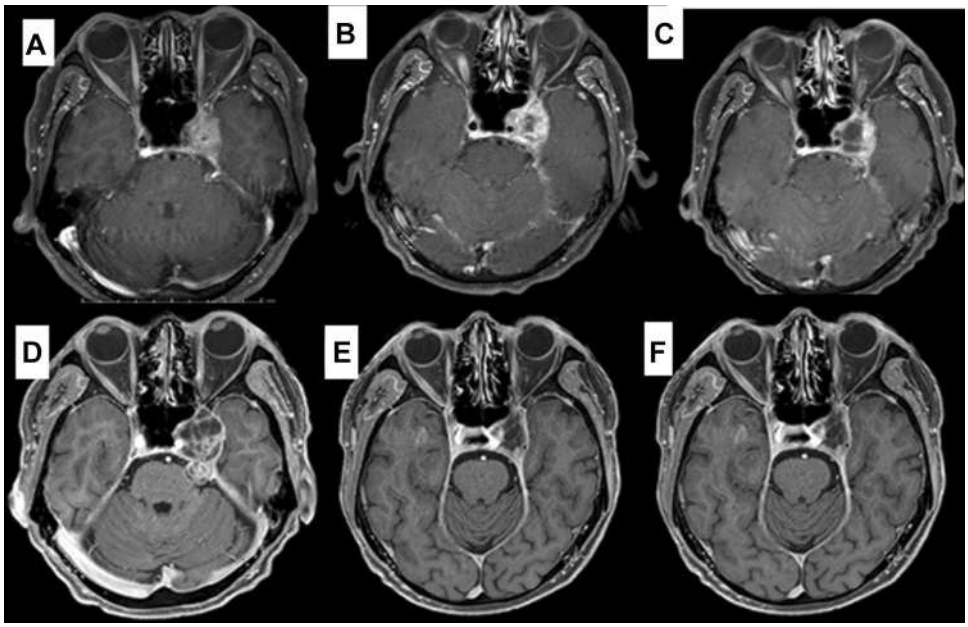

Fig. 4 Axial MRI showing a trigeminal schwannoma adhering to the left optic nerve: **a** 1-, 2-, and 3-year follow-up MRI; **b–d** continuously increased size and necrotic area are observed; **e, f** however, at the 4- and 6-year follow-up, the tumor shows a less bulbous appearance. This finding is consistent with pseudoprogression after hypofractionated stereotactic radiotherapy (HSRT)

Discussion

Perioptic tumors are tumors that originate from the pituitary fossa, tuberculum sella, cavernous sinus, sphenoid wing, orbital apex, or optic nerve sheath that can compromise the anterior visual pathways. Maximum safety resection, particularly for optic nerve decompression, is the treatment of choice. Radiation therapy (RT) plays an important role in an adjuvant setting after residual tumor or in recurrence cases. Definitive RT is also recommended in patients who are not candidates for surgery. Stereotactic irradiation, including single-dose radiosurgery (SRS) and fractionated stereotactic radiotherapy (FSRT), has been reported as an efficacious treatment for various types of benign brain tumors. SRS yielded a tumor control rate of greater than 90% in many benign parasellar tumors [2–4]. However, SRS is not recommended in perioptic tumors located adjacent to the optic apparatus, because single large-dose radiation can cause more injury to late-responding tissue. Previous studies reported high risk of visual injury if the optic nerve is irradiated more than 8–10 Gy in a single fraction [5, 6]. FSRT delivered with a small daily dose per fraction (1.8–2 Gy/day) accumulates to a total dose of 45–50 Gy in 25–30 fractions, and this was found to be of radiobiological advantage by sparing late-responding tissue. Accordingly, FSRT is generally recommended in tumors located adjacent or very close to the optic apparatus. From previous studies in perioptic tumors, FSRT yielded favorable long-term tumor control rates that ranged from 80 to 100%, and a radiation-induced optic neuropathy (RION) rate of 0–5% [7–12]. A notable disadvantage of FSRT to the patient is the longer treatment time that is associated with conventional fractionation schedules (4–5 weeks).

In recent years, advanced frameless radiosurgery with hypofractionated stereotactic radiotherapy (HSRT) has been developed, and has become an attractive alternative approach to treating perioptic tumors. HSRT has shown several treatment benefits in perioptic benign tumors, including the radiobiological advantage of delivering a high biologically effective dose (BED) and low radiation toxicity to the optic apparatus [13–15]. Moreover, the 2–5 fractions required for HSRT is more convenient for patients than the aforementioned lengthy 4–5 week fractionation schedule. Given the relatively recent release of HSRT, previous studies in perioptic tumors are still limited. In this study, we report the findings of a relatively large number of perioptic tumor patients treated with HSRT by CK at a university-based national tertiary referral hospital.

The 97.5% tumor local control (LC) and 100% vision preservation rates found in this study are comparable with the 94–100% LC rates and 94–100% visual preservation rates reported in previous studies [13, 16–22] (Table 2). The dose/fraction selection in a hypofractionated schedule to treat perioptic tumors still needs to be established. Various hypofractionated dose regimens are described in the literature, with variations that range from 20 to 25 Gy in 3–5 fractions [13, 16, 22]. The aforementioned gray range is equal to a BED of 76–120 Gy using an α/β value of 2. The average dose/fraction used in our protocol was 25 Gy in 5 fractions with a BED of 87.5 Gy_2 that falls within the BED range of 76–120 Gy_2 reported in the immediately aforementioned studies. Compared to the BED Gy_2 of SRS and FSRT, which clearly demonstrated high tumor control probability [23],

Table 2 Literature review of previous studies that reported local control rates in patients treated for perioptic tumor with HSRT

Author	Number of patients	Prescribed dose (Gy), median (range)	Number of fractions	Type of HSRT system	Follow-up (mo), median (range)	Volume (mL), median (range)	Local control (%)	Vision preservation (%)
Adler et al. [14]	Total (49) -Meningioma (27) -Pituitary adenoma (19) -Craniopharyngioma (2) -Germ cell tumor (1)	20.3 (15–30)	2–5	CK	46 (13–100)	7.7 (1.2–42)	94.0	94.0
Kim et al. [17]	Total (22) -Meningioma (13) -Pituitary adenoma (3) -Craniopharyngioma (3) -Schwannnoma (1) -Hemangioblastoma (1) -Hemangioma (1)	19 (15–20)	3–4	GKS	29 (14–44)	3.99 (3.08–11.4)	96.0	96.0
Killory et al. [18]	Pituitary adenoma (20)	25 (15–25)	3–5	CK	26.6 (10.5–41)	17.5 (2.3–42.3)	100	100
Jee et al. [19]	Total (24) -Meningioma (22) -Craniopharyngioma (6) -Pituitary adenoma (6) -Schwannoma (2) -Hemangioma (2)	20 (16–20)	4	GKS	50 (19–87)	3.85 (3.08–16.8)	94.6	94.7
Liao et al. [20]	Pituitary adenoma (34) Meningioma (62)	21	3	Novalis®	36.8 (16–72)	5.06 (0.82–12.69)	100	100
Conti et al. [13]	Retrospective data (25)	23 (18–34)	2–5	CK	57.5 (48–82)	4.95 (0.3–18.8)	100	100
	Prospective data (39)	25 (19.5–40)	5 (2–5)		15 (3–38)	7.5 (1.2–44.1)	100	100
Puataweepong et al. [21]	Pituitary adenoma (40)	25 (20–28)	5 (3–5)	CK	38.5 (14–71)	3.35 (0.8–25.9)	97.5	100
Lee et al. [22]	Total (26) -Meningioma (17) -Hemangioma (4) -Pituitary adenoma (2) -Schwannoma (2) -Craniopharyngioma (1)	27.8 (25.6–32.2)	5	CK	20 (6–46)	8.2 (0.1–26.5)	100	100

HSRT hypofractionated stereotactic radiotherapy, *CK* CyberKnife® stereotactic radiosurgery system, *GKS* gamma knife surgery system

the average BED used in the hypofractionated studies that ranged from 76 to 120 Gy_2 seems to be lower than the BED Gy_2 of 13–14 Gy for SRS that was 97.5–112 Gy_2 and for FSRT that was 100 Gy_2. However, the lower BED of hypofractionated schedules did not compromise local control, as shown in the previous studies.

Radiation-induced optic neuropathy (RION) is the potential complication of most concern after radiation, because the optic apparatus is a radiosensitive structure that has a low tolerance for radiation. Leavitt et al. [24] and Pollock et al. [25] reported the dose tolerance of optic apparatus after SRS of 10 and 9.2 Gy, respectively. These were consistent with the review from Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) showing that the optic apparatus has a dose tolerance in the range of 8–10 Gy for SRS, and 55–60 Gy for conventional fractionation schedules [26]. Given that HSRT is still a relatively new treatment for perioptic tumor, the true dose tolerance of the optic apparatus and the incidence of RION are not yet fully understood. Conti et al. [13] reported the normal tissue complication probability (NTCP) on the optic apparatus to be 0.02, 0.12, and 2.98% relative to a Dmax of 24, 25 and 27.5 Gy in 5 fractions to the optic nerve and chiasm, respectively. The use of 22–25 Gy in 5 fractions (BED range 70–87.5 Gy_2), with a dose limit at the optic apparatus of 5 Gy per fraction is safe for the optic apparatus, as confirmed by the clinical data [13, 16, 27–29]. The use of a more aggressive protocol (i.e., 21 Gy in 3 fractions with a BED Gy_2 of 94.5) was associated with visual deterioration in 1 patient [16]. More importantly, most of the patients who developed visual deterioration had tumor progression [16, 28]. At present, the issue of tumor progression seems to be of more concern than RION relative to the currently used hypofractionated regimen. Conti et al. [13] estimated the BED of the commonly used hypofractionated regimen of 22–25 Gy in 5 fractions to range from 70 to 87.5 Gy_2 and to have a TCP of $\leq$31%, while the total higher dose of 27.5 Gy in 5 fractions, which is equivalent to a BED of 103 Gy_2, increases the TCP to 91% according to their model. However, this dose cannot be delivered to the optic apparatus since the risk of optic neuropathy is 100 times higher than when using 24 Gy in 5 fractions, which carries a near zero risk of toxicity according to the NTCP model. The most recent pooled data from the AAPM working group on SBRT [30] which analyzed dosimetric and clinical predictors of RION after stereotactic RT (1–5 fractions) reported that prior irradiation was associated with a crude 10-fold increased RION risk. They also reported the incidence of RION of less than 1% if the maximum point dose to optic apparatus was 12 Gy in 1 fraction, 20 Gy in 3 fractions, and 25 Gy in 5 fractions. To date, strategies to achieve the best TCP/NTCP ratio vary from center to center depending on institute protocol. At our center, the prescribed dose of 25 Gy in 5 fractions is commonly used. However, if it is determined that the optic apparatus will be exposed to a total dose that exceeds its tolerance threshold, a lower prescribed dose will be used. In contrast, Conti et al. [13] recommended 15 fractions that escalate to a total dose of 40 Gy in cases where a 5 fraction regimen is not sufficient to achieve the best possible TCP/NTCP ratio. The most effective hypofractionated schedule has not yet been established. Nevertheless, conventional fractionation, which was safe and effective (perhaps more effective than lower the prescribed treatment dose if the prescribed dose would be subtherapeutic) could also be another feasible option. The decision regarding dose fraction selection is dependent on multiple factors, including tumor volume, relationship with and extent of optic apparatus involvement, and previous history of radiation. Further study in a large number of patients over a long-term period is needed to evaluate the most appropriate dose fractionation schedules.

While fractionation schedule seems to have no impact on local control, the impact of fractionation schedule on the rate of hormone normalization is still being debated. Most series reported endocrine remission that varies widely from 5 to 63% after SRS treatment [31–33], and from 20 to 42% following FSRT treatment [11, 34]. Some reports suggest that the decline in serum growth hormone is faster after gamma knife SRS than after fractionated RT [35, 36]. The 54% hormone normalization rate observed in this study is similar to the rates reported in other HSRT studies [18, 20], and also comparable to the rates observed after SRS and FSRT. However, variations in study design, differences in pretreatment hormone level, the use of different criteria to define hormone normalization, the use of concurrent medical therapy, and variations in follow-up duration make it difficult to interpret published results, relative distinguishing efficacy between various fractionation schedules.

HSRT is associated not only with a low incidence of RION, but also with a low rate of hypopituitarism. Stereotactic radiation technique has an advantage over conventional radiation therapy, because it reduces set-up error and planning target volume with rapid dose fall-off outside the tumor volume, so the nearby pituitary gland and hypothalamus should be exposed to less radiation. The incidence of hypopituitarism was reported to be greater than 50% after conventional RT in previous studies [37, 38], and less than 20% after treatment with SRS [17]. In this study, we found no newly detected hypopituitarism after HSRT—a finding that is comparable with that of a previous study [20]. However, our study was retrospective in nature without systematic regular checkup of hormone level. Therefore, the exact rate of newly-developed hypopituitarism may have been missed. Although it is still possible to develop the late RT effects (i.e. hypopituitarism or RION) within 3 years, our follow-up time may be not long enough to draw a conclusion that they will not occur later.

Conclusion

The findings of this study revealed excellent tumor control and vision preservation after HSRT by CK using 25 Gy in 5 fractions in perioptic tumor patients. The short treatment time suggests HSRT as the recommended treatment for perioptic tumors located within 2–3 mm of the optic apparatus. Continued study with long-term follow-up to evaluate for hormonal control, and long-term complications, such as RION, hypopituitarism, and radiation-induced malignancy, is needed to further understand the long-term efficacy of this radiation modality in this patient population.

Compliance with ethical standards

Conflict of interest All authors declare no personal or professional conflicts of interest, and no financial support from the companies that produce and/or distribute the drugs, devices, or materials described in this report.

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