学 術
Arts and Sciences
原 著

Optimization of radiation exposure to the eye lens in stereotactic radiosurgery

定位放射線治療における水晶体線量の最適化

Kohei Kawasaki[1), Osamu Nagano[2), Kyoko Aoyagi[2), Takahiro Kageyama[1)

1) Department of Radiology, Chiba Cardiovascular Center
2) Gamma Knife House, Department of Neurosurgery, Chiba Cardiovascular Center

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【Abstract】
In 2012, International Commission on Radiological Protection (ICRP) published a threshold dose for cataract as 0.5 Gy. However, little evidence is available on determination of radiation dose to the eye lens in gamma knife radiosurgery (GKS). The purpose of this study was to confirm the fact of radiation exposure to the eye lens and produce an appropriate treatment plan for GKS. From January 2015 to December 2016, 57 patients (39 women; age, 27-84 years) with single lesion of meningioma were enrolled in this study. We retrospectively measured the dose to the eye lens in the treatment plans that have been performed for these patients. To investigate whether a reasonable dose distribution could be designed we modified the plans regarding the eye lens as organ at risk in the cases that the lens dose exceeded 0.5 Gy. Then we compared treatment parameters between plans before and after modification. As a result, the maximum dose to the eye lens reached the threshold level for cataract in 13 cases. In the modified treatment plans for all of these cases, the maximum dose to the eye lens was reduced to less than 0.5 Gy although the irradiation time was prolonged by 11.6 minutes on average. There was no significant difference in dose covering 95% of the lesion volume (D95). In conclusion, in 23% of patients who underwent GKS, the eye lenses were exposed beyond the ICRP threshold dose for cataract. Ophthalmological follow-up might be required in these cases. In addition, we could produce optimal treatment plan with reduced lens dose to less than the threshold dose for cataract while keeping D95 with acceptable prolongation of irradiation time.

【要 旨】
2012年，国際放射線防護委員会（ICRP）は白内障のしきい線量を0.5Gyと発表した．この研究の目的は，ガンマナイフ治療における水晶体被ばくの実態を明らかにし，治療計画の最適化を図ることである．まず，単発の髄膜腫57症例に対して実際に施行された治療における水晶体被ばくを遡及的に調べたところ，13例で0.5Gyに達し眼科的経過観察の必要性が示唆された．次に，ICRPのしきい線量を超えたこれらの計画を見直し，変更前後の治療パラメーターを比較した．全症例において病変体積の95%を包含する線量に有意差はなく，臨床的に容認できる照射時間の延長で水晶体線量を0.5Gy未満に減少させることができた．

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1. Introduction

Gamma knife radiosurgery (GKS) is one of the techniques of stereotactic radiosurgery, which is specialized for intracranial lesions [1)]. The steepness of the dose distribution curve of stereotactic radiosurgery raises concern about adverse radiation effects. Thus, it is essential to be cognizant of the spatial relationship between organs at risk of developing side effects, target lesions and the dose distribution. Therefore, there have been several reports to optimize the radiation dose to organ at risk in this field [2-5)].

In International Commission on Radiological Protection (ICRP) publication 118 [6)], it was required to pay particular attention to cataract. The threshold dose for cataract of 0.5 Gy was proposed, which is drastically lower than previously considered. However, little evidence is available on dose optimization for the eye lens involving the new threshold value in GKS. The purpose of this study was to confirm the fact of radiation exposure to the eye lens in GKS and produce an appropriate treatment plan to prevent the lens dose from reaching the ICRP threshold level.

川﨑 康平[1)，永野 修[2)，青柳 京子[2)，景山 貴洋[1)

1）千葉県循環器病センター放射線科　診療放射線技師
2）千葉県循環器病センター脳神経外科ガンマナイフ治療部　医師

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2. Materials and methods

This study was approved by institutional review board (IRB) of our hospital (IRB No. 392). We took care not to infringe on the patients' right to privacy by making the data anonymous. All patients provided written informed consent.

2-1 Patient characteristics

From January 2015 to December 2016, 57 patients with single meningioma were enrolled in the present study. Patient characteristics and the location of the lesions are presented in Table 1. GKS was performed in all the patients using the Leksell Gamma Knife Perfexion (Elekta Instruments AB, Stockholm, Sweden).

Table 1 Patient characteristics

Characteristic	Value
Total no. of patients	57
Men/women	18/39
Age (years), median (range)	64 (27-84)
Lesion location	
Right/left	29/28
Frontal lobe	21
Temporal lobe	14
Occipital lobe	2
Parietal lobe	2
Cerebellopontine angle	12
Cerebellar hemisphere	6

2-2 Confirmation of the fact of radiation exposure to the eye lens

To confirm how much the eye lens was irradiated, we retrospectively calculated the dose to the eye lens in the treatment plans that have been conducted for GKS. The peripheral dose prescribed for the lesions was 12.5-18 Gy. In the cases of the lesion adjacent to the optic nerve, staged GKS was applied and peripheral doses of 8.5-9 Gy were prescribed [7]. On treatment plan system (Leksell GammaPlan 10.1.1; Elekta Instruments AB, Stockholm, Sweden), we newly contoured the eye lens in the original plans and overlaid the dose distribution. And then, we regarded the eye lens as an organ at risk and measured following dose parameters: maximum lens dose; mean lens dose; the volume of the eye lens received beyond 0.5 Gy ($V_{0.5}$). Additionally, we analyzed following factors that might affect the dose parameters: lesion location (anterior, mid, posterior, ipsilateral and contralateral); lesion volume; peripheral dose; number of shots; existence of other organs at risk.

2-3 Optimization of the treatment plan

We further analyzed the cases in which the maximum lens dose reached the threshold level as a result of Sect. 2-2. We modified the original treatment plans to design reasonable dose distribution. We intended to make 0.5 Gy isodose line away from the eye lens without compromising lesion control by employing a hybrid isocenter technique referred to as "composite shot" with collimators of different sizes that are blocked and mixed. Then, we compared following dose parameters between before and after modification: maximum lens dose; dose covering 95% of the lesion volume (D95); irradiation time.

2-4 Statistical analysis

All statistical analyses were performed using EZR (http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmed.html) [8]. We evaluated the factors affecting the dose to the eye lens using multiple regression analysis. We compared the maximum lens dose, the D95 and the irradiation time between original and modified plans using the Wilcoxon signed rank test. The significant level was defined as 0.05.

3. Results

3-1 Confirmation of the fact of radiation exposure to the eye lens

The measurement results of the maximum

and the mean dose to the eye lens and the $V_{0.5}$ are shown in Table 2. The maximum lens dose, the mean lens dose and The $V_{0.5}$ ranged 0-1.1 Gy, 0-0.8 Gy and 0-276.3 mm^3, respectively. Figure 1 shows the frequency distribution of the maximum lens dose. In 13 cases (23%), the eye lenses were exposed beyond 0.5 Gy which is the ICRP threshold dose for cataract.

Table 2 Measurement of the dose parameters

Dose parameter	Value
Maximum lens dose (Gy)	0.1 (0-1.1)
Mean lens dose (Gy)	0.1 (0-0.8)
$V_{0.5}$ (mm^3)	30.4 (0-276.3)

Data are presented as median (range)

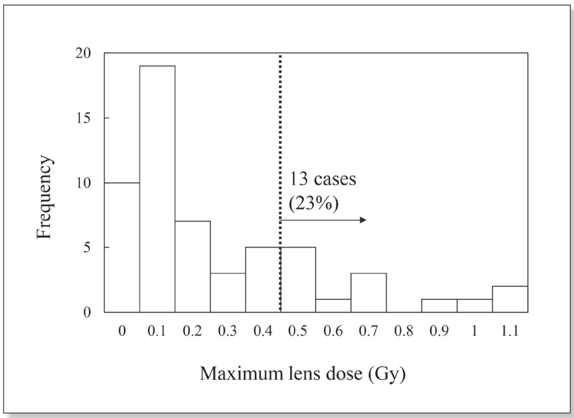

Fig.1 Frequency distribution of the maximum lens dose.

In 13 cases (23%), the maximum lens dose reached 0.5 Gy, the ICRP threshold dose for cataract.

Table 3 demonstrates the result of multiple regression analysis of the factors affecting the dose parameters for the eye lens. There was a significant correlation between the lens dose and the location of the lesions. Besides, the co-existence of organs at risk significantly affected the lens dose. As for the $V_{0.5}$, there were no significant correlated factors.

Figure 2 illustrates the representative case that the lens dose was affected by the existence of the other organ at risk. This 48-year-old man had a left cavernous sinus meningioma. In the original treatment planning, we regarded the optic nerve as the organ at risk [7] and produced the dose plan without

Table 3 Multiple regression analysis regarding the factors affecting the lens dose

Factor	*P* value Max dose	Mean dose	$V_{0.5}$
Lesion location (anterior vs. mid)	<0.05	<0.05	0.236
Lesion location (anterior vs. posterior)	<0.05	<0.05	0.377
Lesion location (ipsilateral vs. contralateral)	0.218	0.268	0.380
Lesion volume	0.642	0.438	0.063
Peripheral dose	0.205	0.648	0.075
No. of shots	0.536	0.885	0.448
Other at-risk organ	<0.05	<0.05	0.232

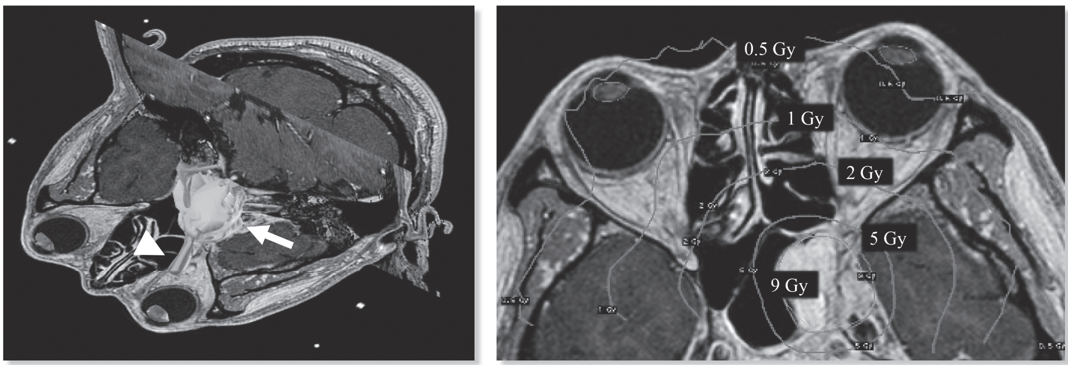

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Fig.2 Unexpected expansion of the dose distribution.

a) This 48-year-old man had a left cavernous meningioma (*arrow*). We regarded the optic nerve as the organ at risk (*arrowhead*) and produced the dose plan.
b) The lesion was irradiated with 9 Gy of peripheral dose. The isodose line for 0.5 Gy was expanded toward the right lens despite lesion was on the left side. The maximum dose to the right lens was 0.7 Gy, greater than the left lens.

concern about radiation exposure to the eye lens. Peripheral dose for this lesion was 9 Gy. The isodose line for 0.5 Gy was unexpectedly expanded toward the right eye lens despite the lesion was on the left side. The maximum doses to the lens were 0.7 Gy in the right and 0.6 Gy in the left, respectively. The dose to the right eye lens which is the contralateral side of the lesion was greater than the left.

3-2 Optimization of the treatment plan

Figure 3 demonstrates the comparison of the maximum lens dose between before and after modification. The dose to the eye lens was significantly reduced in the modified plans. (P<0.05). Further, the radiation exposure to the eye lens were less than 0.5 Gy in the modified plans for all of the cases. The comparison of the D95 is shown in Fig.4. There was no significant difference in the D95. Figure 5 shows the comparison of the irradiation time. The irradiation time was prolonged by 11.6 min on average in the modified plans (P<0.05).

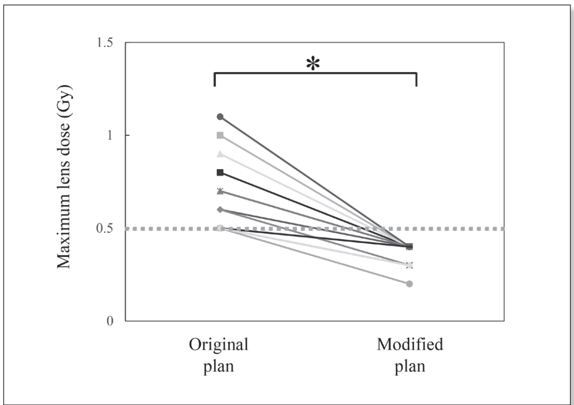

Fig.3 Comparison of the maximum dose to the lens.

The maximum lens dose was significantly reduced in the modified plans on which the eye lens was regarded as the organ at risk. Radiation exposure to the lens were less than 0.5 Gy in all of the plans after modification. *P<0.05

Figure 6 illustrates the representative case that a reduction in the dose to the eye lens could be achieved by modifying the treatment plan. This 62-year-old woman had a meningioma in the olfactory groove. In the original plan, both eye lenses were covered with the 0.5 Gy isodose line. The maximum lens doses were 0.7 Gy in the right and 0.9 Gy in the left, respectively. On the other hand, 0.5 Gy isodose line was away from both eye lenses when the dose distribution was modified with taking the radiation exposure to the eye lens into account. As a result, the maximum lens doses were reduced to 0.4 Gy.

4. Discussion

The fact of the radiation exposure to the eye lens during stereotactic radiosurgery remains to be clarified although ICRP published the threshold dose for cataract as 0.5 Gy. Eye lens does not seem to be dealt with as organ at risk for adverse effect at low radiation dose in treatment planning for GKS. To the best of our

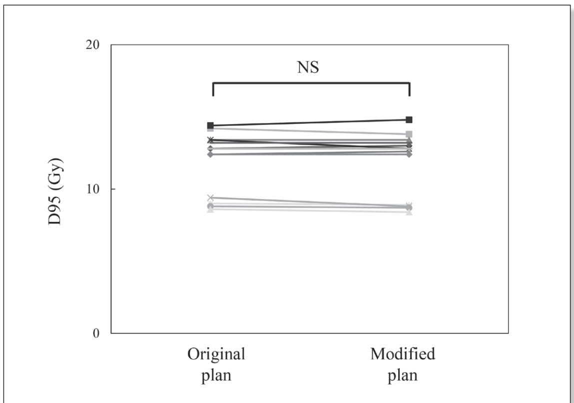

Fig.4 Comparison of the dose covering 95% of the lesion volume (D95).

There was no difference in the D95. NS not significant.

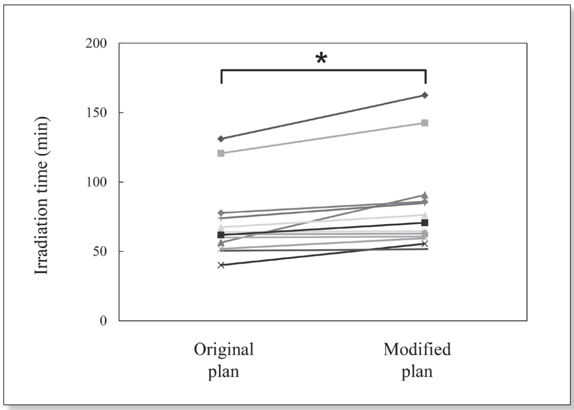

Fig.5 Comparison of the irradiation time.

The irradiation time was prolonged by 11.6 min on average in the modified plans. *P<0.05

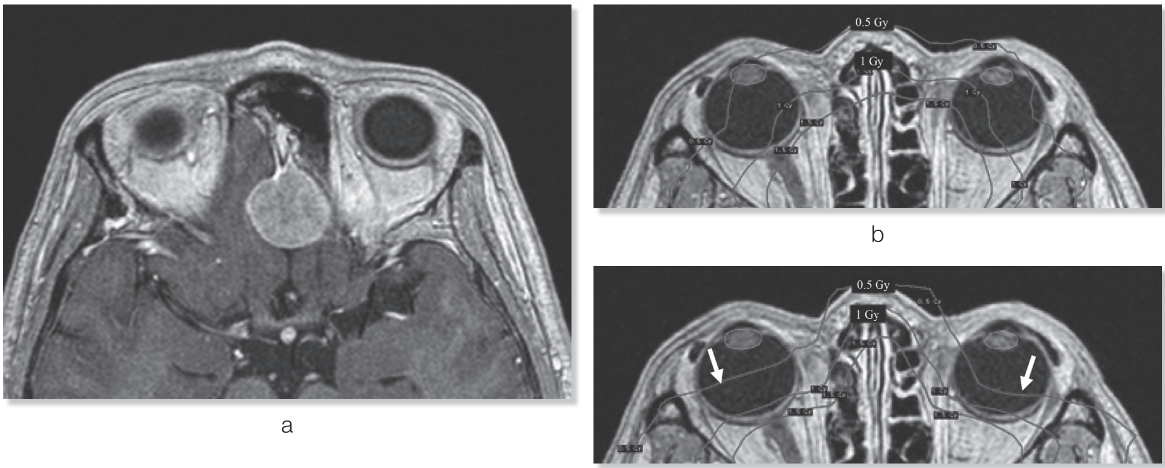

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Fig.6 Dose reduction in the eye lens.

a) This 62-year-old woman had a meningioma in the olfactory groove.
b) In the original plan, both eye lenses were covered with the 0.5 Gy isodose line. The maximum lens doses were 0.7 Gy in right and 0.9 Gy in left, respectively.
c) In the modified plan, the 0.5 Gy isodose line was away from both eye lenses (*arrows*). The maximum lens doses were reduced to 0.4 Gy.

knowledge, the present study is the first report focusing on this important issue. Our data indicates 23% of cases were exposed beyond the ICRP threshold dose in GKS for patients with meningioma (Fig.1). In multiple regression analysis of the factors affecting the lens dose, the location of the lesions and co-existence of organs at risk were significant correlated factors (Table 3). While the former seems to be reasonable because the lesions are close to the eye lens, the latter is a new finding. Careful attention might be necessary to the increase in the dose to the eye lens due to unexpected expansion of dose distribution when producing treatment plan with other organs at risk (Fig.2). In the cases that the lens dose reaches the ICRP threshold dose, ophthalmological follow-up may be recommended to check for cataract induced by stereotactic radiosurgery.

It is possible to distinguish between radiation related cataract and senile cataract[9]. Posterior subcapsular cataract that occurs at back of the lens is typical type of radiation related cataract. Young patients, 40s or less in particular, who undergoing GKS for benign lesions should be observed as long as possible since previous studies indicate radiation related cataract was detected in decades after irradiation[9, 10].

To produce appropriate dose distribution for the cases which exceeded the ICRP threshold dose level for cataract, we regarded the eye lens as organ at risk and modified the original plan. As a result, we could reduce the lens dose to less than 0.5 Gy without making any difference in D95 (Fig.3, 4). Meanwhile, the irradiation time was prolonged by 11.6 min on average in the modified plans (Fig.5). In this regard, the gamma knife model at our hospital, Perfexion is fully robotized and both the radiation beam configuration and the couch positional coordinate setting are automated, which makes patient hospitable and mitigates the workload of the operator[11]. Additionally, for patients which are considered to achieve long-term survival it is required not to raise the level of occurrence of radiation-induced complications in the rest of their life. Thus, the prolongation of irradiation time was short enough to accept clinically although there was a trade-off between a conformal dose plan and irradiation time. Our effort to optimize radiation exposure to the eye lens is meaningful in GKS.

The present study has several limitations. First, this is a single institutional study. Next, relatively small number of subjects were enrolled in this study. Third, we did not take into account the movement of the eye ball during the irradiation when calculating dose to the eye lens. The internal error due to lens motion should be defined in GKS to make dose evaluation more rationally. Finally, in our experience, there are no patients who is diagnosed with radiation related cataract. To address these issues, a long-term observational study with a larger number of subjects is necessary in the future. We believe that the treatment planning with consideration for radiation exposure to the eye lens is a way to advance GKS as minimally invasive treatment. We hope that the relationship between radiation exposure to the eye lens in stereotactic radiosurgery and the occurrence of cataract will be elucidated as further research in this field progresses.

5. Conclusions

In 23% of patients who underwent GKS, the eye lenses were exposed beyond the ICRP threshold dose for cataract. We demonstrated that the treatment plan could be modified in order to reduce the eye lens exposure below the threshold level with clinically acceptable D95 and irradiation time.

We presented this study at the 20th International Society of Radiographers and Radiological Technologists held in Port of Spain, Trinidad and Tobago in April 2018.

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