KISEP
CLINICAL ARTICLE
J Korean Neurosurg Soc 39 : 96-101, 2006

Gamma Knife Radiosurgery for Remnant or Recurred Craniopharyngiomas

Young Sub Kwon, M.D., Yong Sook Park, M.D., Jong Hee Chang, M.D., Ph.D., Jin Woo Chang, M.D., Ph.D., Yong Gou Park, M.D., Ph.D.

Department of Neurosurgery, Yonsei University College of Medicine, Seoul, Korea

Objective : The authors assess the long term effectiveness of gamma knife radiosurgery(GKS) for remnant or recurred craniopharyngiomas on tumor control and possibly set proper radiation dose for tumor control with utmost preservation of the adjacent structures.
Methods : Sixteen GKS were done in 14 patients with recurred or remnant craniopharyngiomas after surgery. Mean follow up duration was 44.2 months (range 11.3~123.6 months). Follow up MR imagings were analyzed.
Results : Mean tumor volume was 3.6cm^3 (range 0.6~18cm^3) and mean margin dose was 12.2Gy (range 8~22.4Gy). Tumor control was achieved in 87.5% (14 of 16 tumors) which were either solid or cystic in nature. Dose to optic apparatus was mean 7.9Gy and no radiation related complications were observed.
Conclusion : GKS seems to be effective treatment modality for craniopharyngiomas regardless of nature of tumor whether it is cystic or solid. Dose of 8 to 8.5Gy may be sufficient to achieve long term tumor control for remnant or recurred craniopharyngiomas.

KEY WORDS : Radiosurgery · Gamma knife · Craniopharyngioma · Optic apparatus.

Introduction

The treatment of craniopharyngioma has long been considered difficult. Although complete removal of tumor is associated with a favorable outcome, mortality and morbidity increases with attempts at radical surgery[32]. Even with complete tumor removal, recurrence rate is 10 to 18% after 2.5 to 10 years and continued tumor growth after partial removal is reported to be 63 to 90%[32]. It is also known that morbidity and mortality increases with subsequent attempts at radical surgery[32]. After the introduction of gamma knife radiosurgery (GKS), it became an effective and less invasive tool for neurosurgeons against benign and malignant tumors. First GKS for craniopharyngioma was done by Backlund et al in 1972[2] and following studies on GKS for remnant craniopharygiomas after surgical removal have been reported[8,10,19,21,22,28,32]. Less radiation related complications and good tumor regression rate make surgeons less aggressive on surgical removal and give chance for multimodal treatment.

Our study was to assess the effectiveness of GKS for craniopharygiomas on tumor control and possibly set a proper radiation dose for tumor control with utmost preservation of adjacent structures.

Materials and Methods

From period of May 1993 to November 2002, total of 14 patients received GKS (201-source cobalt-60 gamma unit, Elekta Instruments, Stockholm, Sweden) with 13 patients receiving once and 1 patient receiving three times. Mean age of patients at time of GKS was 30.3 years (4.4~62.9 years). Five patients were male and 9 were female. All patients received surgical removal before GKS for histological confirmation and tumor debulking. All except one patient received craniotomy for removal of tumor and one exception being transsphenoidal approach. All MR imaging for remnant or recurred tumor were converted using GammaPlan software where tumor volumes were calculated. Enhanced T1 weighted MR

• Received : April 21, 2005 • Accepted : August 3, 2005
• Address for reprints : Yong Gou Park, M.D., Department of Neurosurgery, Yonsei University College of Medicine, 134 Sinchon-dong, Seodaemun-gu, Seoul 120-752, Korea Tel : +82-2-2228-2150, Fax : +82-2-393-9979, E-mail : ygpark@yumc.yonsei.ac.kr

images were used to delineated tumor margin. All measurements were performed by one investigator (Y. K.). Radiologic outcomes were categorized into three groups : decreased (0~80% of original tumor volume), static (80~120%), and increased (more than 120% of original tumor volume). Tumor was considered as recurred if clinical symptom and sign worsened even when increase in tumor volume did not exceed 120%.

Clinical and imaging follow up

Visual and endocrinologic evaluations were routinely done preoperatively. Visual evaluation included visual acuity and field test (Humphrey perimetry) and endocrinologic evaluation was done with combined pituitary function test. Postoperatively, all patients returned for clinical evaluation every month. Patients were questioned subjectively for postoperative changes in vision and hormonal symptoms.

Mean follow up duration was 48.0 months (range 11.3~123.6 months). This study is a follow up version of preliminary study reported at 2001 with added patients and longer follow up period[7].

Results

Radiological Outcome after GKS

Total of 16 procedures were done in 14 patients. Tumor volume ranged from 0.4cm^3 to 18.0cm^3 (mean 3.6 cm^3). Mean margin dose was 12.2 Gy (range 8~22.4Gy) and dose to optic chiasm was mean 7.9Gy (range 4~11Gy).

Of the 16 tumors treated with GKS, 12(75%) decreased in size (0~80% of the original tumor volume). Two (12.5%) of the 16 tumors were considered static (80~120% of the original tumor volume) thus the control rate (decreased and static volume) was 87.5% (14 of 16 tumors). For one patient who received GKS 3 times, the first was considered recurrent and the rest were considered controlled.

For the 14 tumors where tumor control was achieved, mean tumor volume was 3.8cm^3 (range 0.6~18.0 cm^3). For the 2 recurred tumors, mean tumor volume was 1.6cm^3 (0.4 and 2.8cm^3). Comparing the mean margin dose of controlled and recurred tumor, they were 11.8 and 13.3Gy respectively. For the two recurred cases, both tumors were solid in nature. As for the controlled cases, 4 were cystic and the rest were either solid or mixed. Mean follow up period for the controlled cases was 49.1 months (range 11.3~98.0 months) and for the recurred cases, 106.9 months (range 90.2~123.6 months). Time interval to recurrence for the two cases were 57.6 and 123.6 months (Table 1). Statistical significance be-tween the tumor controlled group and recurred group was not tested due to small size of patient population. Tumor volume, radiation dose, and imaging outcome are summarized in Table 2.

One of the two recurred cases was a 15 year old female who

Table 1. Comparison between controlled cases and recurred cases

Parameters	Controlled cases	Recurred cases
Number of cases	14	2
Target volume (cm^3)	0.6–18 (mean 3.8)	0.4/ 2.8 (mean 1.6)
Margin dose (Gy)	8–22.4 (mean 11.8)	14/ 12.6 (mean 13.3)
PreGKS* image	Cystic 4, solid 6, mixed 4	Solid 2
Follow–up duration (months)	11.3–98.0 (mean 49.1)	90.2/123.6 (mean 106.9)
Recurrence (months)	–	57.6/123.6 (mean 90.6)

*PreGKS : preoperative to Gamma knife surgery

Table 2. Summary of cases

Patient No	Age/ sex	PreGKS* treatment	Target volume(cm^3)	Margin dose (Gy)	Results	F/U duration (months)	PreGKS* image
1	4/F	C/R**	3.2	8	Shrunk	39.9	Cystic
2	47/M	C/R	2.4	8.5	Shrunk	98.0	Solid
3	15/F	C/R	0.4	14	Recurred	123.6	Solid
4	16/M	TSA***	18.0	8.5	Shrunk	97.6	Solid
5	63/F	C/R	0.7	15	Static	11.3	Mixed
6†	30/M	C/R	2.8/2.9/0.6	12.6/22.4/14.5	recur/shrunk/static	90 /60 /25	Solid/Solid/Solid
7	8/F	C/R	6.3	11.5	Shrunk	45.1	Mixed
8	15/F	C/R	1.8	10	Shrunk	36.9	Solid
9	43/F	C/R	2.1	10	Shrunk	39.8	Solid
10	38/F	C/R	0.6	13	Shrunk	34.5	Cystic
11	23/M	C/R	8.6	11	Shrunk	21.4	Mixed
12	44/M	C/R	0.6	14	Shrunk	17.3	Cystic
13	4/F	C/R	2.9	10	Shrunk	11.9	Cystic
14	38/F	C/R	1.6	9	Shrunk	14.4	Mixed

*PreGKS : preoperative to Gamma knife surgery, **C/R : Craniotomy and tumor removal, ***TSA : Trans–sphenoidal approach, †GKS was done 3 times where each procedure is divided by a slash(/)

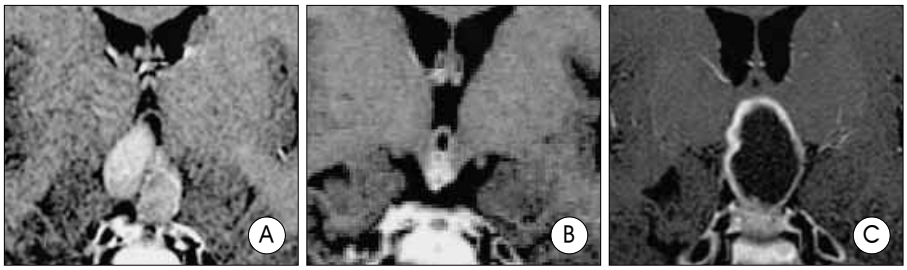

Fig. 1. Serial T1 weighted coronal magnetic resonance(MR) images of 15 a year–old woman with short stature. (A) Preoperative MR image showing a 9X9mm sized solid craniopharyngioma. (B) Postoperative MR image showing remnant mass (C) MR image taken 10 years after GKS showing 2 X2.5cm cystic recurrent tumor.

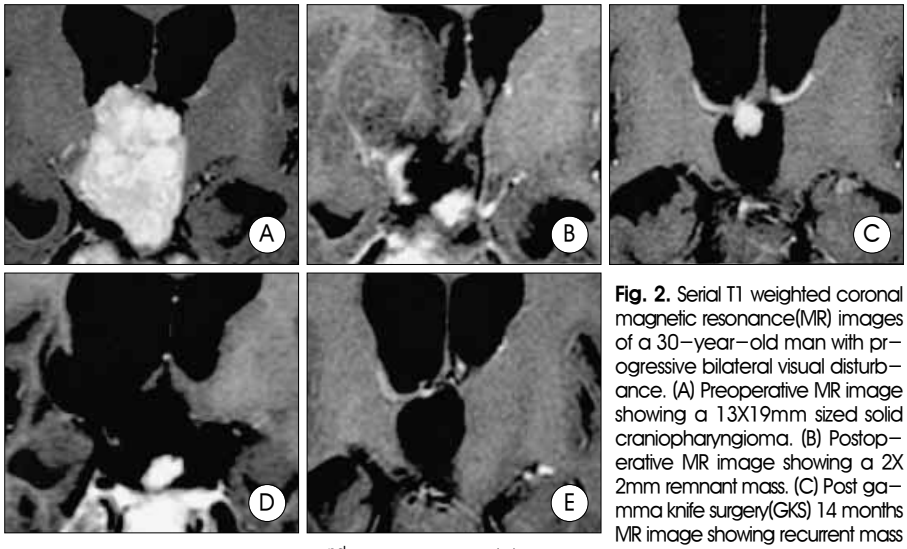

Fig. 2. Serial T1 weighted coronal magnetic resonance(MR) images of a 30-year-old man with progressive bilateral visual disturbance. (A) Preoperative MR image showing a 13X19mm sized solid craniopharyngioma. (B) Postoperative MR image showing a 2X 2mm remnant mass. (C) Post gamma knife surgery(GKS) 14 months MR image showing recurrent mass adjacent to the optic chiasm and 2nd GKS was done. (D) MR image taken 43 months after 2nd GKS where recurrent tumor is found in area of initial remnant tumor. 3rd GKS was done. (E) No tumor is seen after 25 months follow up after the 3rd GKS.

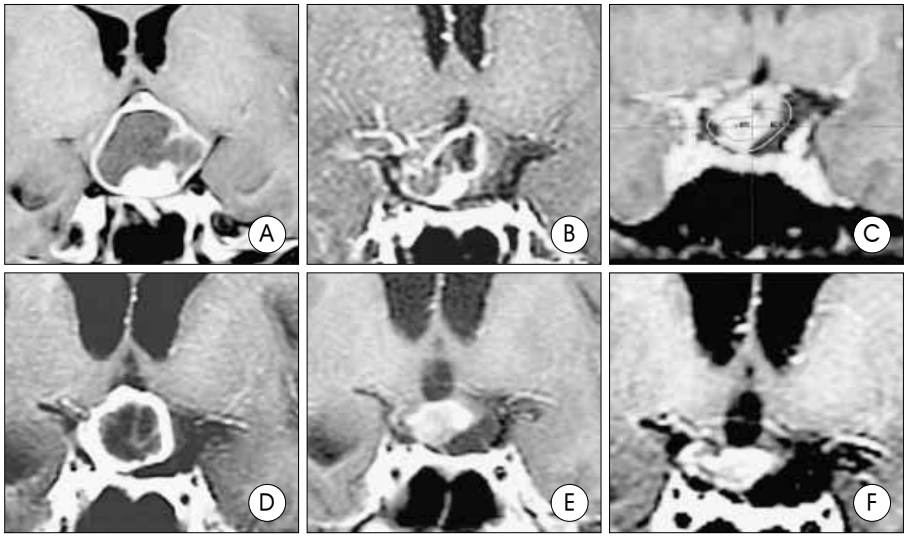

Fig. 3. Serial T1 weighted coronal magnetic resonance(MR) images of a 38-year-old woman with visual disturbance. (A) Preoperative MR image showing a craniopharyngioma with mixed cystic and solid nature. (B) Postoperative MRI showing remnant mass. (C) Postoperative gamma knife surgery(GKS) MR image treated with margin dose of 9Gy. (D) PostGKS 3 months MR image showing typical volume expansion mainly cystic enlargement. (E) & (F) PostGKS 5 months and 8 months follow up MR image with regression of cystic component with stabilized size of solid mass.

had visited our clinic for short stature. Evaluation revealed panhypopituitarism and a 9×9mm suprasellar tumor on her brain MRI. She received craniotomy for removal of tumor where histologic confirmation for craniopharyngioma was made and followed by GKS. She had not visited our clinic since then and had been follow up lost for 10 years. She revisited our clinic 2 years ago and had MRI taken which revealed a 2×2.5cm sized cystic recurrent mass (Fig. 1). She underwent another surgical removal of tumor.

Another case of recurrence was with a 30 year old male patient who had progressive bilateral vision loss. His MRI revealed 13×19mm sized craniopharyngioma and underwent surgical removal (Fig. 2). His postoperative MRI showed 2×2mm sized remnant mass and GKS was done. Fourteen months after GKS, recurrent mass was found adjacent to the optic chiasm. It was not thought to be a recurrence after GKS since no mass was seen adjacent to optic chiasm at postoperative MRI and radiation dose was not included on optic chiasm. Second GKS was done at newly found mass. Forty three months after the 2nd GKS (which is 57 months after the 1st GKS), a recurrent mass was found in the area of initial remnant tumor at follow up MRI. Third GKS was done and no recurrence is yet found at 25 months follow up.

Visual and Endocrinologic Outcome after GKS

Eight of 14 (57%) patients had preoperative visual impairment. In case where tumor was attached or adjacent to the optic apparatus, margin dose was restricted to 8 or 8.5 Gy (Case 1, 2, and 4). However, when patient's preoperative visual loss was severe, vision sparing was no longer of concern and dose as high as 22.4Gy was used for better tumor control (Case 6). No patient had deterioration of vision postoperatively.

Seven of 14 (50%) patients had preoperative hormonal insufficiency. Hormonal replacement was done for these patients with 7.5mg methyl prednisolon, 100ug levothyroxine sodium, and 0.05mg desmopressin preoperatively. Hormonal status remained stable in all patients including patients without preoperative hormonal deficiency.

Volume response after GKS

Volume response of tumor after GKS varied among cases. Ten (62.5%) had progressive volume reduction (<80% of original volume), while two (Case 1 and case 14) had transient volume expansion followed by marked reduction at next follow up imaging (Fig. 3). For case 1, volume expansion began as

Table 3. The results of gamma knife radiosurgery for craniopharygiomas reported in the literature

Authors	Number of Patients/tumors	Mean or median volume (cm^3)	Margin dose (Gy)	Control rate (%)	Follow-up (years)
Prasad[28]	8	?	5-30	88	0.5-4
Mokry[22]	23	8	9-15.4	74	2
Kobayashi[19]	100	5.8	11.5	77	5.46
Chung[10]	31	9	9.5-16	87	2.7
Chiou[8]	10/12	1.35	16.4	58	5.25
Ulfarsson[32]	21/22	7.8	<3-25	33	7.5
Kim[18]	18	2.7	17.6 (4-35)	72.2	4.9
Barua[4]	7	?	14.2	83.3	5
Present	14/16	3.6	12.2 (8-22.4)	87.5	3.7

early as 3rd month and shrunk dramatically at 4th follow up month. In case 14 however, the volume expansion was found at 6th follow up month and expansion lasted until 11th month where tumor markedly shrunk at next follow up imaging.

Discussion

Treatment modalities

Adjuvant therapy such as radiation therapy(RT) has shown good results. 10-year survival rates of 81 to 91% after subtotal removal followed by RT has been reported[15,29] and adjuvant radiotherapy has been the preferred practice for neurosurgeons. However, radiotherapy is not without hazard. Radiation necrosis, optic neuritis, malignancies, and cognitive disturbances in young children following RT is reported to be 6 to 18% of patients[6,29]. Tumor recurrence is also reported to be 14 to 22% 5 to 10 years after RT[12,13,25,29] and mortality rate of patients suffering recurrence after RT is 83 to 100%[12,25,29,30,34,35].

Alternative treatments such as neuroendoscopy and intracavitary brachytherapy have been introduced to decrease surgery related mortality and morbidity[2,3,16,23,37]. Intracavitary radiation and chemotherapy can be effective modality for cystic tumors but it also harbors considerable hazards such as visual deterioration and tumor regression may not be satisfactory[5,24,26,33]. Our institution has discarded the use of intracystic treatment and radiation therapy and substituted with surgical removal of tumor plus GKS for remnant or recurred cases.

Tumor control and associated factors in GKS treated craniopharyngiomas

On tumor control of craniopharyngiomas after GKS, much have been mentioned on nature of tumor (whether solid or cystic), treated tumor volume, and radiation dose to tumor, but these characteristics are yet to be statistically proven and need prospective or controlled study with bigger patient population. Attempts at justifying radiosurgery for craniopharyngiomas have started since Backlund[2] and subsequent reports followed supporting its effectiveness. Mokry et al[22] reported tumor control rate of 56% and Kobayashi et al[19] reported a much improved tumor control of 85% (Table 3). Although tumor control rate tends to fall with longer follow up period, short term treatment failure of GKS is often observed in cystic tumors[1,17]. Backlund et al[2] suggested the use of intracystic brachytherapy for cystic components, and Ulfarsson's study[32] also observed high rate of cystic enlargement after GKS. Although statistical difference is yet to be proven, many institutions defer the use of GKS in cystic craniopharyngiomas. Cystic tumors are result of diffusion of plasma from the capillaries of the tumor and Gardner[16] suggested inability of brain getting rid of this fluid. In our study, the two recurred cases were both solid tumor in nature and we inferred that cystic recurrence can be minimized by surgically removing the tumor cyst and treating rest of the tumor with GKS. The principle is not just to puncture the cyst but to remove as much cyst wall as possible. Four cystic tumors and four mixed tumors did not show recurrence as long as 45.1 months follow up.

Volume reponse after GKS

Much of the previous studies concentrate on tumor's volume response following GKS. However, little is known about the actual microbiological change that affects the volume response. Benign tumors such as meningiomas, benign gliomas or schwannomas have transient periods of volume expansion which does not necessarily mean recurrence[27]. There are studies on vestibular schwannomas that after gamma knife surgery, transient increase in tumor volume is observed in 6~39% and decrease after 3 months to 5 years follow up[9,20,27,36]. We also noticed this transient volume expansion for craniopharyngiomas where transient volume expansion of tumor eventually decreased at follow up imaging (case 1 and case 14). This volume expansion was found to be as much as 200% of the original tumor volume, but fortunately did not produce neurological dysfunction thus enabling further observation. Whatever the cause may be, clinicians should be aware that increased volume response does not necessarily mean recurrence and should be open for observation until definite evidence of recurrence emerges.

Proper prescription dose between tumor control and optic pathway sparing

Majority of postoperative recurrence of craniopharyngiomas locate at optic apparatus and hypothalamus[17,31]. This reflects the difficulty of total resection of tumor in these adjacent

structures and importance of GKS adjacent to optic chiasm. Studies demonstrated tolerance of 8 to 12Gy with incidence of radiation optic neuropathy as low as 0~1.8%[11,14]. Kobayashi et al[19] used margin dose of 12.8Gy and gradually reduced margin dose to 11.5Gy, suggesting the optimal dose to be between 11 and 12Gy. Chung et al[10] demonstrated comparable tumor control of 87.2% with use of 9 to 12Gy margin dose. Study of Ulfarsson et al[32] found out that margin dose less than 6Gy is suboptimal, and tumor progression rate was as high as 85%. They demonstrated statistically significant difference with cases using 6Gy or more where tumor progression was 33%. Considering the minimal dose to optic apparatus to achieve tumor control without complication, 3 of our cases where margin dose of 8 and 8.5Gy were used provided adequate tumor control as long as 98 months (mean 78.2 months). Although Ulfarsson[32] recommended optimal dose to be 6Gy or more, we recommend marginal dose of 8 to 8.5Gy for maximal tumor control and minimal radiation related complication.

The exact pathophysiology behind recurrence of craniopharyngiomas after GKS is yet to be proven. In our study, target volume, nature of tumor and radiation dose did not provide reason behind recurrence of craniopharyngiomas. However, our study shares with previous reports that tendency of recurrence rate increases after longer follow up period. This implies that GKS for craniopharyngiomas is not yet a curative modality but a modality for control of tumor. Long term clinical and imaging follow up is mandatory for optimal treatment of tumor.

Conclusion

As difficult as treatment of craniopharyngiomas can be, many diverse tactics of treatment are being conducted. Less aggressive surgical removal and GKS seem to be effective treatment modality regardless of nature of tumor whether it's cystic or solid. Dose of 8 to 8.5Gy may be sufficient to achieve long term tumor control for craniopharyngiomas.

References

1. Backlund EO, Axelsson B, Bergstrand CG, Eriksson AL, Noren G, Ribbesjo E, et al : Treatment of craniopharyngiomas--the stereotactic approach in a ten to twenty-three years' perspective. I. Surgical, radiological and ophthalmological aspects. **Acta Neurochir (Wien) 99** : 11-19, 1989
2. Backlund EO, Johansson L, Sarby B : Studies on craniopharyngiomas. II. Treatment by stereotaxis and radiosurgery. **Acta Chir Scand 138** : 749-759, 1972
3. Barajas MA, Ramirez-Guzman G, Rodriguez-Vazquez C, Toledo-Buenrostro V, Velasquez-Santana H, del Robles RV, et al : Multimodal management of craniopharyngiomas : neuroendoscopy, microsurgery, and radiosurgery. **J Neurosurg 97** : 607-609, 2002
4. Barua KK, Ehara K, Kohmura E, Tamaki N : Treatment of recurrent craniopharyngiomas. **Kobe J Med Sci 49** : 123-132, 2003
5. Bernstein M, Laperriere NJ : A critical appraisal of the role of brachytherapy for pediatric brain tumors. **Pediatr Neurosurg 16** : 213-218, 1990
6. Cavazzuti V, Fischer EG, Welch K, Belli JA , Winston KR : Neurological and psychophysiological sequelae following different treatments of craniopharyngioma in children. **J Neurosurg 59** : 409-417, 1983
7. Chang JH, Chang JW, Park YG, Chung SS : Gamma knife radiosurgery for craniopharyngioma. **J Korean Neurosurg Soc 30** : 561-566, 2001
8. Chiou SM, Lunsford LD, Niranjan A, Kondziolka D, Flickinger JC : Stereotactic radiosurgery of residual or recurrent craniopharyngioma, after surgery, with or without radiation therapy. **Neuro-oncol 3** : 159-166, 2001
9. Chung WY, Liu KD, Shiau CY, Wu HM, Wang LW, Guo WY, et al : Gamma knife surgery for vestibular schwannoma : 10-year experience of 195 cases. **J Neurosurg (Suppl) 102** : 87-96, 2005
10. Chung WY, Pan DH, Shiau CY, Guo WY, Wang LW : Gamma knife radiosurgery for craniopharyngiomas. **J Neurosurg (Suppl 3) 93** : 47-56, 2000
11. Chung WY, Pan HC, Guo WY, Shiau CY, Wang LW, Wu HM, et al : Protection of visual pathway in gamma knife radiosurgery for craniopharyngiomas. **Stereotact Funct Neurosurg (Suppl 1) 70** : 139-151, 1998
12. Danoff BF, Cowchock FS, Kramer S : Childhood craniopharyngioma : survival, local control, endocrine and neurologic function following radiotherapy. **Int J Radiat Oncol Biol Phys 9** : 171-175, 1983
13. Fischer EG, Welch K, Shillito J Jr, Winston KR, Tarbell NJ : Craniopharyngiomas in children. Long-term effects of conservative surgical procedures combined with radiation therapy. **J Neurosurg 73** : 534-540, 1990
14. Girkin CA, Comey CH, Lunsford LD, Goodman ML, Kline LB : Radiation optic neuropathy after stereotactic radiosurgery. **Ophthalmology 104** : 1634-1643, 1997
15. Hetelekidis S, Barnes PD, Tao ML, Fischer EG, Schneider L, Scott RM, et al : 20-year experience in childhood craniopharyngioma. **Int J Radiat Oncol Biol Phys 27** : 189-195, 1993
16. Kim MS, Lee SI, Sim JH : Brain tumors with cysts treated with Gamma Knife radiosurgery : is microsurgery indicated? **Stereotact Funct Neurosurg (Suppl 1) 72** : 38-44, 1999
17. Kim SK, Wang KC, Shin SH, Choe G, Chi JG, Cho BK : Radical excision of pediatric craniopharyngioma : recurrence pattern and prognostic factors. **Childs Nerv Syst 17** : 531-537, 2001
18. Kim YS, Lee DH, Ra DS, Chun YI, Ahn JS, Jeon SR : Long-term results of gamma knife radiosurgery for craniopharynioma. **J Korean Neurosurg Soc (Suppl 2) 30** : S289-S293, 2001
19. Kobayashi T, Kida Y, Hasegawa T : Long-term results of gamma knife surgery for craniopharyngioma. **Neurosurg Focus 14** : 13, 2003
20. Kobayashi T, Tanaka T, Kida Y : The early effects of gamma knife on 40 cases of acoustic neurinoma. **Acta Neurochir (Suppl) 62** : 93-97, 1994
21. Kobayashi T, Tanaka T, Kida Y : Stereotactic gamma radiosurgery of craniopharyngiomas. **Pediatr Neurosurg (Suppl 1) 21** : 69-74, 1994
22. Mokry M : Craniopharyngiomas : A six year experience with Gamma Knife radiosurgery. **Stereotact Funct Neurosurg (Suppl 1) 72** : 140-149, 1999
23. Nicolato A, Foroni R, Rosta L, Gerosa M, Bricolo A : Multimodality stereotactic approach to the treatment of cystic craniopharyngiomas. **Minim Invasive Neurosurg 47** : 32-40, 2004
24. Nishizawa S, Ryu H, Yokoyama T, Ninchoji T, Shimoyama I, Yamamoto S, et al : Post-irradiation vasculopathy of intracranial major arteries in children--report of two cases. **Neurol Med Chir (Tokyo) 31** : 336-341, 1991
25. Onoyama Y, Ono K, Yabumoto E, Takeuchi J : Radiation therapy of craniopharyngioma. **Radiology 125** : 799-803, 1977
26. Pan DH, Lee LS, Huang CI, Wong TT : Stereotactic internal irradiation for cystic craniopharyngiomas : a 6-year experience. **Stereotact Funct Neurosurg 54-55** : 525-530, 1990
27. Park YG, Kim EY, Chang JW, Chung SS : Volume changes following gamma knife radiosurgery of intracranial tumors. **Surg Neurol 48** : 488-493, 1997
28. Prasad D, Steiner M, Steiner L : Gamma knife surgery for craniopharyngioma. **Acta Neurochir (Wien) 134** : 167-176, 1995
29. Rajan B, Ashley S, Gorman C, Jose CC, Horwich A, Bloom HJ, et al : Craniopharyngioma-a long-term results following limited surgery and radiotherapy. **Radiother Oncol 26** : 1-10, 1993
30. Regine WF, Kramer S : Pediatric craniopharyngiomas : long term results of combined treatment with surgery and radiation. **Int J Radiat Oncol**

Biol Phys 24 : 611-617, 1992
31. Reyes Oliveros F : Craniopharyngioma. Recurrence. **An R Acad Nac Med (Madr) 118** : 263-273, 2001
32. Ulfarsson E, Lindquist C, Roberts M, Rahn T, Lindquist M, Thoren M, et al : Gamma knife radiosurgery for craniopharyngiomas : long-term results in the first Swedish patients. **J Neurosurg 97** : 613-622, 2002
33. Van den Berge JH, Blaauw G, Breeman WA, Rahmy A, Wijngaarde R : Intracavitary brachytherapy of cystic craniopharyngiomas. **J Neurosurg 77** : 545-550, 1992
34. Weiss M, Sutton L, Marcial V, Fowble B, Packer R, Zimmerman R, et al : The role of radiation therapy in the management of childhood craniopharyngioma. **Int J Radiat Oncol Biol Phys 17** : 1313-1321, 1989
35. Yasargil MG, Curcic M, Kis M, Siegenthaler G, Teddy PJ, Roth P : Total removal of craniopharyngiomas. Approaches and long-term results in 144 patients. **J Neurosurg 73** : 3-11, 1990
36. Yu CP, Cheung JY, Leung S, Ho R : Sequential volume mapping for confirmation of negative growth in vestibular schwannomas treated by gamma knife radiosurgery. **J Neurosurg (Suppl 3) 93** : 82-89, 2000
37. Yu X, Liu Z, Li S : Combined treatment with stereotactic intracavitary irradiation and gamma knife surgery for craniopharyngiomas. **Stereotact Funct Neurosurg 75** : 117-122, 2000

Commentary

This is an attractive review about long term effect (mean 3.7 years, ranging 1 to 10 years) of GKS for 14 cases of remnant or recurred craniopharyngiomas on tumor control and about suggesting proper radiation dose (8~8.5Gy) both for tumor control and preserving the nearby crucial structures (optic apparatus and hypothalamus).

Craniopharyngiomas, pathologically benign but clinically malignant neoplasia owing to their inevitable recurrence, impose considerable challenges on the operators who wish to remove tumors as much as possible while without residual deficits. In most cases, the primary cause for incomplete removal is a lack of anatomical dissection plane between tumor and the hypothalamus or optic apparatus. Concern for hypothalamic dysfunction or optic neuritis would also arise from radiation to these regions, irrespective of detailed delivery methods (whole brain irradiation, brachytherapy or GKS). Margin dose, showing maximum effect to withhold tumor regrowth whereas showing minimum adverse effect to the adjacent structures, has to be individualized, therefore. Eight to 8.5Gy, as suggested in this review, appears as a little bit smaller than any previous articles[2,3]. In this point of view, it is very fortunate that your results showed very low rate of morbidity and I want to know the reason more specifically.

Authors have written that target volume, tumor nature (solid or cystic) and radiation dose did not seem to affect the post-operative recurrence for craniopharyngiomas. I agree with this conclusion in some aspects, however, due to the small cohort number and random allocation (tumor nature, individual surgical approach, main complaints), external validity and statistical verification (such as reducing type 2 error) should be established by multi-center prospectively designed study and enrolling a large volume of patients in near future. It is generally believed that the longer the follow up period, the more the number of recurrence after GKS (decrease in rate of tumor control)[1,4]. I think the accumulated effect of radiation has been diminished as time went by (i.e. more than 5 years post-GKS). For this reason, I'm on the same side with you that GKS for craniopharyngiomas is not yet a definite, curative method for tumor control especially only in a certain limited period of time.

I want to address congratulation on your excellent clinical outcome.

Suck Jun Oh, M.D., Ph.D.
Department of Neurosurgery, Hanyang University

References

1. Chiou SM, Lunsford LD, Niranjan A, Kondziolka D, Flickinger JC : Stereotactic radiosurgery of residual or recurrent craniopharyngioma, after surgery, with or without radiation therapy. **Neuro-oncol 3** : 159-166, 2001
2. Chung WY, Pan DH, Shiau CY, Guo WY, Wang LW : Gamma knife radiosurgery for cranoipharyngiomas. **J Neurosurg (Suppl 3) 93** : 47-53, 2000
3. Kobayashi T, Kida Y, Hasegawa T : Long-term results of gamma knife surgery for craniopharyngioma. **Neurosurg Focus 14** : 13, 2003
4. Ulfarsson E, Lindquist C, Roberts M, Rahn T, Lindquist M, Thoren M, et al : Gamma knife radiosurgery for craniopharyngiomas. long-term results in the first Swedish patients. **J Neurosurg 97** : 613-622, 2002