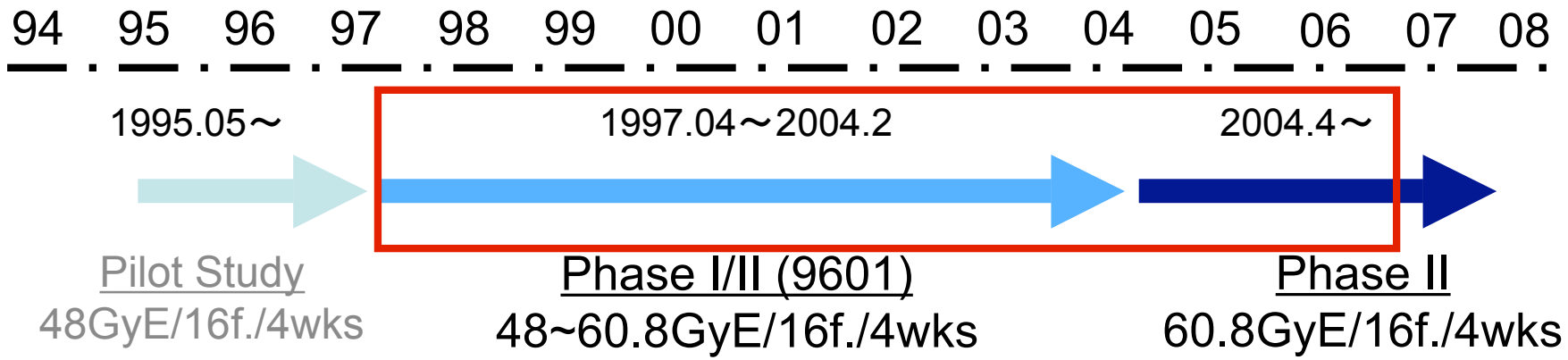
Carbon Ion Radiotherapy for Skull Base and Paracervical Chordomas

Azusa Hasegawa, Jun-etsu Mizoe and Hirohiko Tsujii

Research Center Hospital for Charged Particle Therapy
National Institute of Radiological Sciences
Corresponding Author: Jun-etsu Mizoe, e-mail address: j_mizoe@nirs.go.jp
Azusa Hasegawa, e-mail address: azusa@nirs.go.jp

Skull Base and Paracervical Tumors



Subjects：

Chordoma, meningioma, chondrosarcoma and other tumors originating from skull base or paracervical spine located C1 and C2 vertebra

Eligibility criteria：

1. Age ranged from 15 to 80 years
2. Measurable and histologically proven tumor
3. KPS：60% or higher, Neurological Function (NF) ： grade 1or 2
4. Expected prognosis of at least 6 months or longer
5. Absence of prior RT for target
6. Proceeded chemotherapy must be concluded at least 4 weeks before C-ion RT
7. No distant metastasis

Classification by Carbon Ion Dose and Histological Type

April 1997～August 2007

	Total	48.0GyE	52.8GyE	57.6GyE	60.8GyE
Chordoma	29	1	3	6	19
Chondrosarcoma	7	1	0	1	5
Meningioma	6	2	3	0	1
ON*	3	0	0	1	2
GCS**	1	0	0	1	0
Total	46	4	6	9	27

* ON: Olfactory neuroblastoma

** GCS: Giant cell sarcoma

Patients and Treatment Characteristics

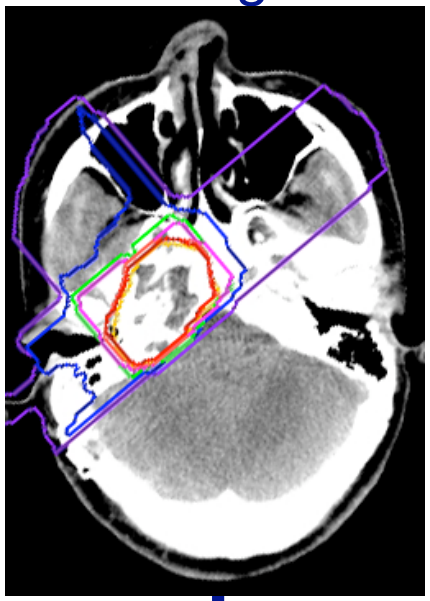
April 1997～ February 2004 phase I/II clinical trial: 15 cases
April 2004 ～August 2007 phase II: 14 cases

Total of 29 patients

Gender	
Male/ Female (n)	12/ 17
Age, years	
Median (range)	47 (16-76)
Tumor sites	
Skull base	10
Clivus	10
Cervical spine/ paraspine	7
Other sites	2

Previous treatment	
Surgery	23
	Subtotal (3)
	Partial (15)
	Biopsy (5)
Recurrence after surgery	6
Gross tumor volume, (ml)	
Median (range)	29.8（2-328）

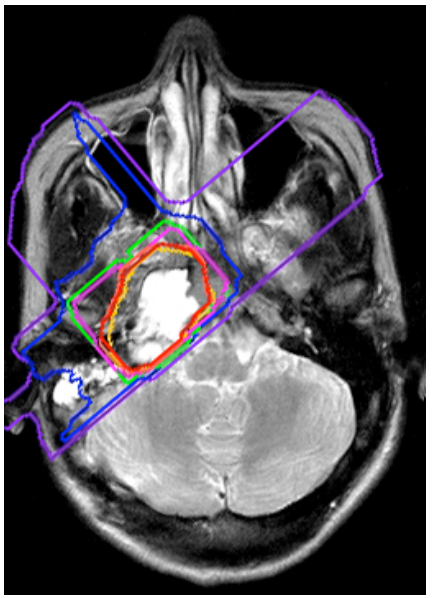
Planning CT



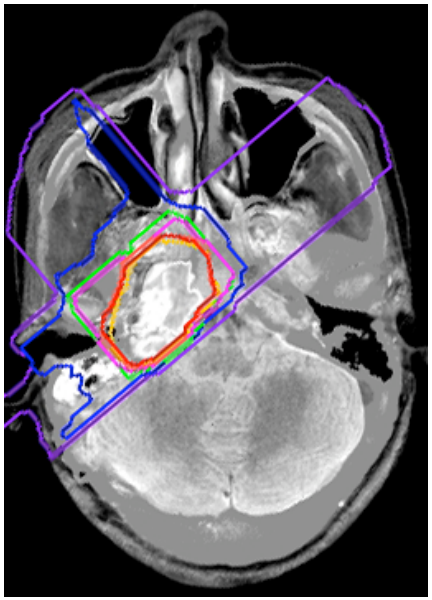
MRI

Fusion

Reconstructed MRI



Fusion Image



Treatment Planning

1. Delineation of CTV

1) A margin of 3-5mm was usually added to the GTV.

2) CTV included the suspected subclinical lesions.

3) When the tumor was located close to the brainstem, spinal cord optic chiasma and optic nerves, the margin was reduced.

2. Maximum dose for critical organs (PROG)

1) Surface of Brainstem and Spinal cord: 60 GyE

2) Center of Brainstem and Spinal cord: 50 GyE

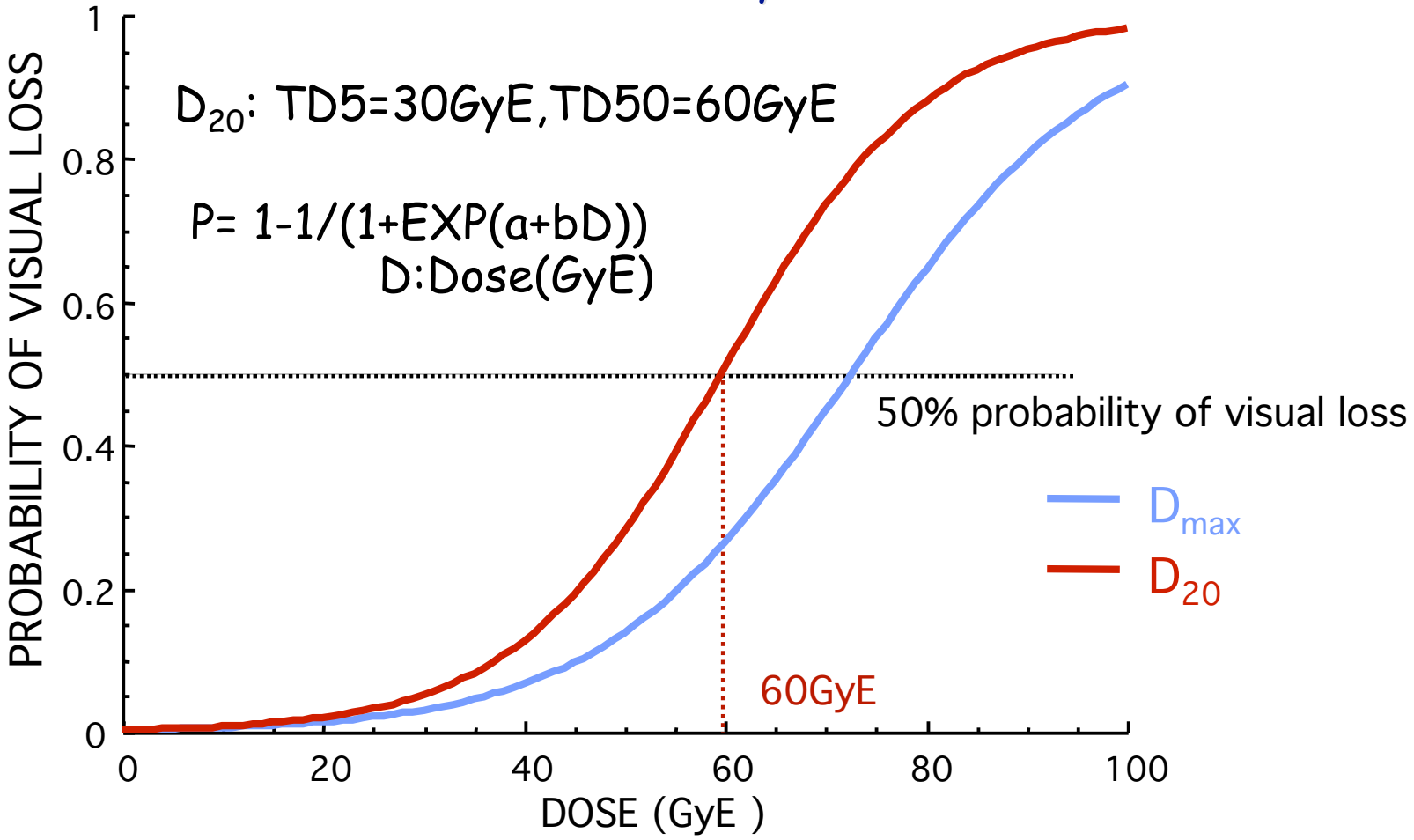
3) Chiasma and contralateral Optic nerve: 55 GyE

Retrospective DVH Analysis of Optic Nerve in Carbon Ion Radiotherapy

Dose-complication probability curves

Treated from June 1994 to March 2000.

Fifty-four ONs with 11 visual loss.



Retrospective DVH Analysis of Optic Nerve in Carbon Ion Radiotherapy

Treated from June 1994 to March 2000.

Fifty-four ONs with 11 visual loss.

Result

D_{max} : 0% (0/35) < 55 GyE < 58% (11/19)

D_{20} : 0% (0/31) < 40 GyE < 48% (11/23)

D_{max} less than 55 GyE or D_{20} less than 40 GyE were recommended.

(Int. J Radiation Oncology Biol. Phys., Vol. 64, 2006)

Acute and Late Radiation Morbidities

29 patients

Acute: Skin

RTOG

Dose (n)	grade 0	1	2	3
48 GyE (1)	0	1	0	0
52.8 GyE (3)	1	1	1	0
57.6 GyE (6)	3	3	0	0
60.8 GyE (19)	12	7	0	0
Total (29)	16	12	1	0

Late: Skin

RTOG / EORTC

Dose (n)	grade 0	1	2	3
48 GyE (1)	1	0	0	0
52.8 GyE (3)	2	1	0	0
57.6 GyE (6)	5	1	0	0
60.8 GyE (19)	19	0	0	0
Total (29)	27	2	0	0

Acute: Mucosa

RTOG

Dose (n)	grade 0	1	2	3
48 GyE (1)	1	0	0	0
52.8 GyE (3)	1	0	2	0
57.6 GyE (6)	3	3	0	0
60.8 GyE (17)	10	3	4	0
Total (27)	15	6	6	0

Late: Mucosa

RTOG / EORTC

Dose (n)	grade 0	1	2	3
48 GyE (1)	1	0	0	0
52.8 GyE (3)	2	1	0	0
57.6 GyE (6)	6	0	0	0
60.8 GyE (17)	16	1	0	0
Total (27)	25	2	0	0

Acute and Late Radiation Morbidities

29 patients

Acute: Brain

RTOG

Dose (n)	grade 0	1	2	3
48 GyE (1)	1	0	0	0
52.8 GyE (3)	3	0	0	0
57.6 GyE (6)	6	0	0	0
60.8 GyE (19)	19	0	0	0
Total (29)	29	0	0	0

Late: Brain

RTOG / EORTC and LENT SOMA

Dose (n)	grade 0	1	2
48 GyE (1)	1	0	0
52.8 GyE (3)	3	0	0
57.6 GyE (6)	6	0	0
60.8 GyE (19)	14	4	1
Total (29)	24	4	1

Grade 1: Occasional non-narcotic medication
Grade 2: Persistent non-narcotic medication, intermittent low dose steroids

Acute: Spinal cord

RTOG

Dose (n)	grade 0	1	2	3
48 GyE (1)	1	0	0	0
52.8 GyE (3)	3	0	0	0
57.6 GyE (6)	6	0	0	0
60.8 GyE (15)	15	0	0	0
Total (25)	25	0	0	0

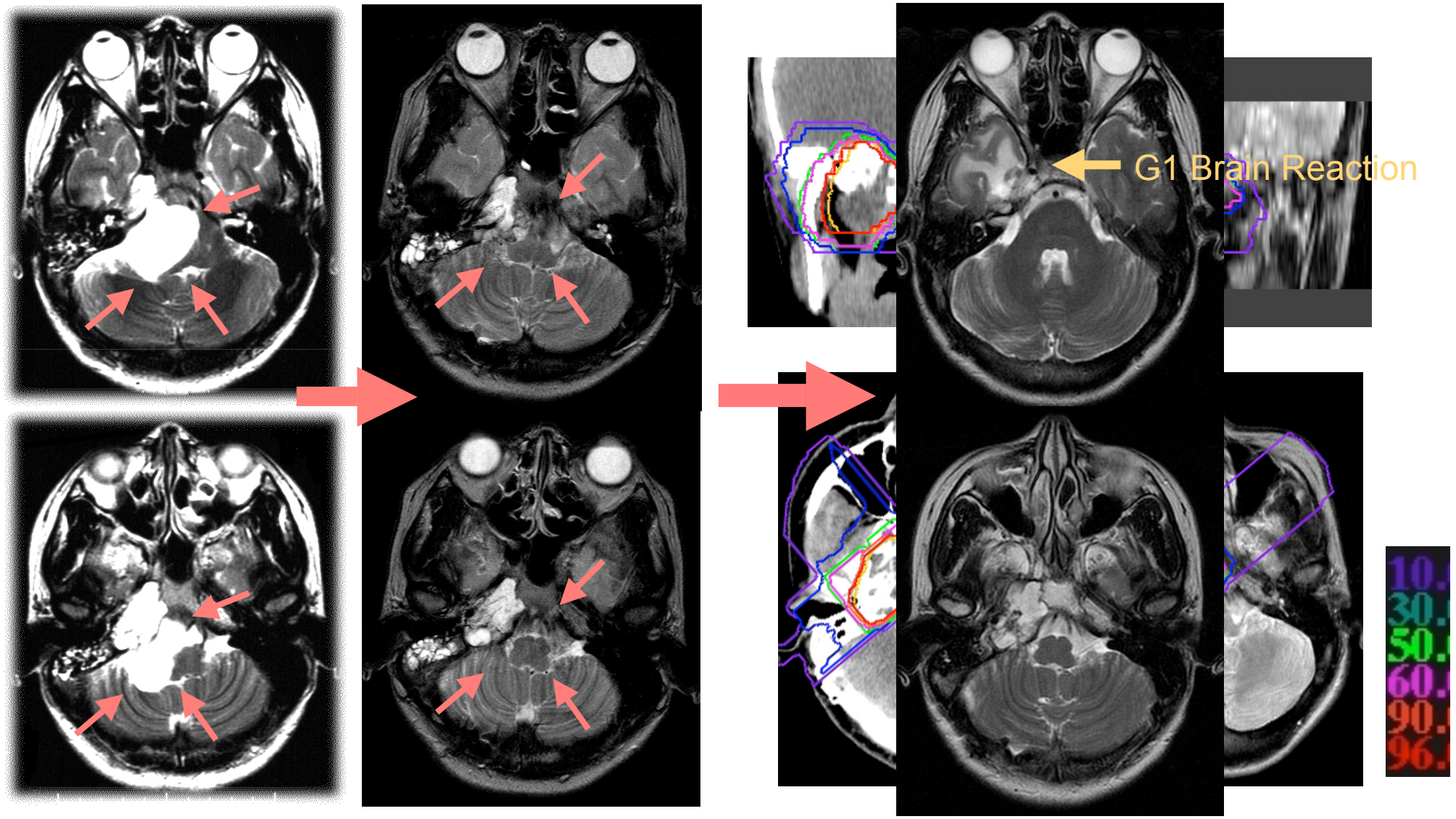
Late: Spinal cord

RTOG / EORTC and LENT SOMA

Dose (n)	grade 0	1	2
48 GyE (1)	1	0	0
52.8 GyE (3)	3	0	0
57.6 GyE (6)	6	0	0
60.8 GyE (15)	15	0	0
Total (25)	25	0	0

Postoperative Chordoma in the Right Clivus

Carbon ion dose: 60.8 GyE/16 frs.



Pre ope

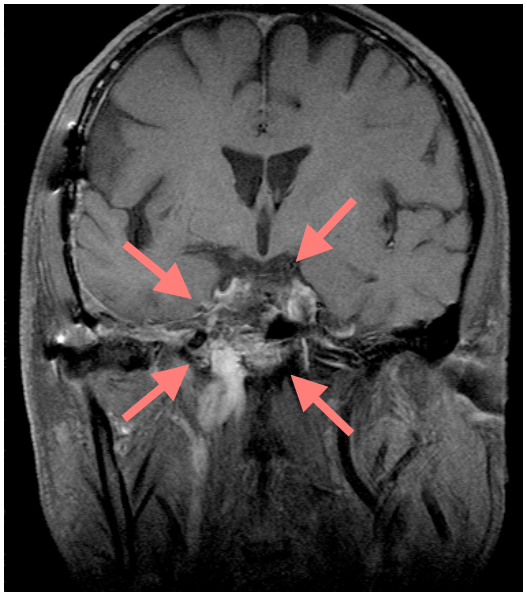
Pre c-ion RT

Dose distribution and reconstructed MRI

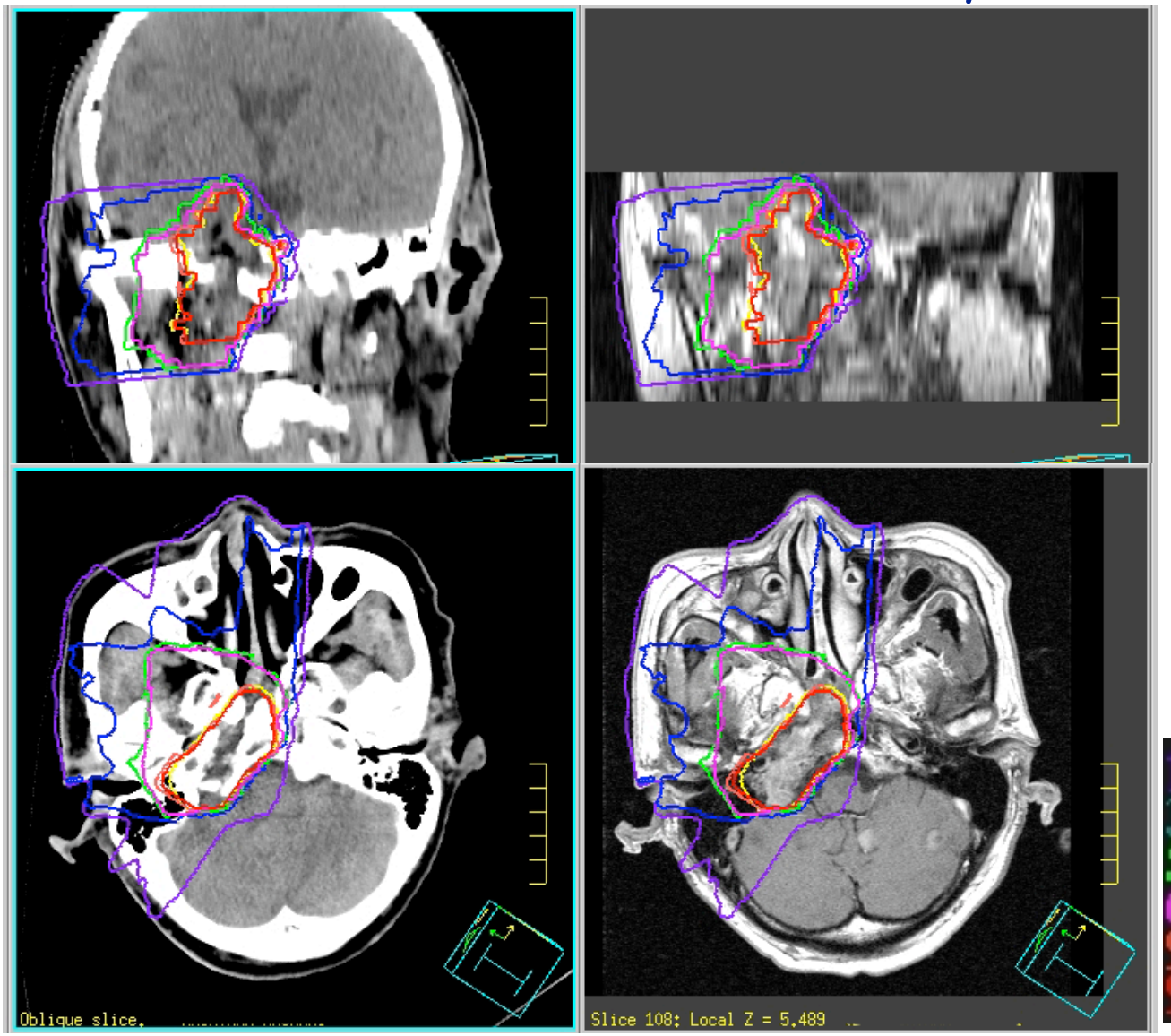
Post 59 months

Postoperative Chordoma in the Right Clivus

Carbon ion dose: 60.8 GyE/16 frs.



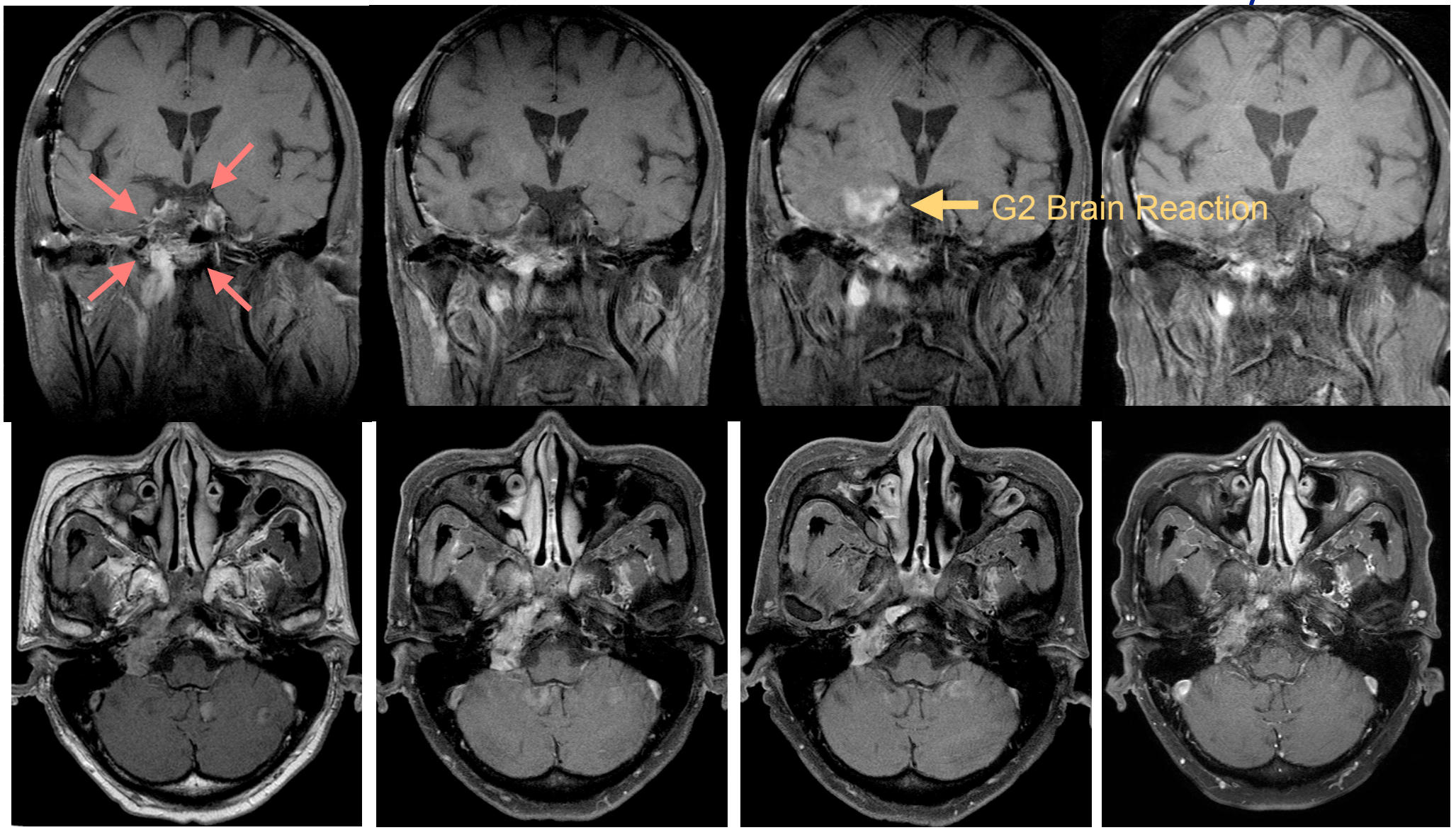
Pre c-ion RT



Dose distribution and Reconstructed MRI

Postoperative Chordoma in the Right Clivus

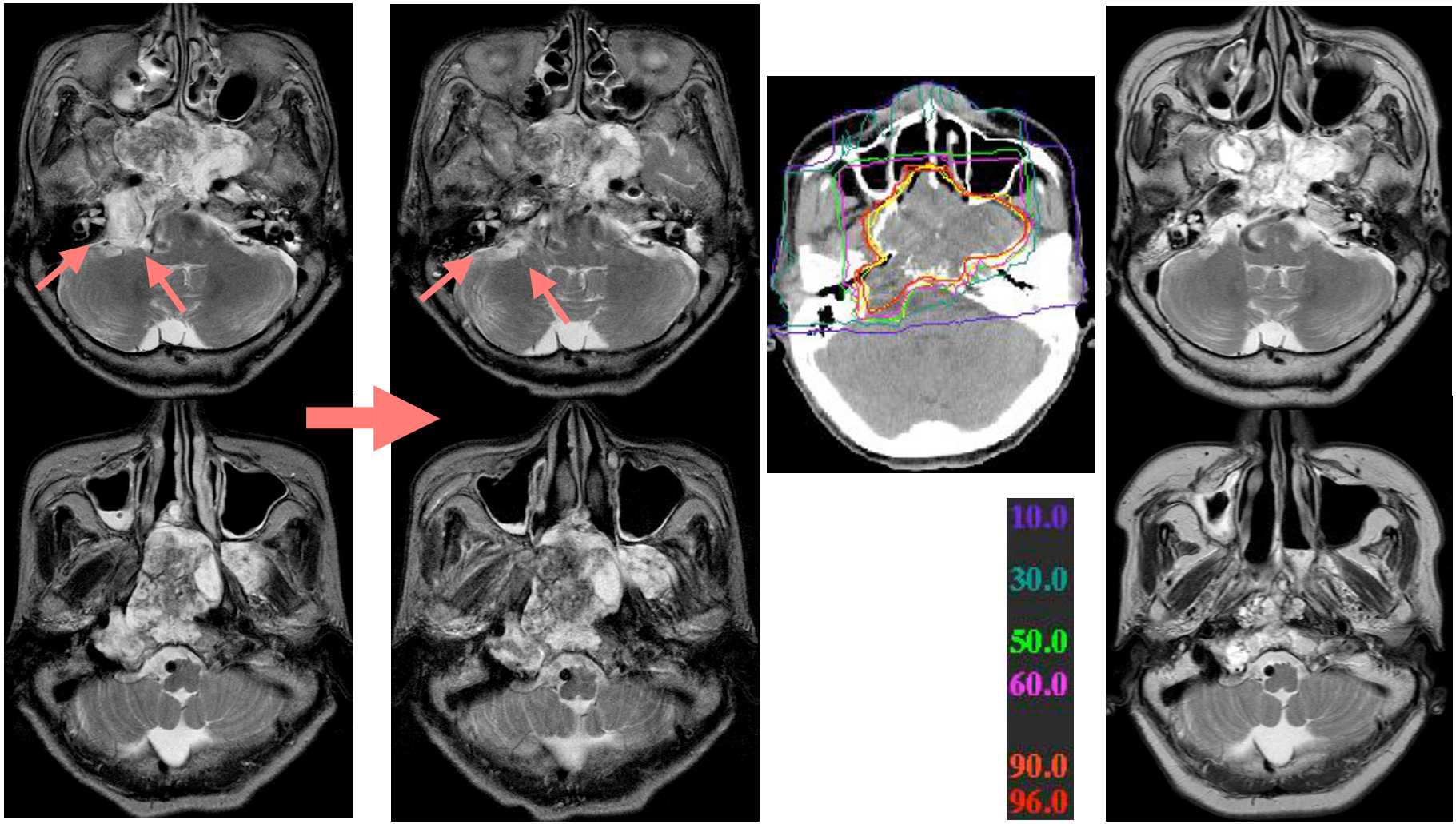
Carbon ion dose: 60.8 GyE/16 frs.



Pre c-ion RT | Post 20 months | Post 26 months | Post 45 months

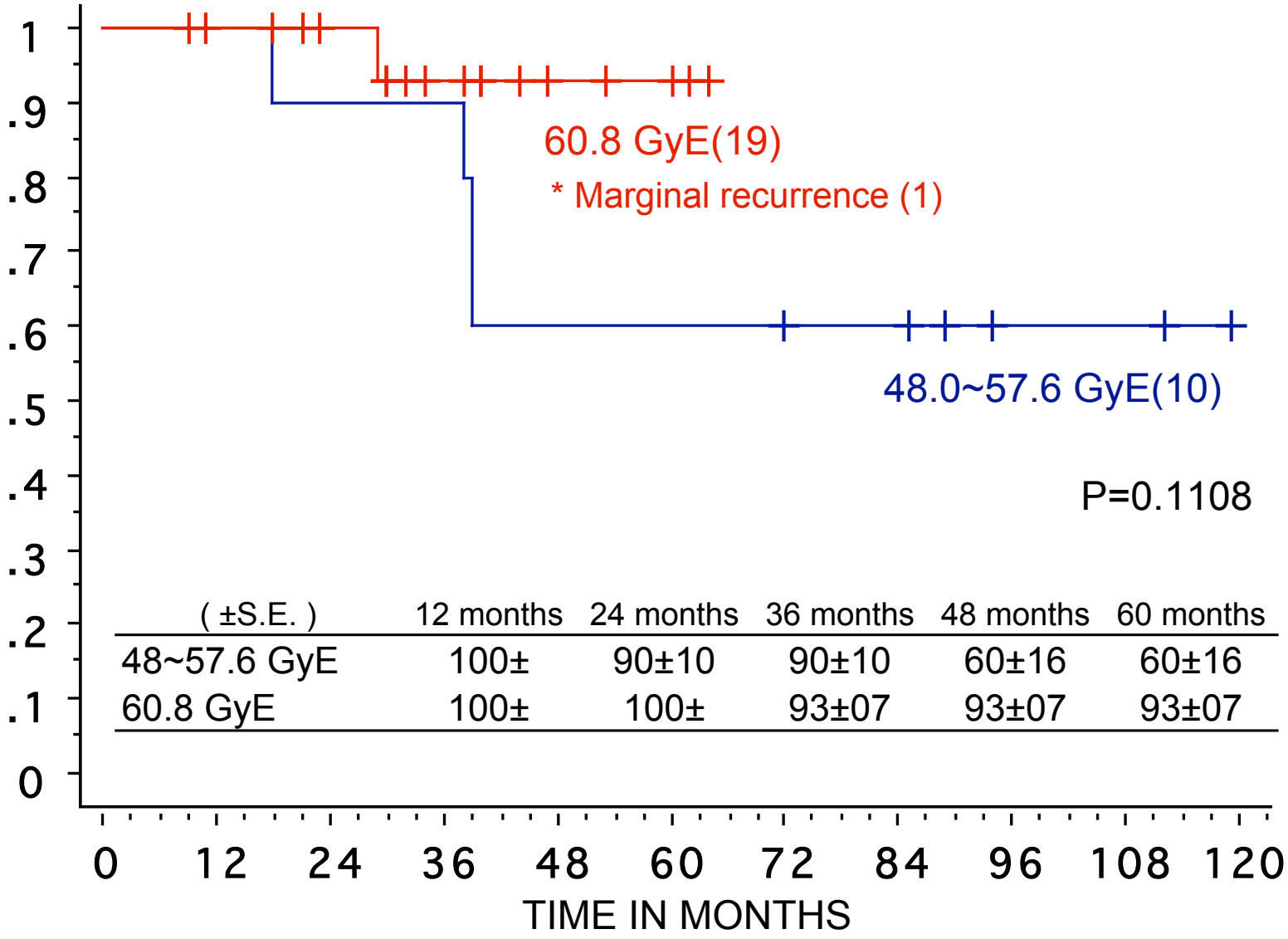
Postoperative Chordoma in the Clivus and Nasopharyngeal Space

Carbon ion dose: 60.8 GyE/16 frs



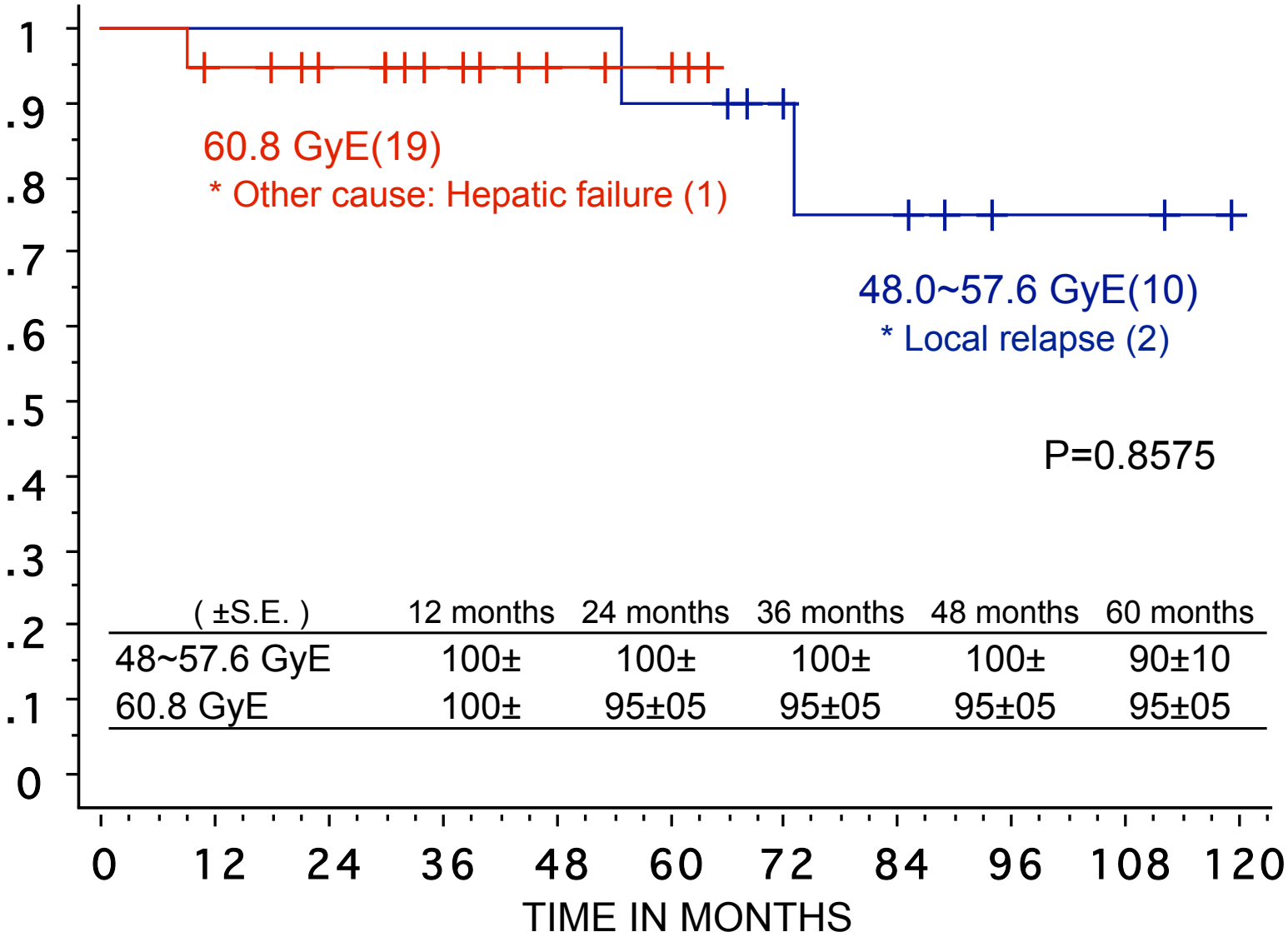
Pre ope | Pre c-ion RT | Dose distribution | Post 40 months

Local control of 29 Chordomas



(±S.E.)	12 months	24 months	36 months	48 months	60 months
48~57.6 GyE	100±	90±10	90±10	60±16	60±16
60.8 GyE	100±	100±	93±07	93±07	93±07

Overall survival of 29 Chordomas



(±S.E.)	12 months	24 months	36 months	48 months	60 months
48~57.6 GyE	100±	100±	100±	100±	90±10
60.8 GyE	100±	95±05	95±05	95±05	95±05

Clinical characteristics of reported cases of chordoma in the skull base and paracervical spine

	Authors	N	Median total dose	Median f/u (y)	Local control rate (% 3-y	5-y	10-y
Photon	Catton et al.	24	50.0	5.2		23	15
	Romero et al.	18	50.1	3.1		17	
	Forsyth et al.	39	50.0	8.3		39	31
	Magrini et al.	12	58.0	6.0		25	25
Proton	Munzenrider et al. (MGH)	169	66-83	3.4		73	54
(+/- photon)	Noel et al (CPO)	100	67.0	2.6	86 (2-y)	54 (4-y)	
	Hug et al. (MGH: 2002)	33	71.9	2.8	67	59	
	Hiroshi I et al (Tsukuba)	13	72.0	5.8	67	46	
Helium	Castro et al. (LB)	53	65.0	4.3		63	
Carbon	Shults-Ertner et al. (GSI)	96	60.0	2.6 (Mean)	81	70	
	NIRS	29	48-60.8	3.7		89 (SE ±10)	
	NIRS	19	60.8	2.7		93 (SE ±07)	

Conclusion

1. The carbon ion dose in 60.8 GyE improves local control. Additionally, we did not observe severe toxicity for the critical organs such as brainstem, spinal cord and optic nerves.

2. Carbon ion radiotherapy for chordoma compared with photon, proton and helium ion radiotherapy will deliver a high local control rates with low toxicity to the surrounding normal tissues.