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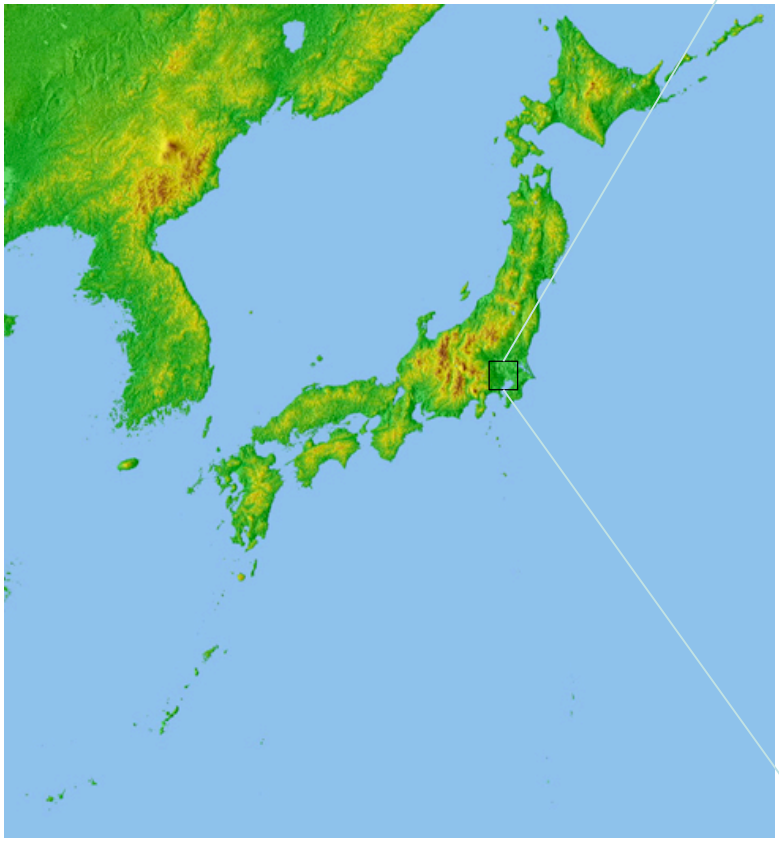
Five Years Comprehensive Experience in Proton Radiotherapy in PMRC Tsukuba

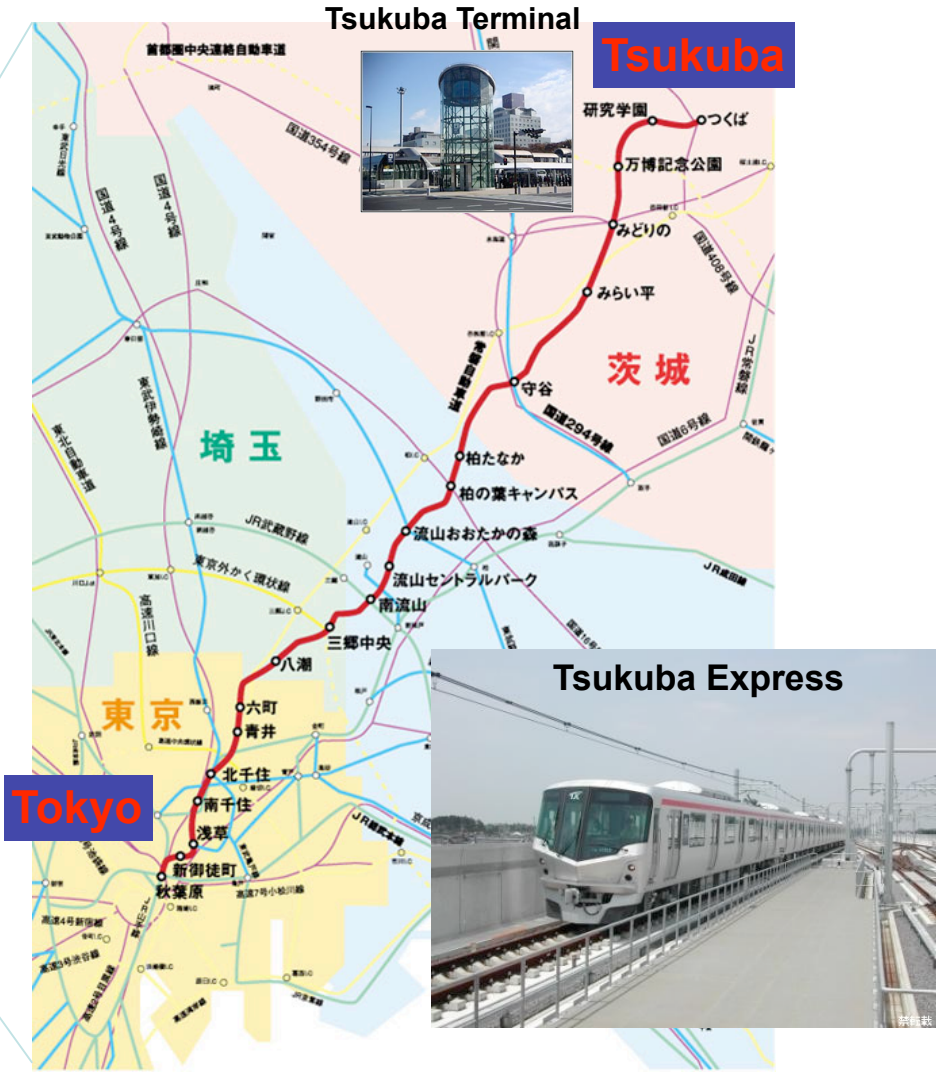
Koji Tsuboi M.D., Ph.D.

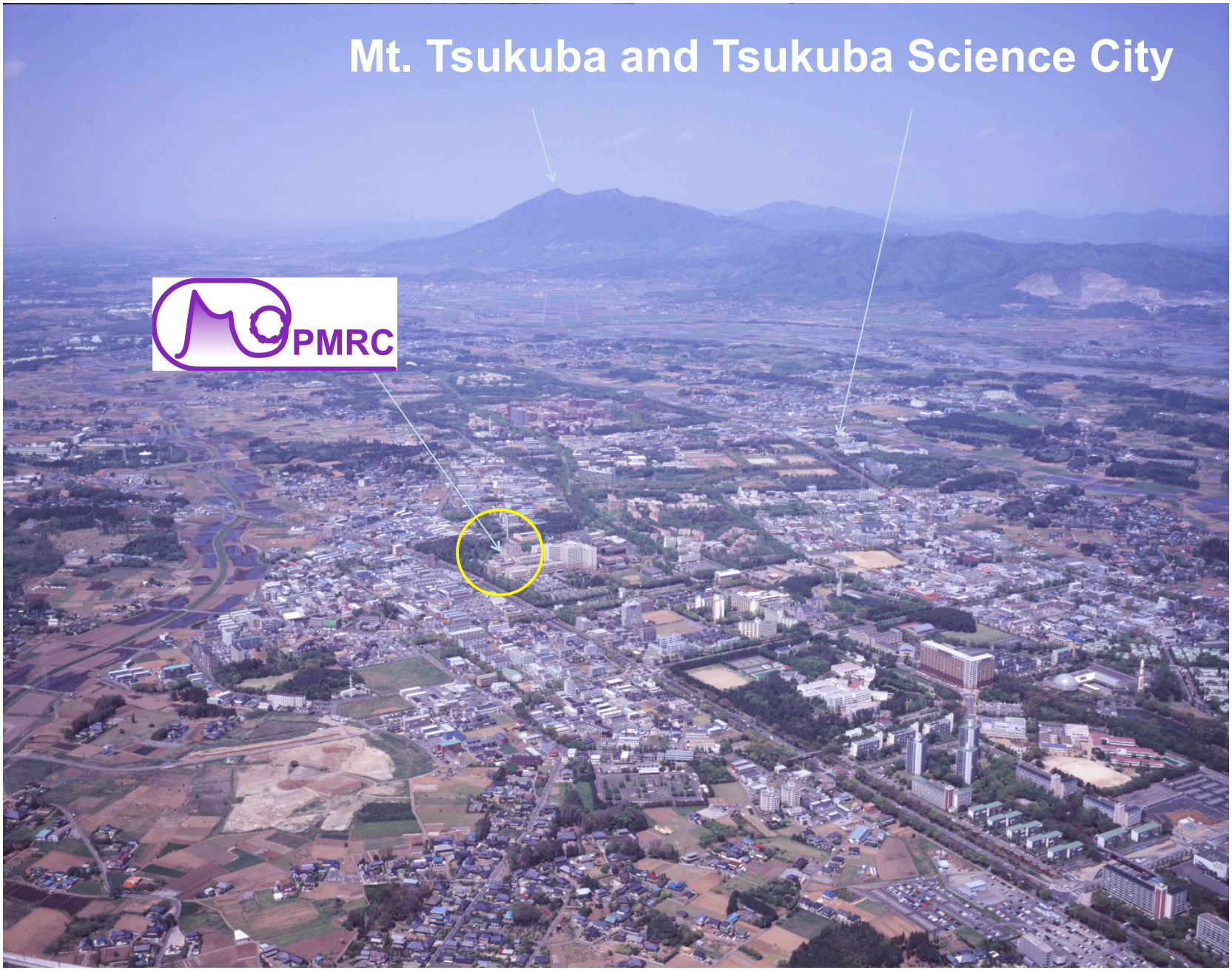
Proton Medical Research Center,
University of Tsukuba,
JAPAN

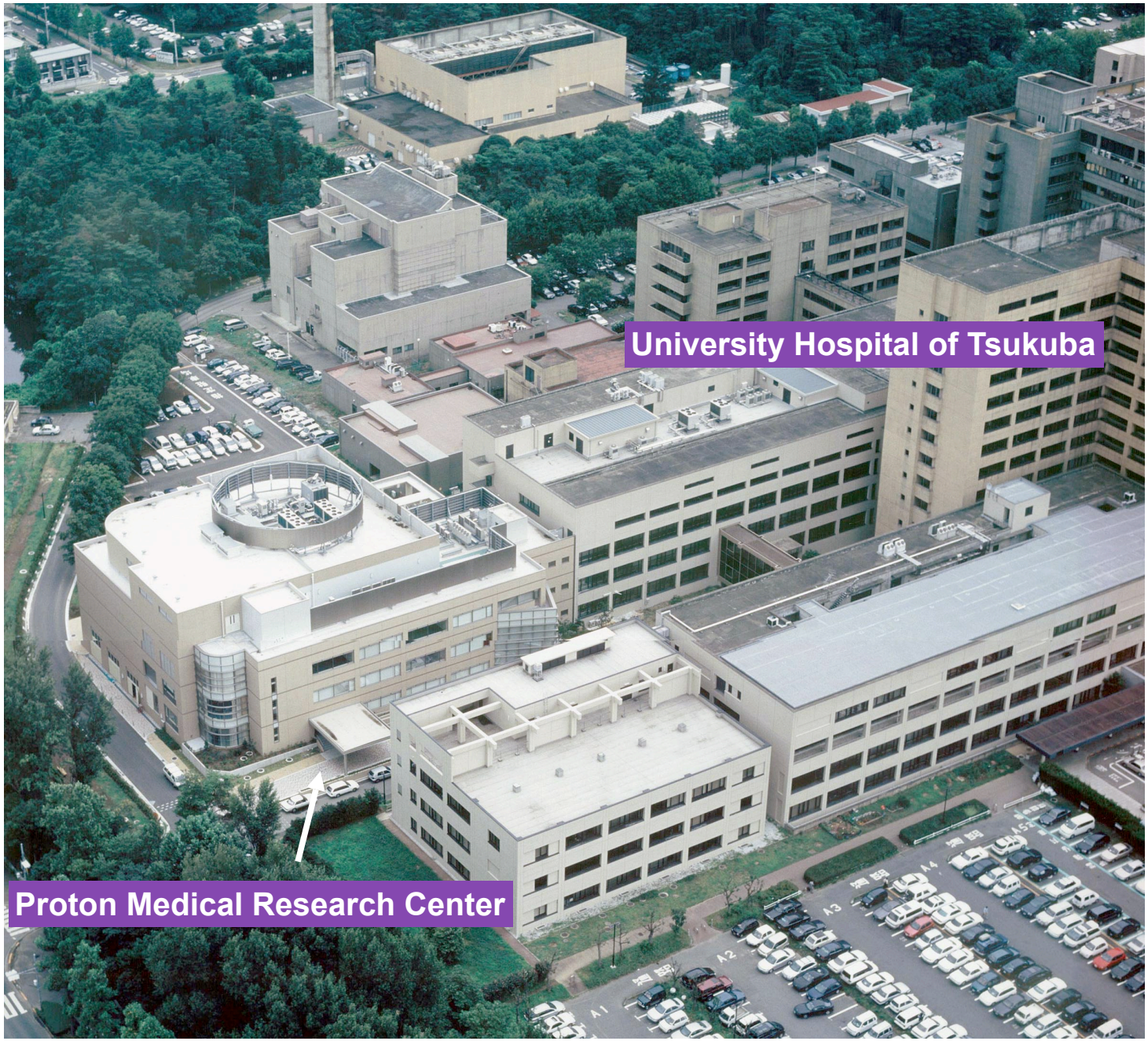
筑波大学
University of Tsukuba

Where is Tsukuba ?

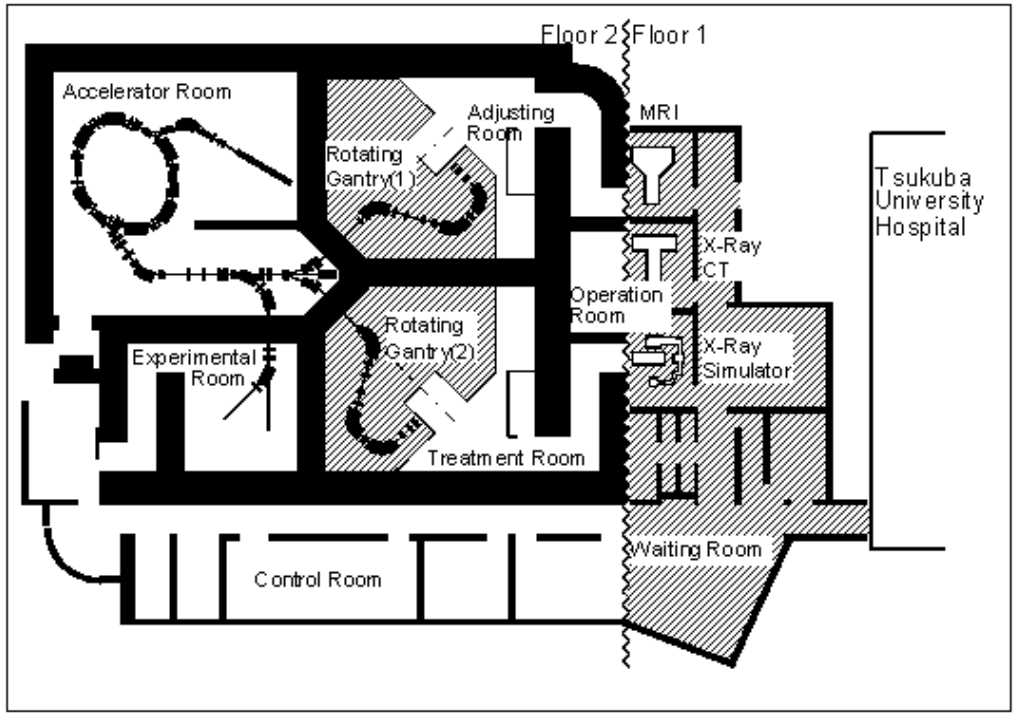


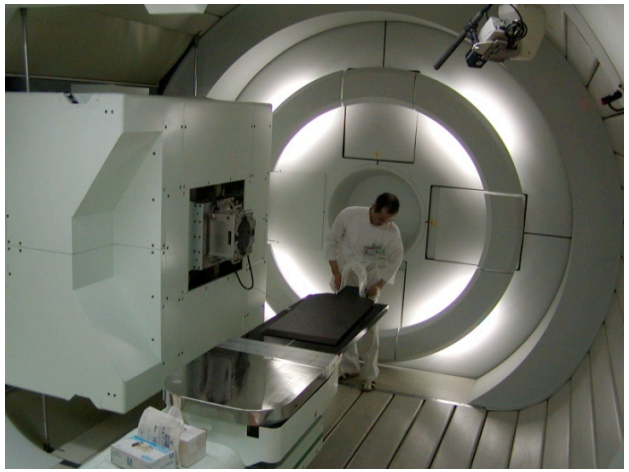


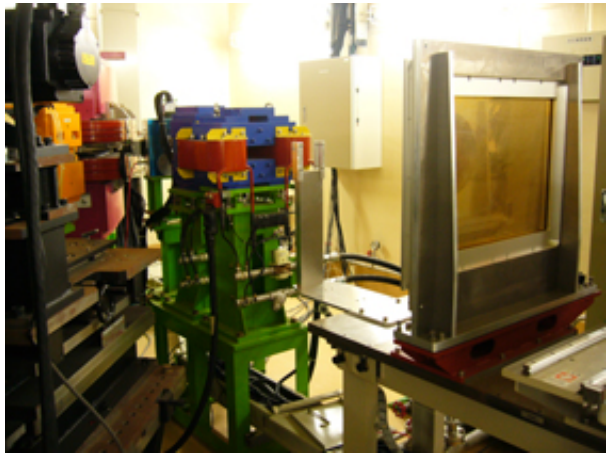

Mt. Tsukuba and Tsukuba Science City
PMRC


University Hospital of Tsukuba
Proton Medical Research Center

Layout of the proton therapy facility







Cases treated at PMRC during the last 5 years (2003.1 – 2007.12)

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Cases treated at PMRC during the last 5 years (2003.1 – 2007.12)

1024

Hepatocellular carcinoma (HCC)

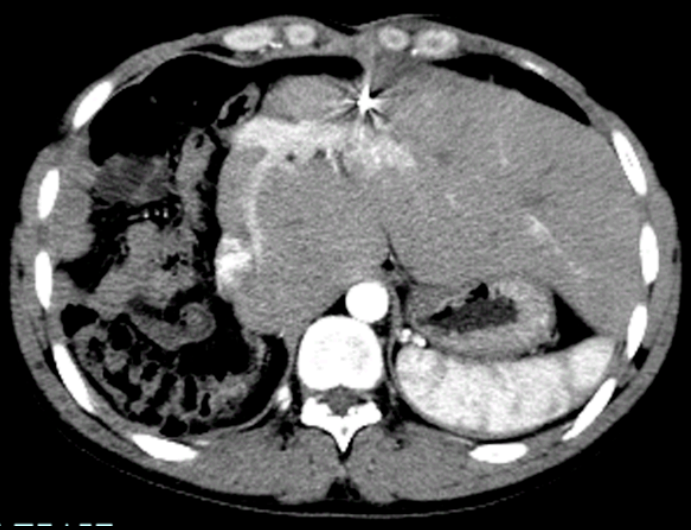
1) 66 GyE / 10 fractions
Solitary tumor
10 cm or less in diameter
2 cm away form the port hepatis or the GI tract
Child-Pugh A or B
→ 51 cases

2) 72.6GyE / 22 fractions
Within 2 cm from the port hepatis
→ 53 cases

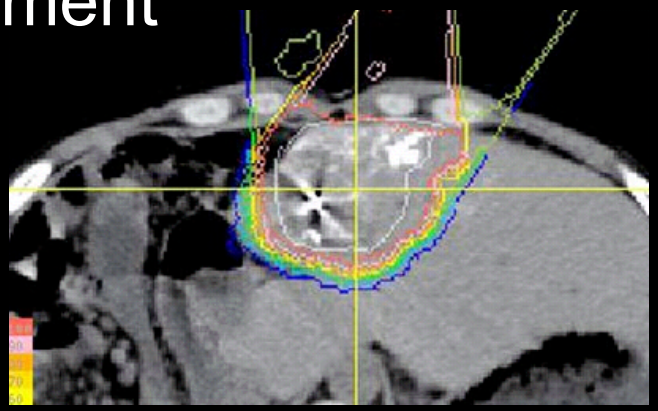
3) 70.0 GyE / 35 fractions
within 2 cm from the GI tract

26 y.o. man 66 GyE/10 fractions

Pre-treatment

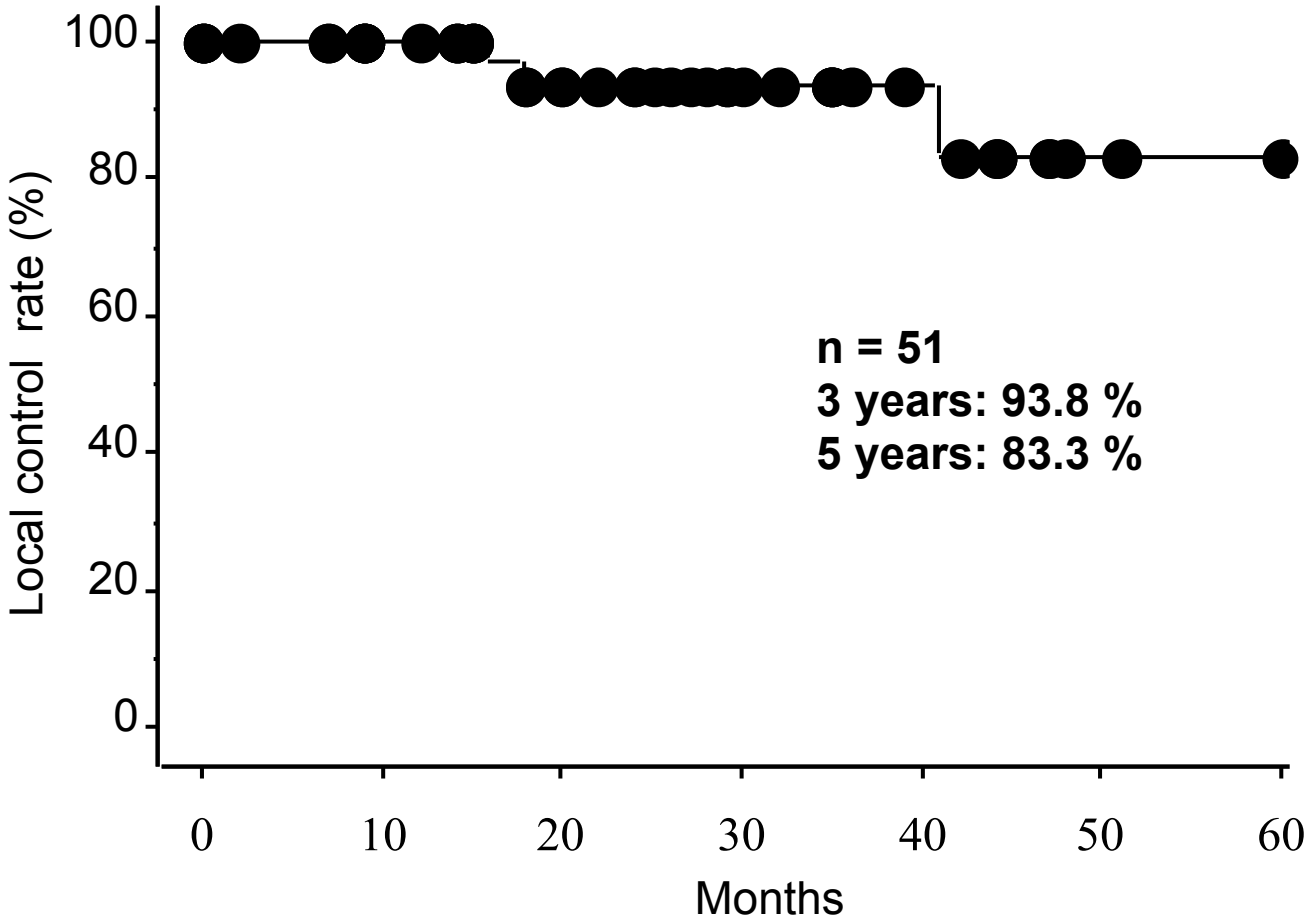


38 months later

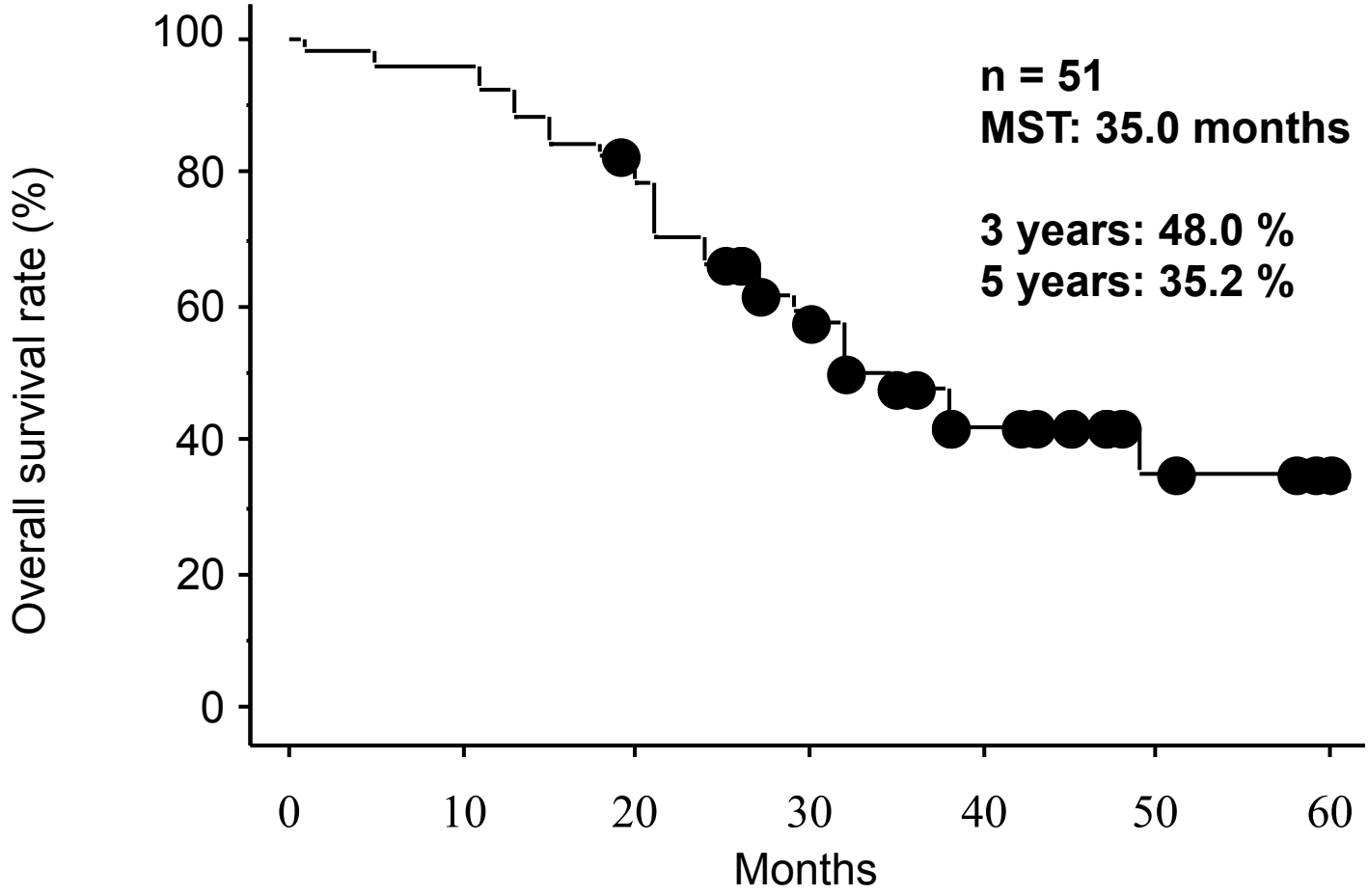


Planning

Local Control Rate of Patients Treated by 66 GyE/10 fractions



Overall Survival of Patients Treated by 66 GyE/10 fractions



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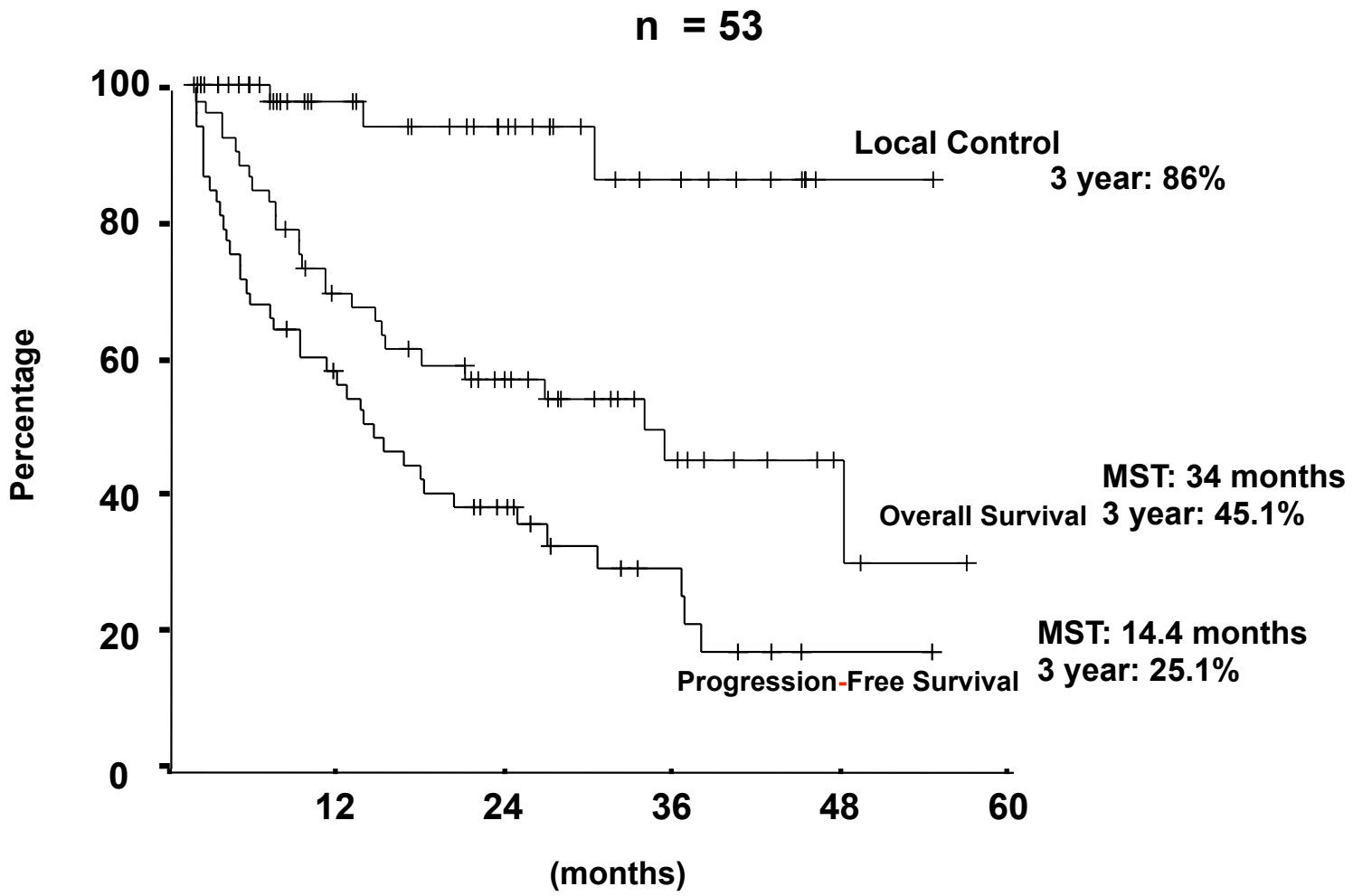
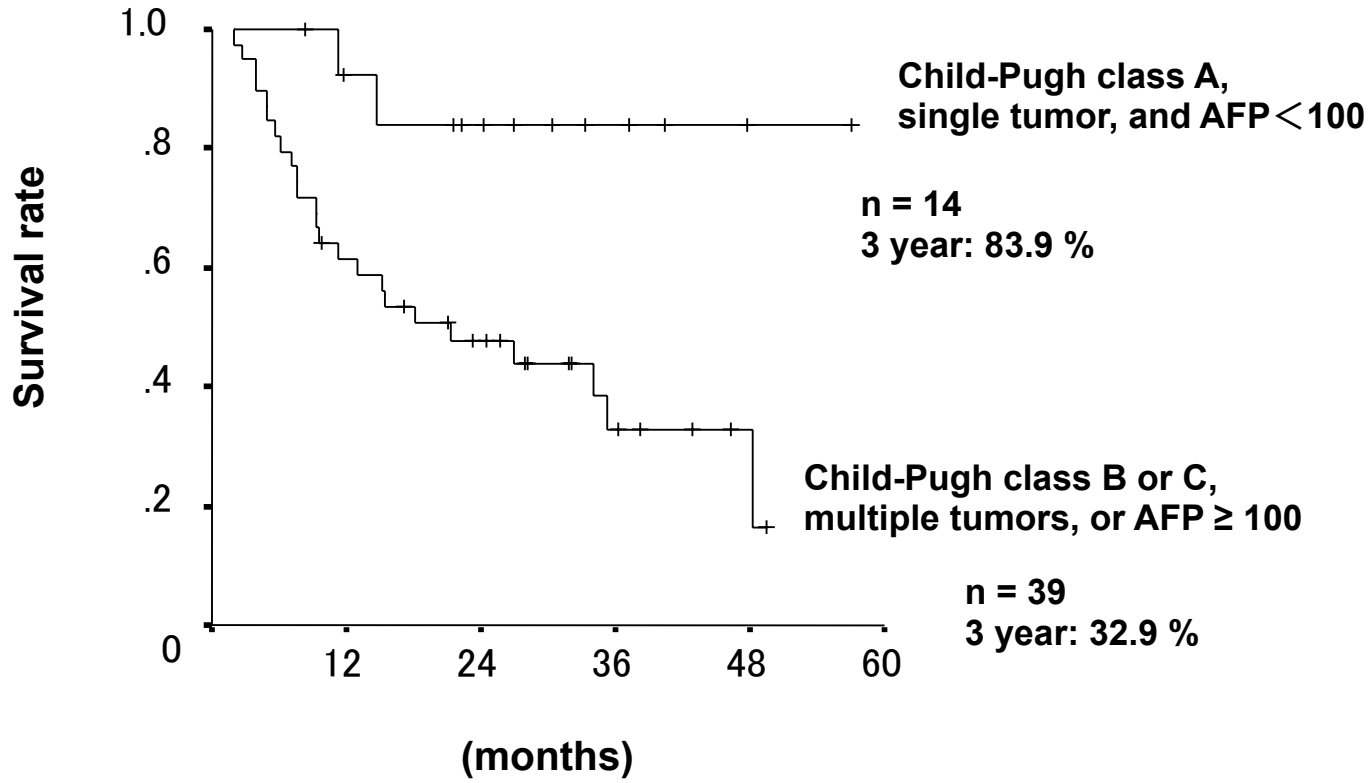
Survival of cases with 72.6GyE/ 22 fractions

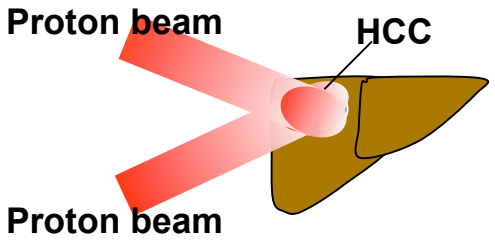


Overall survival of cases with 72.6GyE/ 22 fractions



A current clinical trials in HCC

1) Phase I-IIa trial of combination of proton radiotherapy and novel immunological adjuvant therapy



+

<u>Tumor Specific Immunotherapy</u>
Use of a novel adjuvant

2) Phase II clinical trial of proton radiotherapy for HCC with portal vein tumor thrombus.

- Tumor thrombus at the main portal vein and its first branches
- 72.6GyE / 22 fractions

Non-small cell lung cancers

Stage I: 37 cases Phase II trial

Peripheral: Tumors in the zone outside of the proximal bronchial tree :

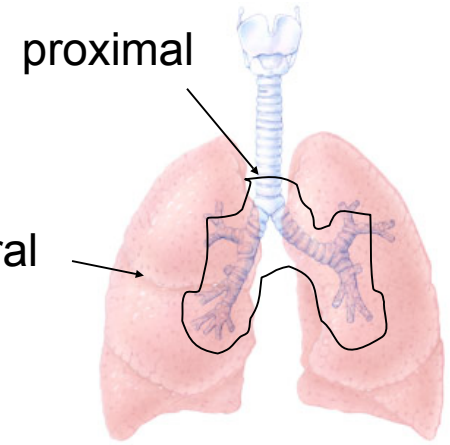
24 cases

CTV = GTV + 5 -10 mm
PTV = CTV + 5 -10 mm
66GyE/ 10 fractions

Proximal: Tumors in the zone of the proximal bronchial tree defined in RTOG 0618

13 cases

CTV = GTV + 5 -10 mm
PTV = CTV + 5 -10 mm
72.6 GyE/22 fractions



Stage II-III: 34 cases Retrospective analysis

CTV1 = GTV1 (primary) + 5 -10 mm
CTV2 = GTV2 (LN) + 5 -10 mm
PTV= CTV1 + CTV2 + 5 -10 mm

Local control of stage I peripheral type

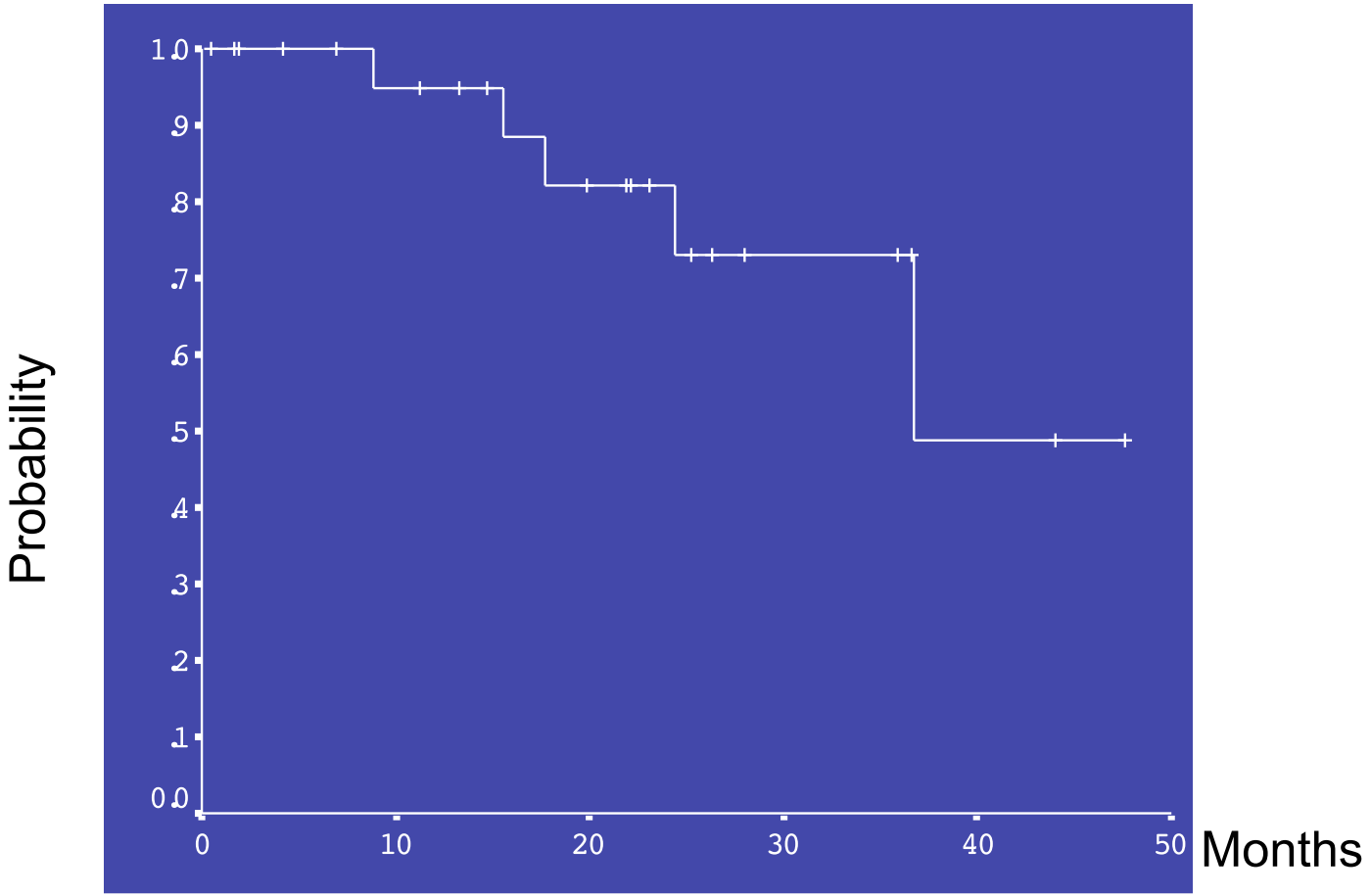
CR: 79.1%（19/24）

PR: 16.7%（4/24）

SD: 4.0%（1/24）

PD: 0%（0/24）

Progression free survival of stage I peripheral type



1 year	2 years	3 years	4 years
94.7%	82.1%	73.0%	48.7%

Overall survival of stage I peripheral type

Median observation time: 22.9 months

Alive 23

Dead 1

83.3 y.o. woman cT1NOMO

Died of NSCLC at 39.9 months

Non-small cell lung cancers

Stage I: **37 cases** **Phase II clinical study**

Peripheral: Tumors in the zone outside of the proximal bronchial tree :

24 cases

CTV = GTV + 5 -10 mm
PTV = CTV + 5 -10 mm
66GyE/ 10 fractions

Proximal: Tumors in the zone of the proximal bronchial tree defined in RTOG 0618

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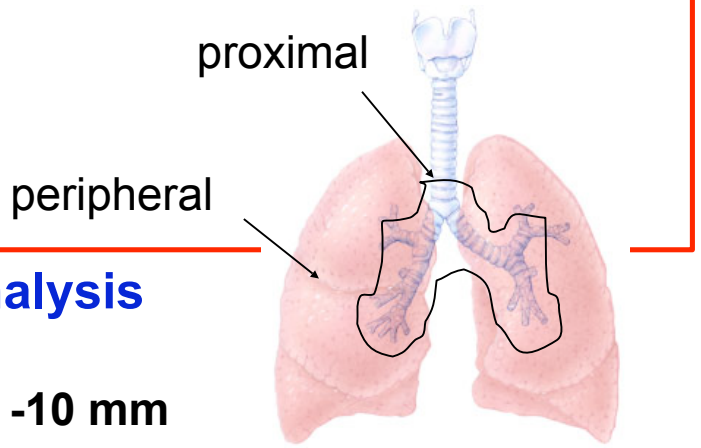


Stage II-III: **34 cases** **Retrospective analysis**

CTV1 = GTV1 (primary) + 5 -10 mm
CTV2 = GTV2 (LN) + 5 -10 mm
PTV= CTV1 + CTV2 + 5 -10 mm

Local control rate of stage I proximal type

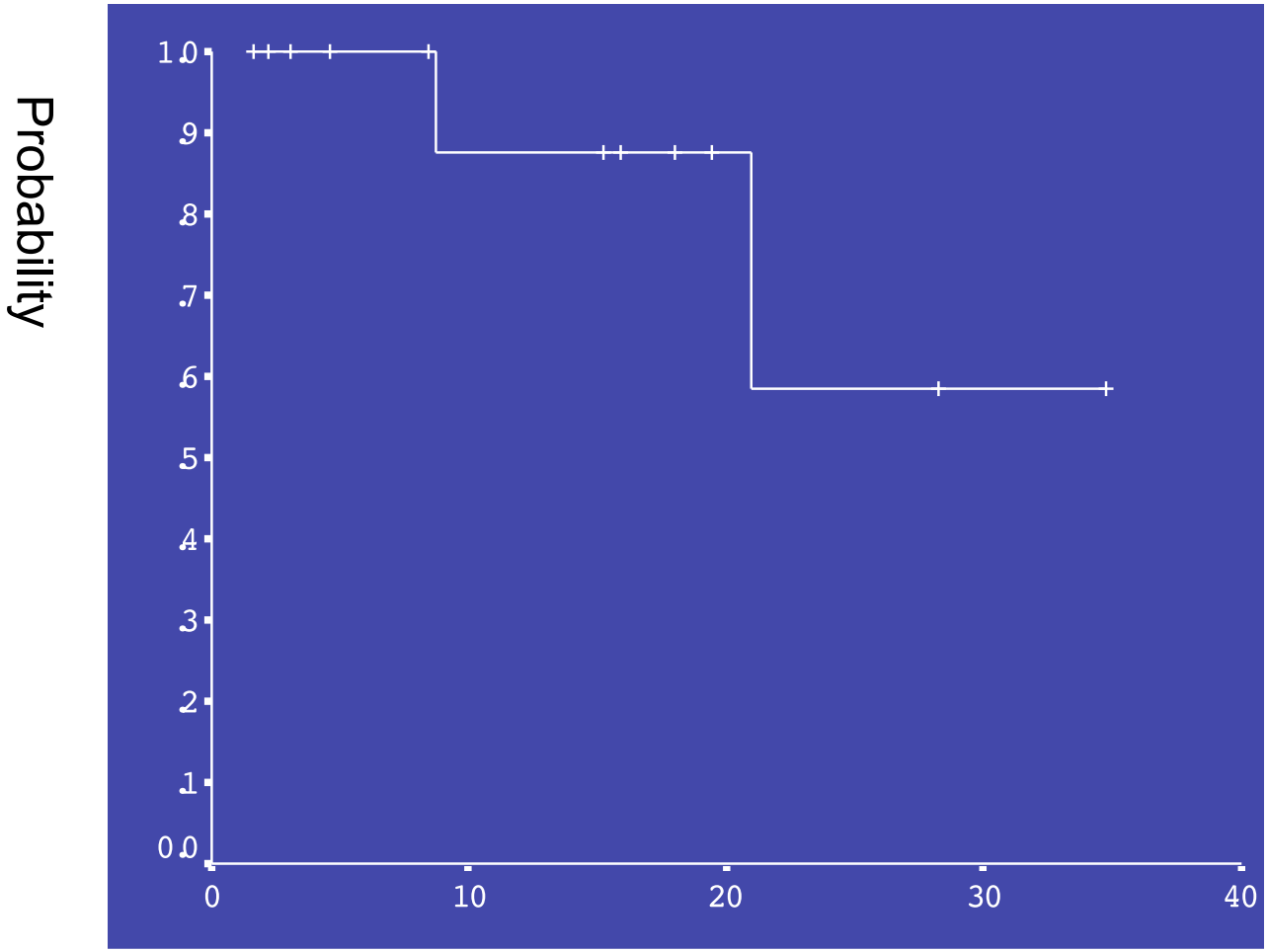
CR: 69.2%（9/13）

PR: 15.4%（2/13）

SD:　7.6%（1/13）

PD:　7.6%（1/13）

Progression free survival of stage I proximal type



1 year	2 years	3 years
87.5	58.3	58.3

Overall survival of stage I proximal type

Median observation time: 15.2 months

Alive: 13 cases

Dead: none

Non-small cell lung cancers

Stage I: 37 cases

Peripheral: Tumors in the zone outside of the proximal bronchial tree :

24 cases

CTV = GTV + 5 -10 mm
PTV = CTV + 5 -10 mm
66GyE/ 10 fractions

Proximal: Tumors in the zone of the proximal bronchial tree defined in RTOG 0618

13 cases

CTV = GTV + 5 -10 mm
PTV = CTV + 5 -10 mm
72.6 GyE/22 fractions

Stage II-III: 34 cases

These patients did not underwent surgery and chemotherapy for some reasons.

CTV1 = GTV1 (primary) + 5 -10 mm
CTV2 = GTV2 (LN) + 5 -10 mm
PTV= CTV1 + CTV2 + 5 -10 mm

Prescribed doses to stage II-III

(Retrospective analysis)

66 GyE/10 frac **3cases**

(α/β=3, 108 GyE)

72.6 GyE/22 frac **9 cases**

(α/β=3, 83.2 GyE)

77 GyE/35 frac **14 cses**

(α/β=3, 80.1 GyE)

83.6 GyE/38 frac **8 cases**

(α/β=3, 86.9 GyE)

Local control rate of stage II-III

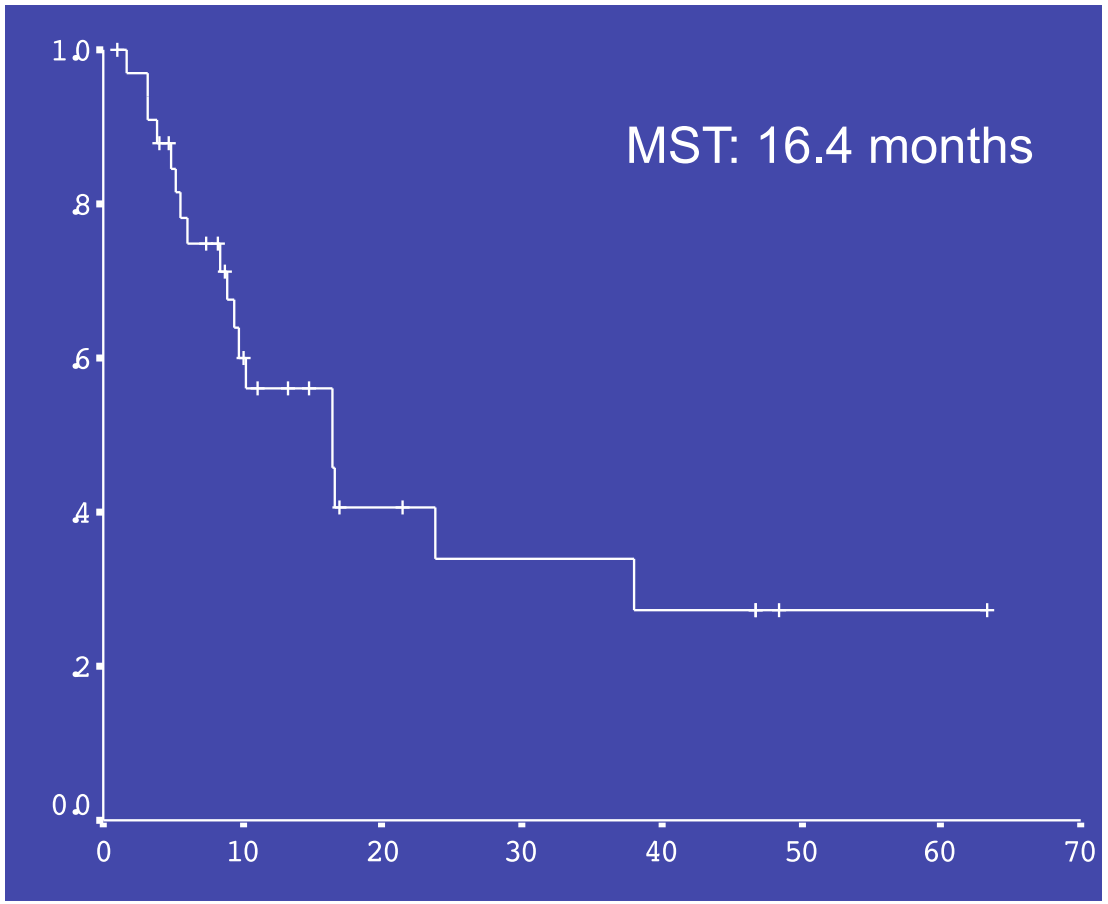
CR: 14.7%（5/34）

PR: 52.9%（18/34）

SD: 17.6%（6/34）

PD: 29.4%（5/34）

Progression free survival of stage II-III



1 year	2 years	3 years	4 years	5 years
56.0	34.0	34.0	27.2	27.2

No chemotherapy
No surgery

A current clinical trials in NSCLC

Phase I/II clinical trail of proton radiotherapy with concurrent chemotherapy for stage II, IIIA and IIIb NCSLC

- **Dose escalation form 74GyE/37 frac to 78GyE/39 frac**
- **Concurrent administration of cisplatin and vinorelbine**

Intracranial lesions

Malignant gliomas

Meningiomas

Neurinomas

A 

Proton therapy for AVM in PMRC (1990-1999)

- 33 cases, M/F =23/10, Age: 35.6 y.o.
  - Treatment
    - SRS: 28 cases
    - SRT: 5 cases （2 frac: 2, 3 frac:2, 15 frac:1）
    - Dose：17Gy-25Gy (Av. 22.5Gy）
    - 3 – 6 ports
  - Results

• Complete cure	21 / 25	(75%)
• Decrease in size	3 / 25	(11%)
• No change	2 / 25	(7%)
• Enlargement	2 / 25	(7%)
• hemorrhage	1 / 25	(4%)
• Necrosis	2 / 25	(7%)

18 cases with AVM ≥3 cm at Tsukuba

Modality	Proton	γ-knife
Number	11	7
Re-bleeding	1 (9.1%)	2 (28.6%)
Cure after 3 years	7 (63.7%)	1 (14.3%)
Nidus remaining after 3 years	4 (36.4%)	6 (85.7%)
Radiation necrosis	1 (9.1%)	1 (14.3%)

α/β-values for AVM cure

Kocher M, et al. (2004)
3.54 (>3.5 cm)
4.6-6.4 (<3.5 cm)

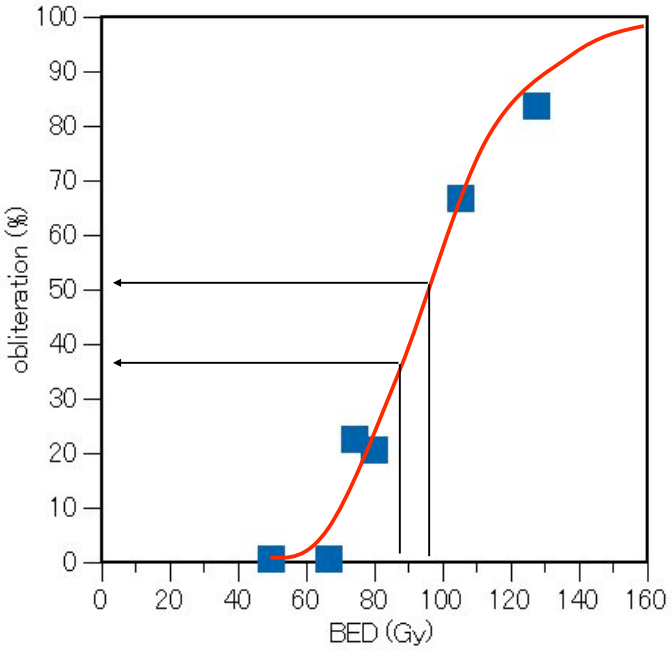
Thus, we assumed that α/β-value for AVM ≥ 3 cm obliteration is 3.5.

Reported series of fractionated radiotherapy for large AVM

Author/Year	method	cases	dose/frac	follow	cure (%)
Redekop/1993	LINAC	10	45-50/15-28	4-10.5	20
Kocher/2004	LINAC	40	50/25	>2	5
		5	20/4	>2	0
Venzendaroglu/2004	LINAC	7	42/6	2	83
		23	30/6	3.5	22
Chang/2004	LINAC	33	25-35/4	4.3	66
Silander/2004	Proton	9	20-25/2	3	22
		6	20-25/4	3	0

α/β **= 3.5**

Fx size	Fx (D)	BED (Gy)	Oblit (%)
8	4 (32)	104.0	66
7	6 (42)	126.0	83
6	4 (24)	65.1	0
5	4 (20)	48.6	0
	6 (30)	72.9	22
2	25 (50)	78.6	20



→ **6 GyE/fx, Total 36 GyE: BED = 97.7 Gy** $_{3.5}$

3 GyE/fx, Total 45 GyE: BED = 83.6 Gy $_{3.5}$

Recent cases

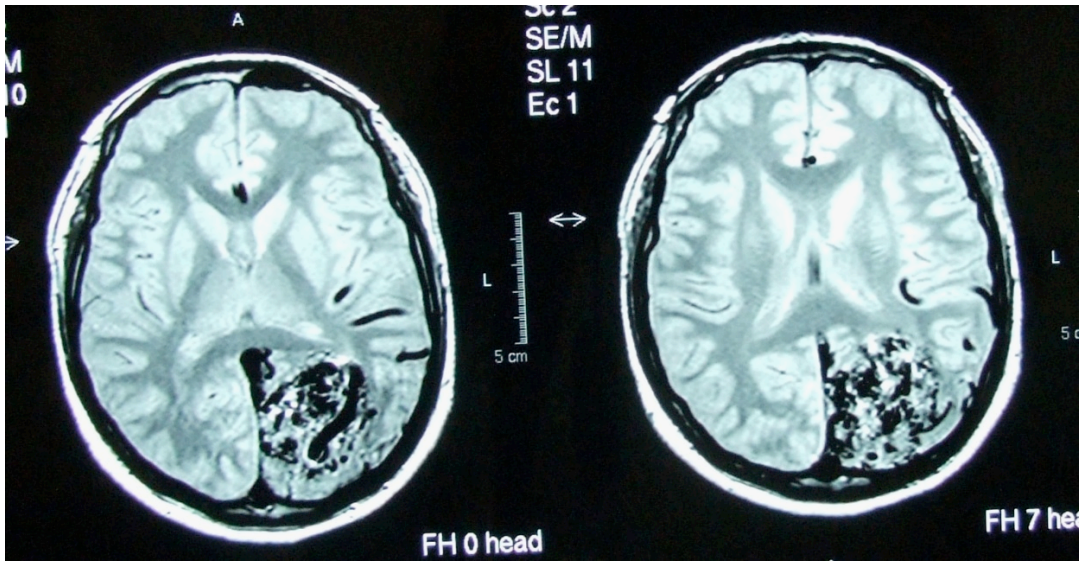
(2008.4.20)

	Age Gender	Size (mm)	S-M Grade	Pre-treatment	Proton	Follow-up
1	23/M	48×45×45	5	Emboli×3	6×6	44 months
2	28/M	40×42×38	5	Emboli×4	6×6	5 months
3	71/M	35×25×22	4	None	3 ×15	4 months
4	28/F	52×48×36	5	None	6×6	2 months
5	25/F	45×23×30	4	None	6×6	2 months
6	40/M	32×25×20	4	None	6×6	1 month

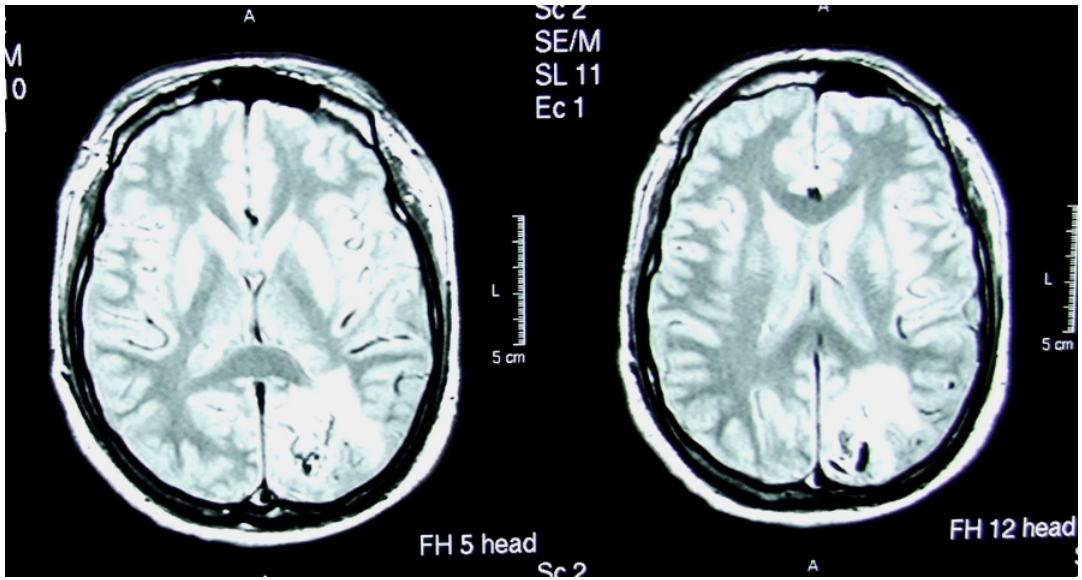
23 y.o. man **Left occipital AVM with Spezler -Martin grade 5**

(48×45×45 mm)

36 GyE / 6 fractions



36 months later



Acknowledgement

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筑波大学
University of Tsukuba

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