

**March 20th, 2014**

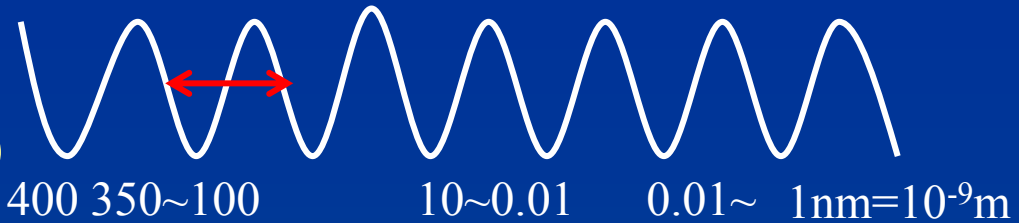
# **Advanced Radiation Therapy of Cancer by Proton Beam**

**Fukui Prefectural Hospital  
Proton Therapy Center  
Yamamoto, Kazutaka**



# (Ionizing) Radiation

Wave (electromagnetic wave)



IR



UV

X-ray  $\gamma$ -ray



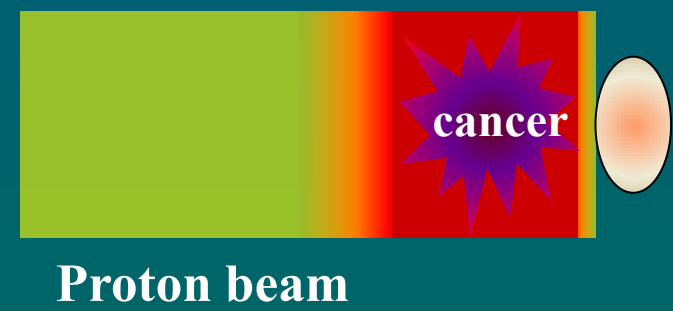
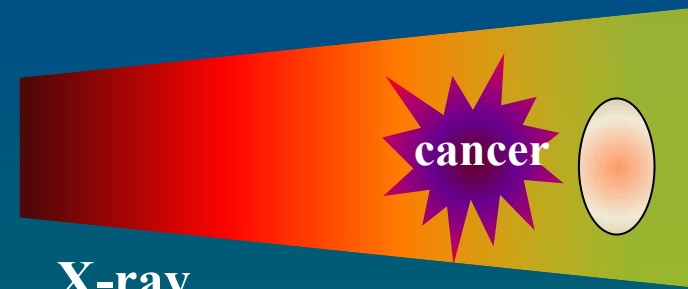
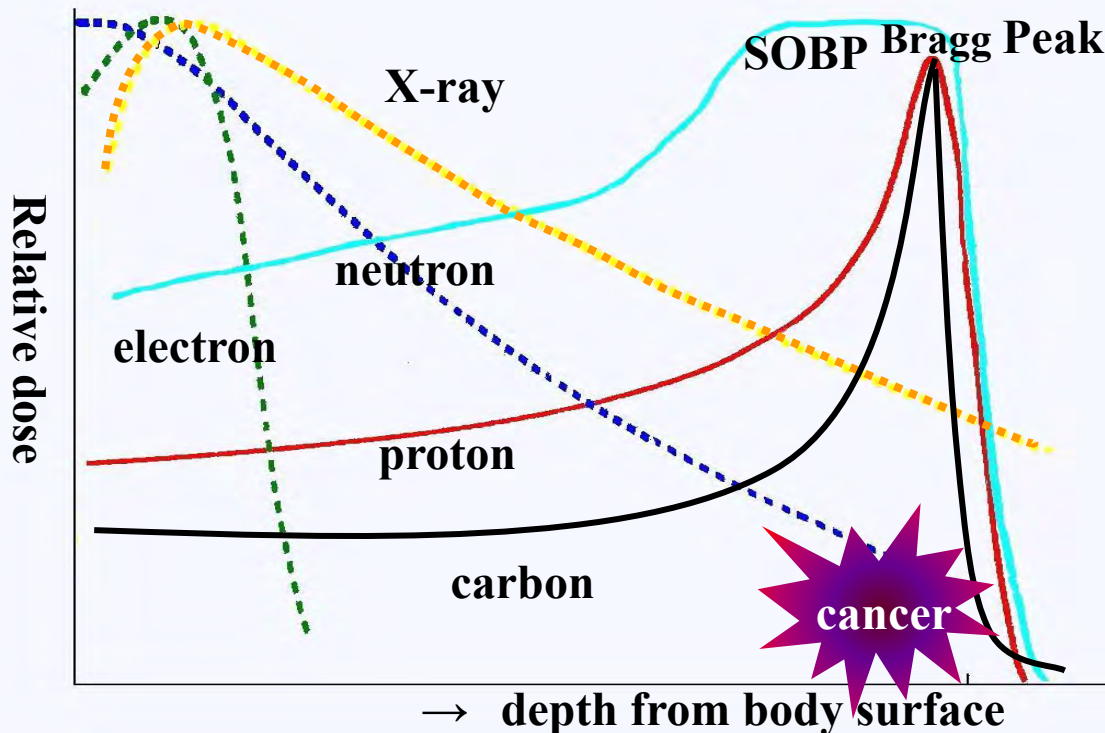
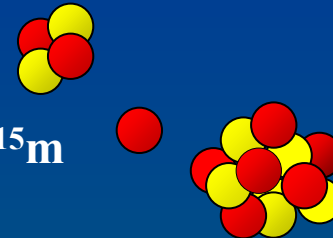
**Ionizing radiation**

## Particle (particle beam)

Alfa ( $\alpha$ ) ray Helium nucleus (p+2n2)

Proton beam Proton (p+) diameter  $\sim 10^{-15}m$

Carbon beam Carbon nucleus ion (p+6n6)



# Biological effect of ionizing radiation

Gene (DNA chain) damage

→ cell death (apoptosis, necrosis)

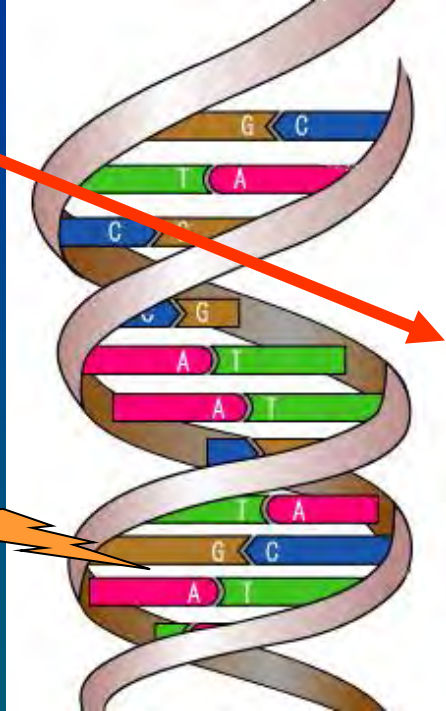
Direct effect

Indirect effect

(Oxygen effect)

Water, Oxygen

Free Radical



Hypoxic cell

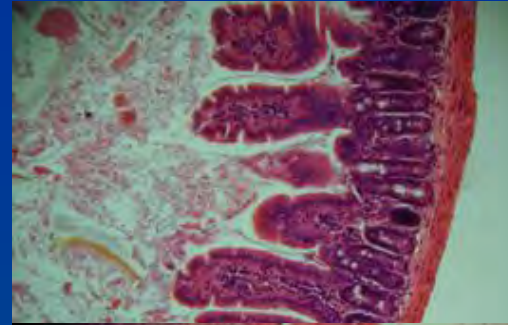
radiosensitivity ↓

(anoxic state; X-ray ~ 1/3)

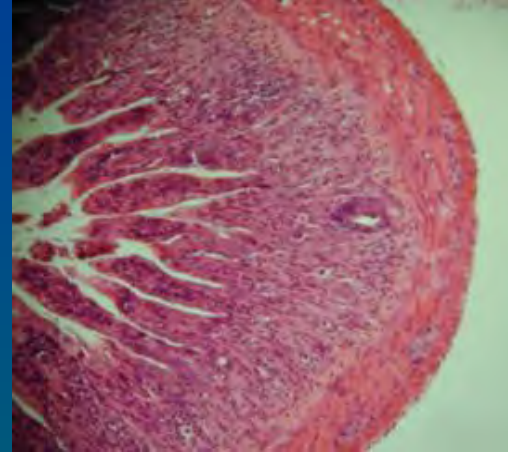
OER (Oxygen Enhancement Ratio)

Irradiation under hypoxic condition (colon 26)

Mouse intestinal crypt



control



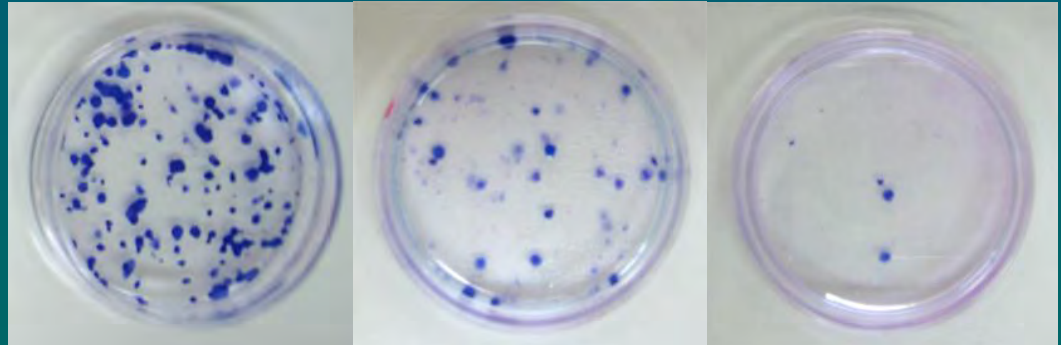
Proton  
14Gy

RBE : proton beam ~ 1.1

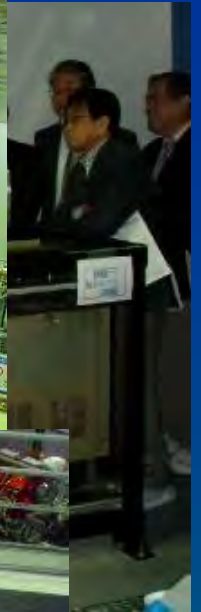
Control

X-ray 9Gy

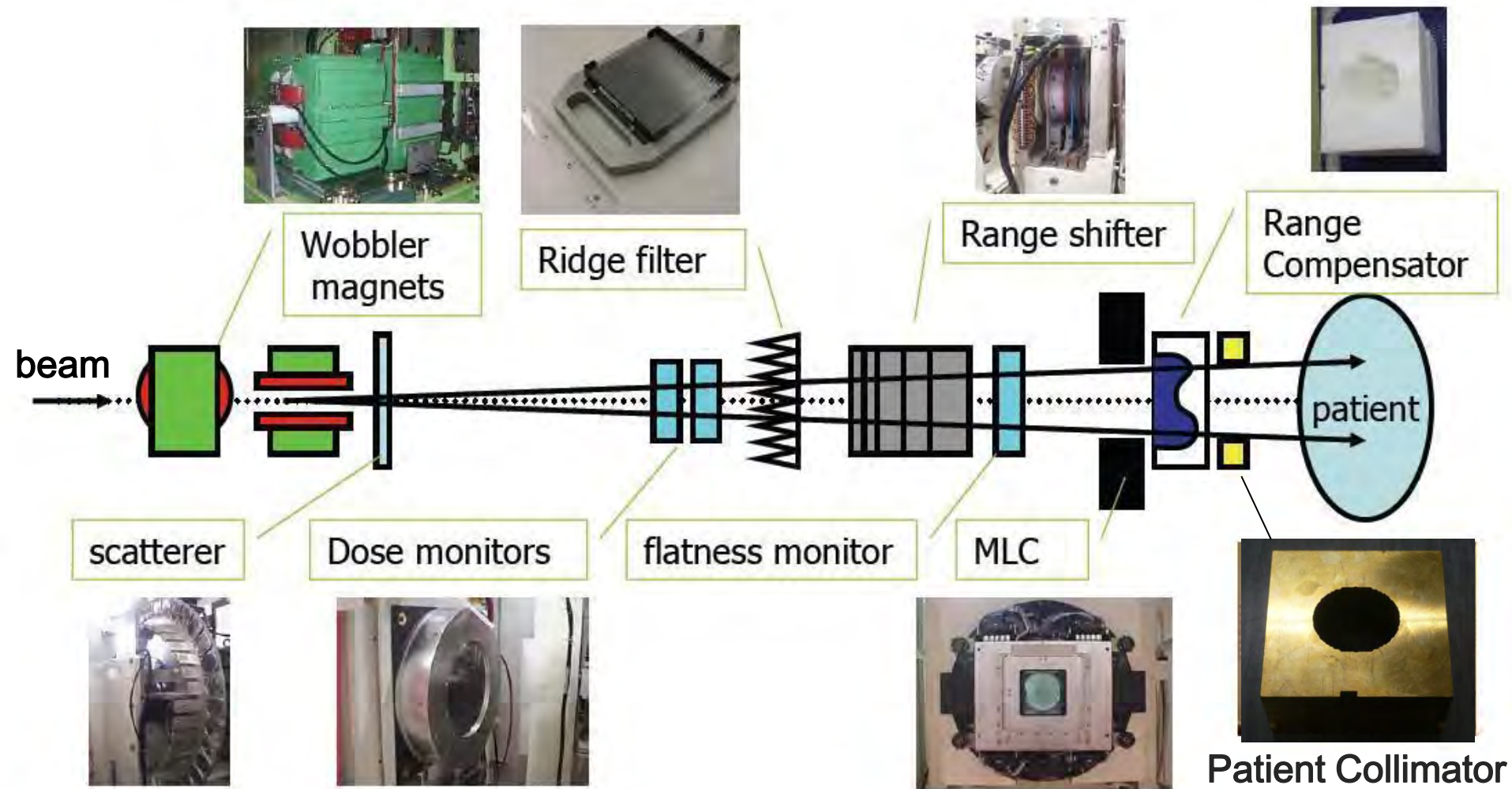
Proton 9Gy







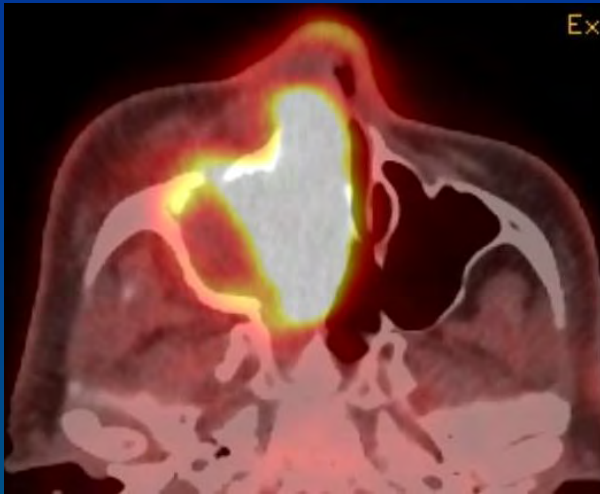
# 3-Dimensional Irradiation Field Forming Method (Broad-Beam Method)



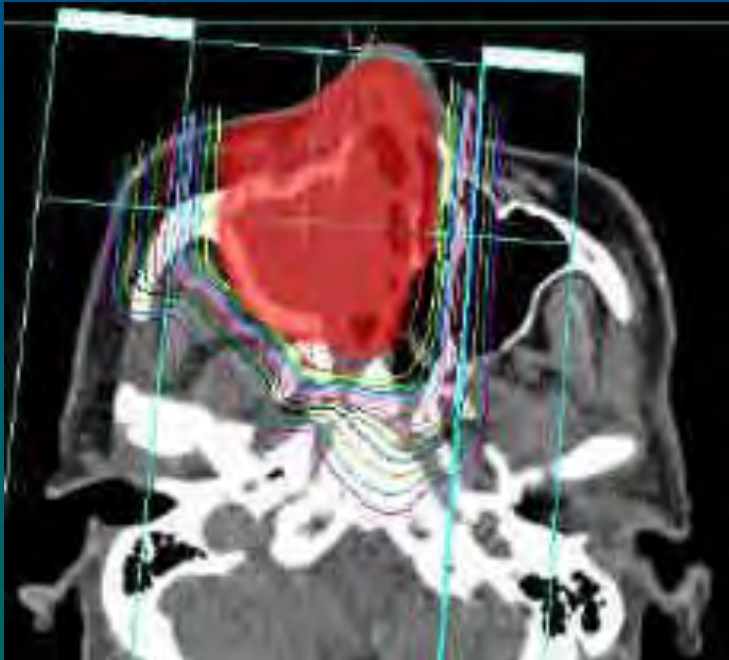
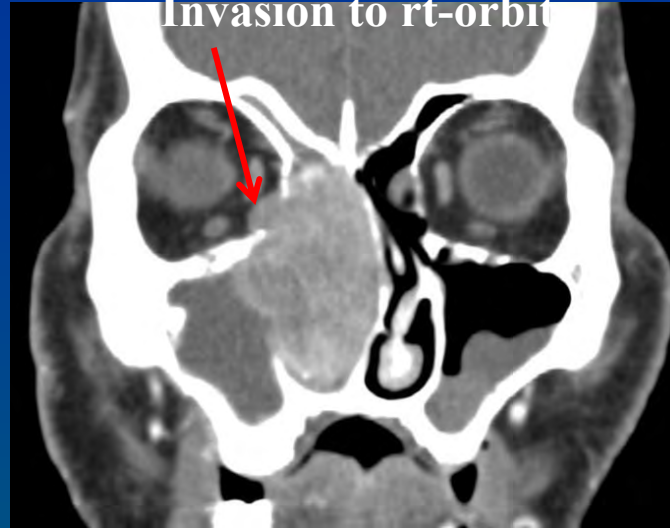


# Rt-nasal cavity basaloid squamous cell cancer 57yo male

Before therapy



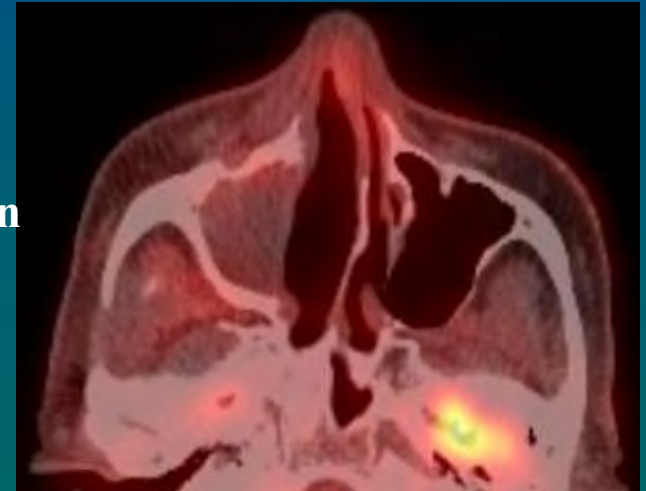
Invasion to rt-orbit



Treatment plan  
2.0Gy(RBC) x 35Frs

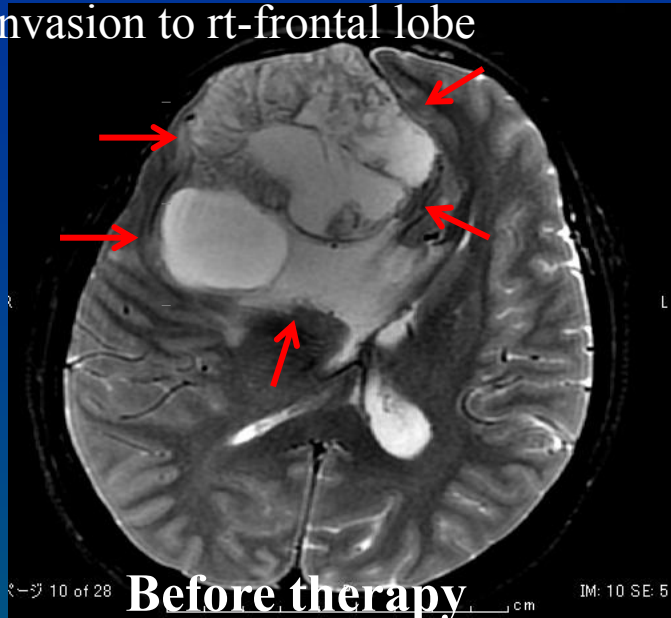
Almost no irradiation  
to lt-eyeball and  
brain stem

One year after therapy



# Nasal cavity adenoid cystic adenocarcinoma 63yo female

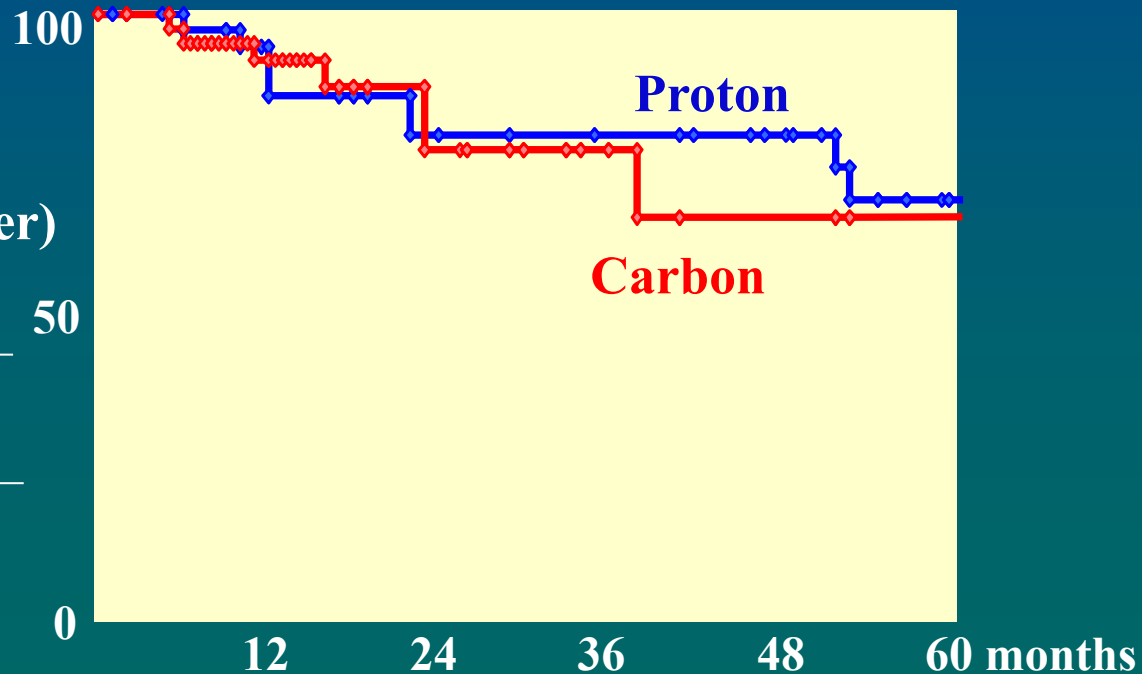
Invasion to rt-frontal lobe



Proton beam  
77.0Gy(RBE)  
2.2Gy(RBE)  
x35Frs

Local control rate of adenoid cystic cancer of head & neck (Hyogo Ion Beam Medical Center)

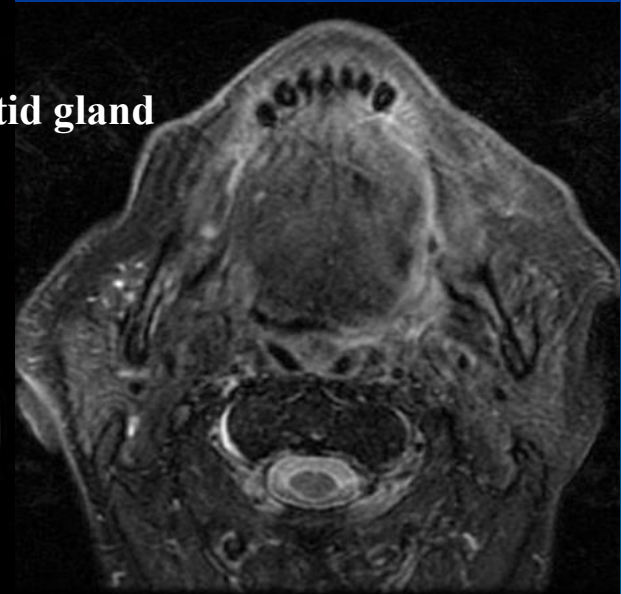
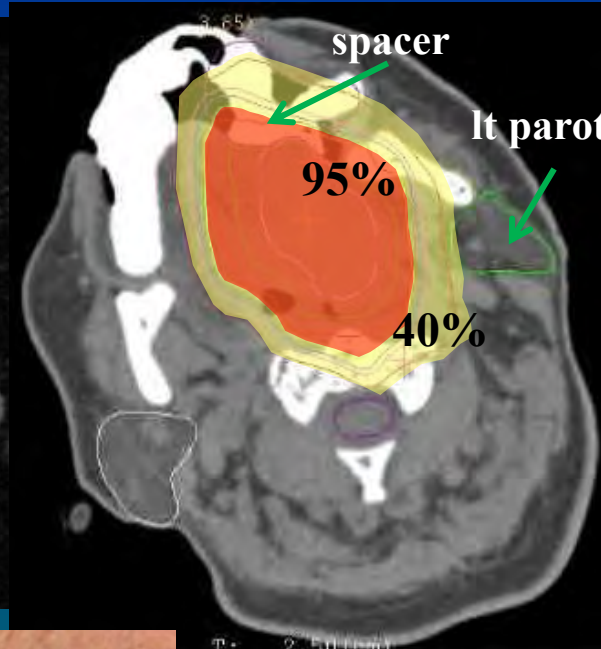
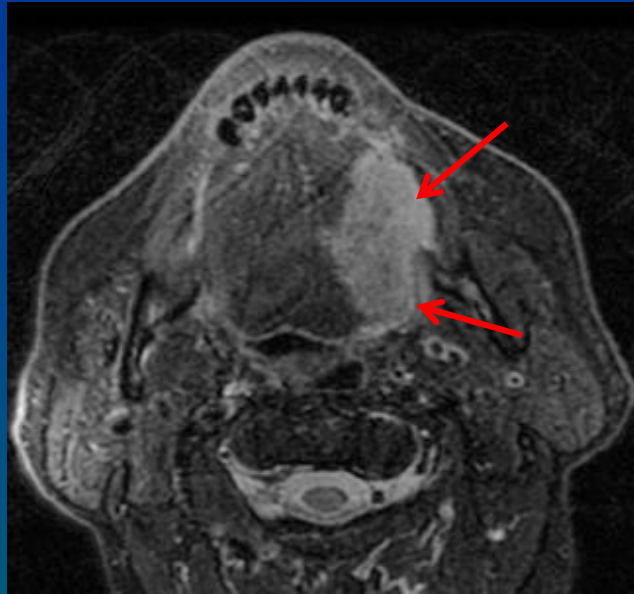
	3 y	5 y
Proton beam	80.1%	69.5%
Carbon beam	77.7%	66.6%
	(N.S.)	



# Tongue cancer 87yo male

Before therapy

Treatment plan 65Gy(RBE)/26fr after therapy

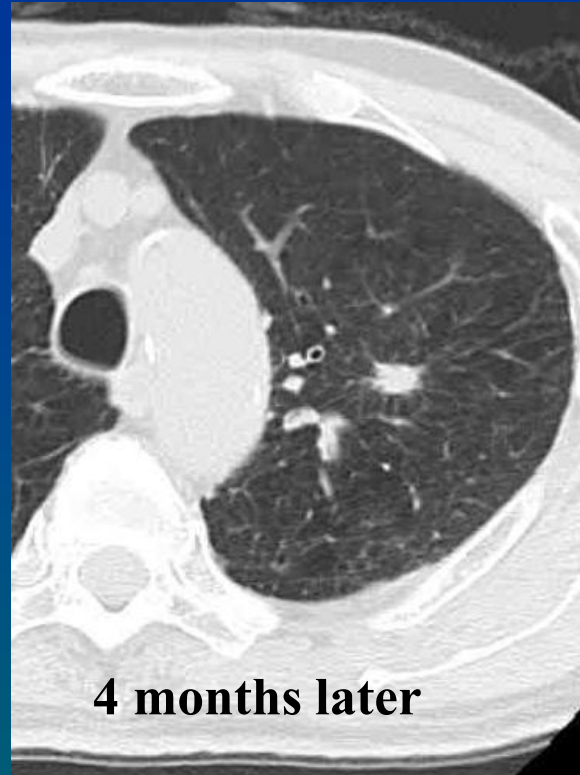


Spacer  
made of dental putty containing silicon

Acute disorders:  
mucositis (oral cavity) Gr2  
dermatitis Gr1-2, taste disorder  
1month after therapy: mucositis and  
taste disorder almost improved  
good salivary excretion



# Lt-lung cancer 84yo male 66.0Gy(RBE)/10 Frs



NSCLC Stage I	cases(IA/IB)	local control	survival rate	late side effect
NCC East	37 (17/20)	80% (2y)	84% <sup>3)</sup>	lung damage 3
Tsukuba Univ	55 (30/28) <sup>1)</sup>	97% (2y)	89% <sup>4)</sup>	pneumonitis 2
Shizuoka CC	24 (6/16/2) <sup>2)</sup>	90% (2y)	66% <sup>4)</sup>	chest wall pain 1
Hyogo IBMC	80 (42/38)	82% (3y)	86% <sup>5)</sup>	lung dysfunction 1

1) Number of lesions ; 58      2) rec after surgery ; 2

3) overall survival rate 4) progression-free survival rate 5) cause-specific survival rate

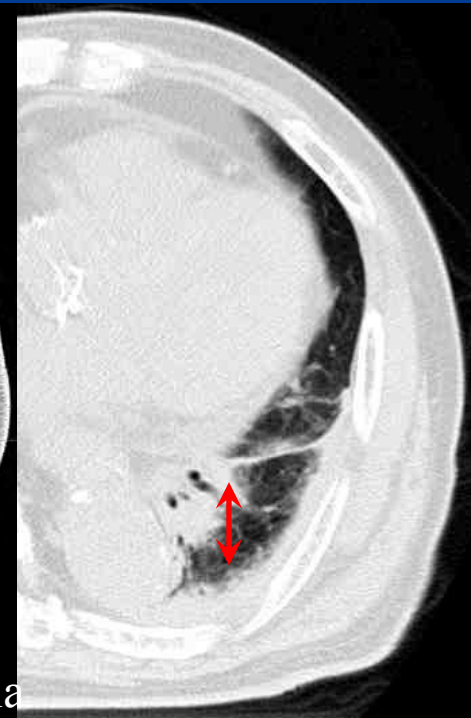
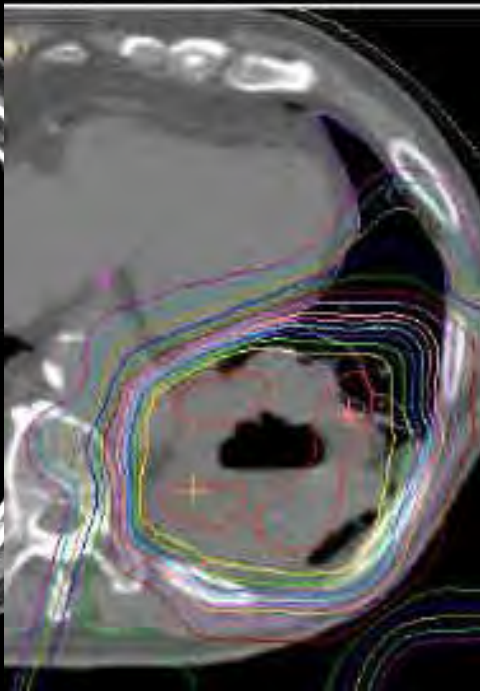
# Lt-lung cancer 81yo male

Emphysema, respiratory function ↓

76 GyE/20 Frs

3months

18months



Rt-lung field : almost no radiation

Spinal cord : less than 10%

Heart : radiation dose ↓↓

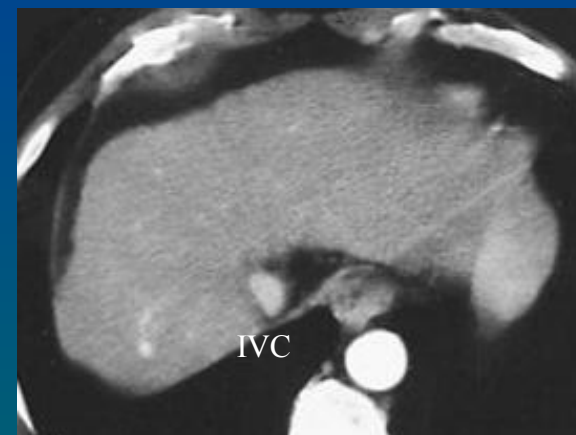
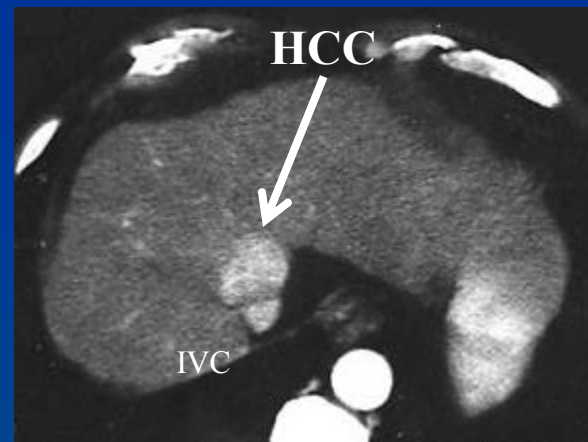
# Hepatocellular Carcinoma (HCC)

**HCC 3 year survival rate**  
**operation\*      Proton therapy\*\***

<b>Number</b>	<b>1</b>	<b>64%</b>	<b>65% (35 cases)</b>
	<b>2</b>	<b>53%</b>	<b>36% (10 cases)</b>
	<b>&gt;3</b>	<b>37%</b>	<b>38% ( 8 cases)</b>
<b>Size</b>	<b>&lt;2cm</b>	<b>73%</b>	<b>75% ( 8 cases)</b>
	<b>2-5cm</b>	<b>64%</b>	<b>51% (39 cases)</b>
	<b>5-10cm</b>	<b>45%</b>	<b>50% ( 6 cases)</b>

\*Japan Liver Tumor Study Group

\*\*Tsukuba Univ.



## Particle beam treatment results for HCC

	<b>materials</b>	<b>methods</b>	<b>no</b>	<b>survival rate</b>	<b>local control rate</b>
<b>Tsukuba</b>	St I-III	P 50-88/10-20	162	24% <sup>1)</sup>	87% <sup>1)</sup>
<b>Hyogo</b>	<13cm	P 76/20, 60/10	104	52% <sup>1)</sup>	87% <sup>1)</sup>
<b>NIRS</b>	St II-IVA	C 49.5-79.5/15	82	26% <sup>1)</sup>	87% <sup>1)</sup>
<b>NCC East</b>	<10cm	P 76/20	30	66% <sup>2)</sup>	96% <sup>2)</sup>

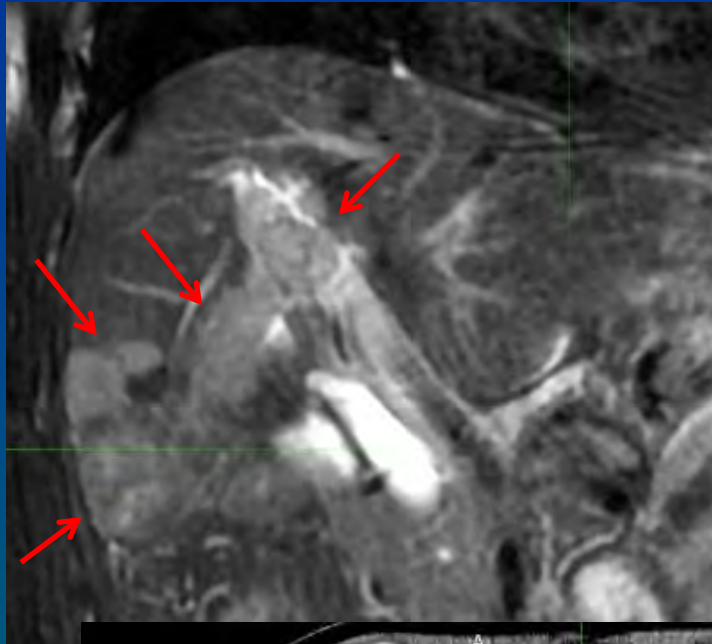
1) 5years

2) 2years

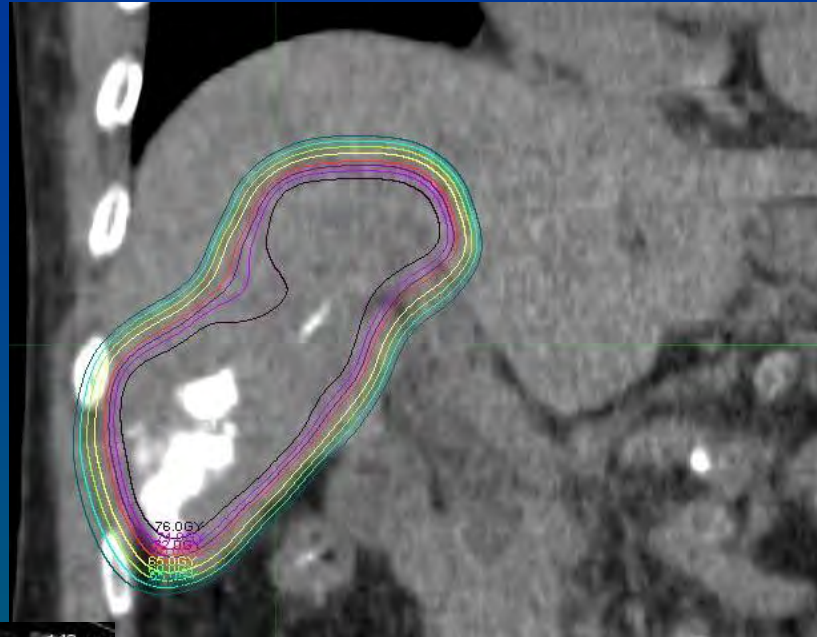


# HCC with portal vein tumor thrombus 71 yo male

MRI before therapy



treatment plan 80.5Gy(RBE)/23Fr



Local control rate 91% (2years)  
Survival rate 48% (2years)  
(Tsukuba Univ)

**CT at 7 months after therapy**

Liver rt-lobe atrophy, lt-lobe enlargement

## Prostate cancer chemically disease-free survival rate

Pre PSA	Prostatectomy (Johns Hopkins)	Proton therapy (LLMU)	Proton therapy (Hyogo)*	Carbon (NIRS)
≤ 4.0	90 % (284)	95 % (100)	100 % ( 9)	100 % ( 3)
4.1 – 10.0	70 % (237)	86 % (595)	99 % (140)	88 % ( 49)
10.1 – 20.0	56 % (105)	67 % (322)	90 % ( 71)	85 % ( 56)
>20.0	45 % ( 40)	56 % (121)	79 % ( 71)	79 % ( 93)

\*3年

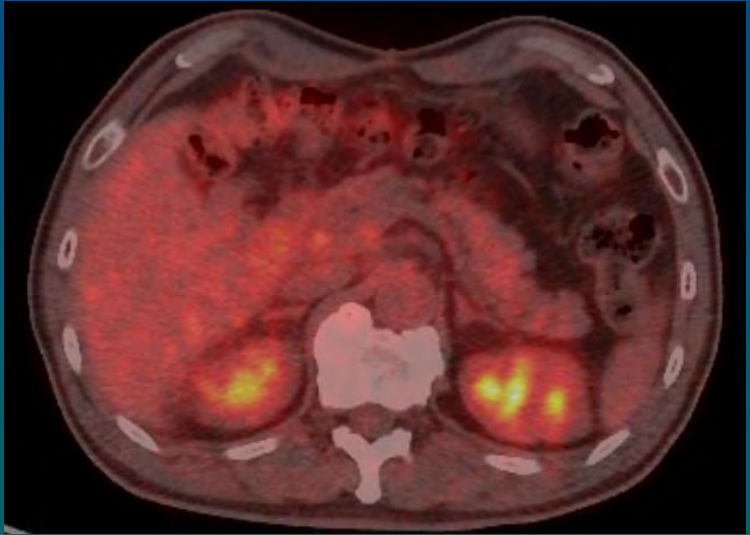
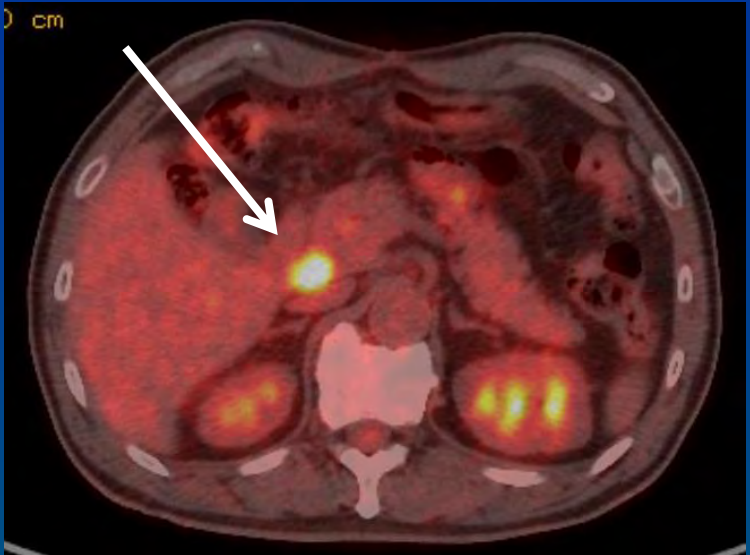
## Late adverse events

	Gy(GyE)	no.	Grade 2 or higher	
			GI	GU
IMRT	81-86.4	772	2.0%	10.0%
Proton	74/37	291	4.0%	4.0%
		1138	3.5%	5.4% (0.3%)
Carbon	66/20	182	1.1%	3.8%

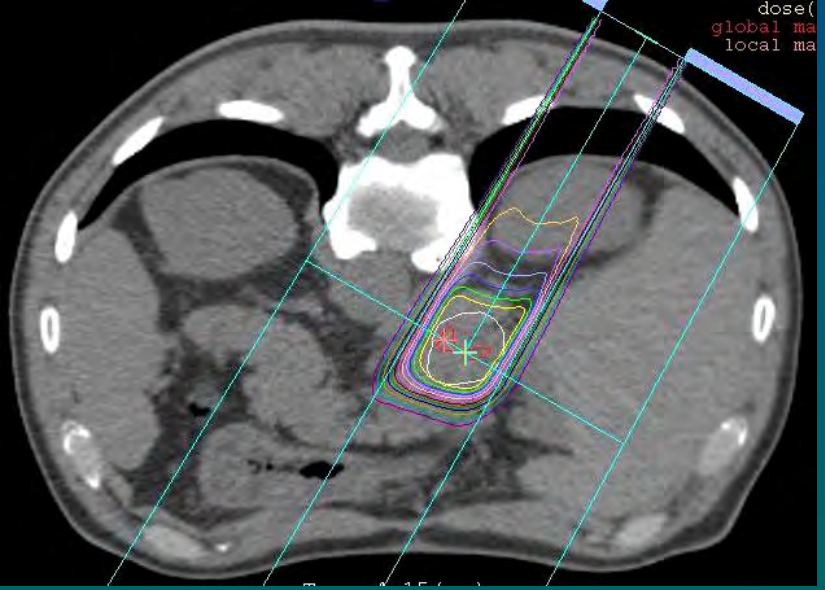
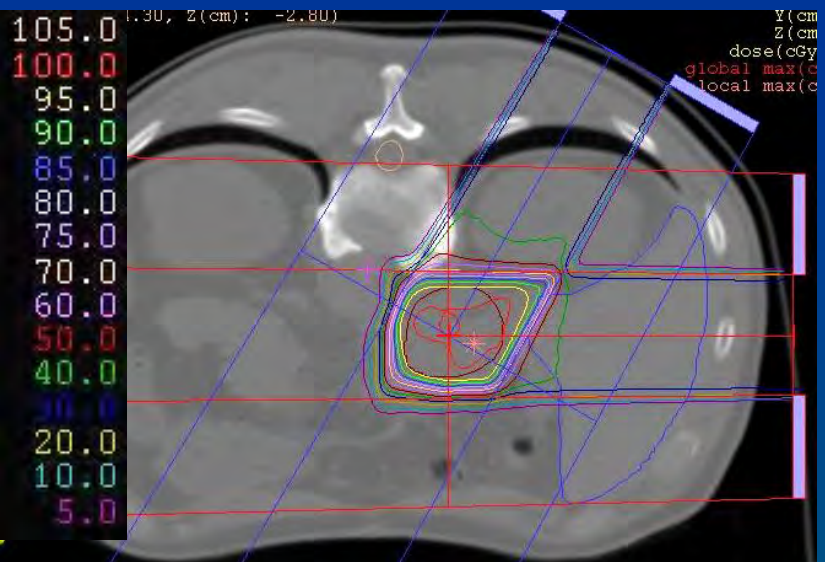
IMRT; Memorial Sloan Kettering Hospital  
 Proton; Hyogo PTC, LLMU      Carbon; NIRS



# Bile duct ca recurrence at pancreas head after surgery 65yo male



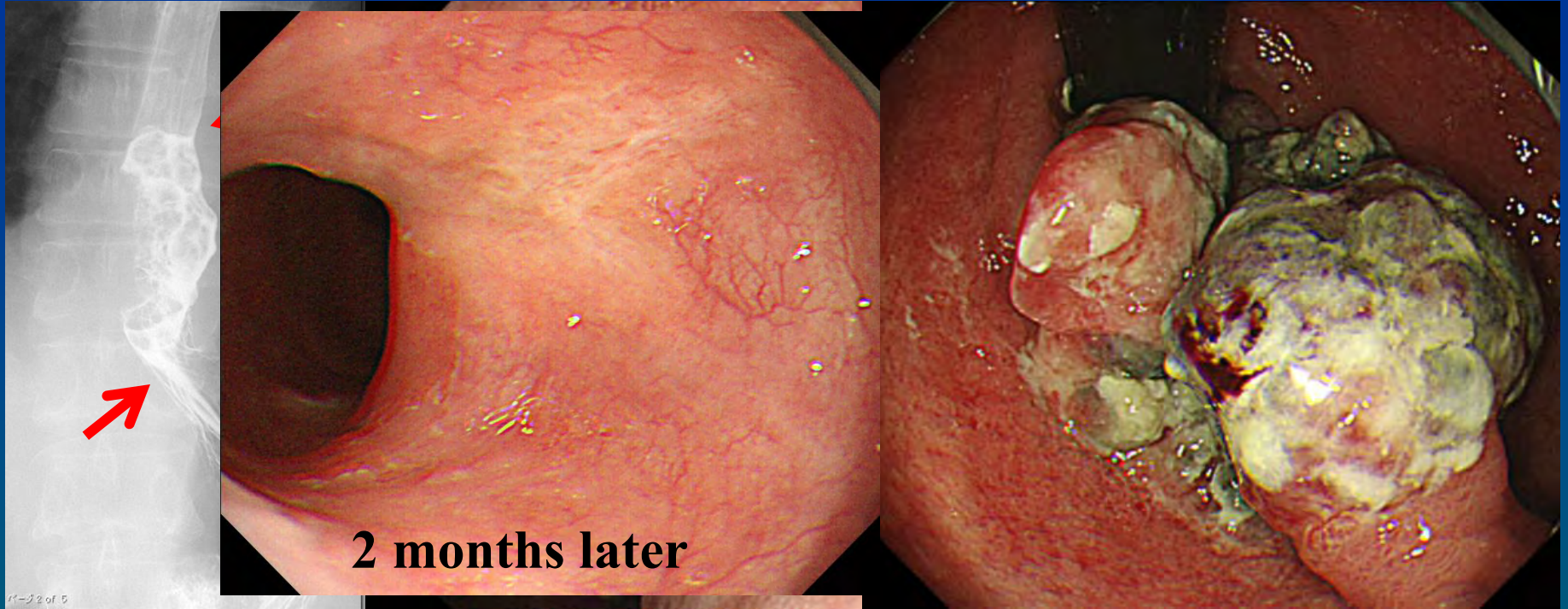
13 months later : No abnormal uptake



66Gy(RBE)/33Frs



# Esophagus ca (T3N1M0; Stage III) 57yo male



## Chemoradiation (X-ray + Proton) Therapy

endoscopy



Chemotherapy

CDDP 70mg/m<sup>2</sup>, day1  
5-FU 700mg/m<sup>2</sup>, day1-4

X-ray

2.0 Gy x 20 回

Proton



endoscopy



CDDP  
5-FU

2.0 Gy x 10-13 回

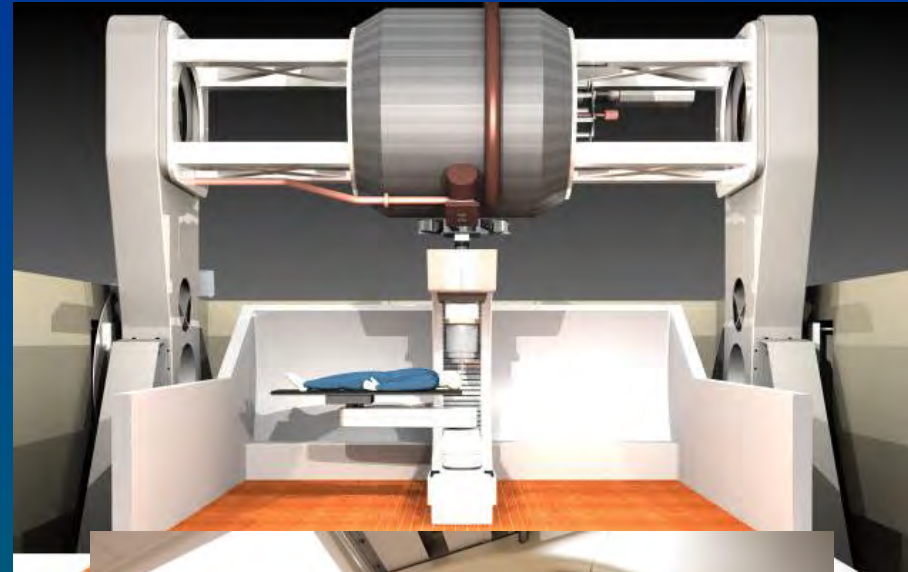
# Proton Therapy System

→ **more compact**  
**lower cost**

Sumitomo Heavy Industries, Ltd.  
short length gantry



**Mevion S250** (Mevion Medical Systems)  
Cyclotron with 10T super-conducting magnet  
( $\Phi 1.8\text{m}$ ) is directly mounted onto the gantry.



# Characteristics of Proton Therapy

**SOBP(Spread-out Bragg peak) of charged particle beam**

**concentrate irradiation to the cancer lesion → therapeutic effect ↑**

**less irradiation to the surround normal tissue → side effects ↓**

**→ low-invasive cancer therapy    gentle for the elderly**

**Biological effect      effective to cancers which are resistant with X-ray  
treatment such as malignant melanoma and so on.**

**Retaining shape and function    QOL (Quality of Life)**

**Time for one irradiation    20~30 minutes      Cancer therapy in outpatient**

**Local therapy method    Therapeutic effect is limited in the radiation area.  
← combination with chemotherapy**

**Accelerator, Proton beam irradiation system → highly expensive**

**Experienced radiation oncologists, Medical Physicists, Radiation technicians  
→ Human resources**