Innovative cancer treatment with carbon ion beams

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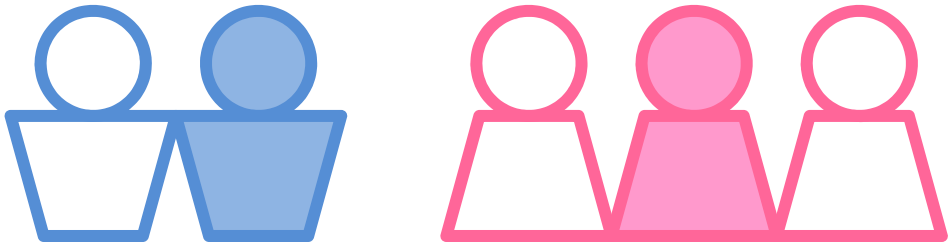
群馬大学
GUNMA UNIVERSITY

GHMC
Gunma university heavy ion medical center

Japanese trend in cancer statistics

- Cancer has been the leading cause of death since 1981, accounting for 30% of all deaths recently.
- Half of male and one third of female are affected with a cancer.



Major cancer treatment

1. Surgery
2. Radiotherapy (RT)
3. Chemotherapy

Country	RT use (%)
Japan	30%
UK	56%
Germany	60%
US	66%

Major cancer treatment

1. Surgery
2. Radiotherapy (RT)
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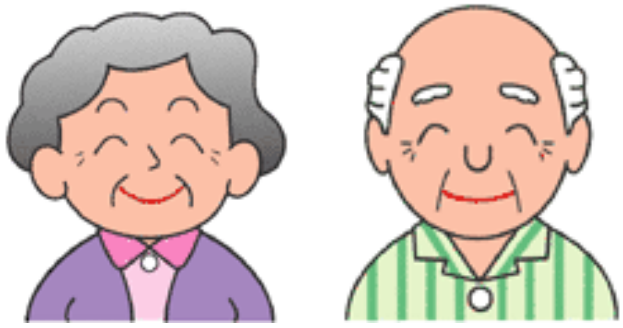
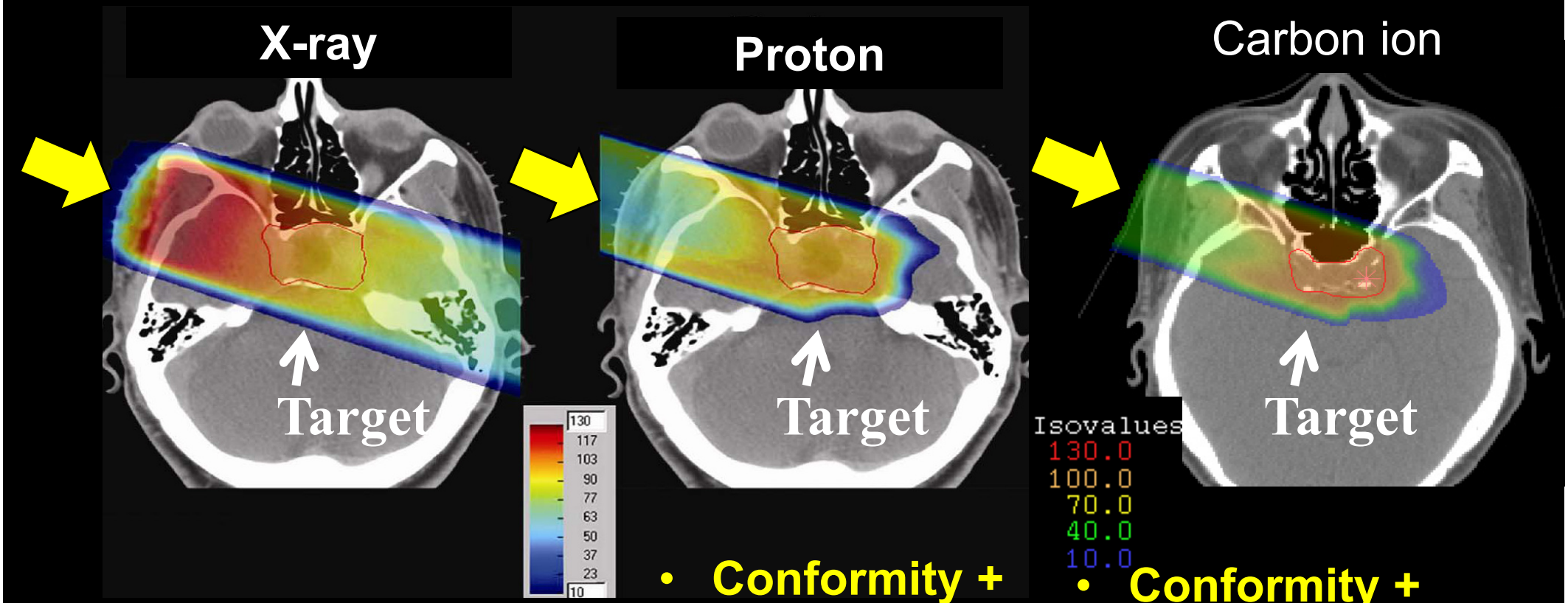
Conventional RT
- X-ray, gamma-ray,
- electron beam

Particle beam RT
- Proton
- **Carbon ion**



X-ray, Proton, and Carbon ion



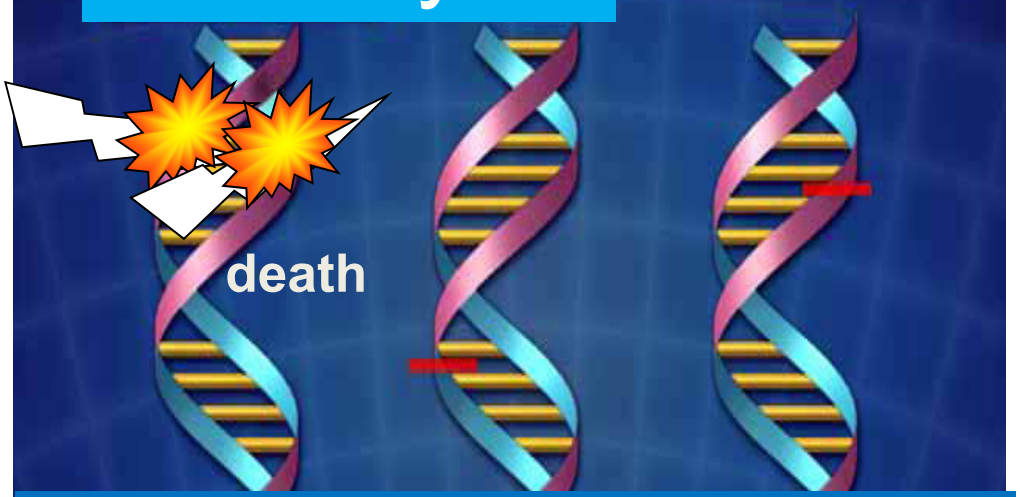
- Conformity +

- Conformity +
- Biological effectiveness +
- Short course +

Little repair possibility with carbon ions

Single-strand break

X-ray



Radiation therapy works by damaging the DNA of cancer cells. X-rays commonly cause single-strand DNA break, and double-strand DNA breaks by 2 hits is essential for cancer cell death. However, cells have mechanisms for repairing single-strand DNA damage, some of them may survive even after treatment.

Double-strand break

Carbon ion

Carbon ions commonly cause double-strand DNA breaks by 1 hit, which results in the most significant event for cancer cell death.

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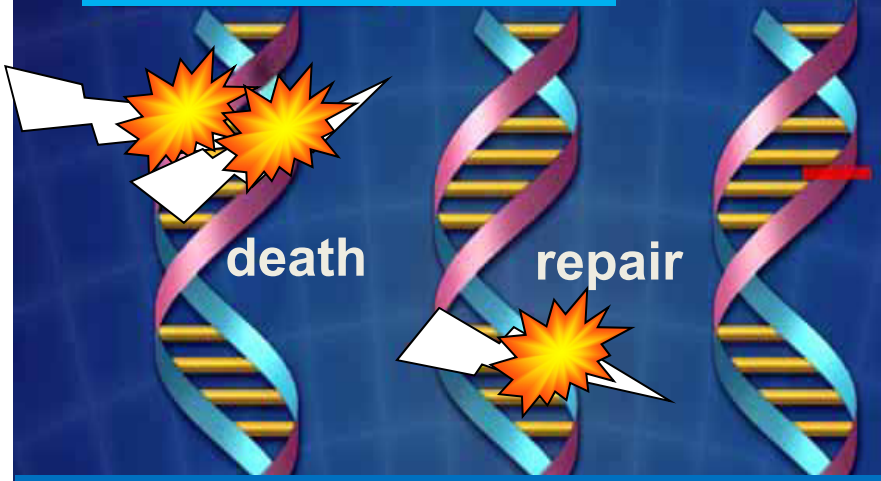
X-ray



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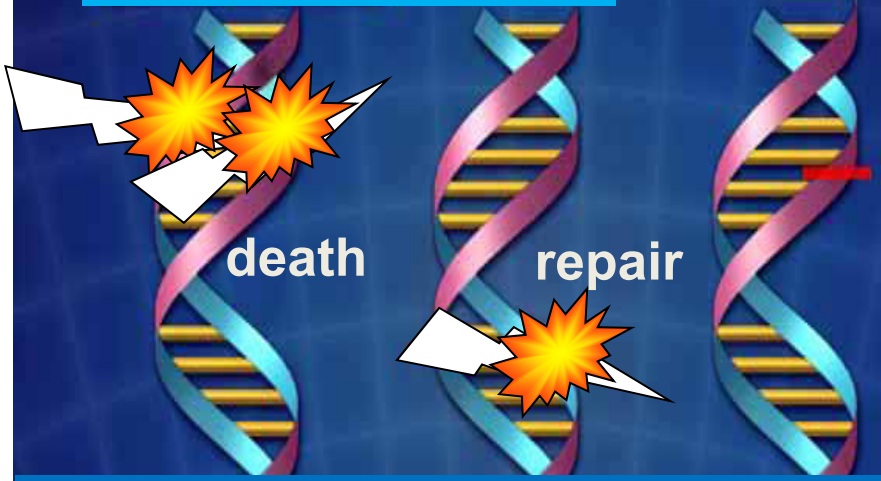

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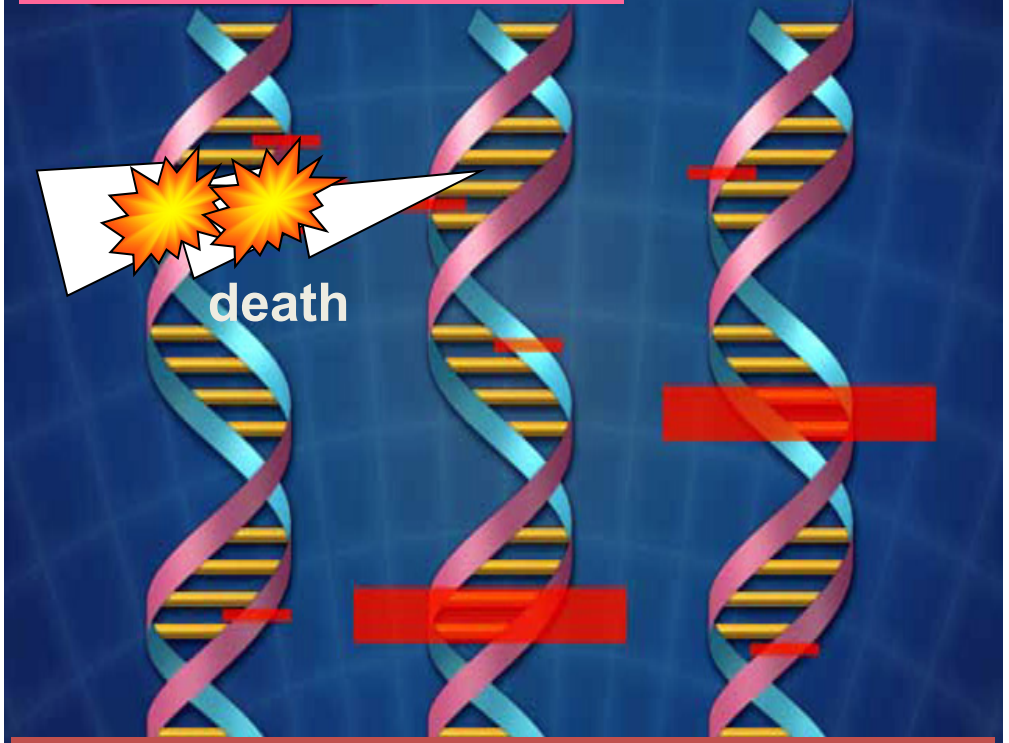

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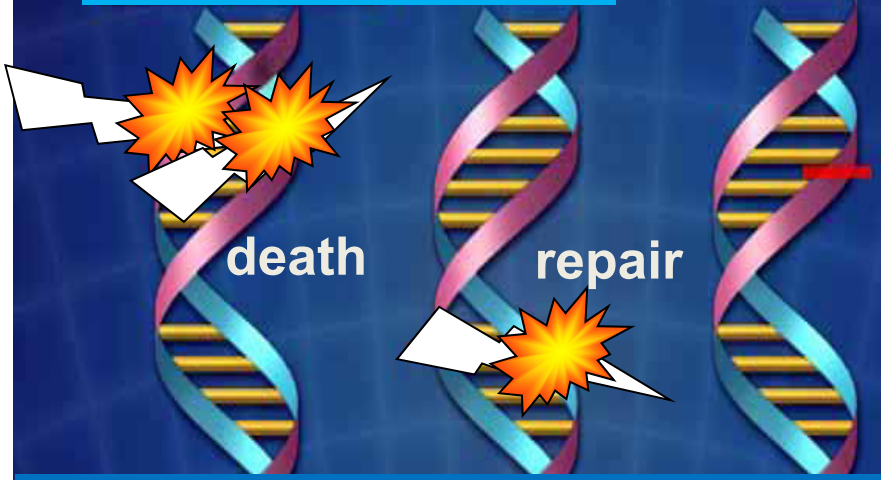

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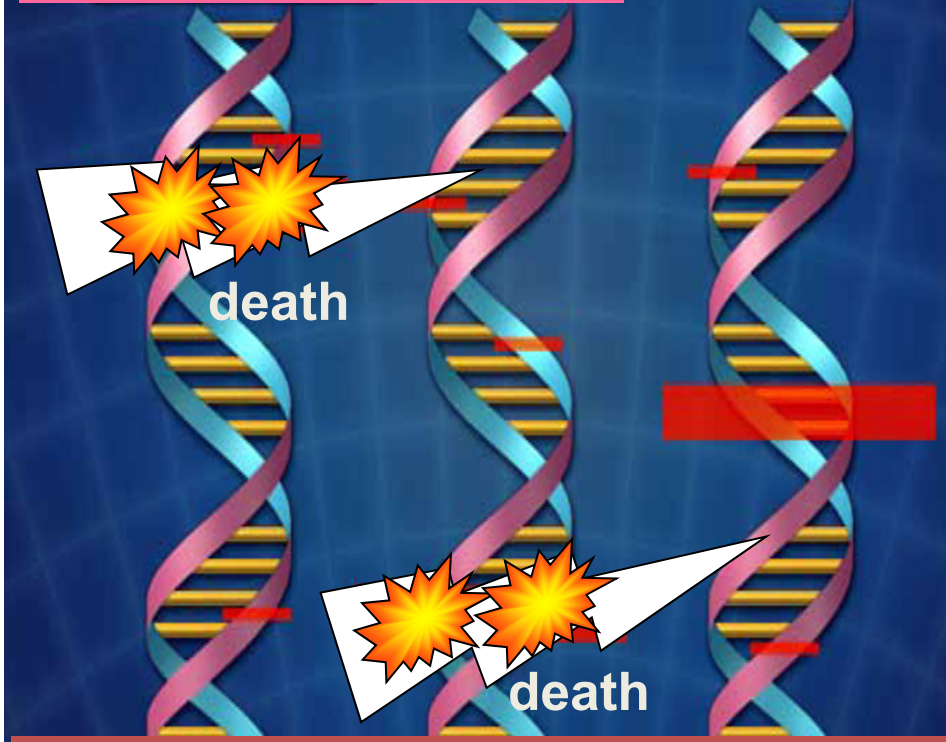

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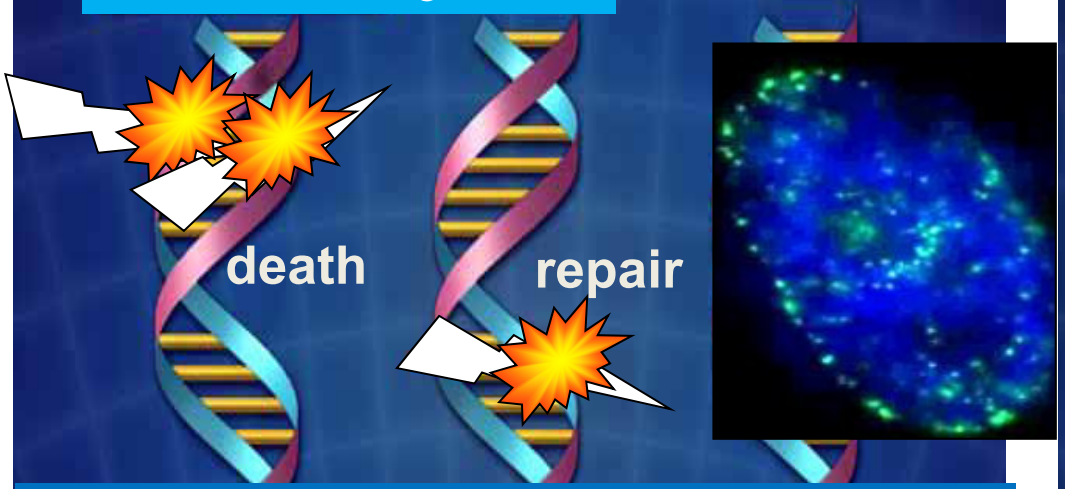

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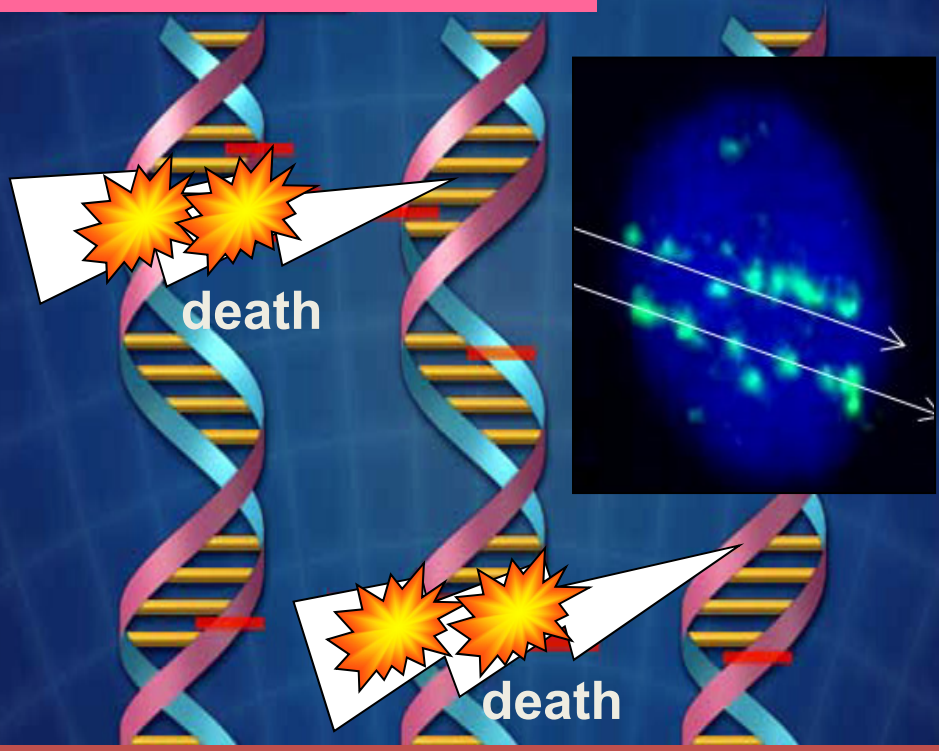

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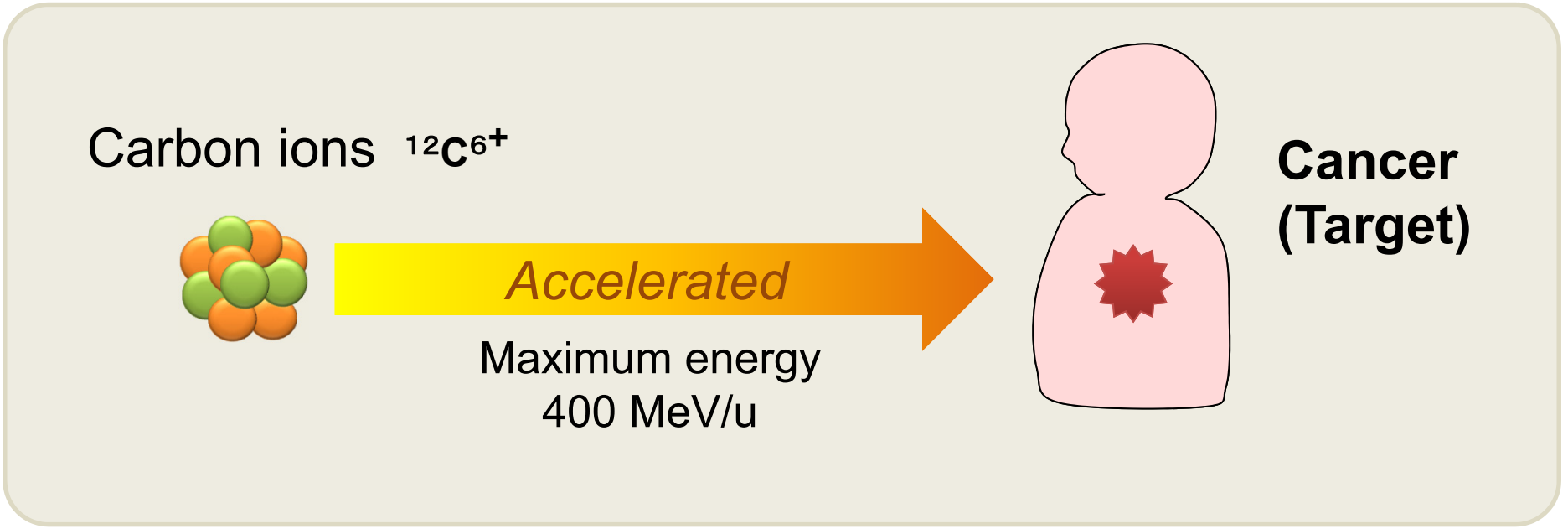
What is carbon ion radiotherapy?



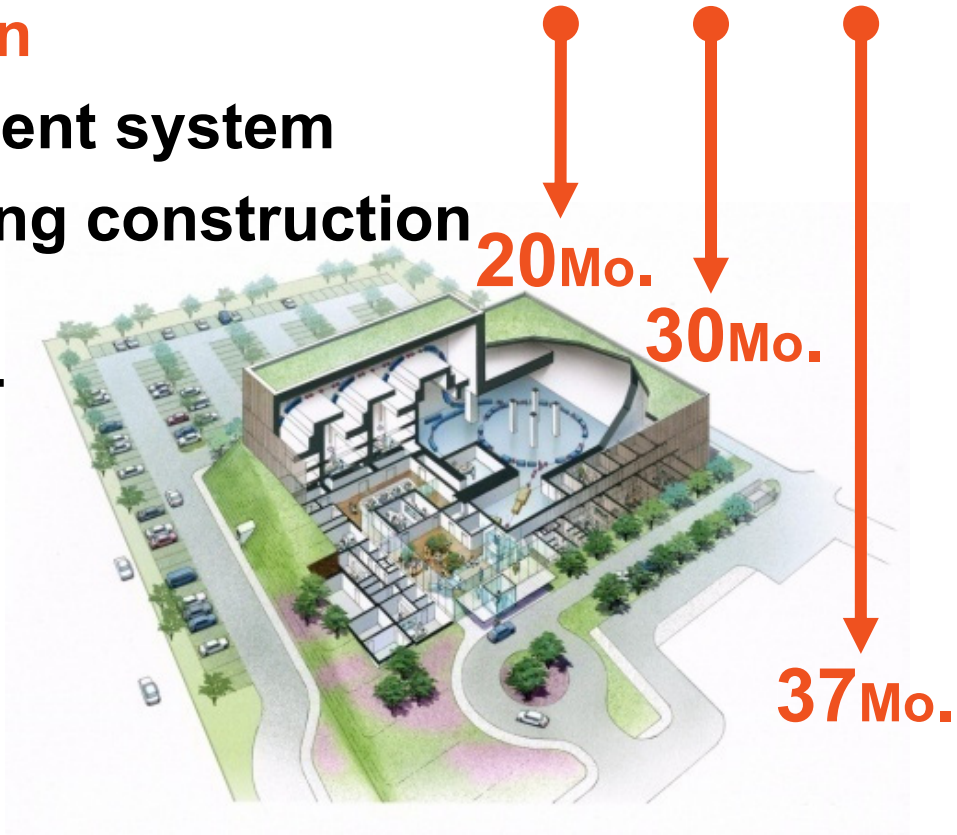
Carbon ion beams are accurately directed to the target by accelerating ions up to 70% of the light speed.
Innovative cancer treatment integrating accelerator engineering, medical engineering, biology, and oncology.

Gunma University Heavy Ion Medical Center (GHMC) since in 2010

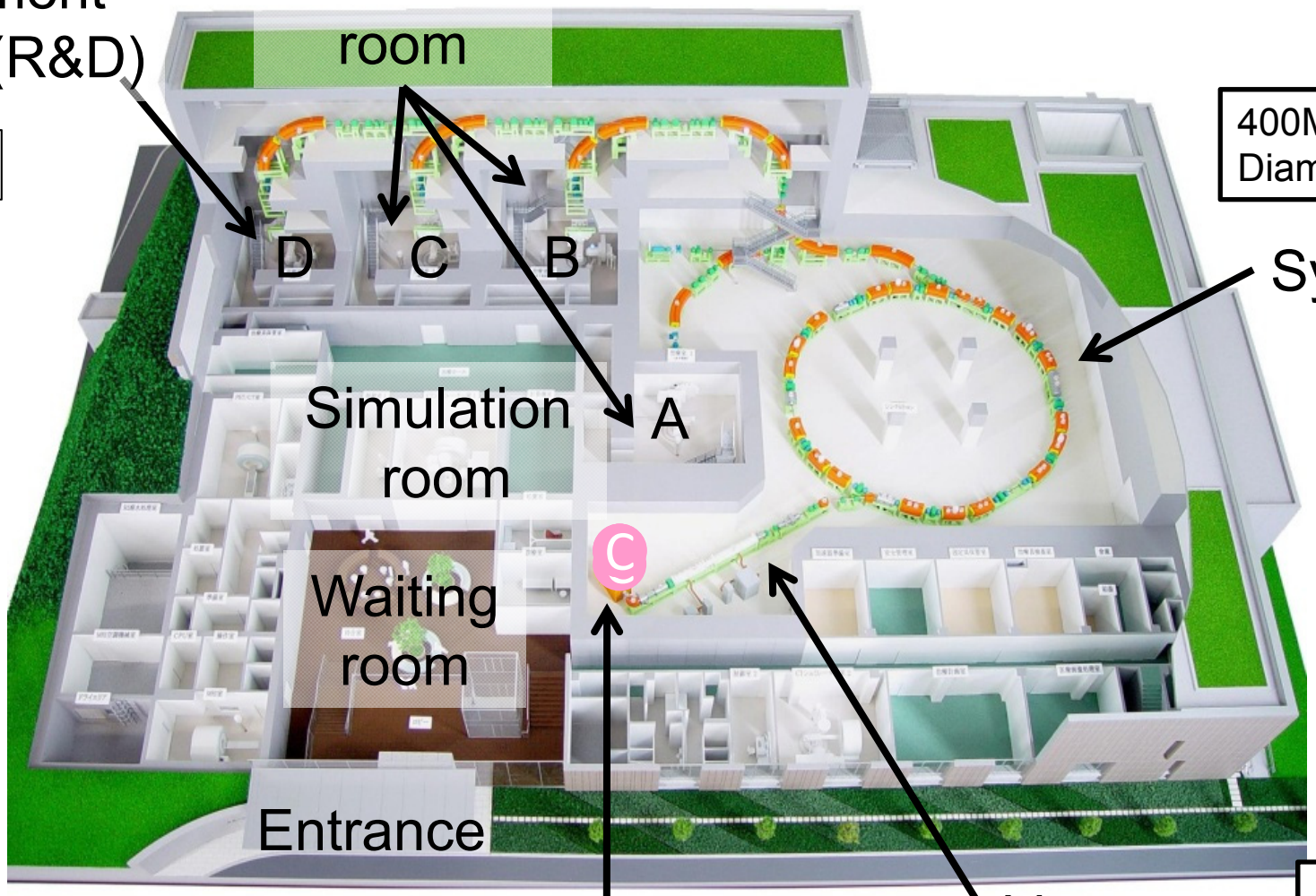
First carbon ion radiotherapy facility in University Hospital in Japan
Supported by Japanese government and local government
Expected number of patients: >600 per year in 3 rooms

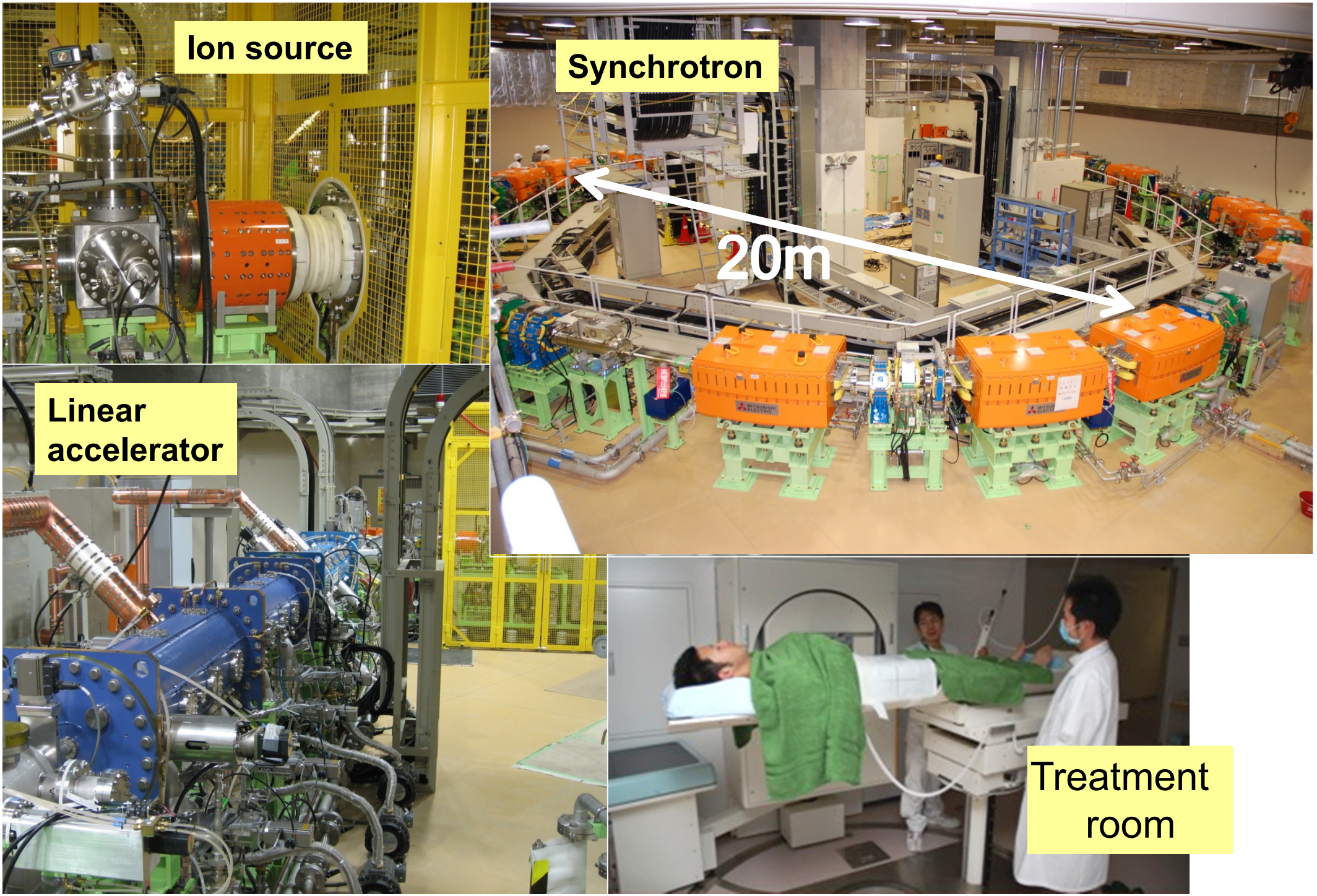
Time-line

2001		**Prof. Nakano came to Gunma Univ. from NIRS.**
2004		*Collaborations with NIRS*
		Design and R&D studies of a facility by NIRS
2006	Apr.	**Facility design at Gunma Univ.**
2007	Feb.	**Building construction**
2008	Aug.	**Installation of treatment system**
2008	Oct.	**Completion of building construction**
2009	Aug.	**Beam test**
2009	Oct.	**Verification by MEXT**
2009	Nov.	**Acceptance**
2010	Jan.	**Commissioning**
2010	Mar.	**First treatment**
2015	May	**Total > 1600 patients**



Equipment

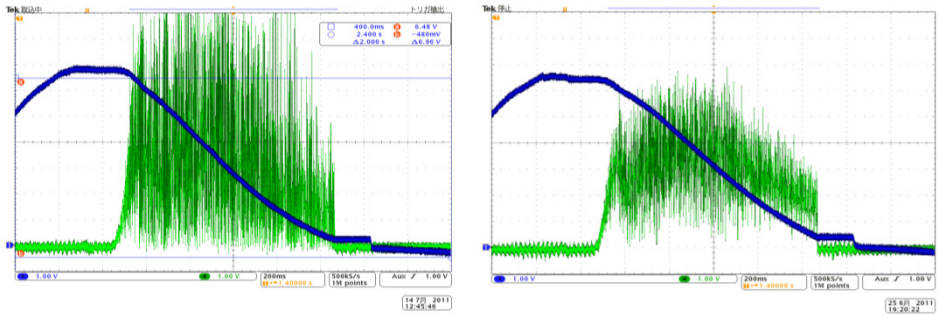

Treatment room (R&D)
scanning
Treatment room
D
C
B
A
Simulation room
Waiting room
Entrance
400MeV/u Synchrotron
Diameter: 20 m
Synchrotron
accelerated up to 70% of light speed
Ion source
Permanent Magnet
Linear accelerator
0.6MeV RFQ
4MeV APF IH-DTL


Ion source
Synchrotron
20m
Linear accelerator
Treatment room

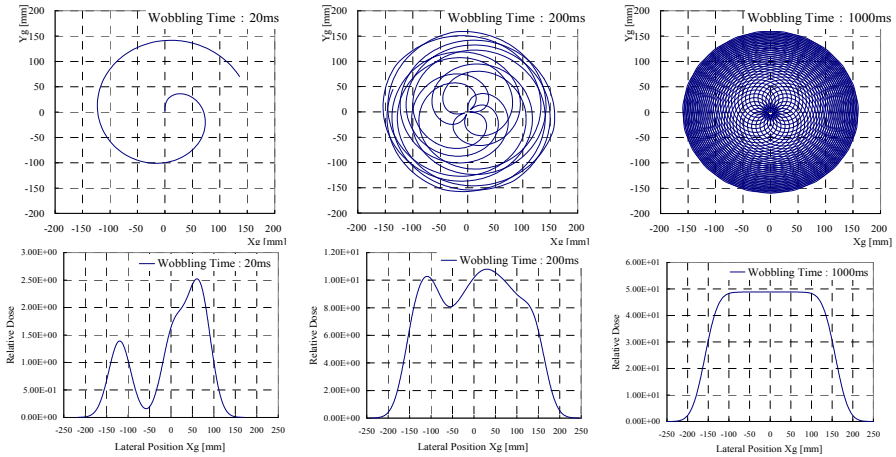
Commissioning

2009.8.19	Injector First Beam
2009.8.26	Synchrotron First Beam
2009.11	Acceptance Test
2010.3.16	First Treatment Irradiation 380MeV Room B
2010.9	Room A in use
2011.4	400MeV/u in use
2011.5	Room C in use
2011.8	Spiral Wobbling in use
2013.1	Layer Stacking in use
2014.6	Mice Experiment (Room D) In use

Spill ripple reduction by changing synchrotron frequency (400Hz→280Hz)
To avoid the ripple of bending magnet PS

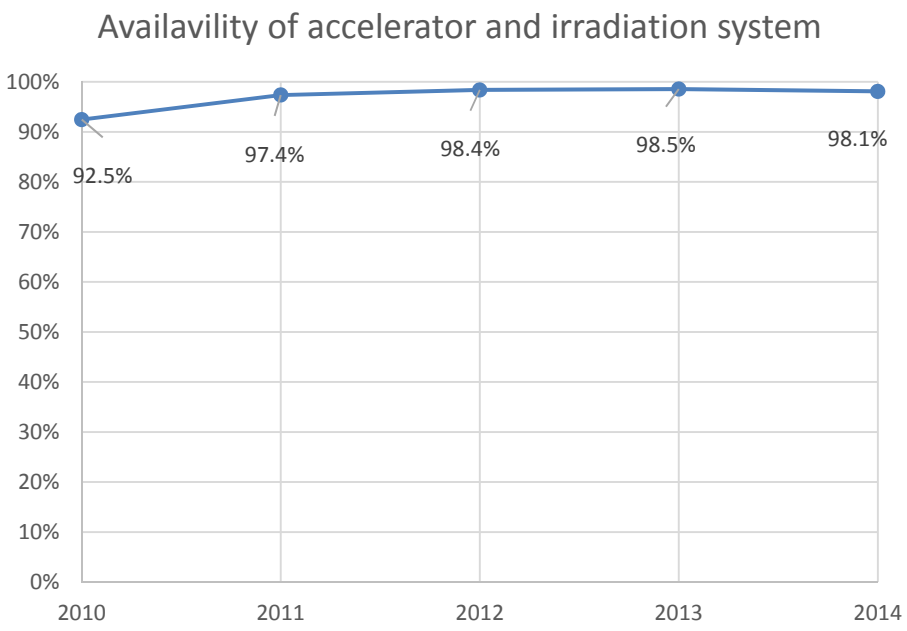


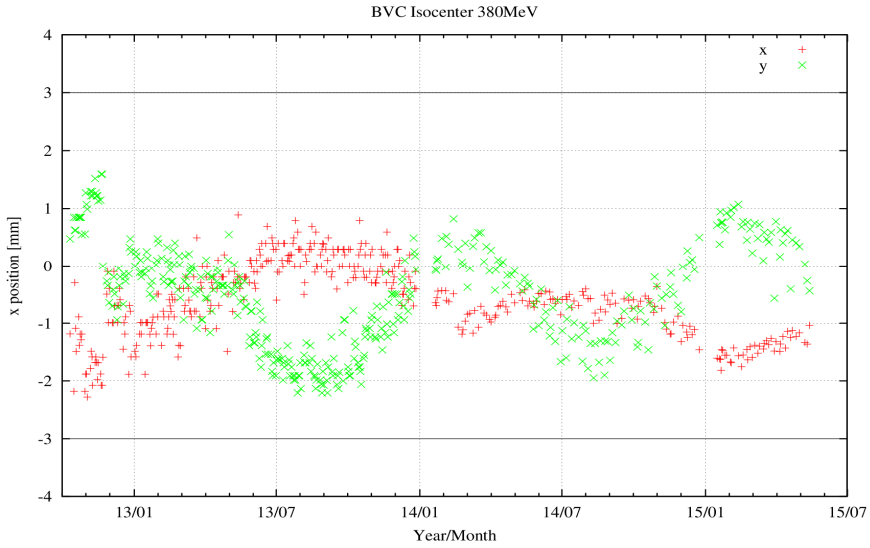
→ Improved dose uniformity of spiral wobbling

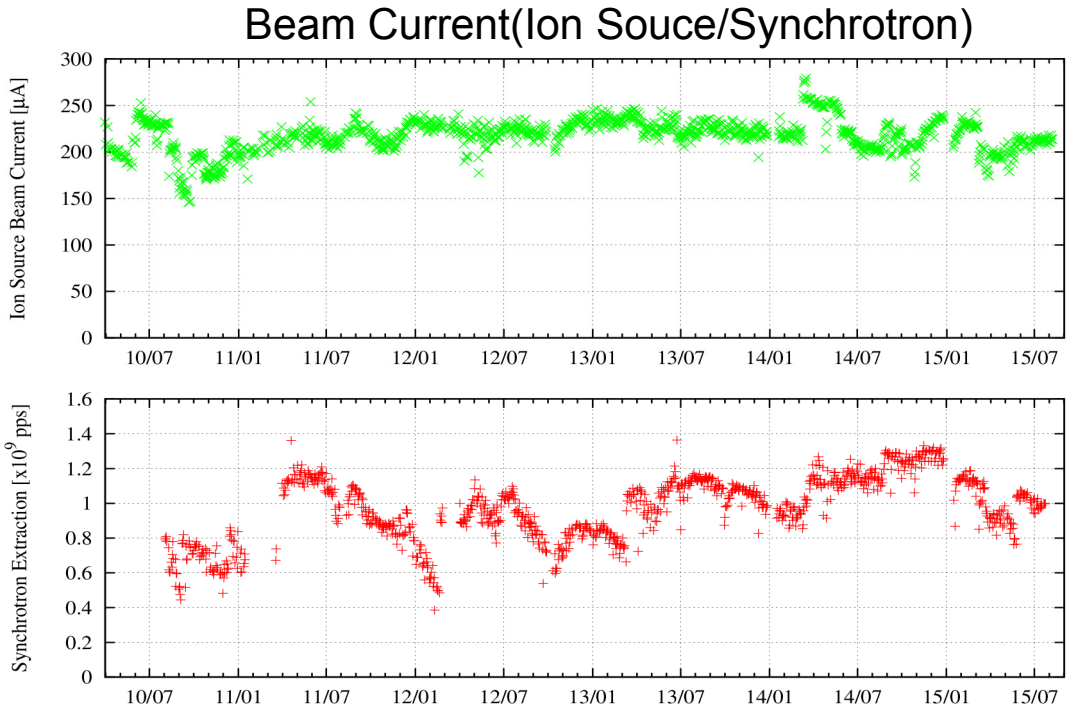


Operation Stability

- No severe breakdown (longer than 1 day) occurred after 2012.
- Ion source, linac, and synchrotron are conditioned to keep the extracted beam current more than $1x10^9$ particles per second (pps) = 5 Gy(RBE)/min

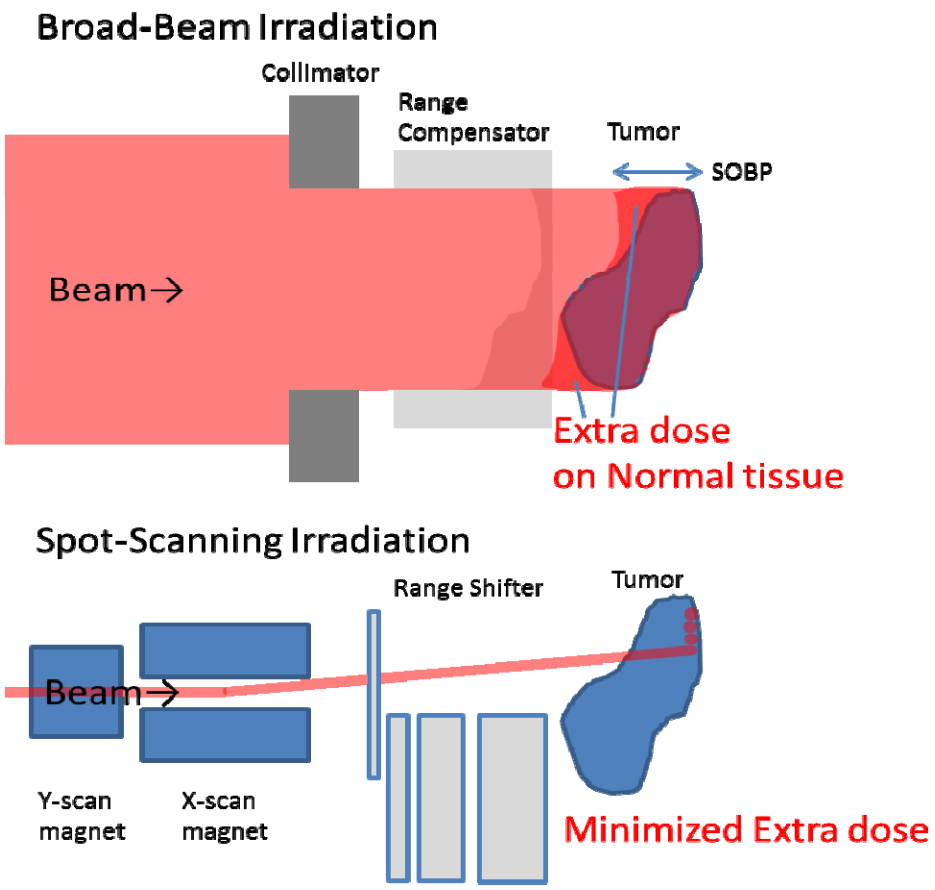




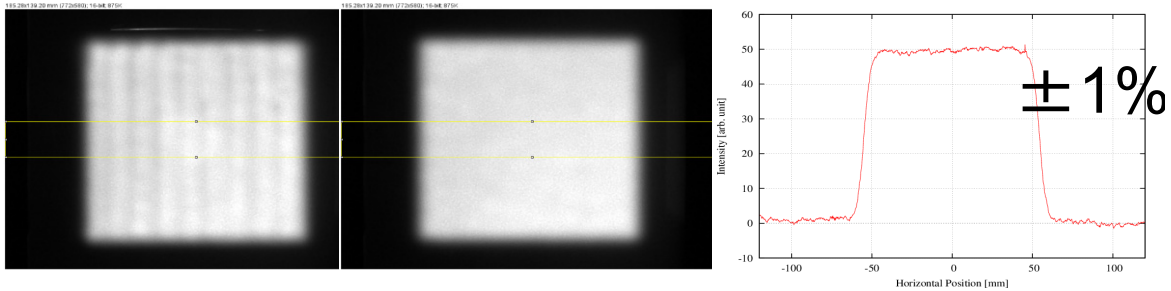


Further Development

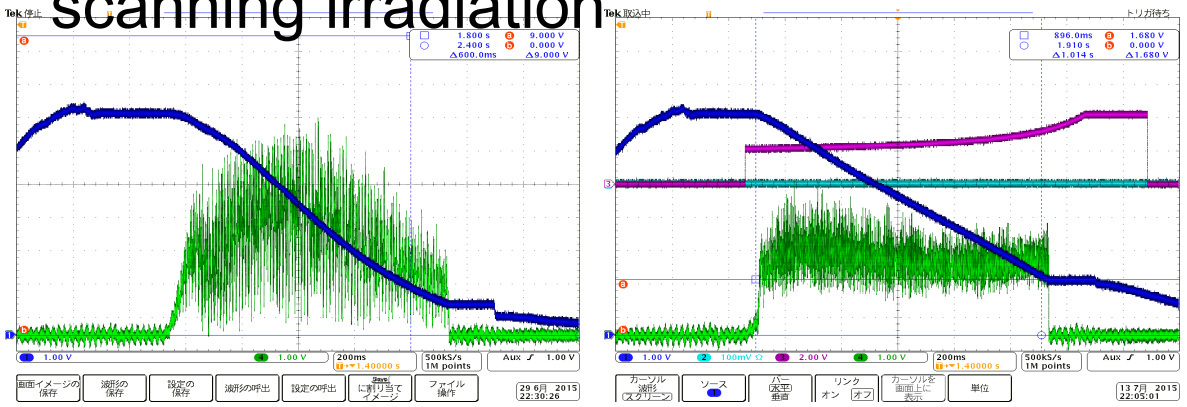
- Development of scanning irradiation



Better uniformity by an improvement of dose monitor and dose control system

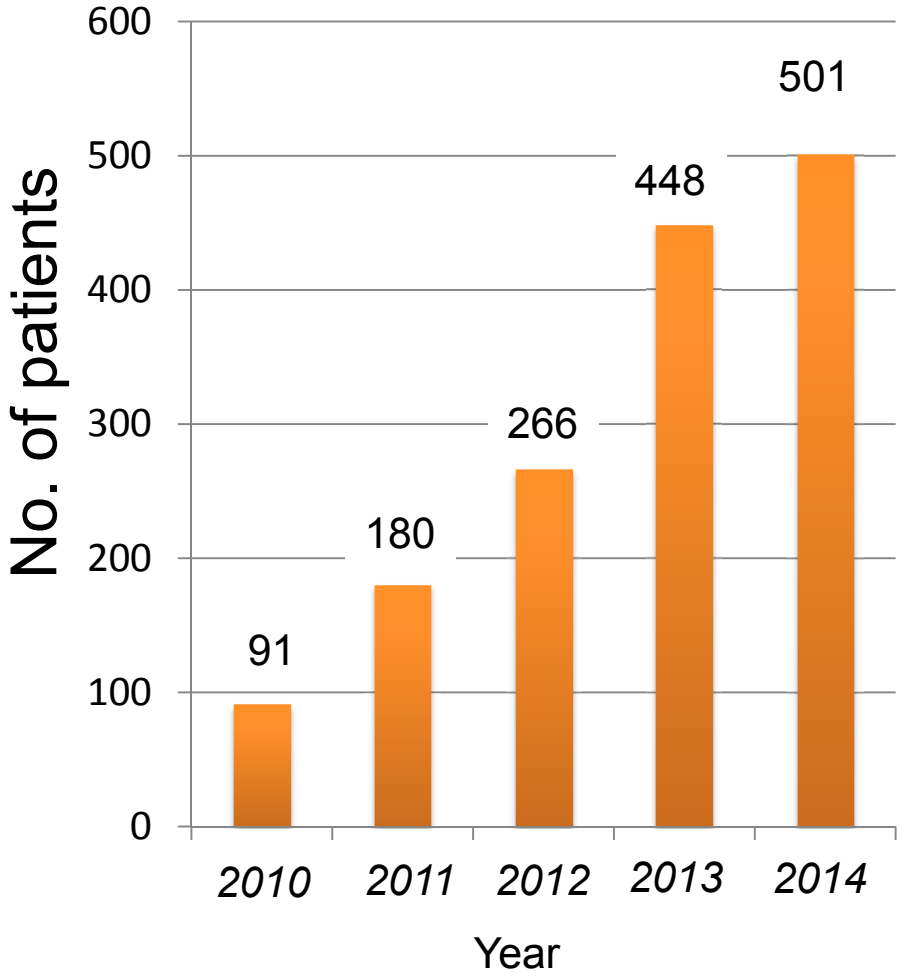


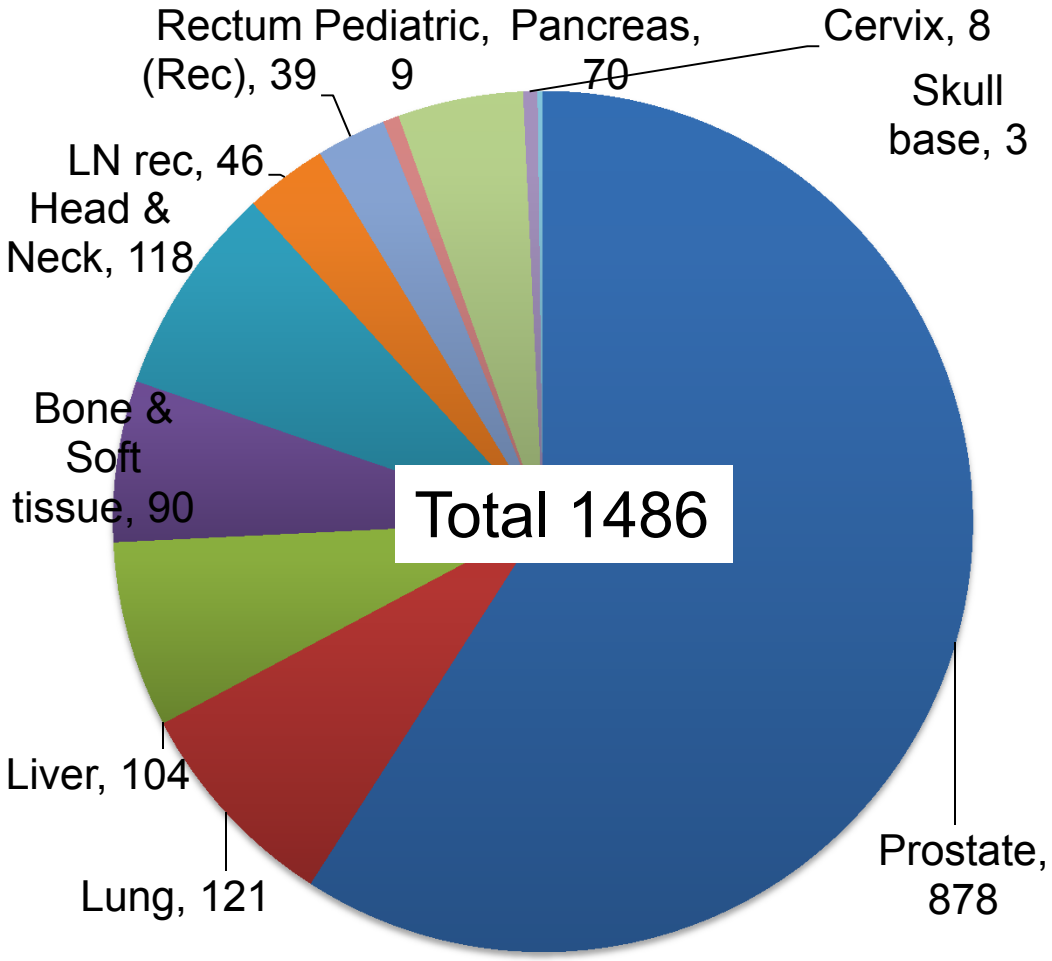
Spill ripple improvement for scanning irradiation



Number and site at Gunma University

(2010 Mar. - 2014 Dec.)





Immobilization with mold and shell

① Fresh mold

② Water injection

③ Lie down

④ Drying

① Warm shell

② Cooling

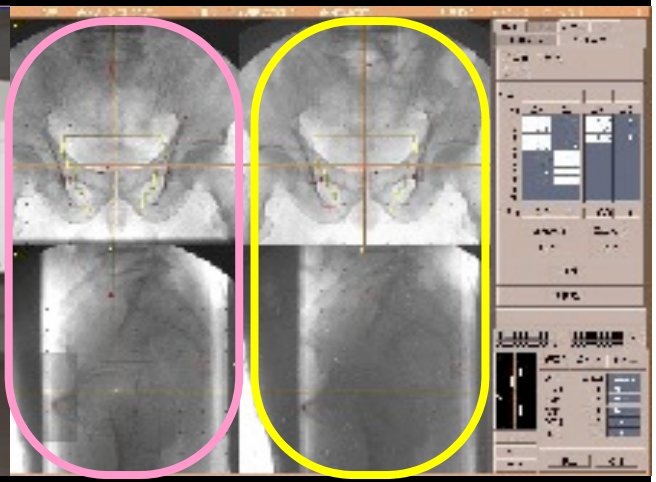
③ Fixed

④ Completed

Prostate cancer: 20 minutes for 1 session

Set up

Image guidance

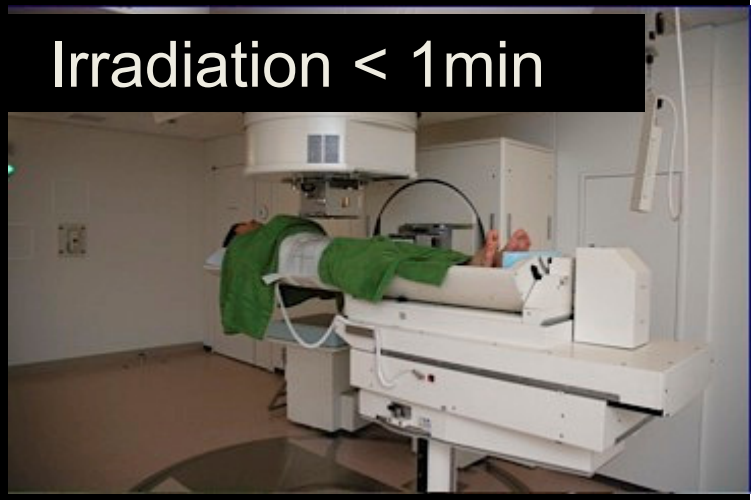


Reference image

Daily Image

Compensator

Irradiation < 1min



Clinical advantage of carbon ion radiotherapy

An advantage for Carbon-ion RT over proton therapy or X-ray RT, suggesting higher biological effects of Carbon-ions, has been demonstrated in:

Head & Neck: non-squamous cell carcinoma (Adenocarcinoma, Adenoid cyctic carcinoma, Malignant melanoma)

Skull base, Para-spinal regions, and Pelvis: Chordoma, Chondrosarcoma, sarcomas

Lung: non small cell lung cancer (Larger than 3cm)

Liver: hepatocellar carcinoma (Larger than 3cm)

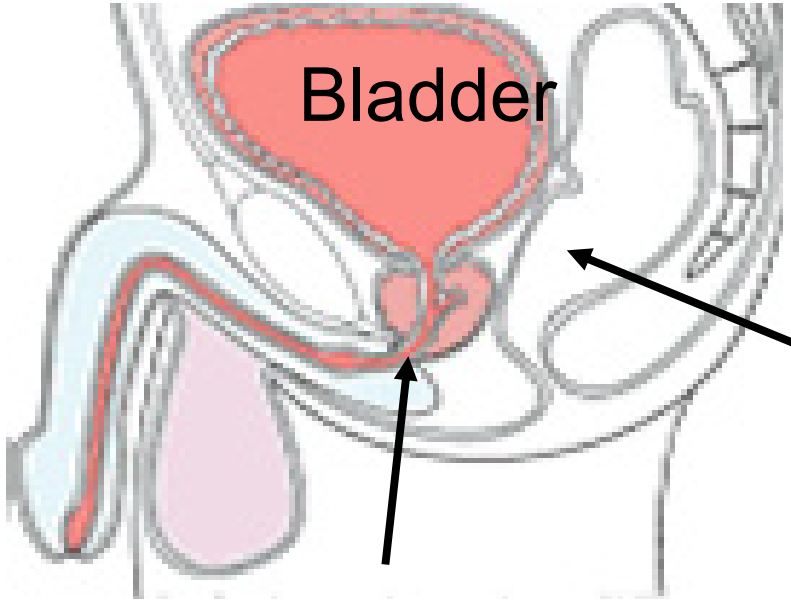
Prostate: intermediate and high risk groups

Locally recurrent rectal cancer after surgery:

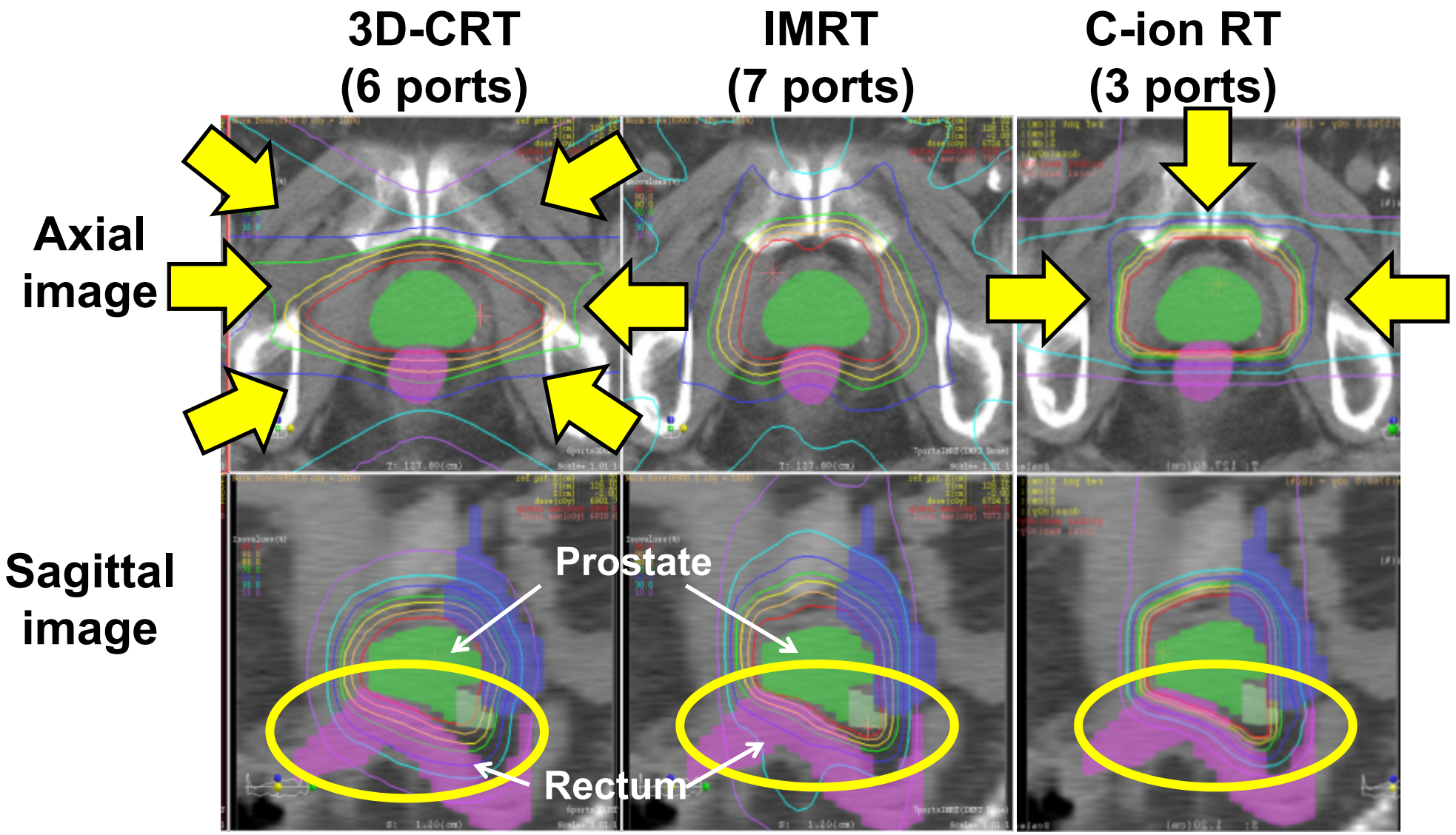
Pancreas: locally advanced unresectable cases

… *In general, bulky and X-ray resistant tumors (mostly inoperable)*

Prostate cancers



Dose distribution of prostate cancer



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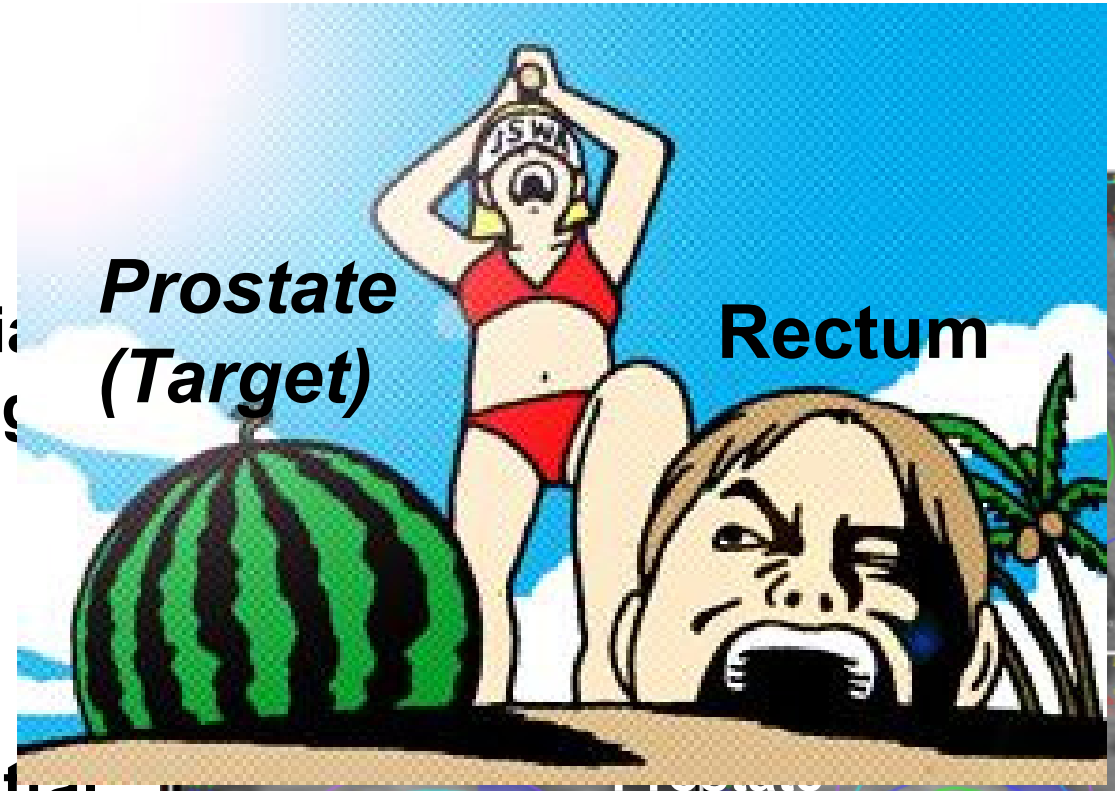
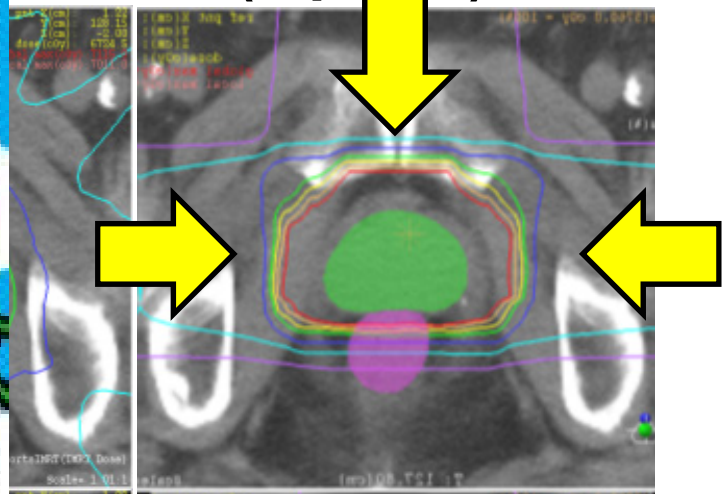
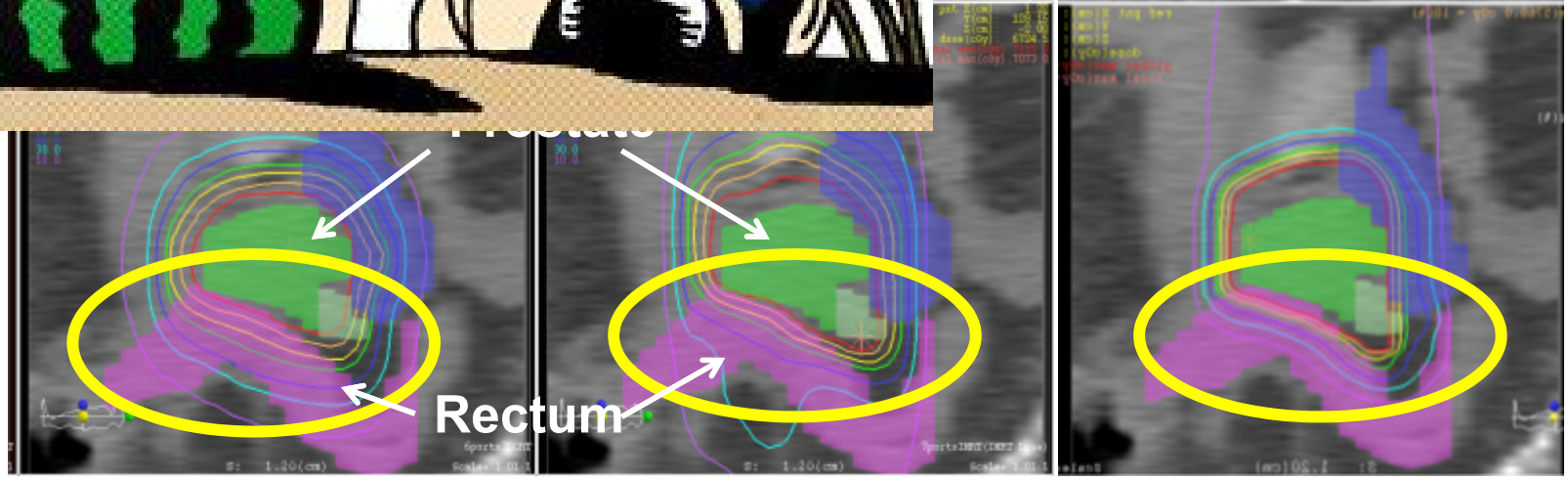


Axia
imag

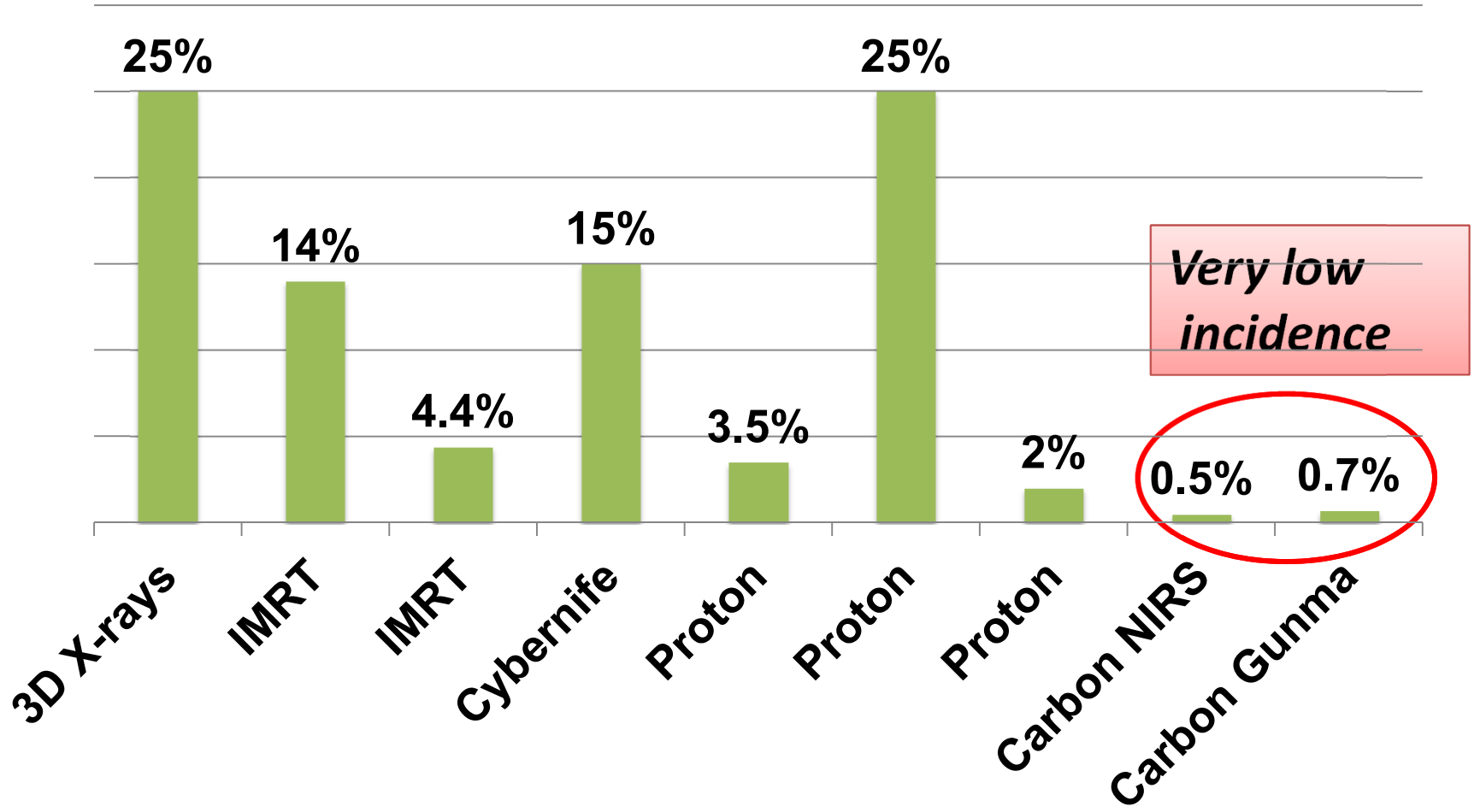
C-ion RT
(3 ports)



Sagittal
image

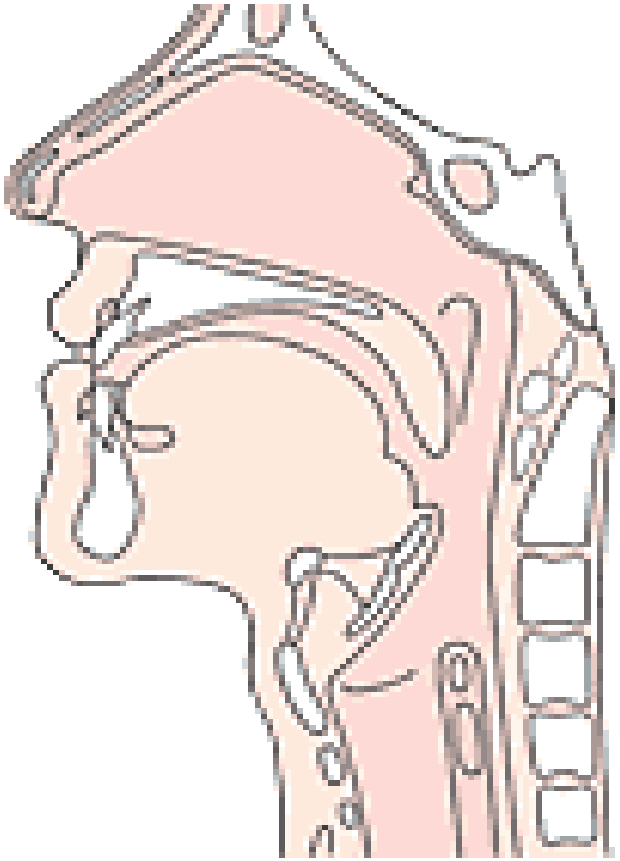


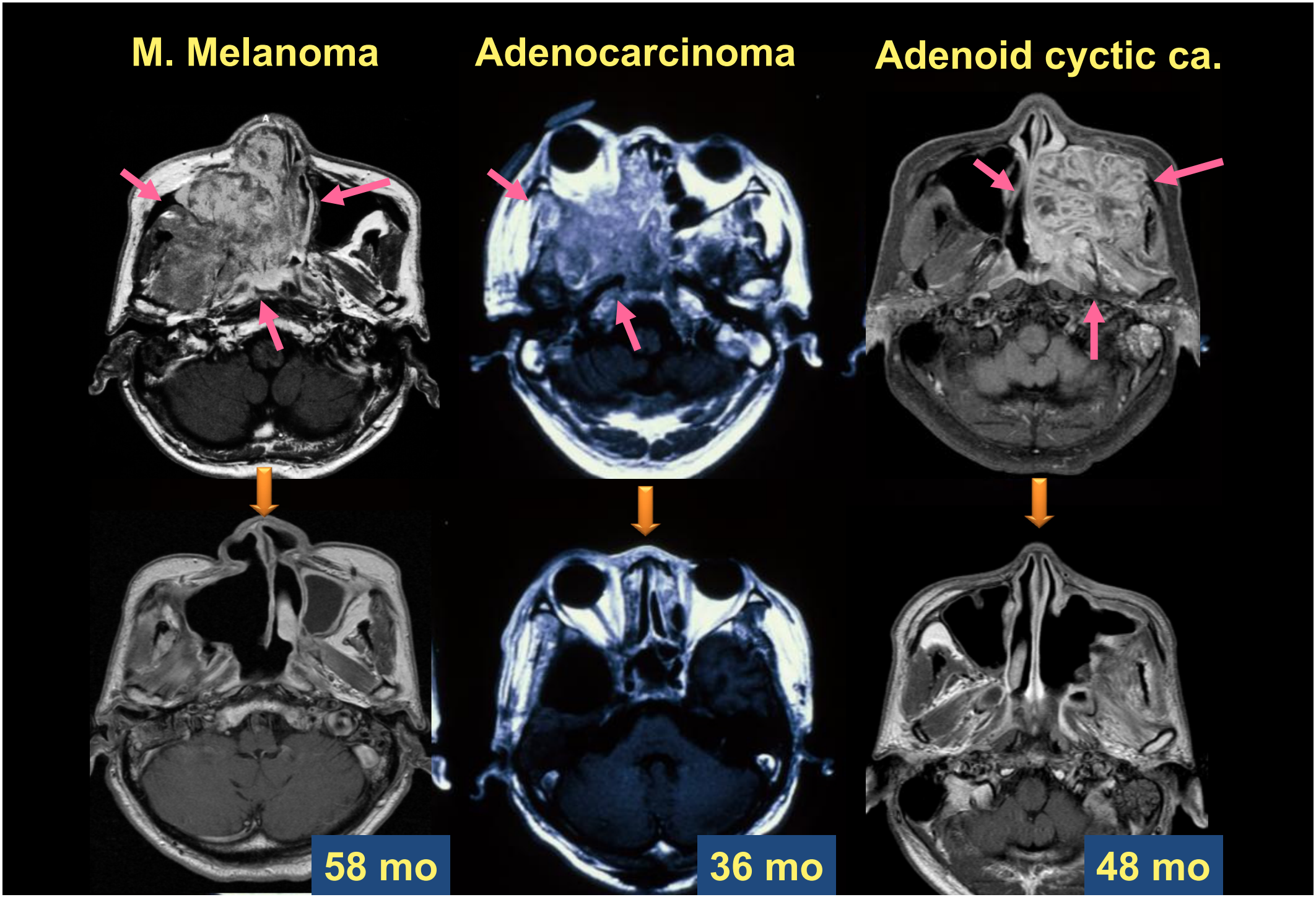
Incidence of late rectal radiation toxicity in prostate cancer (Grade 2 or worse)



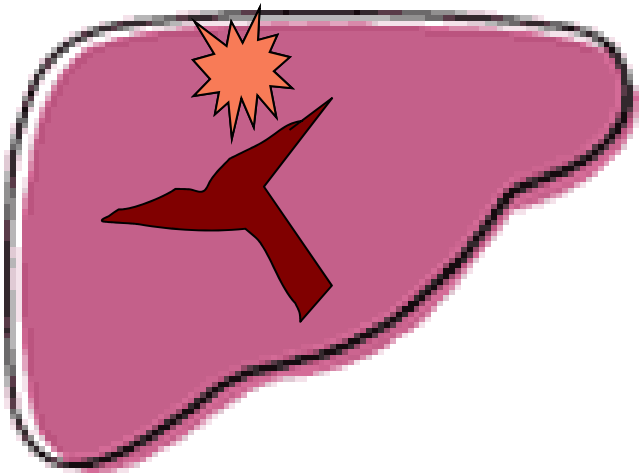
1) Martin JM, IJROBP 2007, 2) Kupelian PA, IJROBP 2007, 3) King CR, IJROBP 2009, 4) Michalski JM, IJROBP 2010, 5) Schulte RW, Strahlenther Onkol 2000, 6) Nihei K, IJROBP 2011, 7) Coen J, IJROBP 2010, 8) Ishikawa H, Int J Uro 2012.

Head & Neck cancers




M. Melanoma
Adenocarcinoma
Adenoid cyctic ca.
58 mo
36 mo
48 mo

Liver cancers

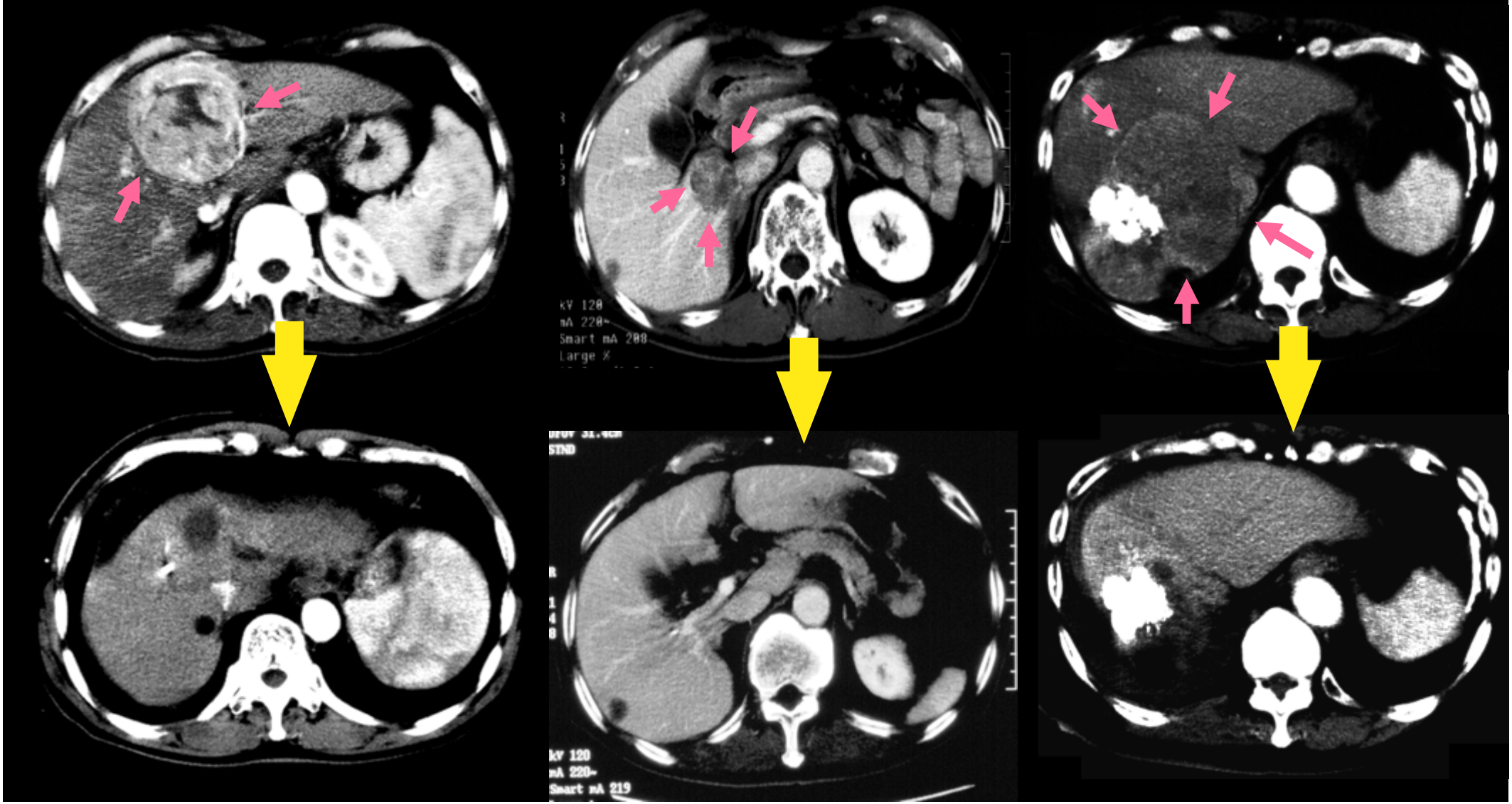


Hepatocellar carcinoma

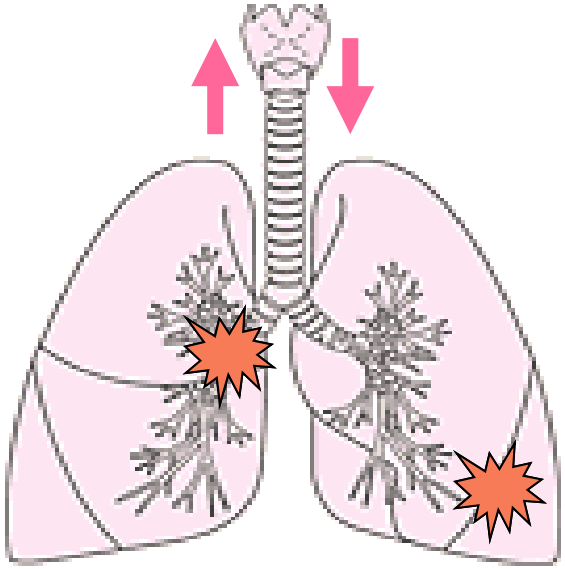
Large sized HCC

Not indicated for RFA

Rec. after TACE

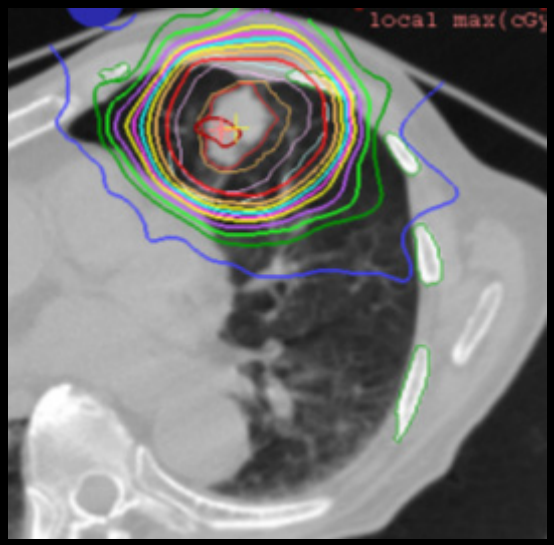


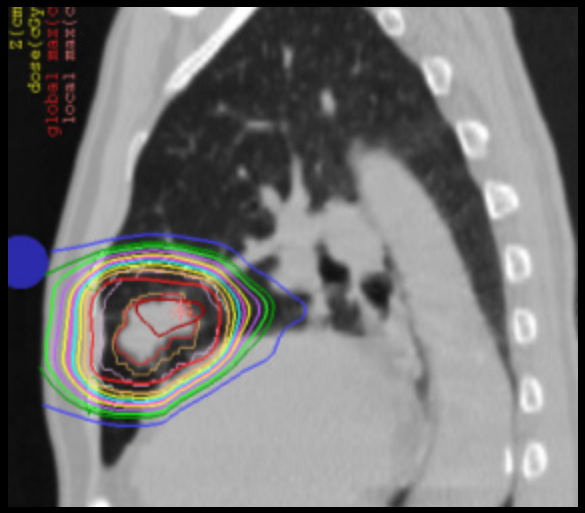
Lung cancers



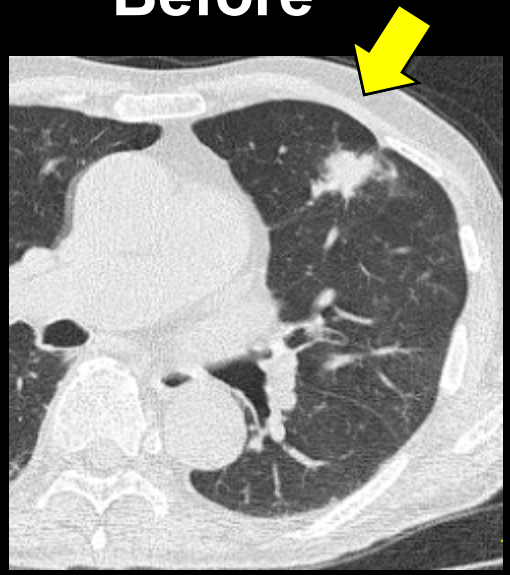
Lung cancer (T1b) 52.8GyE/4fr/w

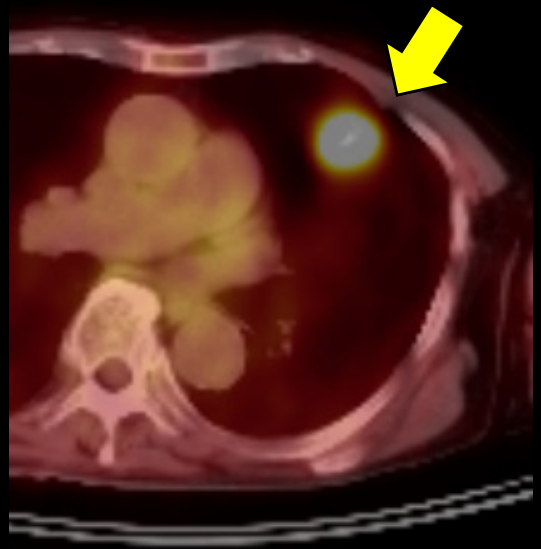
Treatment planning



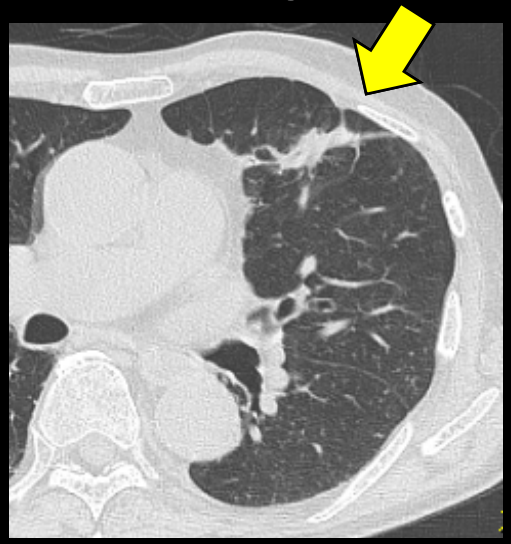


Before

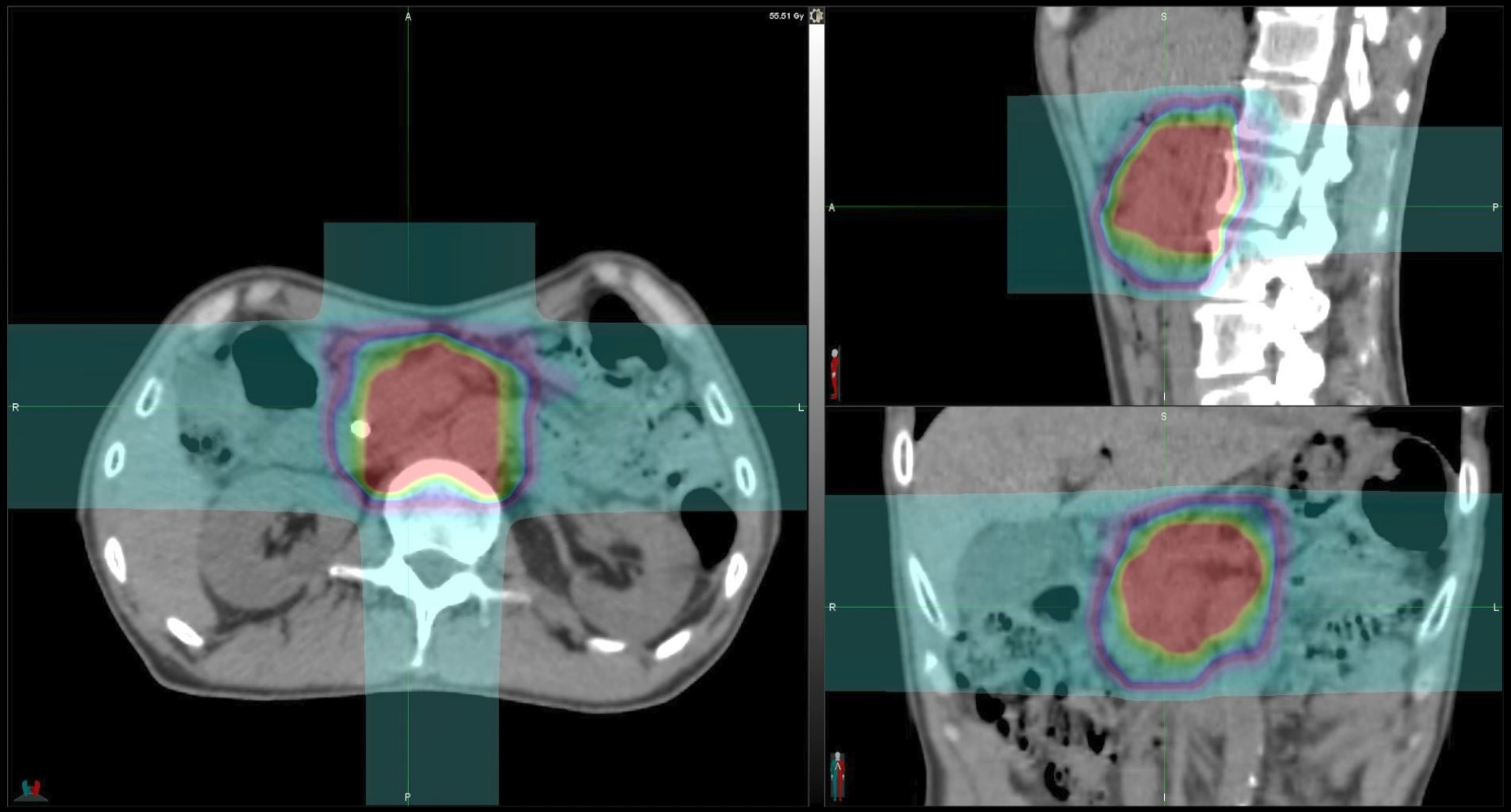




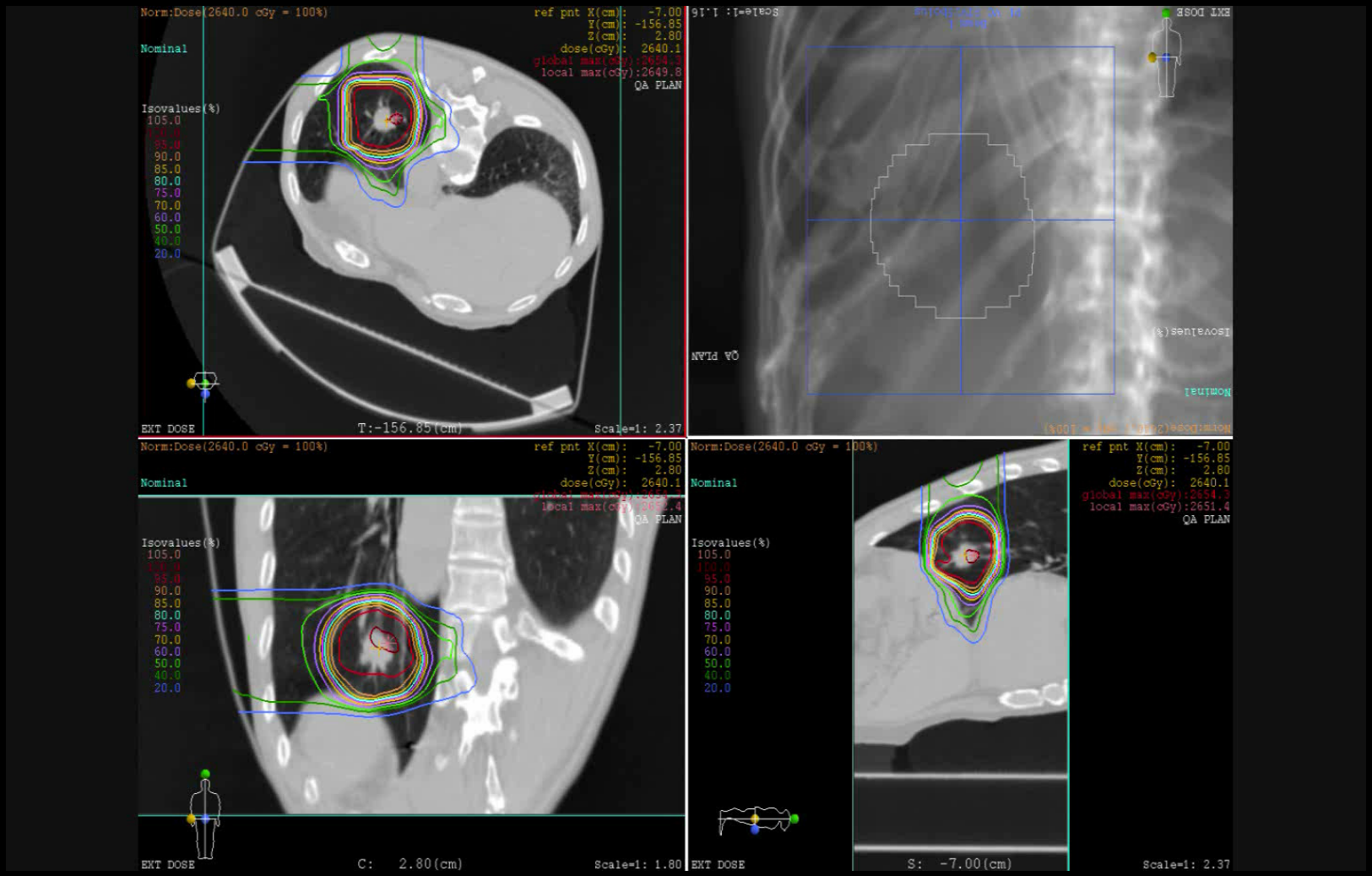
1 Mo.



Respiratory-gated irradiation



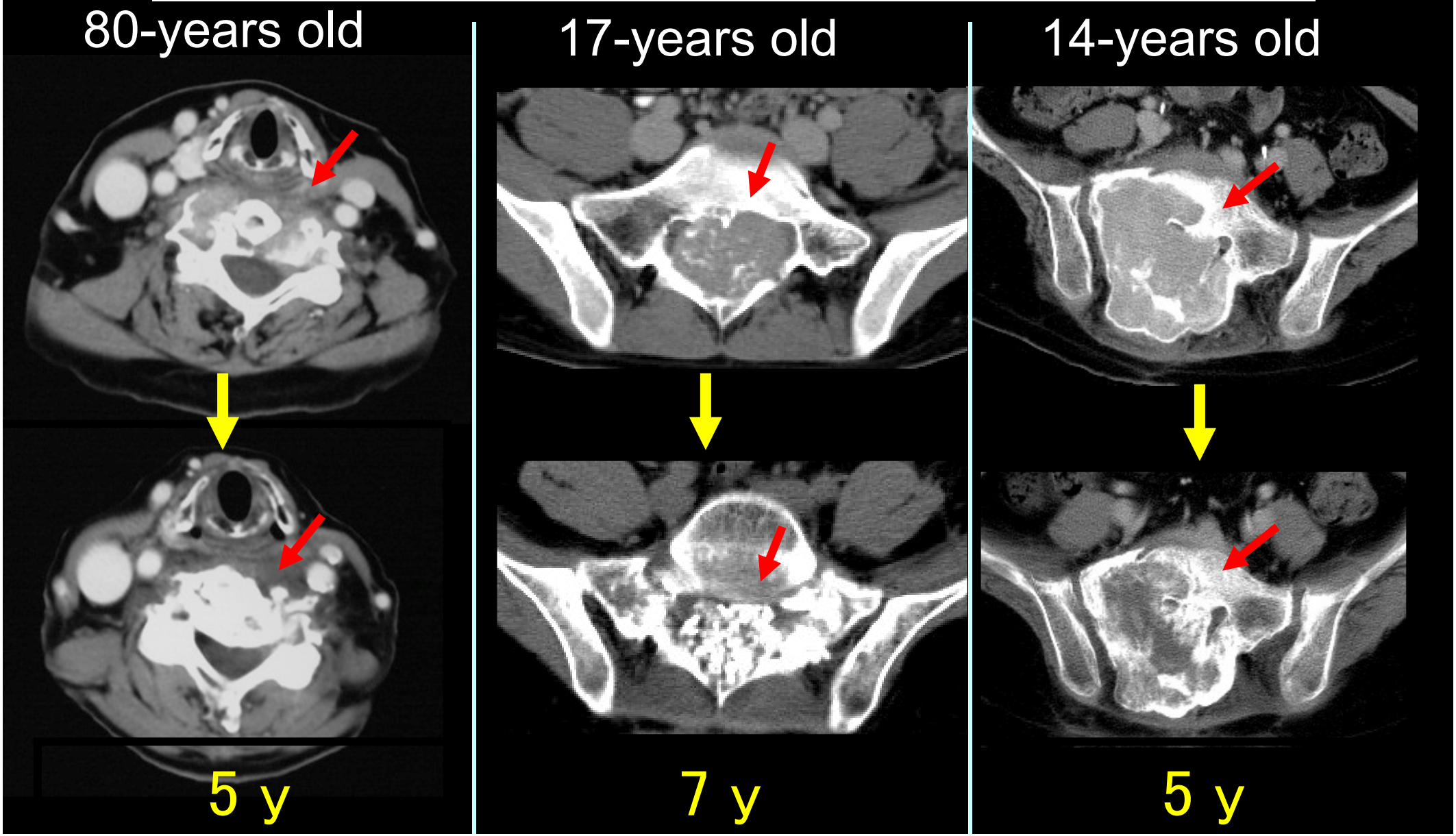
Respiratory-gated irradiation



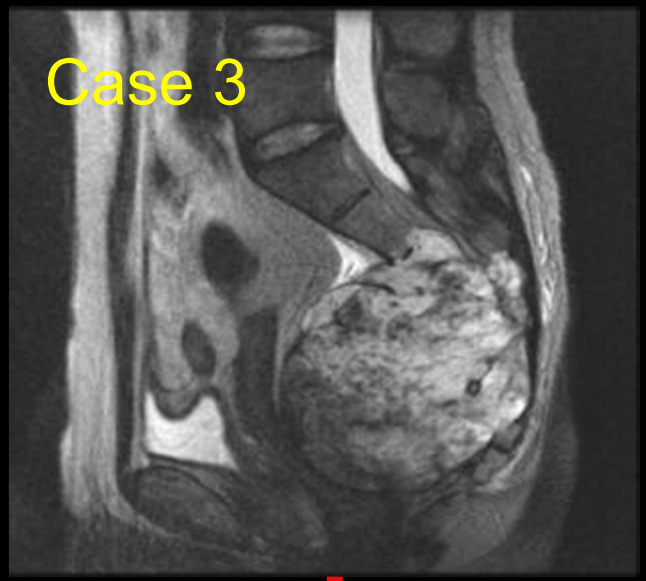
Bone and soft tissue

Osteosarcoma of the trunk

The first results of clinical trial was published in J Clin Oncol in 2002.



Sacral chordoma

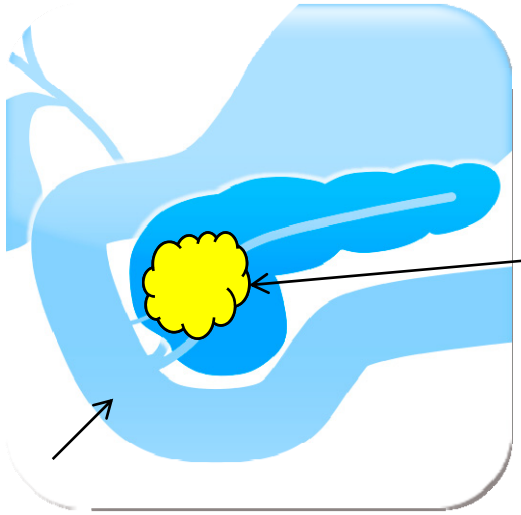


4 years

4 years

4.5 years

Pancreatic cancers

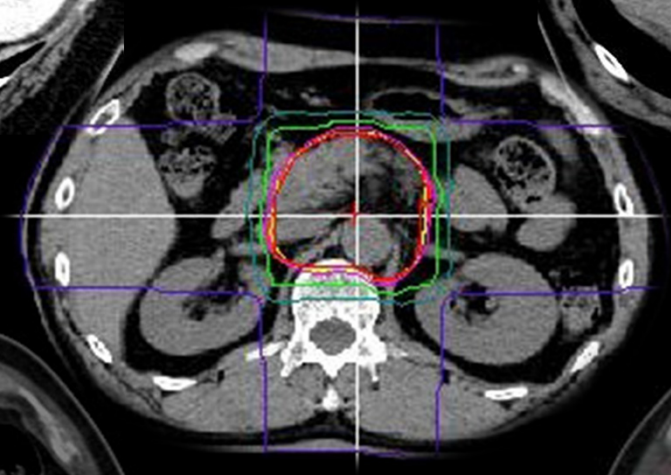


X-ray resistant tumor
of the pancreas

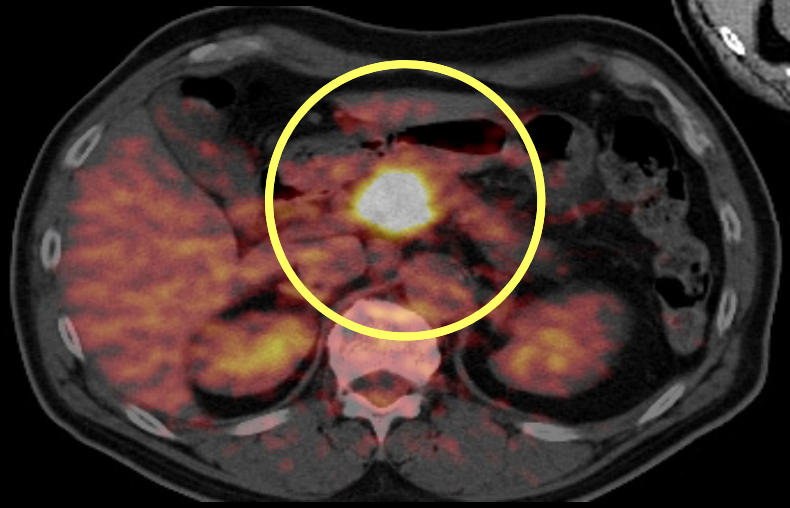
Small bowel
Sensitive to irradiation

Pancreatic cancer: locally advanced unresectable case

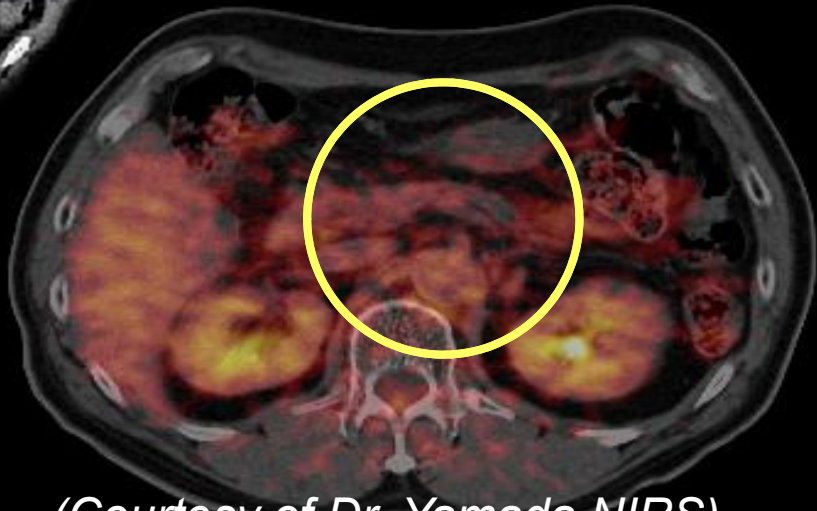
Before Treatment



40M after treatment

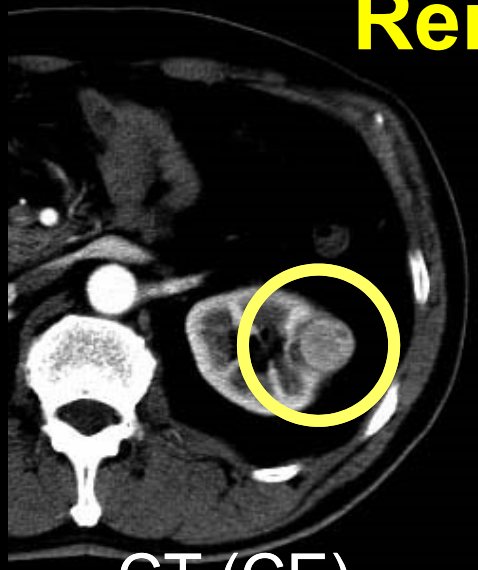


2yOS=49%

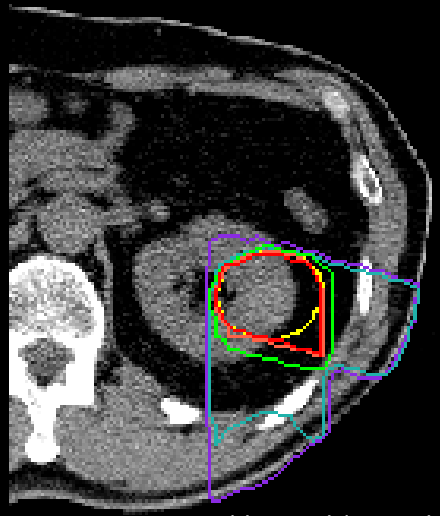


(Courtesy of Dr. Yamada NIRS)

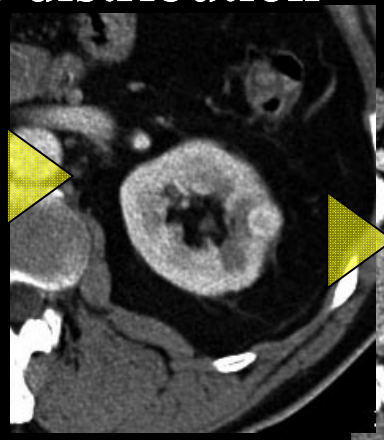
Renal Cell Carcinoma (55y M)



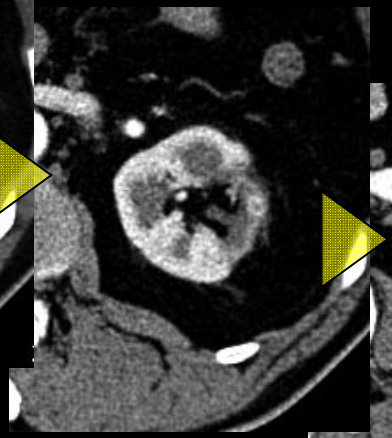
CT (CE)



Dose distribution

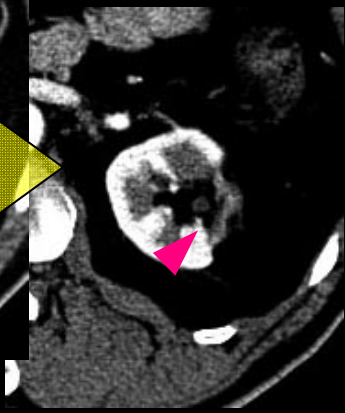


1y



2.5y

4.5y



5.5y

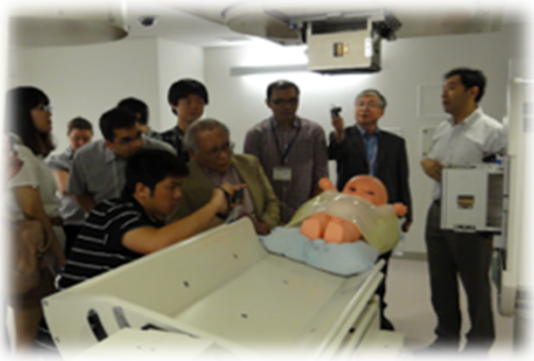
(Nomiya et al. IJROBP 2008)

International Patients have been treated

Opportunity for study at Gunma University

Gunma University is the only educational institute of heavy ions in Japan. To cultivate experts in heavy ion therapeutics and engineering, the university has launched a new doctoral program aimed at producing top-rated radiation oncologist, medical physicists, and drug and device developers.

With state-of-the-art heavy ion facilities, Gunma University is increasingly attracting for visiting researchers from Asia, Europe and the rest of the world.



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Spotlight on Gunma (Nature, 2012)

GUNMA PREFECTURAL NIPPON SILK CENTER

GUNMA, JAPAN

A leader in industry and innovation

The prefecture of Gunma may not be as widely known as the urban areas of Tokyo and Osaka, but it has long contributed to the creation and development of Japan's core manufacturing industries. Today, many breakthrough technologies are springing up in Gunma as the region stands at the frontline of technological innovation.

Spotlight on Gunma (Nature, 2012)




HEAVY-ION MEDICAL RESEARCH CENTER, GUNMA UNIVERSITY

NATIONAL UNIVERSITY CORPORATION
Gunma University

GUNMA PREFECTURAL NIPPON SILK CENTER

Trained to kill

A leader in industry and innovation

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Thank you very much!