

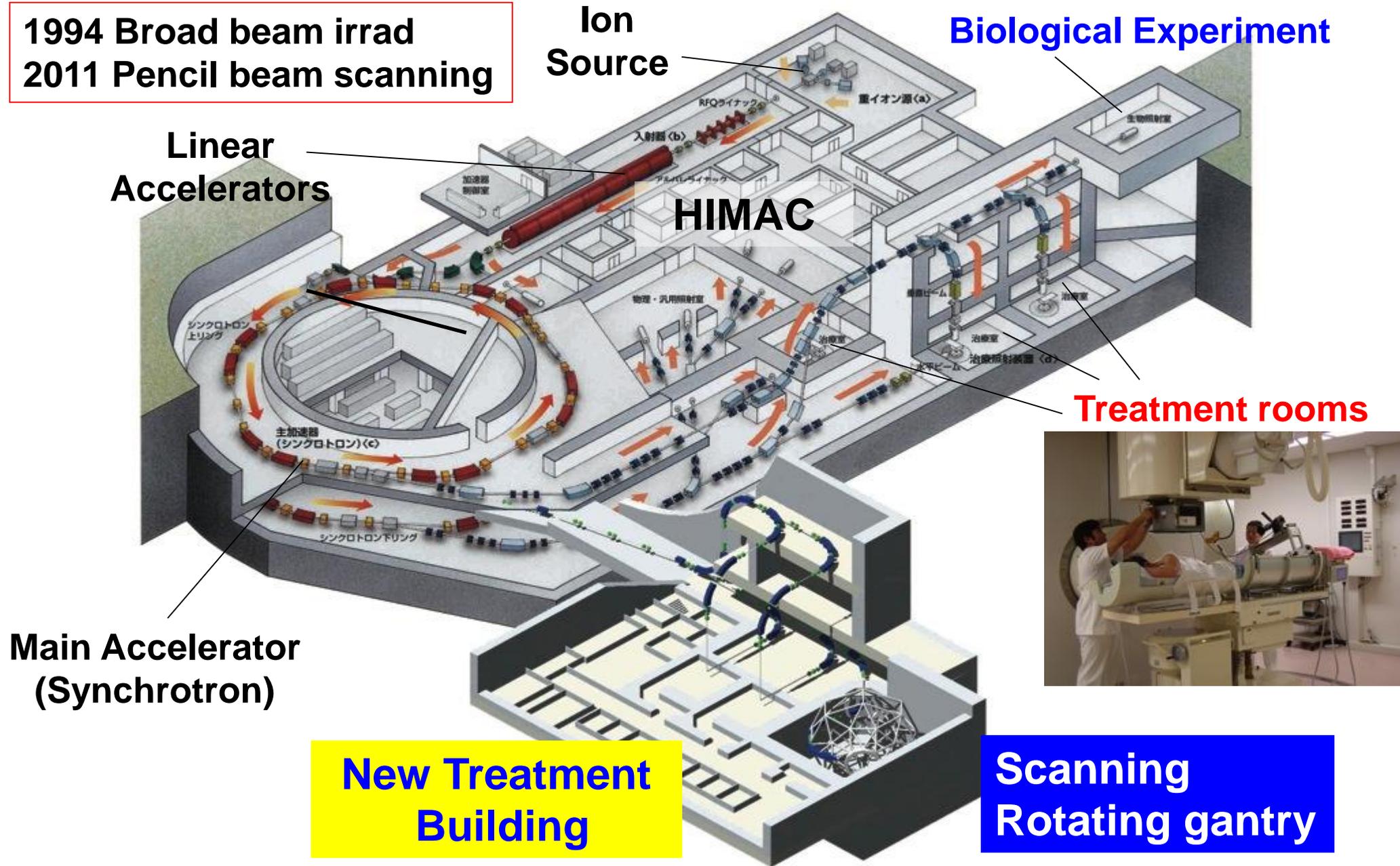
# Clinical Trials for Charged Particle RT in Japan

*H. Tsujii*

*National Institute of Radiological Sciences (NIRS)*

# HIMAC (Heavy Ion Medical Accelerator in Chiba)

1994 Broad beam irradiation  
2011 Pencil beam scanning



Linear Accelerators

Ion Source

Biological Experiment

HIMAC

Treatment rooms

Main Accelerator (Synchrotron)

New Treatment Building

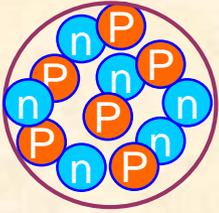
Scanning Rotating gantry



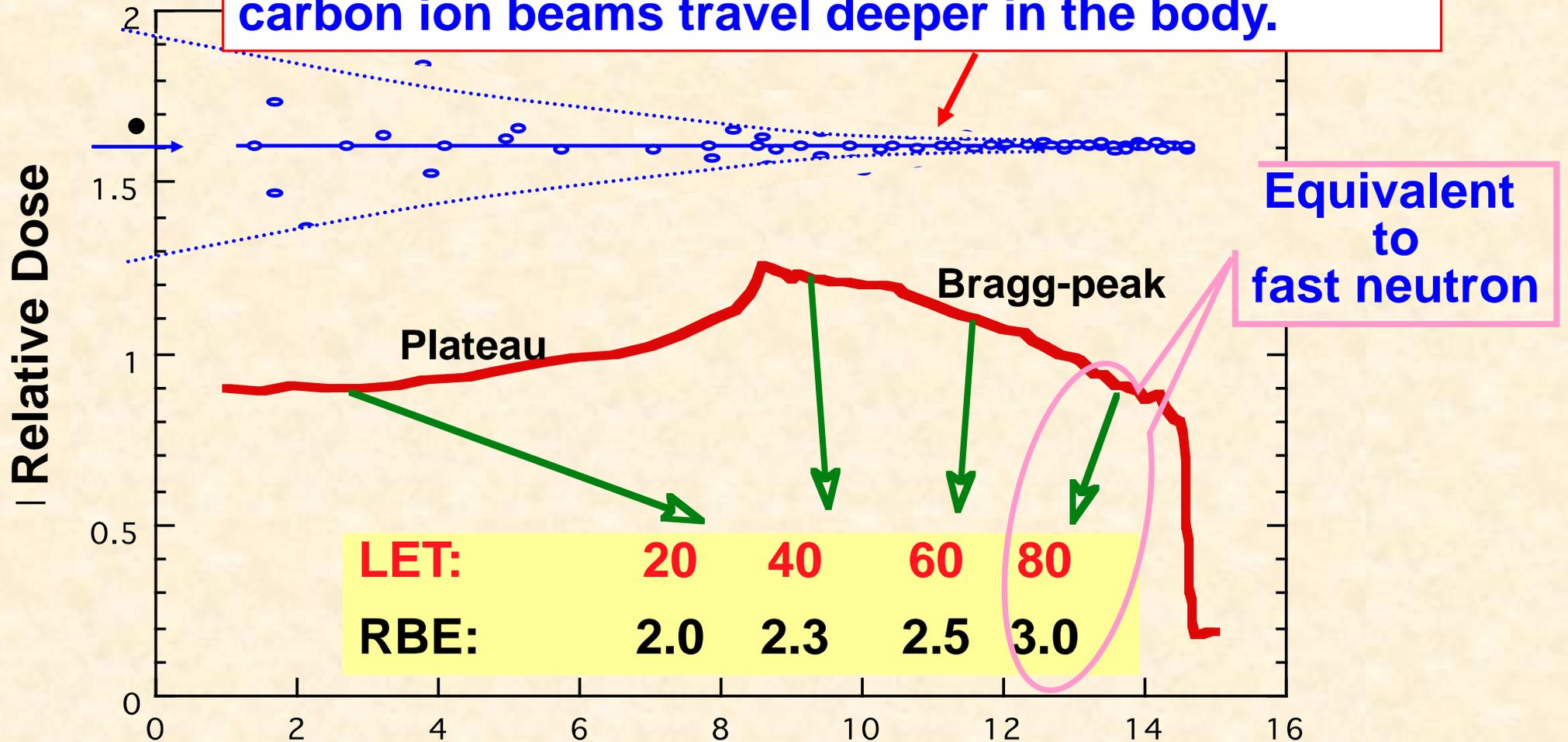
**Carbon ion (6+)**

# LET & RBE Values of Carbon Ions

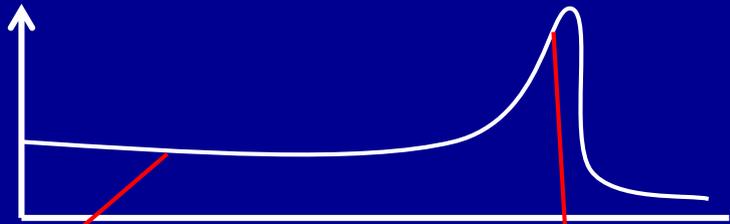
(Carbon ion, 290MeV, SOBP=60mm)



Ionization density increases with depth, thereby the biological effectiveness increases as carbon ion beams travel deeper in the body.



# Carbon-ions

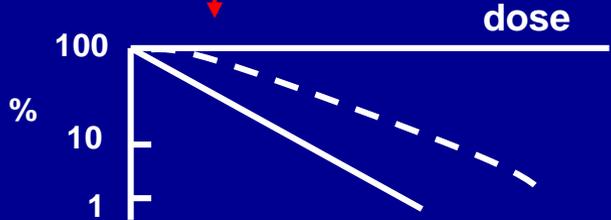
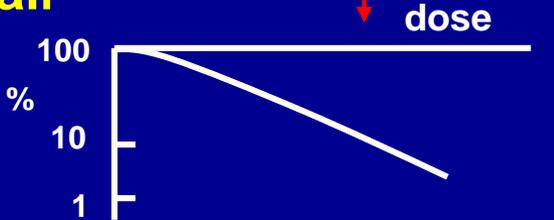


**Plateau**

**Bragg peak**

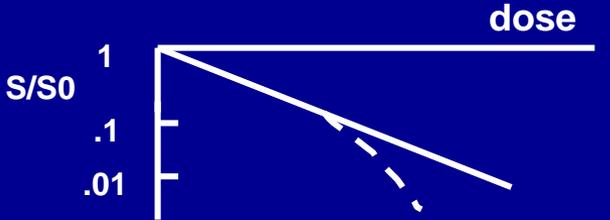
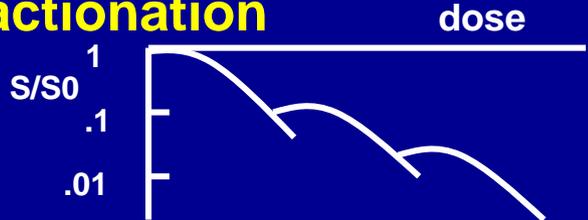
**RBE: 2~3.5**

## Repair



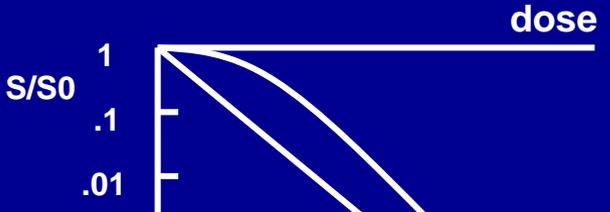
**Repair is smaller**

## Fractionation



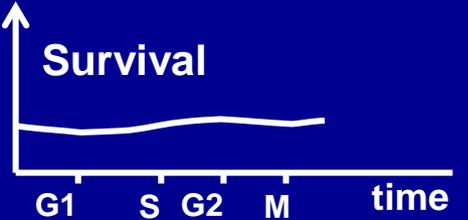
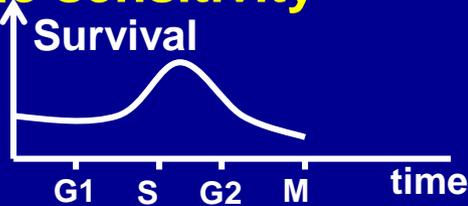
**Effect from fractionation is smaller**

## Oxygen effect



**OER is smaller**

## Cell cycle sensitivity



**Cell cycle difference of sensitivity is smaller**

(Courtesy of G.Kraft)

# *Tumor Types and Clinical Situations Where Carbon Ion Radiotherapy Offers a Therapeutic Advantage*

## ◆ Hypofractionated RT is feasible

Treatment time is reduced to half or even shorter as compared to other RT

**Average : 12.0 fr / 3 wks**

**Stage I Lung → single fr、 Hepatpma → 2 fr**

**Prostate → 12 fr**

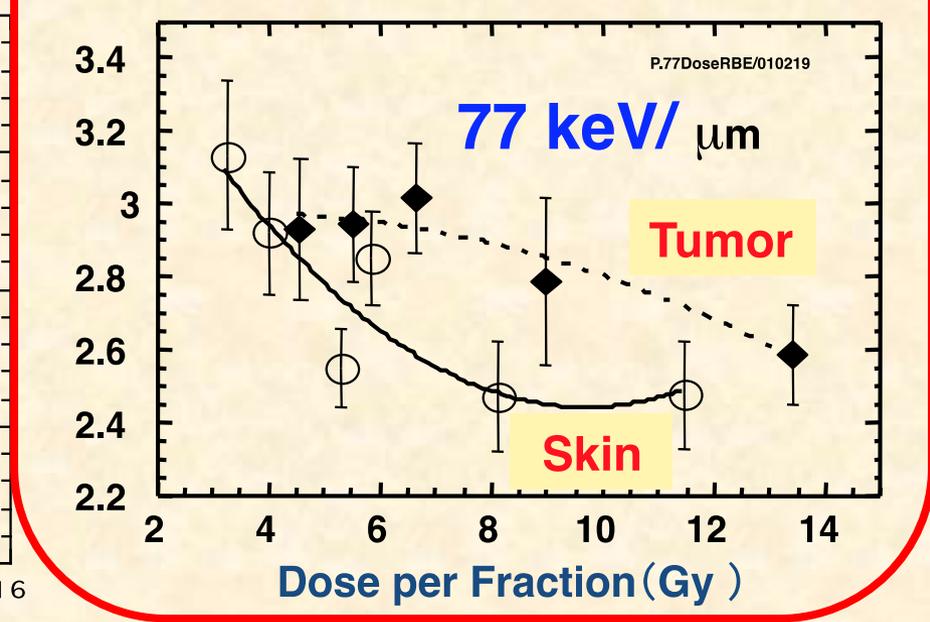
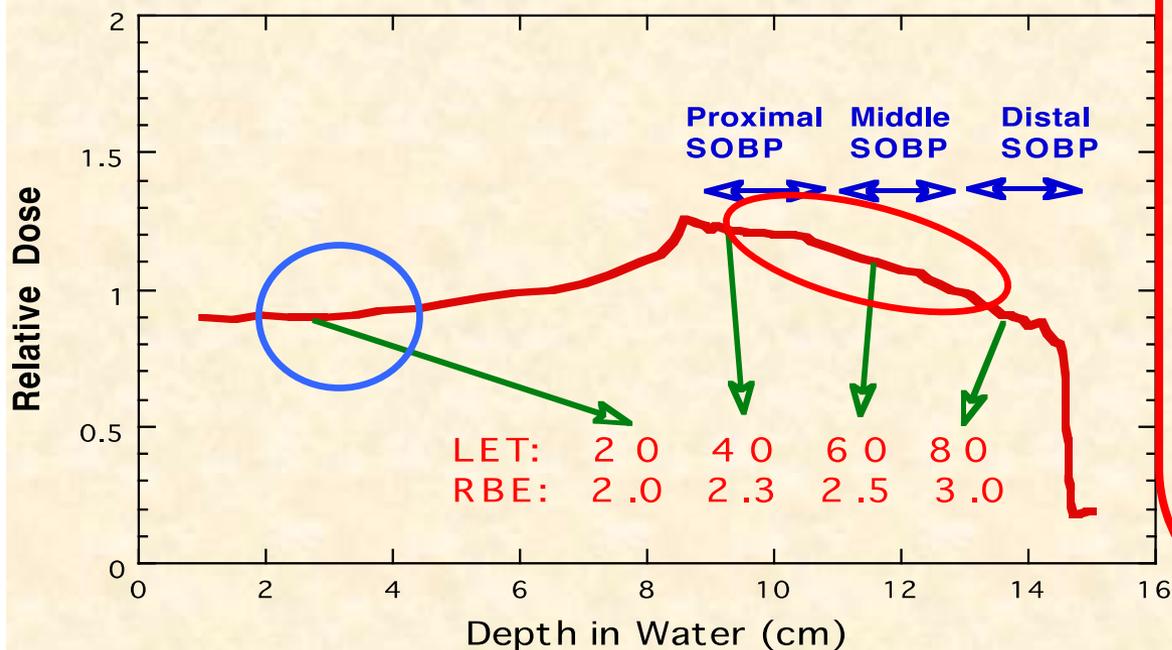
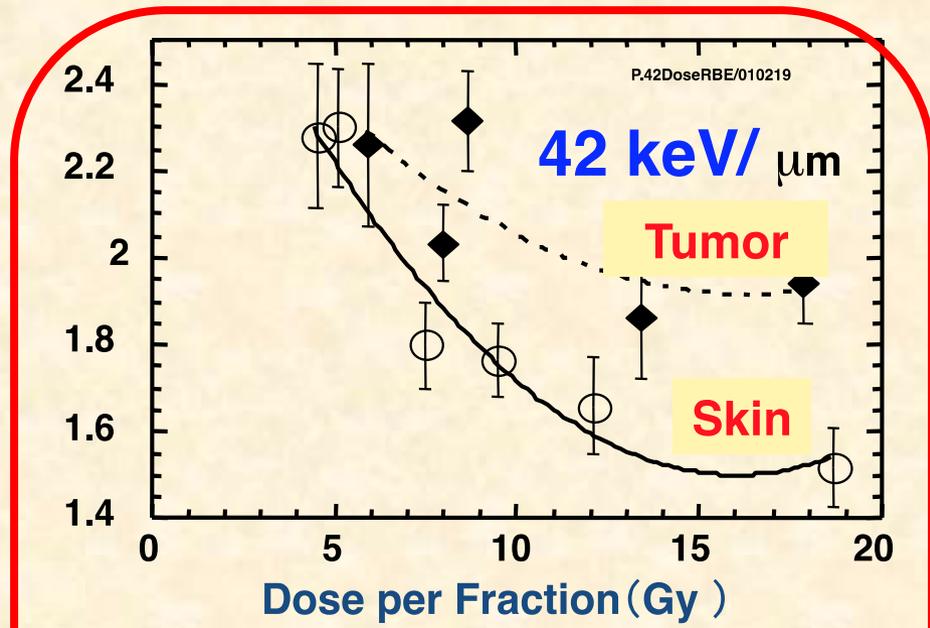
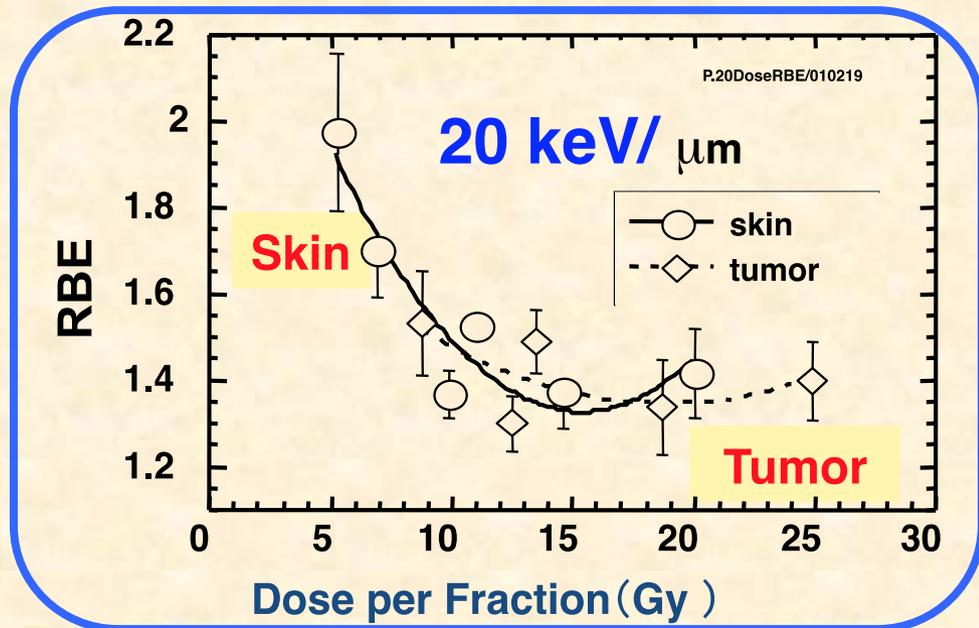
## ◆ Effective to unresectable tumors

Skull base、 Head & neck、 Pelvis, etc

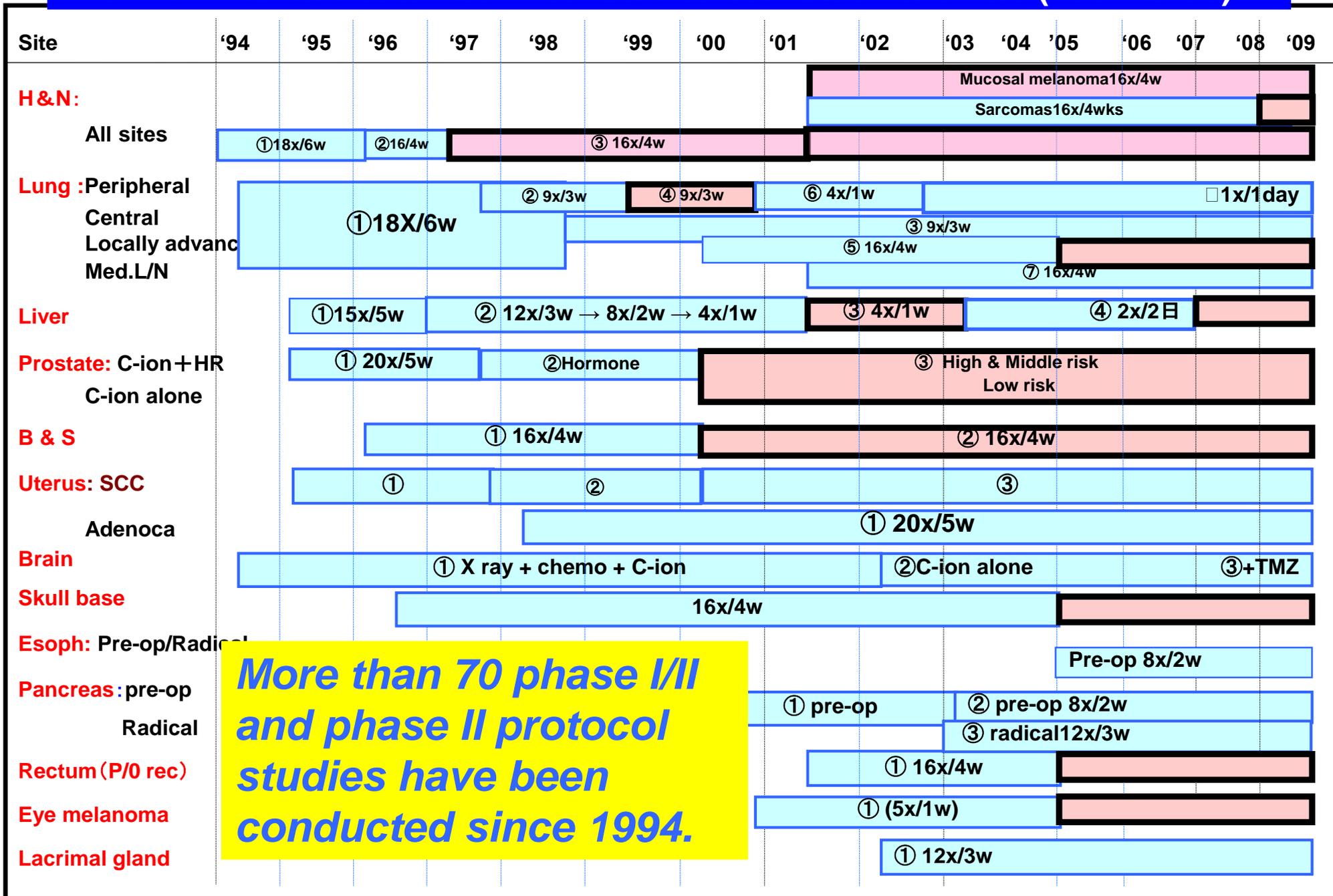
## ◆ Effective to photon-resistant tumors

Sarcoma、 Melanoma、 Adenoca、 Adenoid cystic ca, etc.

# RBE vs. Fraction Size in Carbon Beam Irradiation



# Protocols and Time Line of Carbon Ion Clinical Trials (1994-2009)



# ***Dose Escalation Phase I/II Studies***

## **The NIRS clinical study in the early days :**

- The patients whose tumor was invading or close to the overlying skin often developed severe skin reactions at the higher dose levels delivered.
- In CIRT of prostate and uterine cervix cancer, those patients who were treated with higher dose levels frequently developed severe intestinal side effects.
- **After the cause of these side effects was examined in detail, the safe dose was determined and irradiation techniques were improved when no more similar side effects were observed.**

# Dose-fractionations for carbon ion RT at NIRS

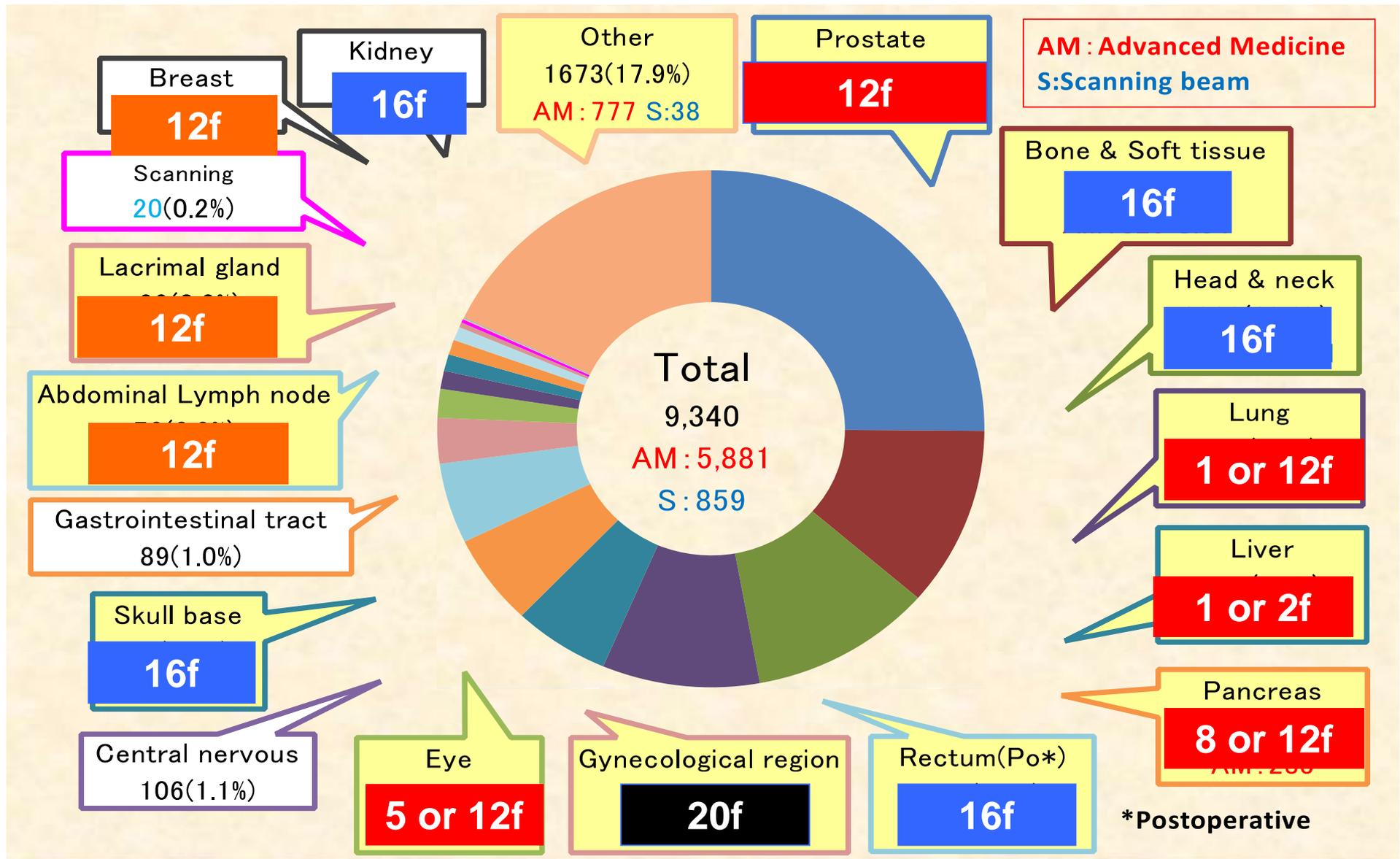
| Site               | Tumor type                            | GyE / Fr./ Wk                   | GyE / fr  | BED ( $\alpha/\beta=10$ ) | BED ( $\alpha/\beta=2.5$ ) |
|--------------------|---------------------------------------|---------------------------------|-----------|---------------------------|----------------------------|
| Head & Neck        | Adenoca, ACC                          | 57.6 / 16 / 4                   | 3.6       | 78.3                      | 140.5                      |
|                    | MMM                                   | 64.0 / 16 / 4                   | 4.0       | 89.6                      | 166.4                      |
|                    | Sarcoma                               | 70.4 / 16 / 4                   | 4.4       | 101.4                     | 194.3                      |
| Skull base         | Chordoma & Chondrosarc                | 60.8 / 16 / 4                   | 3.8       | 83.4                      | 153.2                      |
| Lung               | Peripheral                            | 60.0 / 4 / 1<br>50.0 / 1 / 1 dy | 15.0<br>- | 150.0<br>-                | 420.0<br>-                 |
|                    | : Mediastinum                         | 48.0 / 12 / 3                   | 4.0       | 67.2                      | 124.8                      |
|                    | Hilar : Superficial                   | 54.0 / 9 / 3                    | 6.0       | 86.4                      | 183.6                      |
|                    | : Bulky                               | 68.4 / 12 / 3                   | 5.7       | 107.4                     | 224.4                      |
| Liver              | Hepatocellular ca                     | 48.0 / 2 / 2dys                 | 24.0      | 163.2                     | 508.8                      |
|                    | Metastasis of colon ca                | > 50.0 / 1 / 1dy                | 50.0      | -                         | -                          |
| Bone & Soft tissue | Sarcoma                               | 70.4 / 16 / 4                   | 4.4       | 101.4                     | 193.4                      |
|                    | Chordoma                              | 67.2 / 26 / 4                   | 4.6       | 95.4                      | 180.1                      |
| Prostate           | Low / Medium / High risk              | 57.6 / 16 / 4                   | 3.6       | 78.3                      | 140.5                      |
|                    |                                       | 51.6 / 12 / 3                   | 4.3       | 73.8                      | 140.4                      |
| Pancreas           | Post-operative C-ion RT               | > 35.2 / 8 / 2                  | 4.4       | 50.7                      | 97.2                       |
|                    | C-ion (+ CDDP 1000mg/m <sup>2</sup> ) | 55.2 / 12 / 3                   | 4.6       | 80.6                      | 156.8                      |
| Rectum             | Post-ope pelvic rec.                  | 73.6 / 16 / 4                   | 4.6       | 107.5                     | 209.0                      |
|                    | Re-irradiation                        | 70.4 / 16 / 4                   | 4.4       | 101.4                     | 194.3                      |
| Eye                | Melanoma                              | 70.0 / 5 / 1                    | 14.0      | 168.0                     | 462.0                      |
|                    | Lacrymal gland                        | 55.1 / 12 / 3                   | 4.6       | 80.6                      | 156.8                      |
| Standard photon RT |                                       | 60 / 30 / 8                     | 2.0       | 72                        | 108                        |

# Dose-fractionations for carbon ion RT at NIRS

| Site               | Tumor type                            | GyE / Fr./ Wk                   | GyE / fr  | BED ( $\alpha/\beta=10$ ) | BED ( $\alpha/\beta=2.5$ ) |
|--------------------|---------------------------------------|---------------------------------|-----------|---------------------------|----------------------------|
| Head & Neck        | Adenoca, ACC                          | 57.6 / 16 / 4                   | 3.6       | 78.3                      | 140.5                      |
|                    | MMM                                   | 64.0 / 16 / 4                   | 4.0       | 89.6                      | 166.4                      |
|                    | Sarcoma                               | 70.4 / 16 / 4                   | 4.4       | 101.4                     | 194.3                      |
| Skull base         | Chordoma & Chondrosarc                | 60.8 / 16 / 4                   | 3.8       | 83.4                      | 153.2                      |
| Lung               | Peripheral                            | 60.0 / 4 / 1<br>50.0 / 1 / 1 dy | 15.0<br>- | 150.0<br>-                | 420.0<br>-                 |
|                    | : Mediastinum                         | 48.0 / 12 / 3                   | 4.0       | 67.2                      | 124.8                      |
|                    | Hilar : Superficial                   | 54.0 / 9 / 3                    | 6.0       | 86.4                      | 183.6                      |
|                    | : Bulky                               | 68.4 / 12 / 3                   | 5.7       | 107.4                     | 224.4                      |
| Liver              | Hepatocellular ca                     | 48.0 / 2 / 2dys                 | 24.0      | 163.2                     | 508.8                      |
|                    | Metastasis of colon ca                | > 50.0 / 1 / 1dy                | 50.0      | -                         | -                          |
| Bone & Soft tissue | Sarcoma                               | 70.4 / 16 / 4                   | 4.4       | 101.4                     | 193.4                      |
|                    | Chordoma                              | 67.2 / 26 / 4                   | 4.6       | 95.4                      | 180.1                      |
| Prostate           | Low / Medium / High risk              | 57.6 / 16 / 4                   | 3.6       | 78.3                      | 140.5                      |
|                    |                                       | 51.6 / 12 / 3                   | 4.3       | 73.8                      | 140.4                      |
| Pancreas           | Post-operative C-ion RT               | > 35.2 / 8 / 2                  | 4.4       | 50.7                      | 97.2                       |
|                    | C-ion (+ CDDP 1000mg/m <sup>2</sup> ) | 55.2 / 12 / 3                   | 4.6       | 80.6                      | 156.8                      |
| Rectum             | Post-ope pelvic rec.                  | 73.6 / 16 / 4                   | 4.6       | 107.5                     | 209.0                      |
|                    | Re-irradiation                        | 70.4 / 16 / 4                   | 4.4       | 101.4                     | 194.3                      |
| Eye                | Melanoma                              | 70.0 / 5 / 1                    | 14.0      | 168.0                     | 462.0                      |
|                    | Lacrymal gland                        | 55.1 / 12 / 3                   | 4.6       | 80.6                      | 156.8                      |
| Standard photon RT |                                       | 60 / 30 / 8                     | 2.0       | 72                        | 108                        |

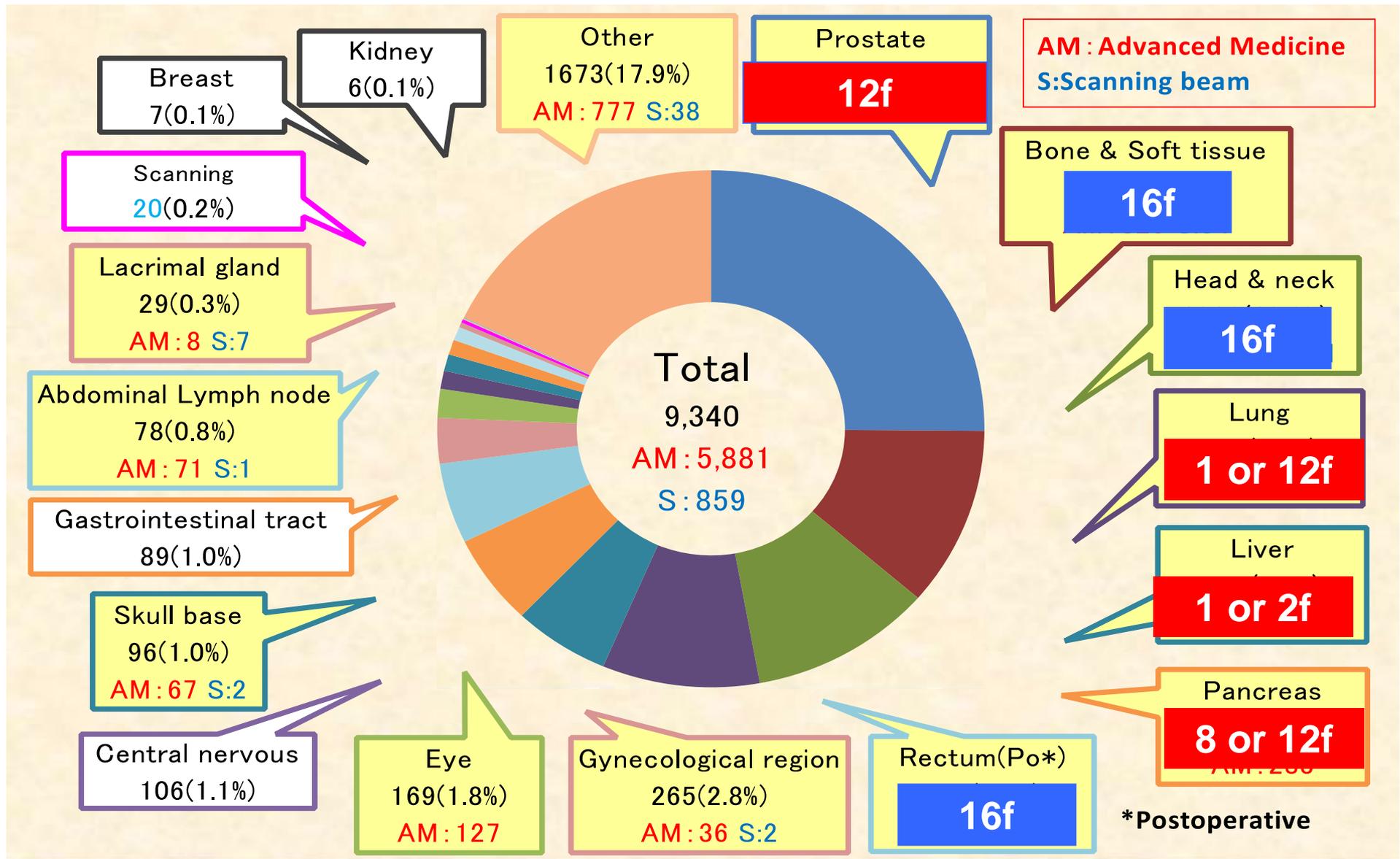
# Tumor Sites in Carbon Ion Therapy at NIRS

## June.1994 ~ August 2015



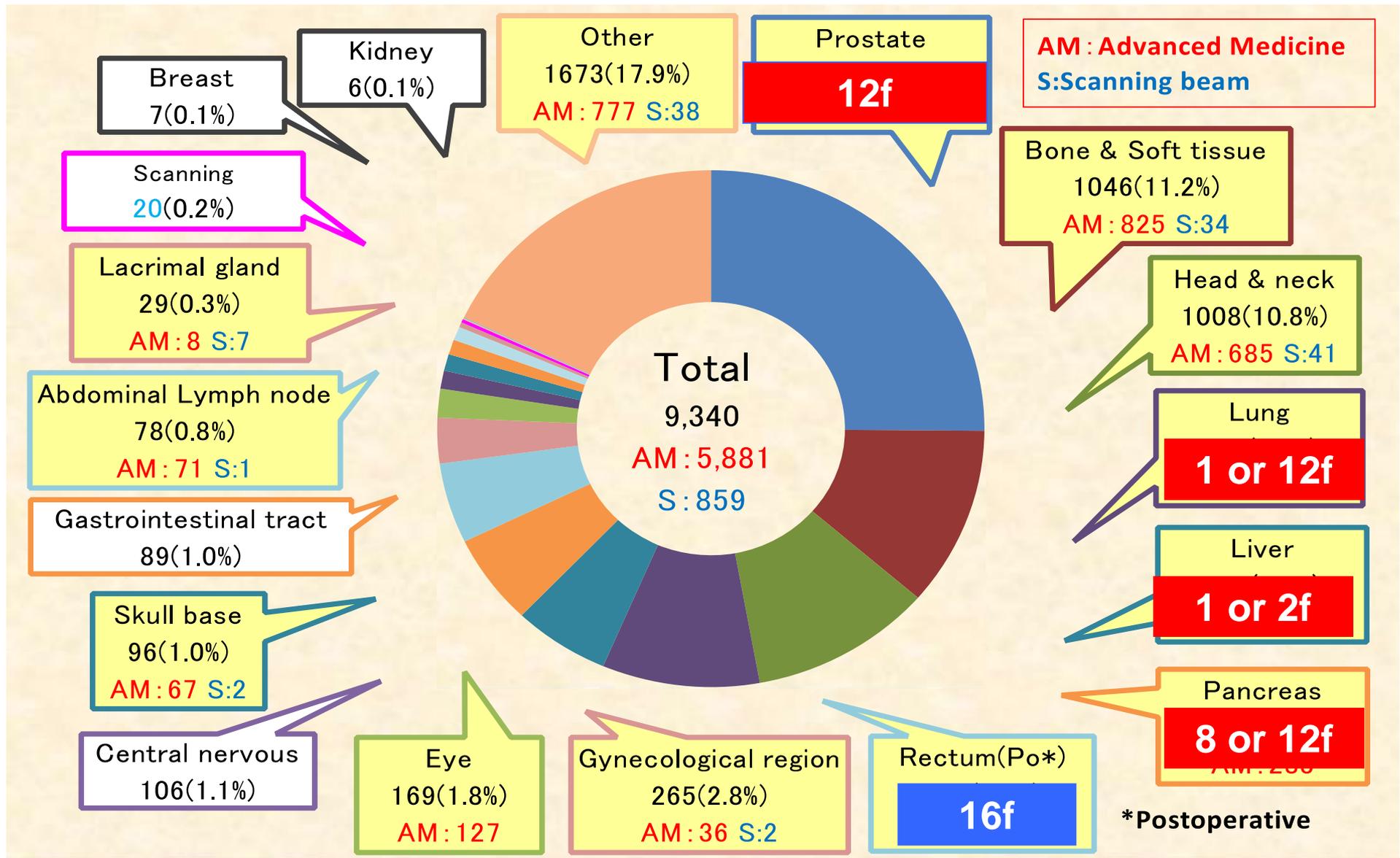
# Tumor Sites in Carbon Ion Therapy at NIRS

## June.1994 ~ August 2015



# Tumor Sites in Carbon Ion Therapy at NIRS

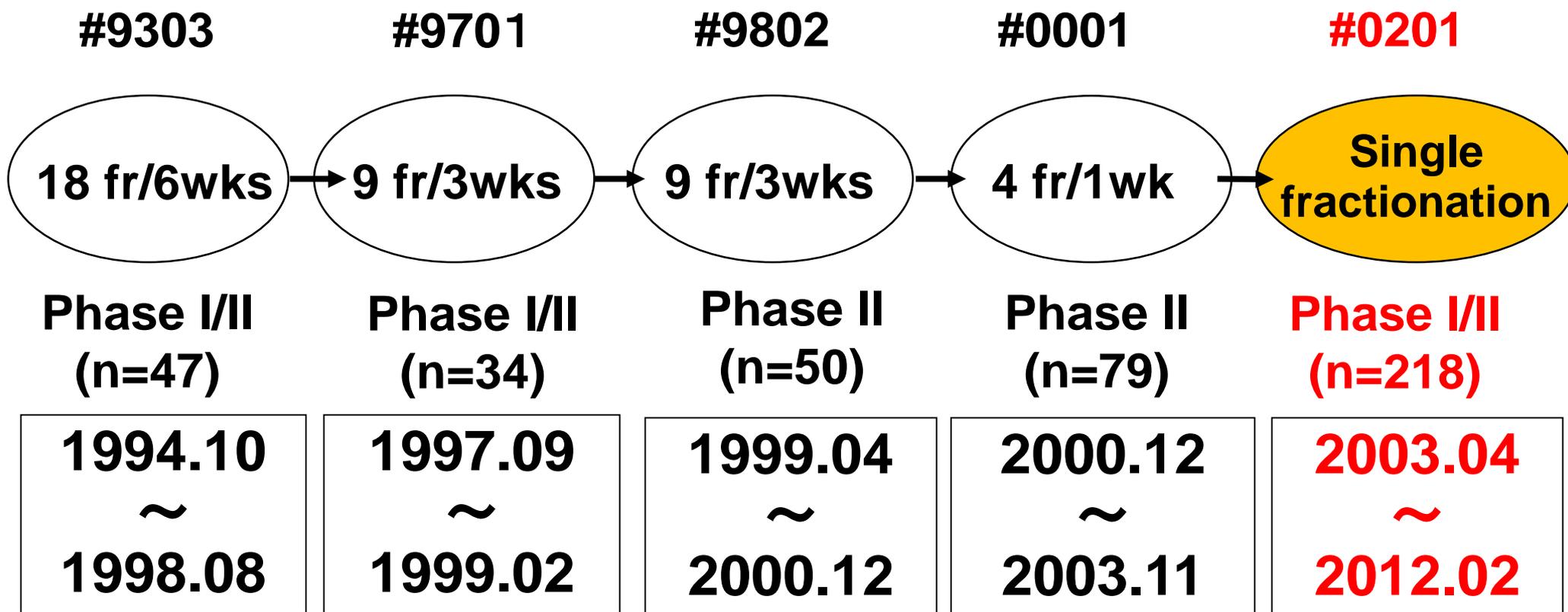
## June.1994 ~ August 2015



# Carbon-ion RT regimens for non-small cell lung cancer

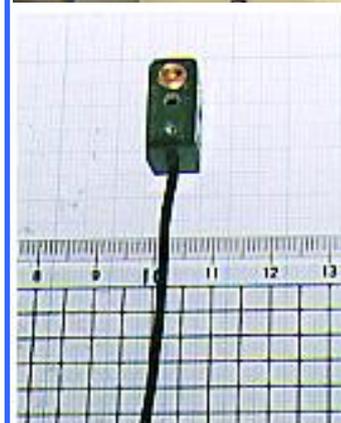
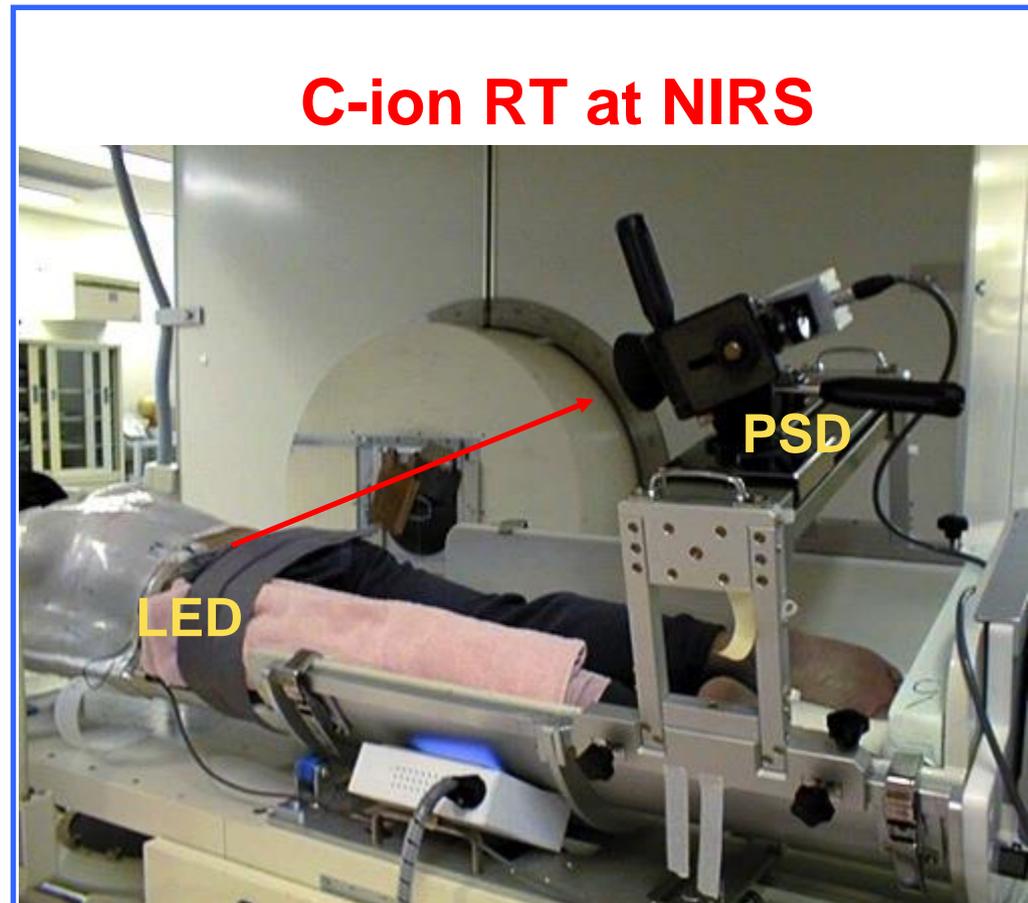
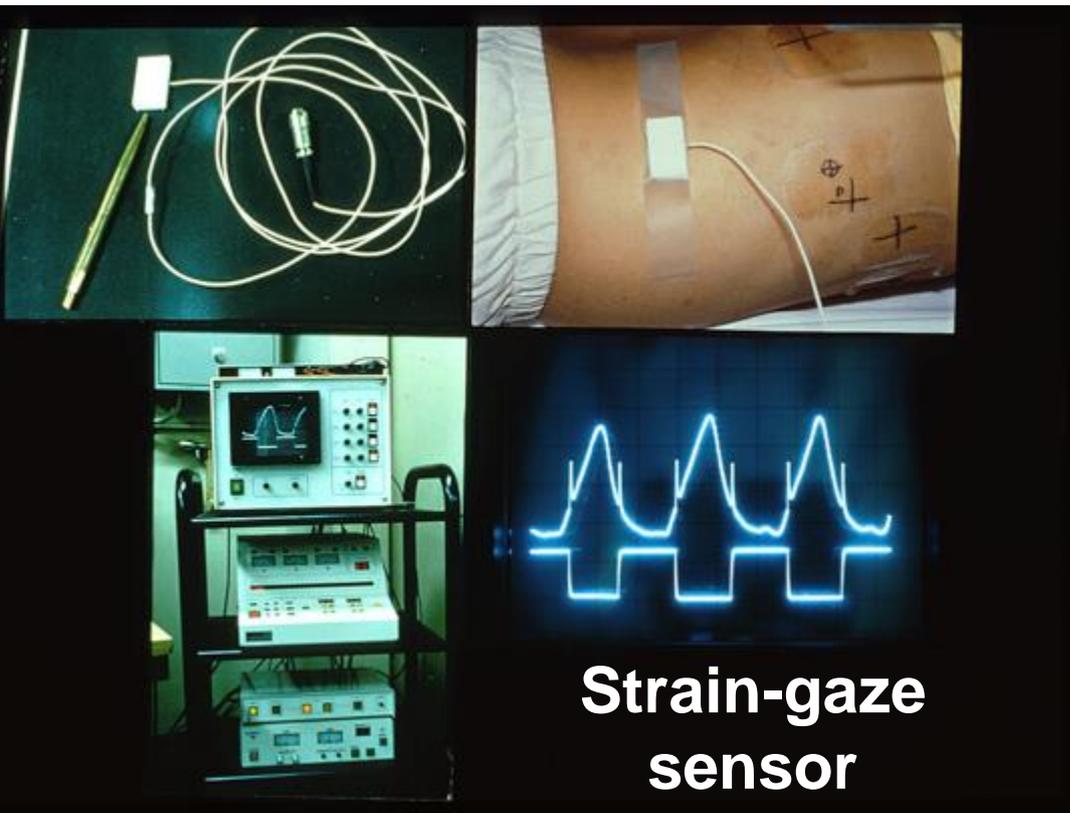
|   | Prescribed Dose (GyE) (dose / fr) |              |
|---|-----------------------------------|--------------|
|   | /fraction                         |              |
| <b>T1-2 N0 M0</b><br><b>Peripheral Stage I</b>        | <b>50.0 / 1</b>                   | <b>50.0</b>  |
| <b>Central type</b><br><b>Early lung cancer</b>       | <b>61.2 / 9</b>                   | <b>(6.8)</b> |
| <b>T1-2 N0 M0</b><br><b>Hilar nodules</b>             | <b>68.4 / 12</b>                  | <b>(5.7)</b> |
| <b>T1-3 N1-2 M0</b><br><b>Locally advanced tumors</b> | <b>72.0 / 16</b>                  | <b>(4.5)</b> |
| <b>Metastatic mediastinal</b><br><b>lymph node</b>    | <b>48.0 / 12</b>                  | <b>(4.0)</b> |

# Clinical trials of CIRT for peripheral Stage I NSCLC



# Respiratory gaited irradiation

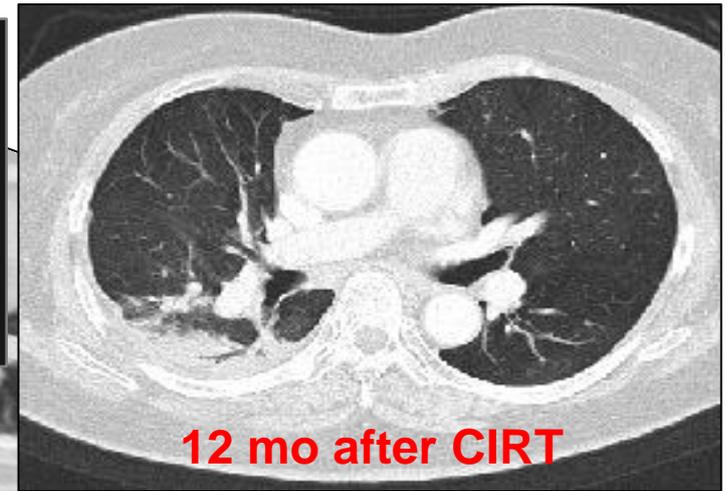
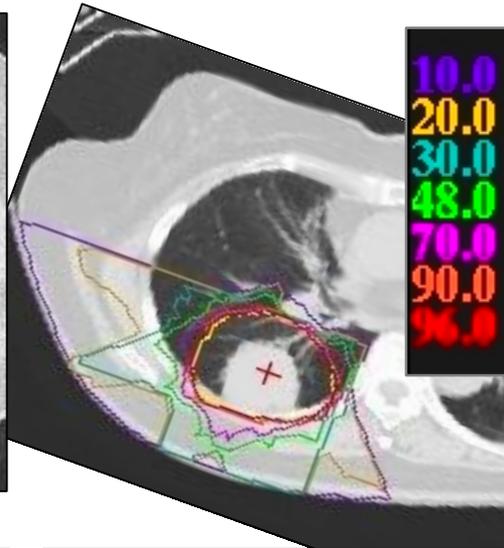
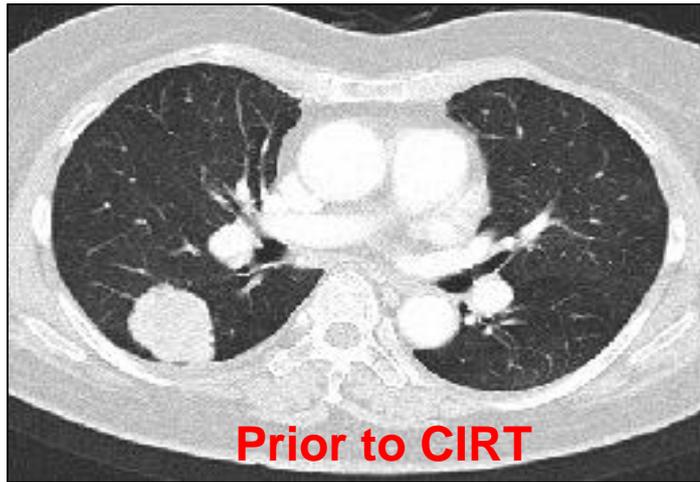
Proton therapy  
at Tsukuba Univ.



Respiratory sensor :  
Semiconductor  
+  
position-sensitive  
detector (PSD)

Infrared LED

# cT2N0M0 Adenocarcinoma 48.0GyE/single fraction

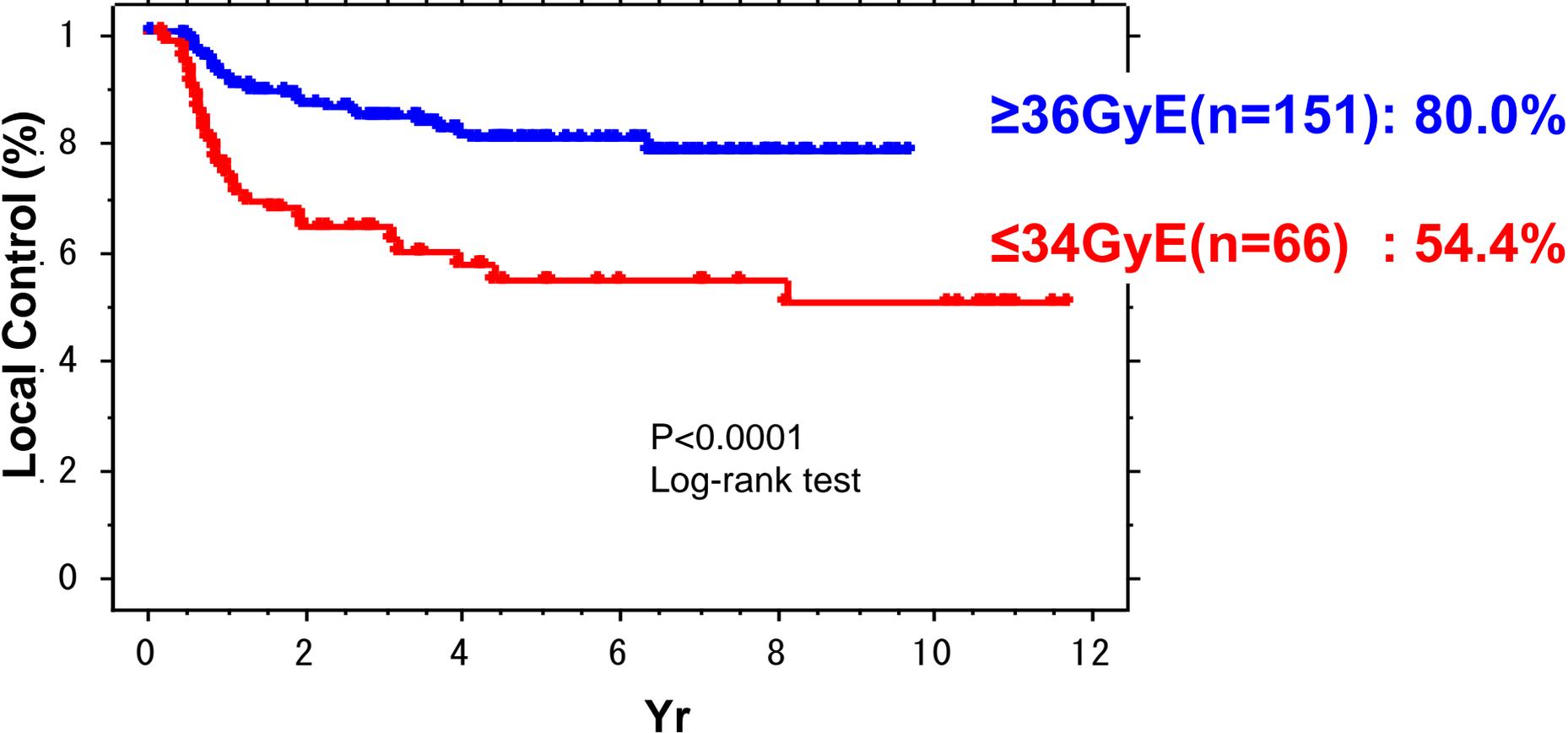


**Grade 1  
skin reaction**

# Lung adverse reaction **single fraction**

| Total dose   | Early (NCI-CTC) |           |            |          |          |          | Late (RTOG/EORTC) |           |            |          |          |          |
|--------------|-----------------|-----------|------------|----------|----------|----------|-------------------|-----------|------------|----------|----------|----------|
|              | No.             | Grade     |            |          |          |          | No.               | Grade     |            |          |          |          |
|              |                 | 0         | 1          | 2        | 3        | 4≤       |                   | 0         | 1          | 2        | 3        | 4≤       |
| 28.0         | 6               | 4         | 2          | 0        | 0        | 0        | 6                 | 2         | 4          | 0        | 0        | 0        |
| 32.0         | 26              | 13        | 13         | 0        | 0        | 0        | 25                | 3         | 22         | 0        | 0        | 0        |
| 34.0         | 34              | 19        | 14         | 1        | 0        | 0        | 33                | 0         | 33         | 0        | 0        | 0        |
| 36.0         | 18              | 12        | 6          | 0        | 0        | 0        | 17                | 2         | 15         | 0        | 0        | 0        |
| 38.0         | 14              | 9         | 5          | 0        | 0        | 0        | 13                | 2         | 11         | 0        | 0        | 0        |
| 40.0         | 20              | 10        | 10         | 0        | 0        | 0        | 19                | 4         | 15         | 0        | 0        | 0        |
| 42.0         | 15              | 10        | 5          | 0        | 0        | 0        | 15                | 1         | 14         | 0        | 0        | 0        |
| 44.0         | 44              | 6         | 37         | 1        | 0        | 0        | 43                | 2         | 40         | 1        | 0        | 0        |
| 46.0         | 20              | 0         | 20         | 0        | 0        | 0        | 19                | 0         | 19         | 0        | 0        | 0        |
| 48.0         | 10              | 0         | 8          | 2        | 0        | 0        | 10                | 0         | 10         | 0        | 0        | 0        |
| 50.0         | 10              | 0         | 10         | 0        | 0        | 0        | 10                | 0         | 10         | 0        | 0        | 0        |
| <b>Total</b> | <b>217</b>      | <b>83</b> | <b>130</b> | <b>4</b> | <b>0</b> | <b>0</b> | <b>210</b>        | <b>16</b> | <b>193</b> | <b>1</b> | <b>0</b> | <b>0</b> |

# 5-Yr Local Control of Single Fraction C-ion RT in Stage I SCSLC

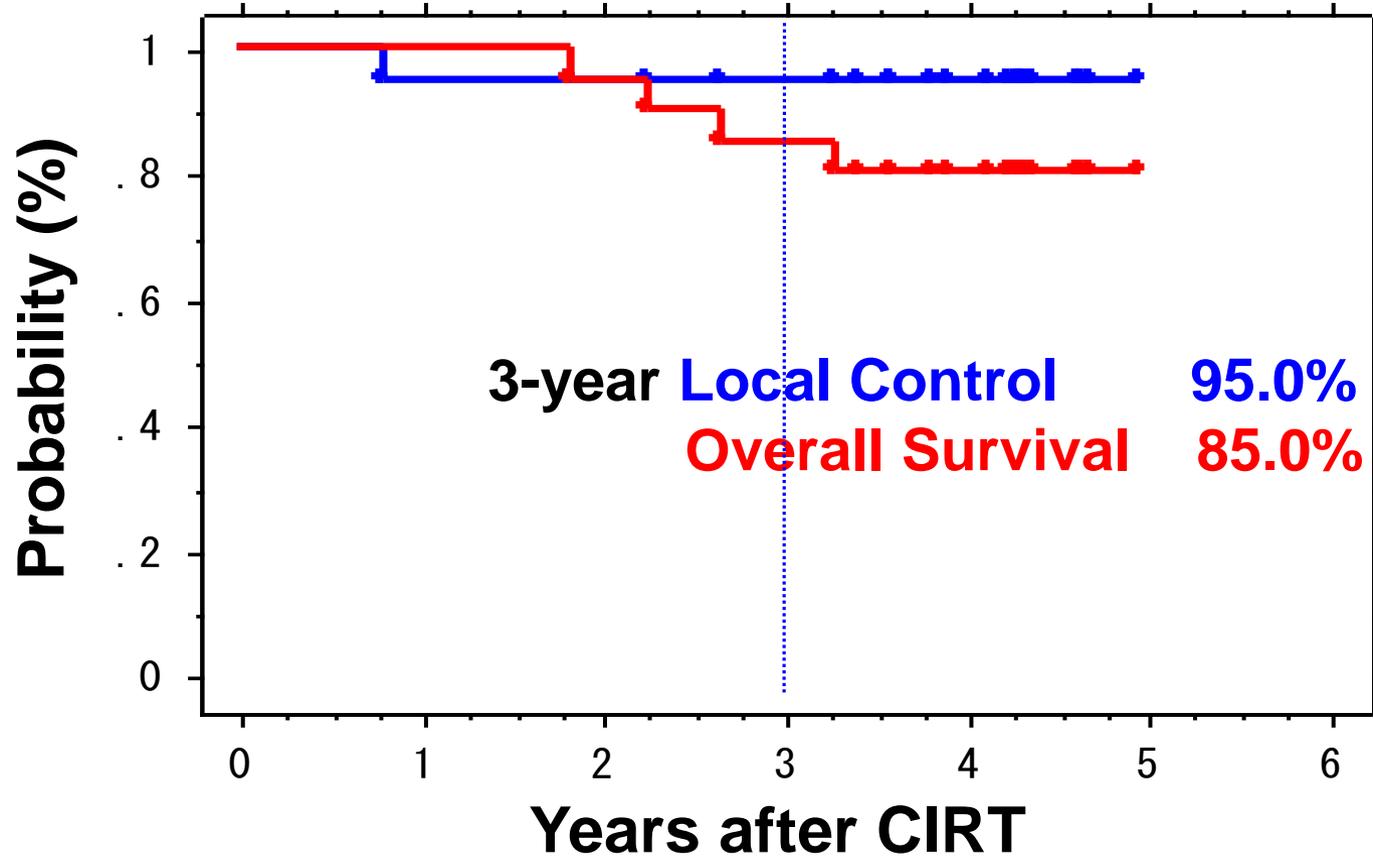


# Toxicities in Pats receiving $\geq 36\text{GyE}$

|                   | Early(NCI-CTC) |            |          |          |          | Late (RTOG/EORTC) |            |          |          |          |
|-------------------|----------------|------------|----------|----------|----------|-------------------|------------|----------|----------|----------|
|                   | No.            | Grade      |          |          |          | No.               | Grade      |          |          |          |
|                   |                | 1          | 2        | 3        | 4 $\leq$ |                   | 1          | 2        | 3        | 4 $\leq$ |
| <b>Skin</b>       | <b>151</b>     | <b>146</b> | <b>3</b> | <b>0</b> | <b>0</b> | <b>151</b>        | <b>143</b> | <b>1</b> | <b>0</b> | <b>0</b> |
| <b>Lung</b>       | <b>151</b>     | <b>101</b> | <b>3</b> | <b>0</b> | <b>0</b> | <b>151</b>        | <b>134</b> | <b>1</b> | <b>0</b> | <b>0</b> |
| <b>Chest Wall</b> | <b>151</b>     | <b>0</b>   | <b>0</b> | <b>0</b> | <b>0</b> | <b>151</b>        | <b>17</b>  | <b>6</b> | <b>1</b> | <b>0</b> |

***For the skin and lung, no toxic reactions greater than grade 2 were observed.***

# Local control and survival rates with $\geq 48.0$ GyE(48.0-50.0GyE) n=20



median follow-up period: 50months (22 to 60)

No toxicities greater than grade 2 were observed in the lungs or skin.



**26-31 JANUARY 2016**  
**WREST POINT, TASMANIA**



**PROFESSOR ANATOLY ROZENFELD,**  
General Chair MMND ITRO  
CMRP, University of Wollongong

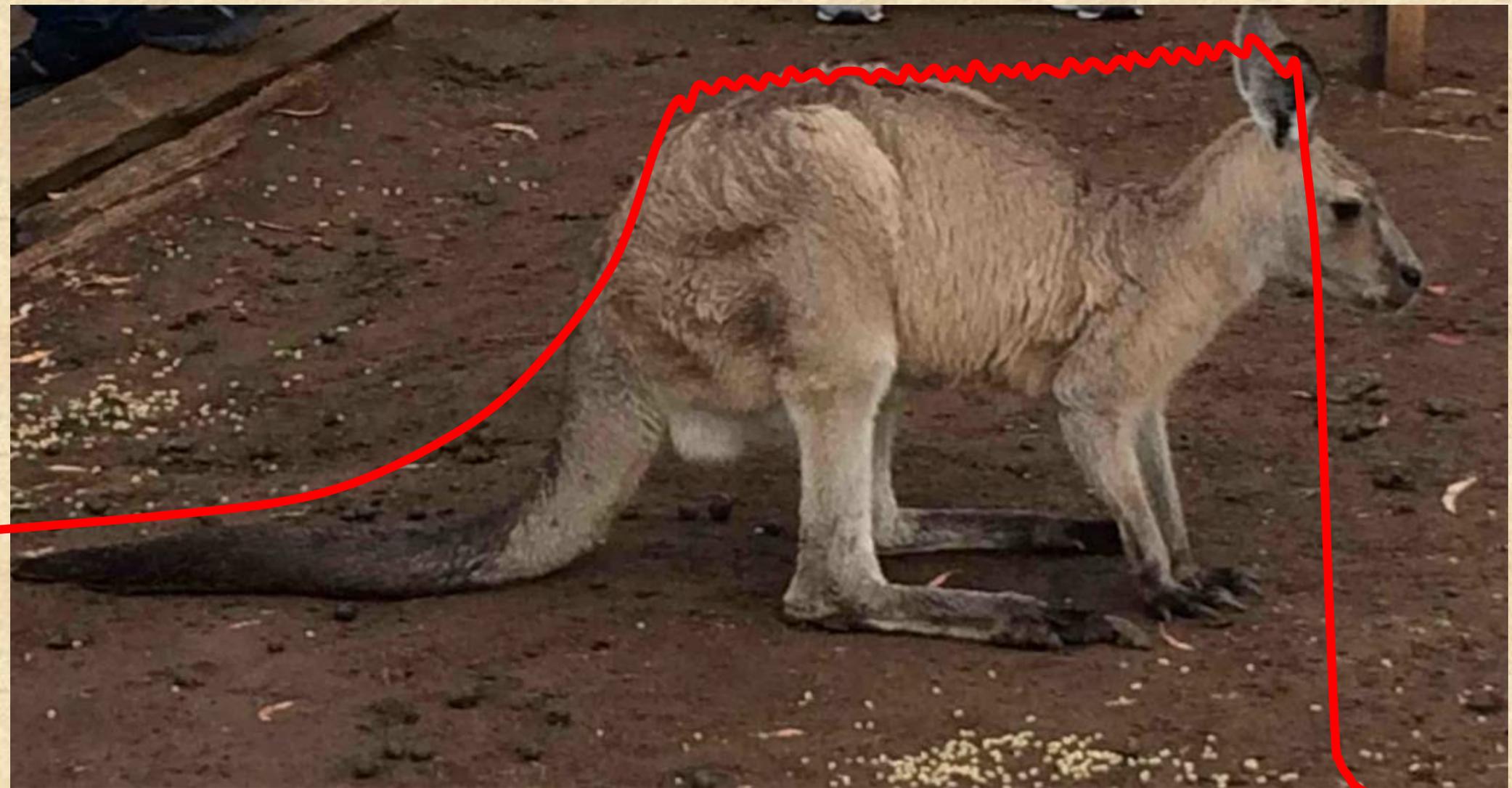


**DR. JOSH YAMADA, MD**



**Bonorong Wildlife Sactuary in Hobart, Tasmania**

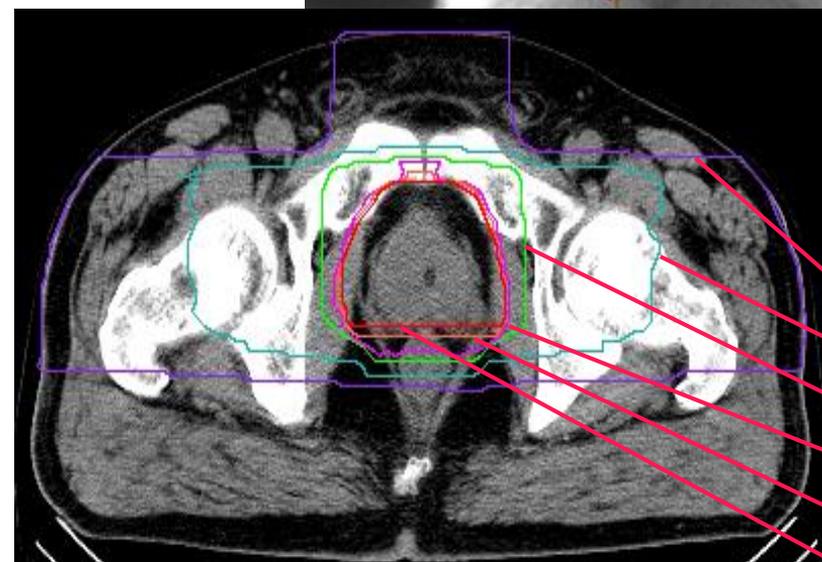
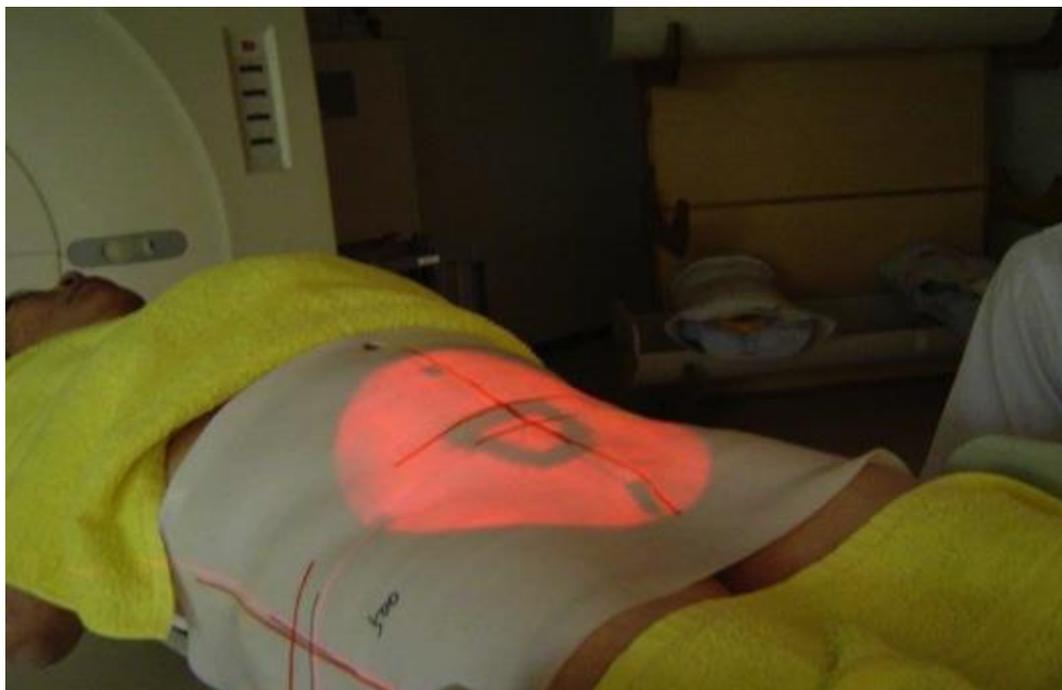
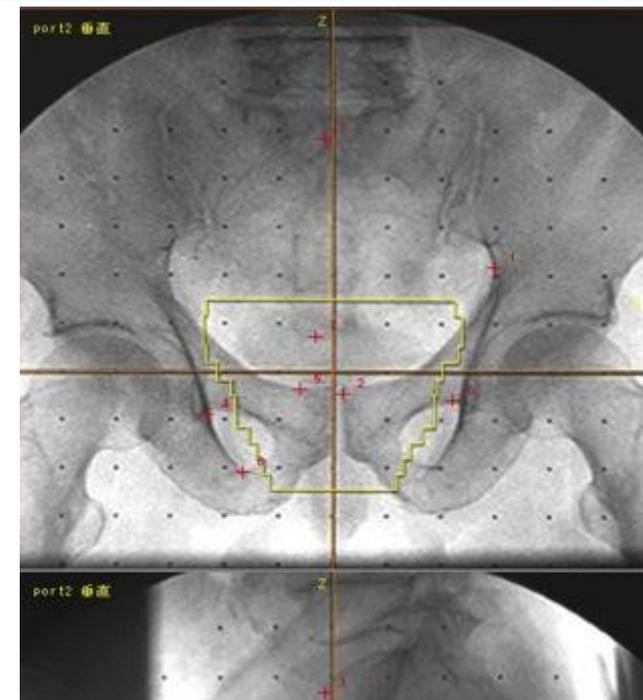




**Bonorong Wildlife Sactuary in Hobart, Tasmania**

# C-ion RT for Prostate Ca

- Rigid immobilization by **body cast + foot rest**.
- Rectum is emptied by laxative or enema, if needed.
- Rectal balloon, metal marker and respiratory gating have **not** been used.



10%  
30%  
50%  
70%  
90%

# C-ion RT for Prostate Cancer at NIRS

Total treated: 2245 pts. Period:95.Jun. ~ 15.Mar.

20fr / 5wks; 562pts, 16f / 4wks; 1107pts, 12f / 3wks; 576pts

| Fractionation                   | Period     | Dose           | No.pts |
|---------------------------------|------------|----------------|--------|
| <u>20fr./5weeks</u>             |            |                |        |
| Phase I/II                      | 95.6~00.2  | 54~72GyE / 20f | 96     |
| Phase II ~ HAMT*<br>(Nov.2003~) | 00.4~07.8  | 63~66GyE / 20f | 466    |
| .....                           |            |                |        |
| <u>16fr./4weeks</u>             |            |                |        |
| HAMT*                           | 03.12~13.2 | 57.6GyE / 16f  | 1,107  |
| .....                           |            |                |        |
| <u>12fr./3weeks</u>             |            |                |        |
| Phase I/II ~ HAMT*              | 10.7~15.3  | 51.6GyE / 12f  | 576    |
| Total                           | 95.6~15.3  |                | 2,245  |

\*AM; Highly Advanced Medicine Technology

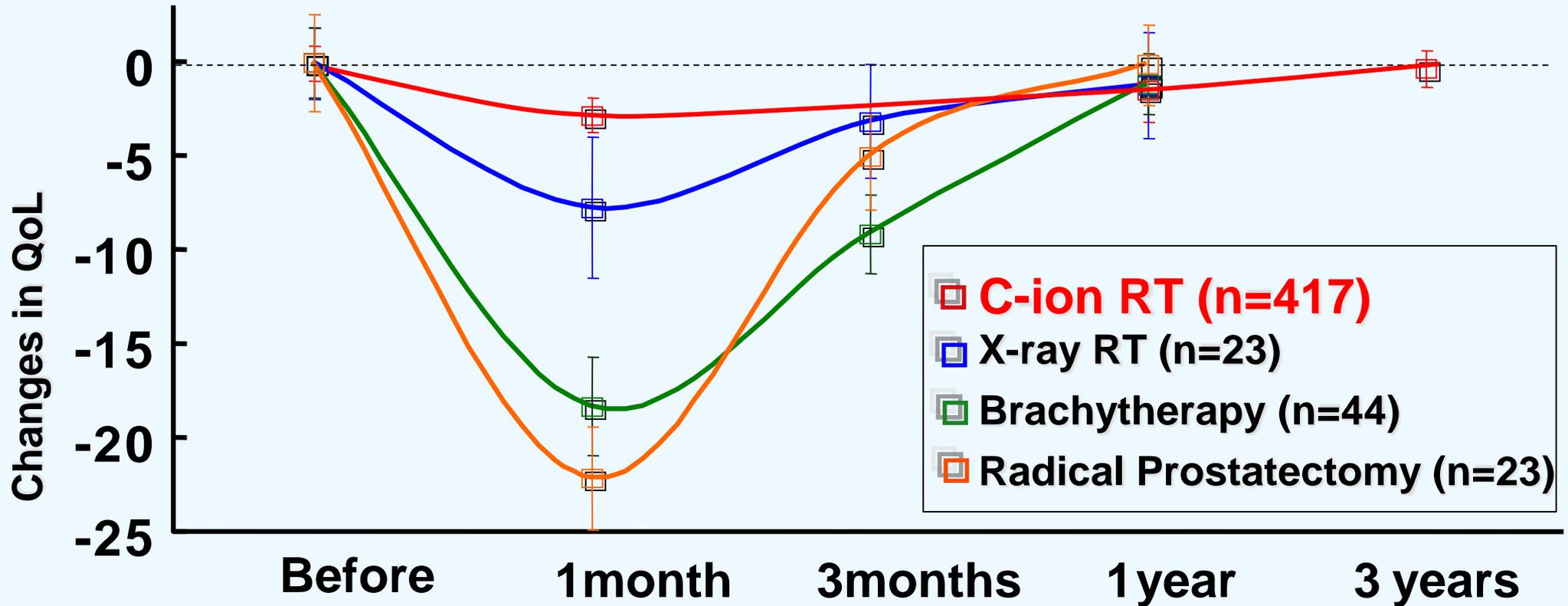
# Late toxicity in Prostate Cancer

| Institutes                        | Treatment | Dose /Fractions         | No. Pts | Late $\geq$ G2 Injury |         |
|-----------------------------------|-----------|-------------------------|---------|-----------------------|---------|
|                                   |           |                         |         | Rectal                | Urinary |
| Princess Margaret H. <sup>1</sup> | IMRT      | 60Gy/20fr               | 92      | 6.3%                  | 10.0%   |
| Cleveland CF. <sup>2</sup>        | IMRT      | 70Gy/28fr               | 770     | 4.4%                  | 5.2%    |
| Stanford U. <sup>3</sup>          | SBRT      | 36.25Gy/5fr             | 41      | 15.0%                 | 29.0%   |
| RTOG 9406 <sup>4</sup>            | 3DCRT     | 68.4-79.2Gy<br>/38-41fr | 275     | 7-16%                 | 18-29%  |
|                                   | 3DCRT     | 78.0Gy/39fr             | 118     | 25-26%                | 23-28%  |
| Loma Linda U. <sup>5</sup>        | Proton    | 75.0Gy(RBE)/39fr        | 901     | 3.5%                  | 5.4%    |
| Japanese PBT group <sup>6</sup>   | Proton    | 74.0Gy(RBE)/37fr        | 151     | 2.0%                  | 4.1%    |
| ACR 0312 <sup>7</sup>             | Proton    | 82.0Gy(RBE)/41fr        | 85      | 25.0%                 | 25.0%   |
| NIRS <sup>8</sup>                 | Carbon    | 57.6Gy(RBE)/16fr        | 1107    | 0.4%                  | 3.7%    |
| Gunma U.                          | Carbon    | 57.6Gy(RBE)/16fr        | 459     | 0.8%                  | 2.8%    |

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.

# Prospective Investigation of Patient Quality of Life After C-ion RT

## Changes of Patient Quality of Life according to Treatment Modality

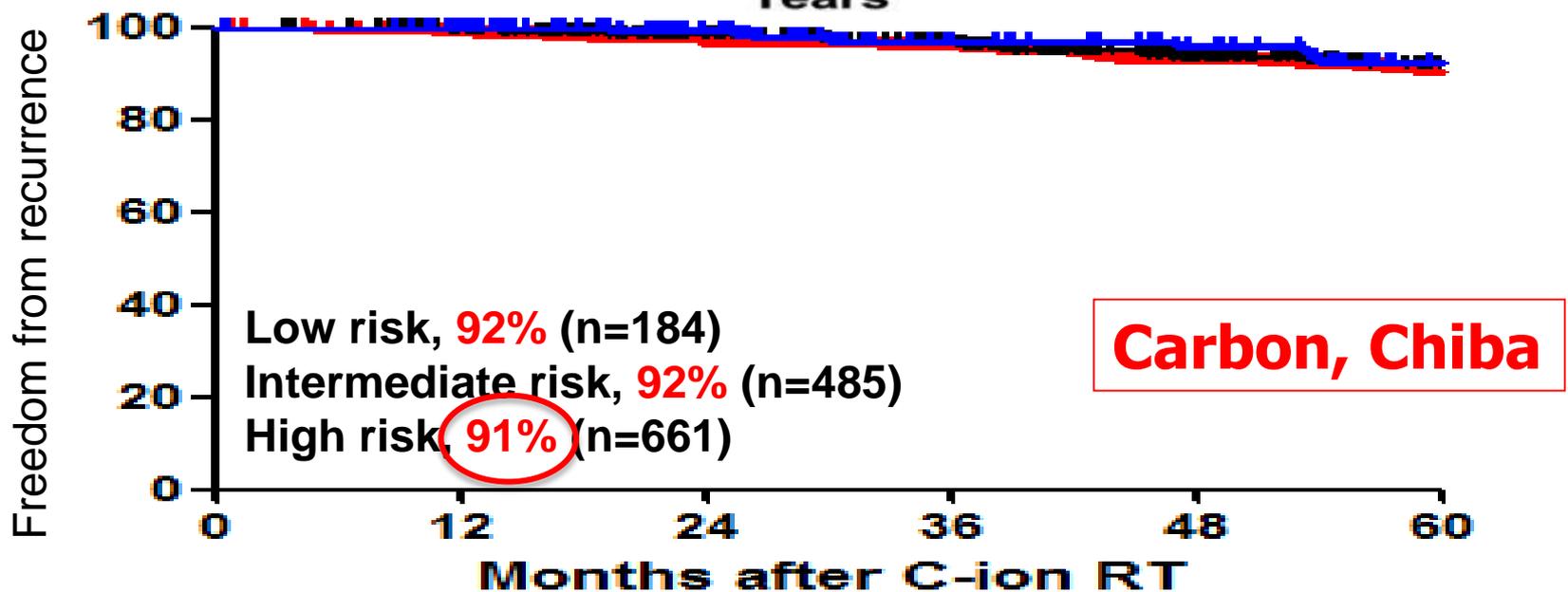
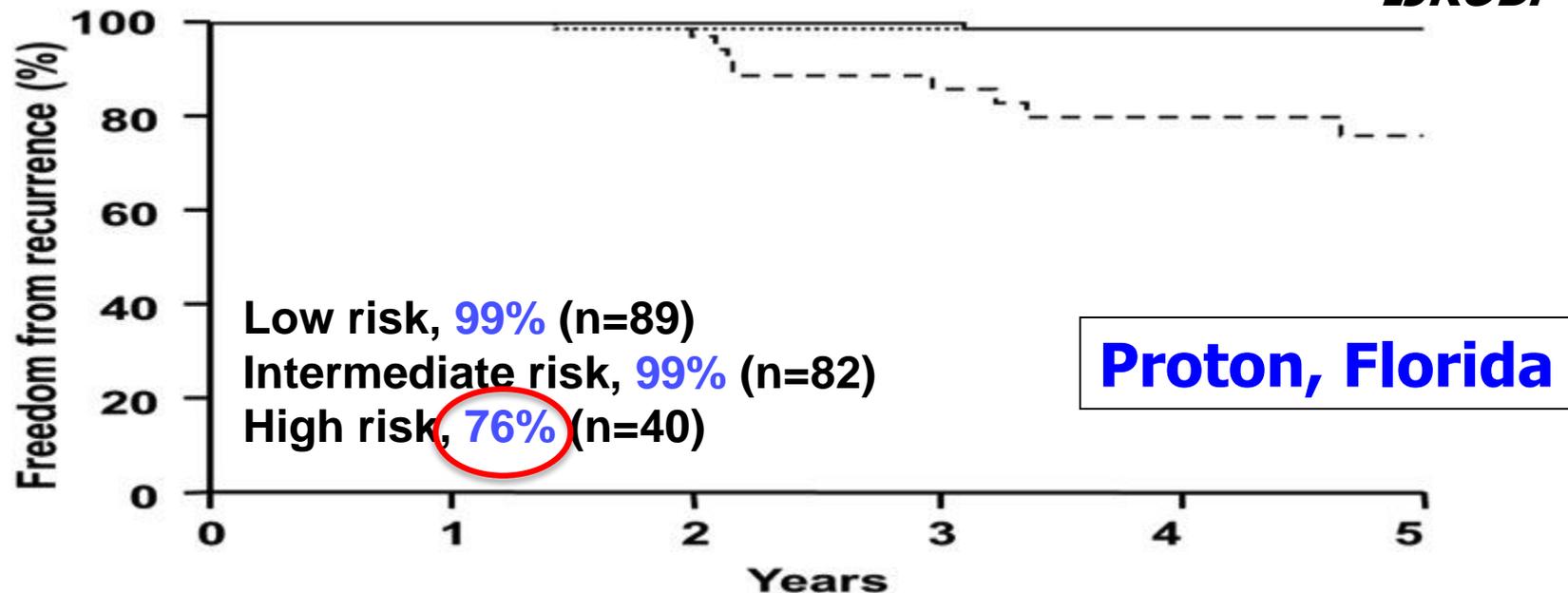


# Outcomes of Radiation Therapy for Prostate Cancer

| Author      | RTx             | No. of patients | Total dose (Gy, GyE / fr.) | 5-year biochemical relapse free rate |              |            |
|-------------|-----------------|-----------------|----------------------------|--------------------------------------|--------------|------------|
|             |                 |                 |                            | Low                                  | Intermediate | High       |
| Zelefsky    | 3DCRT           | 743             | 64.8-81.0 / 36-45          | 85%                                  | 65%          | 35%        |
| Vora        | 3DCRT           | 416             | 66.0-71.0 / 33-38          | 89%                                  | 68%          | 49%        |
| Zelefsky    | IMRT            | 561             | 81.0 / 45                  | 85%                                  | 76%          | 72%        |
| Cahlon      | IMRT            | 478             | 86.4 / 48                  | 98%                                  | 85%          | 70%        |
| Johansson   | 3DCRT + Proton  | 265             | 70.0 / 30                  | 100%                                 | 95%          | 74%        |
| Mendenhall  | Proton          | 211             | 78.0-82.0 / 34-41          | 99%                                  | 99%          | 76%        |
| <b>NIRS</b> | <b>C-ion RT</b> | <b>1649</b>     | <b>51.6-66.0 / 12-20</b>   | <b>92%</b>                           | <b>91%</b>   | <b>90%</b> |

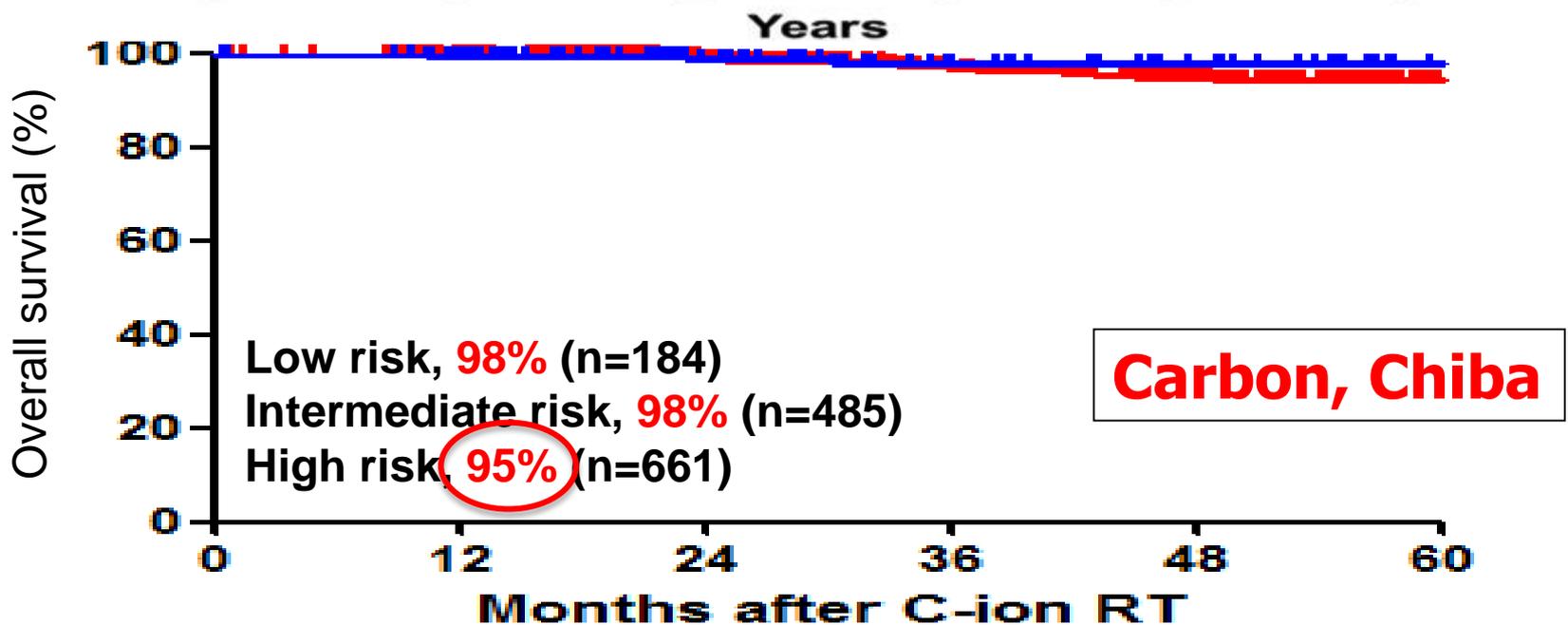
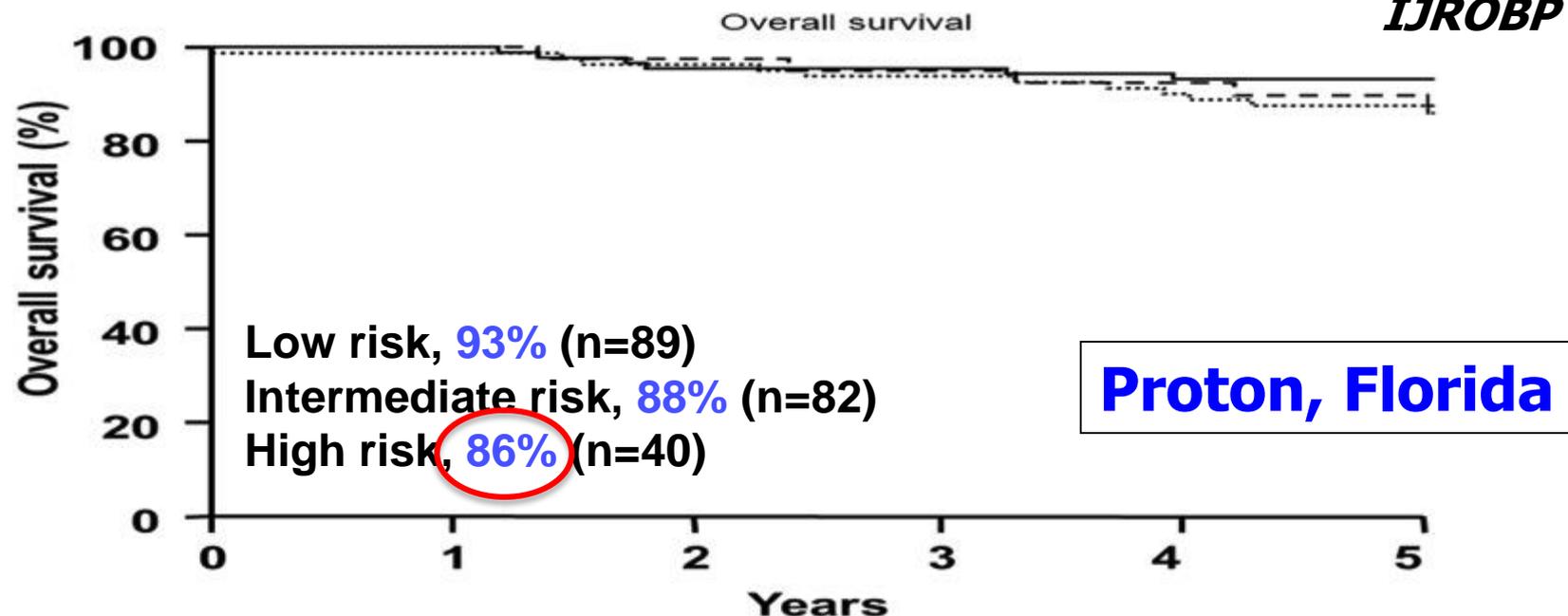
# Biochemical Control Rate Compared with Image-guided Proton Tx

*IJROBP 88, 2014*



# Overall Survival Rate Compared with Image-guided Proton Therapy

*IJROBP 88, 2014*



# *C-ion RT for rectal cancer*

2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014

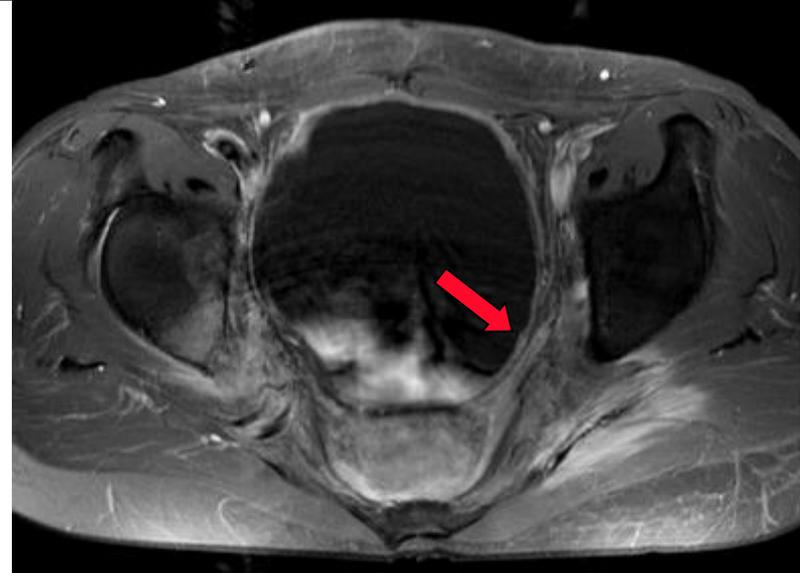
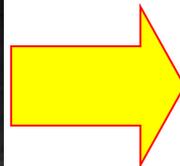
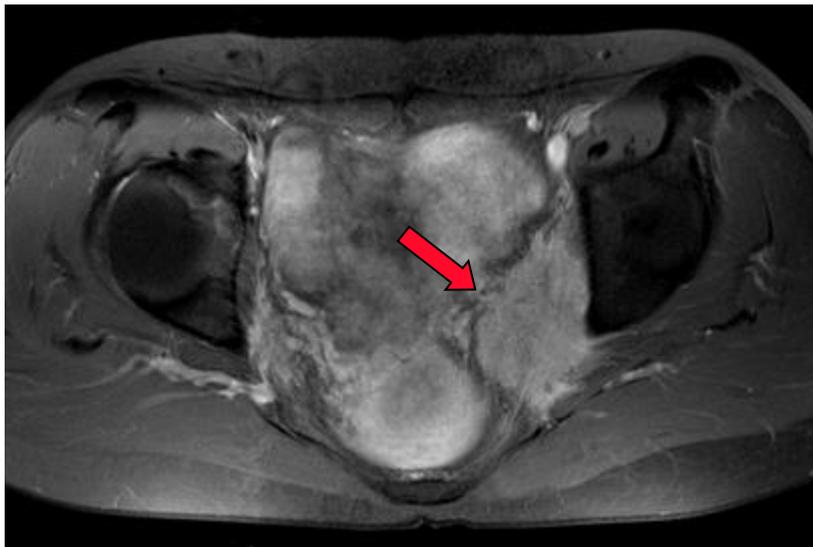
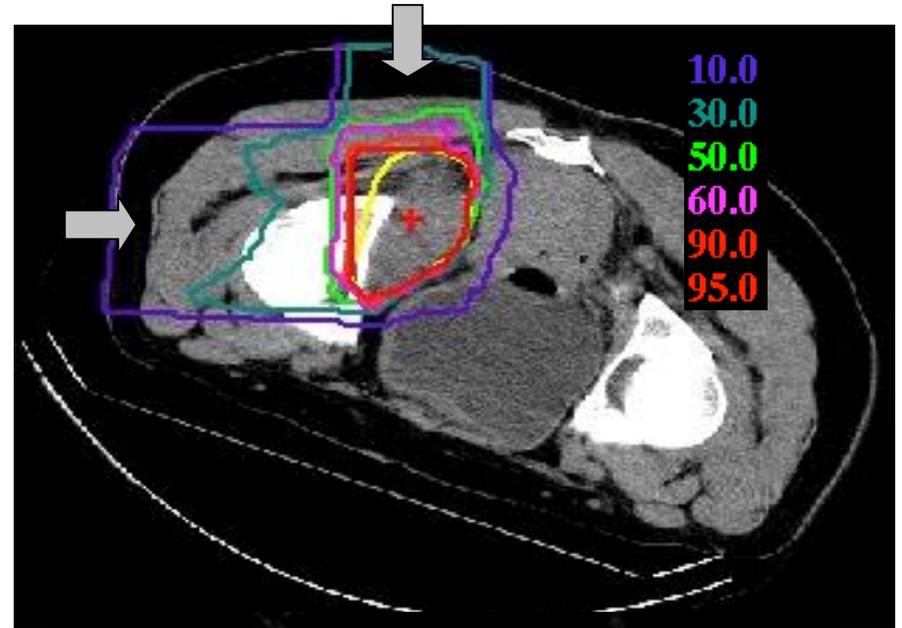
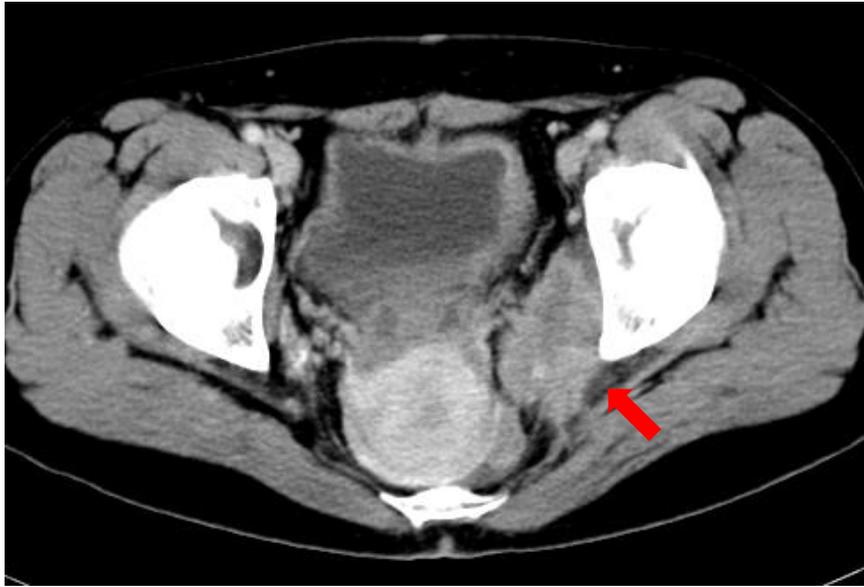
## **C-ion RT for post-op pelvic recurrence**

Indications extended to colon ca and the tumor with bone destruction or distant meta

Development of spacer technique

Re-irradiation after photon RT

59y/o F, 73.6GyE/16fr



**Before**

**12 mo.**

# ***Acute and Late toxicities*** ***by NCI-CTC and RTOG/EORTC Scoring System***

(202 lesions in 189patients)

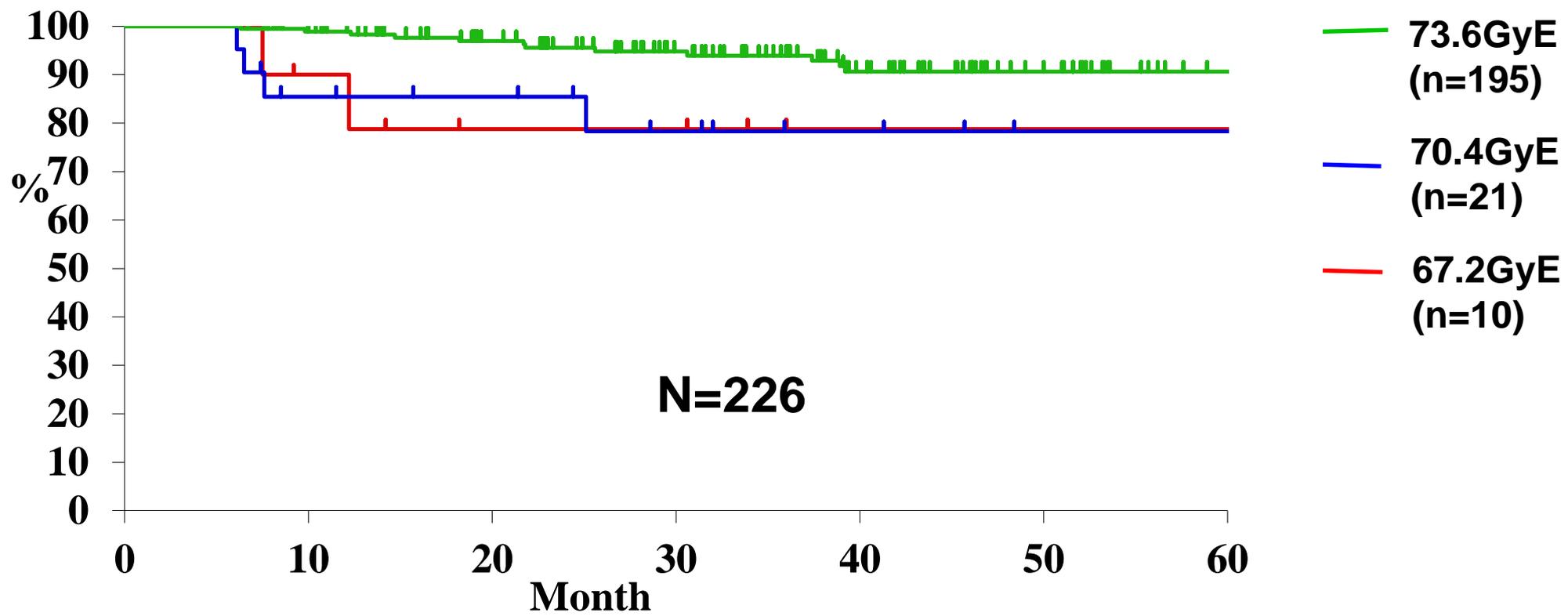
## **Acute(NCI-CTC)**

## **Late(RTOG/EORTC)**

|                 | No. of lesions | Gr0        | Gr1        | Gr2      | Gr3      | Gr4      | No. of lesions | Gr0        | Gr1       | Gr2      | Gr3      | Gr4      |  |
|-----------------|----------------|------------|------------|----------|----------|----------|----------------|------------|-----------|----------|----------|----------|--|
| <b>Skin</b>     | <b>214</b>     | <b>56</b>  | <b>150</b> | <b>8</b> | <b>0</b> | <b>0</b> | <b>214</b>     | <b>127</b> | <b>84</b> | <b>1</b> | <b>2</b> | <b>0</b> |  |
| <b>GI tract</b> | <b>214</b>     | <b>210</b> | <b>0</b>   | <b>4</b> | <b>0</b> | <b>0</b> | <b>214</b>     | <b>210</b> | <b>1</b>  | <b>1</b> | <b>1</b> | <b>0</b> |  |
| <b>Urinary</b>  | <b>214</b>     | <b>213</b> | <b>1</b>   | <b>0</b> | <b>0</b> | <b>0</b> | <b>214</b>     | <b>211</b> | <b>1</b>  | <b>2</b> | <b>0</b> | <b>0</b> |  |

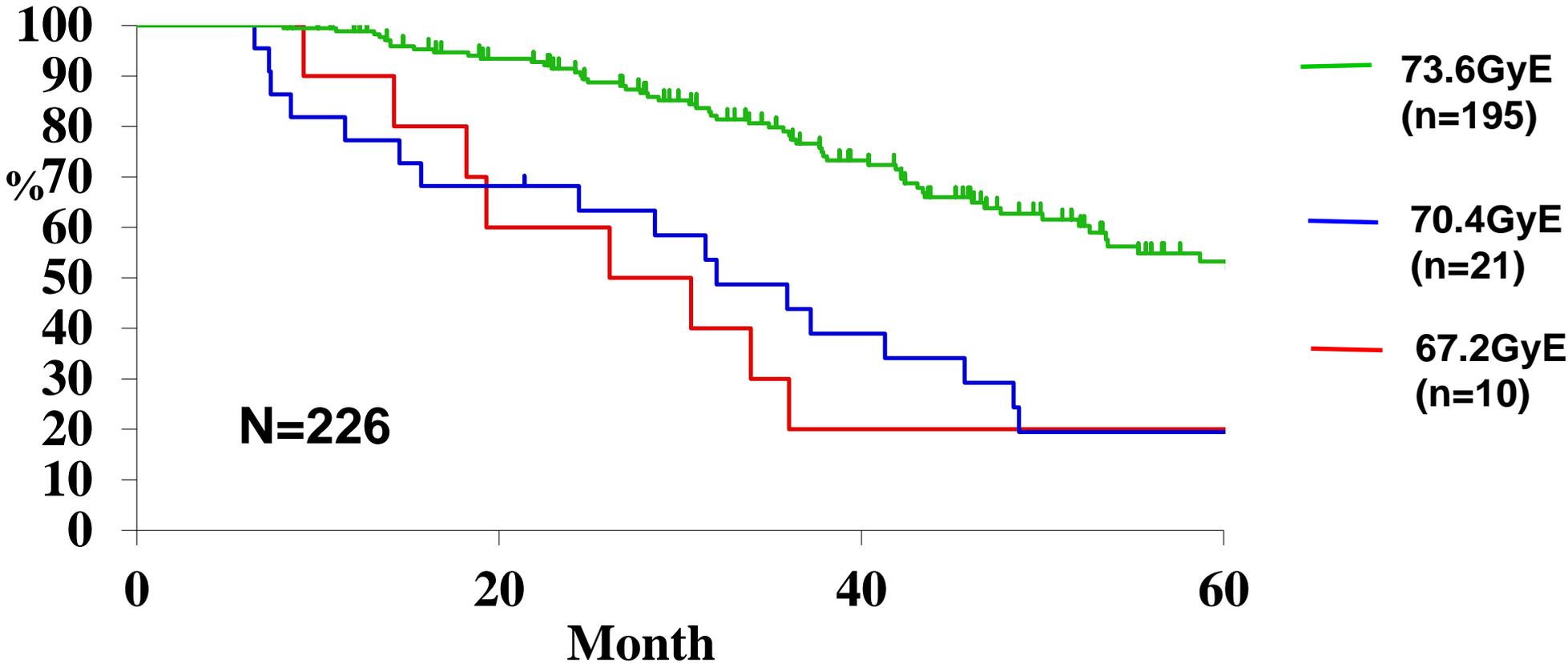
**No grade 3 to 5 toxicity was observed.**

# Local Control by Total Dose



|         | No  | 1 yr  | 3 yr  | 5 yr  |
|---------|-----|-------|-------|-------|
| 67.2GyE | 10  | 90.0% | 78.8% | 78.8% |
| 70.4GyE | 21  | 86.1% | 79.5% | 79.5% |
| 73.6GyE | 195 | 98.4% | 93.9% | 90.9% |

# Survival by Total Dose



|         | No  | 1 yr  | 3 yr  | 5 yr  |
|---------|-----|-------|-------|-------|
| 67.2GyE | 10  | 90.0% | 20.0% | 20.0% |
| 70.4GyE | 21  | 77.3% | 43.4% | 19.5% |
| 73.6GyE | 195 | 98.4% | 74.6% | 50.5% |

# Comparison of C-ion RT with **surgery** in post-op pelvic recurrence of rectal cancer

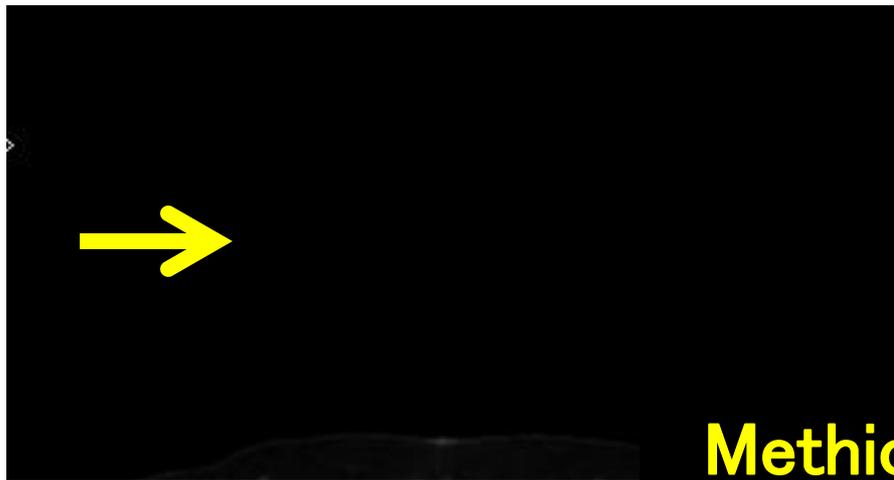
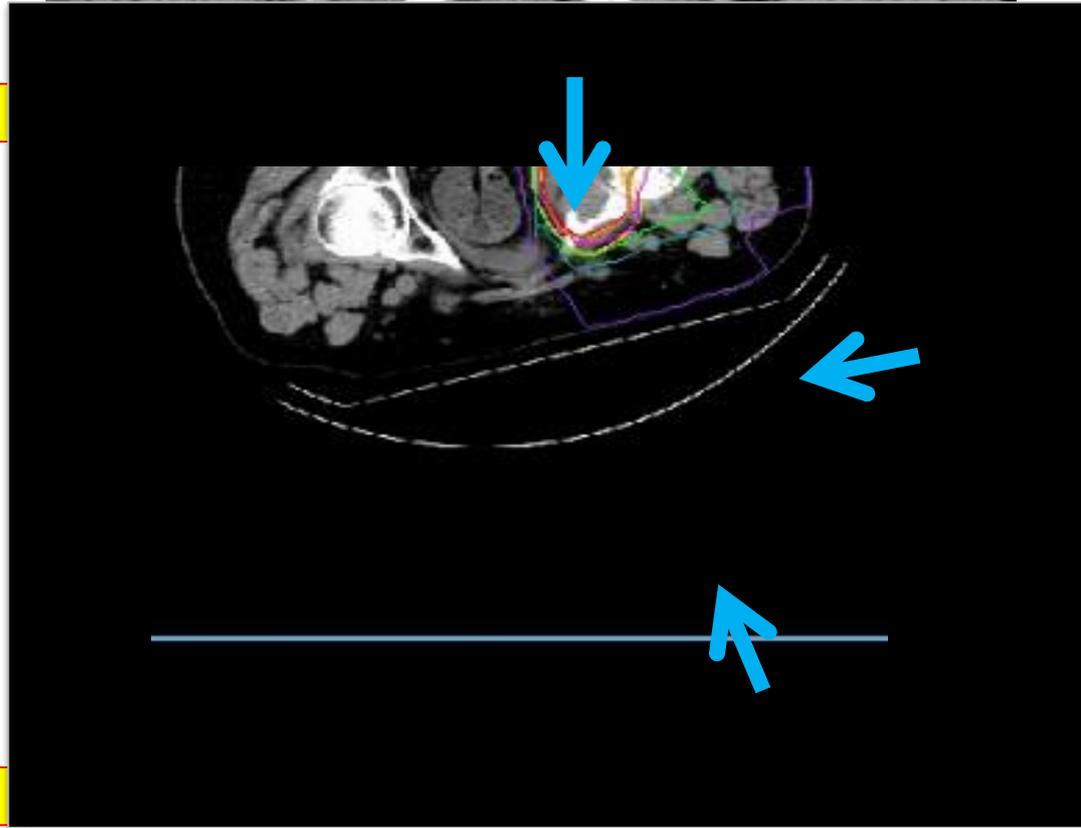
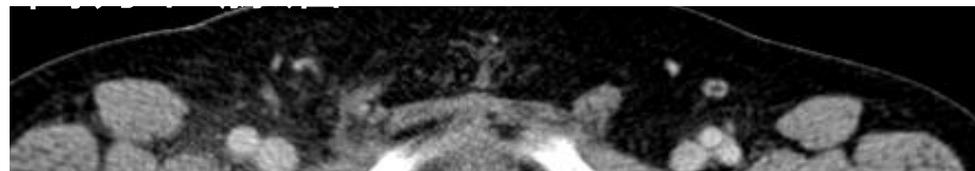
| Author           | Yr          | No         | Survival rate |            |            |
|------------------|-------------|------------|---------------|------------|------------|
|                  |             |            | 1 yr          | 2 yr       | 5 yr       |
| Kato             | 1994        | 32         | 93%           | 82%        | 46%        |
| Garcia-Aguilar J | 1999        | 42         | 88%           | 62%        | 35%        |
| Wanebo           | 1999        | 53         | 91%           | 62%        | 31%        |
| Salo JC          | 1999        | 71         | 88%           | 75%        | 31%        |
| Saito N          | 2003        | 43         | 91%           | 78%        | 39%        |
| Moriya           | 2004        | 48         | 95%           | 76%        | 36%        |
| <b>NIRS</b>      | <b>2015</b> | <b>195</b> | <b>98%</b>    | <b>91%</b> | <b>51%</b> |

1) Gastroentero Surg 21:105, 1982) Dis Colon Rectum 42:1438, 1999, 3) Dis Colon Rectum 42:1438, 1999, 4) Ann Surg Oncol 6:171, 1999, 5) Dig Surg 20:192, 2003, 6) Dis Colon Rectum 47:2047, 2004, 7) 48th ASTRO meeting, 2006

61y/o M, 73.6GyE/16fr



Before



Methionine PET



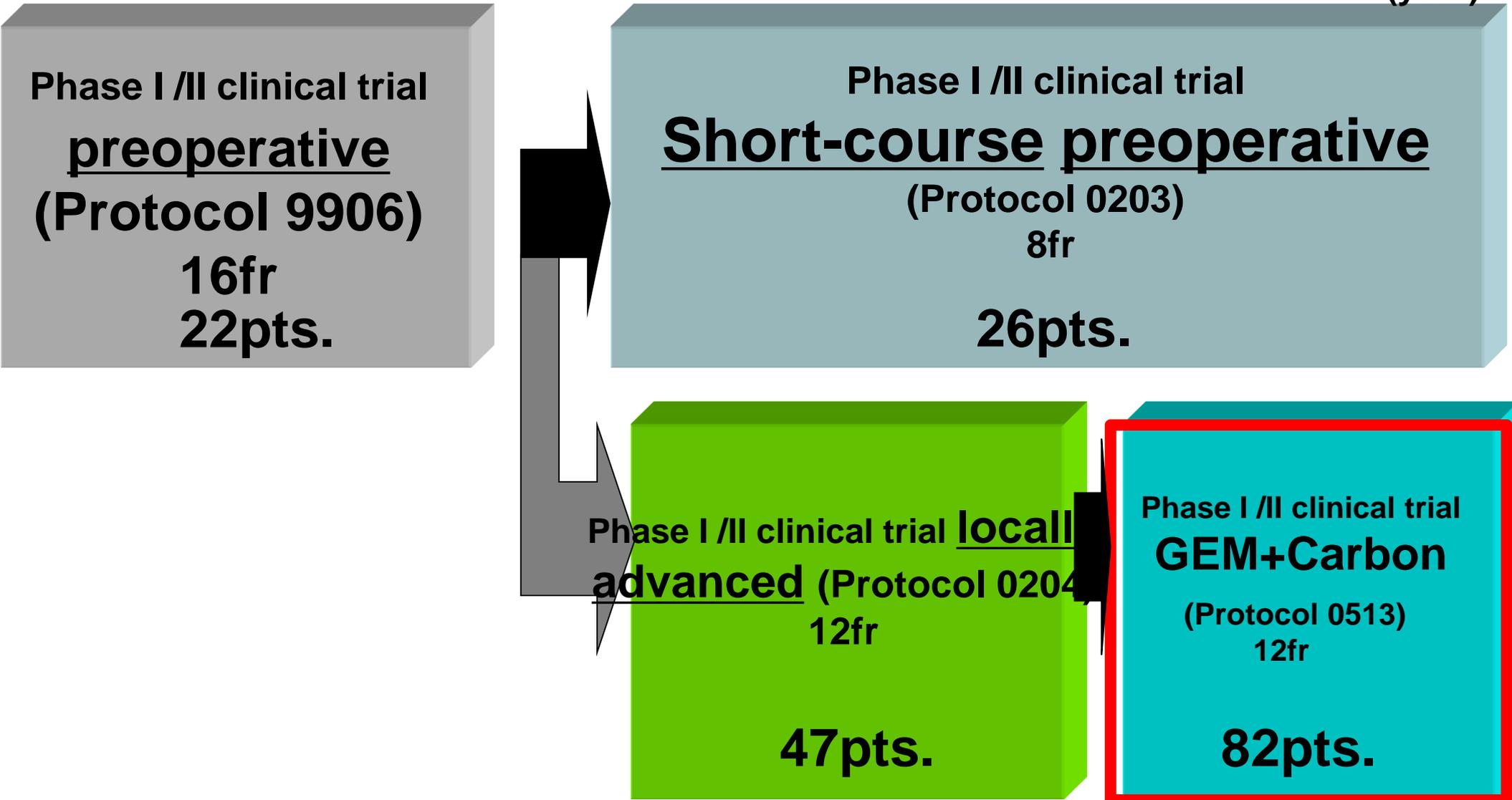
**Bonorong Wildlife Sactuary in Hobart, Tasmania**



**Bonorong Wildlife Sactuary in Hobart, Tasmania**

# C-ion RT for Pancreas Cancer at NIRS

2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 (year)

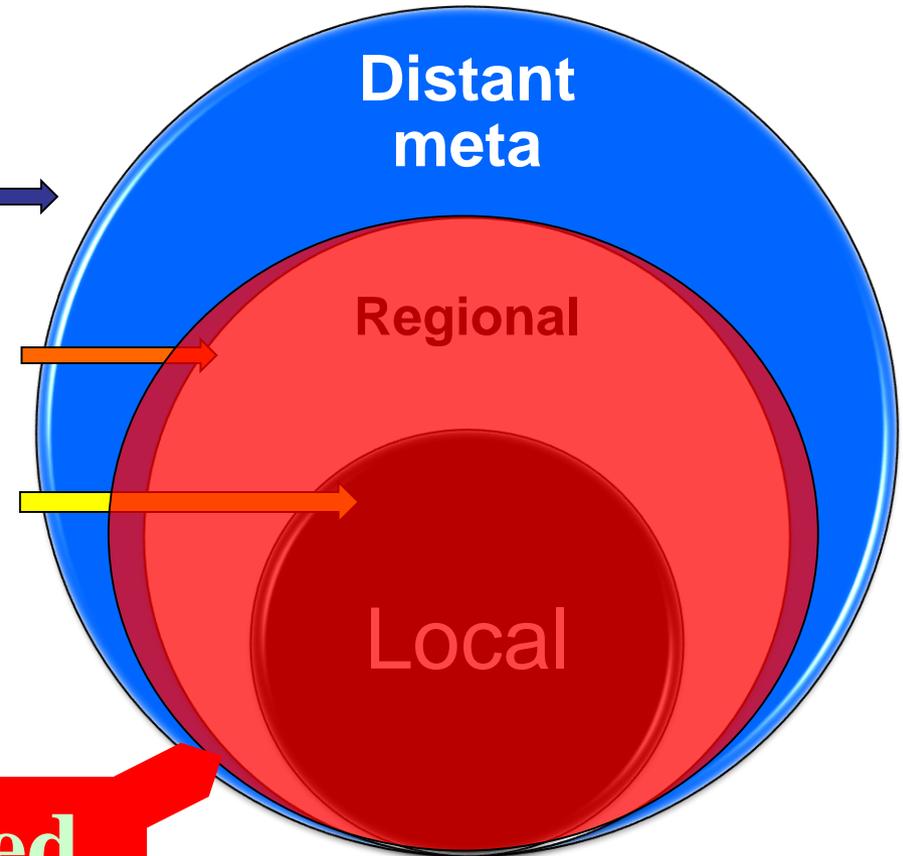


# Pattern of Local Recurrence after Operation in Pancreatic Cancer

|                          |                  |
|--------------------------|------------------|
| <b>Recurrent sites</b>   | <b>140 cases</b> |
| <b>Neuroplexus</b>       | <b>120 (86%)</b> |
| <b>Residual Pancreas</b> | <b>28 (20%)</b>  |

# Sites of failures in pancreatic cancer

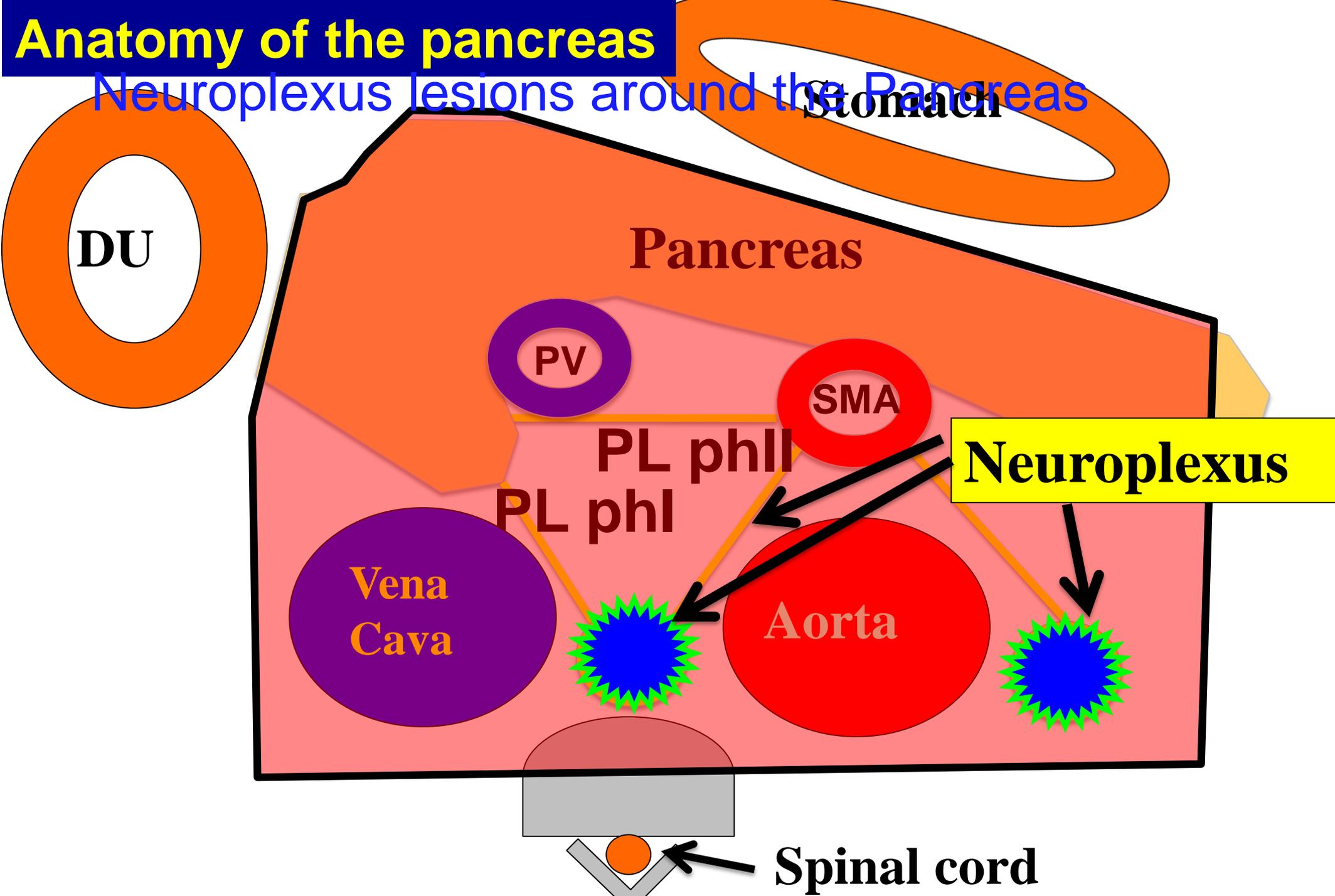
1. Easy distant metastasis
2. Easy infiltration of neuroplexus
3. Large radioresistant cell fraction



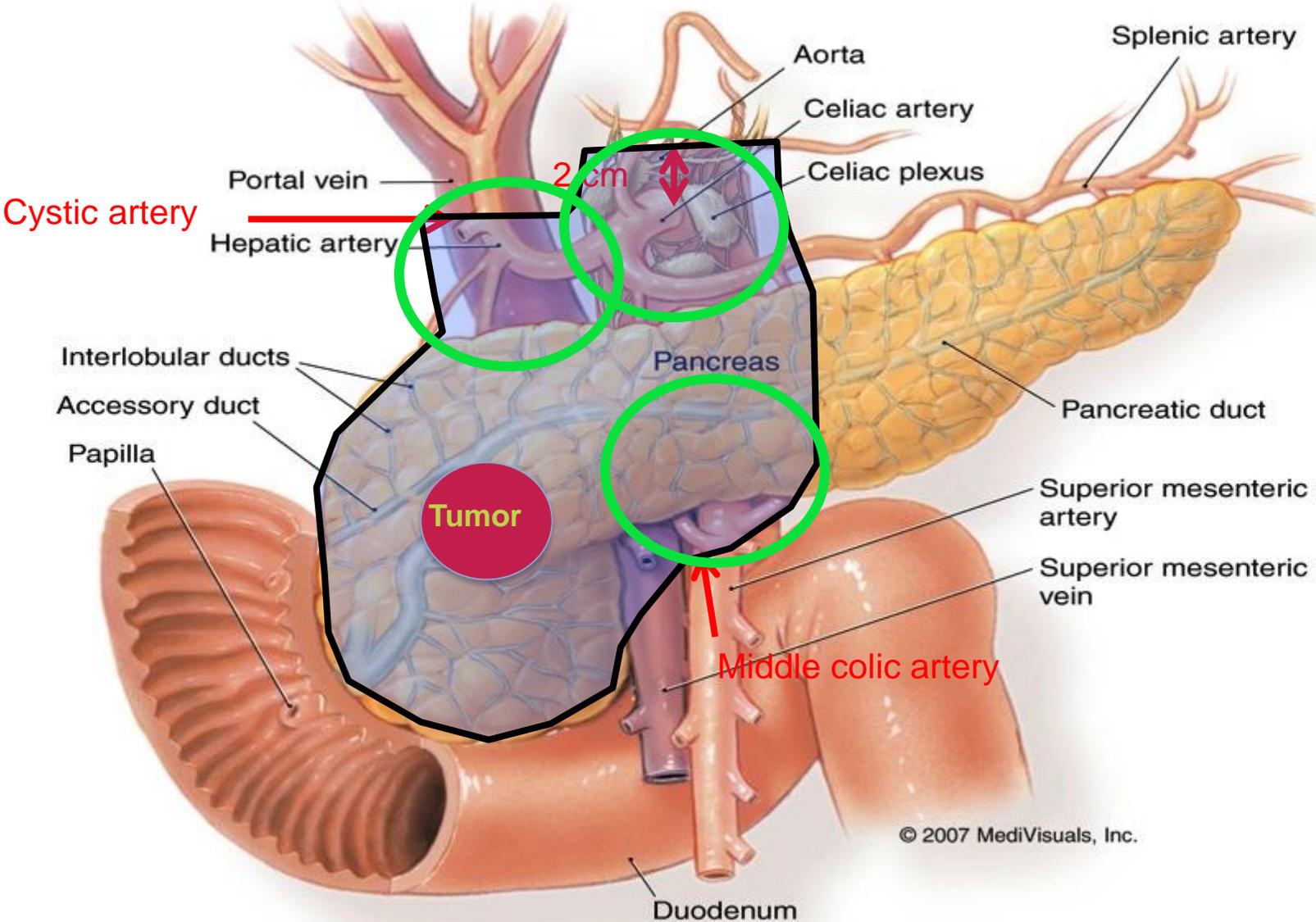
**Carbon-ion can be expected to control these regions.**

# Anatomy of the pancreas

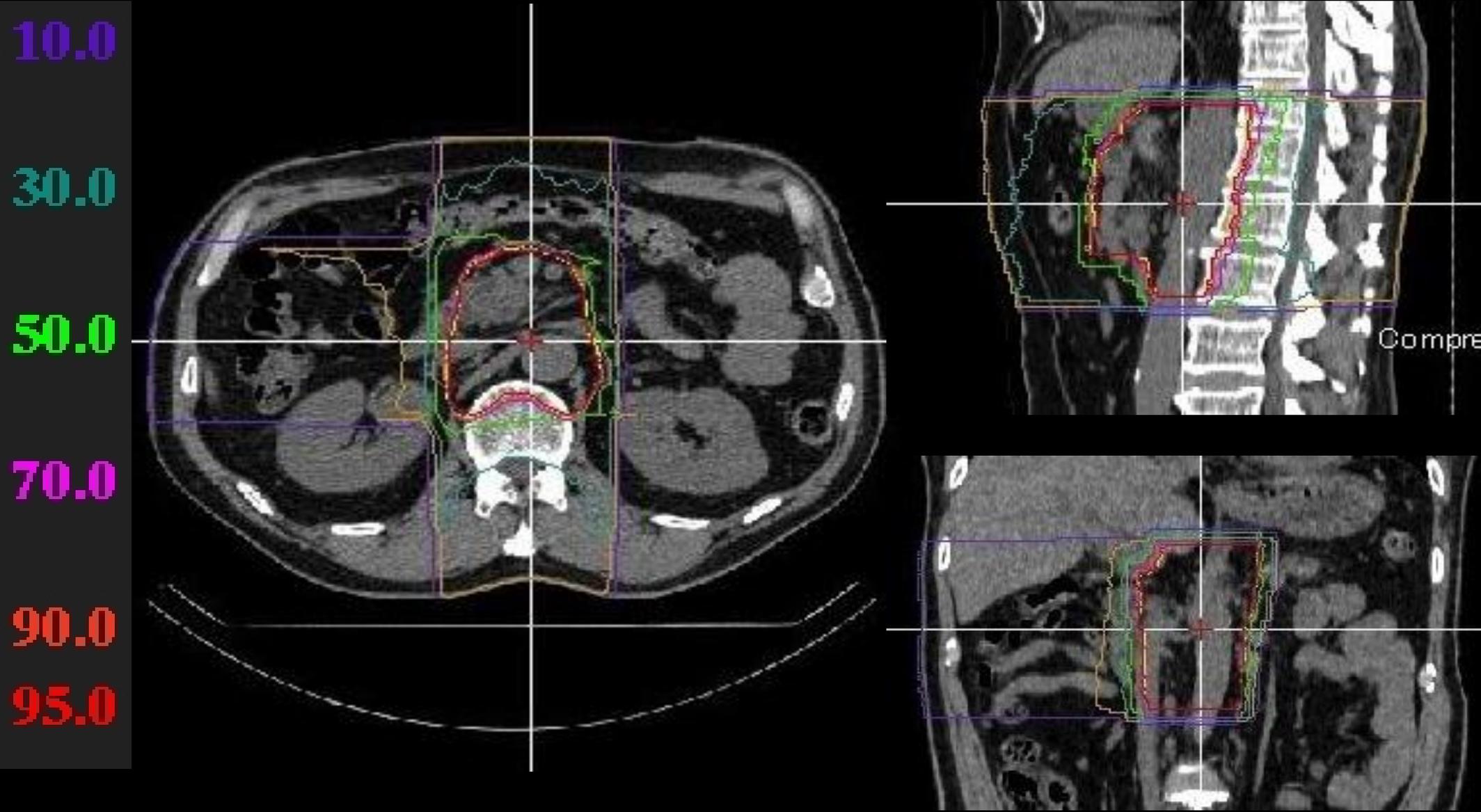
## Neuroplexus lesions around the Pancreas

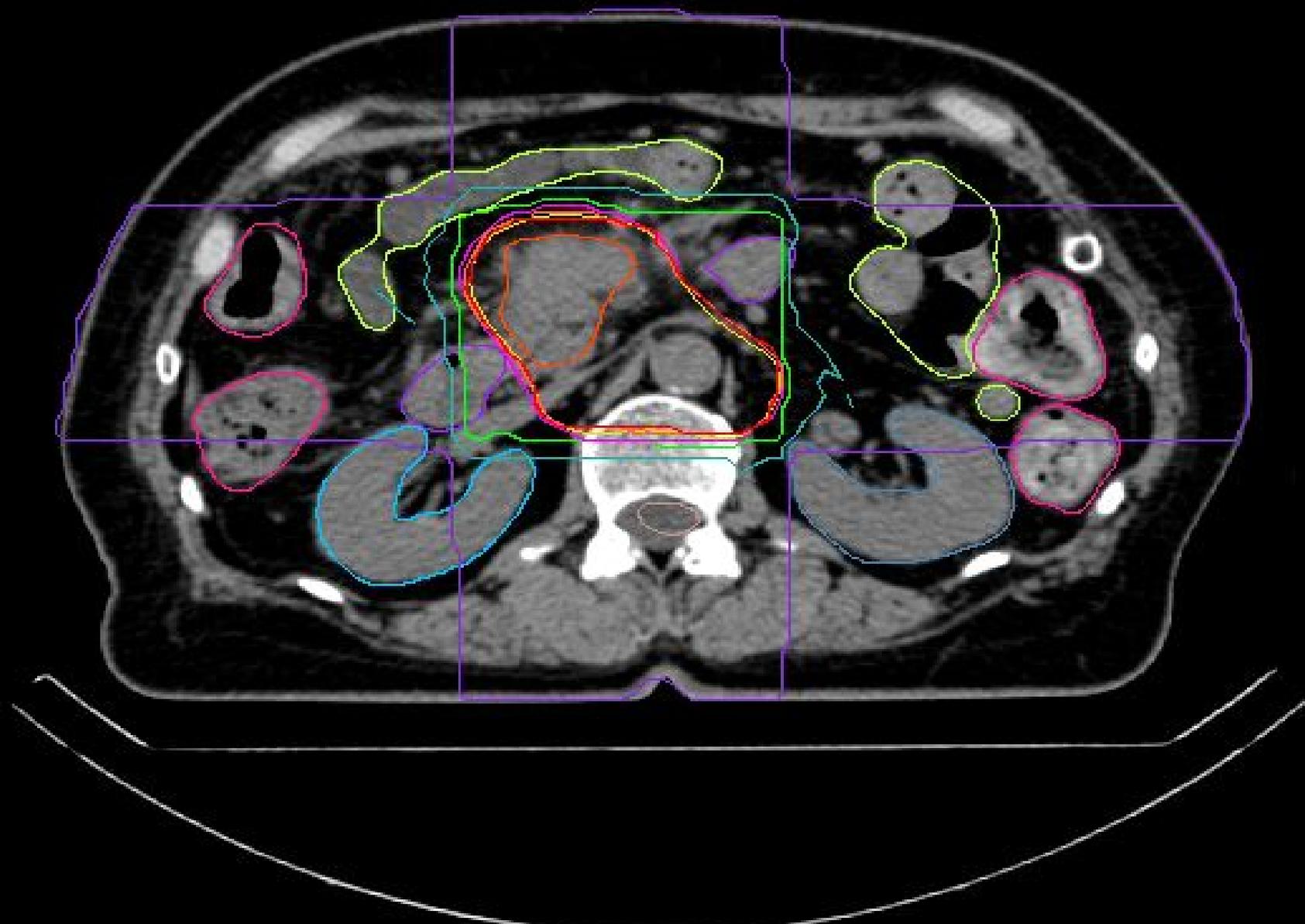


# Radiation Field for Pancreatic head cancer



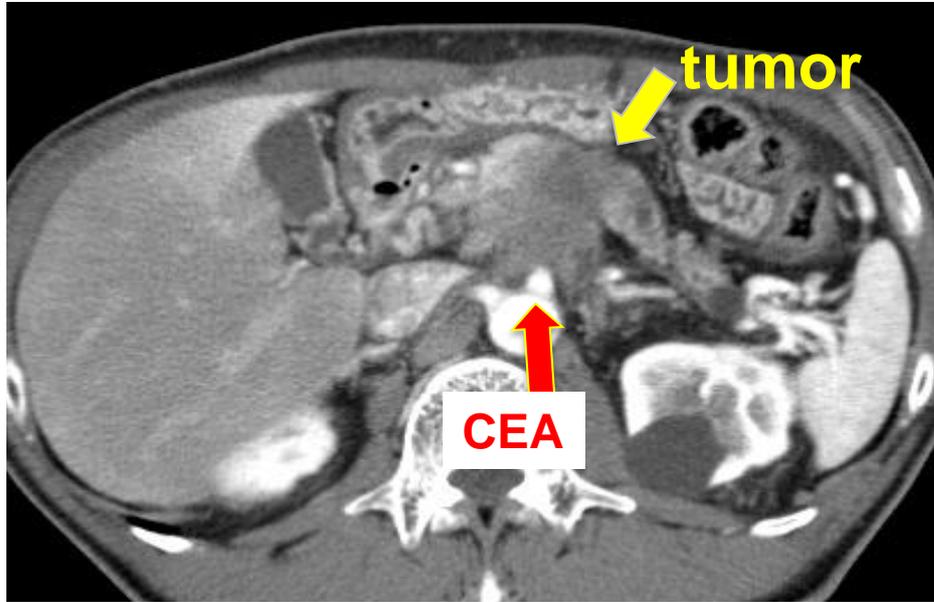
# Dose Distribution of Pancreas Head Ca





# Case: 56y Male Pancreatic body cancer

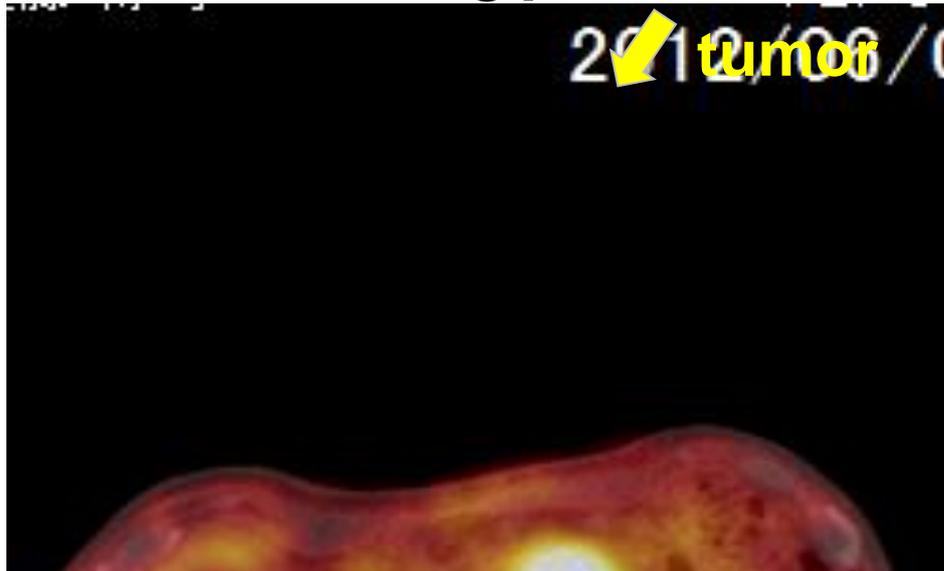
52.8GyE/12fr



CT



12 M after treatment



FDG PET



12 M after treatment

Clinical Investigation

# Carbon Ion Radiation Therapy With Concurrent Gemcitabine for Patients With Locally Advanced Pancreatic Cancer

Makoto Shinoto, MD,<sup>\*,†,‡</sup> Shigeru Yamada, MD, PhD,<sup>\*</sup>  
Kotaro Terashima, MD, PhD,<sup>‡</sup> Shigeo Yasuda, MD, PhD,<sup>\*</sup>  
Yoshiyuki Shioyama, MD, PhD,<sup>†</sup> Hiroshi Honda, MD, PhD,<sup>‡</sup>  
Tadashi Kamada, MD, PhD,<sup>\*</sup> Hirohiko Tsujii, MD, PhD,<sup>\*</sup>  
and Hiromitsu Saisho, MD, PhD,<sup>§</sup> the Working Group for Pancreas  
Cancer

*<sup>\*</sup>Hospital of Research Center for Charged Particle Therapy, National Institute of Radiological Sciences, Chiba, Japan; <sup>†</sup>Ion Beam Therapy Center, SAGA HIMAT Foundation, Tosu, Japan; <sup>‡</sup>Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; and <sup>§</sup>Department of Internal Medicine and Clinical Oncology, Kaken Hospital, Chemotherapy Research Institute, Chiba, Japan*

Received Sep 17, 2015, and in revised form Dec 14, 2015. Accepted for publication Dec 15, 2015.

## Summary

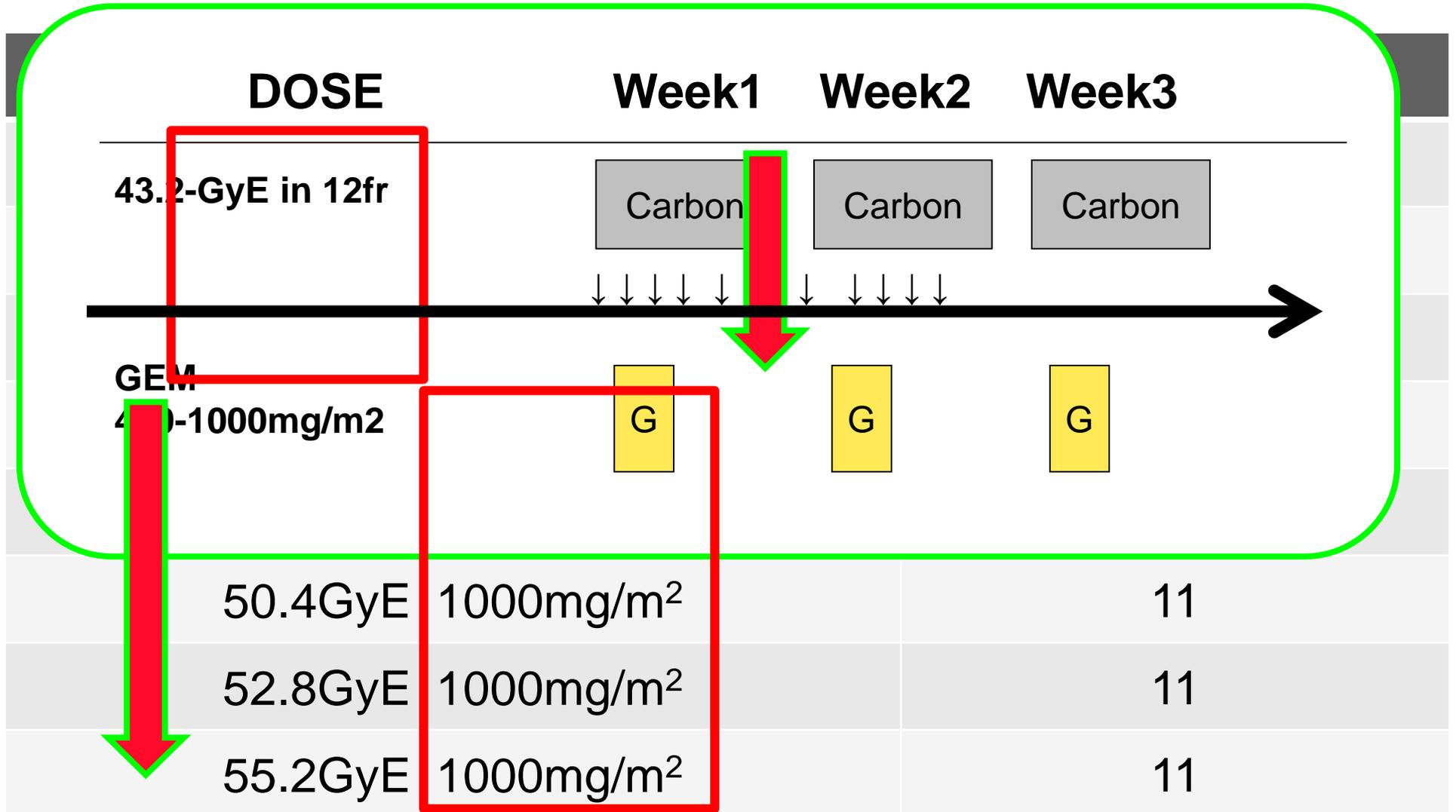
Carbon ion radiation therapy is a unique external radiation therapy that has an excellent dose conformity and higher biological effectiveness compared with conventional radiation therapy. We performed a dose escalation study of carbon ion radiation therapy plus concurrent gemcitabine in 72 patients with locally advanced

**Purpose:** To determine, in the setting of locally advanced pancreatic cancer, the maximum tolerated dose of carbon ion radiation therapy (C-ion RT) and gemcitabine dose delivered concurrently and to estimate local effect and survival.

**Methods and Materials:** Eligibility included pathologic confirmation of pancreatic invasive ductal carcinomas and radiographically unresectable disease without metastasis. Concurrent gemcitabine was administered on days 1, 8, and 15, and the dose levels were escalated from 400 to 1000 mg/m<sup>2</sup> under the starting dose level (43.2 GyE) of C-ion RT. The dose levels of C-ion RT were escalated from 43.2 to 55.2 GyE at 12 fractions under the fixed recommended gemcitabine dose determined.

**Results:** Seventy-six patients were enrolled. Among the 72 treated patients, dose-limiting toxicity was observed in 3 patients: grade 3 infection in 1 patient and grade 4 neutropenia in 2 patients. Only 1 patient experienced a late grade 3 gastric ulcer and bleeding 10 months after C-ion RT. The recommended dose of gemcitabine with C-ion

# Dose escalation in LAPC

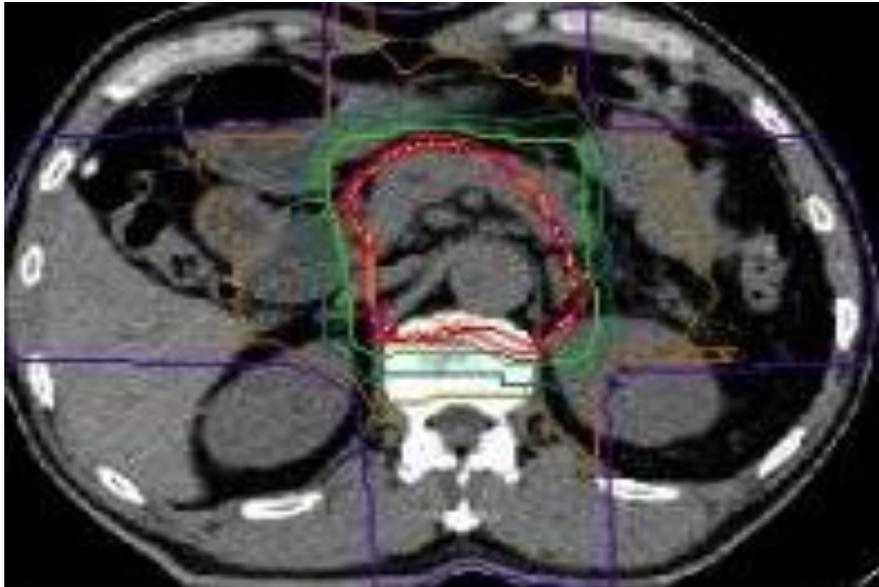


# Upper GI acute and late toxicity by total dose

| Carbon · GEM                                   | n  | 0  | 1 | 2 | 3 | 4 | 5 |
|--|----|----|---|---|---|---|---|
| 43.2GyE ·<br>400 · 700 · 1000mg/m <sup>2</sup> | 24 | 24 | 0 | 0 | 0 | 0 | 0 |
| 45.6GyE · 1000mg/m <sup>2</sup>                | 7  | 7  | 1 | 0 | 0 | 0 | 0 |
| 48.0GyE · 1000mg/m <sup>2</sup>                | 8  | 8  | 1 | 0 | 0 | 0 | 0 |
| 50.4GyE · 1000mg/m <sup>2</sup>                | 11 | 10 | 0 | 1 | 1 | 0 | 0 |
| 52.8GyE · 1000mg/m <sup>2</sup>                | 11 | 10 | 1 | 3 | 0 | 0 | 0 |
| 55.2GyE · 1000mg/m <sup>2</sup>                | 11 | 6  | 0 | 5 | 0 | 0 | 0 |

**Dose distribution**

Case 1

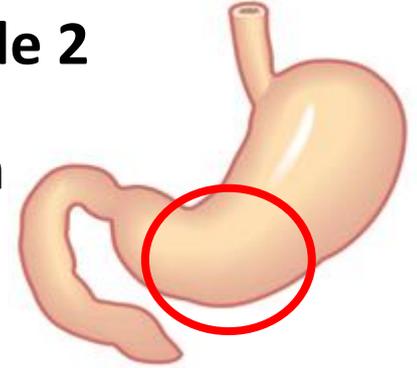


**0513-67 71y Male**

**55.2GyE · 1000mg/m<sup>2</sup>**

**Gastric Ulcer Grade 2**

**Moderate abdominal pain  
PPI for 2months**



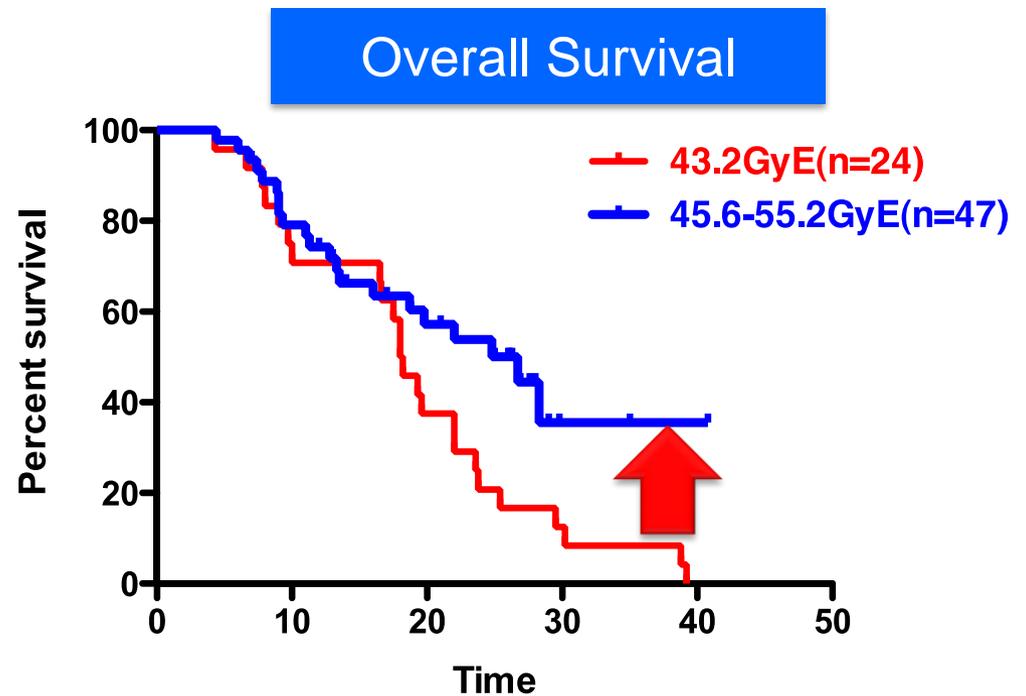
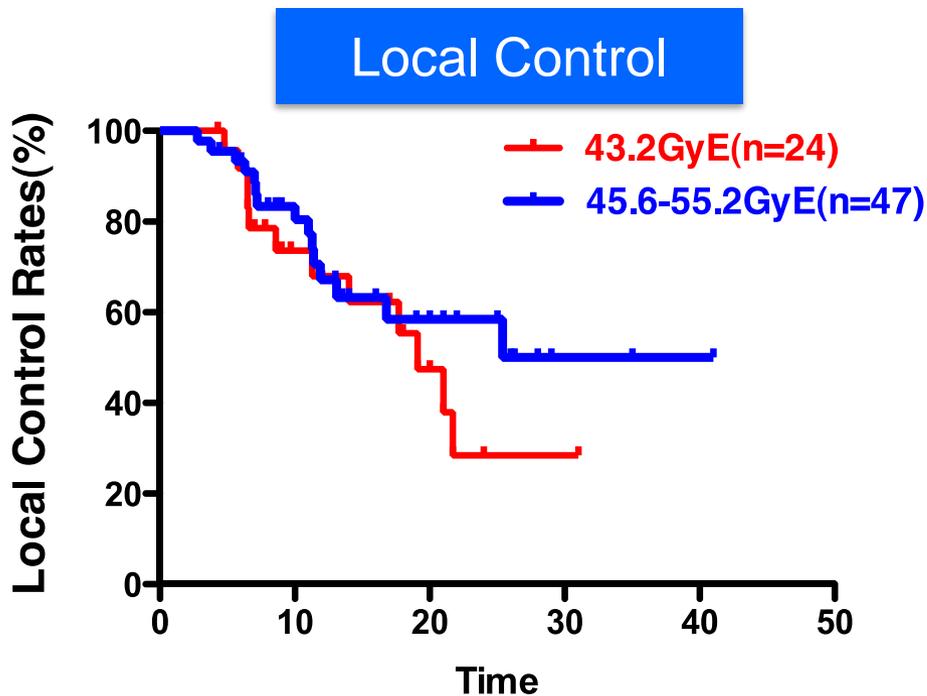
**1 month after CIRT**

**3M after CIRT**



# GEM+CIRT for locally advanced

|                         | Total dose         | n  | 12mo       | 24mo       |
|-------------------------|--------------------|----|------------|------------|
| <b>Local Control</b>    | 45.6GyE<           | 47 | <b>66%</b> | <b>46%</b> |
|                         | 43.2GyE            | 24 | <b>63%</b> | <b>10%</b> |
| <b>Overall Survival</b> | 45.6GyE<(StageIII) | 42 | <b>79%</b> | <b>48%</b> |
|                         | 43.2GyE            | 24 | <b>71%</b> | <b>21%</b> |



# GEM+C-ion RT for locally advanced

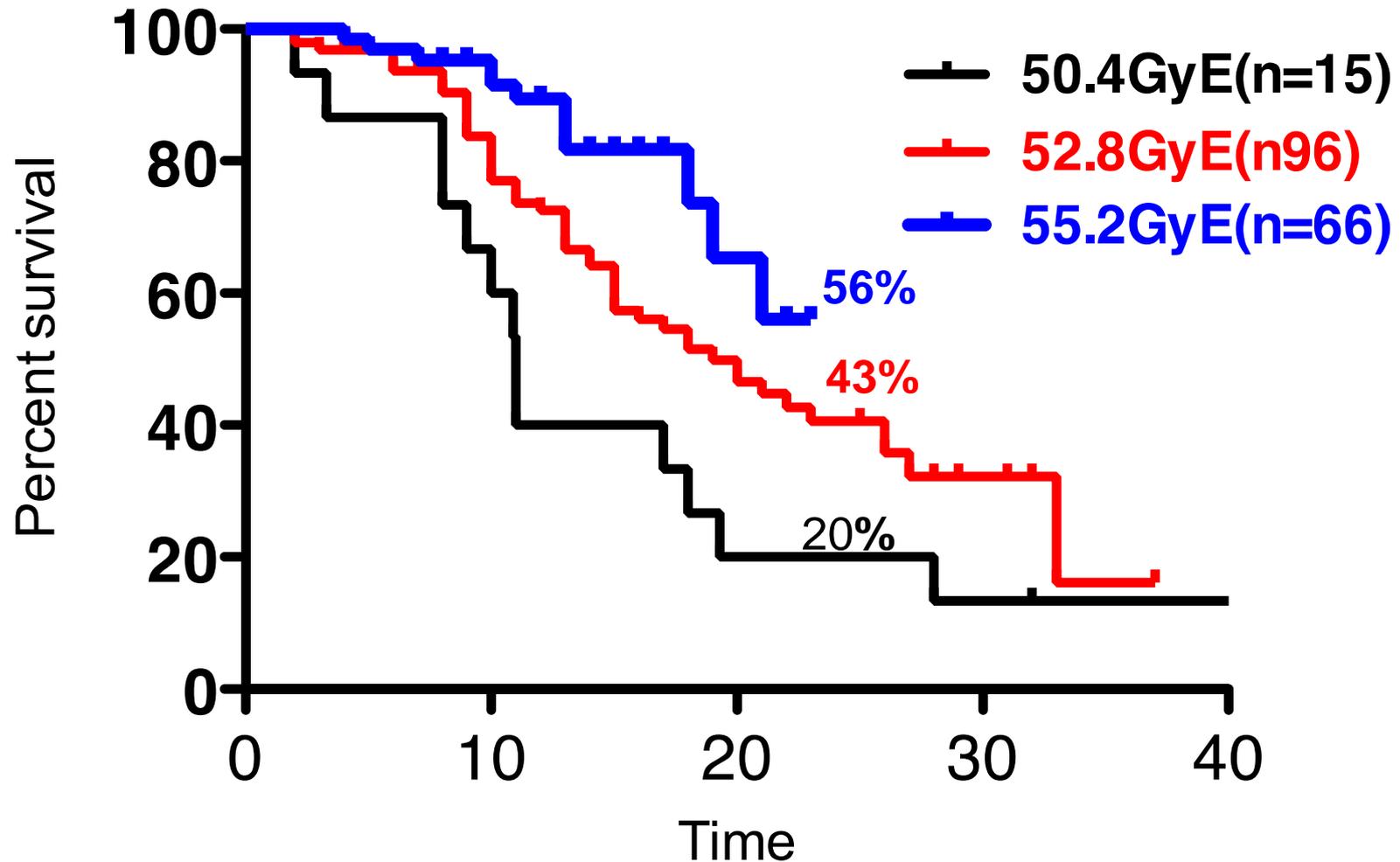
|              | Year | n  | Treatment      | Dose             | Survival |     |
|--------------|------|----|----------------|------------------|----------|-----|
|              |      |    |                |                  | 1yr      | 2yr |
| ECOG         | 2008 | 34 | GEM+RT         | 50.4Gy           | 50%      | 12% |
|              |      | 37 | GEM            | -                | 32%      | 4%  |
| Ishii        | 2010 | 50 | GEM            | -                | 64%      | 14% |
| Sudo         | 2011 | 34 | S-1+RT         | 50.4Gy           | 71%      | 25% |
| Small        | 2011 | 28 | GEM+BZ*+R<br>T | 36Gy/15fr.       | 45%      | 17% |
| Schellenberg | 2011 | 20 | GEM+SBRT       | 25Gy/1fr.        | 50%      | 20% |
| NIRS         | 2015 | 42 | GEM+CIRT       | 45.6-55.2<br>GyE | 79%      | 48% |

\*Bevacizumab

# 1201G C-ion RT for Locally Advanced Pancreatic Ca.

先進医療

(重粒子線治療開始日からの生存曲線)



## A Review of Update Clinical Results of Carbon Ion Radiotherapy

Hirohiko Tsujii\* and Tadashi Kamada

Lancet Oncology, 2015; 16: e93-100

Policy Review

### Carbon ion radiotherapy in Japan: an assessment of 20 years of clinical experience



CrossMark

**Kamada T, Tsujii H, Blakeley E, Debus J, Durante M, Jaekel O, Mayer R, Orecchia R, Poetter R, Vatnitsky S, Chu W**

Lancet Oncol 2015; 16: e93-100

active in the USA, Europe, and Asia, but only a few centres use heavy ions, even though these ions are much more effective than x-rays owing to the special radiobiological properties of densely ionising radiation. The National Institute of Radiological Sciences (NIRS) Chiba, Japan, has been treating cancer with high-energy carbon ions since 1994. So far, more than 8000 patients have had this treatment at NIRS, and the centre thus has by far the greatest experience in carbon ion treatment worldwide. A panel of radiation oncologists, radiobiologists, and medical physicists from the USA and Europe recently completed peer review of the carbon ion therapy at NIRS. The review panel had access to the latest developments in treatment planning and beam delivery and to all updated clinical data produced at NIRS. A detailed comparison with the most advanced results obtained with x-rays or protons in Europe and the USA was then possible. In addition to those tumours for which carbon ions are known to produce excellent results, such as bone and soft-tissue sarcoma of the skull base, head and neck, and pelvis, promising data were obtained for other tumours, such as locally recurrent rectal cancer and pancreatic cancer. The most serious impediment to the worldwide spread of heavy ion therapy centres is the high initial capital cost. The 20 years of clinical experience at NIRS can help guide strategic decisions on the design and construction of new heavy ion therapy centres.

#### Introduction

Control of tumours non-invasively by use of charged

Cancer Institute (NCI) provided long-term support to translational research in charged particle therapy.† After

National Institute of Radiological Sciences, Chiba, Japan (T Kamada MD, H Tsujii MD); Lawrence Berkeley National Laboratory, Berkeley, CA, USA (E A Blakeley PhD, W T Chu PhD); University of Heidelberg and Heidelberg Ion Therapy Centre, Heidelberg, Germany (Prof J Debus MD, Prof O Jaekel PhD); University of Ghent, Ghent, Belgium (Prof W De Neve MD); GSI Helmholtz Center for Heavy Ion Research and Darmstadt University of Technology, Darmstadt, Germany (Prof M Durante PhD); MedAustron, Wiener Neustadt,

# How many patients need particle beam therapy?

Based on available data, there are two estimation methods:

- 13% to 16% of all irradiated cancer patients
- 0.02% to 0.04% of the population

| Author                             | Population (2013) | No. pats treated with RT / yr | Pats for particle therapy (per year) |                    |                 |
|------------------------------------|-------------------|-------------------------------|--------------------------------------|--------------------|-----------------|
|                                    |                   |                               | % of all RT pats                     | No. pats           | % of population |
| Bengt (Sweden) <sup>1)</sup>       | 9,593,000         | 16,000                        | 14-15%                               | 2,200-2,500        | 0.02            |
| Orrecchia (Italy) <sup>2),3)</sup> | 59,830,000        | -                             | -                                    | 11,000             | 0.02            |
| Baron (France) <sup>4)</sup>       | 66,030,000        | 158,620                       | 14.5%                                | 23,000             | 0.04            |
| Mayer (Austria) <sup>5)</sup>      | 8,474,000         | 15,132                        | 13.5%                                | 2,044              | 0.02            |
| Mack Roach (USA)                   | 318,900,000       | 700,000                       | -                                    | SF-Bay area >1,848 |                 |
| Tsujii (Japan)                     | 127,300,000       | 201,000                       | 14.9%                                | 30,000             | 0.02            |
| Olav Mella (Norway)                | 5,100,000         | 16,000-19,000                 | 7-8%                                 | 1,100-1,500        | 0.03            |

1. Bengt G, et al. Acta Oncol. 44: 836-849, 2005.
2. Orrecchia R, et al. Tumori 84:205-208, 1998.
3. Krengli M, et al. Radiother Oncol. 73 (Suppl 2):/21-23, 2004.
4. Baron MH, et al. Radiother Oncol. 73 (Suppl 2):15-17,2004.
5. Mayer R, et al. Radither Oncol. 73 (Suppl 2):24-28, 2004.

# ***Particle therapy facilities in operation in the world***

|                                  | <b>Country</b>   | <b>Proton</b> | <b>Carbon</b> | <b>P + C</b> | <b>Total</b> |                   |
|----------------------------------|------------------|---------------|---------------|--------------|--------------|-------------------|
| <b>West &amp; Central Europe</b> | <b>UK</b>        | <b>1</b>      |               |              | <b>1</b>     | <b>14 (24.1%)</b> |
|                                  | <b>France</b>    | <b>2</b>      |               |              | <b>2</b>     |                   |
|                                  | <b>Germany</b>   | <b>4</b>      | <b>1</b>      | <b>1</b>     | <b>6</b>     |                   |
|                                  | <b>Italy</b>     | <b>2</b>      |               | <b>1</b>     | <b>3</b>     |                   |
|                                  | <b>Sweden</b>    | <b>1</b>      |               |              | <b>1</b>     |                   |
|                                  | <b>Swiss</b>     | <b>1</b>      |               |              | <b>1</b>     |                   |
| <b>East Europe</b>               | <b>Czech</b>     | <b>1</b>      |               |              | <b>1</b>     | <b>2 (3.5%)</b>   |
|                                  | <b>Poland</b>    | <b>1</b>      |               |              | <b>1</b>     |                   |
| <b>Russia</b>                    | <b>Russia</b>    | <b>3</b>      |               |              | <b>3</b>     | <b>3 (5.2%)</b>   |
| <b>Africa</b>                    | <b>S. Africa</b> | <b>1</b>      |               |              | <b>1</b>     | <b>1 (1.7%)</b>   |
| <b>Asia</b>                      | <b>Japan</b>     | <b>8</b>      | <b>4</b>      | <b>1</b>     | <b>13</b>    | <b>18 (31.0%)</b> |
|                                  | <b>China</b>     | <b>1</b>      | <b>1</b>      | <b>1</b>     | <b>3</b>     |                   |
|                                  | <b>Korea</b>     | <b>1</b>      |               |              | <b>1</b>     |                   |
|                                  | <b>Taiwan</b>    | <b>1</b>      |               |              | <b>1</b>     |                   |
| <b>North America</b>             | <b>Canada</b>    | <b>1</b>      |               |              | <b>1</b>     | <b>20 (34.5%)</b> |
|                                  | <b>USA</b>       | <b>19</b>     |               |              | <b>19</b>    |                   |
|                                  | <b>Total</b>     | <b>48</b>     | <b>6</b>      | <b>4</b>     | <b>58</b>    | <b>100%</b>       |

***(PTCOG, 2015)***

# *CIRT Facilities Worldwide*

| Owner/Operator            | Country        | Carbon Ion | Proton | Starting Year      |
|---------------------------|----------------|------------|--------|--------------------|
| <b>NIRS/HIMAC</b>         | <b>Japan</b>   | ●          |        | <b>1994</b>        |
| <b>GSI</b>                | <b>Germany</b> | ●          | ●      | <b>1997</b>        |
| <b>HIBMC</b>              | <b>Japan</b>   | ●          | ●      | <b>2001</b>        |
| <b>IMP</b>                | <b>China</b>   | ●          |        | <b>2006</b>        |
| <b>HIT</b>                | <b>Germany</b> | ●          | ●      | <b>2009 (2012)</b> |
| <b>GHMC</b>               | <b>Japan</b>   | ●          |        | <b>2010</b>        |
| <b>CNAO</b>               | <b>Italy</b>   | ●          | ●      | <b>2011/2013</b>   |
| <b>SAGA HIMAT</b>         | <b>Japan</b>   | ●          |        | <b>2014</b>        |
| <b>SPHIC</b>              | <b>China</b>   | ●          | ●      | <b>2014</b>        |
| <b>iROCK</b>              | <b>Japan</b>   | ●          |        | <b>2015</b>        |
| <b>Marburg University</b> | <b>Germany</b> | ●          |        | <b>2016</b>        |

# ***CIRT Facilities Under Construction***

| <b>Owner/Operator</b>    | <b>Country</b> | <b>Carbon Ion</b> | <b>Proton</b> | <b>Starting Year<br/>(planned)</b> |
|--------------------------|----------------|-------------------|---------------|------------------------------------|
| <b>MedAustron</b>        | <b>Austria</b> | ●                 | ●             | <b>2016</b>                        |
| <b>Wuwei</b>             | <b>China</b>   | ●                 |               | <b>2016</b>                        |
| <b>Lanzhou</b>           | <b>China</b>   | ●                 |               | <b>2017</b>                        |
| <b>KIRAMS</b>            | <b>Korea</b>   | ●                 |               | <b>2018</b>                        |
| <b>Facility in Osaka</b> | <b>Japan</b>   | ●                 |               | <b>2018</b>                        |
| <b>Yamagata Univ.</b>    | <b>Japan</b>   | ●                 |               | <b>2019</b>                        |

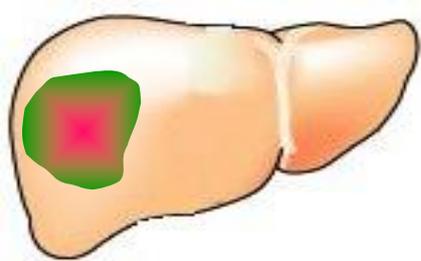
# Hospital-based Facilities for Carbon-ion RT

| Institute /Hospital | Company              | Start year            | Method  | No. Treatment Rooms |        |        |   |   |     |      | Res |
|---------------------|----------------------|-----------------------|---------|---------------------|--------|--------|---|---|-----|------|-----|
|                     |                      |                       |         | Total               | Ions   | Gantry | V | H | H+V | Ob+H |     |
| Hyogo (HIBMC)       | Mitsubishi Japan     | 2001~                 | Passive | 5                   | Carbon | 2      |   | 1 | 1   | 1    |     |
|                     |                      |                       |         |                     | Proton |        |   |   |     |      |     |
| Gunma Univ. (GHMC)  | Mitsubishi Japan     | 2010~                 | Passive | 4                   | Carbon |        | 1 | 1 | 1   |      | V   |
| Heidelberg (HIT)    | Siemens Germany      | 2009~                 | Active  | 3                   | Carbon | 1      |   | 2 |     |      |     |
|                     |                      |                       |         |                     | Proton |        |   |   |     |      |     |
| Pavia (CNAO)        | CNAO/CERN Italy      | P: 2011~<br>(C: 2012) | Active  | 3                   | Carbon |        |   | 2 | 1   |      |     |
|                     |                      |                       |         |                     | Proton |        |   |   |     |      |     |
| Shanghai            | Siemens Germany      | 2013                  | Active  | 4                   | Carbon |        |   | 1 | 1   | 1    | H   |
|                     |                      |                       |         |                     | Proton |        |   |   |     |      |     |
| Marburg             | Siemens Germany      | 2009~                 | Active  | 3                   | Carbon | 1      |   | 2 |     |      |     |
|                     |                      |                       |         |                     | Proton |        |   |   |     |      |     |
| Saga (Saga-HIMAT)   | Mitsubishi Japan     | 2013                  | Passive | 3                   | Carbon |        |   |   | 1   | 1    |     |
|                     |                      |                       | Active  |                     |        |        |   |   |     |      |     |
| Kanagawa (iROCK)    | Toshiba Japan        | 2015                  | Active  | 4                   | Carbon |        |   |   | 2   | 1    | H   |
| Med-Austron         | Austria/CERN Austria | 2013                  | Active  | 4                   | Carbon | 1      |   | 1 | 1   |      | H   |
|                     |                      |                       |         |                     | Proton |        |   |   |     |      |     |
| Yamagata            | Toshiba Japan        | 2019                  | Active  | 3                   | Carbon | 1      |   |   | 1   |      | H   |

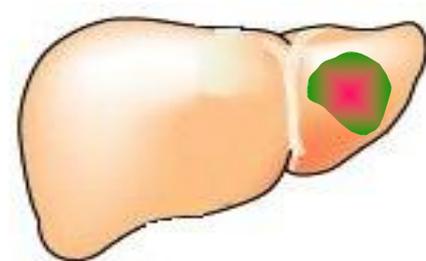
# **Trials for PBRT and CIRT in Japan**

# Trials for Proton Beam Radiotherapy

| Tumor sites                 | Status  | Method           |       | To be compared with  |
|-----------------------------|---|------------------|-------|----------------------|
| Liver                       | Resectable                                      | Proton           | 2 arm | Surgery              |
|                             | Unresectable                                    | Proton           | 1 arm | TACE                 |
| Intrahepatic bile duct      | Unresectable,<br>Not responsive to chemotherapy | Proton + Chemo   | 1 arm | Best supportive care |
| Lung, locally advanced      | Inoperable,<br>Unsuitable for XRT               | Proton + Chemo   | 1 arm | Chemo                |
| Head & neck                 | Re-irradiation                                  | Proton           | 1 arm | Chemo or No Tx       |
| Esophagus, locally advanced | Operable  | Proton + Chemo   | 1 arm | Surgery              |
| Pancreas, locally advanced  | Inoperable                                      | Proton + Chemo   | 1 arm | Chemo                |
| Prostate                    | Intermediate risk                               | Proton + Hormone | 1 arm | IMRT                 |



# Proton trial in Japan



**Non-randomized controlled study  
comparing PBT and hepatectomy for resectable  
HCC**

**Newly diagnosed solitary & nodular HCC**

- 3 - 12 cm, age 20-80 y/o
- Child-Pugh 5-7, PS 0 - 1

**registration**

**Treatments (S or P) can be chosen by patient**

**surgery**

66Gy / 10 fr.

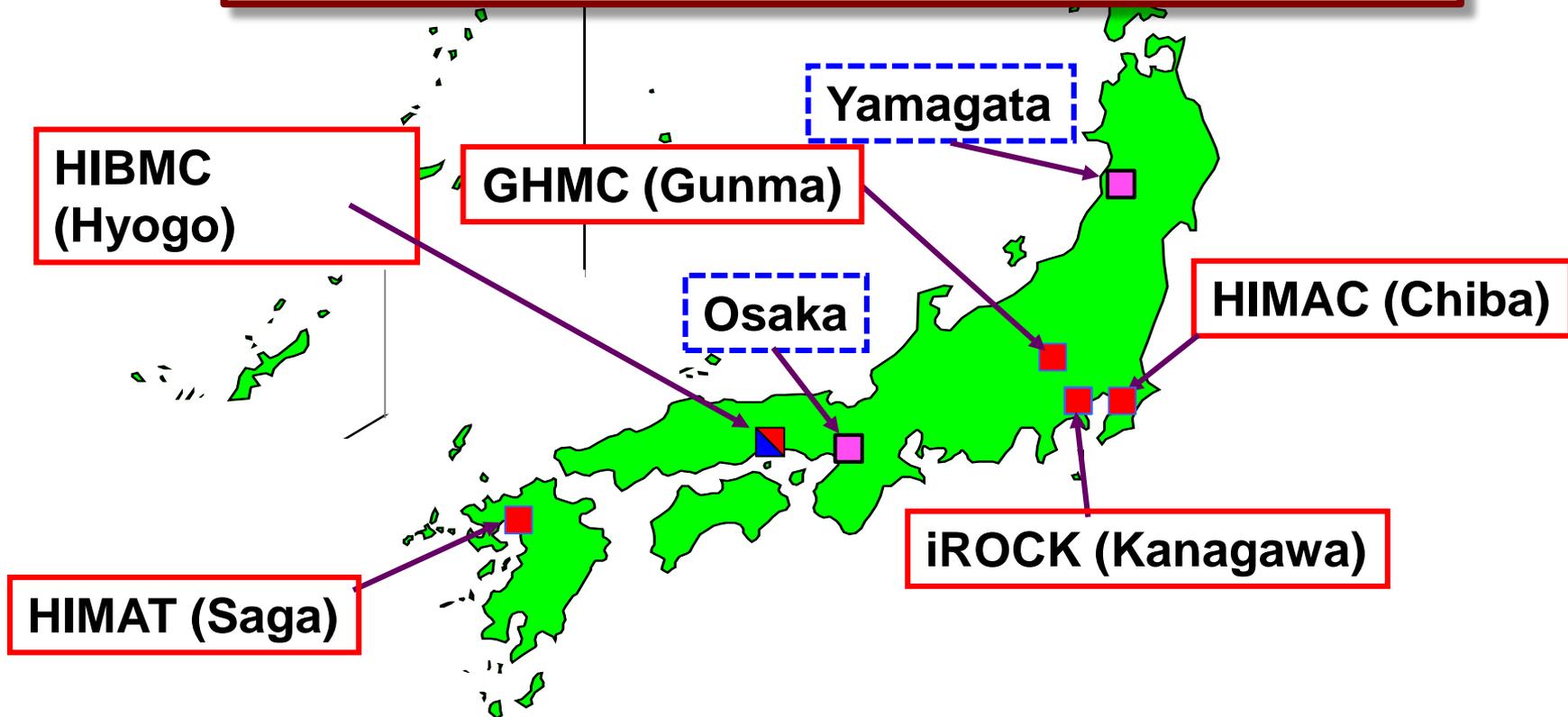
**Proton**

72.6Gy / 22 fr.

# JaCROS

(Japan Carbon-ion Radiation Oncology Study Group)

To Establish a Bench Mark of C-ion RT  
To Conduct Prospective Clinical Trials,  
*'including a RCT'*  
To Standardize C-ion RT in Various Tumors



# ***Planned prospective studies by J-CROS***

| <b>J-CROS Protocols</b> |                             |                       |   |
|-------------------------|-----------------------------|-----------------------|---|
| <b>Study Design</b>     | <b>Protocol No.</b>         | <b>Tumor Site</b>     | <b>Notes</b>                              |
| <b>Prospective</b>      | <b>J-CROS 1501 NSCLC</b>    | <b>Lung</b>           | <b>Stage I, Peripheral non-small cell</b> |
|                         | <b>J-CROS 1502 Pancreas</b> | <b>Pancreas</b>       | <b>Locally advanced</b>                   |
|                         | <b>J-CROS 1505 HCC</b>      | <b>Liver</b>          | <b>Unresectable</b>                       |
|                         | <b>J-CROS 1506 Rectum</b>   | <b>Rectum</b>         | <b>Post-operative locally recurrent</b>   |
|                         | <b>J-CROS 1509 Prostate</b> | <b>Prostate</b>       | <b>Localized high-risk</b>                |
|                         | <b>J-CROS 1510 Prostate</b> | <b>Prostate</b>       | <b>Localized low to intermediate-risk</b> |
|                         | <b>J-CROS 1511 Gyne.</b>    | <b>Uterine Cervix</b> | <b>Cervical adenocarcinoma</b>            |
|                         | <b>J-CROS 1512 Breast</b>   | <b>Breast</b>         | <b>Stage I, Low risk</b>                  |
|                         | <b>J-CROS 1513 HN</b>       | <b>Head and Neck</b>  | <b>Ear canal, SCC</b>                     |
|                         | <b>J-CROS 1514 Gyne.</b>    | <b>Uterine Cervix</b> | <b>Locally advanced scc</b>               |
|                         | <b>J-CROS 1515 Gyne.</b>    | <b>GYN Region</b>     | <b>Mucosal malignant melanoma</b>         |

# Trials for Carbon-ion Radiotherapy

| Tumor sites                   | Status                           | Method              | To be compared with |              |
|-------------------------------|----------------------------------|---------------------|---------------------|--------------|
| Liver                         | Unresectable,                    | Carbon              | 1 arm               | TACE         |
| Lung,<br>Early stage          | Unresectable,<br>Surgery refused | Carbon              | 1 arm               | IMRT         |
|                               |                                  |                     | 2 arm               | Proton       |
| Pancreas,<br>locally advanced | Inoperable                       | Carbon +<br>Chemo   | 1 arm               | Chemo        |
|                               |                                  |                     | 2 arm               | IMRT + Chemo |
| Rectum                        | Post-operative<br>recurrence     | Carbon              | 1 arm               | Chemo or XRT |
| Prostate                      | High risk                        | Proton +<br>Hormone | 1 arm               | IMRT         |
|                               |                                  |                     | 2 arm               | Proton       |

## **J-CROS 1502: Pancreas**

**A clinical trial for validation of CIRT and concurrent GEM chemotherapy efficacy on locally advanced pancreatic cancer**

### **Institutional clinical study**

**A phase I clinical study of preoperative C-ion RT for resectable pancreas cancer**

**Period: 2003-2011**

**Number of patients: 26**

**Recommended dose 36.8GyE / 8 fr.**

**5 years survival rate; 42%**

*Cancer 2013*

**A Phase I/II clinical trial of C-ion RT combined with GEM for locally advanced pancreas cancer**

**Period: 2007-2012**

**Number of patients: 71**

**Recommended dose: C-ion RT; 55.2GyE / 12 fr.**

**GEM; 1000mg/m<sup>2</sup>**

**Adverse events (Grade3/4):**

**Leucopenia 50%, Infection 1%, Gastric ulcer 1%**

**2-year survival: 39%、**

**Median survival time; 19 months**

*IJROBP, 2016*

### **Multi-institutional study**

**A clinical trial for validation of CIRT and concurrent GEM CTx: Efficacy on locally advanced pancreatic ca**

**Period; 2 years, Planned no. of patients : 64**

**Primary endpoint: 2-year survival rate**

**Secondary endpoints: Survival time, Local control rate, Disease-free survival rate, Adverse event, Quality of life (QOL), Cost-effectiveness**

#### **Inclusion criteria:**

**Pathologically confirmed locally advanced pancreas ca w/o distant metastasis, w/o digestive ulcer**

**No previous treatment, Age between 20-80**

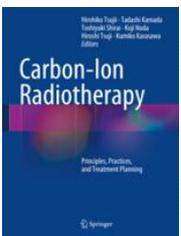
**PS; 0 – 2**

#### **Exclusion criteria:**

**Invasion to mucosal membrane of digestive tract**

**Ascites, Metallic stent, other malignancy**

**C-ion RT: 55.2GyE/12fr.**



## Carbon-Ion Radiotherapy

Principles, Practices, and Treatment Planning

Tsuji, H.; Kamada, T.; Shirai, T.; Noda, K.; Tsuji, H.; Karasawa, K. (Eds.)

2014, XII, 312 p. 237 illus., 199 illus. in color.

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**Published  
in Jan, 2014  
Springer**

### About this book

- Essential practical guide
- Clinical data of more than 20 years at the National Institute of Radiation Physics and Chemistry are highlighted. The book covers the basic biology, and the second section is a systematic review by tumor site, concentrating on the role of therapeutic techniques and the pitfalls in treatment planning.
- Discusses the improvement of clinical results

This book serves as a practical guide for more than 20 years at the National Institute of Radiation Physics and Chemistry are highlighted. The book covers the basic biology, and the second section is a systematic review by tumor site, concentrating on the role of therapeutic techniques and the pitfalls in treatment planning.

of clinical  
20 years at the  
of this modality  
physics and

Readers will learn of the superior outcomes obtained with carbon-ion therapy for various types of tumors in terms of local control and toxicities. It is essential to understand that the carbon-ion beam is like a two-edged sword: unless it is used properly, it can increase the risk of severe injury to critical organs. In early series of dose-escalation studies, some patients experienced serious adverse effects such as skin ulcers, pneumonitis, intestinal ulcers, and bone necrosis, for which salvage surgery or hospitalization was required. To preclude such detrimental results, the adequacy of therapeutic techniques and dose fractionations was carefully examined in each case. In this way, significant improvements in treatment results have been achieved and major toxicities are no longer observed. With that knowledge, experts in relevant fields expand upon techniques for treatment delivery at each anatomical site, covering indications and optimal treatment planning.

With its practical focus, this book will benefit radiation oncologists, medical physicists, medical dosimetrists, radiation therapists, and senior nurses whose work involves radiation therapy, as well as medical oncologists and others who are interested in radiation therapy.

**Content Level** » Professional/practitioner

**Keywords** » Cancer radiotherapy - HIMAC - Heavy ion - Ion beams - Protons - Relative biological effectiveness

Tsuji · Kamada · Shirai · Noda  
Tsuji · Karasawa  
Eds.



Carbon-Ion Radiotherapy

Hirohiko Tsuji · Tadashi Kamada  
Toshiyuki Shirai · Koji Noda  
Hiroshi Tsuji · Kumiko Karasawa  
Editors

# Carbon-Ion Radiotherapy

Principles, Practices,  
and Treatment Planning

# International Training Course on Carbon-ion Radiotherapy

9-14 November, 2015

Venue: NIRS and Kanagawa (iROCK)

## International Training Course on Carbon-ion Radiotherapy

9-14 November 2015 Chiba & Kanagawa, Japan

### Course Program

AM

PM

| November  | History & Overview<br>of Ion Beam Radiotherapy  | Biology 1. Biological Characteristics   |
|-----------|---|---|
| 9 (Mon.)  | Physics 1. Basic Knowledge  | Physics 2. Accelerators<br>Clinical 1. Overview   |
| 10 (Tue.) | Biology 2. Biological Models<br>Physics 3. Beam Delivery & Dosimetry                          | Clinical 2. Head & Neck, Skull Base<br>CNS, Lung Tumors, Esophagus<br>Clinical 3. Pancreas, Rectum, Liver             |
| 11 (Wed.) | Physics 4. Treatment Planning<br>Physics 5. Facility Design<br>Physics 6. Radiation Shielding | Clinical 4. Genitourinary, Breast Cancer<br>Eye, Gynecologic Tumors<br>Tour Patient Positioning<br>Treatment Planning |
| 12 (Thu.) | Physics 7. Facility Set-up & Operation<br>Clinical 5. Diagnostic Imaging<br>Case study 1      | Clinical 6. Clinical Trial<br>Clinical 7. Cost Effectiveness<br>Clinical 8. Multi Modality Approach<br>Case study 2   |
| 13 (Fri.) | Move To Kanagawa  | Tour i-ROCK   |
| 14 (Sat.) | Free discussion   |   |

### Course Director

Hirohiko Tsujii, M.D., Ph.D.

(Research Fellow, National Institute of Radiological Sciences: NIRS)

Tadashi Kamada, M.D., Ph.D.

(Director, Research Center for Charged Particle Therapy, NIRS)

Yuko Nakayama, M.D., Ph.D.

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(Director, Research Center for Charged Particle Therapy, NIRS)



Yuko Nakayama, M.D., Ph.D.

(Chair, Department of Radiation Oncology Kanagawa Cancer Center)



| Country      | No.       |
|--------------|-----------|
| Asia         | 28        |
| India·UAE    | 3         |
| EU           | 7         |
| USA          | 7         |
| Japan        | 10        |
| <b>Total</b> | <b>55</b> |

*International Training Course  
on Carbon-ion Radiotherapy (ITCCIR)  
Nov 18 – Dec 3, 2016  
Venue: NIRS and Gunma*



*ITCCIR  
9-14 November, 2015  
NIRS / Kanagawa (iROCK)*



***Thank you***

