Proton Beam Therapy (PBT) at the National Cancer Center Hospital East, Kashiwa, Japan

PTCOG47, May 22, 2008

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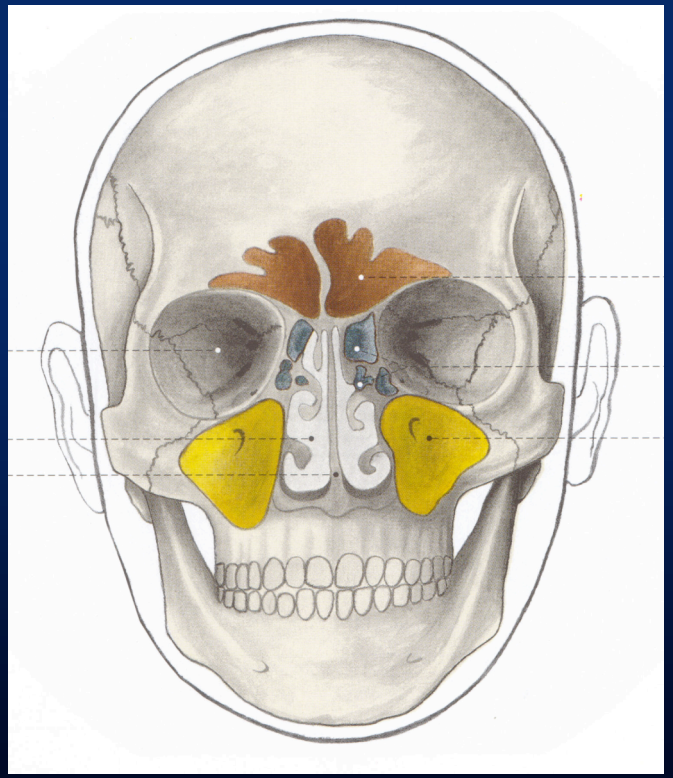
National Cancer Center Hospital East

PBT for Nasal Cavity & Para-nasal Sinus Malignancies

- Retrospectively evaluated the role of proton beam therapy (PBT) in patients with nasal cavity and para-nasal sinus malignancies



Ogino T, et al. ECCO 14, Barcelona, 2007

Patients Characteristics 1

- 1999-2006
- n=93
- Gender: M/F=51/42
- Age: Median 58y (17-88)
- Primary Lesion
  - Nasal Cavity 51
  - Maxillary Sinus 15
  - Ethmoid Sinus 14
  - Sphenoid Sinus 7
  - Others 6

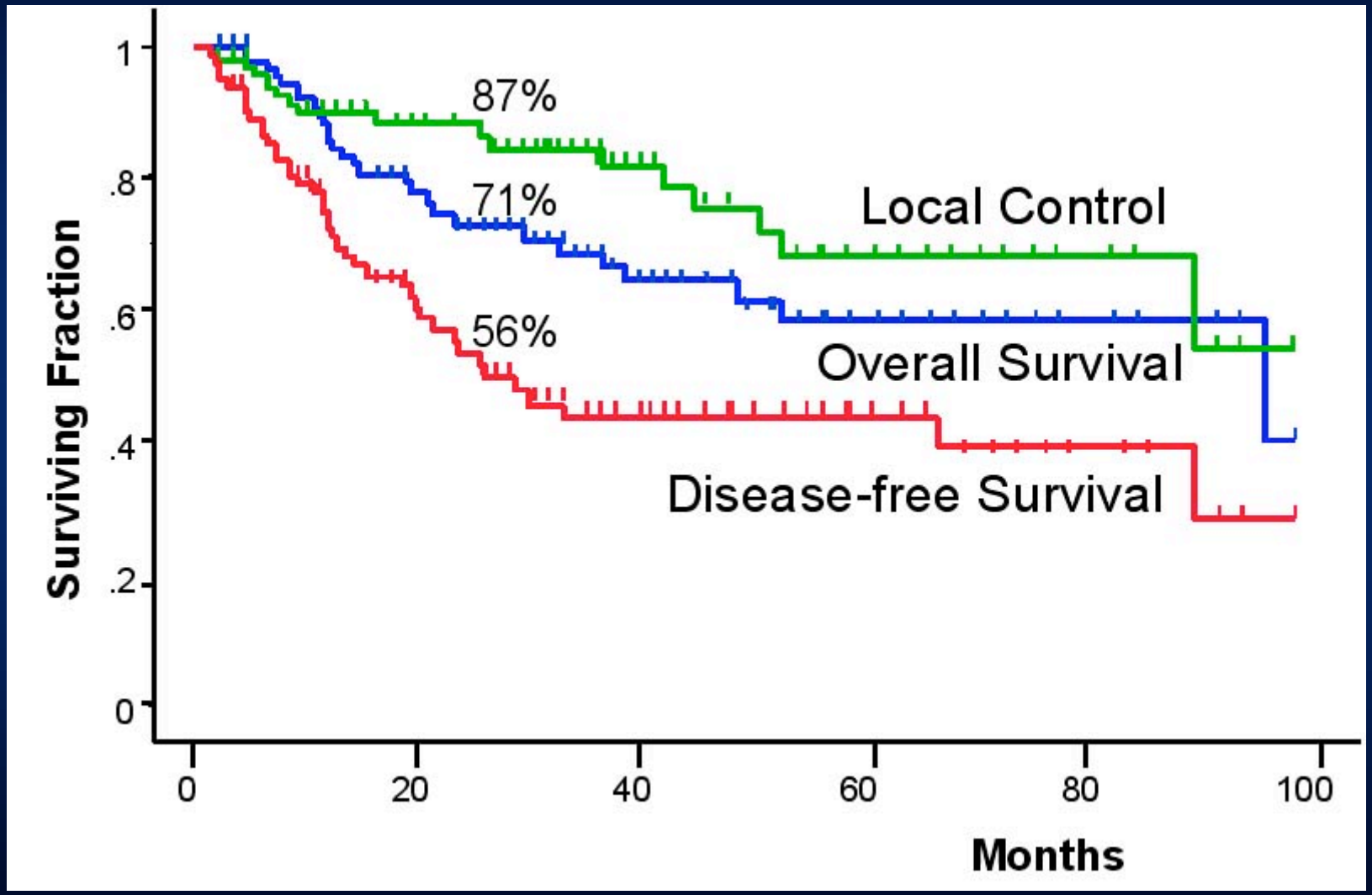
Patients Characteristics 2

- Histology
  - SCC 27
  - Olfactory Neuroblastoma 22
  - Malignant Melanoma 18
  - Adenoid Cystic Ca. 13
  - Undiff. Ca. 4
  - Others 9
- T stage
  - T2/T3/T4/Rec: 14/19/53/7

Methods

- Prior Therapy
  - Reduction Surgery 22
  - Induction Chemo. 18
  - Recurrent Tumor 7
- At this time period, concurrent chemotherapy was not used
- Median Dose: 65 GyE (58.8-70)
  - PBT alone: 2.5 GyE x 26-28 fr = 65-70 GyE
  - Malignant Melanoma: 4.0 GyE x 15 fr = 60 GyE
- Median FU: 18 m (2-95 m)

Local Control (LC), Overall Survival (OAS), and Disease-Free Survival (DFS)



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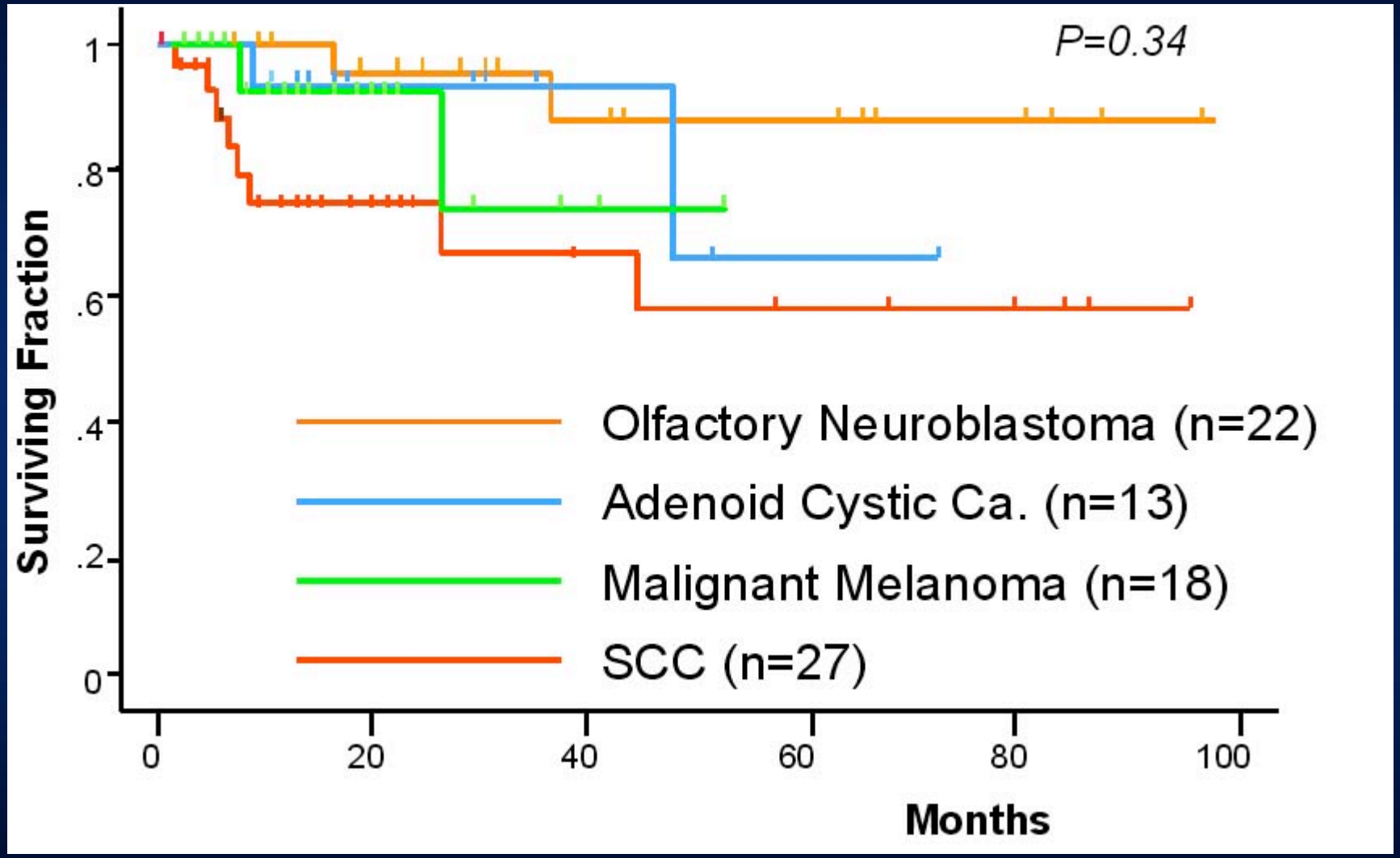
Local Control by Histology



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Late Adverse Events

- No visual loss/weakness
- Cataract: 3
- Asymptomatic brain necrosis by MRI: 2
- Bone necrosis: 1
- Liquorrhea due to shrinkage of the tumor: 1
- Hemorrhage (re-irradaition case): 1
- Surgical soft tissue repair: 2

48y F, Ethmoid Sinus Ca.

Coplanar beam Non-coplanar beam

Pre-PBT **Isodose Curve** **Post-65 GyE PBT**

Alive without disease over 8 yrs

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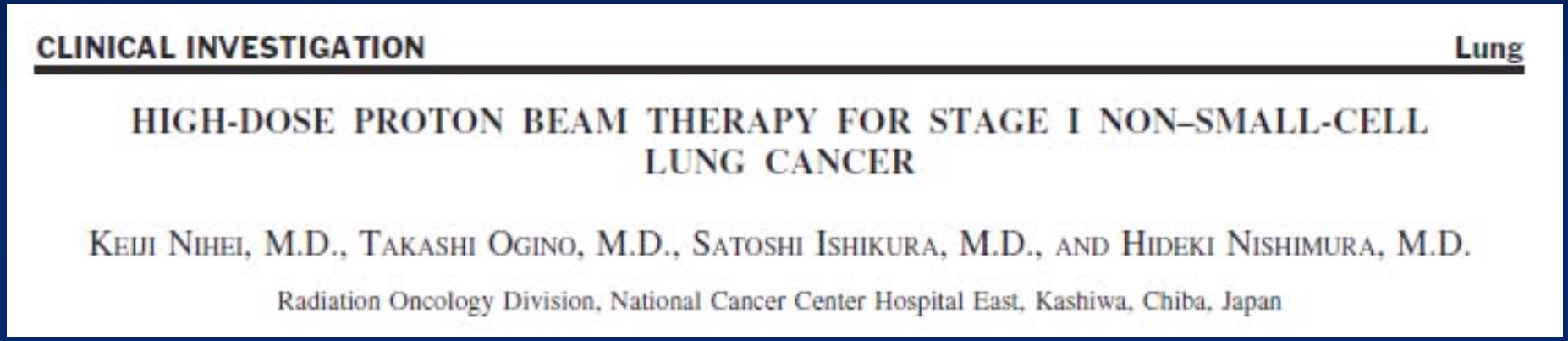
Stage I Non-Small Cell Lung Cancer



CLINICAL INVESTIGATION Lung

HIGH-DOSE PROTON BEAM THERAPY FOR STAGE I NON–SMALL-CELL LUNG CANCER

KEIJI NIHEI, M.D., TAKASHI OGINO, M.D., SATOSHI ISHIKURA, M.D., AND HIDEKI NISHIMURA, M.D.

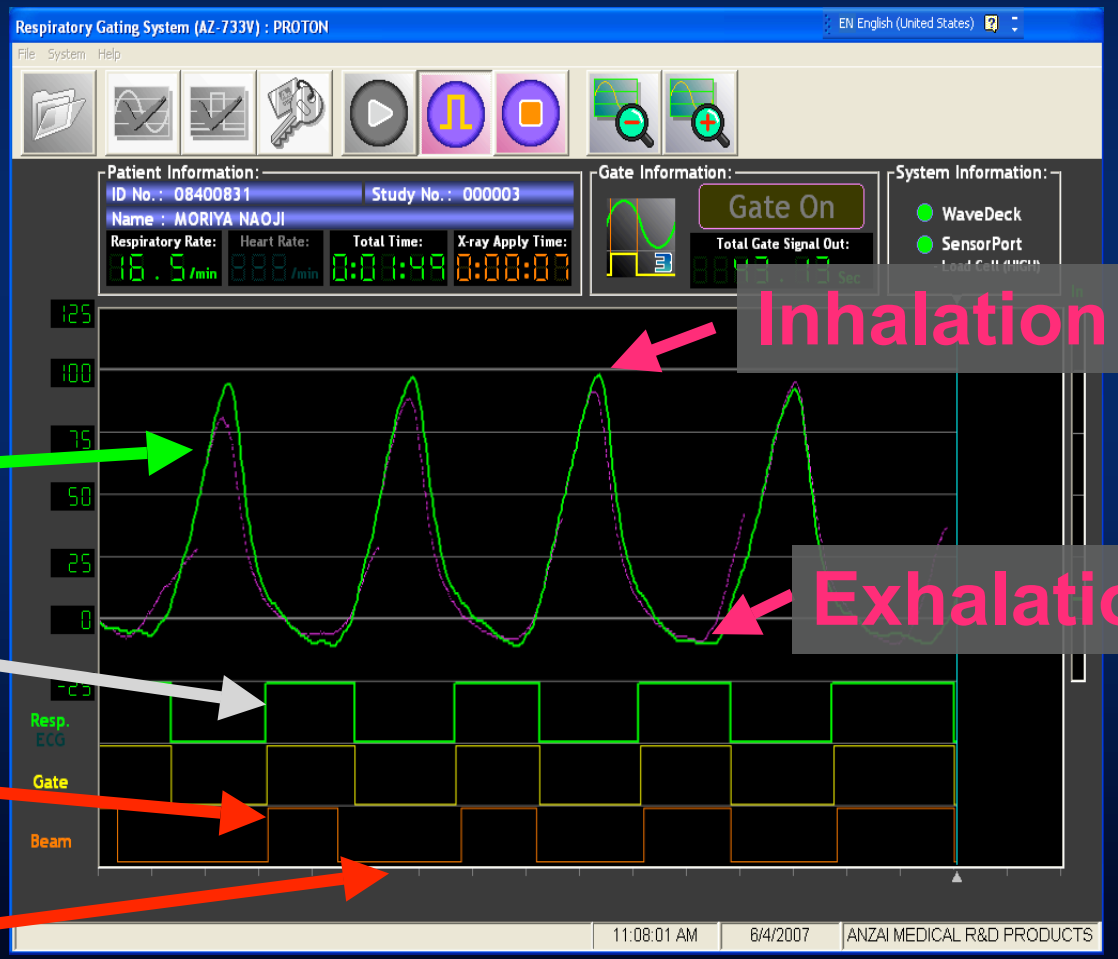
Radiation Oncology Division, National Cancer Center Hospital East, Kashiwa, Chiba, Japan

Initial experience of 37 patients

Nihei K, et al. Int J Radiat Oncol Biol Phys 2006;65:107-111

Respiratory-Gating System

Strain gauge => Laser sensor



Respiratory signal

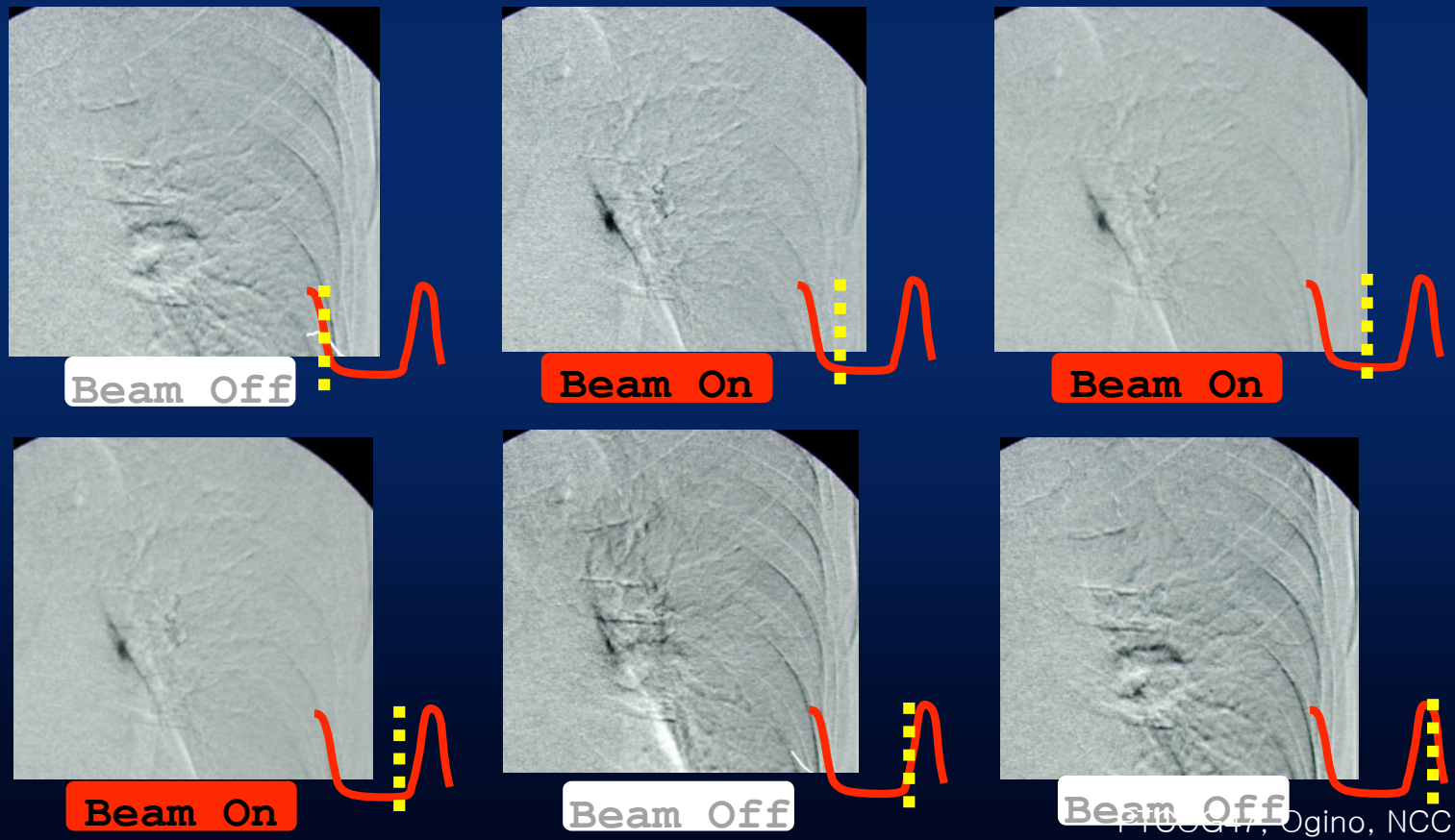
Gating signal

Beam on

Beam off

Respiratory-Gated Irradiation

- End exhalation phase is used
- Currently, high intensity beam (average 8 Gy/min) is used
- Gating at inhalation phase without using active breathing control (ABC) system is under consideration



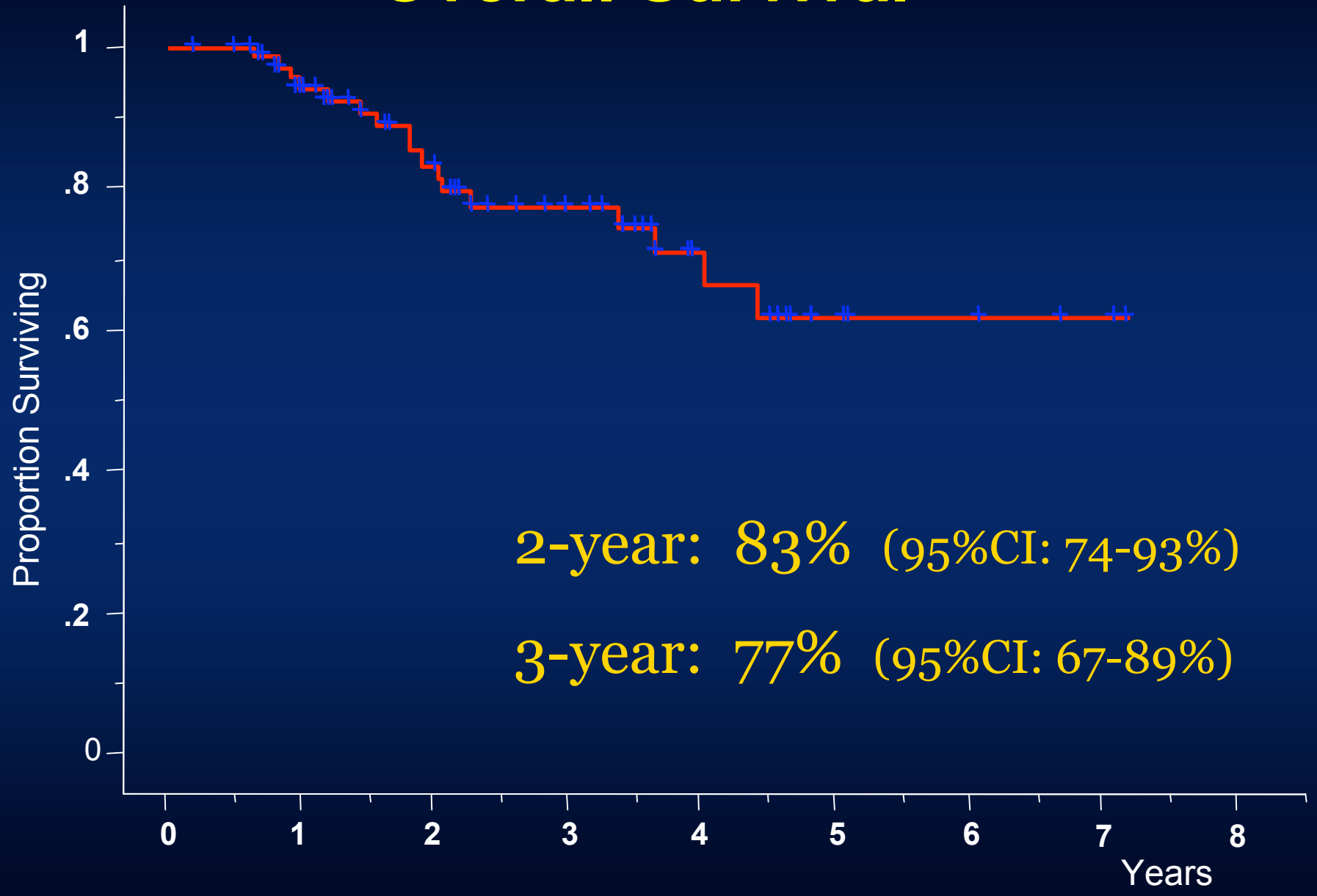
Patients Characteristics

- 2000-2006
- 76 patients with stage I (T1,2N0M0) NSCLC
  - including 10 pts enrolled in our dose escalation study

- Median Age 75 yrs (52-86)
- Male/Female 53/23
- Stage IA/IB 43/33
- Sq/Adeno/NOS 27/23/26
- Inoperable/Refuse Surgery 49/27
- Total Dose 70/80/88/94 GyE 3/56/16/1 in 20 fractions

- Median Follow-Up Duration 27 months (3 - 88 m)

Overall Survival



2-year: 83% (95%CI: 74-93%)

3-year: 77% (95%CI: 67-89%)

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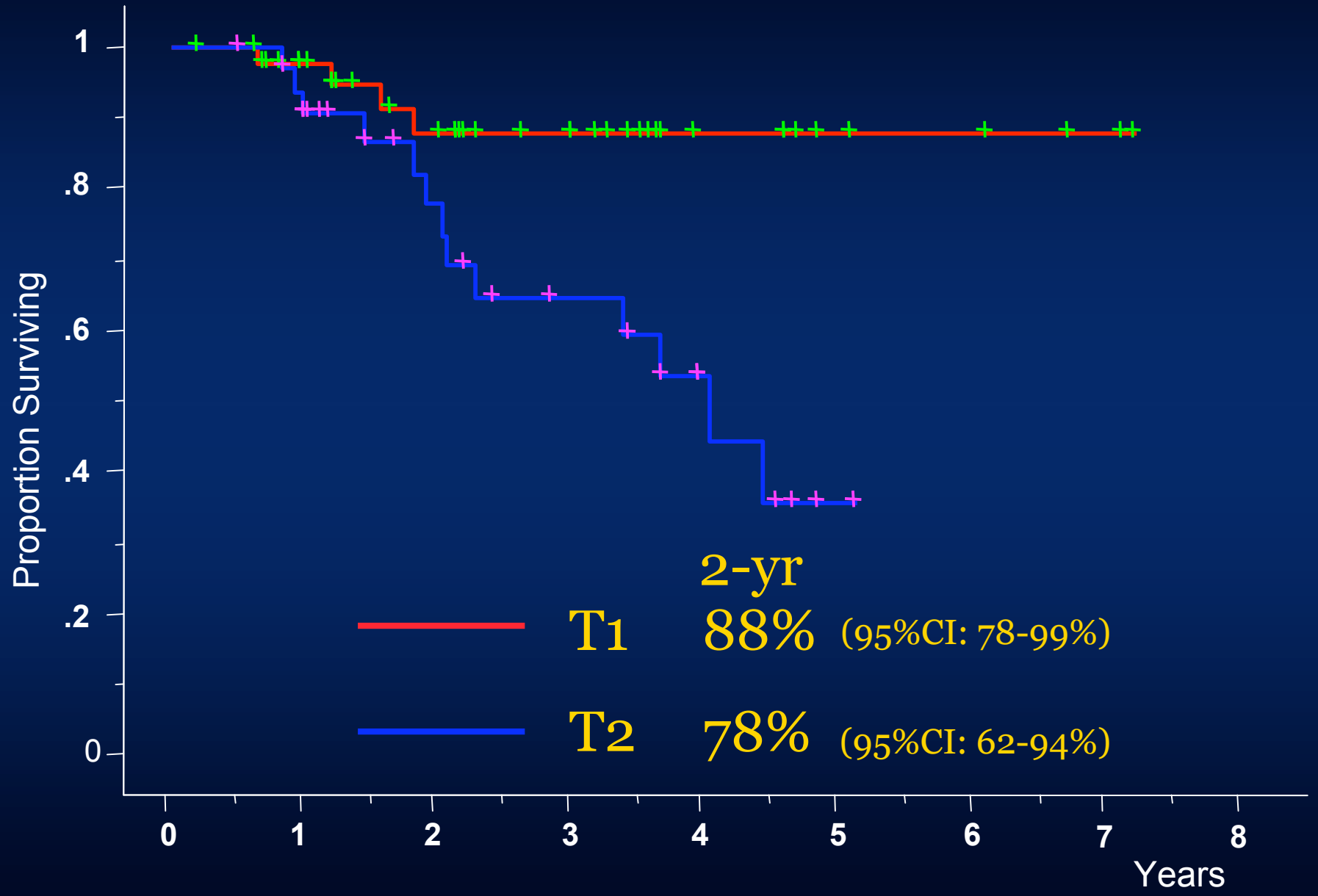
Result 2　T1 vs T2

- Patterns of Failure

	All	T1	T2
	76	43	33
Local	2	0	2
Loco-regional	2	0	2
Regional	10	4	6
Regional + distant	2	0	2
Distant	7	4	3

Overall Survival



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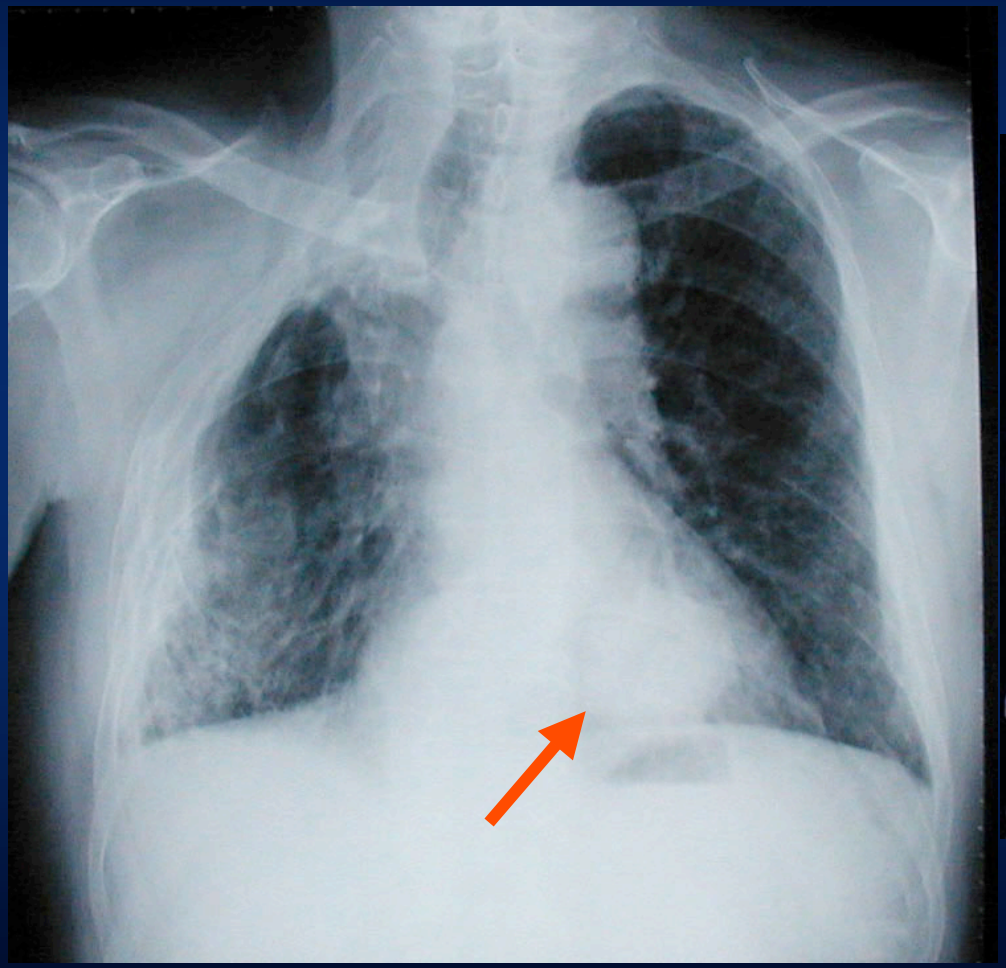
Result 2　T1 vs T2

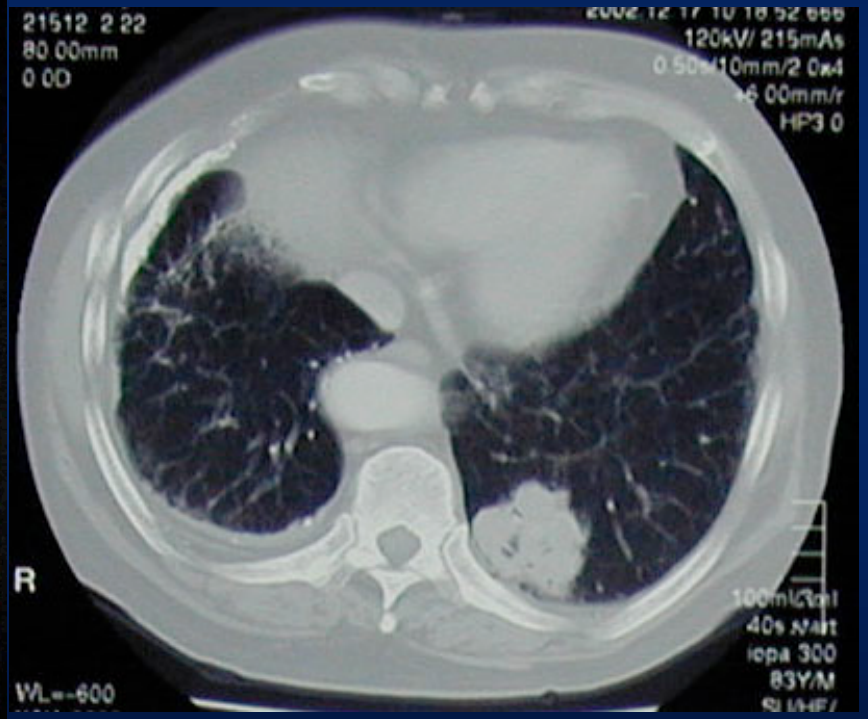
- Late Toxicities

		All	T1	T2
		76	43	33
Chest pain	Gr1	7	5	2
Pulmonary	Gr1	56	33	23
	Gr2	5	2	3
	Gr3	3	0	3
Bone (rib)	Gr4	4	2	2

All received >/= 88 GyE close to the rib

84y M, Inoperable case





70y M, T2N0M0 NSCLC

Pre-PBT

Post-80 GyE PBT

Alive without disease over 5 yrs

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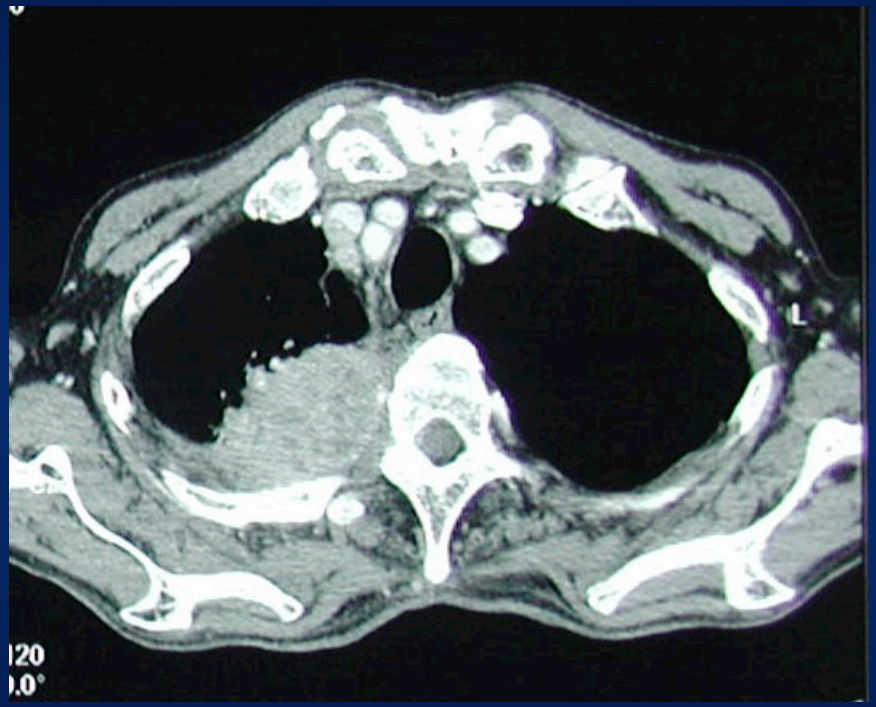
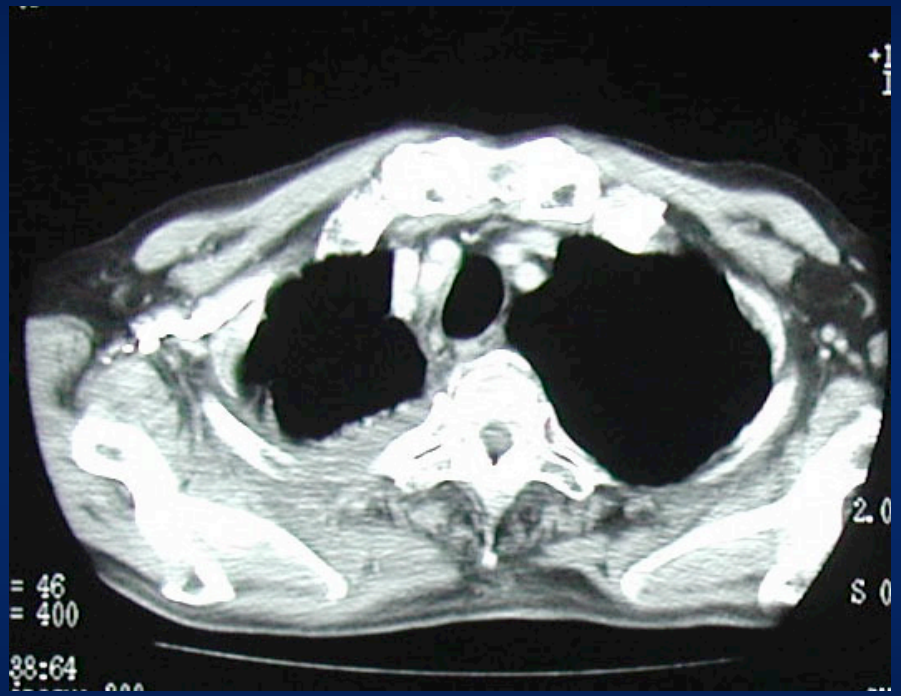
79y M, T3N0M0 NSCLC



Pre-PBT



Post-80 GyE PBT

Alive without disease over 4 yrs

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Hepatocellular Carcinoma

Phase II Study of Radiotherapy Employing Proton Beam for Hepatocellular Carcinoma

Miesuhiko Kawashima, Junji Furuse, Teiji Nishio, Masaru Konishi, Hiroshi Ishii, Taira Kinoshita, Michitaka Nagase, Keiji Nihei, and Takashi Ogino

Kawashima M, et al., J Clin Oncol 2005;23:1839-46

Hepatocellular Carcinoma

- n=30 (1999-2003)
- Age: Median 70y (48-87)
- Gender: M/F = 20/10
- Child-Pugh Classification: A/B/C = 20/10/0
- Tumor Size: Median 45 mm (25-82)
- AFP Level: <300/>=300 = 21/9
- Prior Treatment: No/Surgery/Ablation or TACE = 13/6/11
- PBT Dose
  - 76 GyE / 20 fx

Results

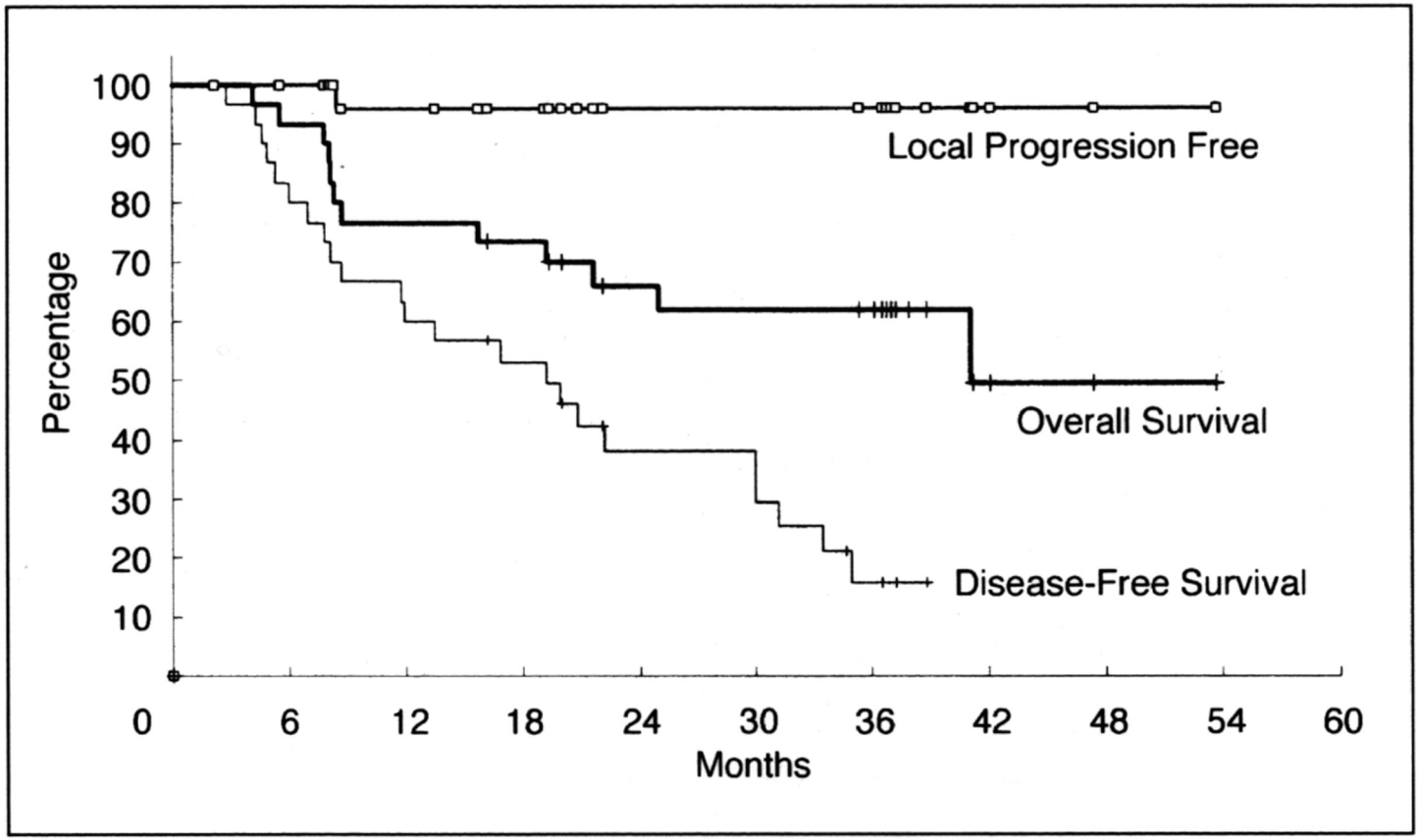
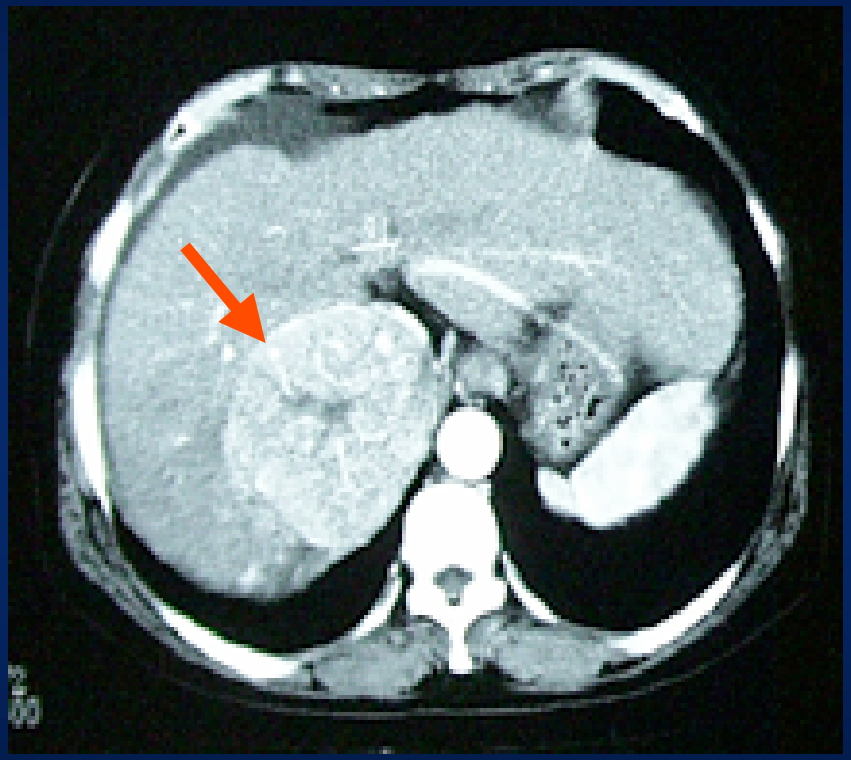
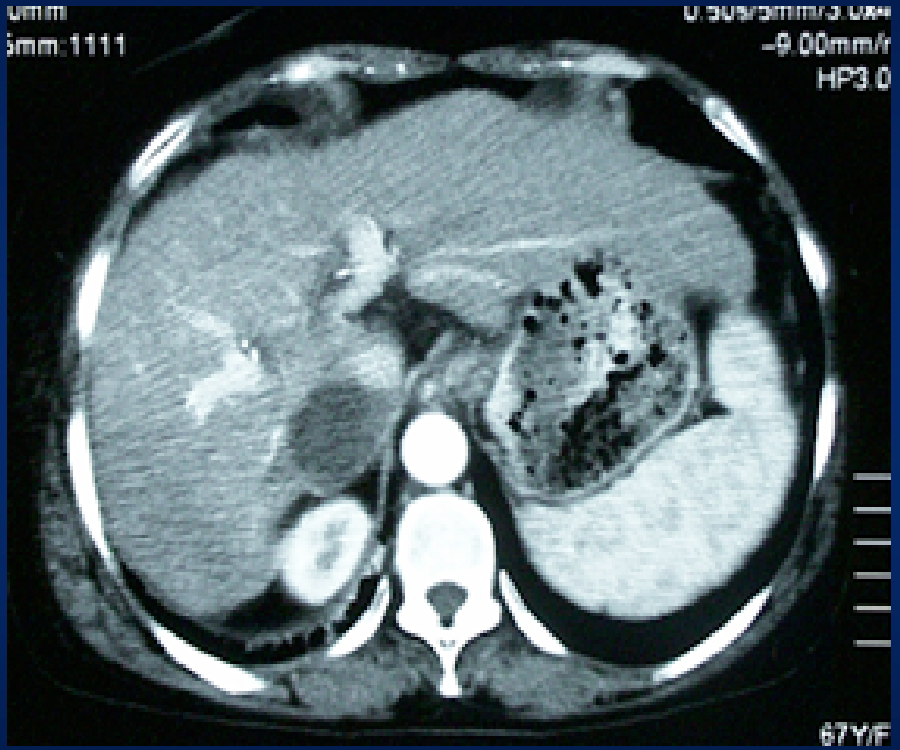


Fig 2. Kaplan-Meier estimate of local progression-free, overall, and disease-free survival rates for all 30 patients enrolled.

67y F, Hepatocellular Carcinoma





Pre-PBT **Post-76 GyE PBT**

Dead by multiple new lesion at 3 years

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Prostate Cancer

Jpn J Clin Oncol 2005;35(12)745–752
doi:10.1093/jjco/hyi193

Phase II Feasibility Study of High-Dose Radiotherapy for Prostate Cancer Using Proton Boost Therapy: First Clinical Trial of Proton Beam Therapy for Prostate Cancer in Japan

Keiji Nihei, Takashi Ogino, Satoshi Ishikura, Mitsuhiko Kawashima, Hideki Nishimura, Satoko Arahira and Masakatsu Onozawa

Radiation Oncology Division, National Cancer Center Hospital East, Kashiwa, Chiba, Japan

Nihei K, et al. Jpn J Clin Oncol 2005;35:745-752

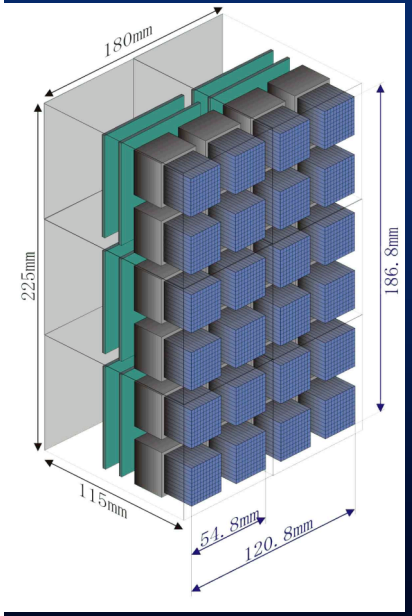
Prostate Cancer

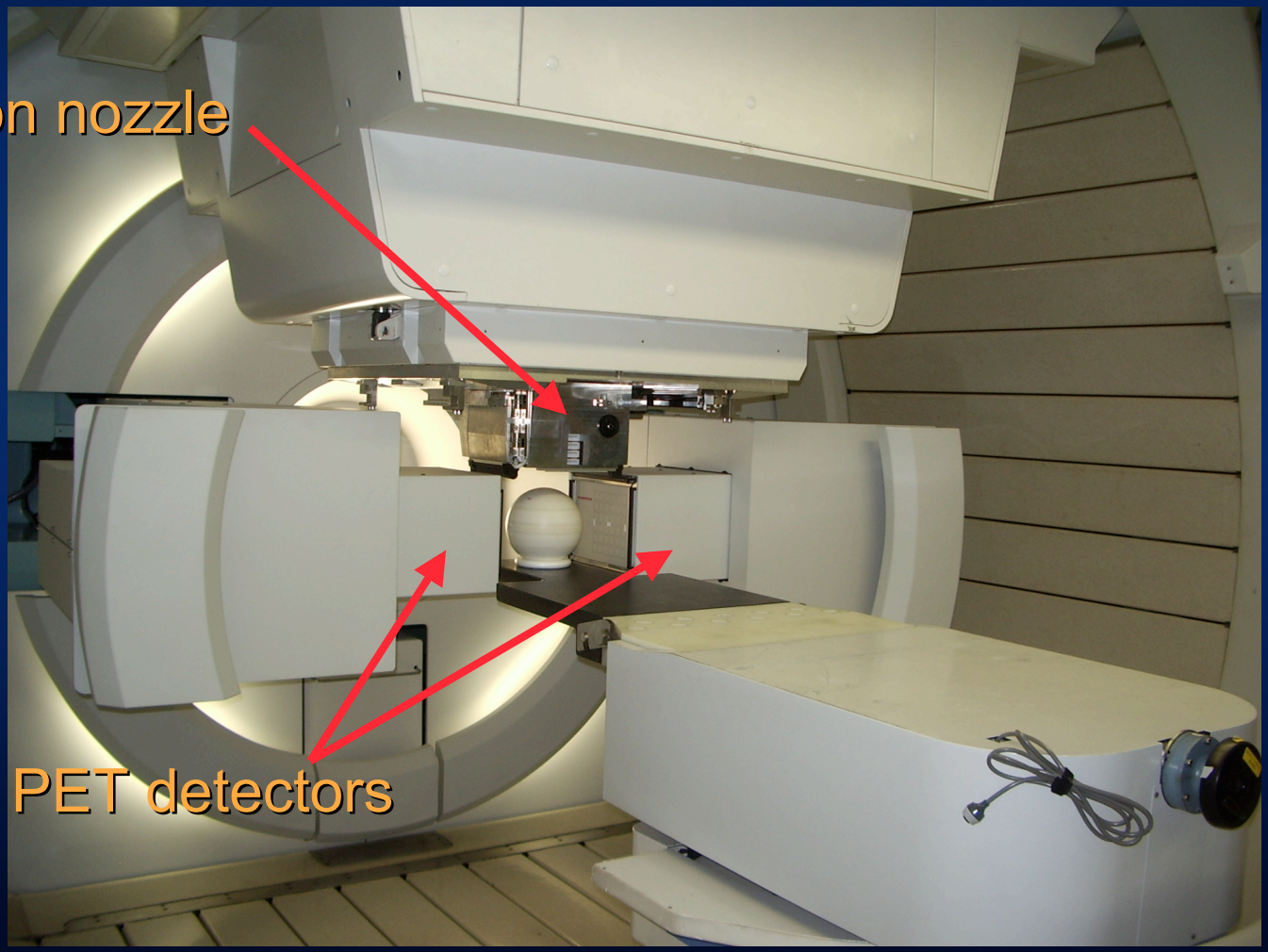
- Multi-institutional Phase II study for low-intermediate risk prostate cancer
  - Objective
    - To evaluate safety and efficacy of proton beam therapy for low-intermediate risk prostate cancer
  - Primary endpoint
    - Incidence of >/= Grade 2 late rectal toxicity
  - PBT
    - 74 GyE/37 fr.
  - Number of accrual patients
    - 150 patients
- Patient accrual has been completed in Mar 2007 !
- Hypofractionated regimen might be the next protocol (matched case control study with protons and carbon-ions)

Adaptive proton beam therapy by beam on-line PET system

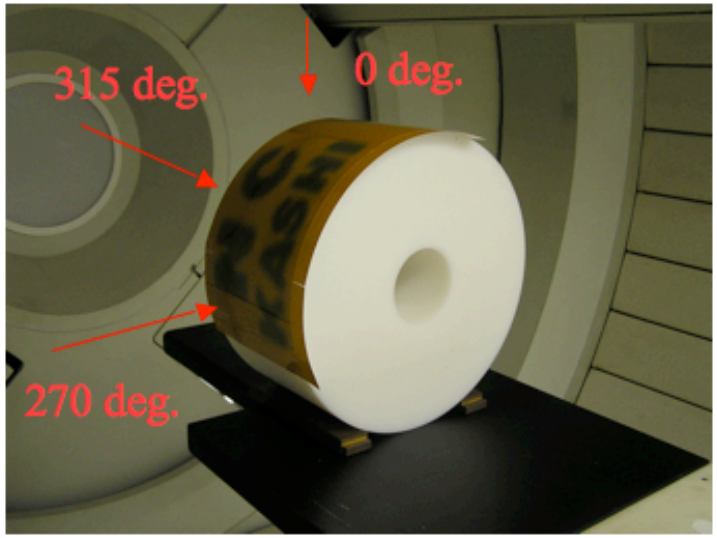
Proton nozzle

Detector head





Scanning Technology



270 deg. : “N” “KA”

315 deg. : “C” “SHI”

0 deg. : “C” “WA”

Final Outlook

- Technological development is always necessary
  - Beam on-line (in-beam CT) PET monitoring system
  - Scanning irradiation
  - Robotic system
  - Dose calculation algorithm (Monte Carlo)
  - MOSFET dosimeter
- PBT has a very promising modality and has the potential to significantly improve clinical outcomes in head & neck, lung, liver and prostate cancer
- So-called radio-resistant tumors (e.g., malignant melanoma, adenoid cystic carcinoma) of the head & neck responded well to PBT
- To conduct multi-institutional clinical trials (domestic & international) is mandatory

Thank you for your attention