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Latest developments in PET verification of proton therapy

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MGH 1811

VE RI TAS

Massachusetts General Hospital
and Harvard Medical School

FZD Forschungszentrum Dresden Rossendorf

Overview

- The advantages and challenges of ion beam therapy
- PET verification of ion beam therapy
  - Motivation and principles
  - Implementations and clinical experiences
  - Technological and methodological improvements
- Conclusion and outlook

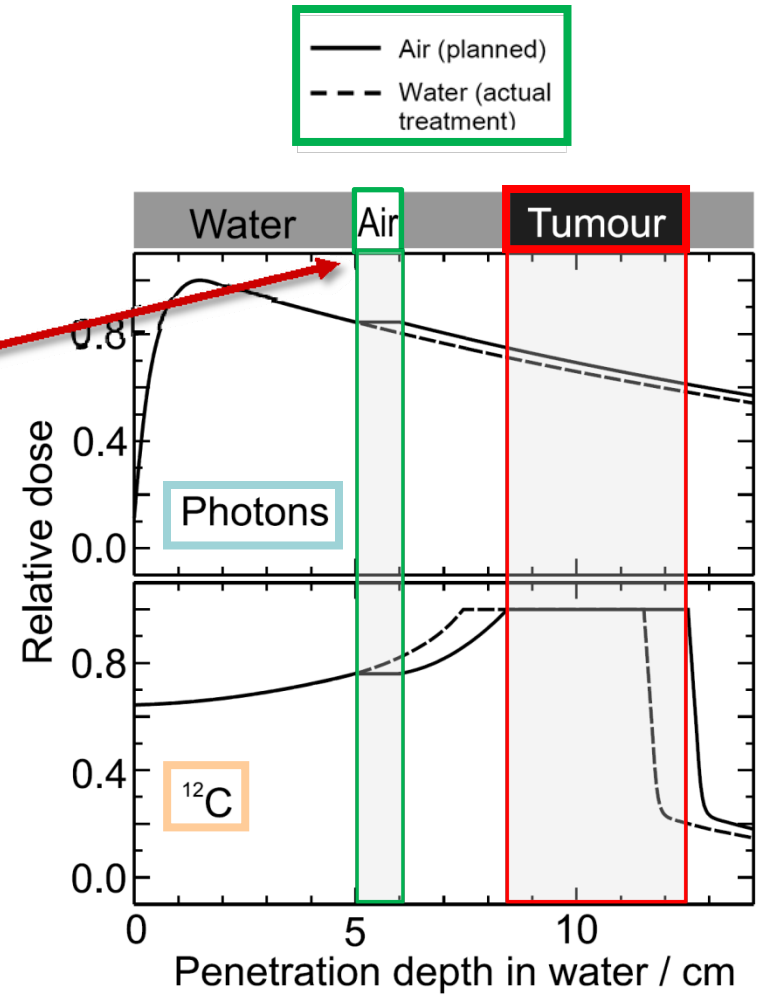
Range uncertainties issues in ion therapy

Difference TP / delivery

- Daily setup variations
- Internal organ motion
- Anatomical / physiological changes

Dose calculation errors

- Conversion CT numbers - ion range
- Inhomogeneities, metallic implants
- CT artifacts



After W. Enghardt, Oncoray Dresden

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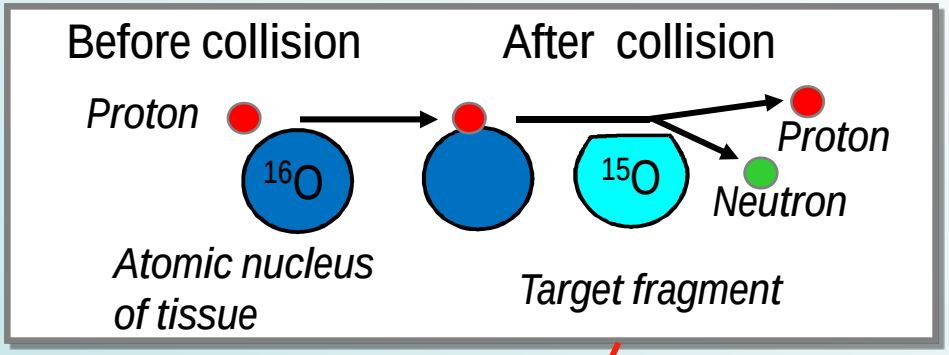
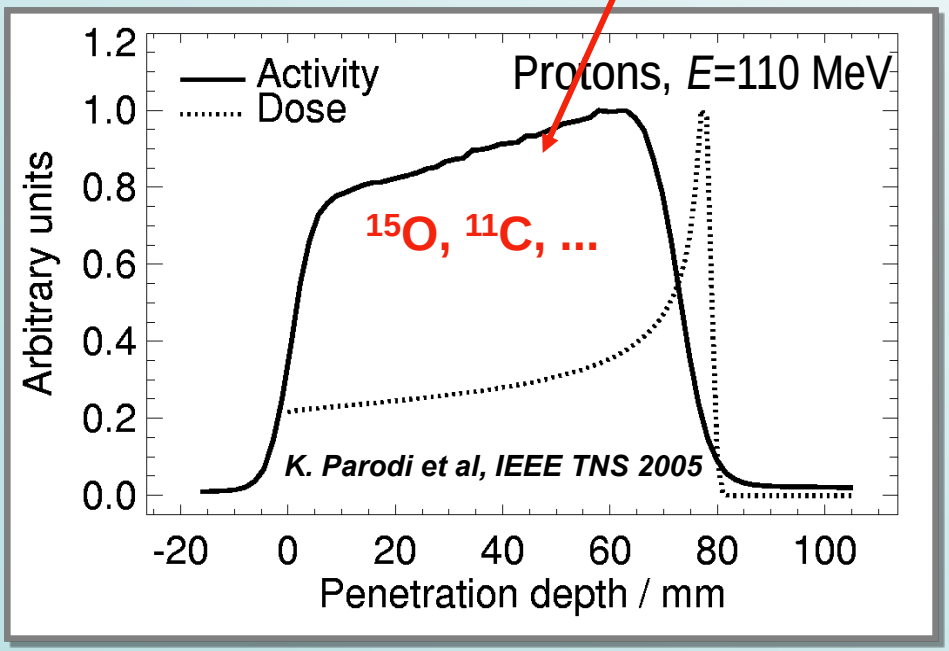
The principle of PET monitoring in ion therapy





By-product of irradiation (^{15}O, ^{11}C, ^{13}N... with $T_{1/2}$ ~ 2, 20 and 10 min)

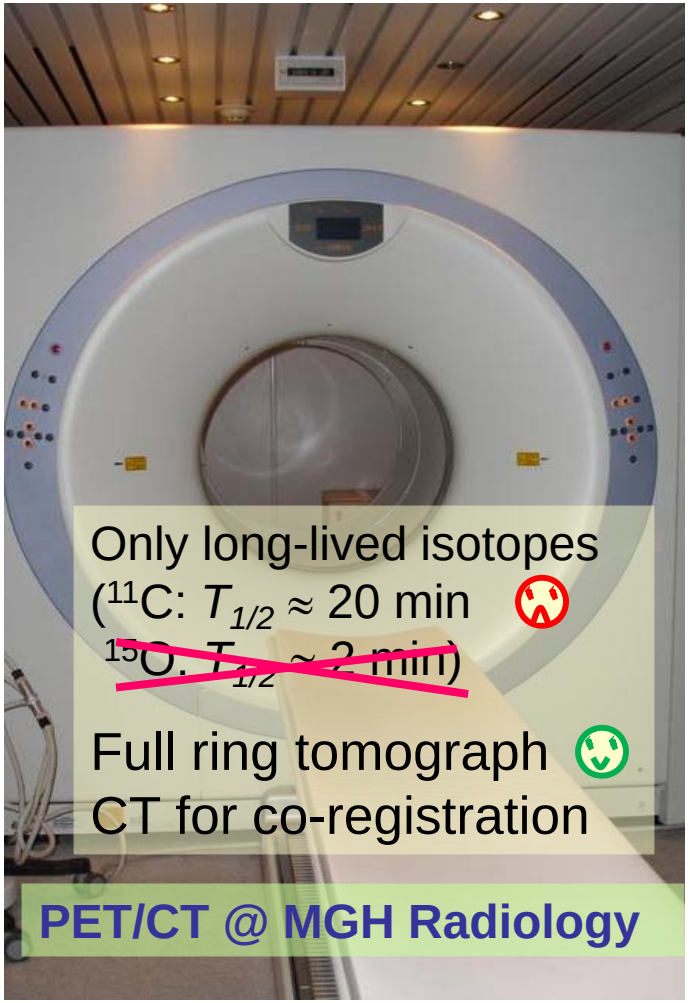
A(r) ≠ D(r): "Dose-guidance" and range - verification from "surrogate„ PET ?

Measured activity compared with Monte Carlo calculation as for ^{12}C therapy at GSI Darmstadt, Germany *(Enghardt et al, NIMA 525, 2004)*

Offline PET/CT after proton Tx @ MGH

Proton Irradiation… ***14-20 min elapsed…*** ***Offline PET/CT***

Passive beam delivery @ Francis H. Burr Proton Therapy Center



Only long-lived isotopes
(^{11}C: $T_{1/2} \approx 20$ min
~~^{15}O: $T_{1/2} \approx 2$ min~~)

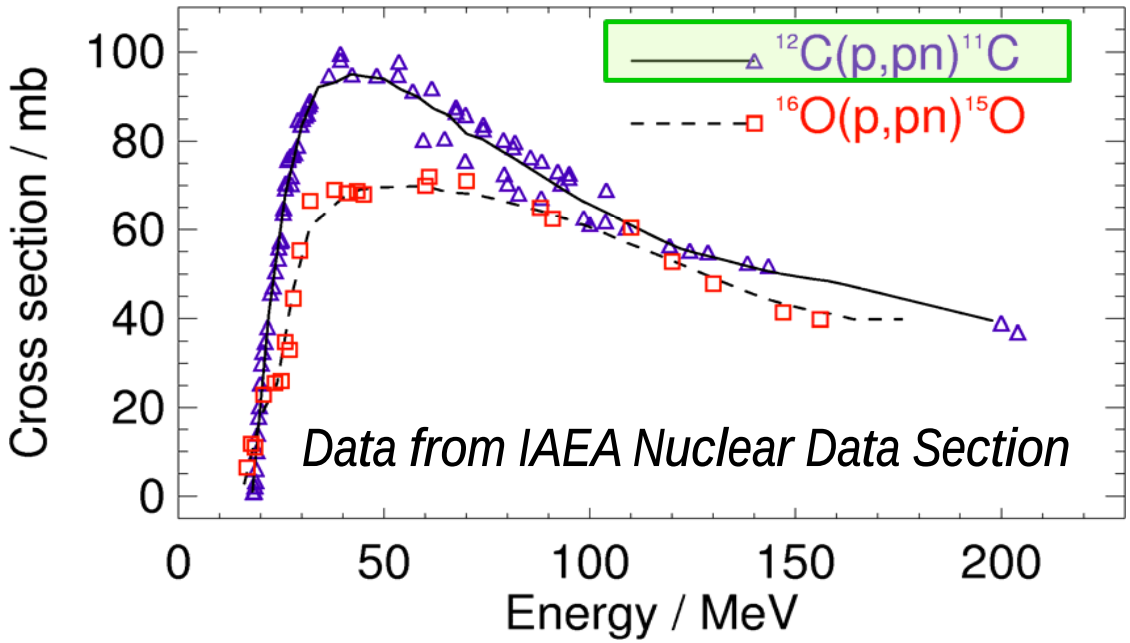
Full ring tomograph
CT for co-registration

PET/CT @ MGH Radiology

Calculation model of β^+-activation

FLUKA Monte Carlo code using

- Field-specific beam source information from Geant4 modeling of the nozzle and beam modifiers ***(Paganetti et al, MP 31, 2004)***
- Planning CT (segmented into 27 material) and same CT-range calibration curve as TPS ***(Parodi et al MP 34, 2007, PMB 52, 2007)***
- Experimental cross-sections for β^+-emitter production
- Semi-empirical biological modeling ***(Parodi et al IJROBP 2007)***
- Convolution with 3D Gaussian kernel (7-7.5 mm FWHM)



…and other reaction channels on N, O, Ca yielding, e.g., ^{13}N, ^{38}K, …

(Parodi et al, PMB 45, 2002, Parodi et al, PMB 52, 2007)

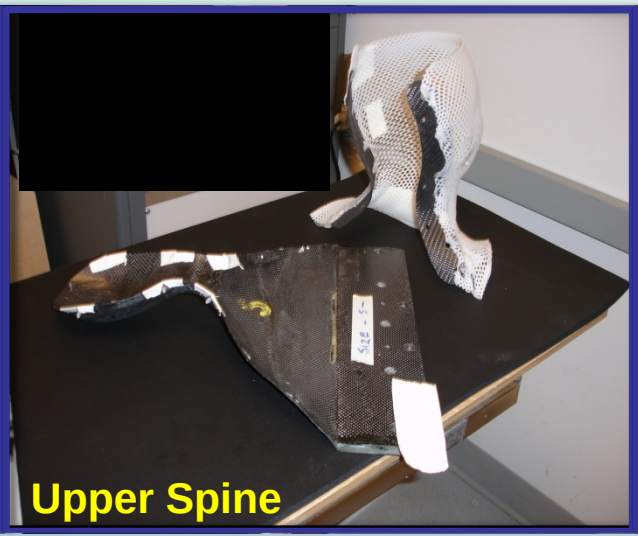
The PET/CT clinical experience @ MGH

Phantom studies: achievable mm-accurate range verification at ~ 2 Gy for t_{meas}~ 20 – 30 min ***(Parodi et al Med Phys 2007, Knopf et al PMB 2008)***

Pilot study *(**9 subjects**: 3 paraspinal, 4 head, 1 sacrum, 1 eye)* followed by

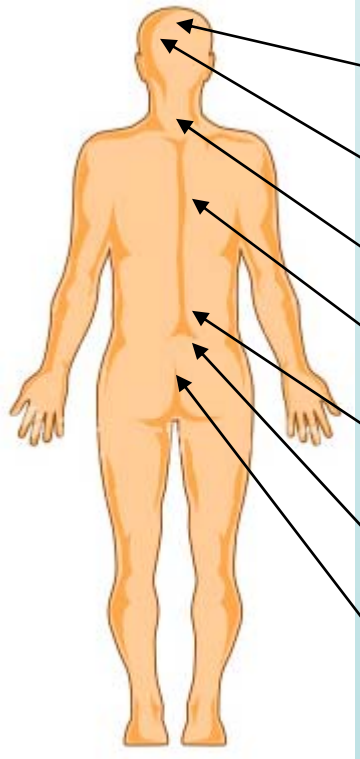
larger study *(**14 subjects**: 8 head, 3 paraspinal, 1 sacrum, 2 prostate)*

- 1 – 2 (3) fields for a typical total dose of ~ 2 GyE
- Same immobilization device at treatment / imaging site
- Post-treatment CT followed by 30 min list mode PET acquisition
- Rigid co-registration of TP-CT and PET-CT



The PET/CT clinical experience @ MGH

- Patients undergoing 1 post-treatment PET/CT (repeated scan in 2 cases)



	# of patients	# of patients that received 1 field	# of patients that received 2 (or 3) fields	Dose per field [GyE]
head	12	3	8 (1)	0.9-3
eye	1	1		10
C-spine	3	1	2	0.6-2.5
T-spine	1		1	1.8
L-spine	2	2		0.9-2
sacrum	2	1	1	1-2
prostate	2	2		2
TOTAL	**23**	**9**	**13 (1)**	**0.6-10**

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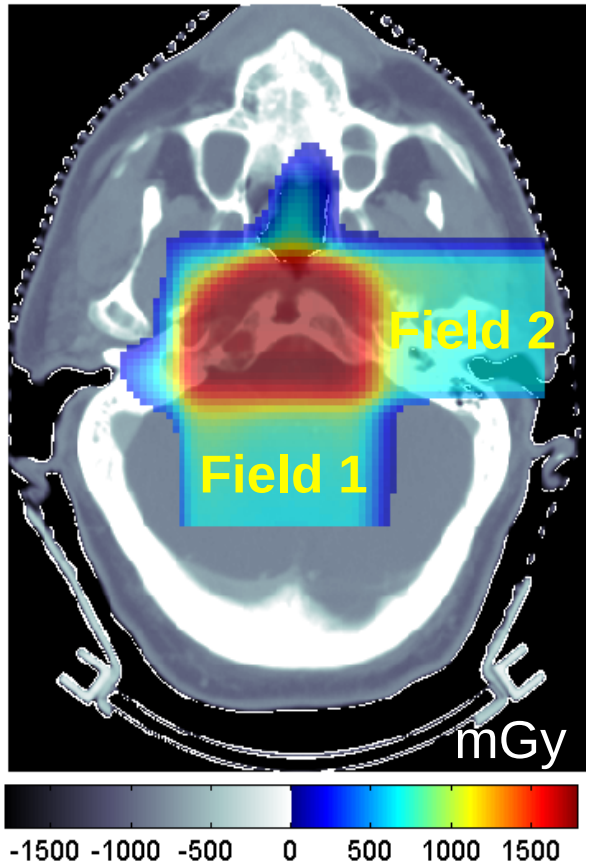
Parodi et al, IJROBP 68, 2007; Knopf et al, PMB 54, 2009

Parodi et al., IJROBP 68 2007

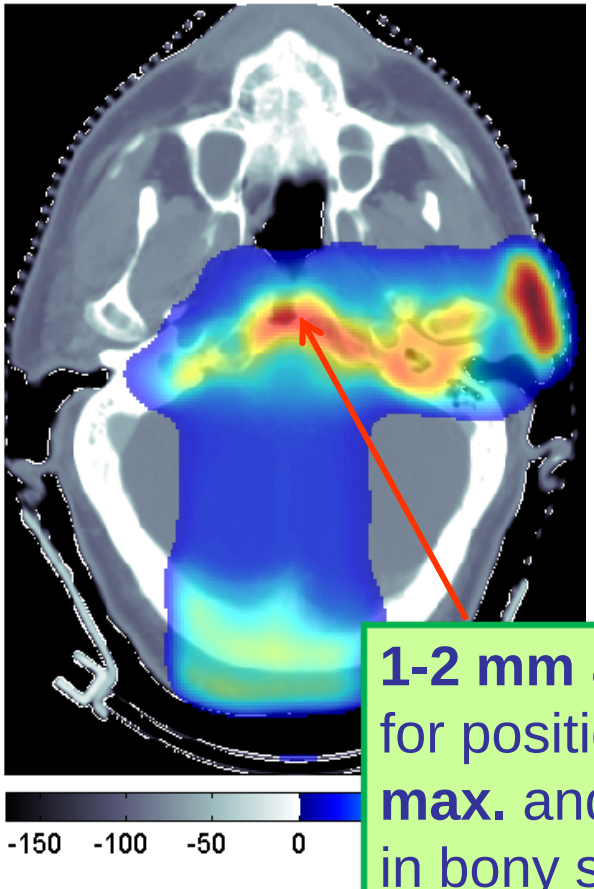
Clival Chordoma
Field 1: 0.87 Gy, ΔT_1 ~ 26 min
Field 2: 0.87 Gy, ΔT_2 ~ 16 min
PET t_{meas}= 30 min

The clinical PET/CT study @ MGH
(skull base tumour)

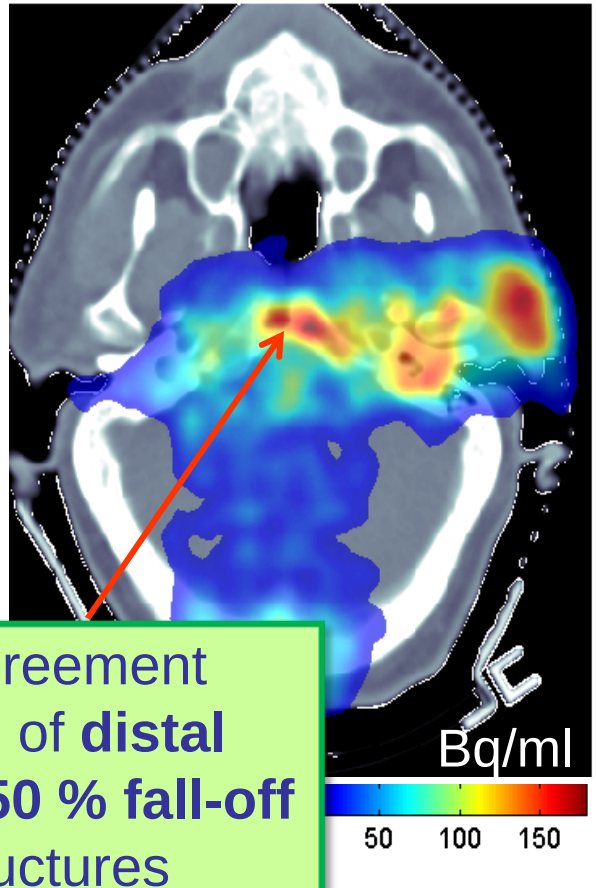
TP Dose Calculation



MC PET Calculation



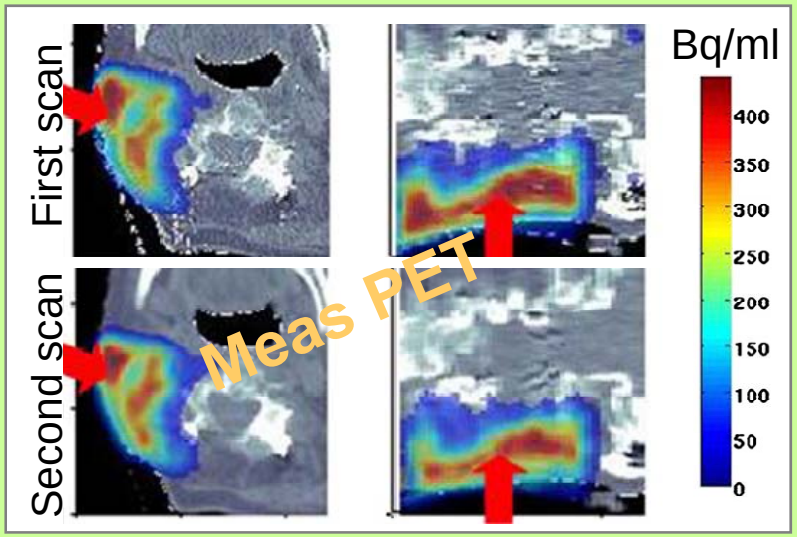
PET/CT Meas.

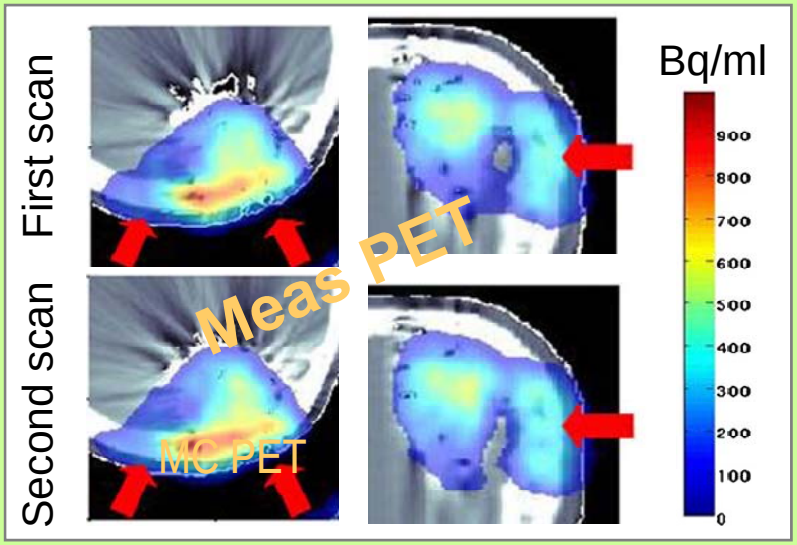


1-2 mm agreement for position of **distal max.** and **50 % fall-off** in bony structures

The clinical PET/CT study @ MGH (c'nt)

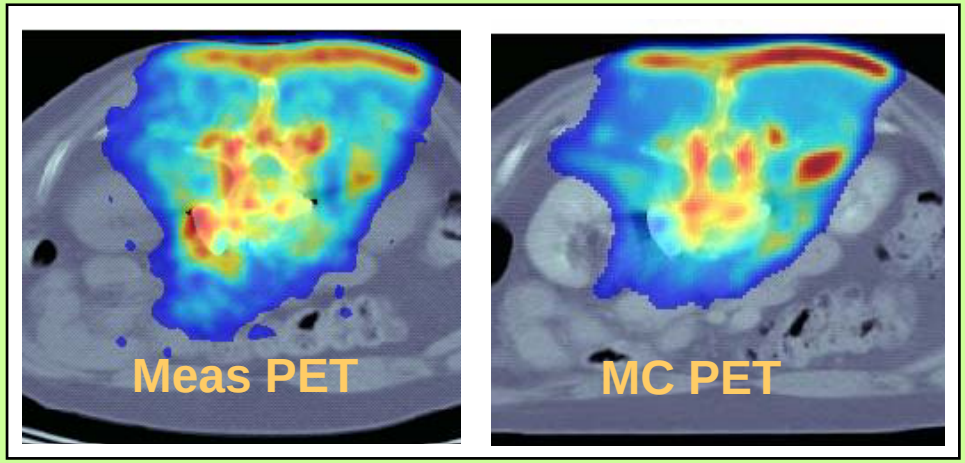
Good reproducibility repeated PET/CT scans (2 H&N cases)

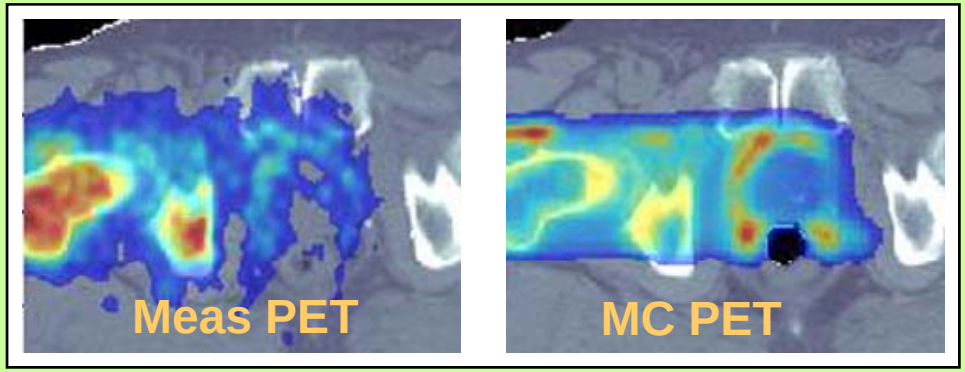




Challenges for abdominopelvic and ocular sites

- Biological washout, motion and co-registration issues
- Uncertainties of CT-based modeling due to overlapping HU domains

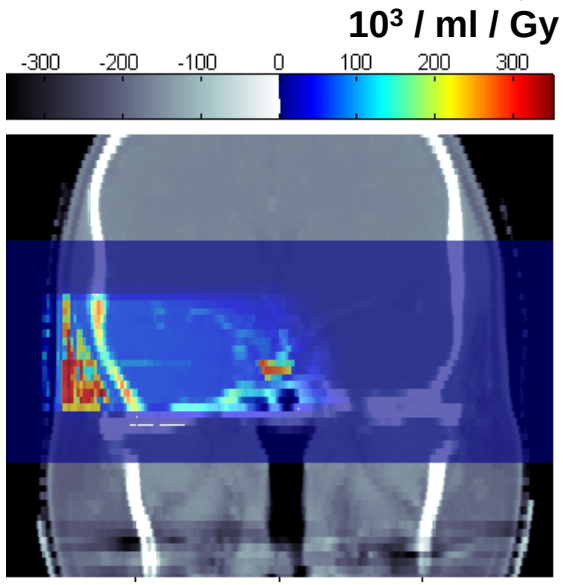




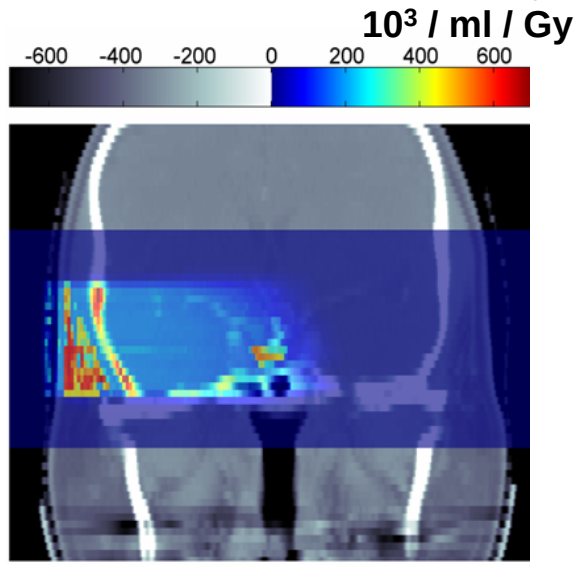
Knopf et al, PMB 54, 2009, Parodi et al, IJROBP 68, 2007

Towards better imaging strategies

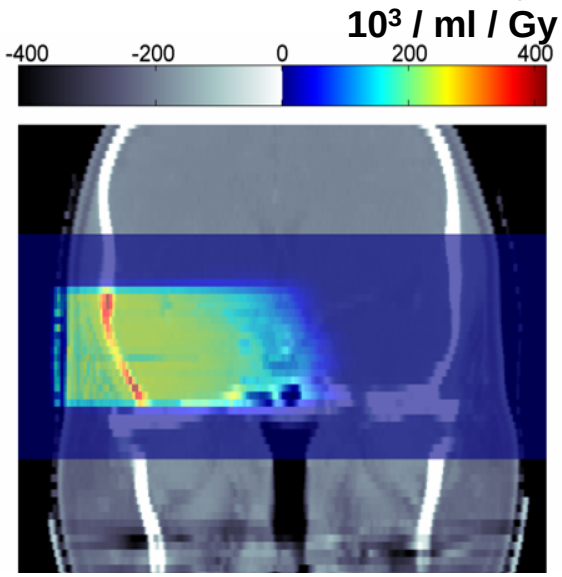
Reducing **delay time** ΔT and **scan time** t_{meas}…



Offline current situation
ΔT = 20 min
PET t_{meas}= 30 min
Total decays: 1.1 10^7



Offline nearby scanner
ΔT = 5 min
PET t_{meas}= 30 min
Total decays: 2.7 10^7



In-beam dedicated
ΔT = 0
PET t_{meas}= 100 s
(60s beam-on with 100% recovery + 40s decay)
Total decays: 2.4 10^7

Parodi et al, IJROBP 71, 2008

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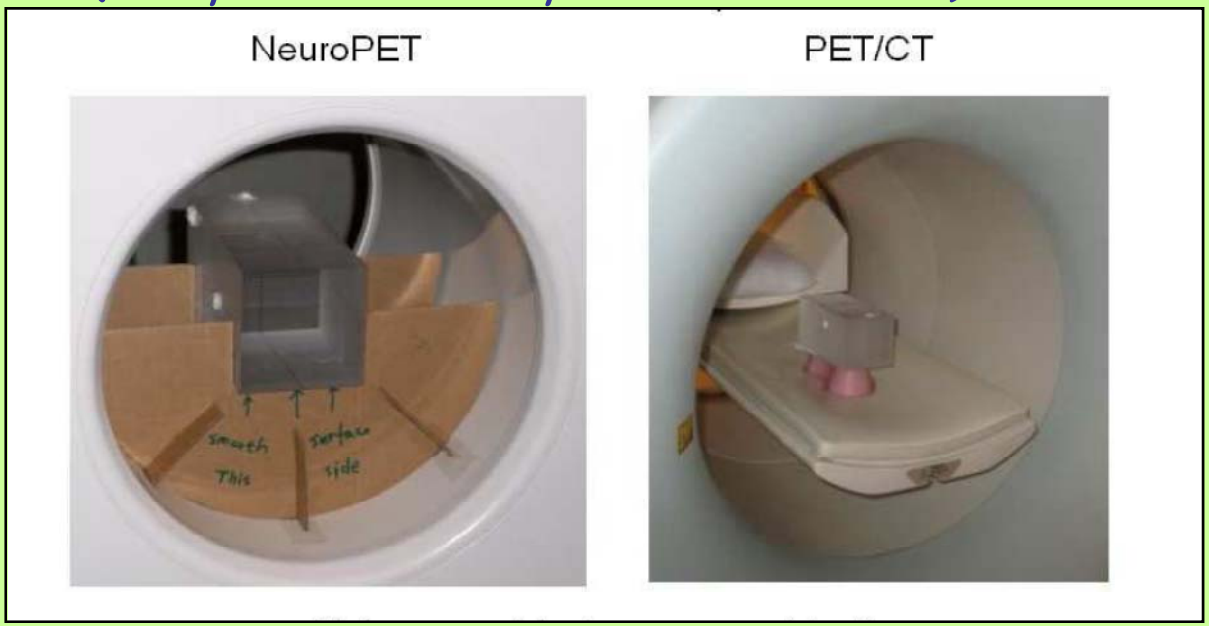
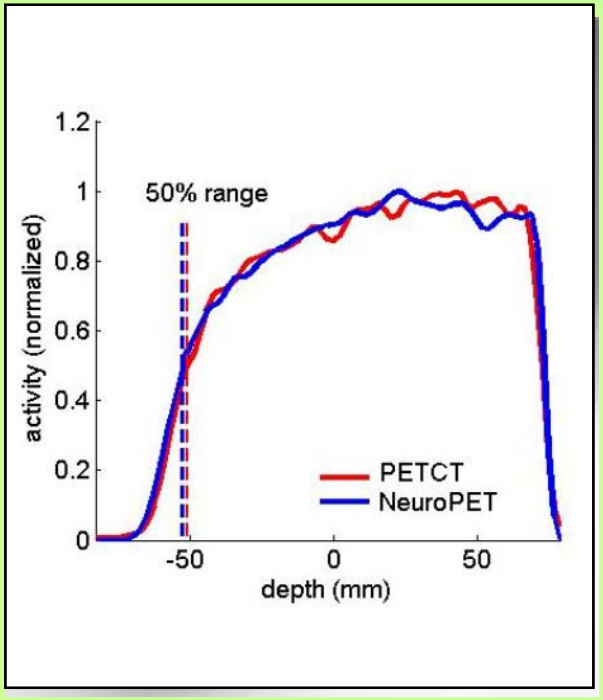
Novel PET systems for in-room imaging (I)

Mobile PET scanner (PhotoDetection Systems Inc) @ MGH

- ≈ Same treatment position and reduced delay irradiation-imaging
- Already benchmarked against offline PET/CT in phantom experiments

(see poster A. Knopf SU-FF-J-129)





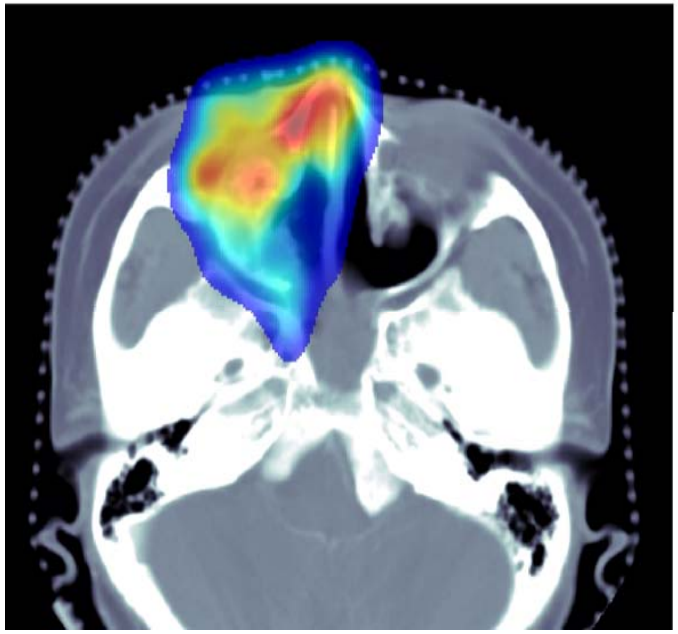
- Clinical investigation ongoing

http://www.photodetection.com

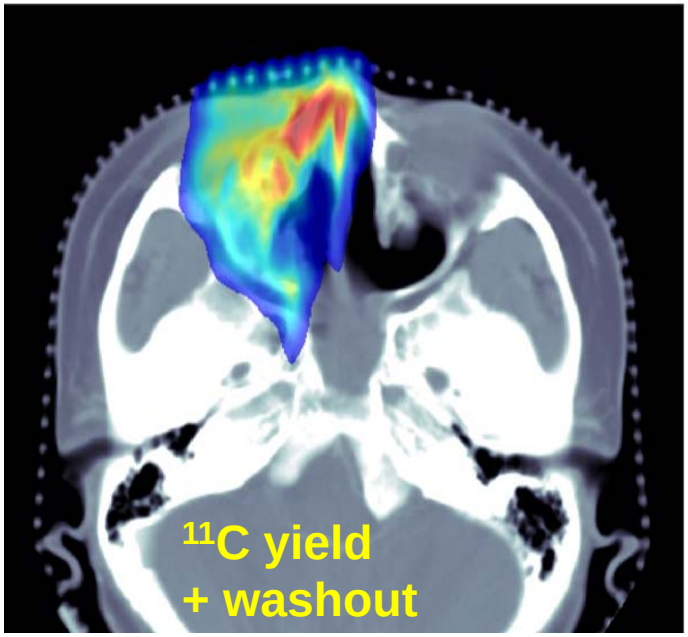
Analytical modeling for in-room imaging

Extend to short-lived emitters a proposed fast analytical approach deriving the PET signal directly from the planned Dose (PET = filter * Dose)

MC-PET (offline PET scan)



Analytically filtered dose



Parodi and Bortfeld, PMB 2006; Parodi et al, AAPM 2006

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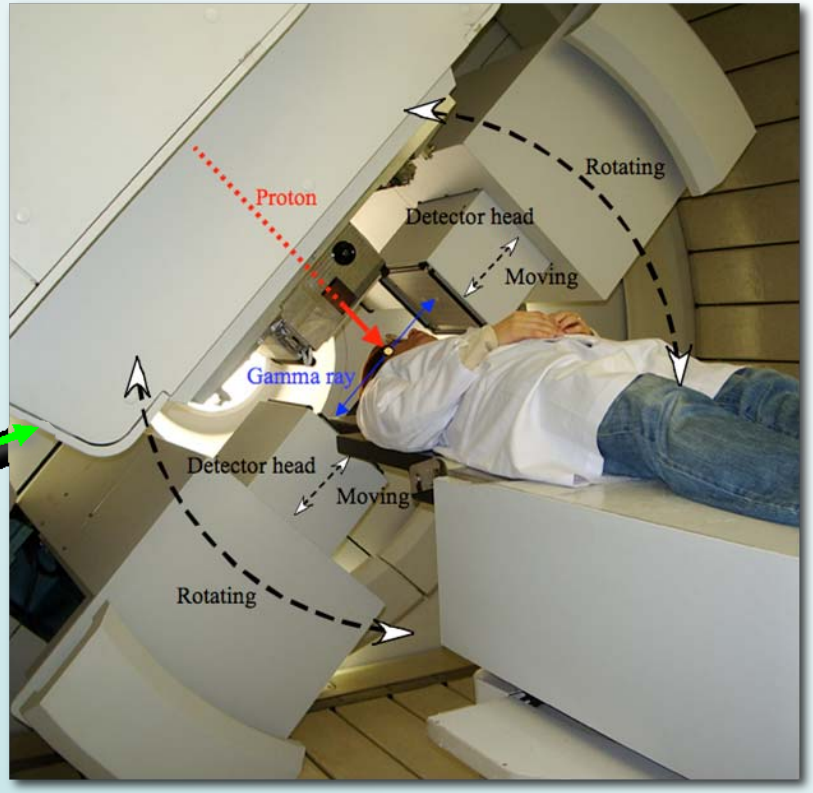
Attanasi et al, Talk TH-D-303A-3

Novel PET systems for in-room imaging (II)

Dual-head scanner mounted on rotating gantry at NCC Kashiwa, Japan

- Distance between two opposing detector heads of 30 - 100 cm
- Icentric rotating of 0 -360 deg.
- Position resolution of 1.6-2.1 mm FWHM
- Detection area of 164.8×167.0 mm^2

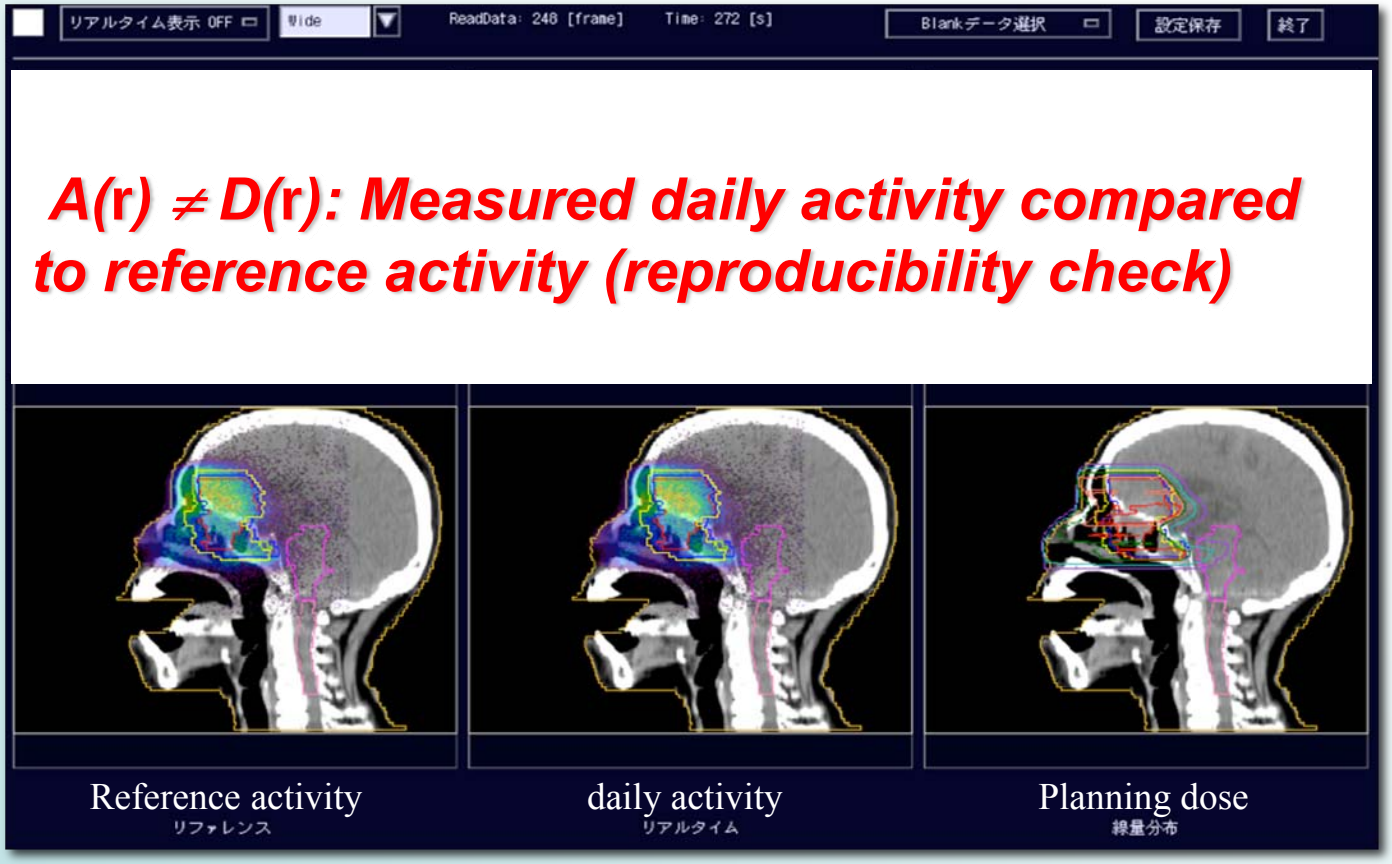
Courtesy of T. Nishio NCC Kashiwa



NCCH-E

Novel PET systems for in-room imaging (II)

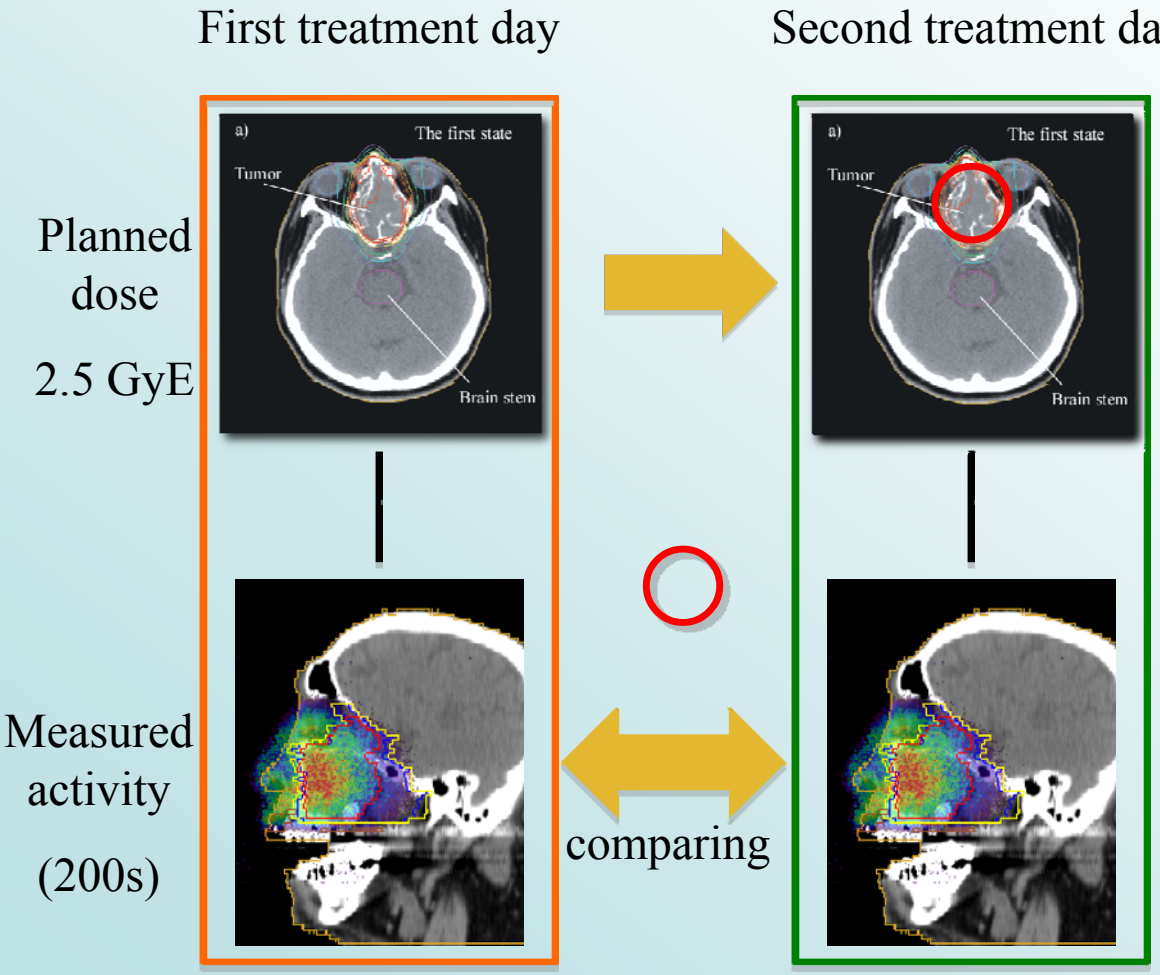
Planar imaging starting immediately after end of irradiation



- 50 patients of H&N, Liver, Lung, Prostate and Brain (2007/10 -)
- Daily measurement of the PET image of every irradiation field for a proton treatment
- Measured PET images of 1000 or more (50 patients)

Courtesy of T. Nishio, NCC Kashiwa

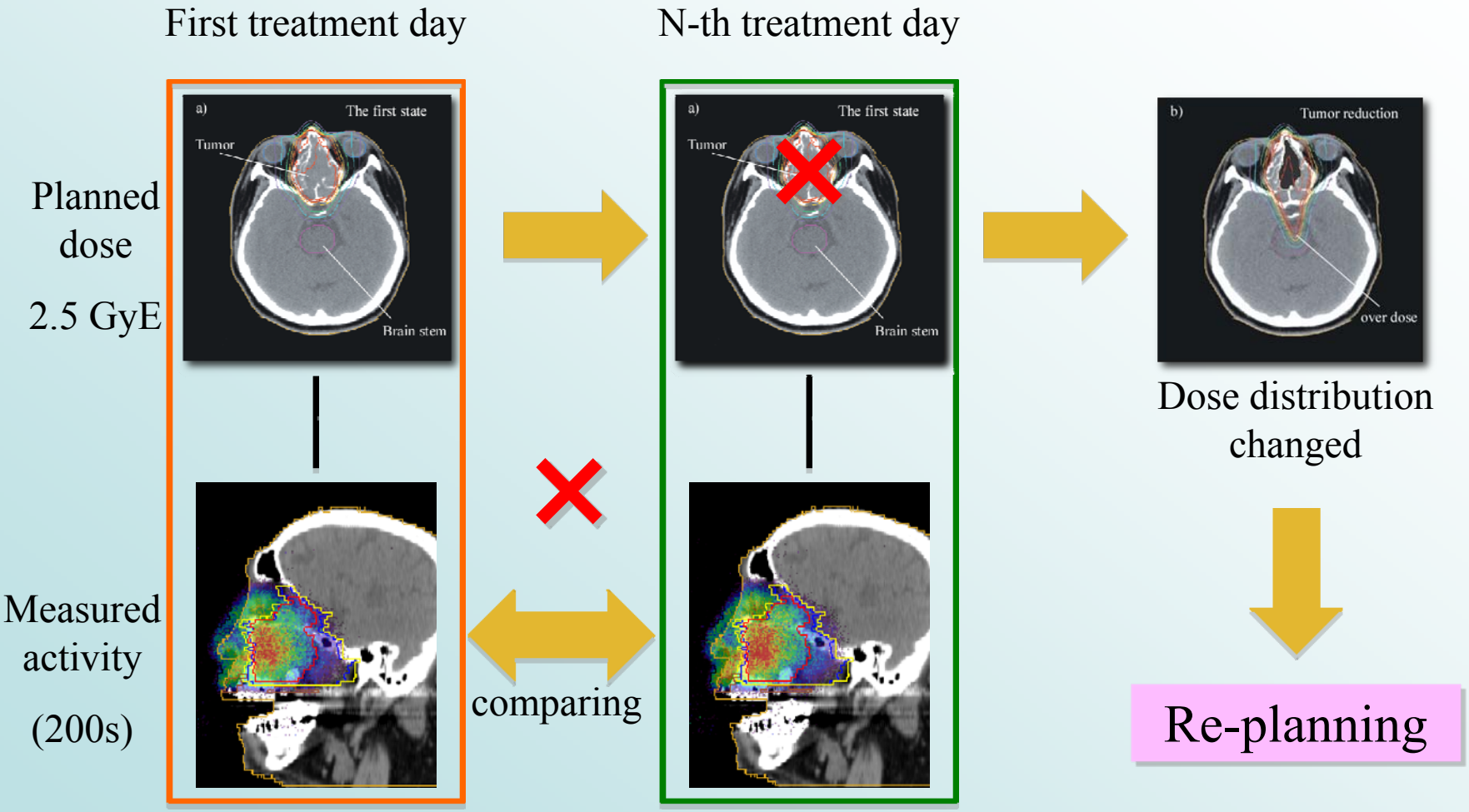
Clinical implementation and experience @ NCC



NCCH-E

Courtesy of T. Nishio, NCC Kashiwa, accepted for publication in IJROBP

Clinical implementation and experience @ NCC

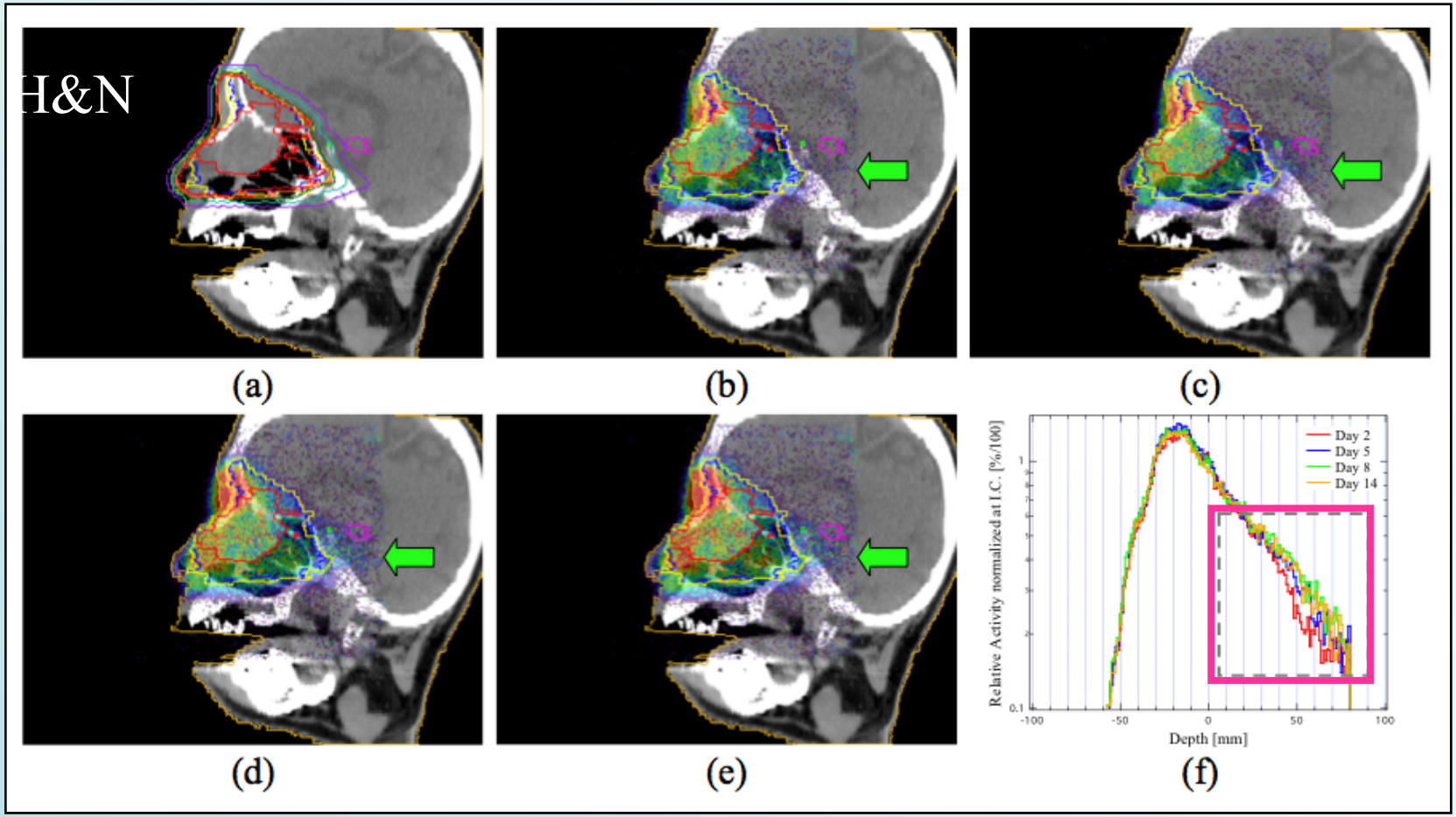


NCCH-E

Courtesy of T. Nishio, NCC Kashiwa, accepted for publication in IJROBP

Change of activity in treatment period

121MeV/SOBP90/G10deg./B20deg. /2.5GyEpfx.: (a) dose distribution

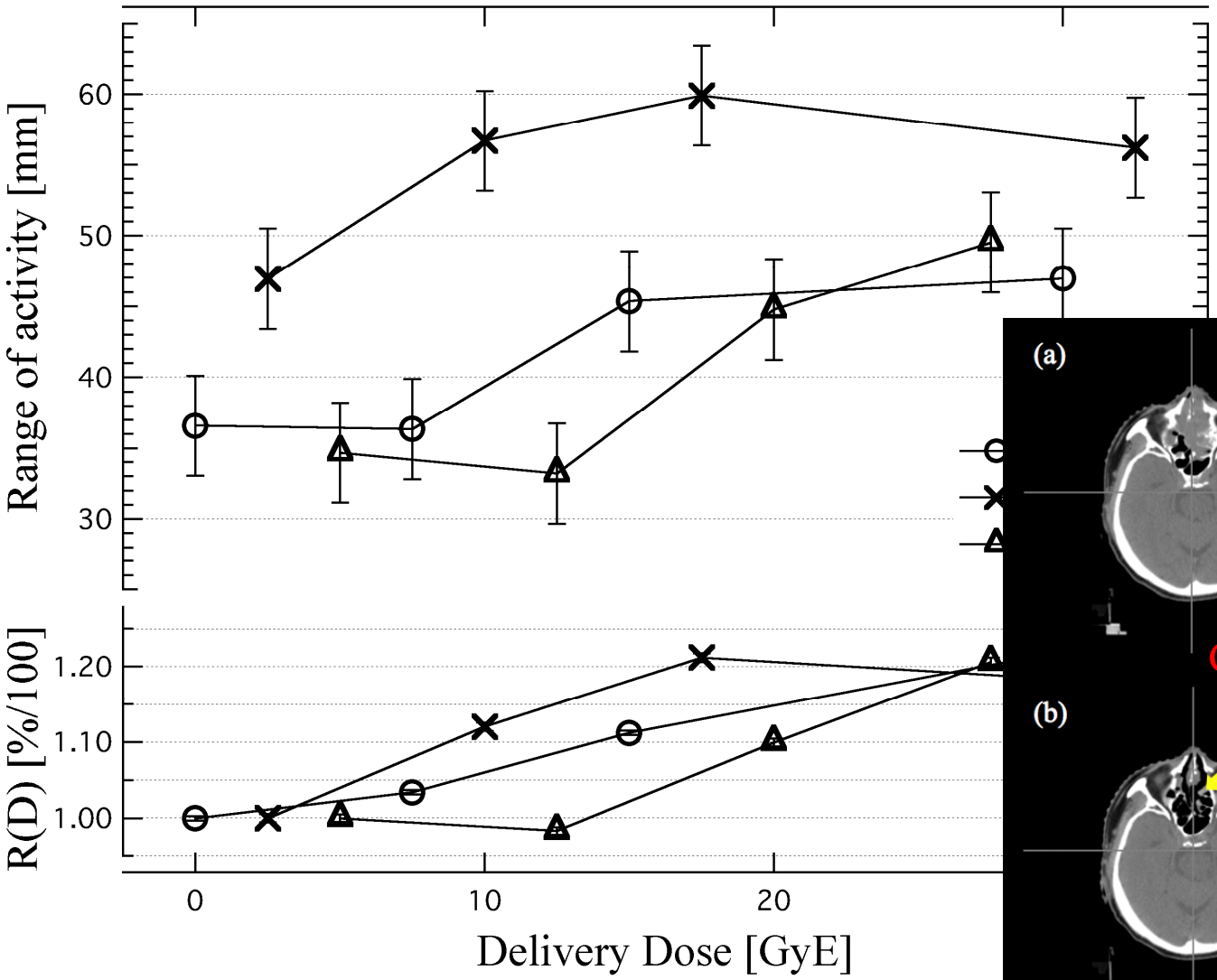


Activity distribution (delivery dose) : (b) 2.5 GyE, (c) 10 GyE, (d) 17.5 GyE, (e) 32.5 GyE, (f) depth profile

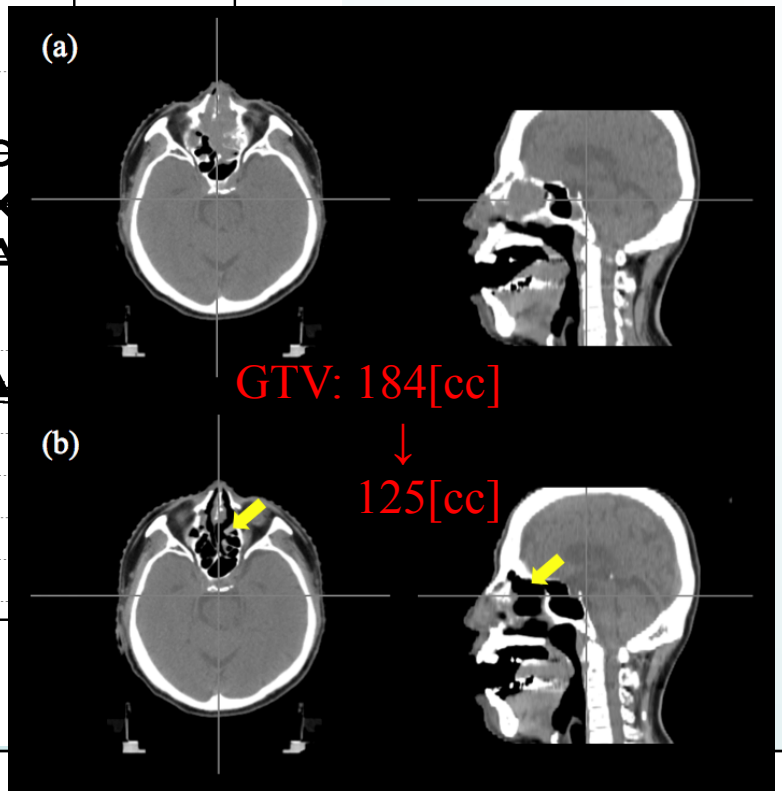
NCCH-E

Courtesy of T. Nishio, NCC Kashiwa, accepted for publication in IJROBP

Change of activity in treatment period



$$\Delta R_{max}(\text{plan(b)} - \text{plan(a)}) = \begin{cases} -21.1 \text{ mmWEl} & : \text{port1} \\ -15.0 \text{ mmWEL} & : \text{port2} \\ -17.2 \text{ mmWEL} & : \text{port3} \end{cases}$$



Courtesy of T. Nishio, NCC Kashiwa, accepted for publication in IJROBP

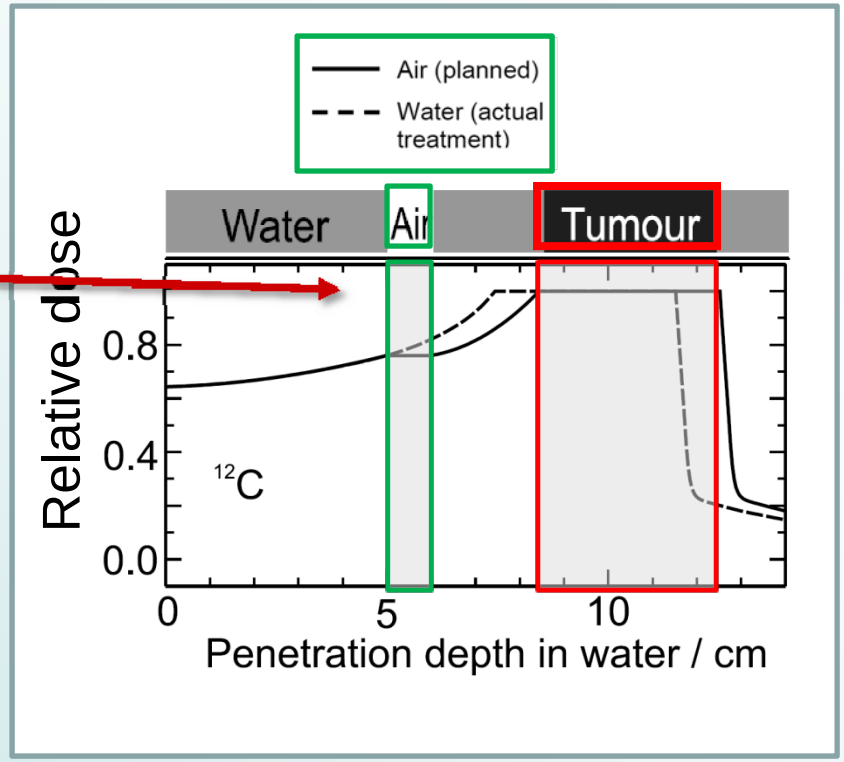
NCCH-E

The issue of moving organs

Detrimental effect of motion not only on imaging BUT also on dose delivery

Sensitivity of ion therapy to density variations is increased in the presence of intra-fractional organ movement, e.g., due to respiration

Motion is accounted for using special motion-compensated beam delivery strategies like gating or beam tracking



Feasibility and potential of time-resolved 4D PET verification

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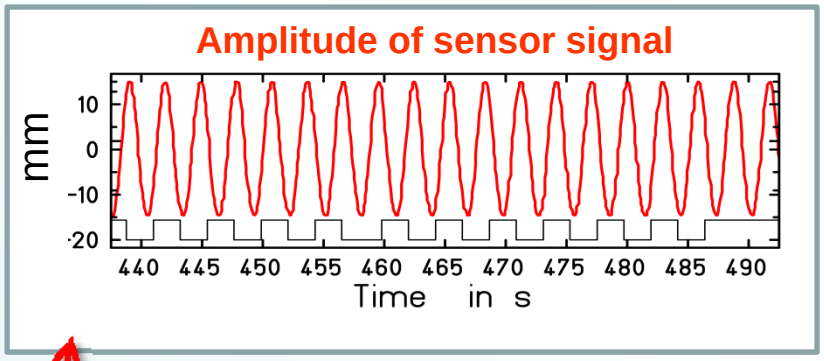
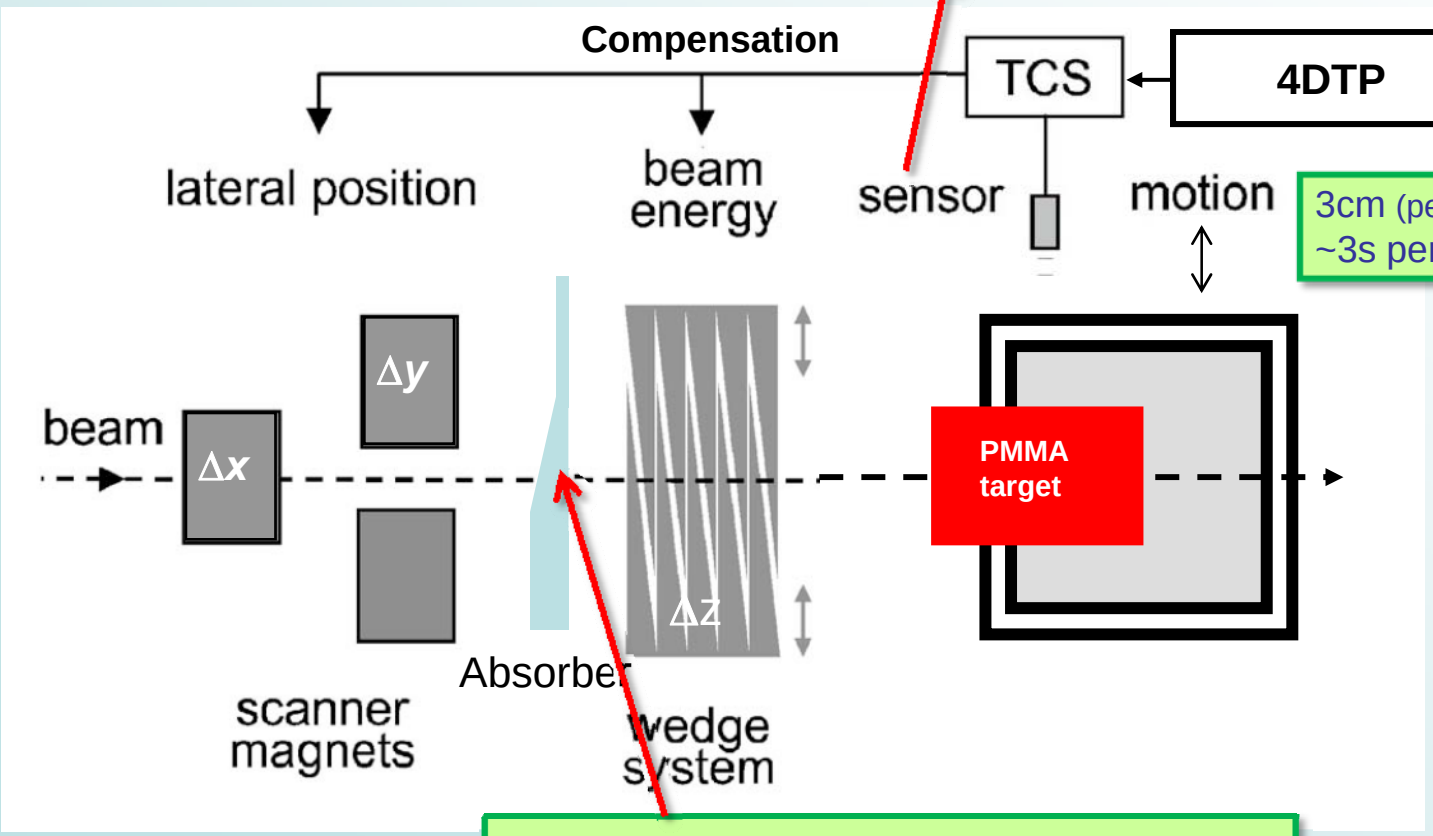
Ion beam tracking at GSI Germany

Bert et al, Med Phys 2007
Bert and Rietzel, Radiat Oncol 2007





Laterally compensated beam goes through different absorber thickness
➔depth compensation with wedge

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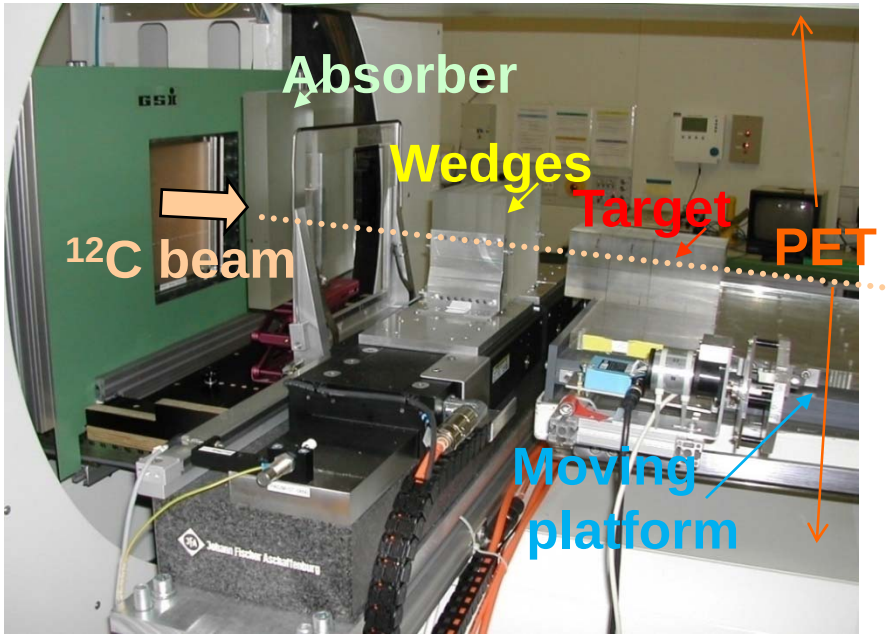
4D in-beam PET experiment @ GSI

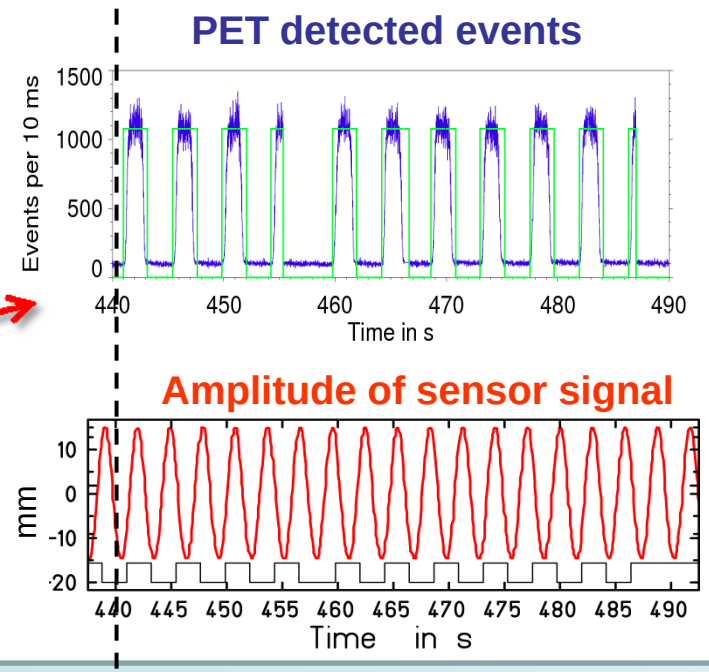
Parodi et al, Med. Phys, in press



The data acquisition

~6min irradiation	~25min decay	~18min decay
In-beam	Offline (I)	Offline (II)
Moving phantom *(static in ref. meas.)*		Static phantom

time



Time correlation between PET acquisition and motion track, both synchronized with pulsed irradiation

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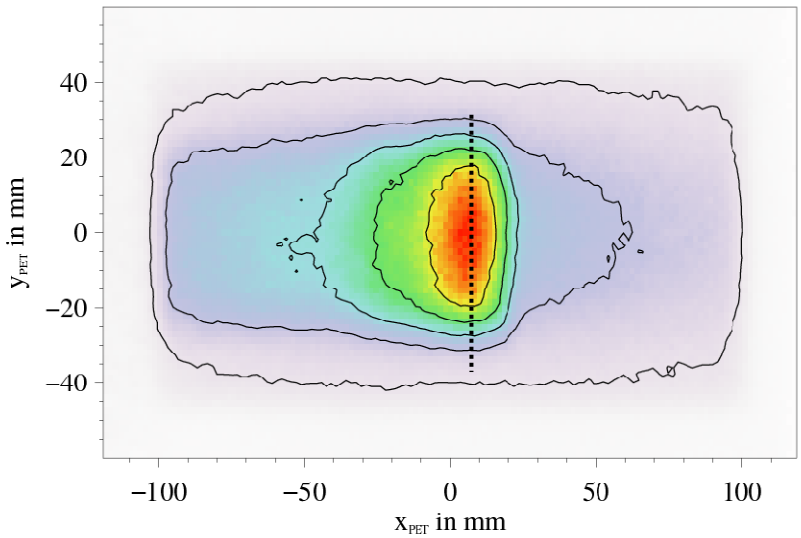
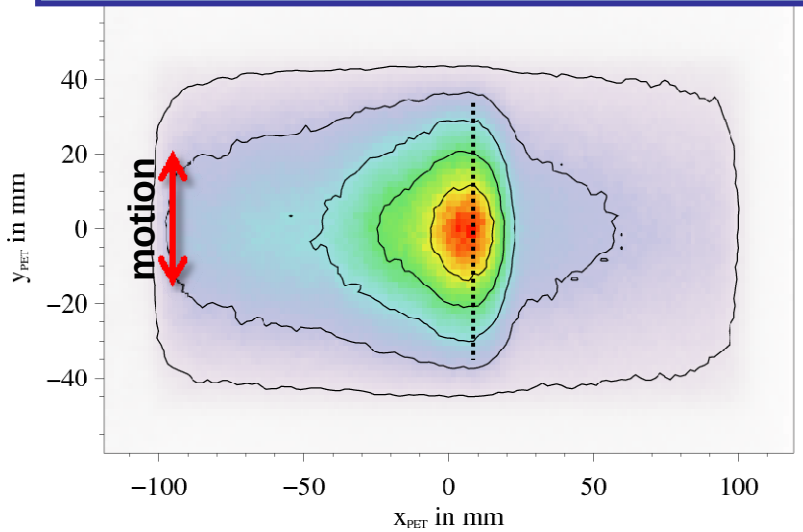
Results: 2D images

Signal recovery implementing
phase-resolved 4D reconstruction
co-registered to a reference phase

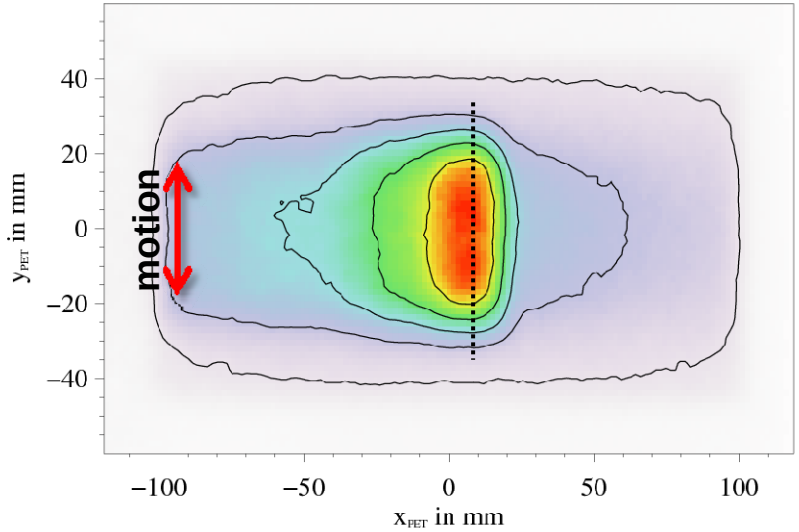
Static reference



Standard 3D reco, no Phase sorting



4D reco + co-registration



Parodi et al, Med. Phys., In press

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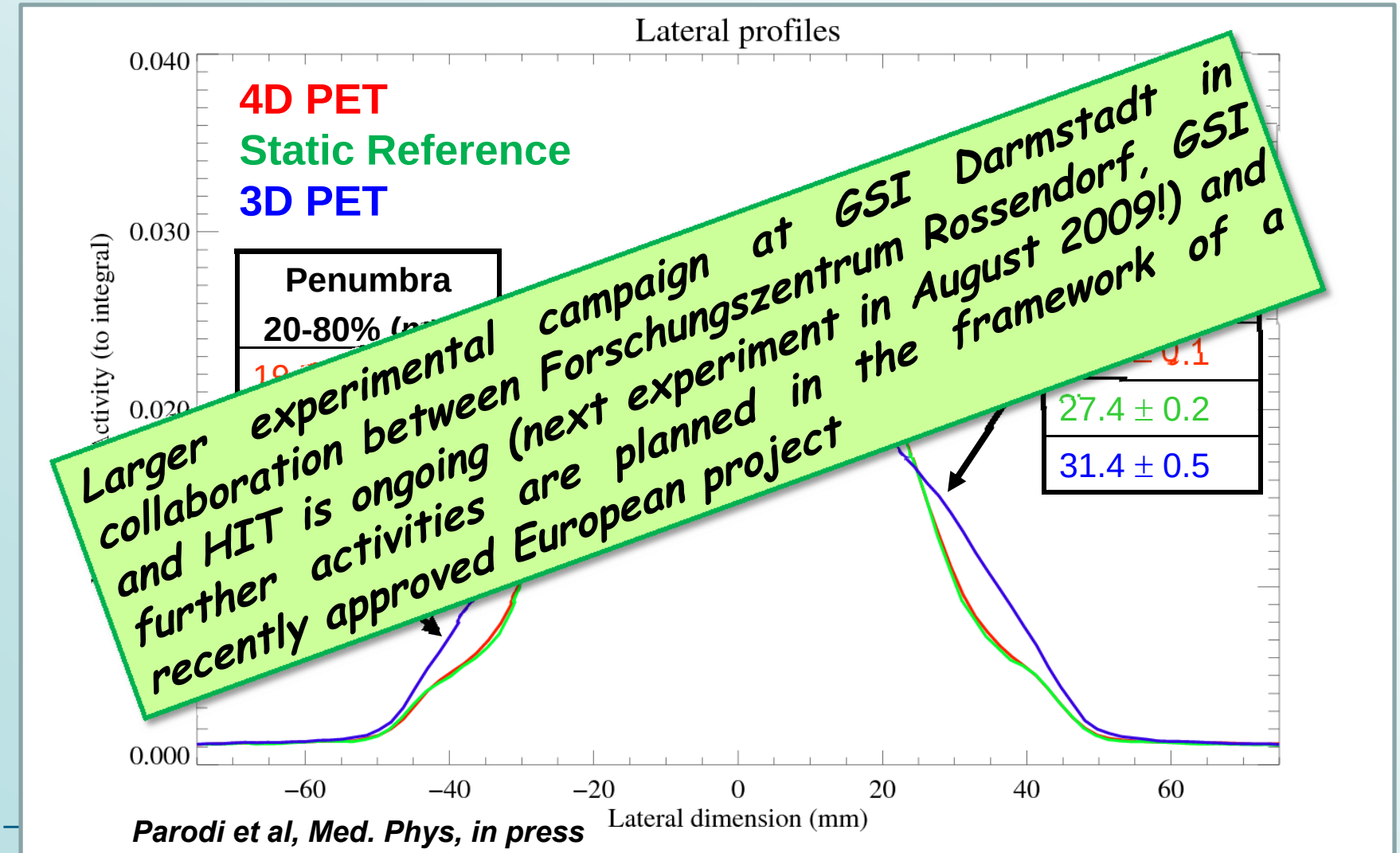
Results: signal recovery in motion direction

Proof-of-principle of 4D in-beam PET verification of ion tracking



Larger experimental campaign at GSI Darmstadt in collaboration between Forschungszentrum Rossendorf, GSI and HIT is ongoing (next experiment in August 2009!) and further activities are planned in the framework of a recently approved European project

Parodi et al, Med. Phys, in press

Conclusion and outlook I

- Ion beam therapy is rapidly spreading worldwide
- Full clinical exploitation of its promise
  - In-vivo imaging of “surrogate” signal, e.g., from escaping secondary radiation to infer information on the primary dose delivery
  - Reliable computational tools for accurate modeling of the “surrogate” signal and the dose deposition
- PET is a mature imaging technique for in-vivo treatment verification
- Ongoing research on technological / methodological improvements to enable optimal quality assurance of ion beam therapy

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Conclusion and outlook II

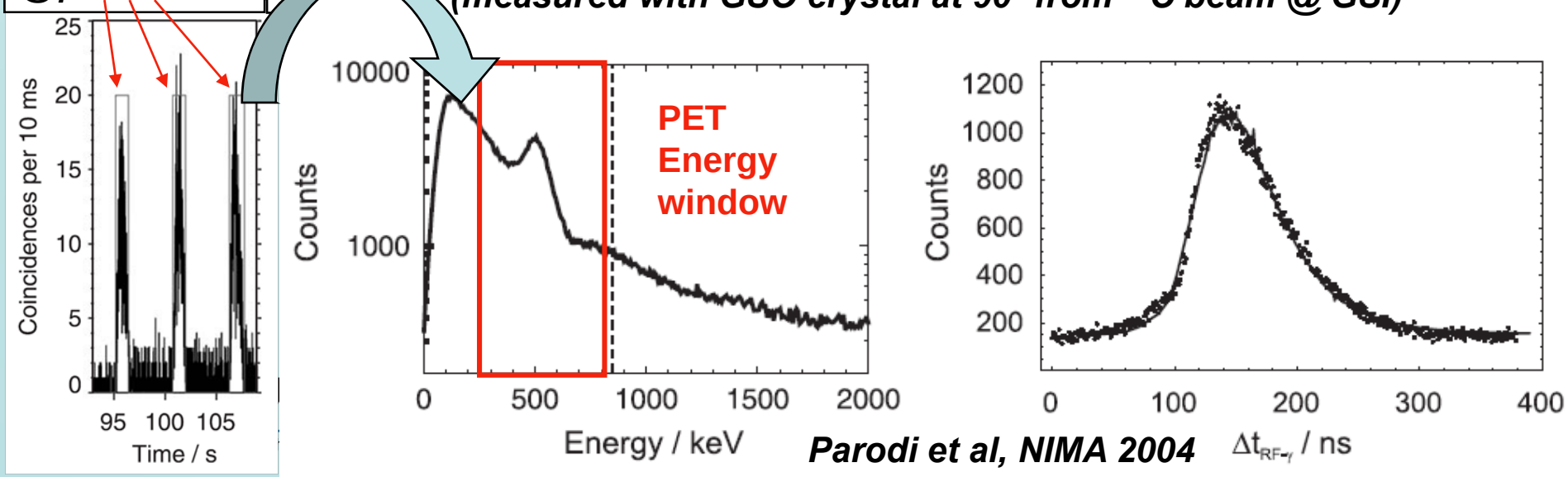
- "In-beam" PET implementation would be method of choice but is technological challenging due to the need of
  - Dedicated, expensive instrumentation (industrial partners?)
  - Dedicated data acquisition solutions to suppress noise form background radiation (γ, *n*, *p*, …) during "beam-on" time

(W. Enghardt, J. Pawelke, K. Parodi and P. Crespo, Patent DE 10 2004 009 784 A1)

See Next Talk…

In-beam PET @ pulsed beam

Measured backround radiation timely correlated to beam micropulses (measured with GSO crystal at 90º from ^{12}C beam @ GSI)



Parodi et al, NIMA 2004

Acknowledgements

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C. Bert, N. Saito, N. Chaudhri, GSI Darmstadt, Germany
E. Rietzel, SIEMENS, Germany
T. Nishio, NCC Kashiwa, Japan

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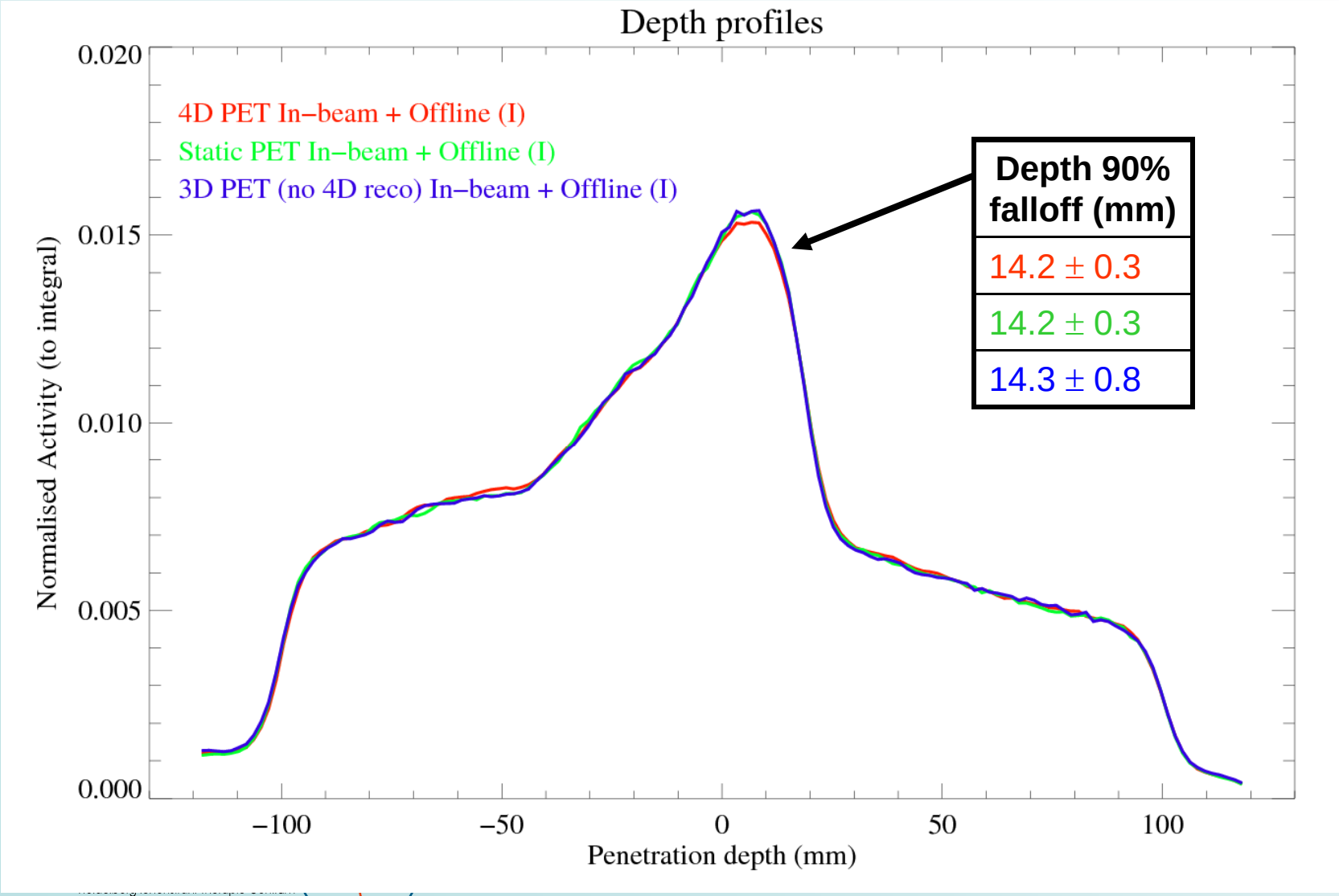
PTCOG 48
28 September - 03 October 2009
Heidelberg Convention Center
http://www.ptcog-meeting.de

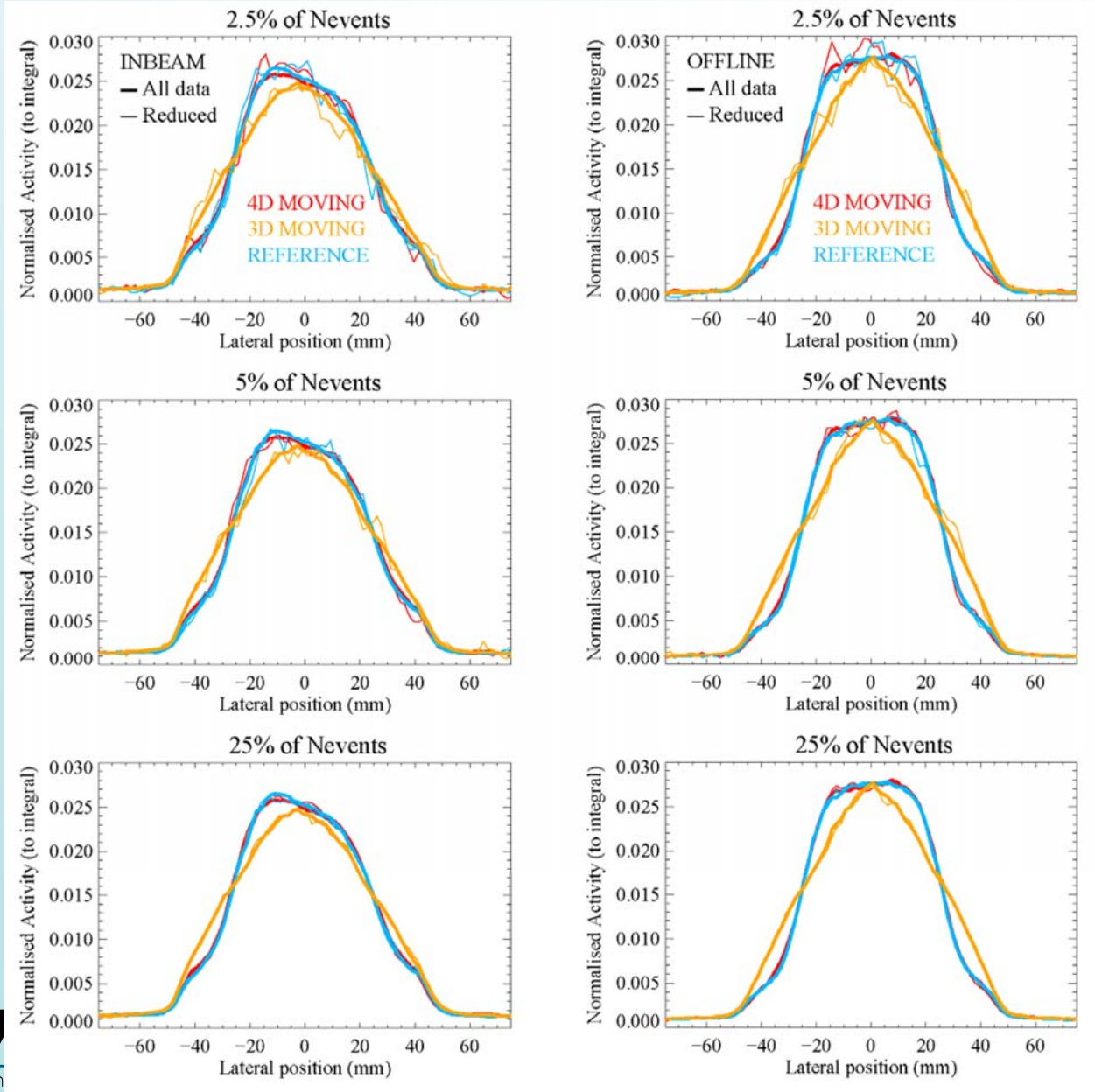
Thank you for your attention

Results: depth profiles

β^+-activity depth-profiles for 4D reco., uncorrected reco. and static ref.



Results: dependence on statistics



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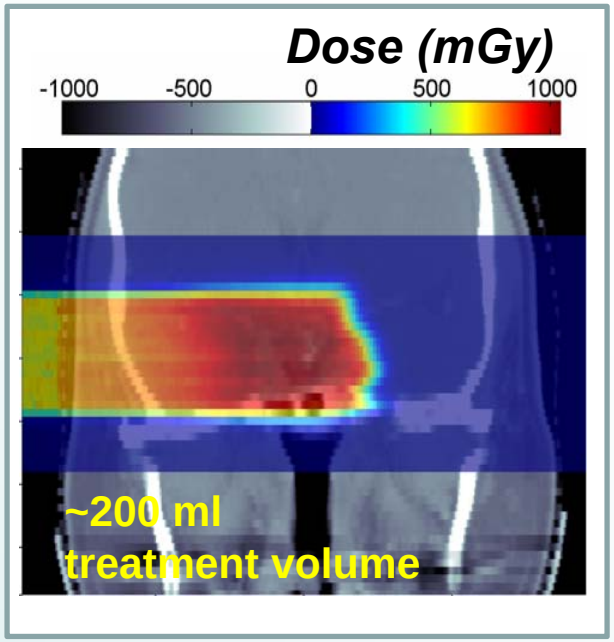
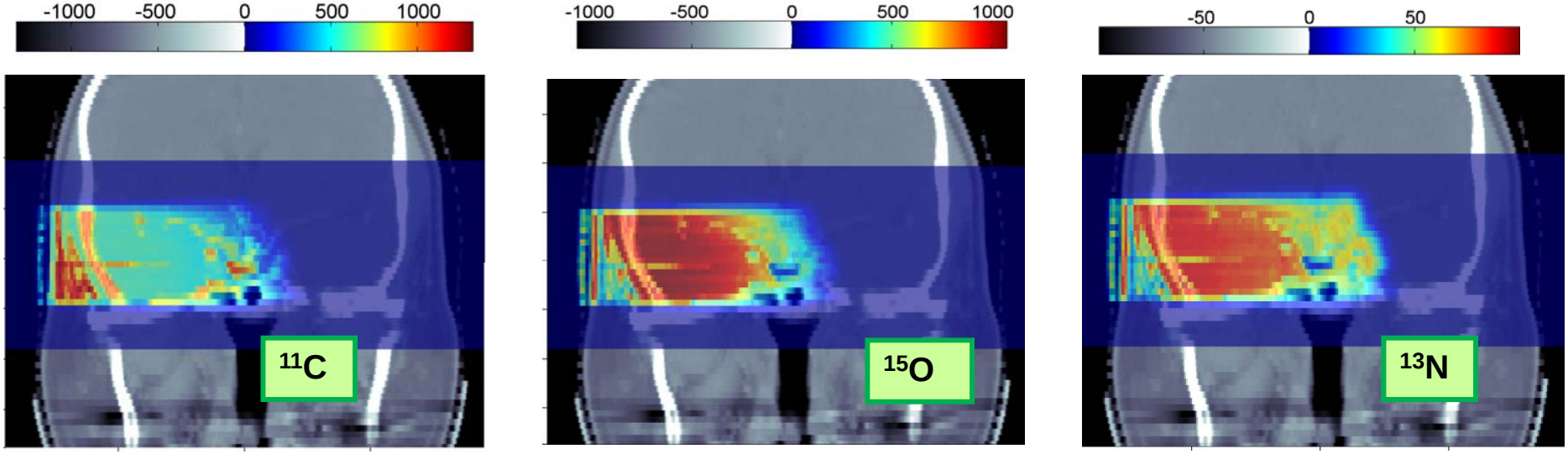
Investigation of optimal imaging strategy

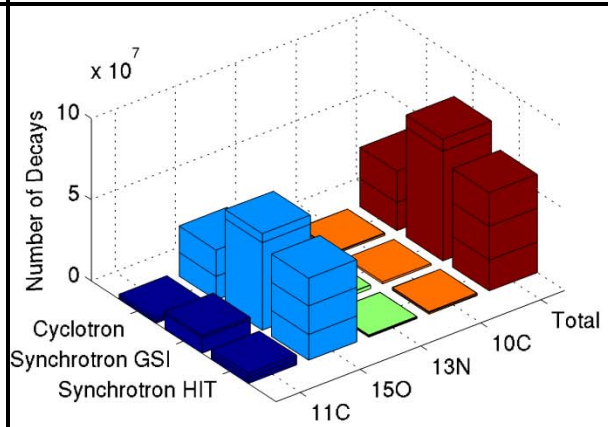
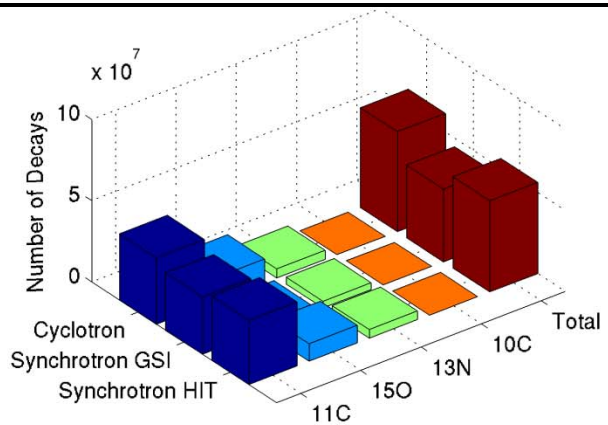
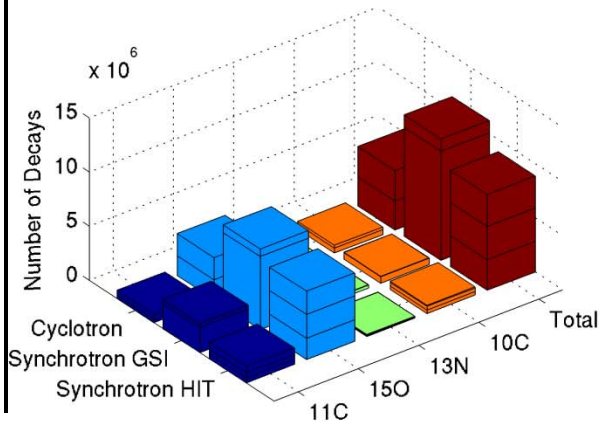
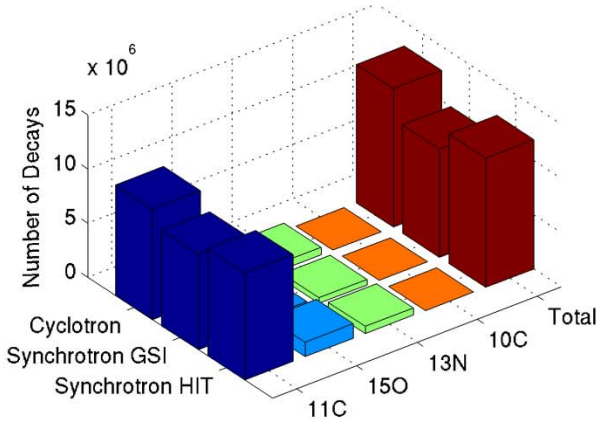
- Calculate β^+**-yield** for ***p*** irradiation
- Model **activity build-up** / **decay** during and after irradiation
- Include biological decay



MC calculated β^+-yield (× 10^3 / ml)

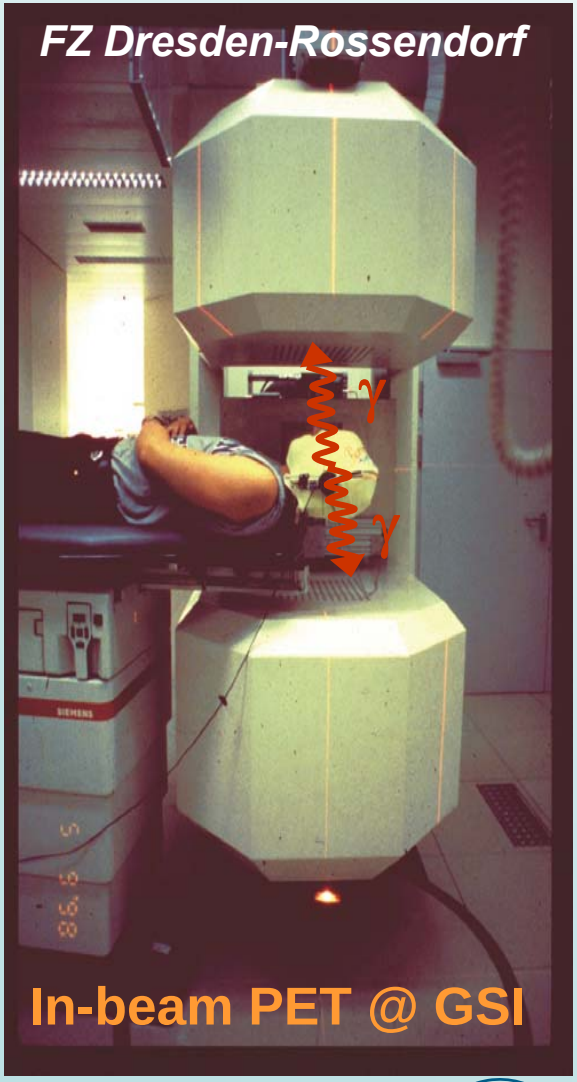


Number of detectable "physical" decays
(base of skull case, 1 Gy)

	In-beam *($t_{meas} \approx t_{irradiation}$)*	***Offline*** *(t_{meas} = 30min, Δt = 5min)*
proton beam		
carbon beam		

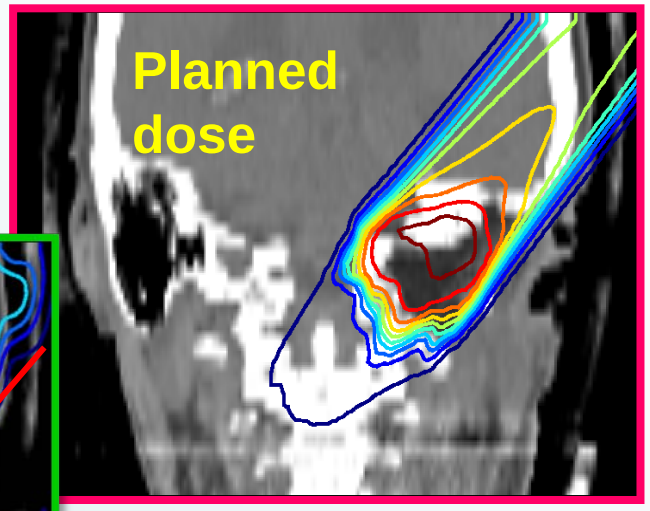
Parodi et al, IJROBP 71, 2008

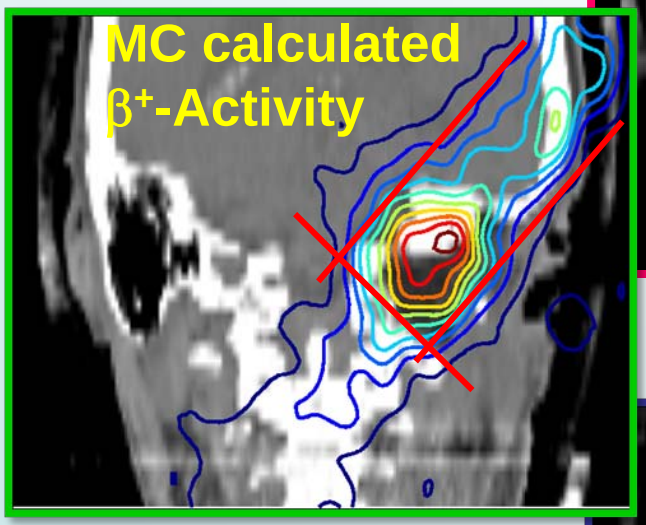
In-beam PET for ^{12}C ion therapy @ GSI

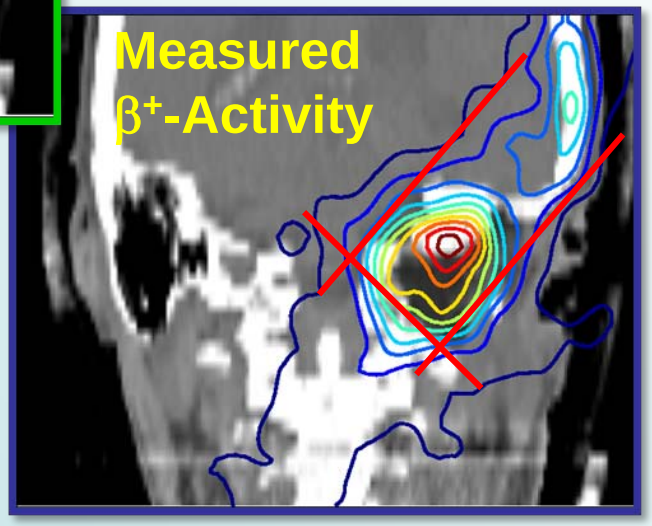


For every treatment fraction (typically 20 d @ 1Gy)

Once







Verification of

- Beam range
- Lateral position

In case of deviation

- Timely reaction

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Enghardt et al, NIMA 525, 2004