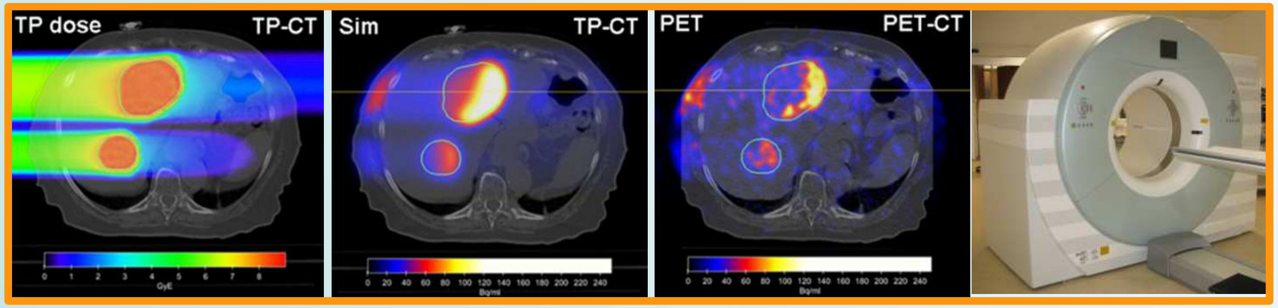
PET Imaging for Treatment Verification

-

Clinical Status



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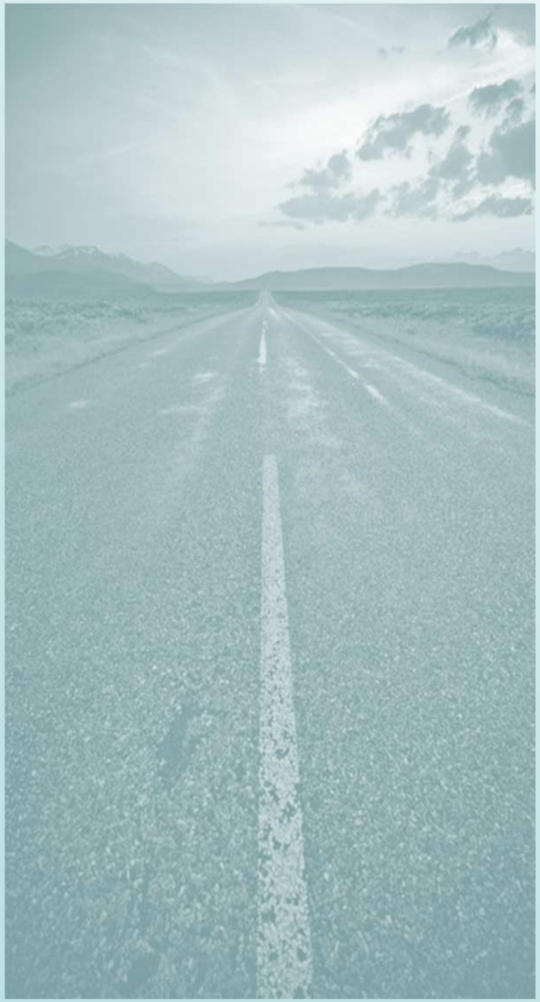
Department of Radiation Oncology, University Hospital Heidelberg

2nd Heidelberg Symposium on Novel Techniques in Ion Beam Radiotherapy

March 11th, 2016

Outline



Introduction *PET-based in-vivo verification*
Different concepts

Technical realization and clinical results for:

In-Beam Installations *(^{12}C, (p))*

In-Room Installation *(p)*

Offline Installations *(^{12}C, p)*

Lessons learned

Outlook

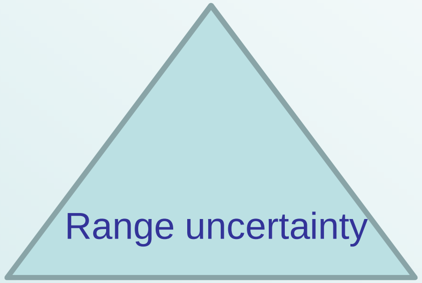
In-vivo verification of PT

Various sources of range uncertainties:

(See also Paganetti et al, PMB 57 (2012))

Planning:

- Imaging artifacts
- HU-water conversion
- Biology models



Lomax' bermuda triangle:

Range uncertainty ranked 2nd!

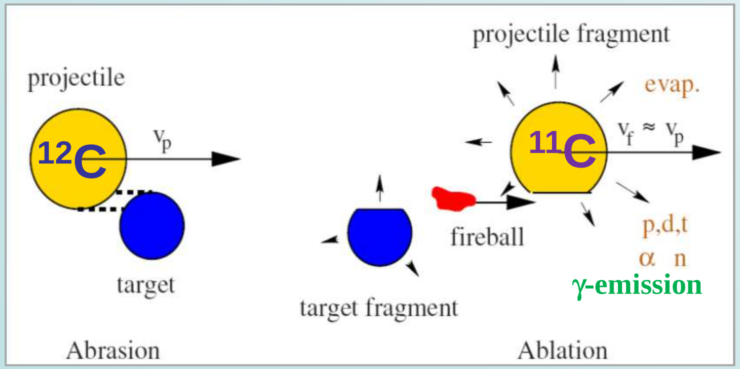
Treatment:

- Anatomic changes
- Positioning of the patient
- Inter-/intra-fractional motion (liver, prostate …)

In-vivo verification

Primaries

Heavy-Ion CT



Secondaries

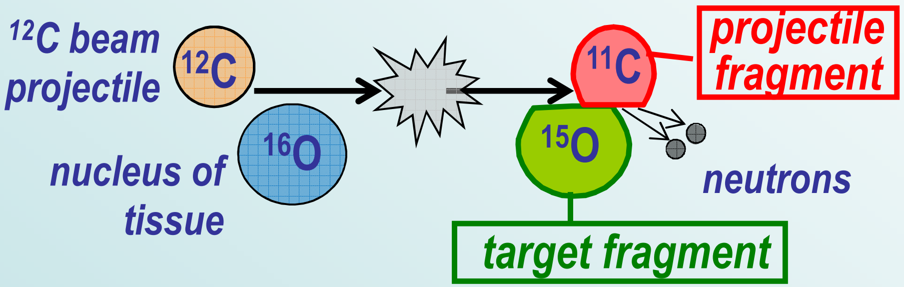
PET

Interaction vtx imaging

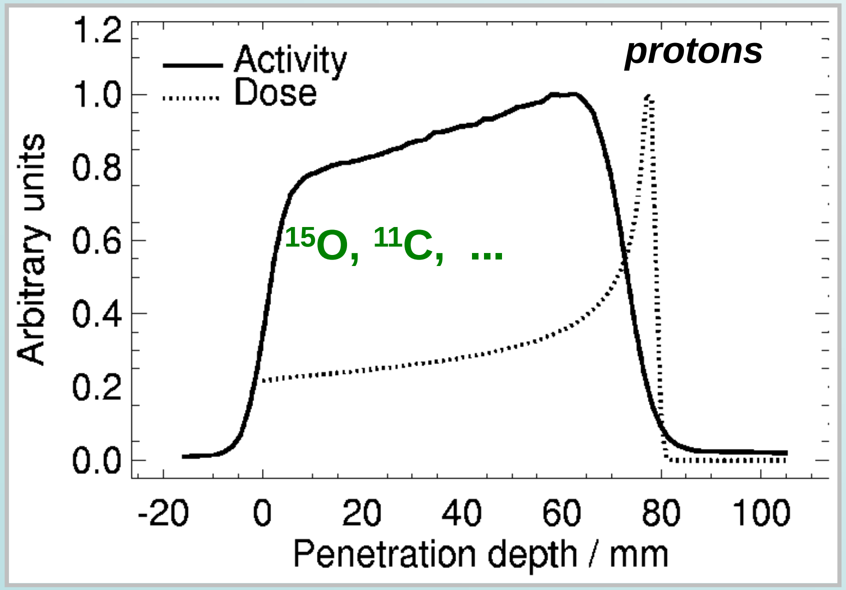
Prompt gamma

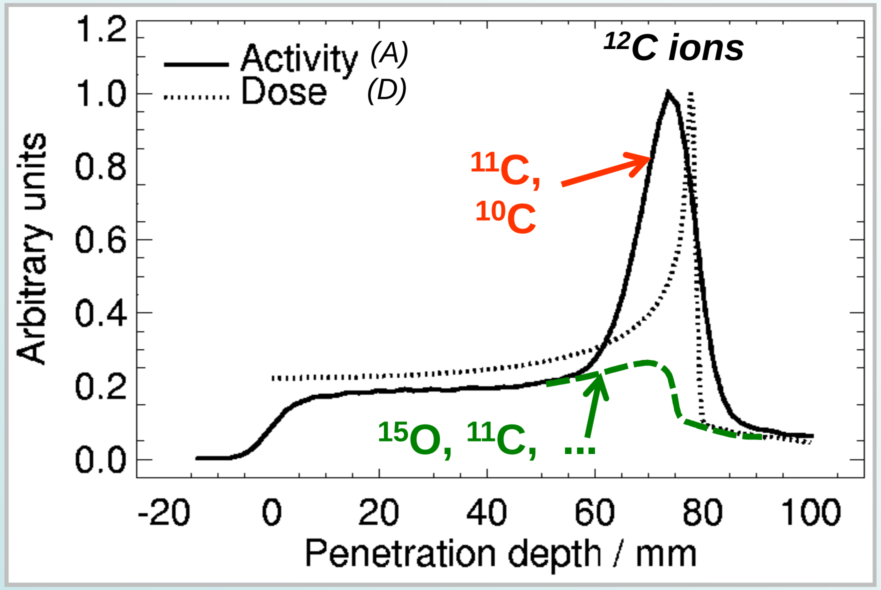
(…)

PET-based treatment verification



β⁺-emitter formed as by-product of irradiation in nuclear fragmentation reactions:
In-situ, non-invasive **detection of β⁺-activity via PET**



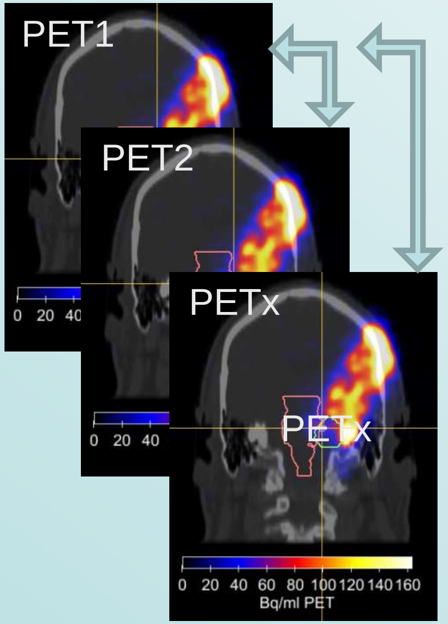


W. Enghardt, Oncoray Dresden, Parodi et al, IEEE 2005

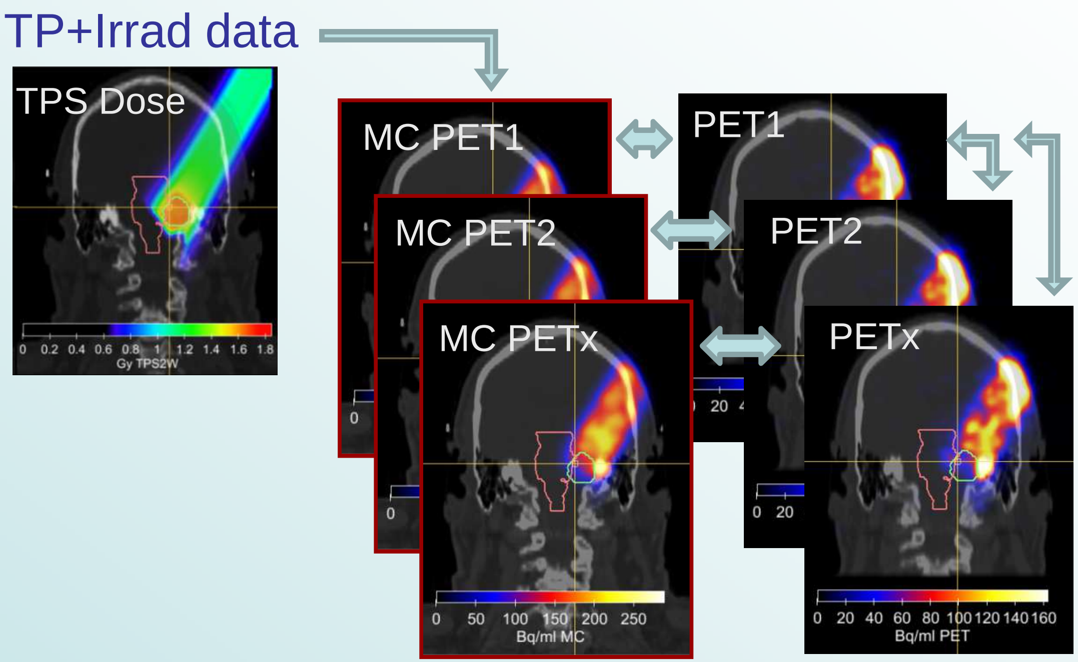
A(r) ≠ D(r)

PET-based treatment verification

Inter-fractional comparison:
PET_x - PET_1
→ **Reproducibility**

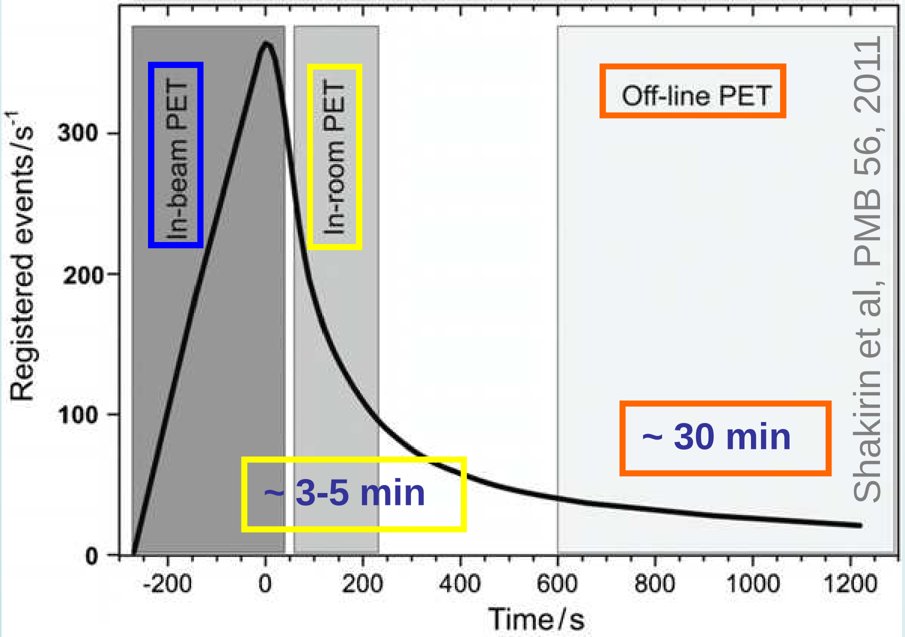


Comparison to expectation (MC):
$MCPET_x$ - PET_x
→ **Accuracy & Reproducibility**



Relevant PET isotopes:
^{10}C, ^{15}O, ^{38}K, ^{13}N, ^{11}C
($t_{1/2}$ ~ 20s, 2min, 8min, 10min, 20min)

Different Implementations



Offline (PET/CT)

+ full ring scanner
+ CT: co-registration PET↔ anatomy
+ comparably low costs (com. product)
- time delay between irradiation and PET scan → washout, low signal (^{11}C)
- re-positioning of patient
- very long acquisition time

In-beam (PET)

+ patient in treatment position
- limited detection area (dual head camera)
- very high integration costs (prototypes)
- high background signal

In-room (PET or PET/CT)

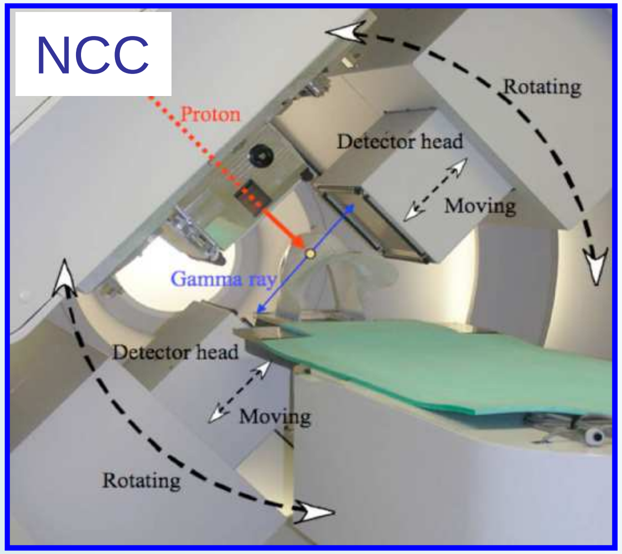
+ patient in treatment position
+ full ring scanner, state-of-the-art imaging

(+ CT: co-registration PET ↔ anatomy)

- limited to cranial indications (NeuroPET)
- required radiation hardness

Overview Clinical Experience

In beam:
GSI (Germany): ^{12}C
NCC (Japan): p



Miyatake et al, MedPhys 37 (2010)

Courtesy of K. Parodi

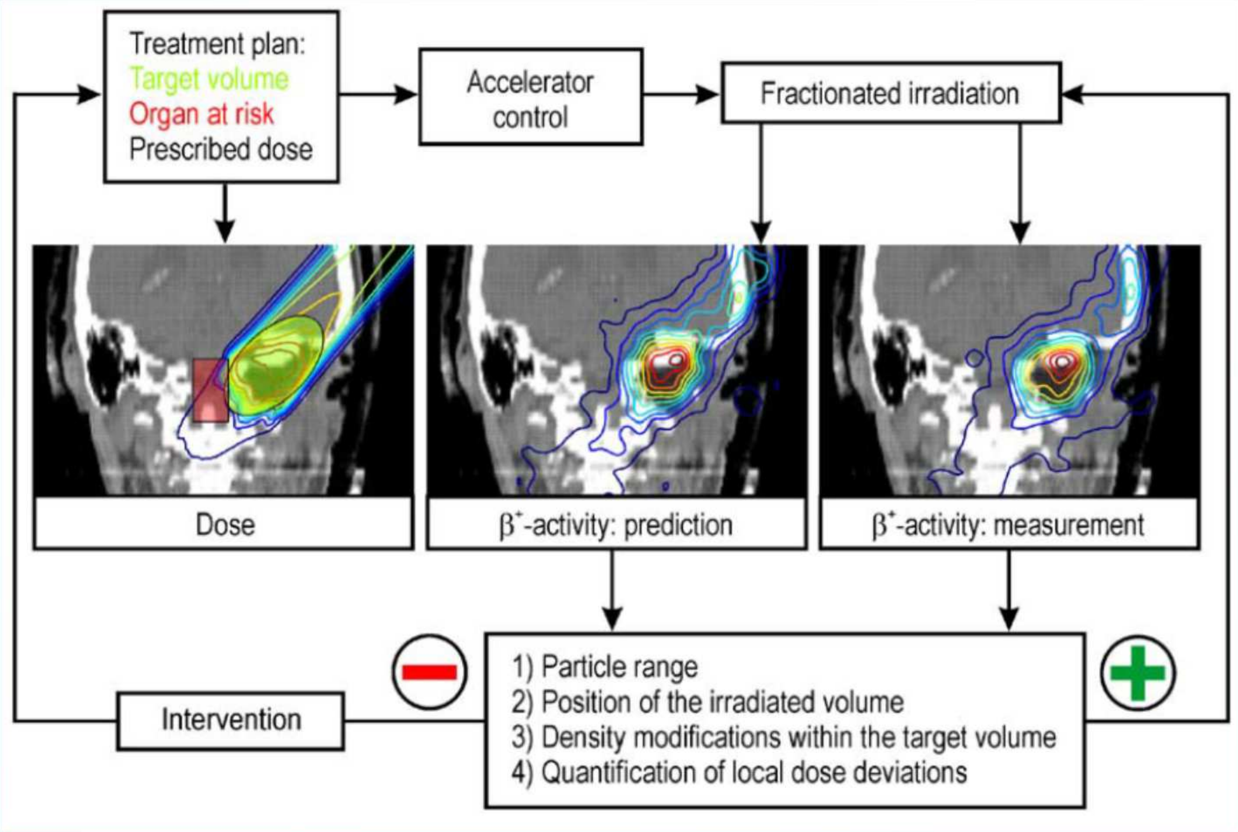
Min et al, IJROBP 86 (2013)

In room: MGH (USA): p

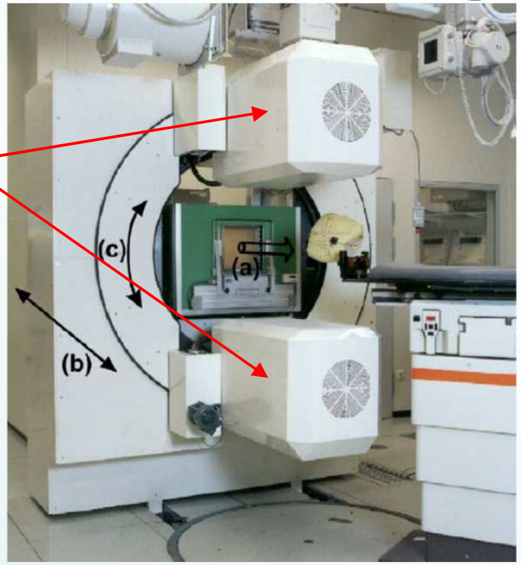
Offline: MGH (USA): p
NCC (Japan): p
HIT (Germany): p, ^{12}C

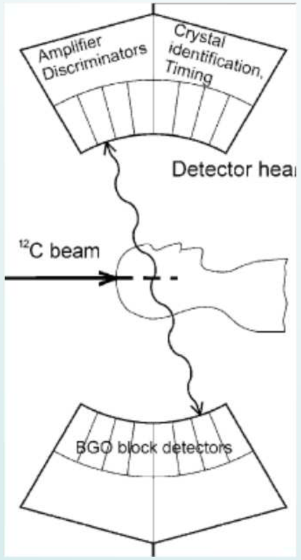
In Beam: GSI$_{12C}$ (1997-2008, >400pts)

- Double head camera @ horizontal beam port (components: ECAT EXACT PET system, BGO)
- Detector head area: 42 x 21 cm²
- Workflow:



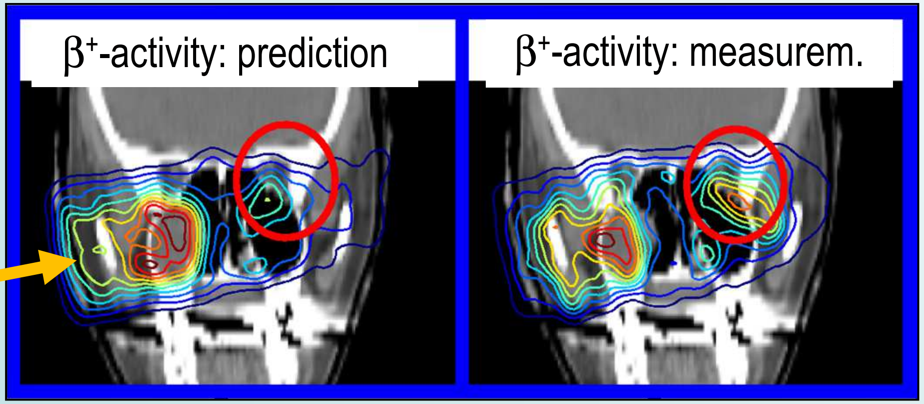
Enghardt et al, Nucl Inst Meth 525, 2004



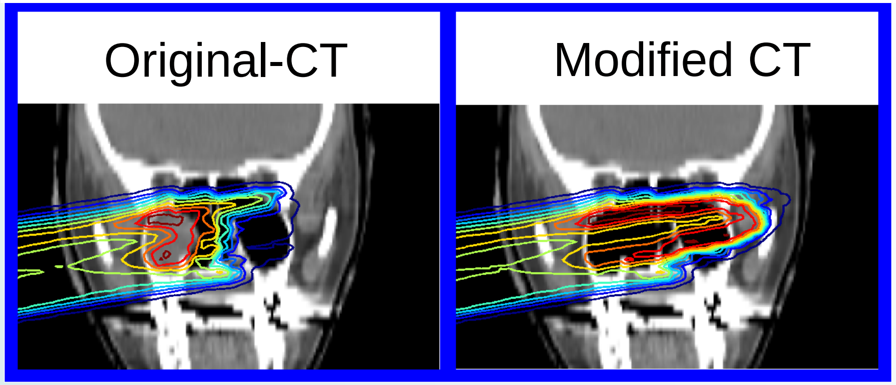


In Beam: GSI$_{12C}$ (1997-2008, >400pts)

- Validation of physical beam model for TP (CT calibration curve)
- Indirect estimation of dose deviation from in-beam PET:

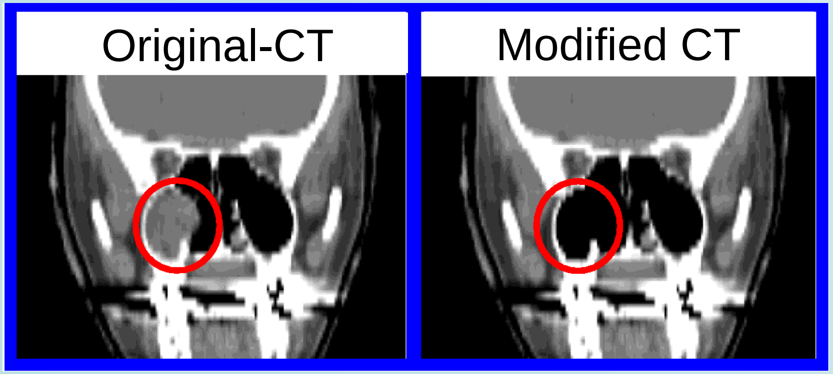


Dose recalculation:

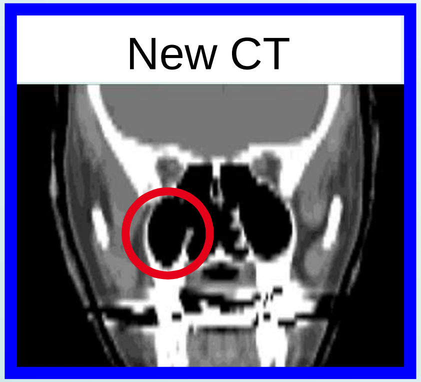


Comparison by visual inspection

Reasons for deviation? → Test!



New CT after PET findings:

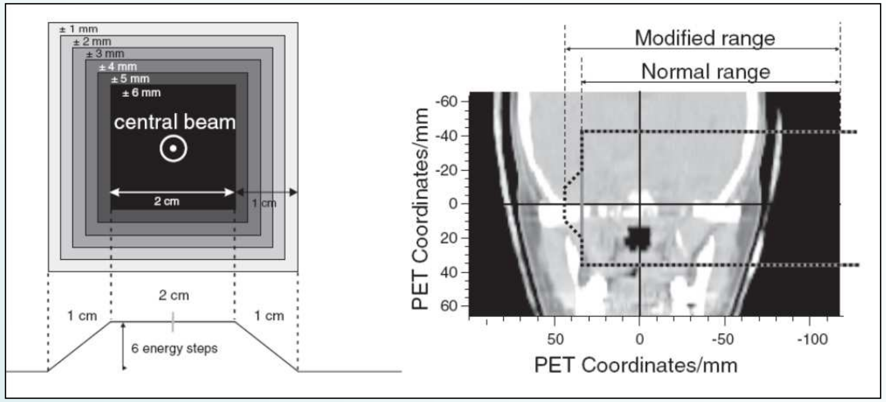


Enghardt et al, Rad Onc 73, 2004
Parodi K PhD Thesis

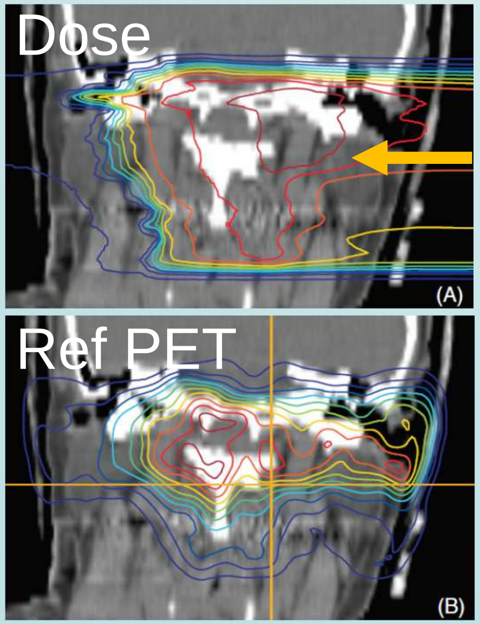
In Beam: GSI$_{12C}$ (1997-2008, >400pts)

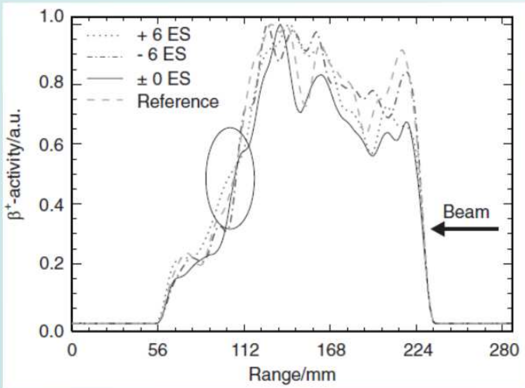
Quantitative study on accuracy of in-beam PET to detect range deviations:

- 6 experienced observes
- 81 patients (head & neck)
- Range modification of up to ± 6mm in water simulated



Fiedler F, et al, PMB 55 (2010)



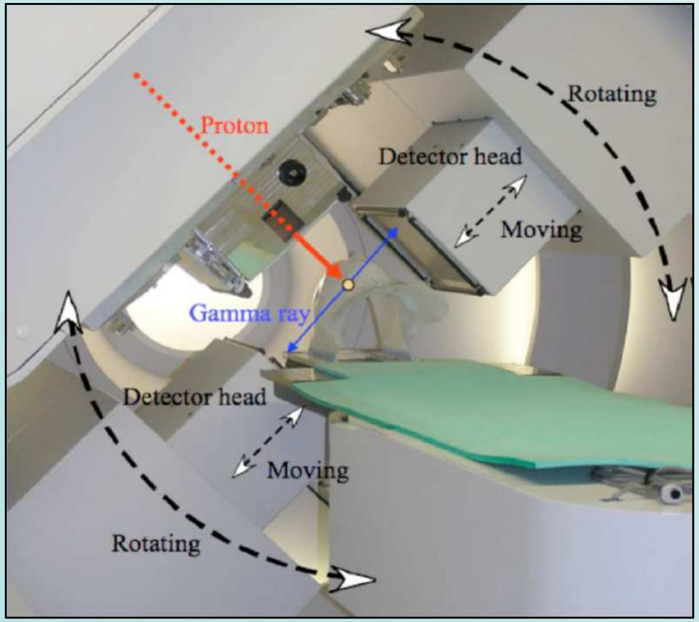


	Overrange detection	*Underrange detection*
Specificity TN/(TN+FP)	96 ± 2 %	96 ± 2 %
Sensitivity TP/(TP+FN)	91 ± 3 %	92 ± 3 %

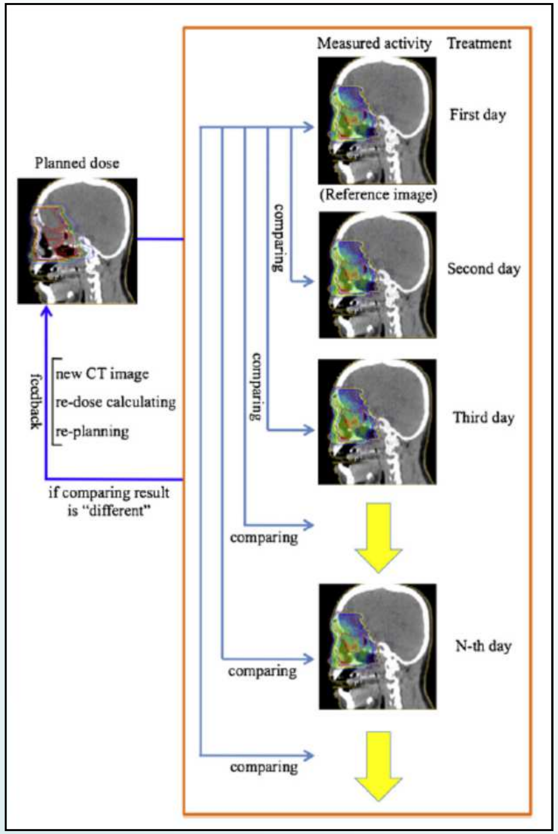
Observed very high specificity and sensitivity
to detect range deviations
→ appropriate tool for monitoring heavy ion therapy

In Room – NCC_p

- Planar detector heads, BGO crystals
- FOV size: 16.48 x 16.7 cm²
- Detector distance adjustable (30 - 100 cm)
- Daily measurement
- t_{frame}: 200s (starting immediately after irradiation)



Miyatake A et al, MedPhys 37 (2010)

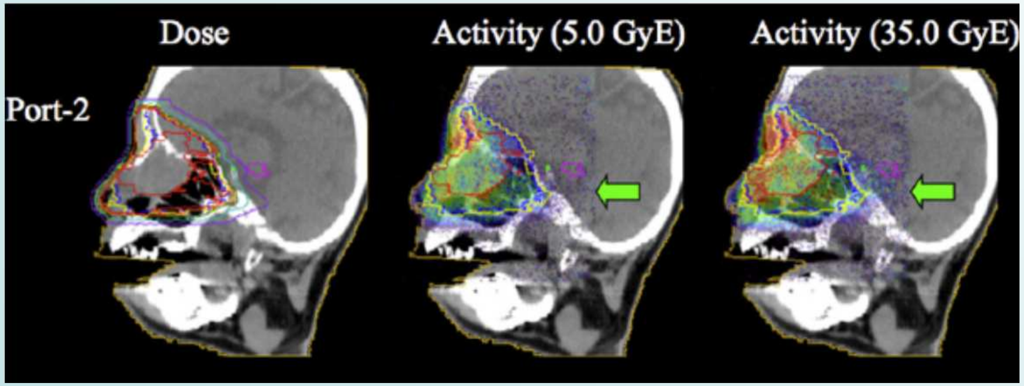


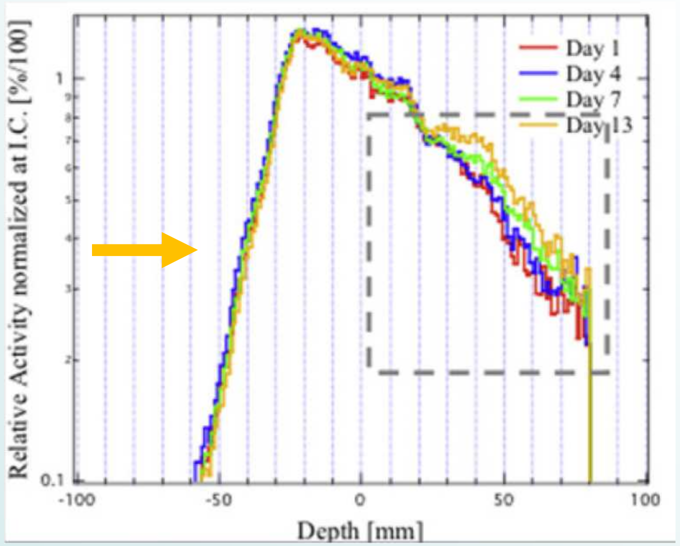
Nishio T et al, IJROBP 76 (2010)

- ➢ Confirmation of reproducibility
- ➢ Changes of activity distribution observed:
  - tumor volume changes
  - patient positioning/body shape variations

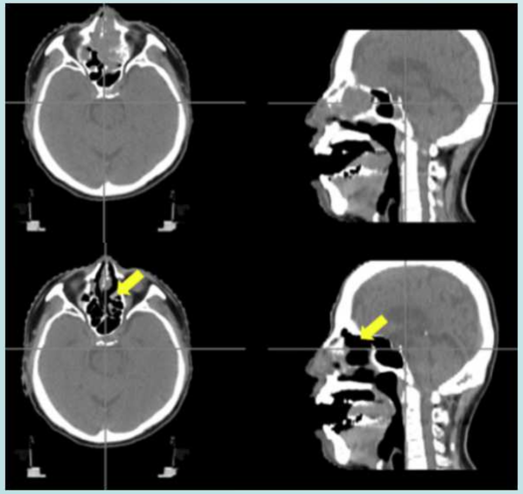
In Room – NCC$_p$

- Clinical analysis of 48 patients
(1 brain, 18 head & neck, 4 liver, 15 lung, 10 prostate)
- Example head & neck: Depth activity profile at different treatment days:





Nishio T et al, IJROBP 76 (2010)



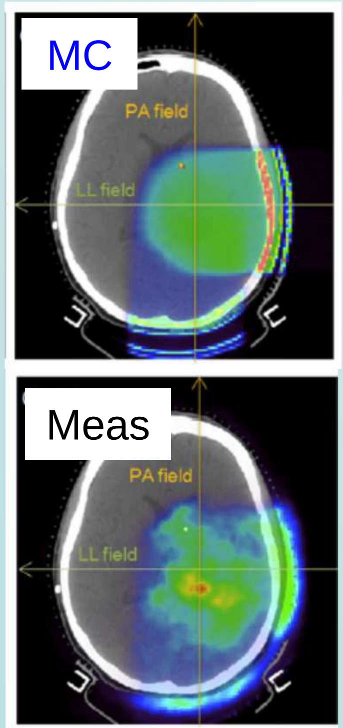
→ Tumor shrinking (184 ml to 125 ml)

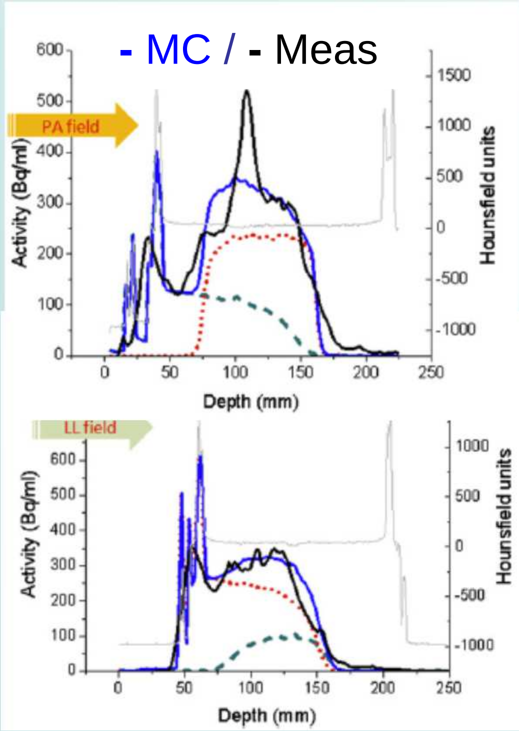
→ 3 patients underwent re-planning triggered by observed activity changes

In Room – MGH_p

- NeuroPET scanner on wheels
- Scan start ~2 min after irradiation
- Image co-reg. via markers (~ 2 mm uncert.)
- 9 patients
- t_{frame} up to 20 min

Min C, IJROBP 86 (2013)



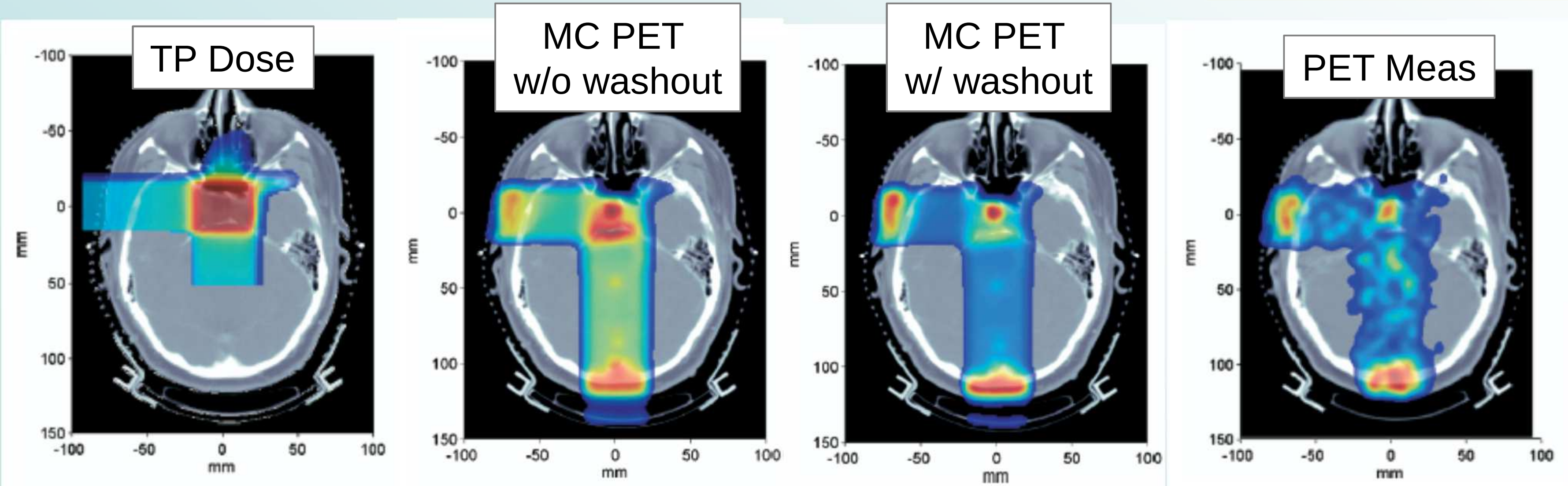


- ➢ Comparable results for 5/20 min scan time for range deviation
- ➢ Week points of MC modelling:
  - Elemental composition of tissue
  - Washout modelling
- ➢ Main issue: image co-registration → in-room PET/CT

Offline - MGH_p

- Remote PET/CT scanner (PET scan delay 13-20 min)
- Refixation with same devices as used for treatment
- Data acquisition: 30 min

→ consider biological washout in MC prediction



Parodi K, IJROBP 68 (2007)

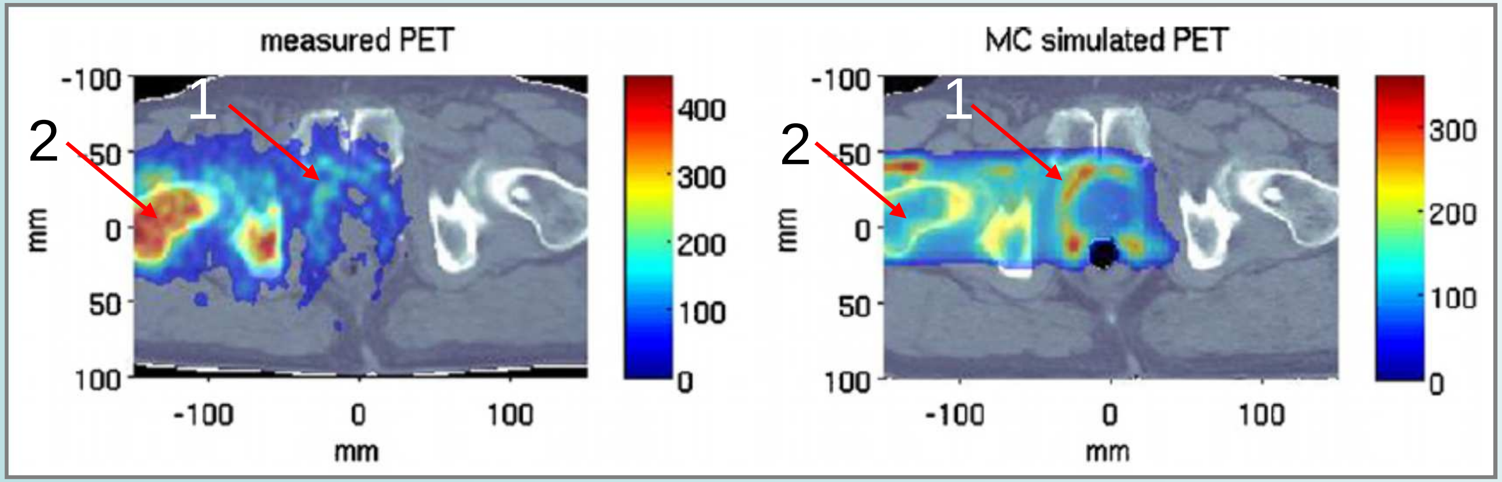
Average range deviation: -0.1 (±2) mm
→ only in low perfused, well co-registered bony structures (head/neck)

Offline - MGH_p

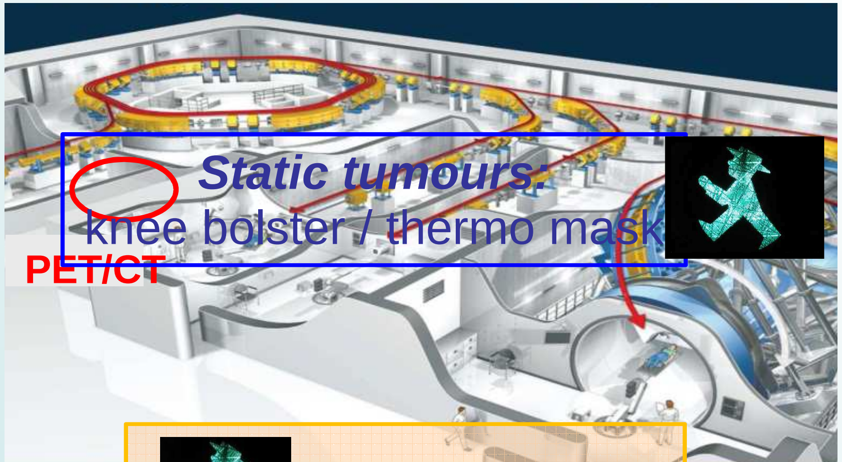
Knopf A, PMB 54 (2009)

<u>Feasibility and accuracy of offline PET/CT based verification:</u>

- Spatial reproducibility of PET vs PET **within 1mm** (however restricted to particular tumor sites)
- Beam stop in soft tissue: washout uncertainty PET-MCPET: **~4mm**
- Motion: spatial deviations **up to 3cm** between PET and MCPET
- Reliability of comparison method (MC):
  - Motion and biological washout difficult to be taken into account in MC
  - Translation HU values → tissue composition critical (p irrad.)



Offline – HIT$_{p,12C}$ (2010-now, >200 pts)



Static tumours:
knee bolster / thermo mask

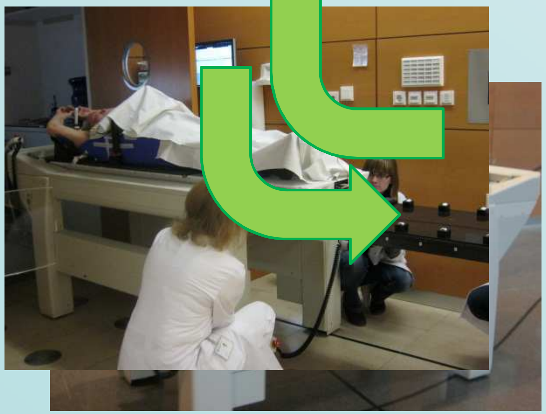

Treatment room

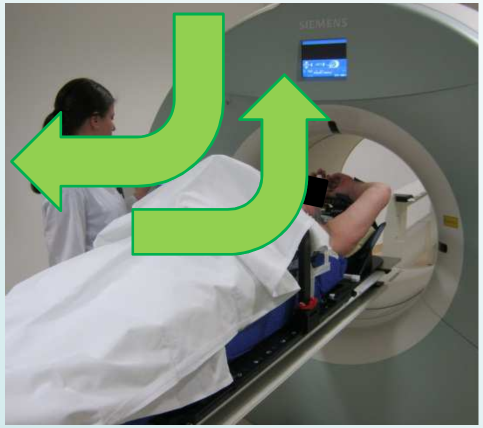

PET/CT room

Δt ~ 5 - 8 min.

Δt ~ 9 -12 min.

t_{PET} = 30 min.



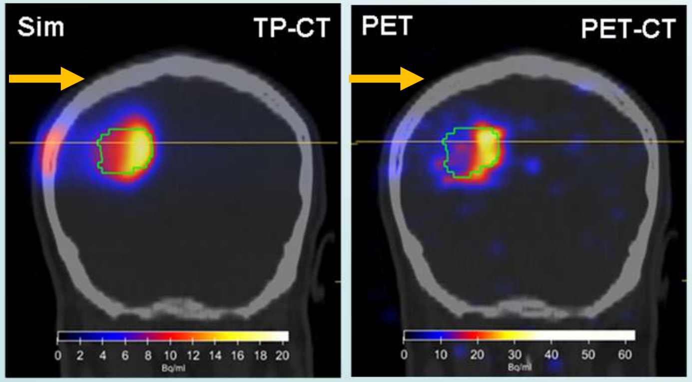


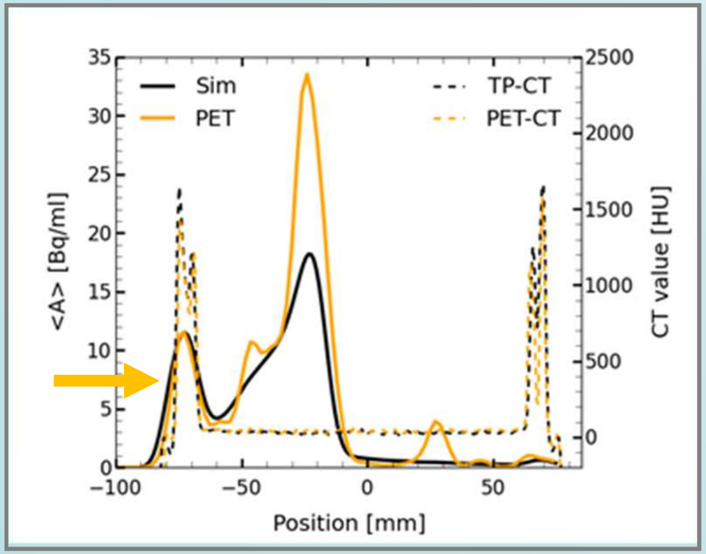
Liver:
vacuum matting,
ANZAI belt (respiration signal),
arm holder, abdominal press (…)

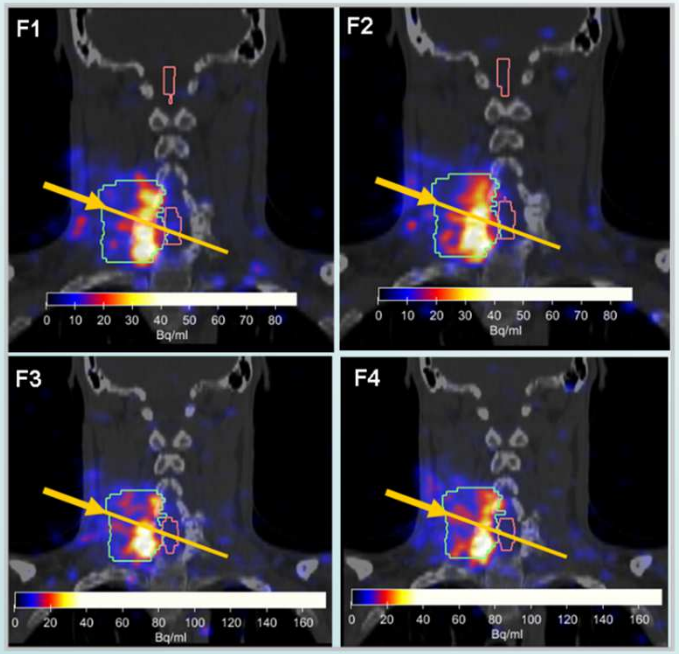
Offline – HIT_{12C} (2010-now, >200 pts)

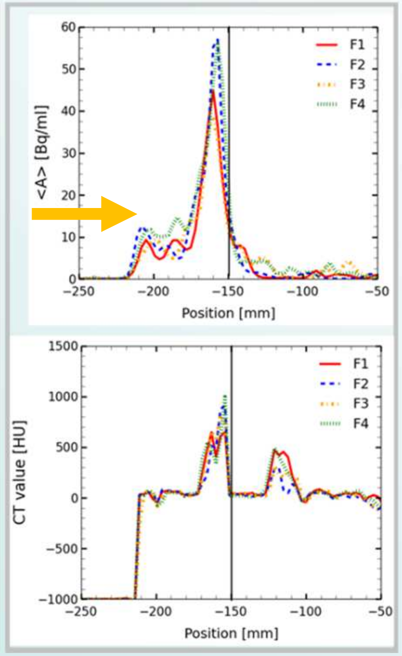
Initial experience with monitoring of ^{12}C patients:

- Extremely low signal strength (~100 Bq/ml)
- Pronounced signal max at distal edge
- Very good range control for ^{12}C in both analysis strategies (MCPET-PET, PET-PET)





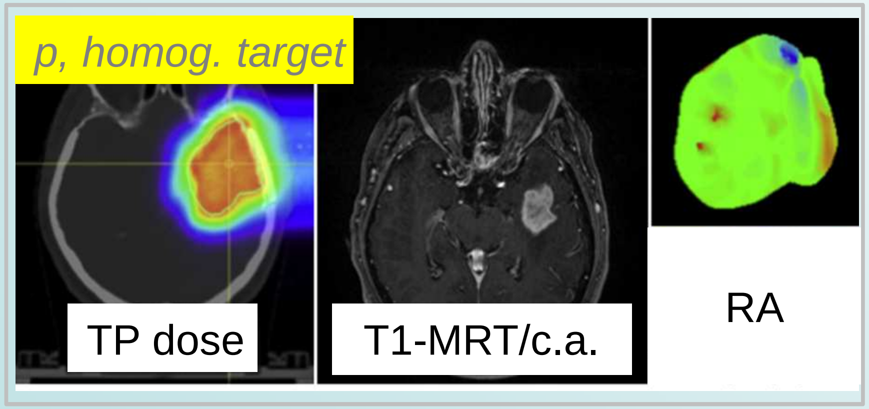


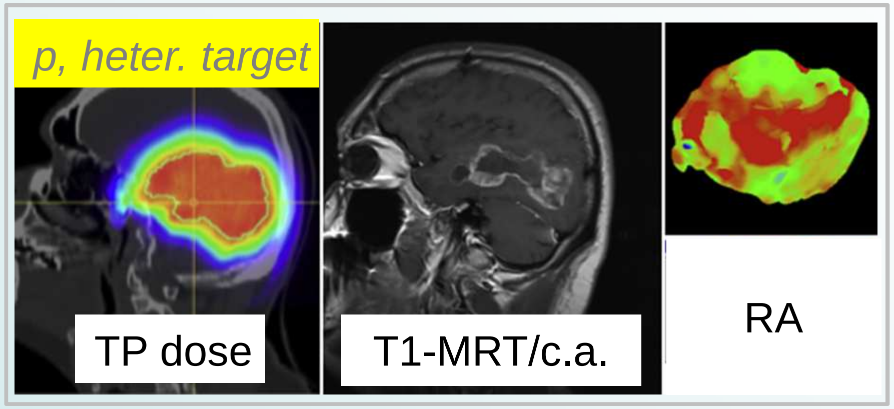


Bauer et al., Radiother Oncol 107 (2013)

Offline – $HIT_{p,12C}$ (2010-now, >200 pts)

- Systematic analysis for cranial lesions: 10 x p/^{12}C each; 1-2 field plans
- PET after 2 selected therapy fractions
- Range analysis (RA): $MCPET_{1,2}$-$PET_{1,2}$ and PET_1-PET_2





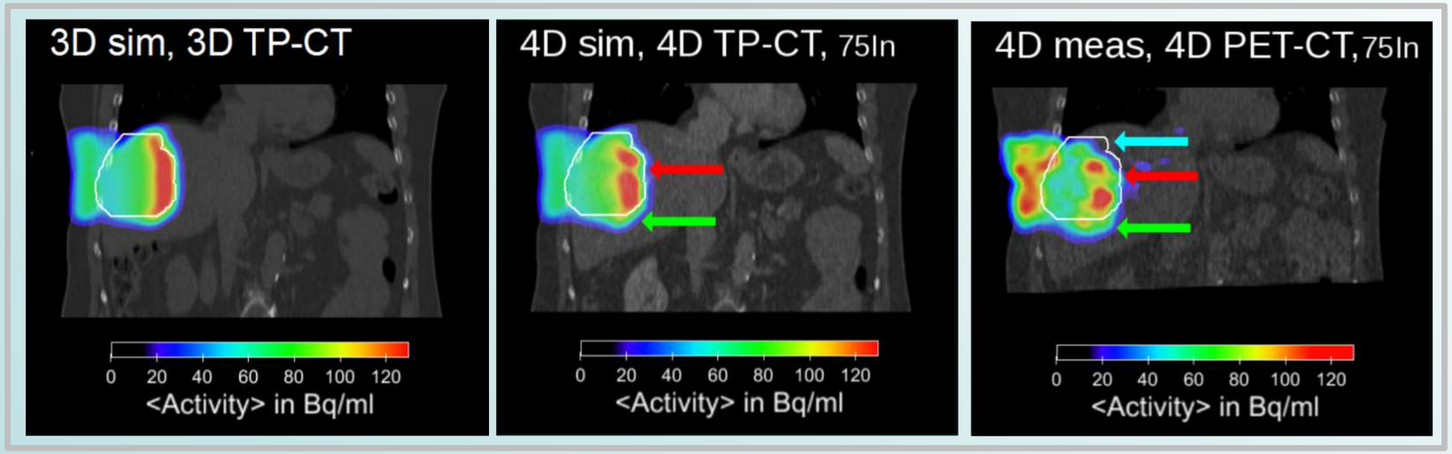
Bauer & Nischwitz, Radiother Oncol 115 (2015)

- PET-PET comparison consistent:
  $\langle\Delta_{dist}\rangle = (0.7 \pm 0.7_p/0.6_{12C})$ mm
- MCPET-PET comparison shows significant differences for p, ^{12}C:
  p: **$\langle\Delta_{dist}\rangle = (4.2 \pm 2.2)$ mm**
  ^{12}C: **$\langle\Delta_{dist}\rangle = (2.3 \pm 1.7)$ mm**
- RA sensitive to tumour homogeneity (washout) & modelling of tissue composition (proton irradiation)

Offline – HIT$_{p,12C}$ (2010-now, >200 pts)

First clinical study for 4D PET/CT verification of moving targets:

- 3 patients (HCC), ^{12}C treatment, single field plans (right-lateral), 4 fractions
- Motion amplitude (MA) of lesion in SI: ~ (2-14) mm
- Recording of respiration signal during TP, irradiation and PET scan
  → 4D sim: considering time structure of beam delivery (interplay effects)
  → 4D meas: time-resolved PET image reconstruction



Kurz, Bauer et al, MedPhys 43 (2016)

- ➢ No benefit of 4D analysis for lesions with MA-SI < 5 mm
- ➢ Improved data evaluation by 4D for lesions with MA-SI ~ 10 mm
- ➢ Low signal level → considerable noise contribution hampers data analysis

Lessons learned

→ Various pre-clinical and clinical studies performed for all imaging configurations

InBeam (^{12}C):

- Only prototype installations → no commercial solution available
- Only double-head configurations → recon and quantification issues

InRoom (p):

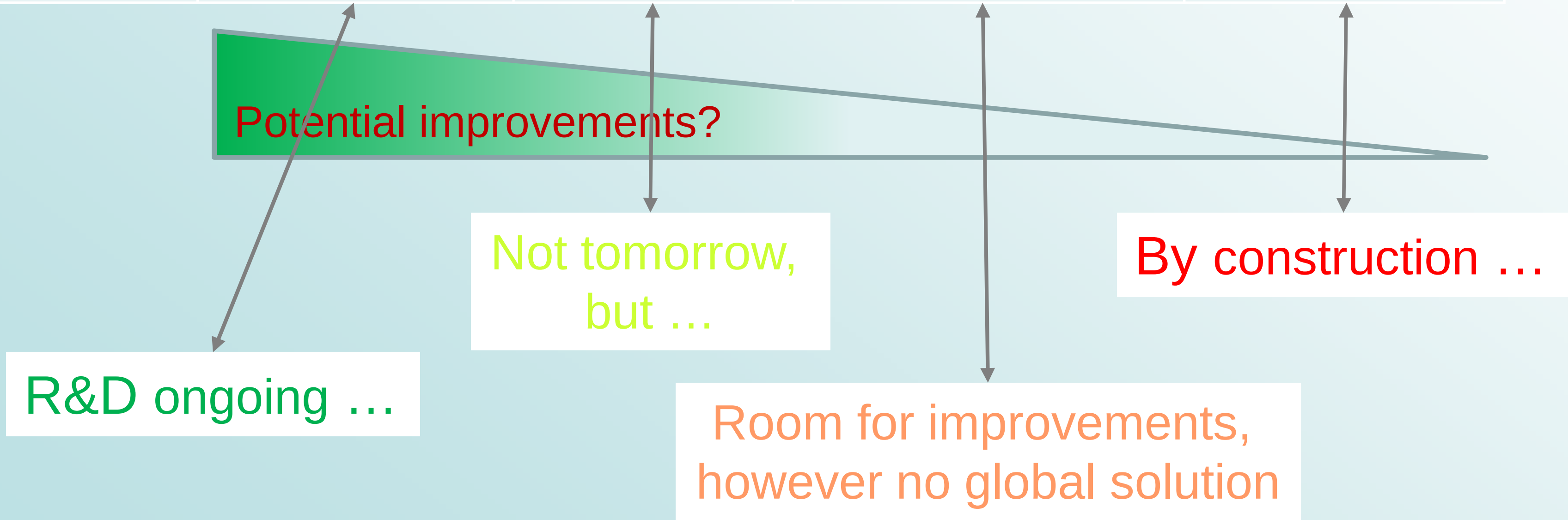
- Standalone full-ring scanner (preferably PET/CT): radiation hardness
- Biological washout has to be considered for MCPET-PET strategy

Offline (p, ^{12}C):

- Good range information for ^{12}C (pronounced max at distal edge)
- Higher signal for p (~ 2-3 times higher), but shallow distal fall-off
- Limited accuracy of PET prediction model (washout/tissue composition) hinders reliable range verification for various clinical scenarios
- Limited to single /parallel field(s) (→ robust treatment?)
- *CT acquisition might rule out PET verification*

Lessons learned

	Imaging performance	System availability	Model uncertainties MC	Clinical workflow compatibility
In-beam	☹	☹	☺	☺
In-room	😐 / ☺	😐	😐	😐
Offline	☺	☺	☹	☹

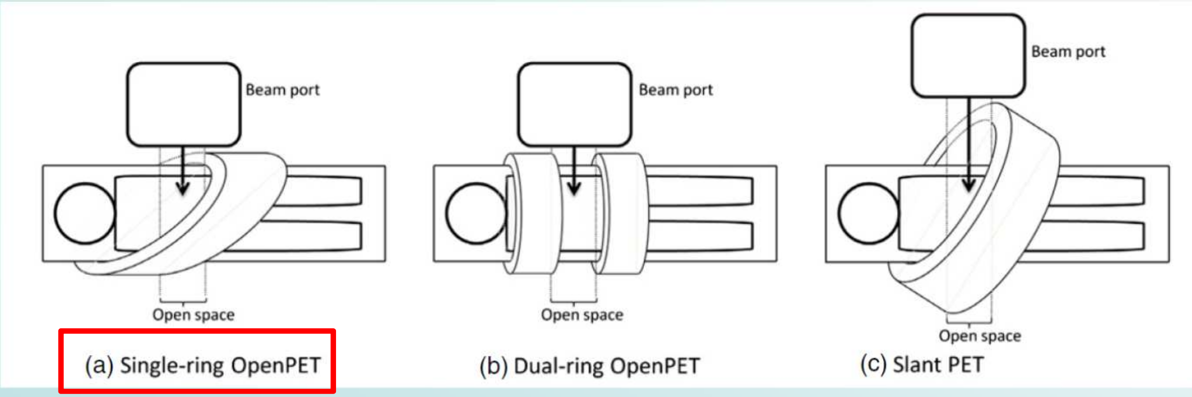


„Quo vadis“ PET verification?

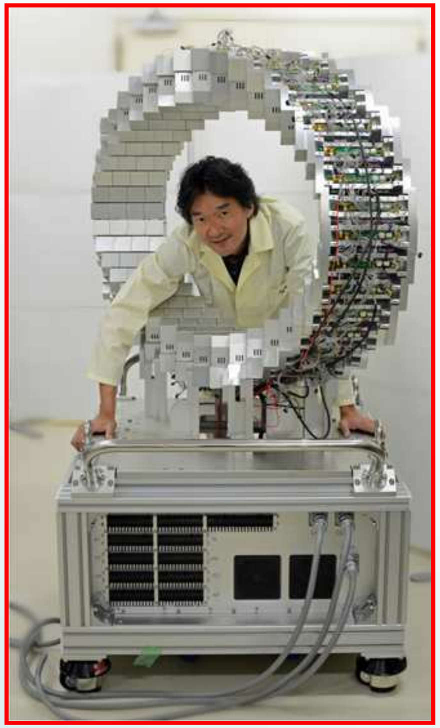
→ ***in-beam!***

Detector Development:

- Double head cameras: fast TOF-PET systems
- „Gantry compatible“ closed-ring configurations:



Tashima et al, PMB 57, 2012



Courtesy of Tashima H

→ advanced pre-clinical studies ongoing

- Combination of in-beam PET with other particle tracking systems (INSIDE project @ CNAO (next talk): in-beam PET + charges secondaries + PG)

> ➢ Clinical routine application at many centers: manufacturer for gantry built-in system mandatory

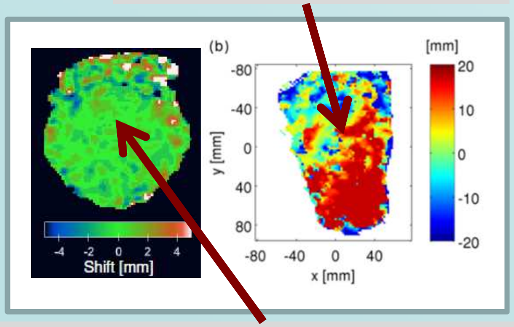
Routine Veri for Adaptive Therapy?

… requires a fast and reliable feedback!

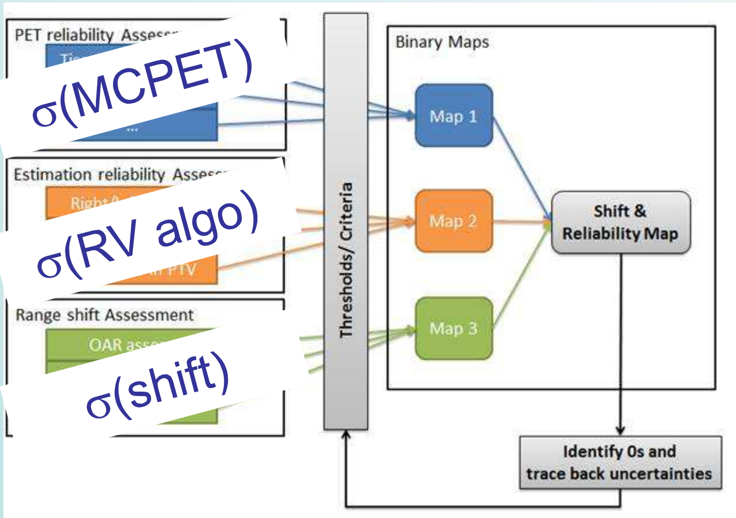
<u>About Reliability:</u>

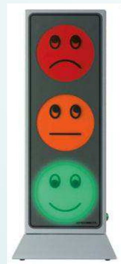
- **In-beam** (Helmbrecht S, PMB 57 (2012)):
  Automated range analysis for GSI data*: promising results for range shifts > 5 mm (soft tissue); however worse than human observer performance
- **Offline:**
  Automated range verification (Frey K, PMB 59 (2014), offline and in-room);
  Larger uncertainties on MCPET modeling → establish decision support system to evaluate reliablity of observed range differences
  (Chen W, Bauer J et al, MMND-ITRO 2016)

What went wrong?



Can I trust the „greenfield“?





SPARTA
Software Platform for Adaptive Multimodal Radio and Particle Therapy with Autarkic Extendibility

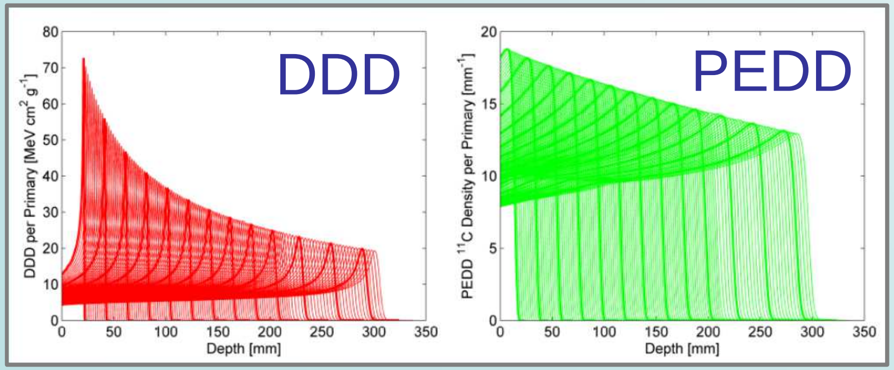
http://www.projekt-sparta.de

Routine Veri for Adaptive Therapy?

About speed:

- GPU based MC for dose calculation → PET?
- Analytical approach to calculate expected positron emitter distribution from planned dose distribution (*)
  → Gaussian based filter functions: translate DDDs to PEDDs
  → first implementation to RayStation (*submitted to ICCR 2016*)

Frey K, Bauer J et al, PMB 59 (2014)



- Confidential -

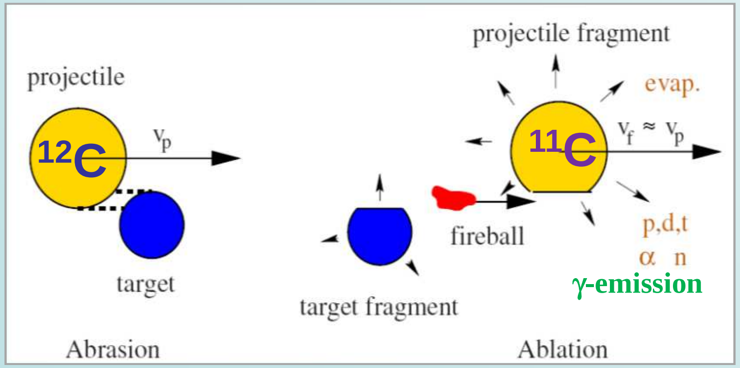
*Parodi PMB 51 (2006), Attanasi PMB 56 (2011)

Concluding Remarks

- Clinically implemented routine in-vivo verification of particle therapy (PT) at operating facilities remains an unsolved challenge

- However deemed to be necessary for a full exploitation of PT‘s advantages compared to conventional RT

- Ongoing research effort in detector and system integration development, not only for PET:



Secondaries

PET

Interaction vtx imaging

Prompt gamma (…)

➢ Will be covered by the following talks ☺

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BACKUP

"Oh, the magic carpets are just for backup."

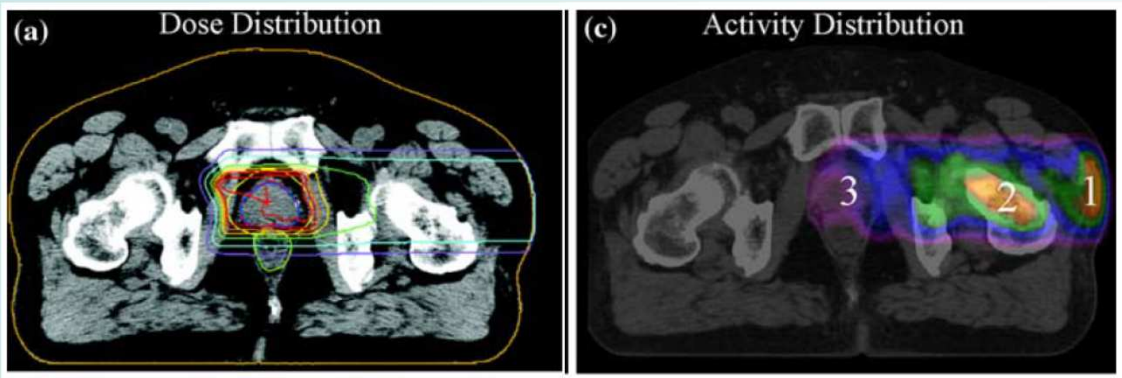
Offline – NCC_p

- PET/CT (Discovery ST (GE Medical Systems)
- Transfer time 5-7 min (~40m distance)
- PET data acquisition: 5 min
- 5 patients: sacrum, prostate, head & neck, 2x liver

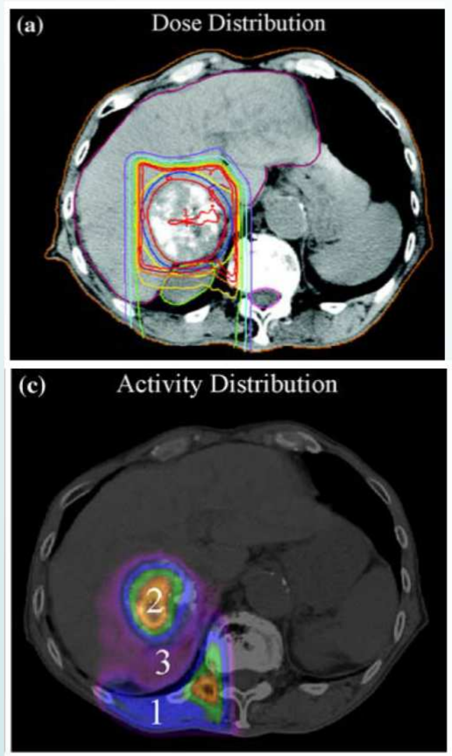
→ lateral field position

→ estimate signal strength for in-beam system

Prostate



Liver (TACE)



Nishio T, Radiol Phys Technol (2008)

<u>Main drawbacks:</u>

- No direct information on proton range
- Problems to quantify washout effect in different tissue categories

Technical workflow @ HIT