# Novel Imaging Systems for in vivo Monitoring and Quality Control during Tumour Ion Beam Therapy: An Introduction

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# Outline

1. The upcoming FP7 call
2. What do we have? In-beam PET
3. What do we need?

# 1. The upcoming FP7 call

**HEALTH-2008-1.2-4: Novel imaging systems for in vivo monitoring and quality control during tumour ion beam therapy.**

**Description:** The focus should be to develop novel imaging instruments, methods and tools for monitoring, in vivo and preferably in real time, the 3-dimensional distribution of the radiation dose effectively delivered within the patient during ion beam therapy of cancer.

The ions should be protons or heavier ions.

The system should typically be able to quantify the radiation dose delivered, to determine the agreement between the planned target volume and the actually irradiated volume, and for decreasing localisation uncertainties between planned and effective positions (e.g. of tissues or organs), and between planned and effective dose distribution during irradiation.

It should aim at improving quality assurance, increasing target site (tumour) to normal tissue dose ratio and better sparing normal tissue.

# 2. What do we have? In-beam PET

## Rationale

3D → Tomography

Non invasive → Highly penetrable signal → X- or γ-rays

In situ → Separation of the signal from the therapeutic irradiation

Real time → Separation of the signal from the therapeutic irradiation

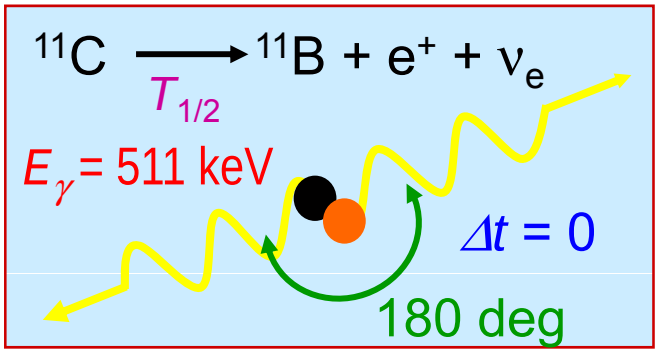
Separation of the signal from the therapeutic irradiation → Signal with:
- well defined energy
- spatial correlation
- time correlation
- time delay

Time efficient → High detection efficiency

Signal with: → Annihilation γ-rays, Positron Emitters ?

Proportional to dose ?

High detection efficiency → PET



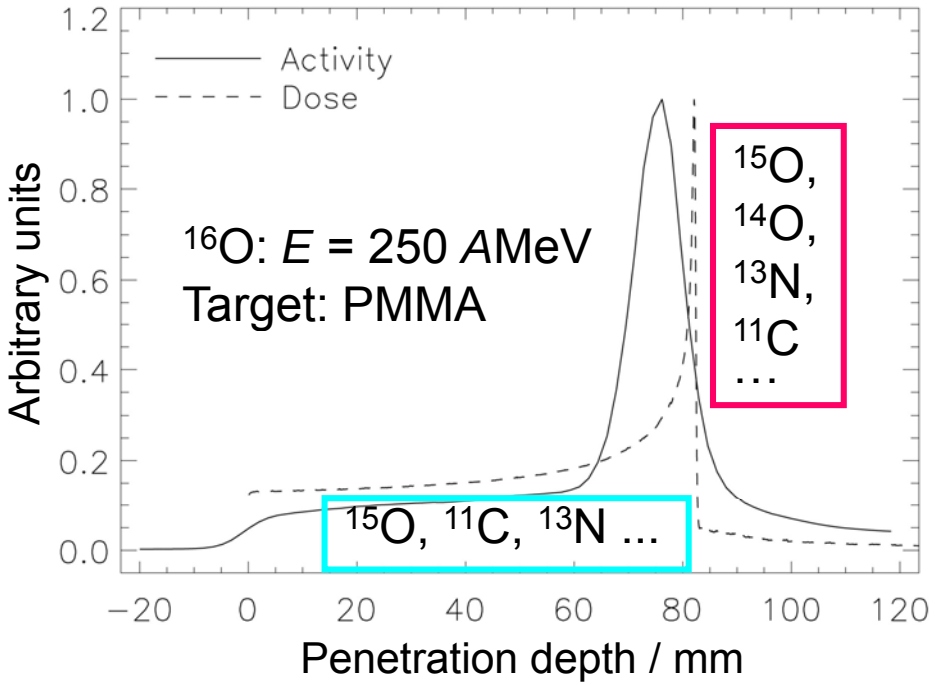
# 2. What do we have? In-beam PET

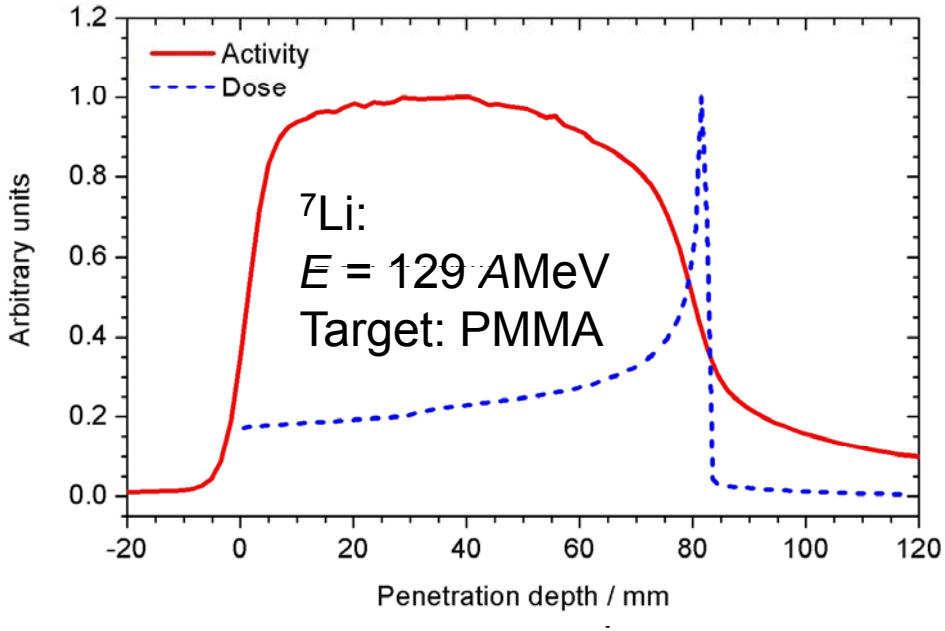
## Physics

Peripheral nucleus-nucleus-collisions, nuclear reactions ($^{A}Z$, *xp*,*yn*), $\Delta \mathbf{p} \approx \mathbf{0}$

$Z \geq 6$ Projectile fragments | Target fragments

$Z < 6$ Target fragments



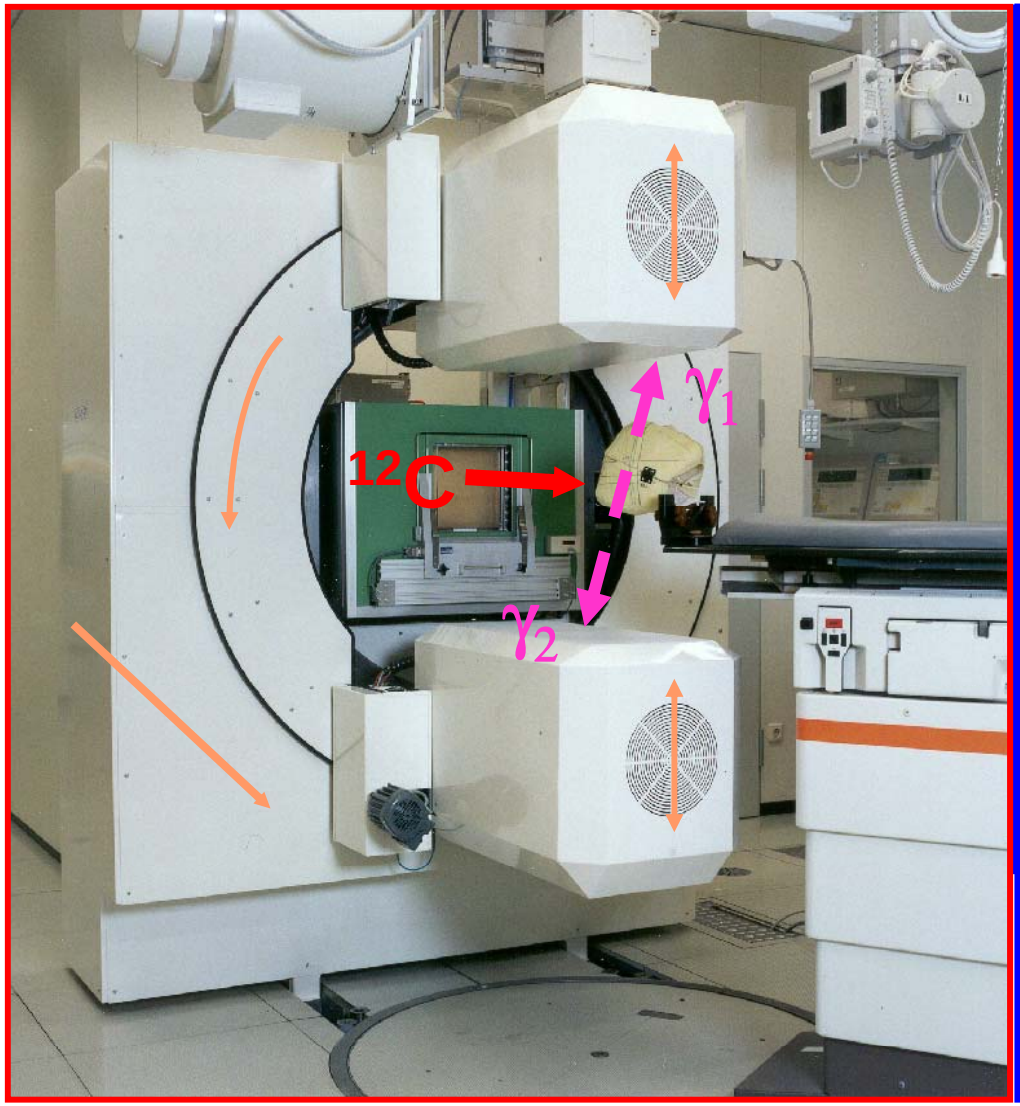

| Therapy beam | $^{1}$H | $^{3}$He | $^{7}$Li | $^{12}$C | $^{16}$O | Nuclear medicine |
|---|---|---|---|---|---|---|
| Aktivity density / Bq cm$^{-3}$ Gy$^{-1}$ | 6600 | 5300 | 3060 | 1600 | 1030 | $10^{4}$ – $10^{5}$ Bq cm$^{-3}$ |


W. Enghardt et al.: Phys. Med. Biol. 37 (1992) 2127;
K. Parodi et al.: IEEE T. Nucl. Sci. 52 (2005) 778;
F. Sommerer et al.: Phys. Med. Biol. (to be published);
J. Pawelke et al.: IEEE T. Nucl. Sci. 44 (1997) 1492;
F. Fiedler et. al.: IEEE T. Nucl. Sci., 53 (2006) 2252;
M. Priegnitz et al.: Phys. Med. Biol. 53 (2008) 4443

# 2. What do we have? In-beam PET

## Instrumentation (I)

In-beam PET: $^{12}$C-therapy at GSI Darmstadt




Off-beam PET: $^{1}$H-therapy at MGH Boston

J. Pawelke et al.: Phys. Med. Biol. 41 (1996) 279
W. Enghardt et al.: Nucl. Instr. Meth. A525 (2004) 284

K. Parodi et al.:
J. Radiat. Oncol. Biol. Phys. 68 (2007) 920

# 2. What do we have? In-beam PET

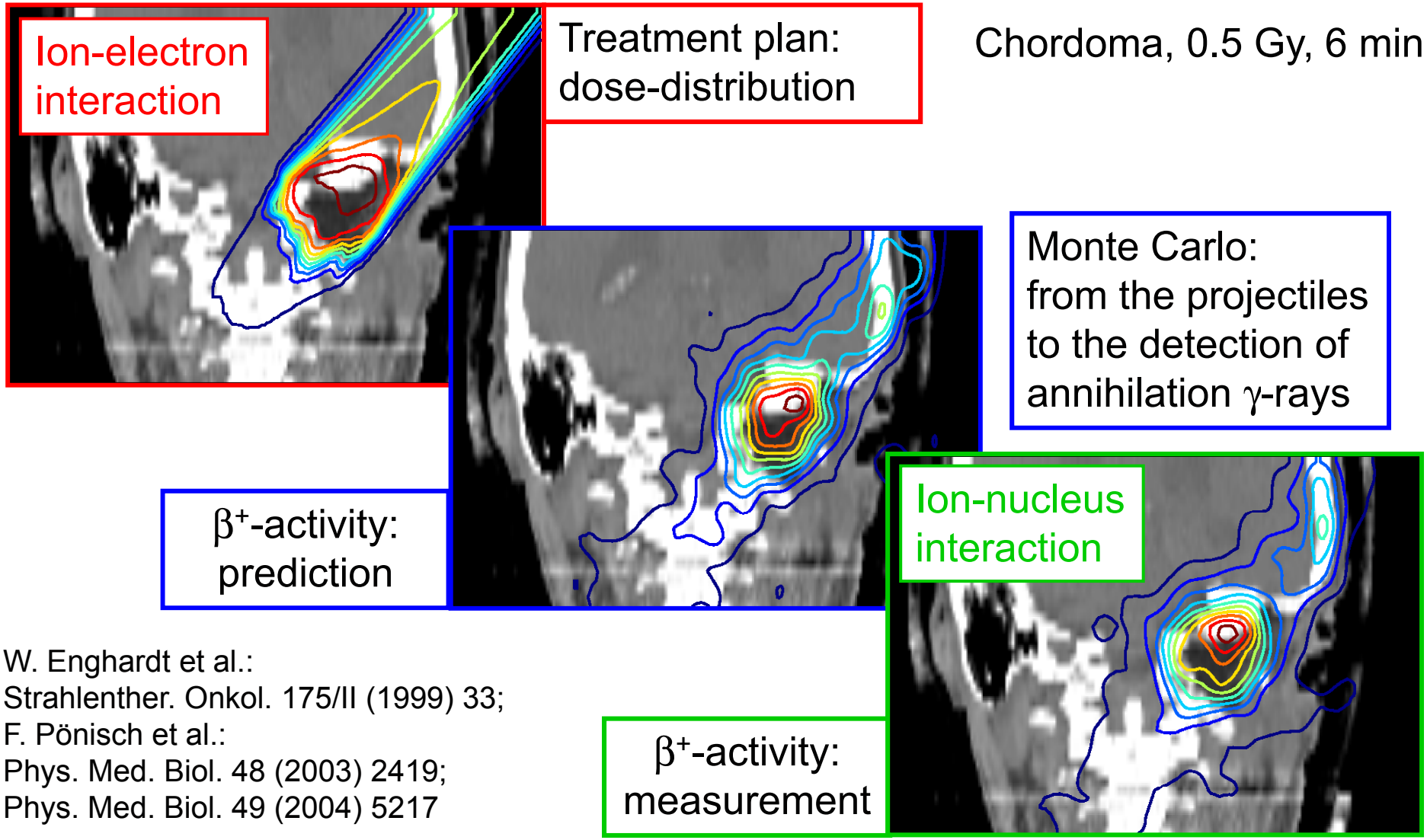
## Instrumentation (II)

| | In-beam | Off-line |
|---|---|---|
| Positron camera | Double head | Conventional ring PET/CT |
| Workflow | (1) Portal 1 + 40 s decay<br>(2) Repositioning (< 5 min)<br>(3) Portal 2 + 40 s decay<br>… | (1) Portals 1, 2, …<br>(2) Transfer to PET (15 min)<br>(3) PET-scan (30 min) |
| Relevant isotopes | $^{11}C$ (20 min), $^{10}C$ (19 s)<br>$^{15}O$ (2 min) … $^{8}B$ (0.8 s) | $^{11}C$ (20 min), |
| Influence of metabolism | Low to medium | Strong |
| Quantitative PET | Difficult | Possible |
| Image correlation planning-CT – PET | Stereotactic coordinates | Additional CT (PET/CT) |
| Range measurements | Portal 1 (no restrictions)<br>Portals 2 … (difficult) | Impossible for opposing portals |

P. Crespo et al.: Phys. Med. Biol. 51 (2006) 2143

# 2. What do we have? In-beam PET

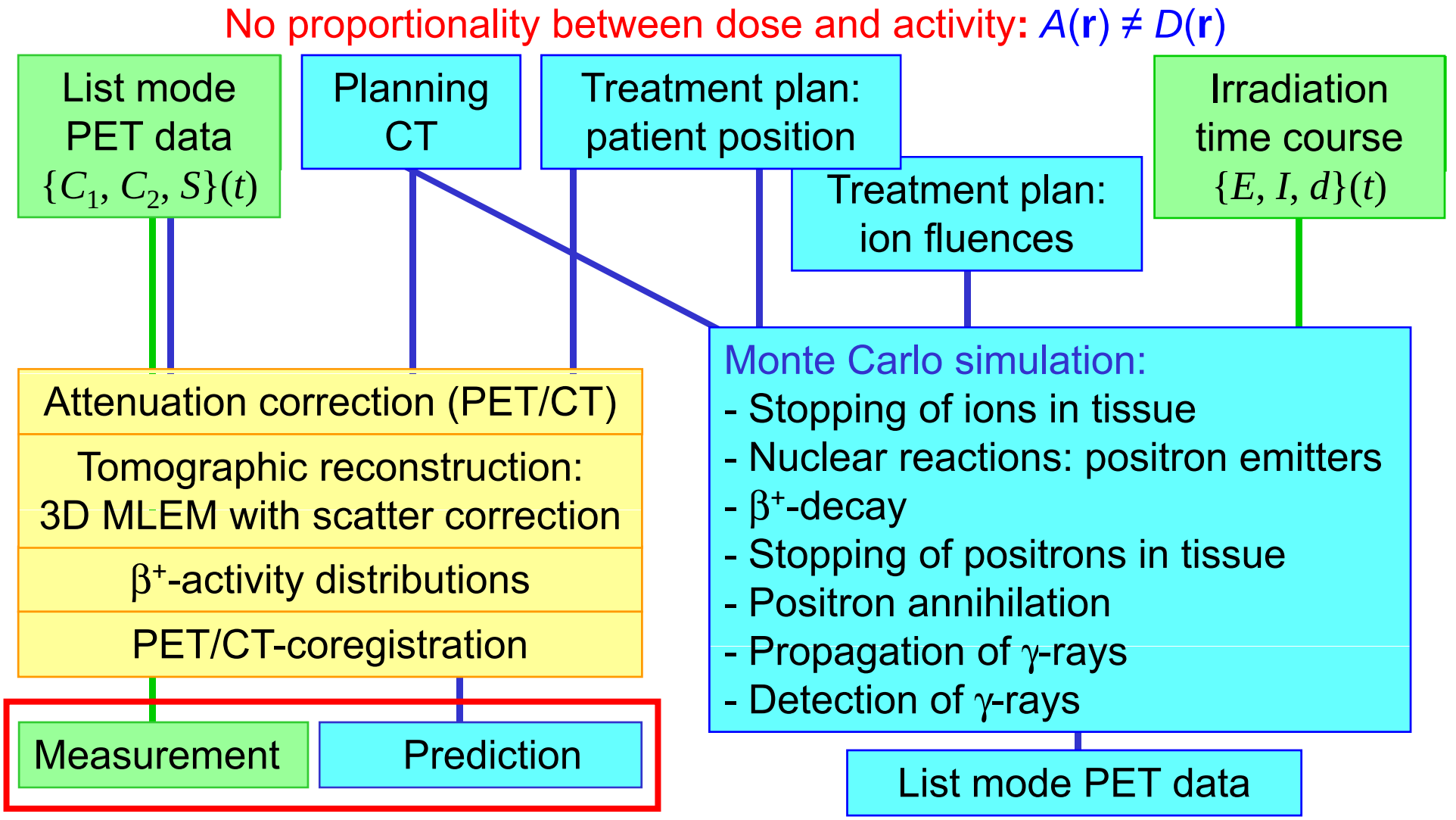
## Clinical implementation (I)




W. Enghardt et al.:
Strahlenther. Onkol. 175/II (1999) 33;
F. Pönisch et al.:
Phys. Med. Biol. 48 (2003) 2419;
Phys. Med. Biol. 49 (2004) 5217

# 2. What do we have? In-beam PET

## Clinical implementation (II)




F. Pönisch et al.: Phys. Med. Biol. 48 (2003) 2419; Phys. Med. Biol. 49 (2004) 5217

# 2. What do we have? In-beam PET

## Clinical implementation (III)

**Accelerator:**

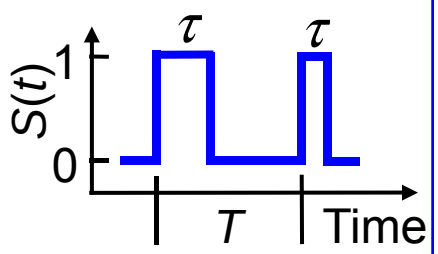
Synchrotron

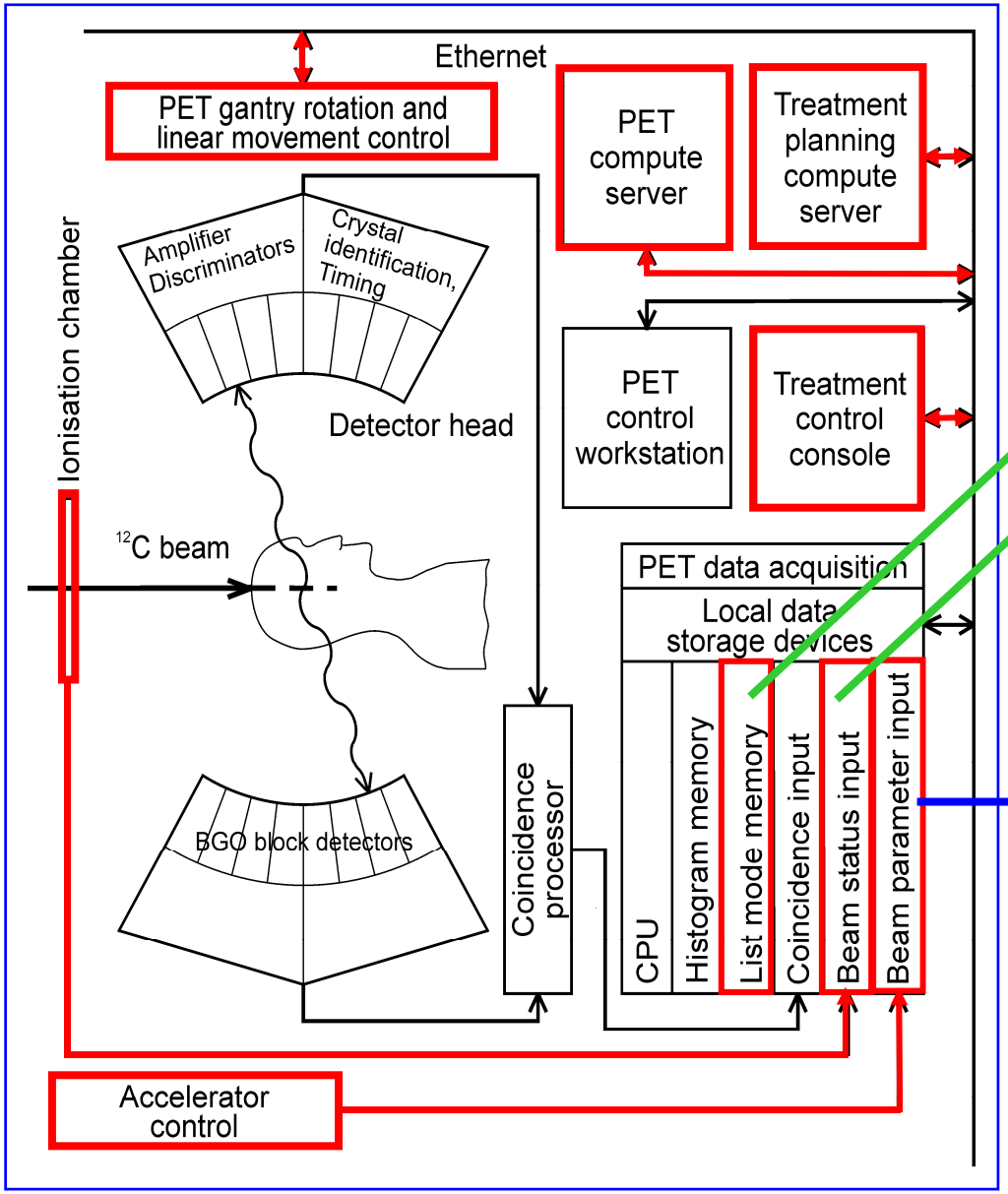
$d \approx 60$ m

**Particle beam:**

pulsed

$T \approx 5$ s, $\tau \leq 2$ s



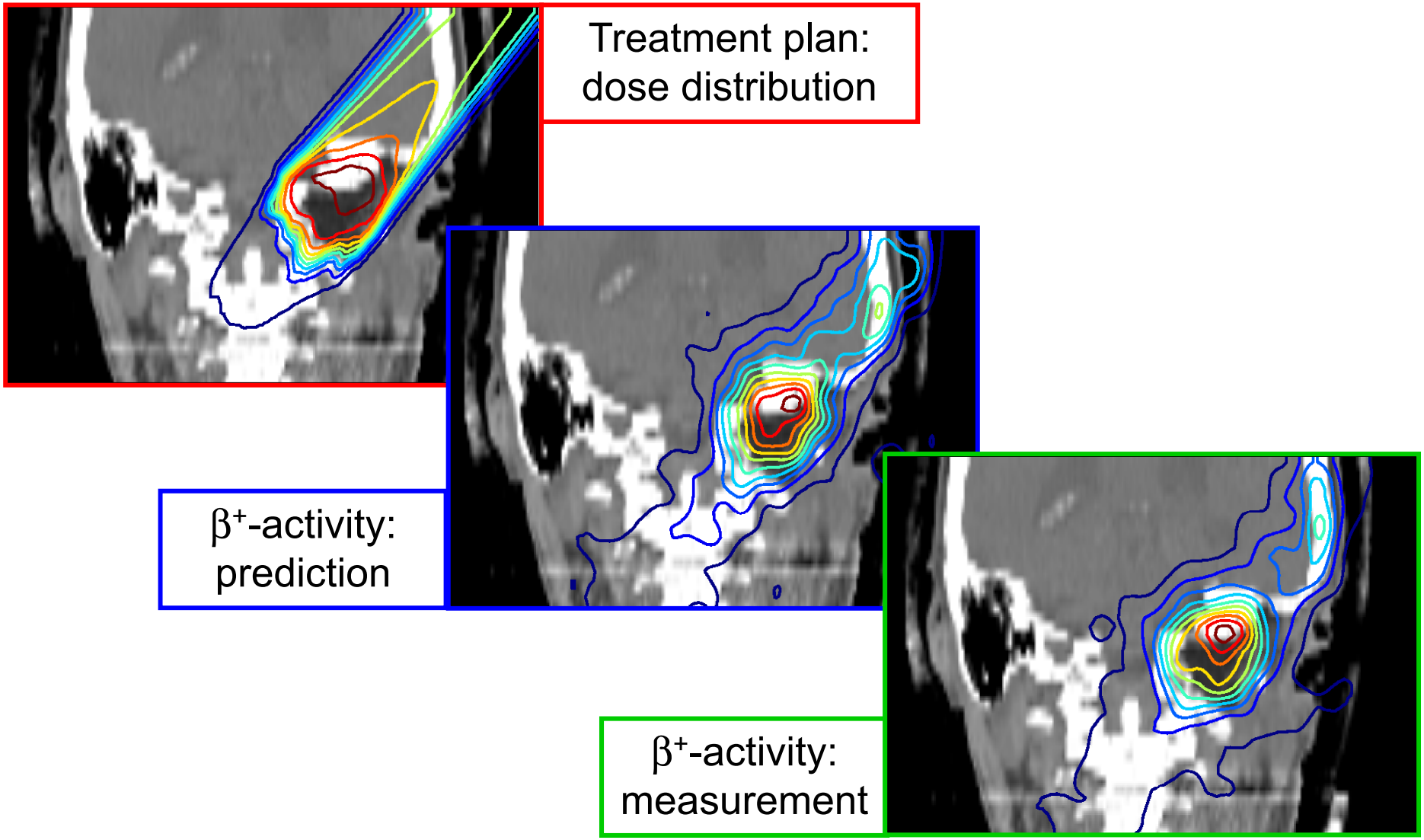




PET data, list mode: $\{K_1, K_2, S\}(t)$

Irradiation-time course: $\{E, I, d\}(t)$

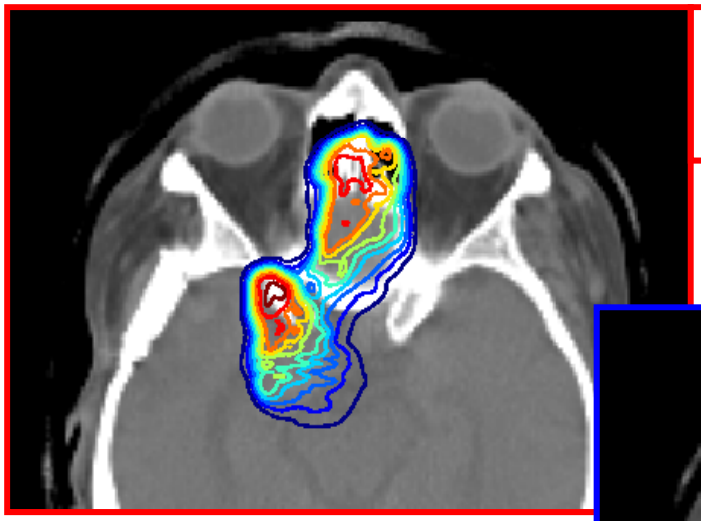
# 2. What do we have? In-beam PET

## Ion range verification

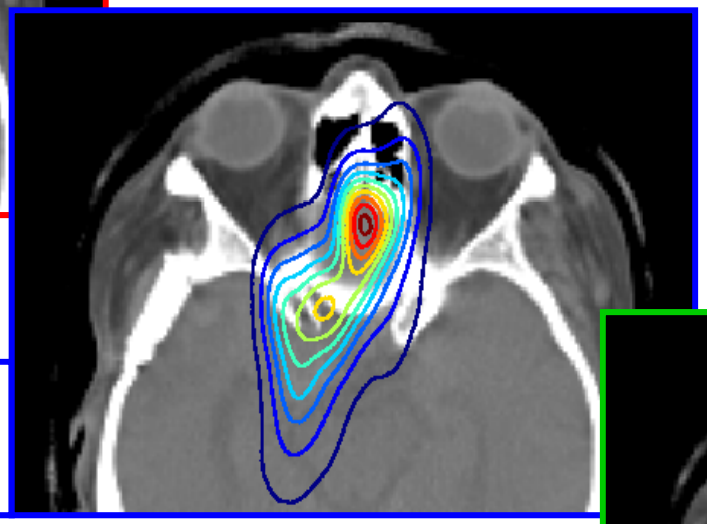


# 2. What do we have? In-beam PET

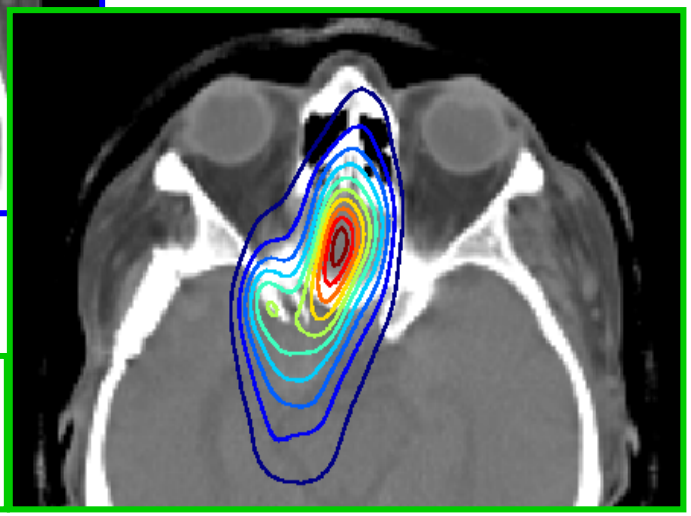
## Field position verification



Treatment plan:
dose distribution



$\beta^+$-activity:
prediction

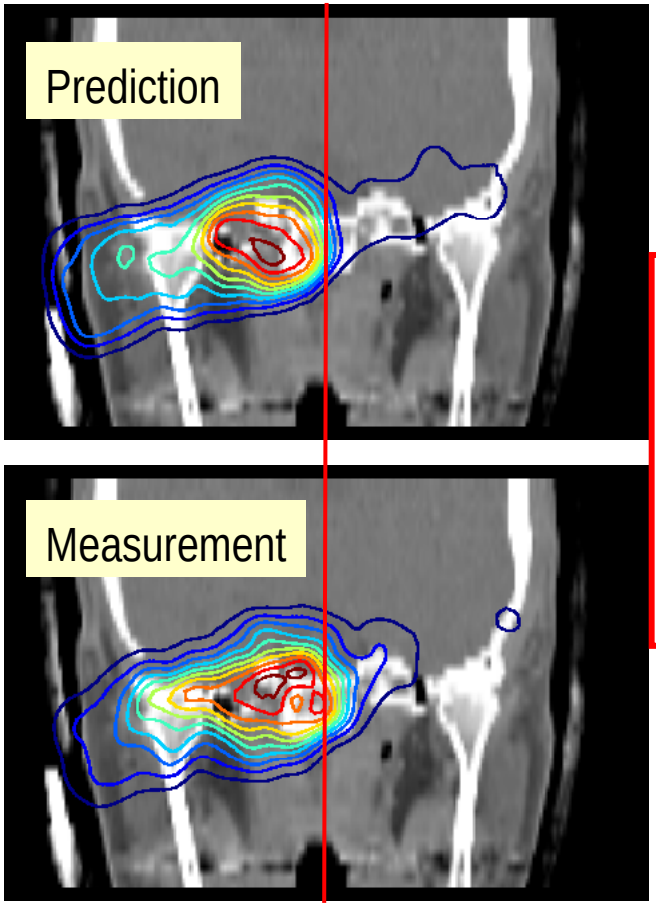


$\beta^+$-activity:
measurement

# 2. What do we have? In-beam PET

## Physical beam model validation

1998



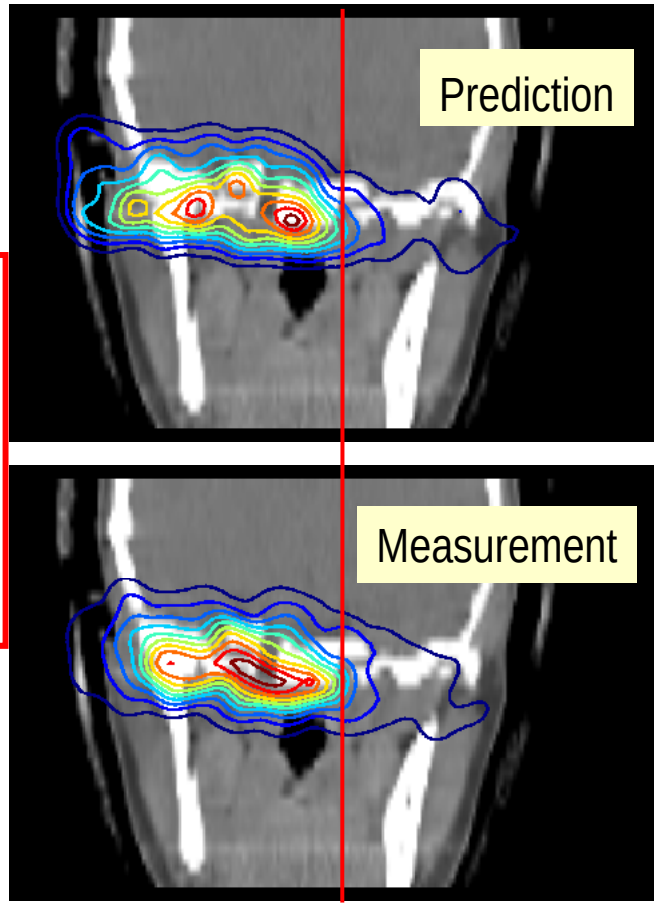

1. Precision measurements:

Range of
$^{12}$C-ions in tissue

2. Modification:

$$R = R(HU)$$

Since 1999

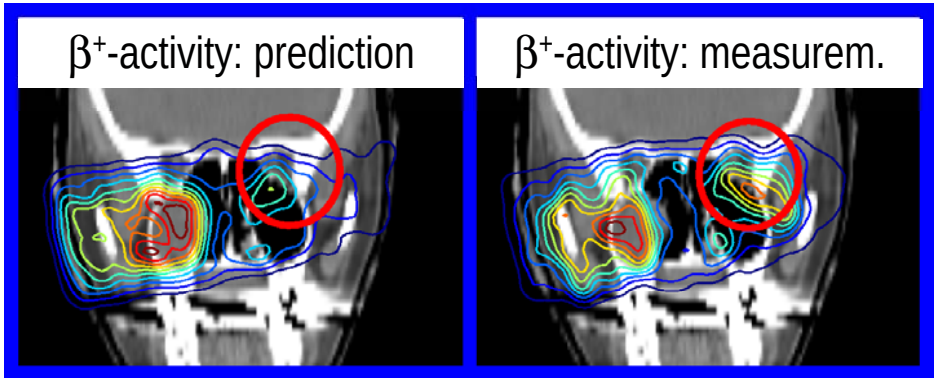





M. Krämer et al.: Radiother. Oncol. 73 (2004) S80

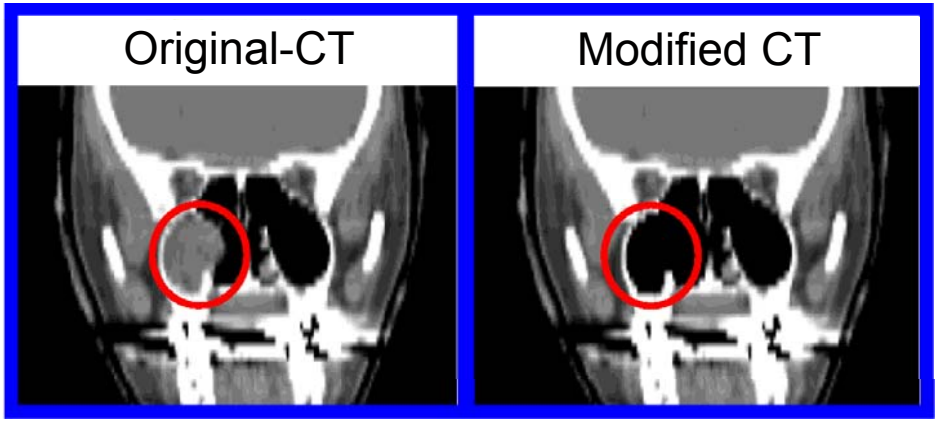
# 2. What do we have? In-beam PET

## Estimation of dose delivery deviations

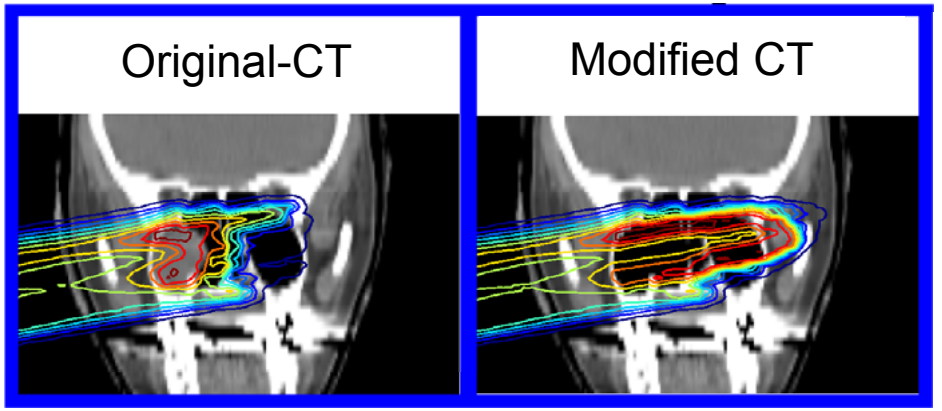


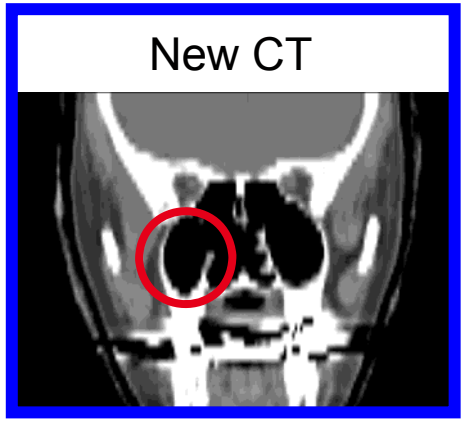

Hypothesis on the reason for the deviation from the treatment plan

Interactive CT manipulation




Dose recalculation




CT after PET findings

W. Enghardt et al.: Radiother. Oncol. 73 (2004) S96

# 2. What do we have? In-beam PET

## Estimation of dose delivery deviations

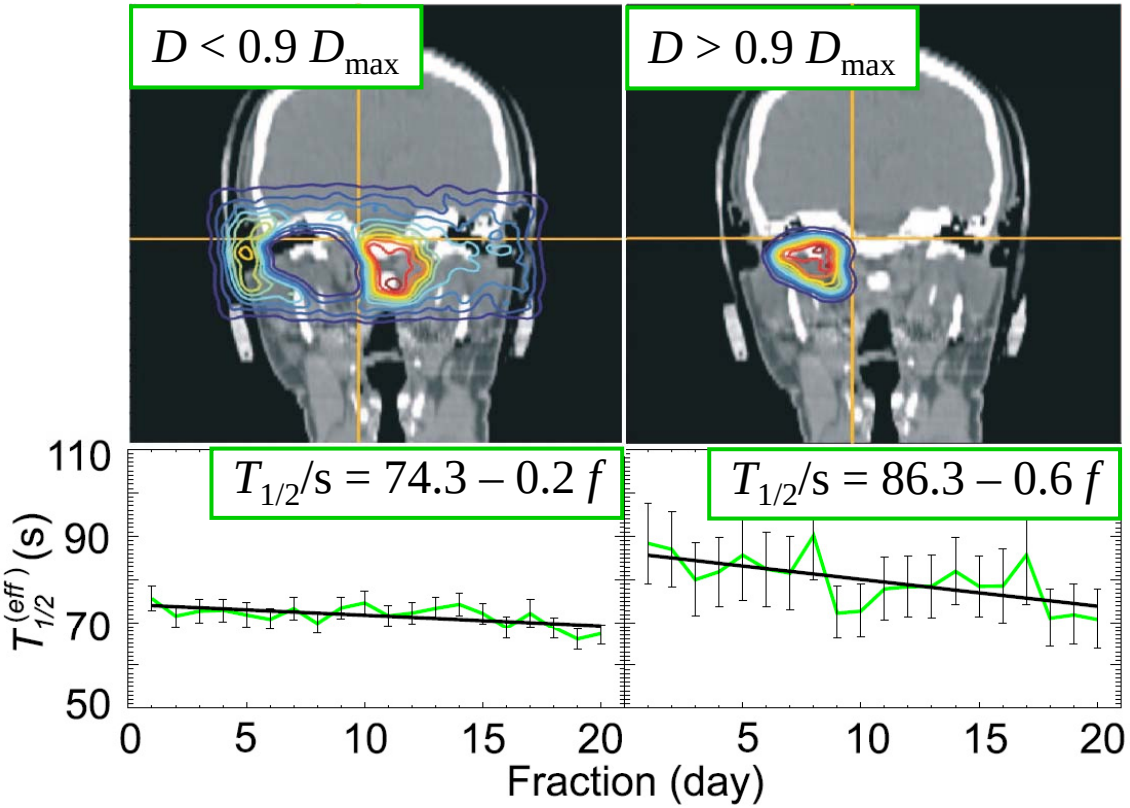
In-beam PET is not applicable to a precise dosimetry

- it seems to be feasible to solve the inverse problem:

$$\mathbf{A(r)} = \mathbf{T}\,\mathbf{D(r)}$$

$\mathbf{A(r)}$ – spatial distribution of activity
$\mathbf{D(r)}$ – spatial distribution of dose
$\mathbf{T}$ – transition matrix

- it seems to be difficult to quantify the metabolic washout of $\beta^+$-radioactivity
  - individual
  - tissue dependent
  - dose dependent
  - fraction dependent
  - disturbed by the tumour
- in-beam PET images are corrupted by limited angle artefacts (non-quantitative)





K. Parodi, T. Bortfeld:
Phys. Med. Biol. 51 (2006) 1991
K. Parodi et al.:
Med. Phys. 33 (2006) 1993
F. Fiedler et al.: Acta Oncol. 2007

# 2. What do we have? In-beam PET

## Advantages

- PET allows for a
  - beam delivery independent,
  - simultaneous or close to therapy (in-beam, offline, resp.),
  - non-invasive

  control of tumour irradiations by means of ion beams
- an in-vivo measurement of the ion range
- the validation of the physical model of the treatment planning
- the evaluation of the whole physical process of the treatment from planning to the dose application
  - new ion species
  - new components, algorithms
  - high precision irradiations
- the detection and estimation of unpredictable deviations between planned and actually applied dose distributions due to
  - mispositioning
  - anatomical changes
  - mistakes and incidents (www.rosis.info, spotlight on in-vivo dosimetry)

# 2. What do we have? In-beam PET

## Disadvantages and open problems

PET is not applicable to

- real time monitoring:
  - too slow
  - $T_{1/2}(^{15}O)$ = 2 min, $T_{1/2}(^{11}C)$ = 20 min
  - dose specific activity: ~ 1000 - 7000 Bq $cm^{-3}$ $Gy^{-1}$
- quantitative imaging, precise dose quantification, feedback to treatment planning and to IGRT
  - limited angle artefacts
  - degradation of activity distributions by the metabolism
  - degradation of activity distributions by moving organs
  - inaccurate prediction of activity distributions from treatment planning due to unknown nuclear reaction cross sections

# 3. What do we need?

## Aim of this FP7-project

- PET: clinical application reached, further development: industry
- Development and proof of principle of really new solutions for
  - non-invasive, real-time, in-vivo monitoring
  - quantitative imaging
  - precise dose quantification
  - feedback to treatment planning
  - real-time feedback to IGRT for moving organs
- Preserve the leading European position in the field

# 3. What do we need?

## WP1: Time-of-flight in-beam PET

- Aim: Remove the influence of limited angle tomographic sampling to quantitative imaging

- Subtask 1.1.: Development of a demonstrator of an in-beam TOF positron camera:
  - $2\tau < 200$ ps
  - $\eta_{singles} > 50$ %
  - $\Delta x < 5$ mm

  $\Rightarrow$ detector technology

  $\Rightarrow$ DAQ

- Subtask 1.2.: Tomographic reconstruction and prediction of measured activity distributions from treatment planning

  $\Rightarrow$ real-time TOF reconstruction

  $\Rightarrow$ simulation TP $\rightarrow$ TOF IBPET (WP5)

# 3. What do we need?

## WP2: In-beam single particle tomography (IBSPAT) (I)

- Aim: Remove the influence of metabolism by detecting prompt nuclear reaction ejectiles (photons, neutrons, charged particles)

- Challenge: Signal acquisition during the huge background of therapy irradiation

- Subtask 2.1.: Development of a demonstrator of an in-beam single photon tomographic detection system (IBSPECT):
  - $\eta_{singles} > 10$ %
  - $\Delta x < 5$ mm

  $\Rightarrow$ detector technology (Anger camera, Compton camera: $\eta_{CC} \approx 100\ \eta_{AC}$)

  $\Rightarrow$ discrimination of background radiation

  $\Rightarrow$ DAQ

  $\Rightarrow$ tomographic reconstruction (CC)

  $\Rightarrow$ simulation: TP $\rightarrow$ IBSPECT (WP5)

S. Chelikani et al.:
Phys. Med. Biol. 49 (2004) 1387

- Subtask 2.2.: Proof of principle of massive particle (*n*, *p* …) based in-vivo dosimetry

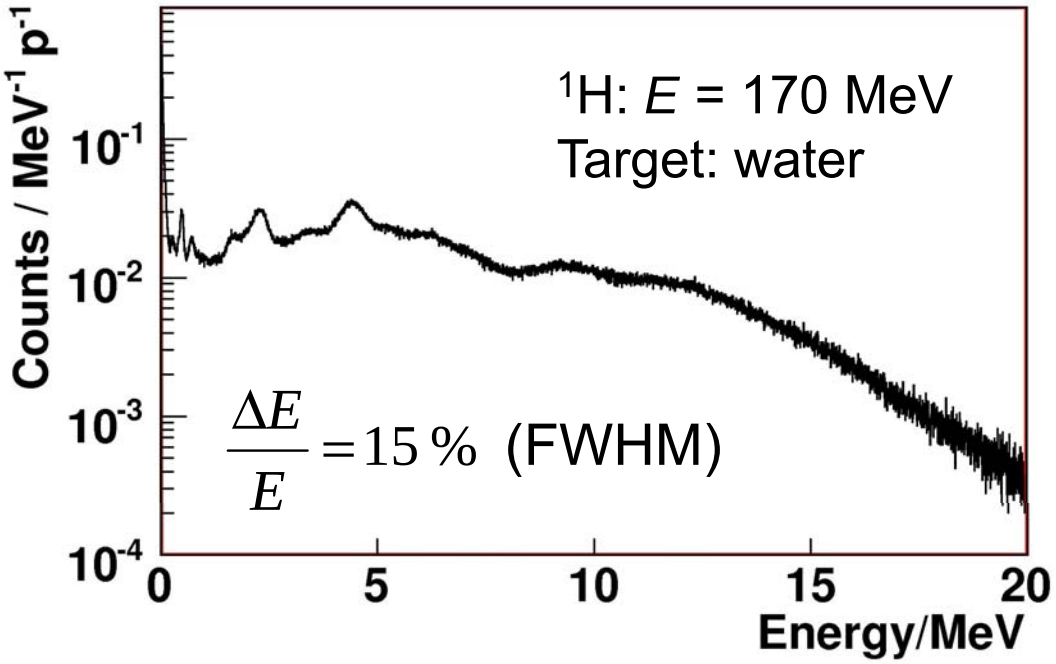
  $\Rightarrow$ simulation: TP $\rightarrow$ IBSPAT (WP5)

  $\Rightarrow$ decision on continuation

# 3. What do we need?

## WP2: In-beam single particle tomography (IBSPAT) (II)

GEANT4: $H_2O$ ($p$, $\gamma$) X




- photon/proton = 0.25
- $N_p > 10^9$
- $N_\gamma > 10^8$

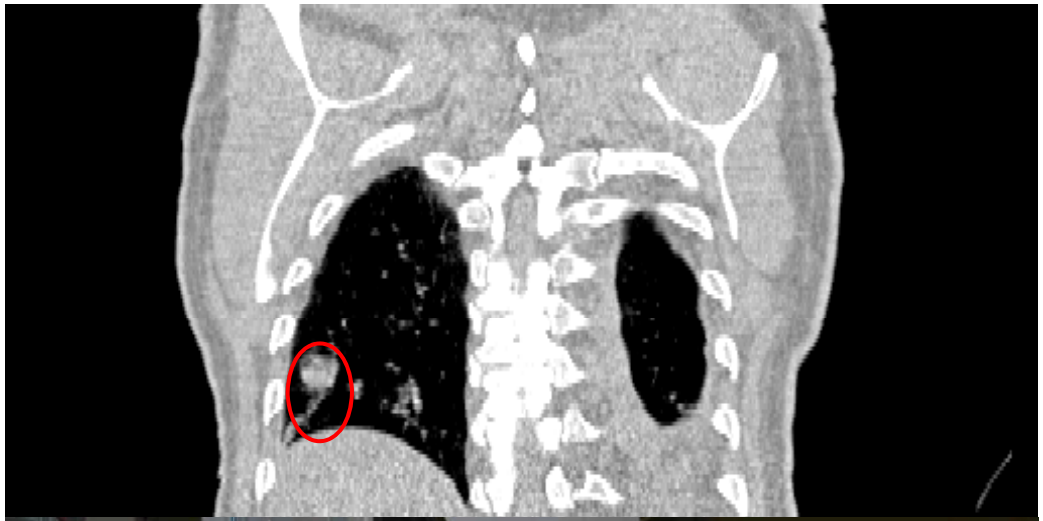
H. Müller:
www.fzd.de/FWK/MITARB/muellerh/G4/FF/index.htm

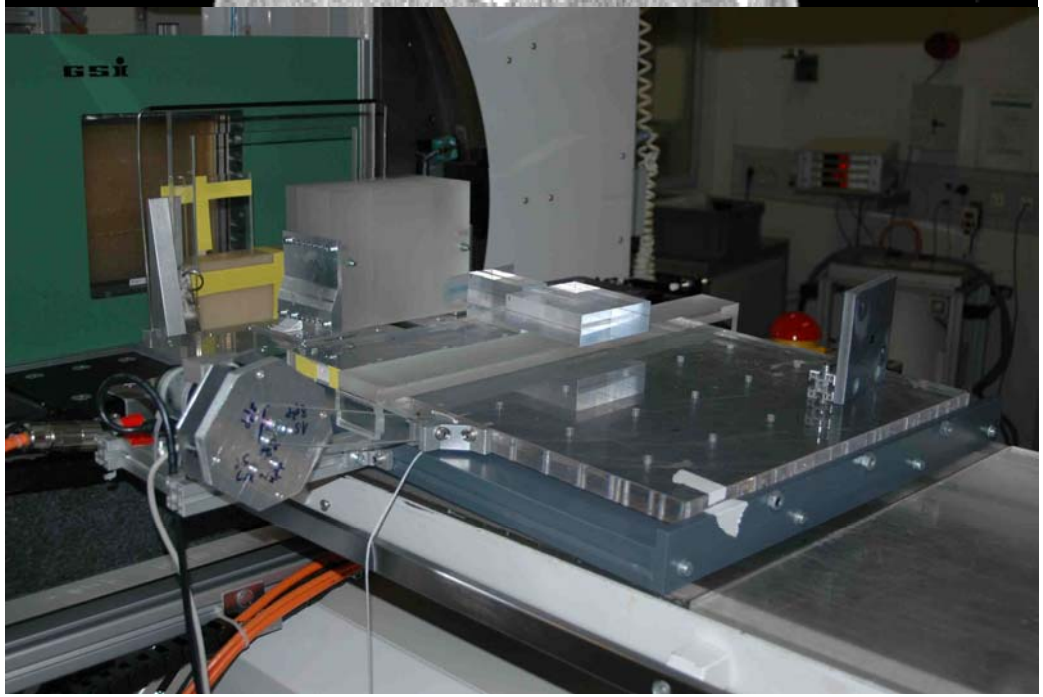
$$\frac{\Delta D}{D_{\max}} < 5\%$$

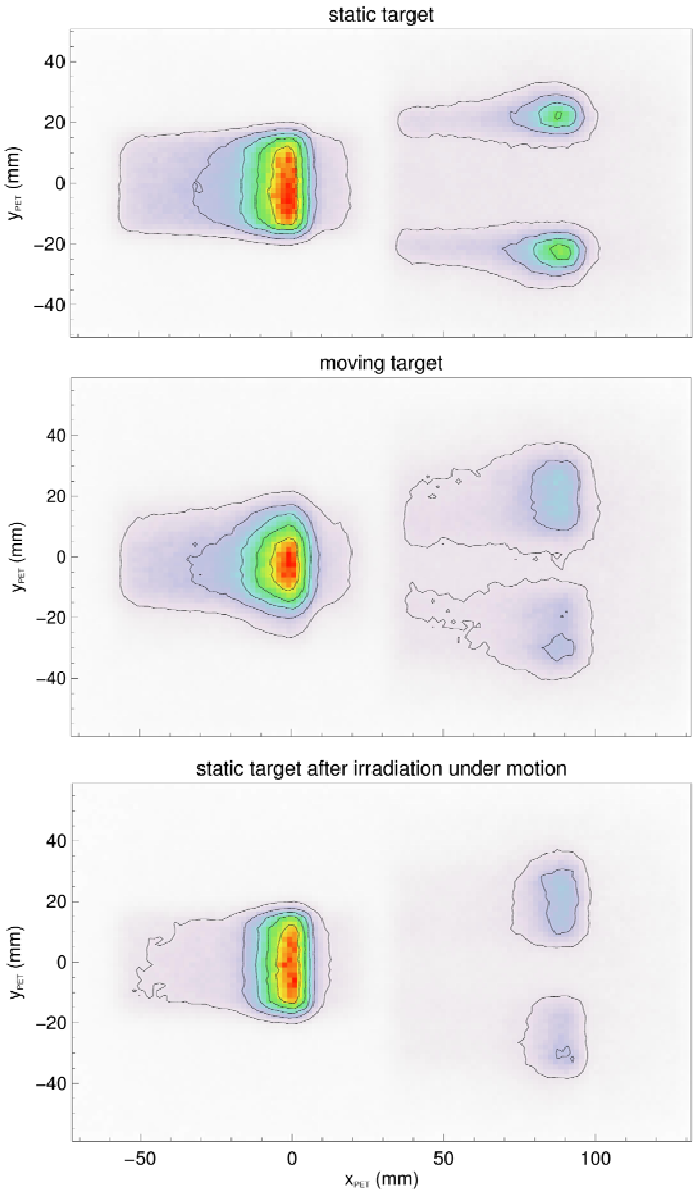
# 3. What do we need?

## WP3: PT in-vivo dosimetry and moving organs (I)

C. Bert, C. Laube, K. Parodi. WE:
In-beam PET and $^{12}$C-beam tracking. Experiment July 2008





# 3. What do we need?

## WP3: PT in-vivo dosimetry and moving target volumes

- Aim: Establish in-vivo dosimetry methods for moving targets in combination with motion compensated beam delivery by gating and tracking

- Subtask 3.1.: Investigation of the potential of in-vivo dosimetry for irradiation of moving targets at the example of in-beam PET (GSI-facility)

  $\Rightarrow$ data acquisition schemes (4D IBPET)

  $\Rightarrow$ motion correction methods for 4D IBPET data

  $\Rightarrow$ time dependent simulation TP $\rightarrow$ 4D IBPET

- Subtask 3.2.: Extension of moving target methodology to the detection of single particles (feasibility study)

  $\Rightarrow$ influence of motion onto IBSPAT: simulation (WP5)

  [$\Rightarrow$ data acquisition schemes (4D IBPET)

  $\Rightarrow$ motion correction methods for 4D IBPET data

  $\Rightarrow$ time dependent simulation TP $\rightarrow$ 4D IBPET (WP5)]

# 3. What do we need?

## WP4: The combination of in-vivo dosimetry and treatment planning

- Aim: Development of fast and clinically applicable procedures for introducing in-vivo dosimetry results into adaptive treatment planning and beam delivery

- Subtask 4.1.: Development of automatic methods of identifying deviations between planned and actually delivered dose distributions:

  ⇒ criteria for deviation detection (comparison with simulations)

  ⇒ identification of reasons for deviations (patient mispositioning, anatomical reasons, incidents)

- Subtask 4.2.: Establishing the feedback between in-vivo dosimetry and treatment planning as well as beam delivery control:

  - fast
  - real time (IGRT), not feasible for IBPET

  ⇒ methods of compensation (patient mispositioning, anatomical reasons, incidents)

  ⇒ delivering information of deviation compensation to TP

# 3. What do we need?

## WP5: Monte Carlo Simulation of in-vivo dosimetry

- Aim: Prediction of IBPET, IBSPECT, IBSPAT measurements from TP data for comparison with measured data

- Challenges: Dose prediction accuracy from in-vivo dosimetry data: $\Delta D/D_{max} < 5\ \%$

  Fast (reaction times of seconds)

- Subtask 5.1.: Development of fast and precise Monte Carlo tools for in-vivo dosimetry

  $\Rightarrow$ TP $\rightarrow$ TOF IBPET (WP1)

  $\Rightarrow$ TP $\rightarrow$ IBSPECT (WP2.1)

  $\Rightarrow$ TP $\rightarrow$ IBSPAT (WP2.2)

  $\Rightarrow$ TP $\rightarrow$ 4D IBPET, 4D IBSPAT, 4D IBSPECT (WP3.2)

- Subtask 5.2.: Compilation of basic physical data for the Monte Carlo tools of WP5.1:

  $\Rightarrow$ basis: experimental data, evaluated data bases

  $\Rightarrow$ generation of implicite data sets, e.g. yields

  $\Rightarrow$ concept for data to be measured (next EU-project)

M. Priegnitz et al.: Phys. Med. Biol. 53 (2008) 4443