Imaging

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What is the role of imaging in modern radiotherapy?

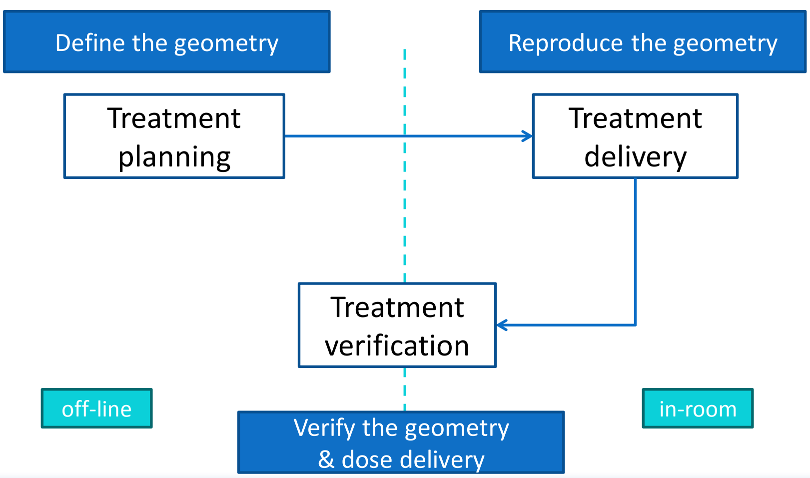
The role of imaging in radiotherapy

If you can´t see it, you can´t hit it,
and if you can´t hit it, you can´t cure it !

Source Wikipedia

Introduction

In order to "hit the target" imaging is used to…



Adapted from C. Gianoli

Imaging for treatment planning

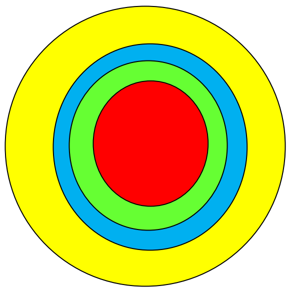
ICRU- concept of therapy relevant volumes

(ICRU 62, 1999)

Time (Movement)

ITV (internal target volume) includes physiological motion

PTV (planning target volume) includes positioning uncertainties



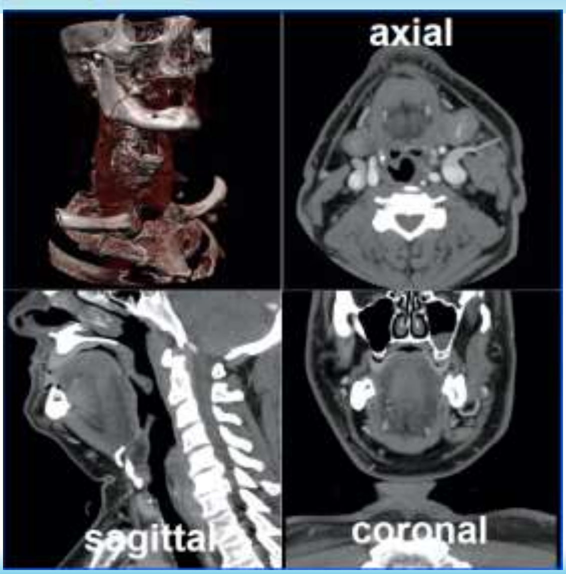
Space (Morphology)

GTV (gross target volume) macroscopic

CTV(clinical target volume) includes microscopic extensions

Courtesy W. Schlegel

Imaging for planning: CT



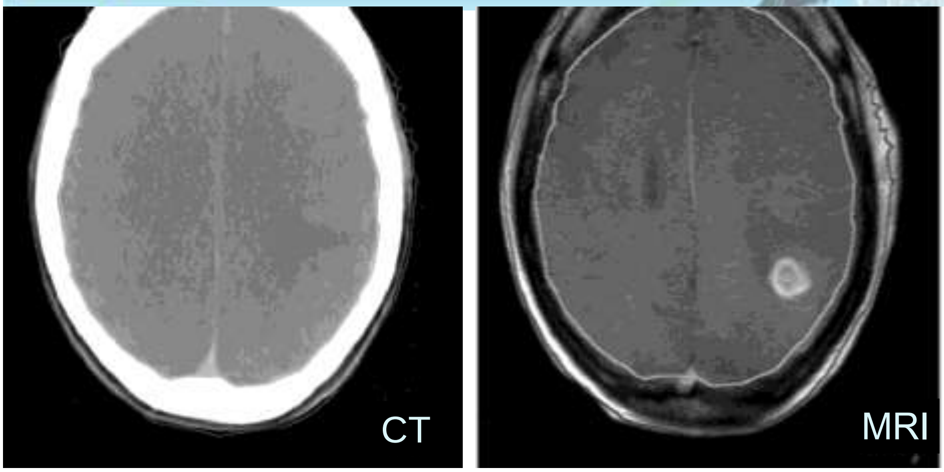
CT Number or Hounsfield Unit (HU)

$$HU = \frac{1000\ (\mu_x - \mu_{water})}{\mu_{water}}$$

Provides the basic patient model information for treatment planning in 3D(4D)

Source: W. Kalendar, E. Rietzel

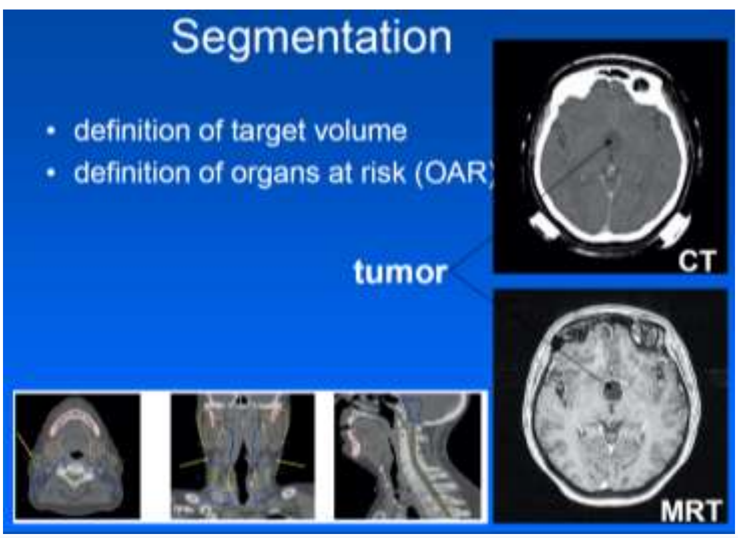
Imaging for planning: MRI



CT imaging lacks of soft tissue contrast and is thus typically complemented by Magnetic Resonance Imaging (MRI)

Source: DKFZ

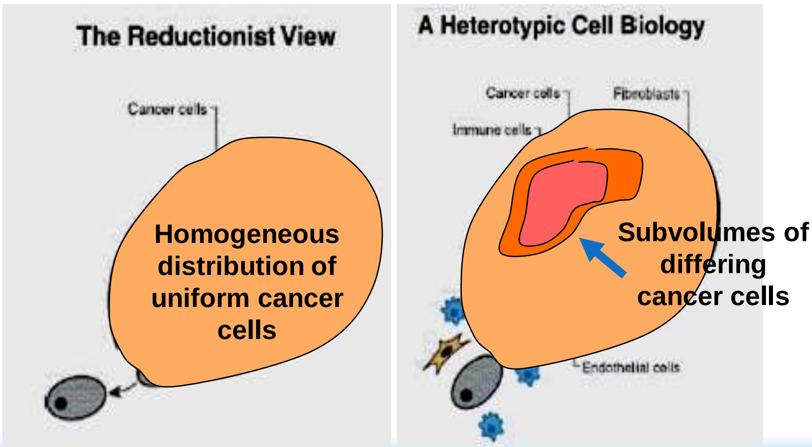
Imaging for planning: CT & MRI



Source: HIT

ICRU- concept of therapy relevant volumes

The paradigm shift in radiation oncology



D. Hanaha, R. A. Weinberg, Cell,Vol. 100, 57-70,2000

ICRU- concept of therapy relevant volumes

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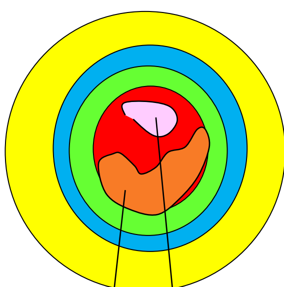


radio-sensitive area

radio-resistant area

BTV (Biological Target Volume) includes biol. heterogeneities

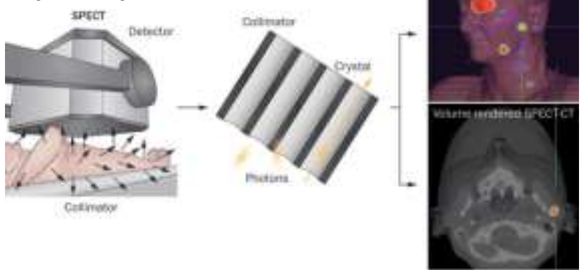
Biology (Metabolism)

Courtesy W. Schlegel

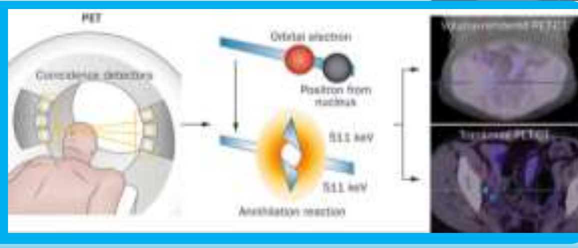
Nuclear medicine imaging

Visualizes radioactive decay of injected tracers

SPECT -
Single photon emission tomography



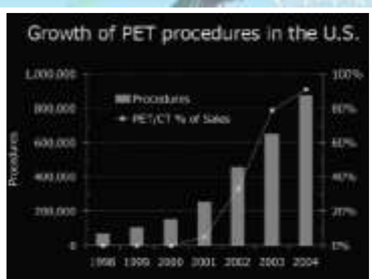
PET -
Positron emission tomography

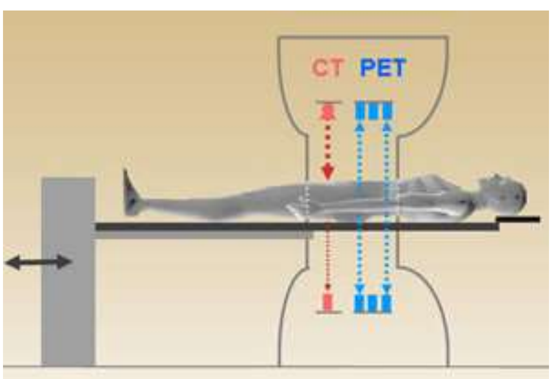


Nature Reviews Clinical Oncology **9**, 712-720 (2012)

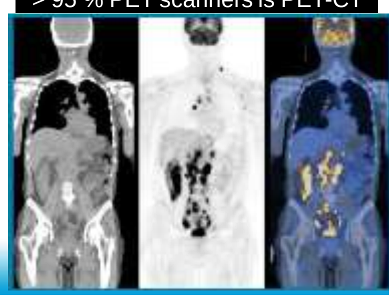
Imaging for planning: PET/CT

Integration of PET and CT in single hybrid scanner





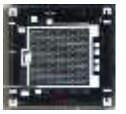
> 95 % PET scanners is PET-CT



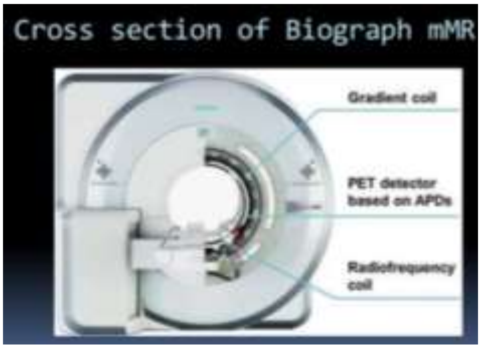
D. Townsend

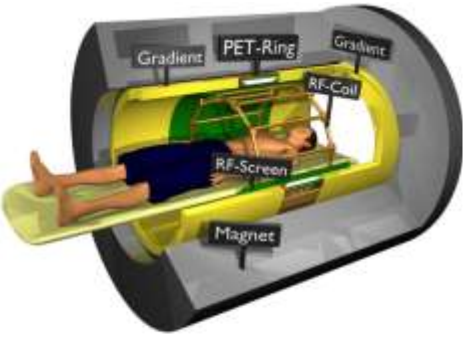
Imaging for planning: PET/MR

Combination of PET and MR in hybrid scanner
(first commercial systems available, but still ongoing research)



SiPM



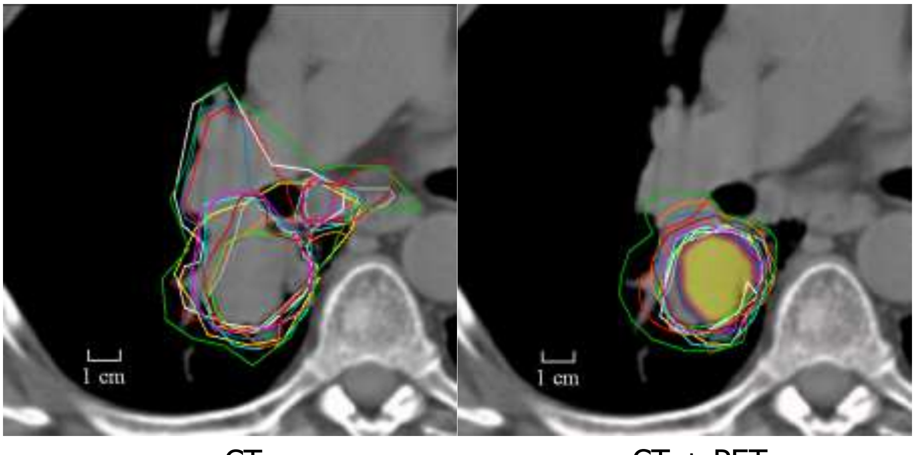


Source Siemens

Hybrid PET MR Project
Philips et al, HYPERimage

Multimodal imaging for planning

Multimodal imaging improves target delineation and reduces inter-observer variability



CT CT + PET

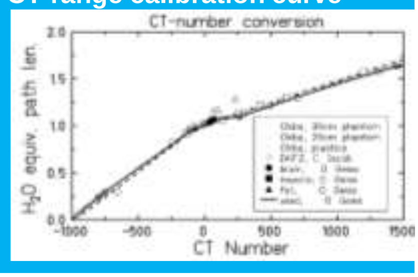
Steenbakkers et al, IJROBP 2005

Treatment planning

CT with target volumes and OARs, dose prescription

Physical beam data in water (biological data)

CT-range calibration curve



How to replicate planning geometry at the treatment site?

Source: HIT, Krämer et al, PMB 2000

Patient positioning

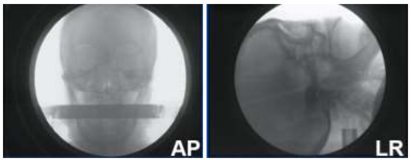
Patient immobilized with mask and special localisers for sterotactic positioning in treatment room using laser alignment and additional optical systems

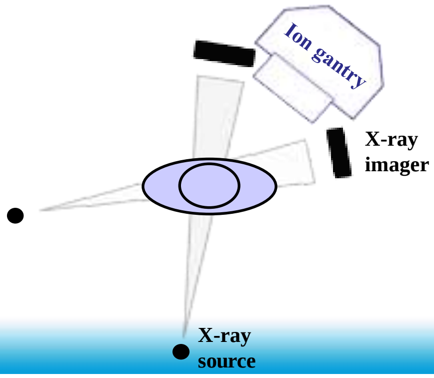
However missing inner anatomy…

Sources: CNAO and DKFZ

In-room imaging for patient positioning

Anatomy confirmation via X-rays





Source HIT

X-ray/CT-simulation

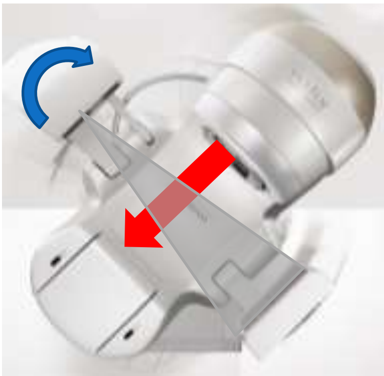
kV-X-ray

Digitally reconstructed radiography from CT

From A. Mahr

In-room imaging for patient positioning

As in photon therapy, use integrated on-board X-ray imager for volumetric so called cone beam imaging (CBCT)

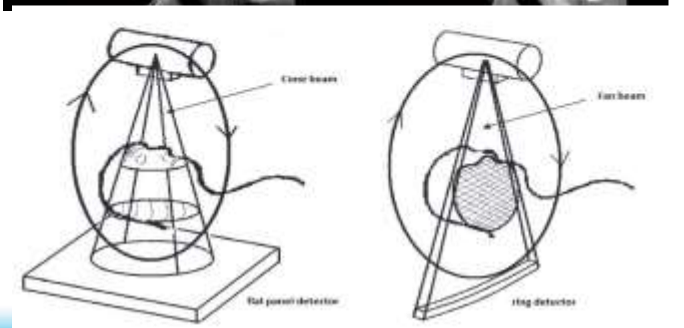



15TH SEPTEMBER , 2014

WORLD'S FIRST PT SPECIFIC CBCT GOES CLINICAL

Source: Varian, IBA

CBCT vs CT



Courtesy G. Landry

CBCT imaging for patient positioning

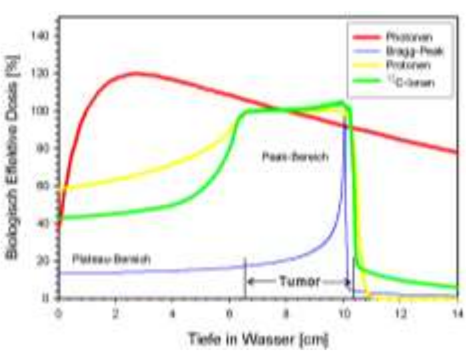
Fast image reconstruction and registration to planning CT for position correction

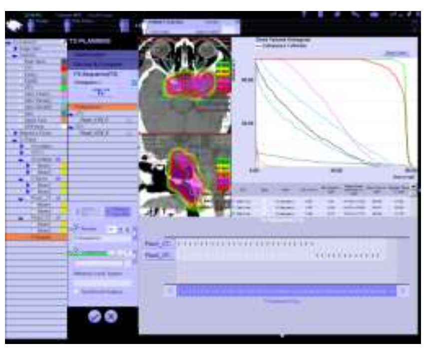
Figure 10. Volumetric registration at the treatment unit. A cone-beam CT acquired at the time of treatment is registered to the treatment planning CT (larger dataset) to properly position the patient on the treatment table (courtesy of Peter Monroe, PhD, Varian Medical Systems).

The British Journal of Radiology, 79 (2006), S99–S108

Treatment delivery uncertainties

We want to exploit clinically the dosimetric advantages of ion beams



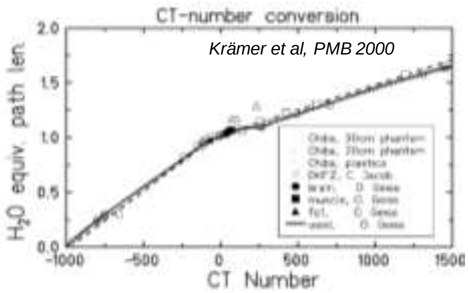


But is what we see in TPS what we really deliver?

Range uncertainties

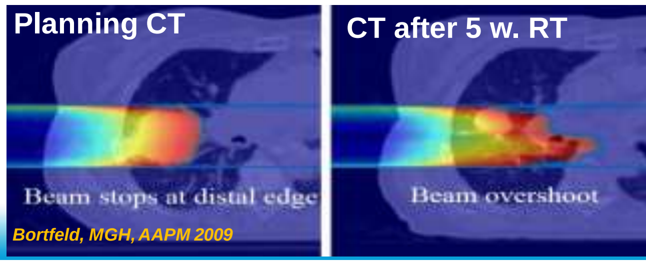
Tx planning uncertainties

- CT-range calibration
- Imaging artefacts
- Calculation models



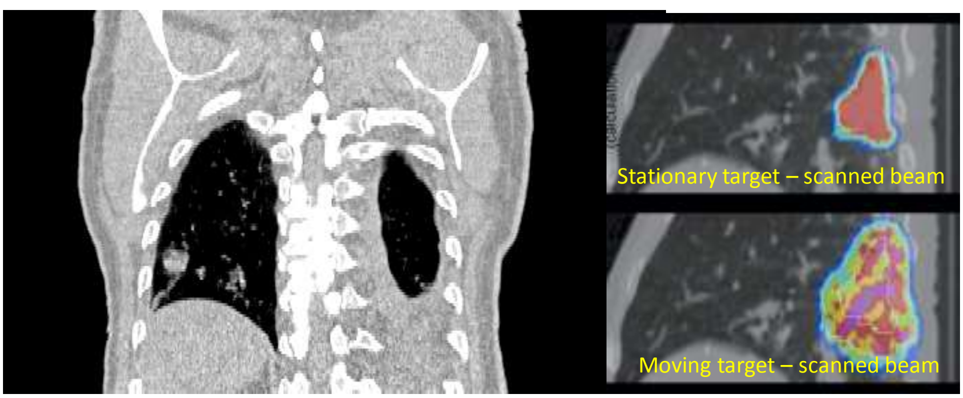
Delivery uncertainties

- Inter- and intra-fractional anatomical changes



Range uncertainties

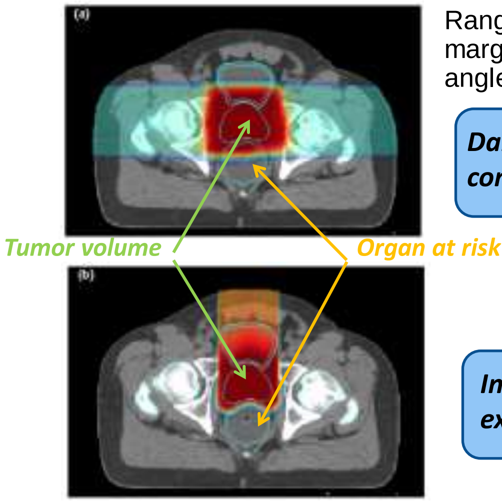
Delivery uncertainties: intrafractional anatomical changes



However not addressed in this lecture for the sake of time…

E. Rietzel et al, MGH; C. Bert et al, GSI Darmstadt

In-vivo verification



Tang et. al. Med.Phys. 2012

Range uncertainties result in conservative margin expansion and choice of beam angles avoiding Bragg peak before OARs

Daily practice of compromising dose conformality for safe delivery

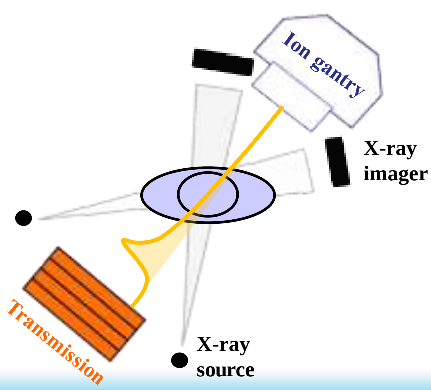
In-vivo verification could enable full exploitation of ion therapy potential

In-room imaging for treatment verification

Current efforts for in-room imaging in ion beam therapy

- Anatomical confirmation via X-rays or transmitted ions

Imaging for confirmation of
- Treatment geometry

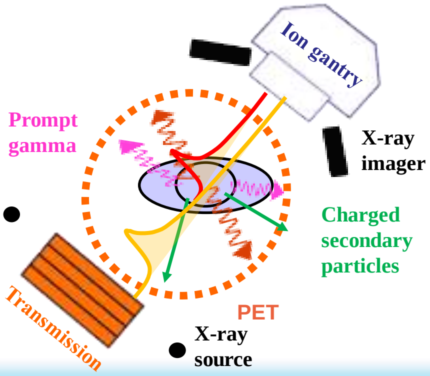


In-room imaging for treatment verification

Current efforts for in-room imaging in ion beam therapy

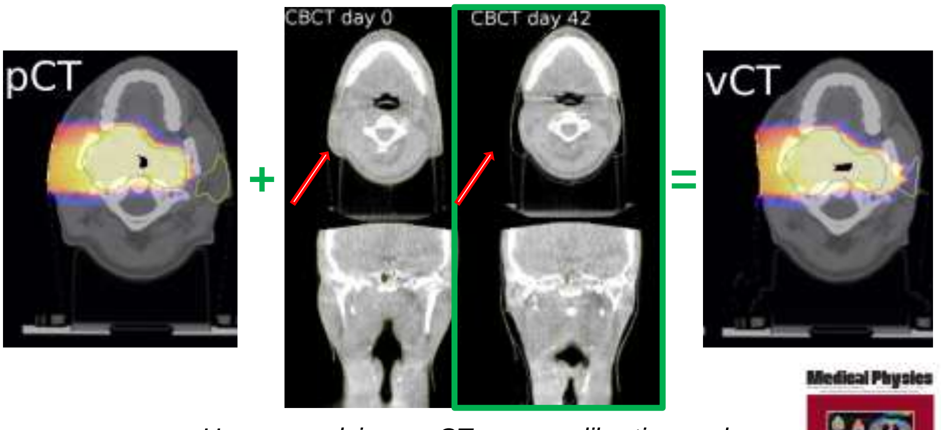
- Anatomical confirmation via X-rays or transmitted ions
- Range monitoring via emerging secondary radiation or transmitted ions

Imaging for confirmation of
- Treatment geometry
- Treatment delivery



In-room imaging for dosimetric assessment

CBCT (and DIR)-based image guidance for dose recalculation on daily anatomy

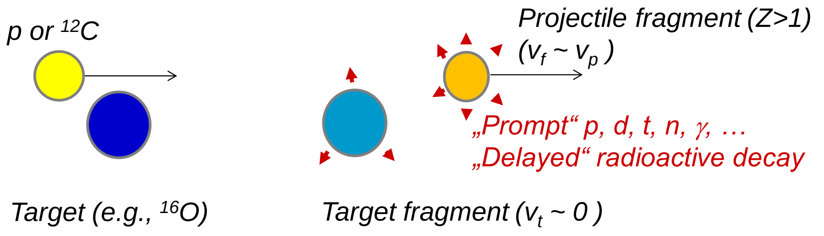


However relying on CT-range calibration and dose calculation engine

Landry...Parodi Med. Phys. 2015

In-room (offline) imaging for in-vivo treatment visualization

- Primary ions are stopped *somewhere* within the patient, with dose and range mainly dependent on Coulomb interaction
- Nuclear reactions induce measurable emerging radiation

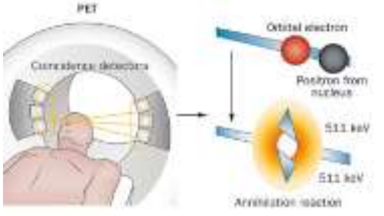


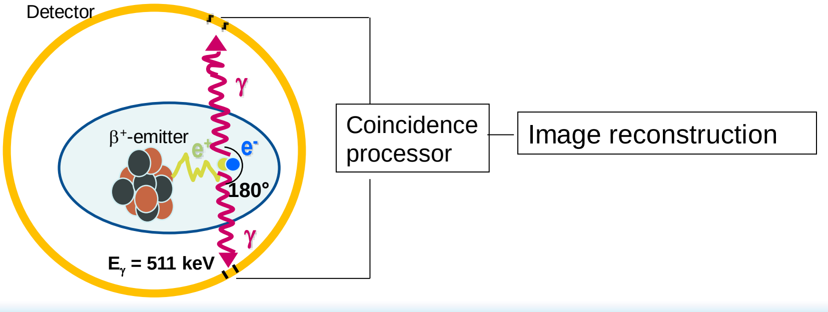
Only Positron-Emission-Tomography clinically investigated so far

Positron-Emission-Tomography

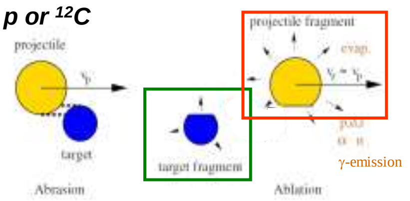
Imaging of β^+-activity

1) β^+-decay A(Z,N) ⟶ A(Z-1,N+1) + e^+ + ν_e
2) Moderation of e^+ in medium (few mm in tissue)
3) Annihilation into 2 opposite γ-rays (511 keV each)
4) Coincident detection and processing

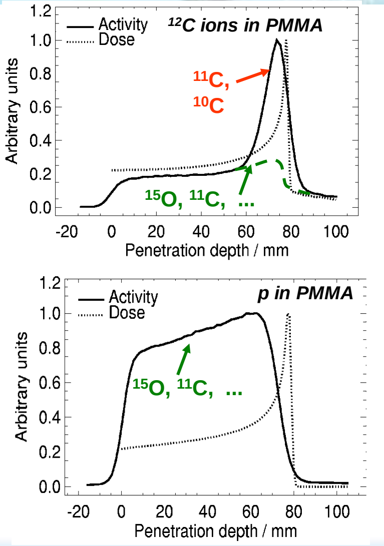




In-vivo PET-based verification



(projectile fragmentation only for Z>1)



β^+-emitter yield (^{15}O, ^{11}C,..., with $T_{1/2}$ ~ 2, 20,... min) as by-product of irradiation

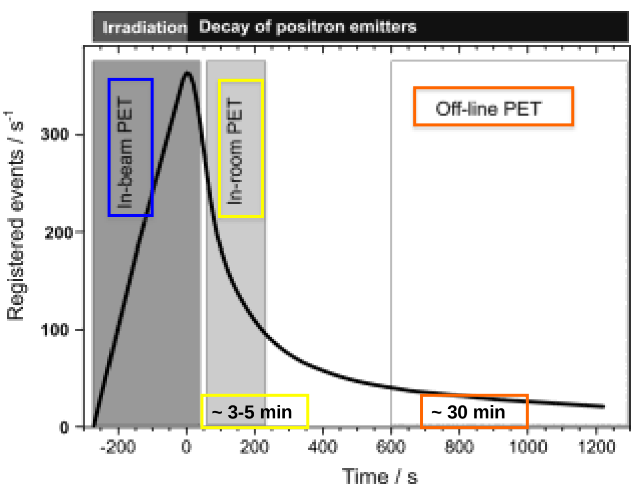
A(r)* $\neq$ *D(r)

Tradeoff between **better spatial correlation** (^{12}C) and **stronger signal** (*p*)

Dose-guidance from comparison of **measured** vs **expected** β^+-activity

K. Parodi et al, IEEE TNS 2005

The possible workflows



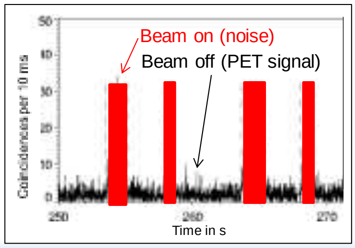
PET is a dynamic process, depending on time of irradiation and acquisition

Shakirin, ..., Parodi, ... PMB 2011

Clinical implementation of in-beam PET

In-beam PET (used clinically at GSI for ^{12}C ions)

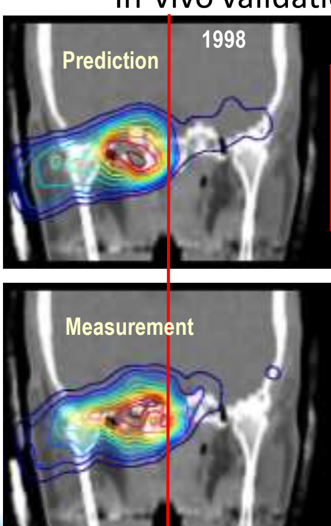
- \+ Patient in treatment position
- \+ Detection of short lived emitters (^{15}O)
- \+ No prolongation of treatment session
- ○ Morphological information from planning CT
- \- Limited-angle detection
- \- High integration costs



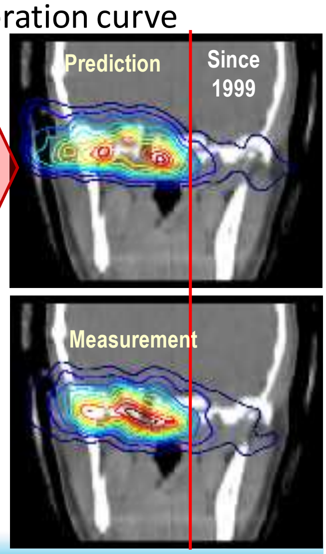
Enghardt, … Parodi … Nucl Instrum Meth A 2004; Parodi et al Nucl Instrum Meth A 2005

Clinical results of ibPET@GSI

In-vivo validation of CT-range calibration curve

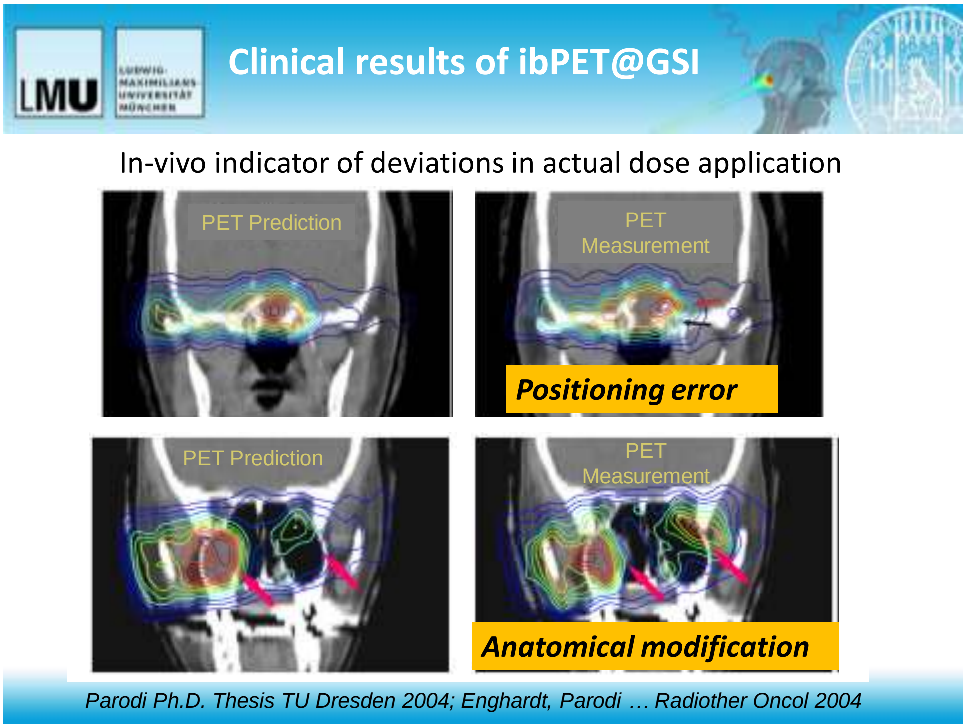


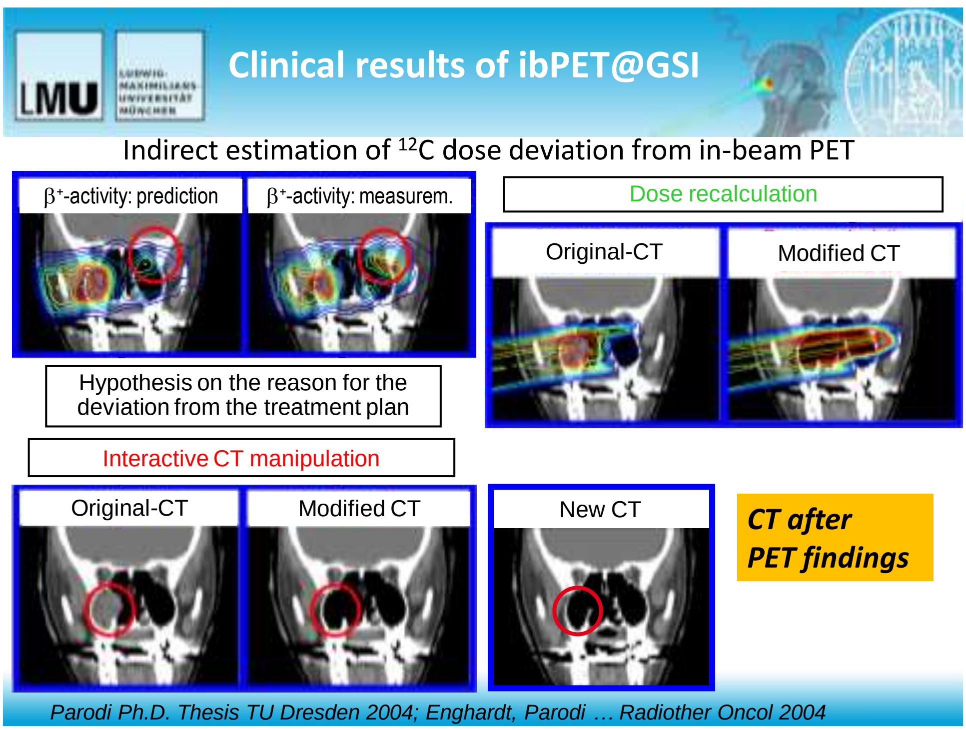
Experimental refinement of R(HU) calibration in tissue samples



Eliminate or reduce systematic error

Enghardt, et al GSI Report 2004; Schardt et al, GSI report 2007; Rietzel et al, Rad Oncol 2007


LMU
LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN
Clinical results of ibPET@GSI
In-vivo indicator of deviations in actual dose application
PET Prediction
PET Measurement
Positioning error
PET Prediction
PET Measurement
Anatomical modification
Parodi Ph.D. Thesis TU Dresden 2004; Enghardt, Parodi … Radiother Oncol 2004


LMU
LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN
Clinical results of ibPET@GSI
Indirect estimation of ^{12}C dose deviation from in-beam PET
β^+-activity: prediction
β^+-activity: measurem.
Dose recalculation
Original-CT
Modified CT
Hypothesis on the reason for the deviation from the treatment plan
Interactive CT manipulation
Original-CT
Modified CT
New CT
CT after PET findings
Parodi Ph.D. Thesis TU Dresden 2004; Enghardt, Parodi … Radiother Oncol 2004

Clinical implementation of offline PET/CT

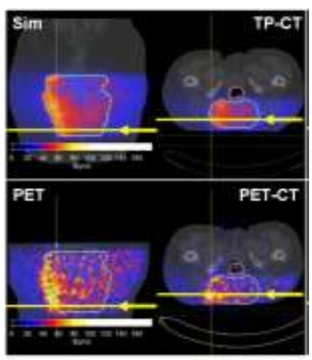
Offline PET/CT

\+ Full ring scanner
\+ Comparably low cost
○ CT-image for co-registration (extra dose)
\- Patient re-positioning (if not using shuttle)
\- ~ 5–20 min time delay from irradiation to imaging (washout, counting statistics)
\- Long scan time (~ 20-30 min)

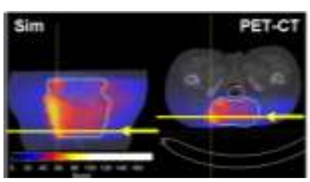
Parodi et al, IJROBP 2007; Parodi et al, IEEE CR 2011; Bauer,.., Parodi, Radiother Oncol 2013

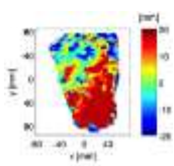
Clinical experience of offline PET/CT ^{12}C @HIT

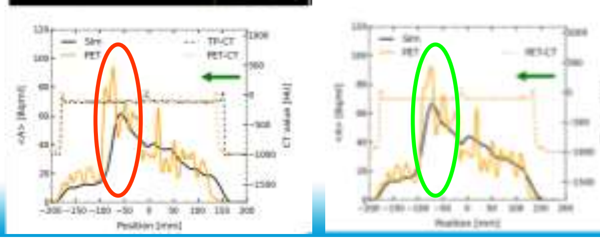
Bauer, ..., Parodi, Radiother Oncol 2013



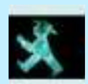
\- Suspected mispositioning supported by new simulation on CT from PET/CT
\- New treatment plan was performed to improve robustness against variations



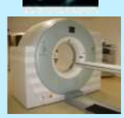




3GyE ^{12}C ~ 17 min

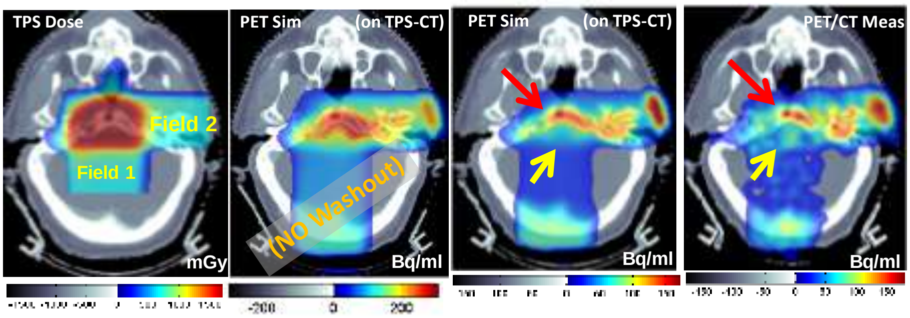


~ 13 min



30 min

Clinical experience of offline PET/CT p @ MGH/HIT



Parodi et al, IJROBP 68, 2007

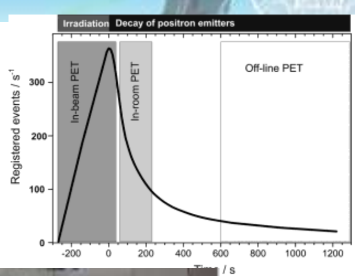
Reliable range in **bony structures**

Challenges from knowledge of **biological washout** and **elemental tissue composition**

Clinical implementation of in-room PET

In-room PET

+ Patient in treatment position
+ Full ring scanner possible
+ Few minutes acquisition sufficient
– Patient throughput
– Co-registration uncertainties if moving table

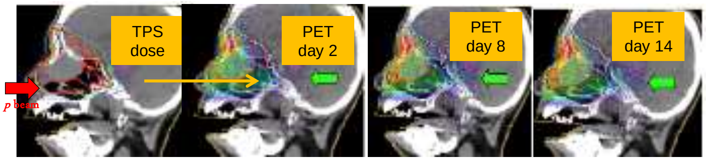


Nishio et al IJROBP 2010, Zhou et al PMB 2011, Shakirin et al PMB 2011, Min et al IJROBP 2013

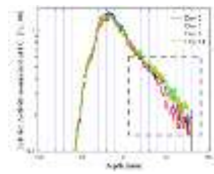
Clinical results of in-room PET@NCC

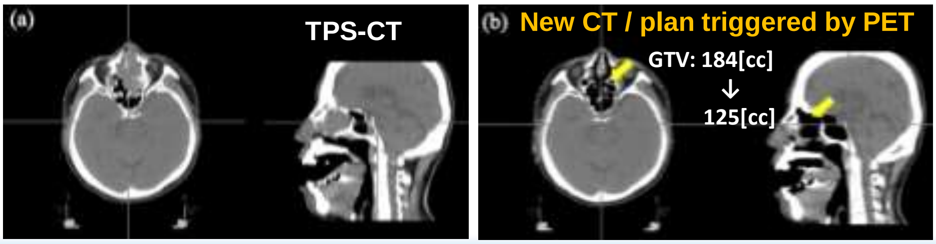
Experience from dual-head in-room PET at NCC Kashiwa (p)

+ 200 s acquisition after end of irradiation found sufficient for imaging
+ Detection of inter-fractional delivery / anatomy changes



Scattered protons



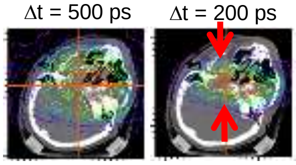


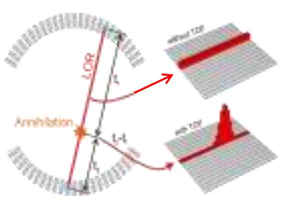
Nishio et al, IJROBP 2010; Courtesy of T. Nishio, NCC Kashiwa

Hardware improvements: dual head solutions

- Detector developments towards ultra-fast Time-of-Flight (TOF) in-beam PET

Crespo et al, PMB 2007





ENVISION

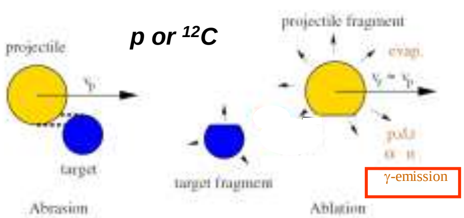
P. Cambraia Lopes et al, presented at IEEE MIC 2013

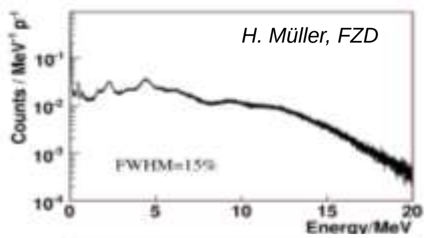
Hardware improvements: full ring solutions

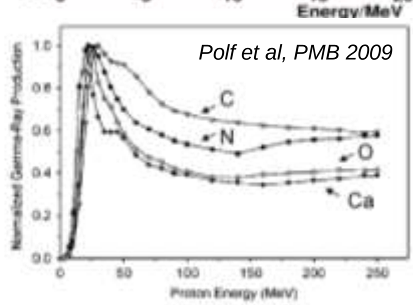
- Prototype small bore PET/CT scanner just started clinical study at MGH
- Large scale in-beam full ring openPET scanner prototype being developed and tested with stable and radioactive ion beams at NIRS

Courtesy G. El Fakhri, PhD

Prompt gamma imaging







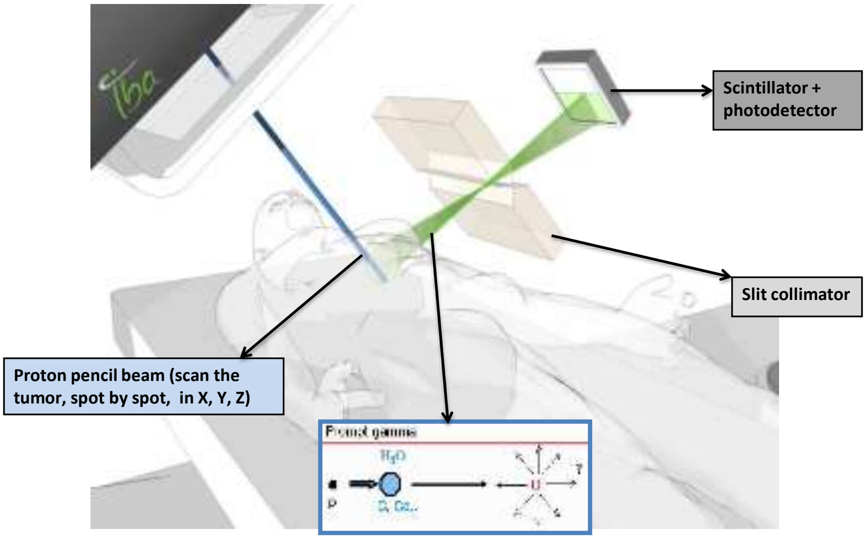
- In addition to β^+- production, nuclear reactions induce **fast (sub-ns)** prompt g emission with broad energy spectrum (up to several MeV)

  ⇒ **Eliminate washout problematic**
- Lower cross section threshold than for positron emitter production

  ⇒ **Closer correlation to Bragg peak**

Challenged detection due to high energies and neutron background

Concept of “slit camera”…

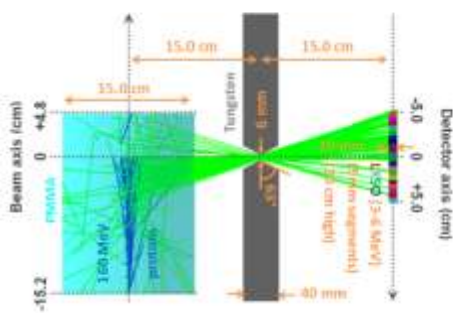


D. Prieels, F. Stichelbaut, F. Roellinghoff et al, IBA and ENVISION

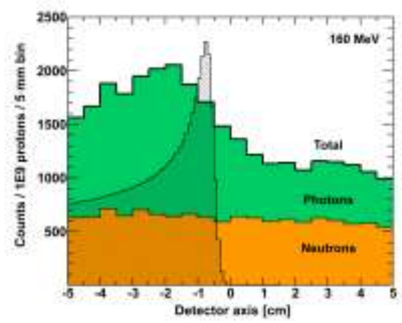
Courtesy A Mazal

IBA slit camera prototype

Realistic geometry was optimized with MC simulation



Detection profile in the scintillator for 10^9 protons (~1 Gy) & for 3-6 MeV window



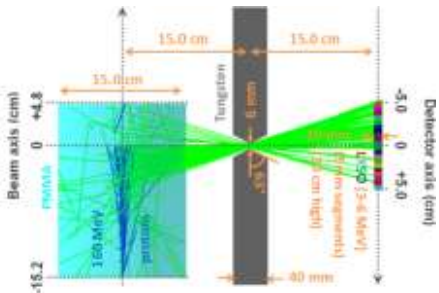
- The 3-6 MeV window gives the best correlation with the Bragg Peak.
- Neutrons give a ca. constant background signal
- Count rate is not very high → detector sensitivity needs to be carefully studied

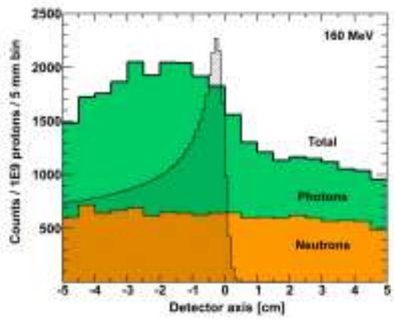
D. Prieels, F. Stichelbaut, F. Roellinghoff et al, IBA et ENVISION

Courtesy A Mazal

IBA slit camera prototype

Detection profile in the scintillator for 10^9 protons (~1 Gy) & for 3-6 MeV window



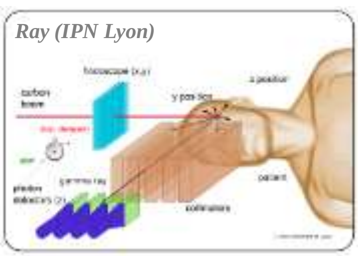


5 mm shifts in proton range generates corresponding shifts in detection profile
(first prototype to be tested soon in clinical scenario)

D. Prieels, F. Stichelbaut, F. Roellinghoff et al, IBA et ENVISION

Courtesy A Mazal

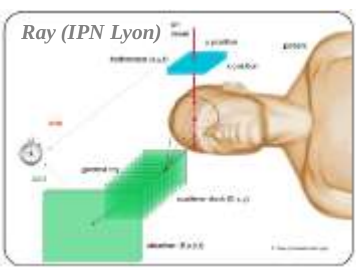
Additional detector concepts



Collimated camera

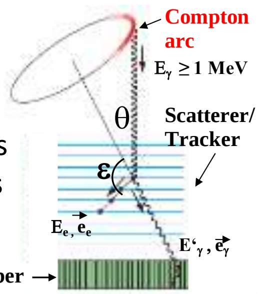
- Multislit collimator
- Time-of-Flight for neutron suppression

Fast position sensitive detector (e.g., hodoscope)



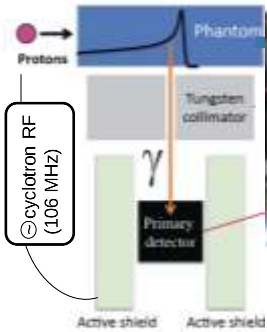
Compton camera

- Electronic collimation
- Several configurations scatterers / absorbers
- Electron tracking possibility

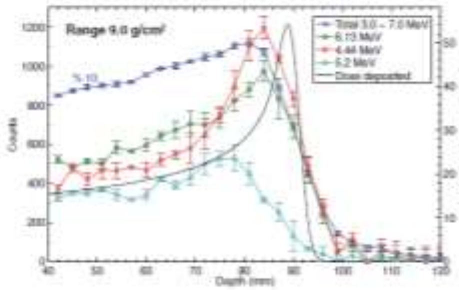


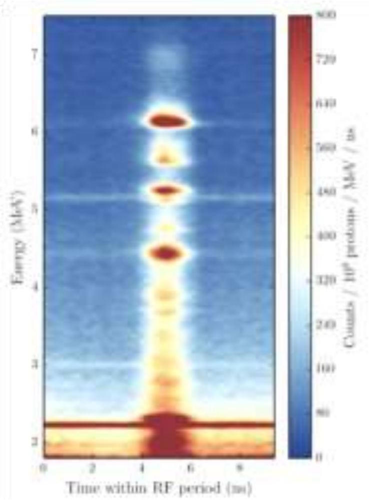
Courtesy Denis Dauvergne et al, IPN Lyon, and Peter Thirolf, LMU

Time- and energy-resolved prompt γ detection



@ MGH Boston



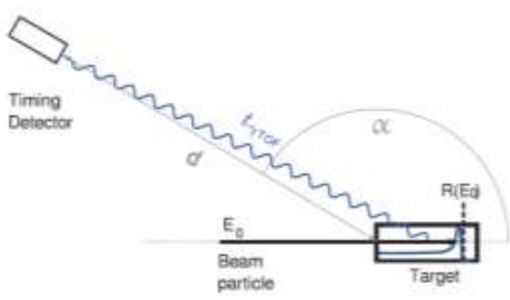


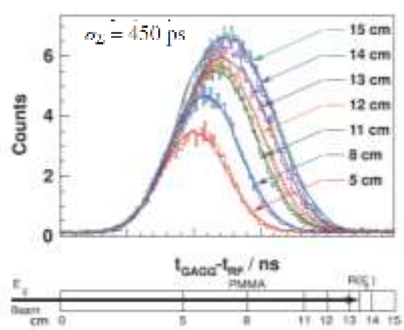
Spectroscopic identification of individual gamma lines

Verbourg et al, PMB 2013

Prompt γ timing (PGT)

New proposed range monitoring concept relying on time spectroscopy without need of directional collimation



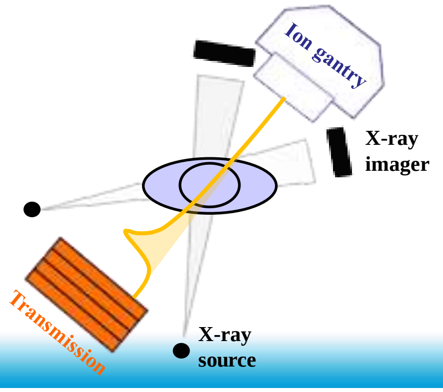


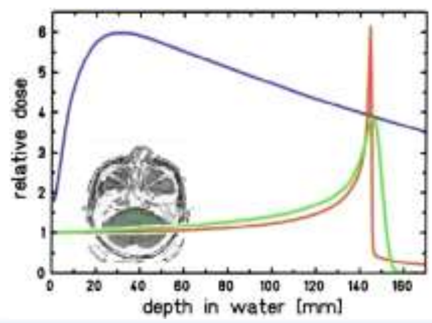
C. Golnik et al, PMB 2014

Ion transmission imaging

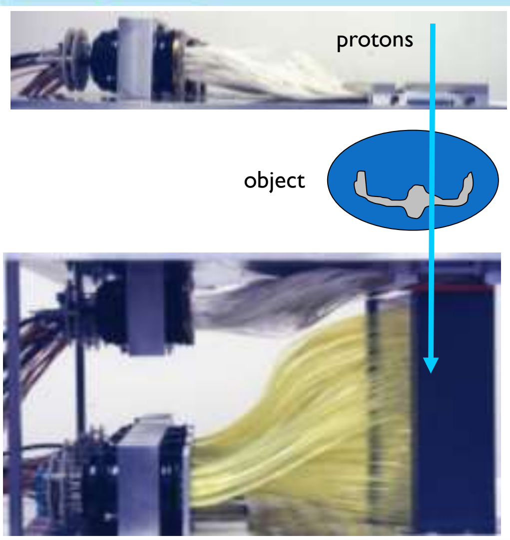
Ion-based radiography / tomography could:

- Decrease range error via direct Relative Stopping Power determination
- Eliminate CT artifacts from metal / dental implants
- Replace X-ray imaging for daily, lower-dose image guidance





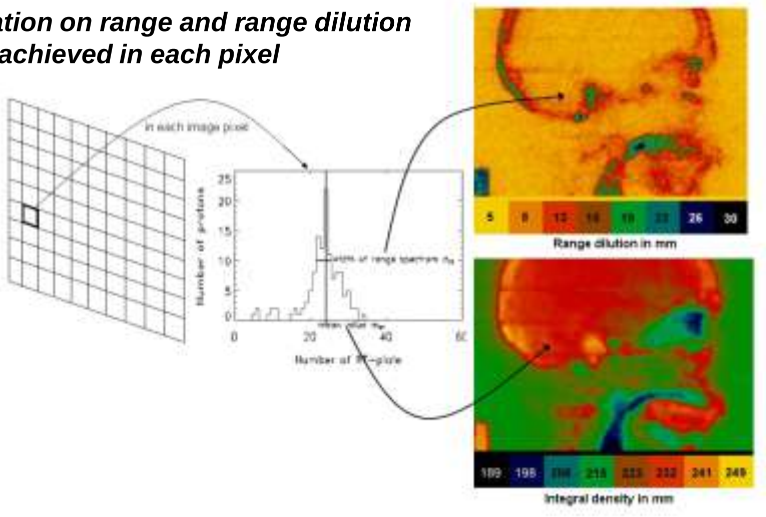
Proton radiography prototype using plastic scintillators @PSI



Courtesy Uwe Schneider

Proton radiography prototype using plastic scintillators @PSI

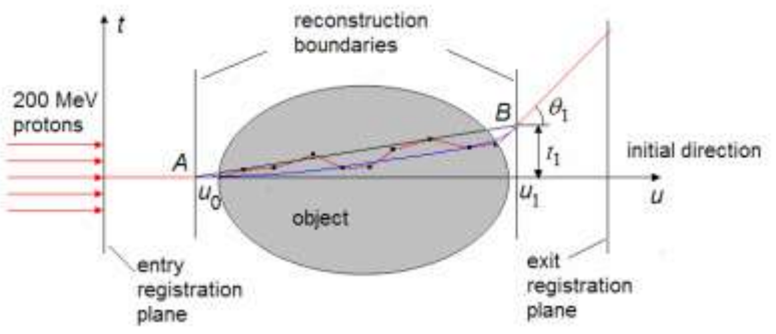
Information on range and range dilution can be achieved in each pixel



Courtesy Uwe Schneider

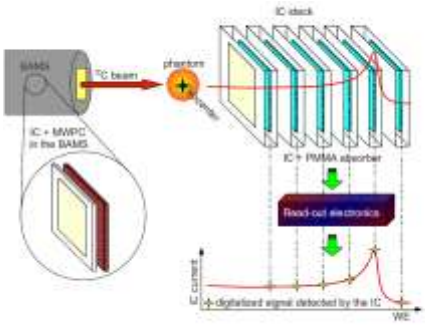
Issues of proton radiography

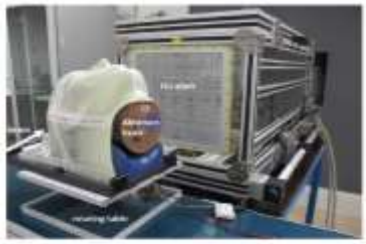
Trajectory of individual protons in tissue has to be estimated, e.g. with concept of Most-Likely-Path in the reconstruction of the radiographic images



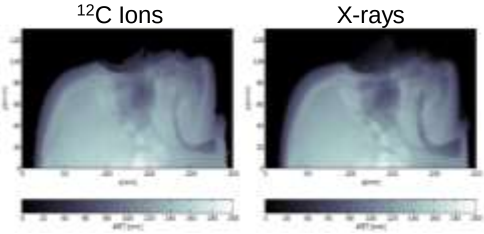
Med Phys. 2006 March ; 33(3): 699–706.

Carbon ion radiography prototype using ionization chambers @HIT





^{12}C Ions | X-rays



- 61 PPIC 30x30 cm^2
- 3 mm PMMA absorber slabs
- 2 read-out modules of 32 channels with real time controller
- Active scanning beam delivery system

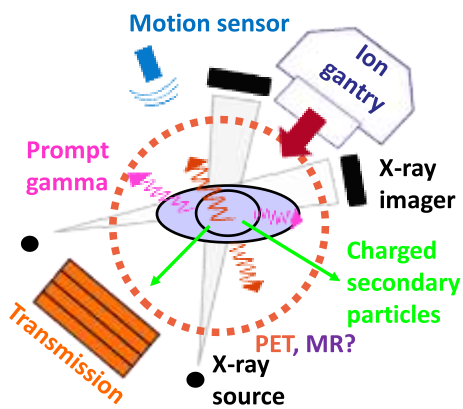
Rinaldi, …, Parodi, PMB 58 2013
Rinaldi, …, Parodi, PMB 59 2014, 2014b

Conclusion and perspectives

Increasing developments towards in-vivo, real time validation of beam range complemented by low-dose anatomical information at the treatment site

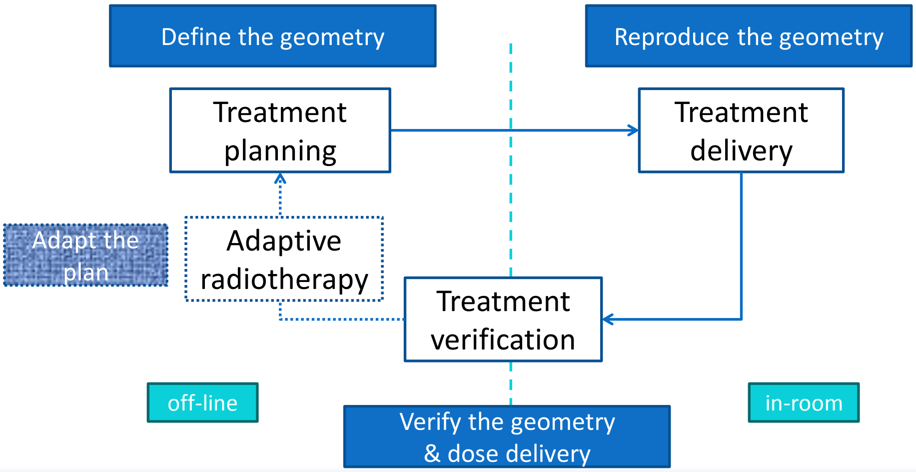
R&D in detector development, experimental validation, clinical integration (depending on beam production / delivery)

Synergy with multimodal diagnostic imaging for planning, follow-up …



Conclusion and perspectives

In order to "hit the target" imaging is used to…



Adapted from C. Gianoli

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