Patient Imaging for Proton Therapy

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LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

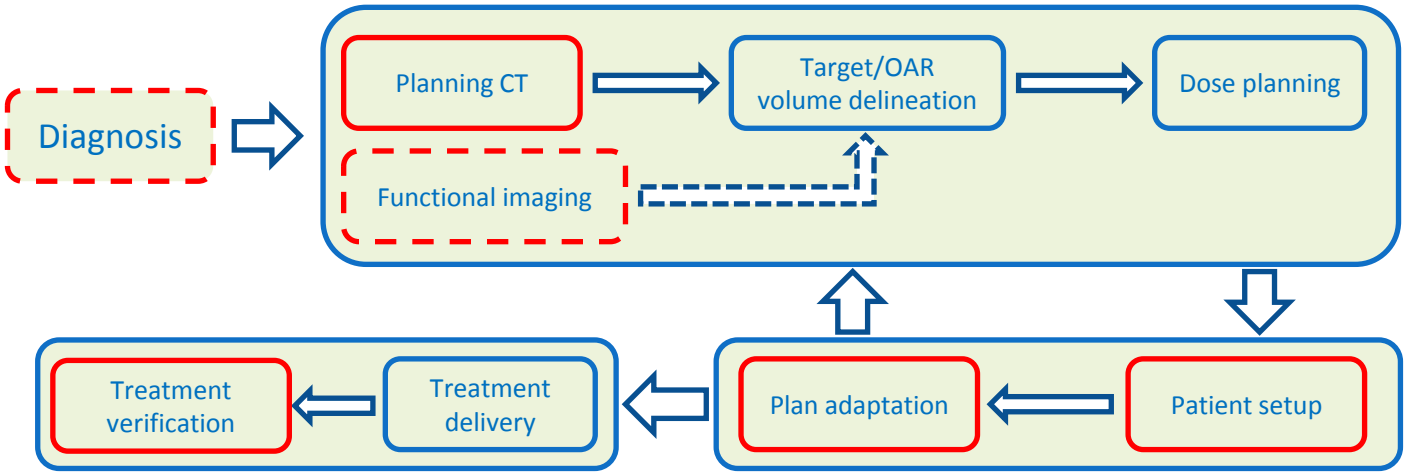
Outline

- Diagnostic (too broad to be covered in this talk)
- **Imaging for treatment planning**
- **Imaging for patient setup and plan adaptation**
- **Imaging for treatment verification**
- Reconstruction algorithms/techniques

Structure of the talk

- For every section shown in the Outline slide, there will be three (four) subsections:
  - **Equipment**
  - **Methods**
  - **Challenges and limitations**
  - **(New approaches)**

Imaging for proton therapy



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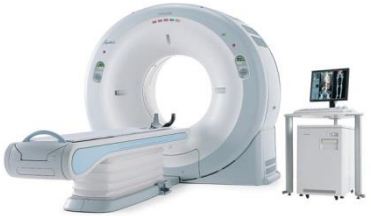
Imaging for treatment planning

Equipment

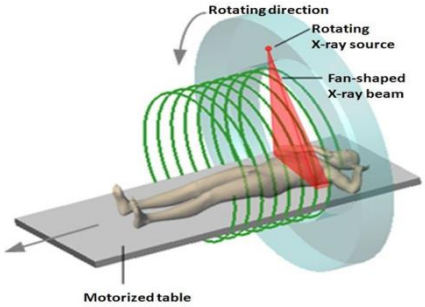
Imaging for treatment planning

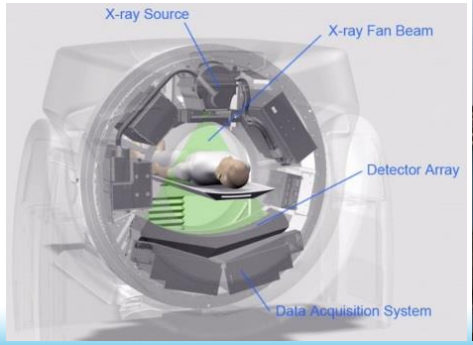
- Treating with particles, imaging with photons
- The high quality CTs used for treatment planning are X-ray CTs
- Some of the state of the art X-ray CT scanners:
  - GE Discovery RT
  - Siemens Somatom
  - Phillips CT Big Bore
  - Toshiba Aquilion
  - …

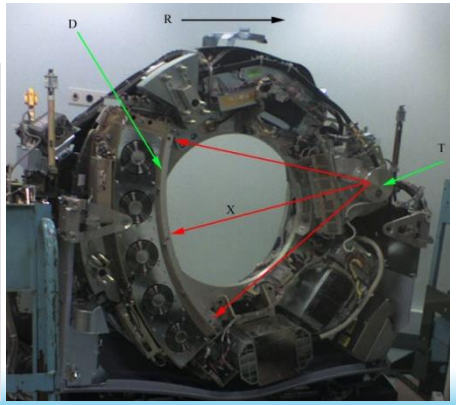


Imaging for treatment planning

- Some scanner characteristics and specifications:
  - Tube voltage: 80 – 140 kV
  - Rotation speed: 1 sec or less
  - Large bore diameter: 60 – 90 cm
  - Scan field of view: 50 – 70 cm
  - Minimum slice thickness: down to 0.5 mm

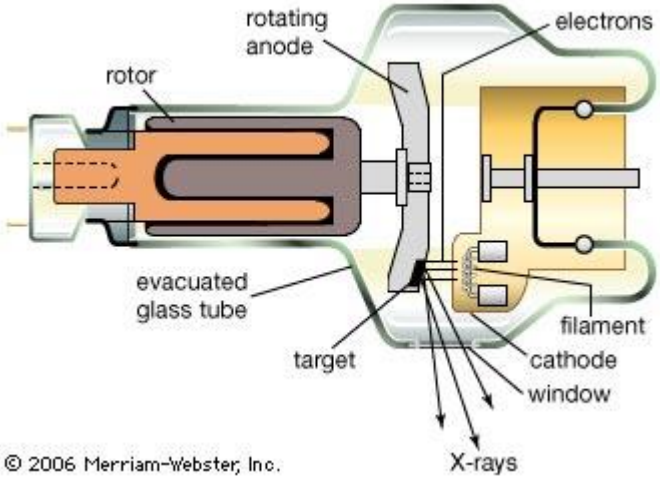


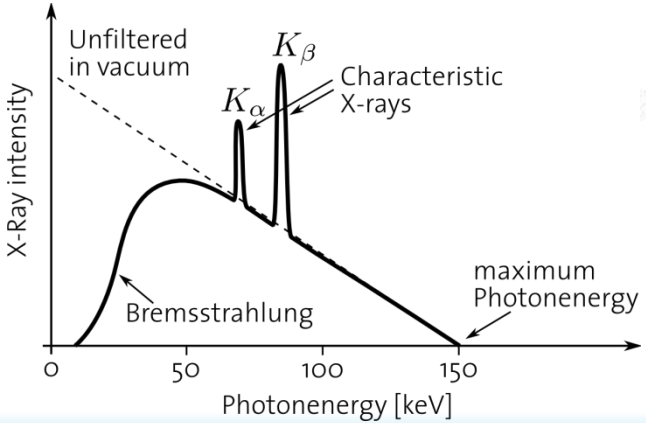




Imaging for treatment planning

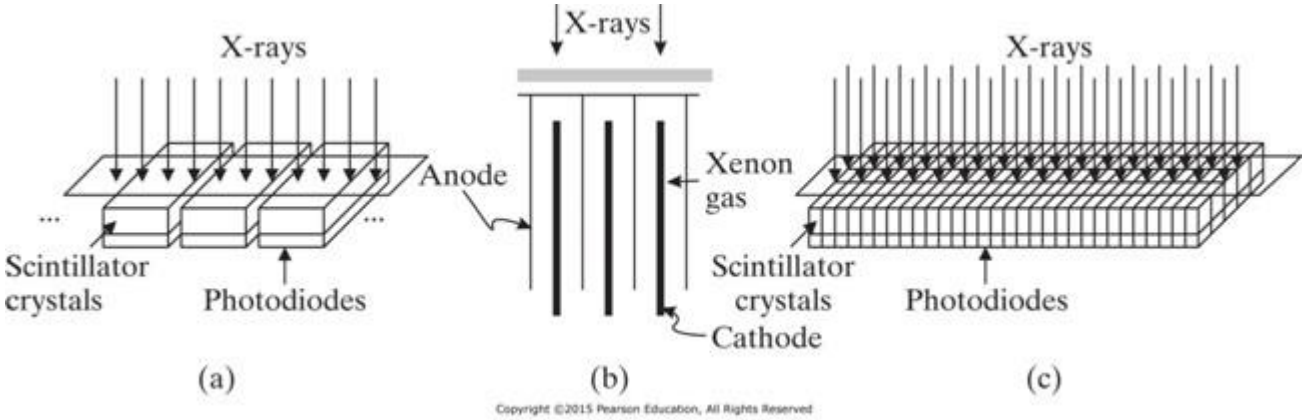
- X-ray tube designs:
  - Focal spot size 0.3-2 mm
  - Max. voltage 150 kV
  - Heating capacity 450 kJ
  - Anode rotation speed 2000 – 10000/min





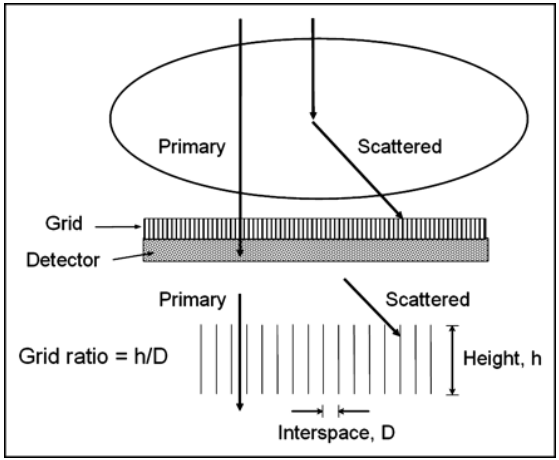
Imaging for treatment planning

- Basic CT detector designs:
  - Nowadays solid state detectors (Xe detectors obsolete)

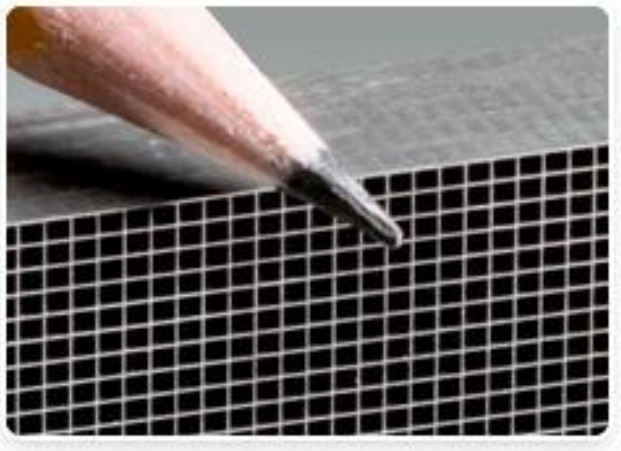


Imaging for treatment planning

- Anti-scatter grids:
  - X-ray absorbing material
  - Ideally eliminates scattered photons



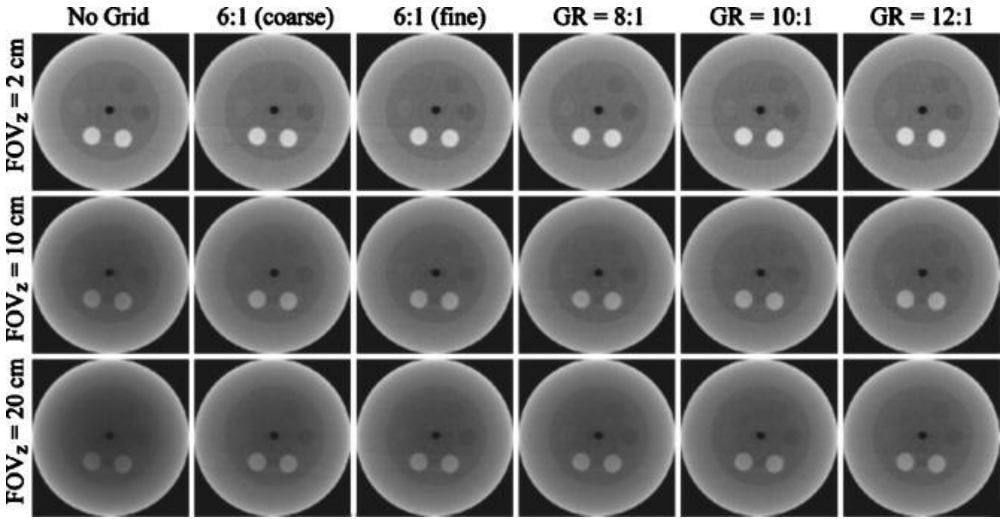
Journal of Nuclear Medicine Technology Volume 33, Number 1, 2005 3-18



http://www.mikrosystems.com/applications/computed-tomography

Imaging for treatment planning

- Anti-scatter grids:
  - The influence of grid granularity (the higher the better) and FOV (the lower the better)



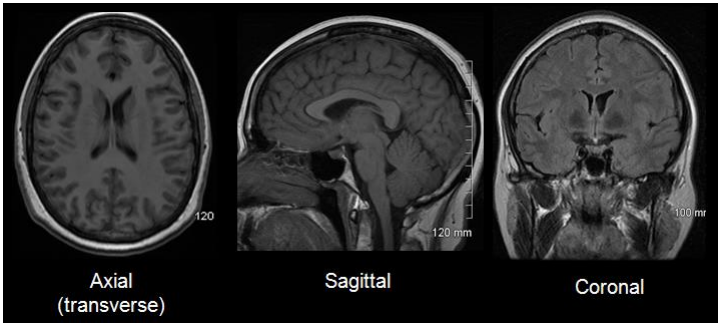
Medical Physics 31(12):3506-20, 2005

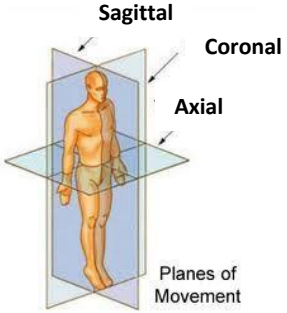
Imaging for treatment planning

Methods

Imaging for treatment planning

- X-ray CT image:
  - Hounsfield Units (HU), representing photon attenuation





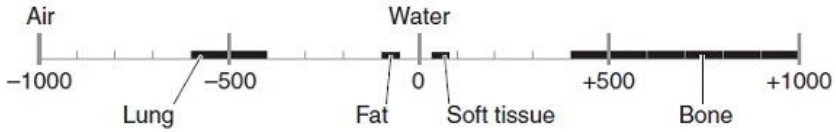
- Proton treatment plan:
  - Based on relative to water stopping power of protons (RSP)
  - Determines where the protons will stop and how much energy they will deposit along their paths

- Need to HU to RSP: No one-to-one correlation!

Imaging for treatment planning

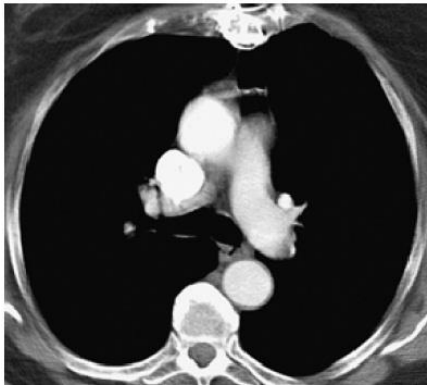
- X-ray CT image:
  - A few basics of what is reconstructed

$$HU = 1000 \times \frac{\mu - \mu_{water}}{\mu_{water}}$$

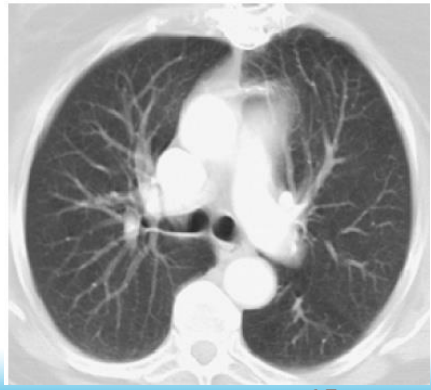


Bone	+400 → +1000
Soft tissue	+40 → +80
Water	0
Fat	−60 → −100
Lung	−400 → −600
Air	−1000

Level= +40 HU and Window = 350



Level= -600 HU and Window = 1500



Imaging for treatment planning

- From HU units to RSP: Stoichiometric calibration **Schneider, Pedroni, Lomax. Phys. Med. Biol. 41 (1996) 111–124**
  - The measured HU is a function of the photon attenuation μ

$$HU = 1000 \times \frac{\mu - \mu_{water}}{\mu_{water}}$$

  - The photon attenuation can be written as a function of the electron density ρN_g, where ρ is the mass density and N_g the number of electrons per unit volume (function of Z)

$$\mu = \rho N_g(Z, A)\{\sigma^{ph} + \sigma^{coh} + \sigma^{incoh}\}$$

  - A parametrization of the cross section is:

$$\mu = \rho N_g(Z, A)\{K^{ph} Z^{3.62} + K^{coh} Z^{1.86} + K^{KN}\}$$

Imaging for treatment planning

- From HU units to RSP: Stoichiometric calibration **Schneider, Pedroni, Lomax. Phys. Med. Biol. 41 (1996) 111–124**

  – Making a set of measurements (HU) of different tissue substitutes of know composition (Z, ρ_e), the K parameters are defined by a fit to the measurement

$$HU = 1000 \times \frac{\mu - \mu_{water}}{\mu_{water}}$$

$$\mu = \rho N_g(Z, A)\{K^{ph} Z^{3.62} + K^{coh} Z^{1.86} + K^{KN}\}$$

  – A full parametrization of the HU (above formula + K factors) has been obtained

  – For a comprehensive set of human tissues (ICRU) the parametrization is used in order to calculate the HU from their chemical composition

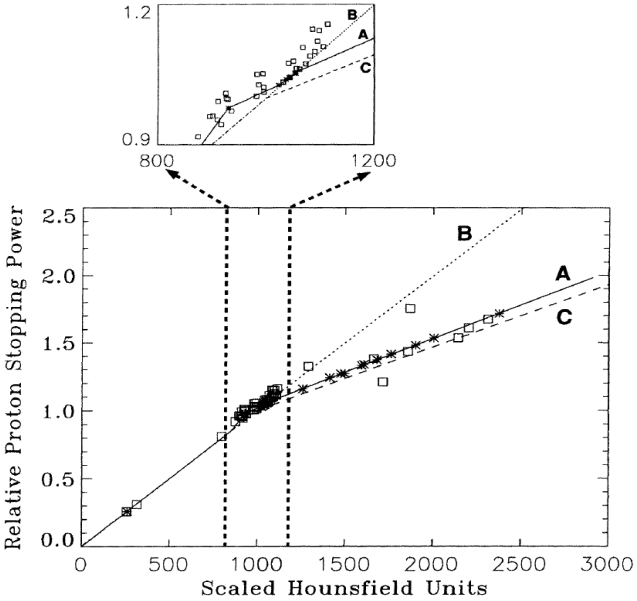
  – Their RSP is also calculated from:

$$RSP = \rho_e\{\log[2m_e c^2\beta^2/I_m(1-\beta^2)] - \beta^2\}/\{\log[2m_e c^2\beta^2/I_{water}(1-\beta^2)] - \beta^2\}$$

Imaging for treatment planning

- From HU units to RSP: Stoichiometric calibration **Schneider, Pedroni, Lomax. Phys. Med. Biol. 41 (1996) 111–124**

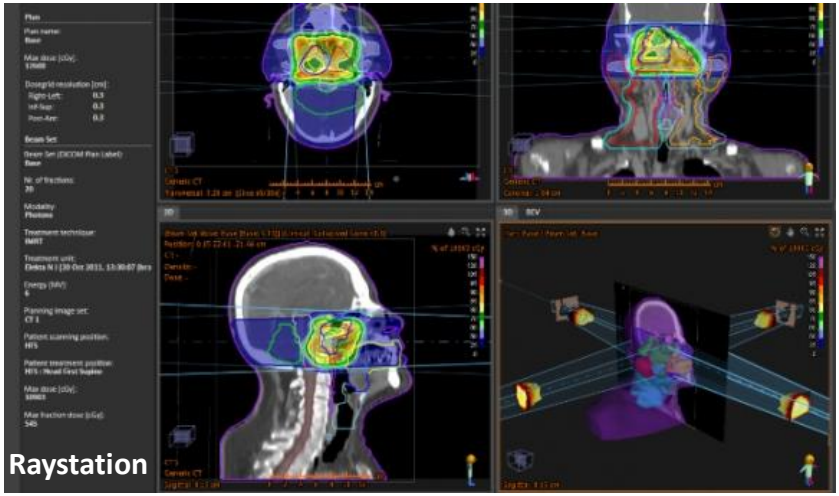
  – From this comprehensive set of human tissues we create an HU to RSP calibration

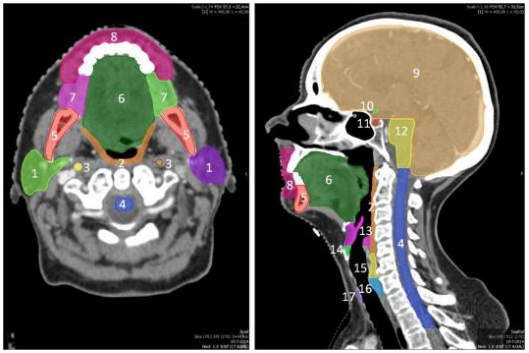


  – Finally, any measured HU of an unknown tissue (voxel) can be converted to RSP, based on this calibration

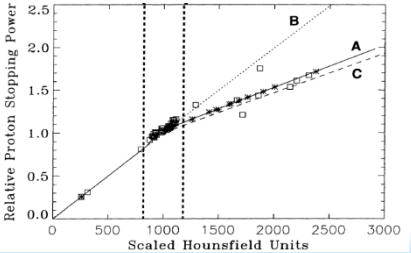
Imaging for treatment planning

- Procedure in a nutshell:
  - "Universal" quantities: facility beam model, dose to water, HU->RSP calibration, …
  - Patient specific quantities: organ contours, prescribed dose to target and OARS, …



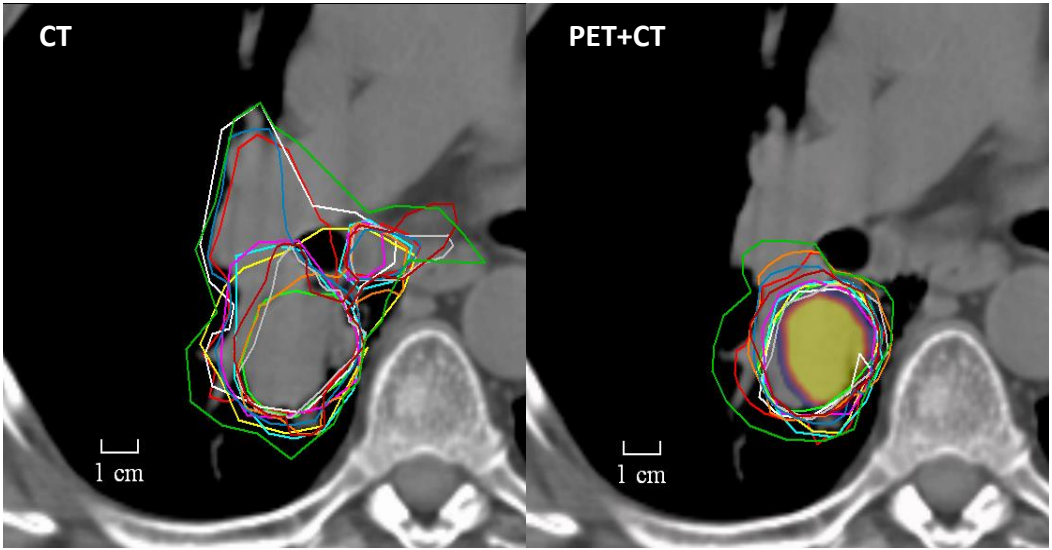


Radiotherapy and Oncology 117(1), 2015



Imaging for treatment planning

- Of course multimodal imaging can improve the procedure:
  - Example of tumor delineation on CT only and on PET+CT



International Journal of Radiation Oncology Biology Physics , Volume 64 , Issue 2 , 435 – 448, 2006

Imaging for treatment planning

Challenges / Limitations

Imaging for treatment planning

- Limitations:

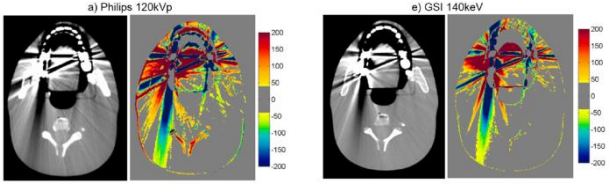
Uncertainty Category	Uncertainty Source
Uncertainties in patient CT imaging	The deviation of HU value from its calibrated value when imaging a patient. The major contributions of uncertainties are from the scatter condition and beam-hardening effect in patient geometry. Minor contributions are from out-of-field objects, such as a portion of the CT couch, immobilization device, and day-to-day variation etc.
Uncertainties the parameterized stoichiometric formula to calculate theoretical CT numbers	This includes the uncertainties in the definition and measurement of equations (1) – (4) using CT imaging for a tissue substitute phantom, including the parameterization of equation (3).
Uncertainties due to deviation of actual human body tissue from ICRU standard tissue	The uncertainties caused by modeling SPR and variations of tissue composition in patient population. The original stoichiometric calibration assumes tissues to follow ICRU standard tissue compositions, which may introduce uncertainties for a given individual with different age or health status.
Uncertainties in mean excitation energies	The value of mean excitation energy is critical in calculating SPR. We evaluated the impact to SPR by the fact that we always made proton range measurement in water during the commissioning process. Only the relative uncertainties (to water) of the mean excitation energy will contribute towards the SPR calculation for a given tissue.
Uncertainty due to energy dependence of SPR not accounted by dose algorithm	For simplicity, some treatment planning systems ignored the SPR dependency on proton energy. This may be specific to a particular situation, but it shows the uncertainty of dose calculation depends on the implementation of dose calculation algorithms.

Phys Med Biol. 2012 Jul 7; 57(13): 4095–4115

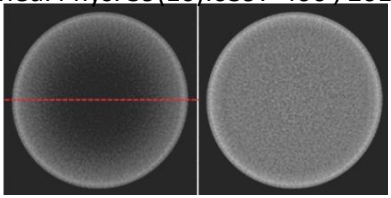
Imaging for treatment planning

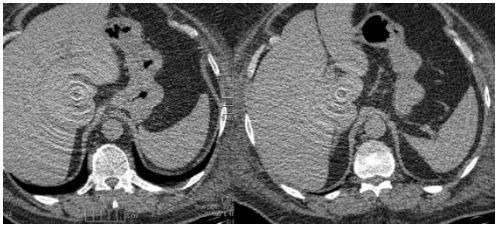
- CT imaging uncertainties:
  - Metal implant artifacts
  - Beam hardening
  - Ring artifacts
  - Motion
  - Anatomical changes, motion, etc

Phys. Med. Biol. **60** 1047, 2015



Med. Phys. 39(10):6397-406 , 2012

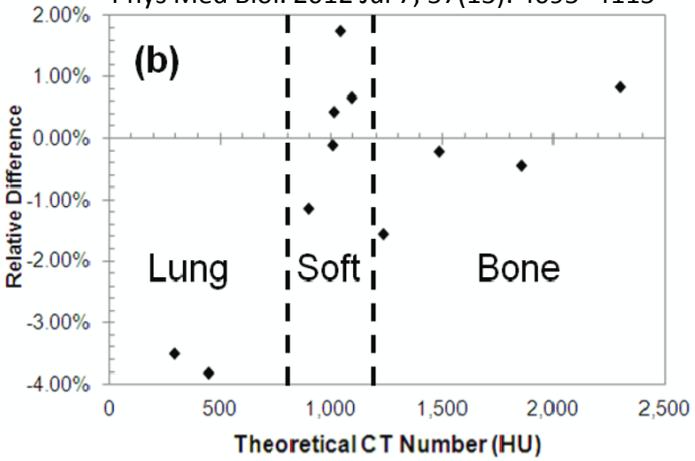




Imaging for treatment planning

- Stoichiometric calibration:
  - Calculation of HU deviates from the real one

Phys Med Biol. 2012 Jul 7; 57(13): 4095–4115

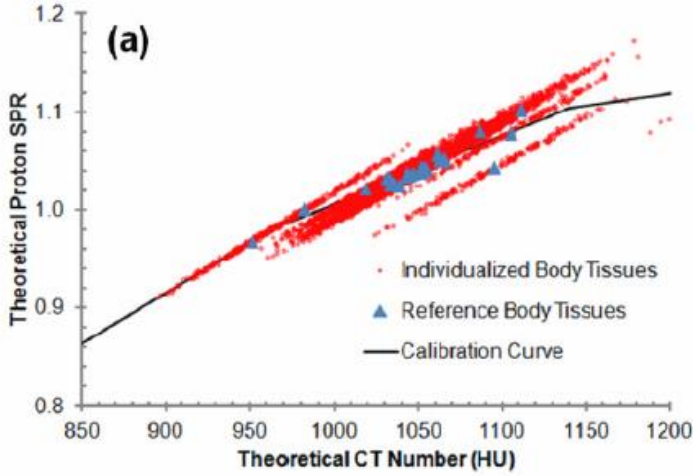


	Uncertainties (1 σ)	
Tissue Group	**CT Number**	**SPR**
Lung	3.7%	3.8%
Soft	1.0%	0.8%
Bone	0.9%	0.5%

Imaging for treatment planning

Phys Med Biol. 2012 Jul 7; 57(13): 4095–4115

- Stoichiometric calibration:
  - Human tissues with slight variations in chemical composition from the reference tissues don't fit well the calibration curve



Tissue Group	Uncertainties (1 σ)	
	Reference Human Tissues	Individualized Human Tissues
Lung	0.00%	0.18%
Soft	0.43%	1.20%
Bone	0.29%	1.60%

Imaging for treatment planning

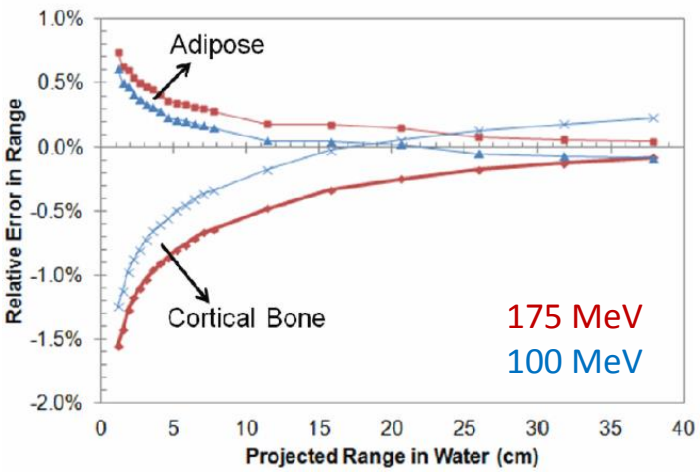
- Stoichiometric calibration:
  - Inaccuracy in calculating I values
  - 10% error in I yields up to 1% error in RSP

Tissue Group	Relative Differences in Theoretical SPRs (1 σ)
Lung	0.17%
Soft	0.23%
Bone	0.65%

Phys Med Biol. 2012 Jul 7; 57(13): 4095–4115

Imaging for treatment planning

- Stoichiometric calibration:
  - Small errors from neglecting the energy dependence of RSP



Phys Med Biol. 2012 Jul 7; 57(13): 4095–4115

Imaging for treatment planning

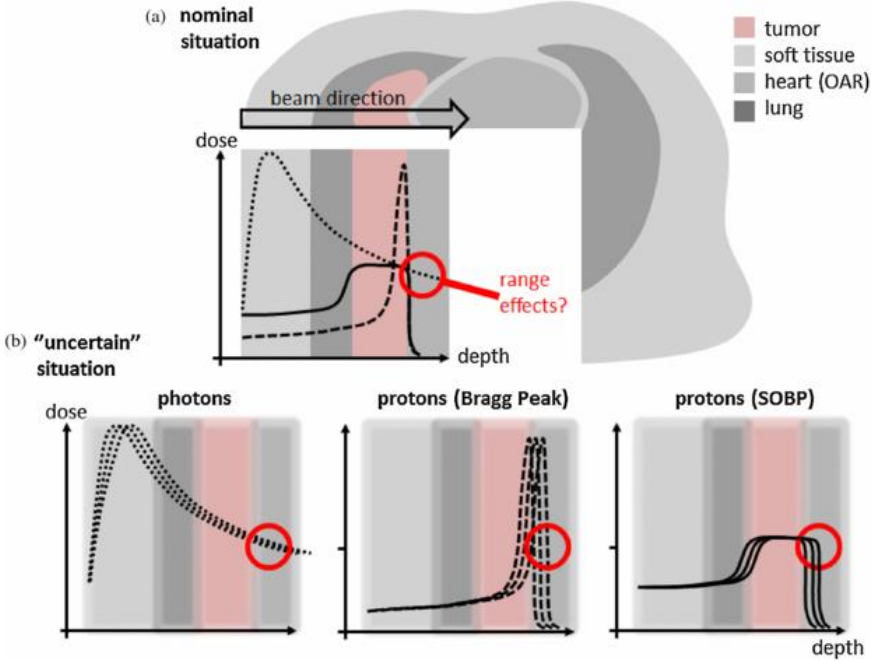
- Stoichiometric calibration:
  - Total RSP uncertainty ranges from 1.6% to 5%
  - 3.5% error covers 95% of the cases studied from three different treatment sites

	Uncertainties in SPR Estimation (1 σ)		
Uncertainty Source	**Lung**	**Soft**	**Bone**
Uncertainties in patient CT imaging	3.3%	0.6%	1.5%
Uncertainties the parameterized stoichiometric formula to calculate theoretical CT numbers	3.8%	0.8%	0.5%
Uncertainties due to deviation of actual human body tissue from ICRU standard tissue	0.2%	1.2%	1.6%
Uncertainties in mean excitation energies	0.2%	0.2%	0.6%
Uncertainties due to energy dependence of SPR not accounted by dose algorithm	0.2%	0.2%	0.4%
Total (root-sum-square)	5.0%	1.6%	2.4%

Phys Med Biol. 2012 Jul 7; 57(13): 4095–4115

Imaging for treatment planning

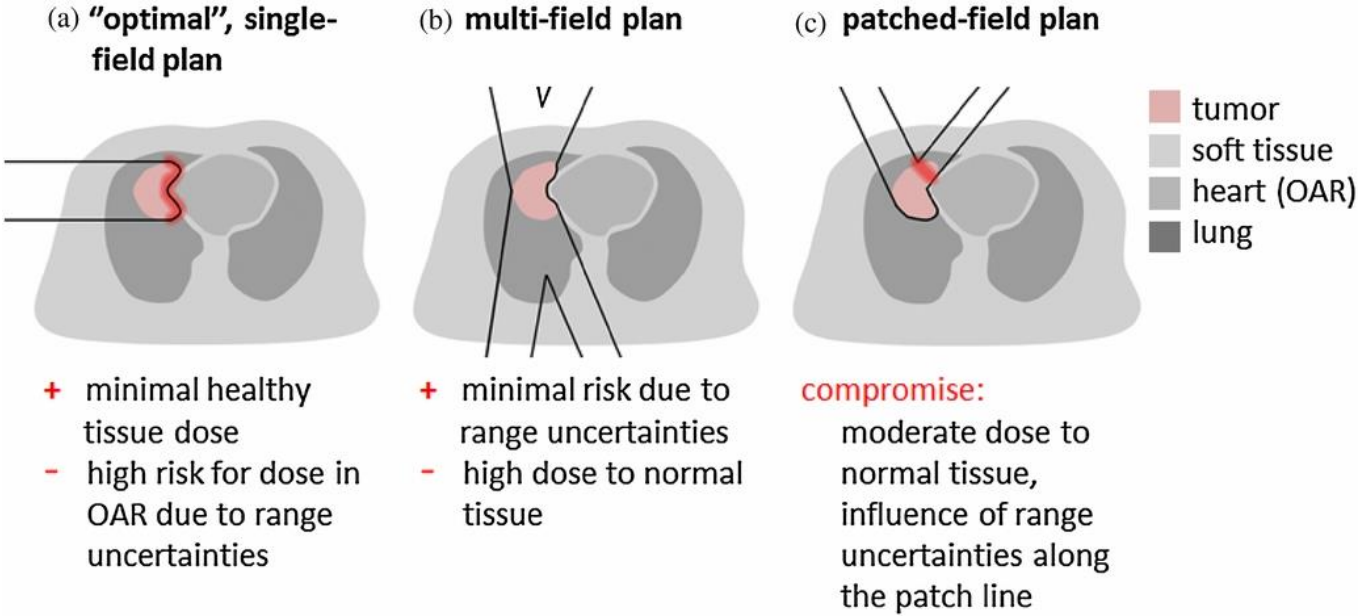
- Impact on range/dose calculations:



Phys. Med. Biol. **58** R131, 2013

Imaging for treatment planning

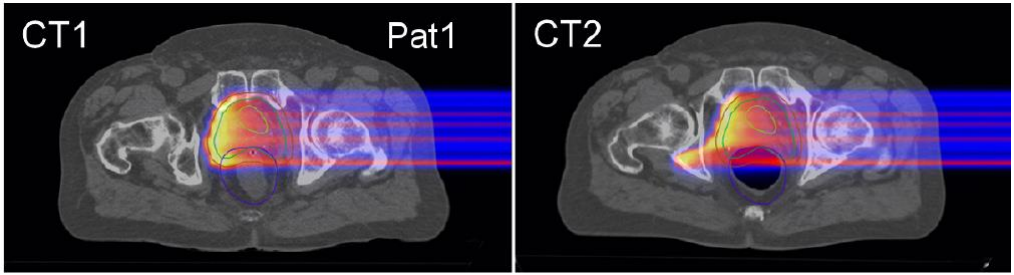
- Impact on range/dose calculations:



Phys. Med. Biol. **58** R131, 2013

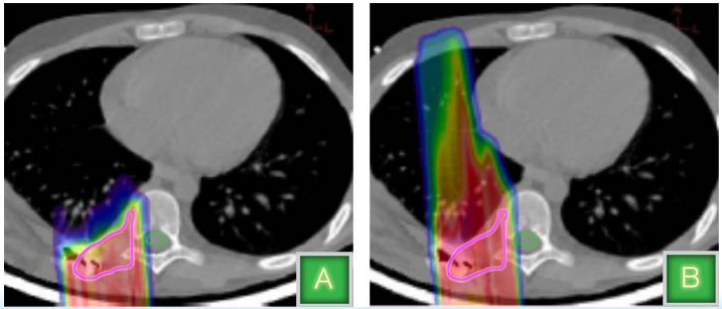
Imaging for treatment planning

- Impact on range/dose calculations:
  - Interfractional anatomical change



Phys. Med. Biol. **60** 9329, 2015

  - RSP determination



Courtesy Prof. R W Schulte

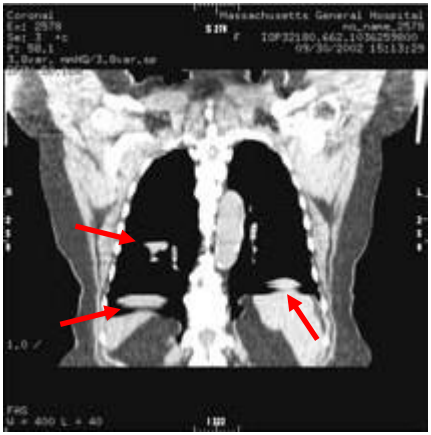
Imaging for treatment planning

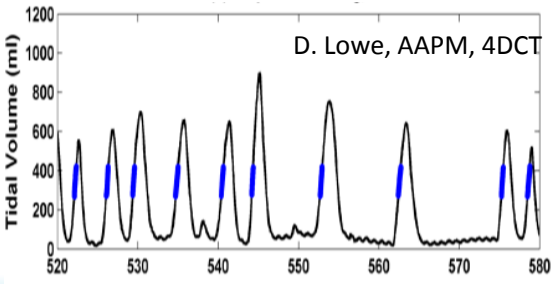
New Approaches

Imaging for treatment planning

- 4DCT:
  - Motion distorts CT images
  - For example breathing:
    Amplitude of motion ~cm, breathing period ~4 sec
  - 4DCT creates a spatio-temporal anatomical dataset
  - Acquisition:
    Most straightforward is gated acquisition: Acquire each slice during the same phase of motion
    Or by oversampling each slice and sorting in reconstruction
  - Motion is usually not perfectly periodic

Image Guided IMRT, Springer, 2006, 4DCT, Chen, Rietzel





D. Lowe, AAPM, 4DCT

Imaging for treatment planning

- 4DCT:
  - Example of 0.4 sec interval
  - Different treatment planning techniques:

Margin expansion to include tumor taking account of motion

Gating: beam at certain phases

Tumor tracking: beam adapted to tumor location

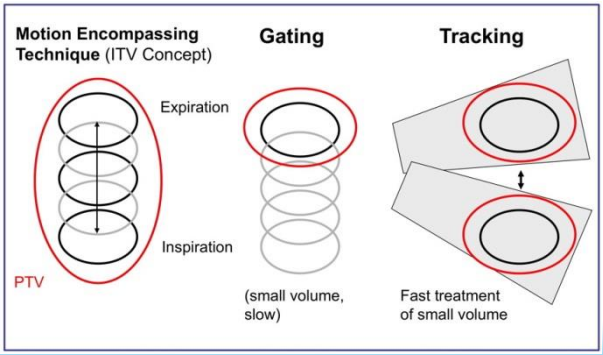
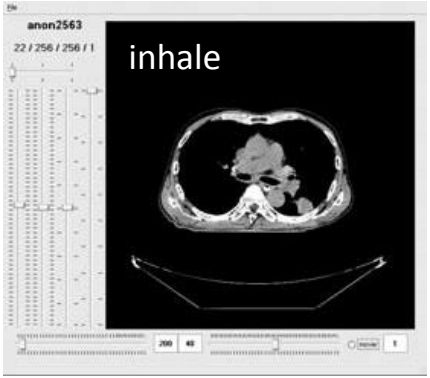
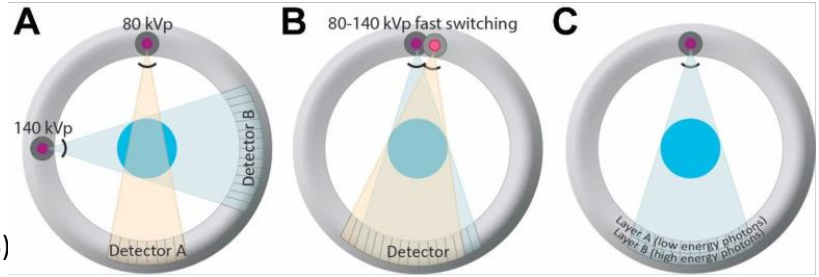


Image Guided IMRT, Springer, 2006, 4DCT, Chen, Rietzel



Imaging for treatment planning

- Dual Energy CT (DECT):



  - Design concept:

Two sources, two detectors (A)

One source, two energies, one detector (B)

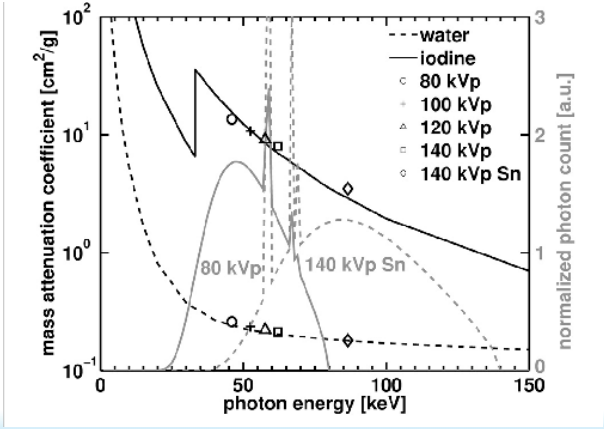
One source, one energy, layered detector (C)

  - Siemens Somatom Force (A)

90kVp – 150 kVp/Sn

Imaging for treatment planning

- Dual Energy CT (DECT):
  - HU related to photon attenuation $HU = 1000 \times \frac{\mu - \mu_{water}}{\mu_{water}}$
  - Photon attenuation is the net result of different processes $\mu \propto C_{\mathrm{Compton}}(E)\boldsymbol{\rho_e} + C_{\mathrm{PE}}(E)\boldsymbol{Z^3}$
  - 2 unknowns, DECT provides two equations (measurements)



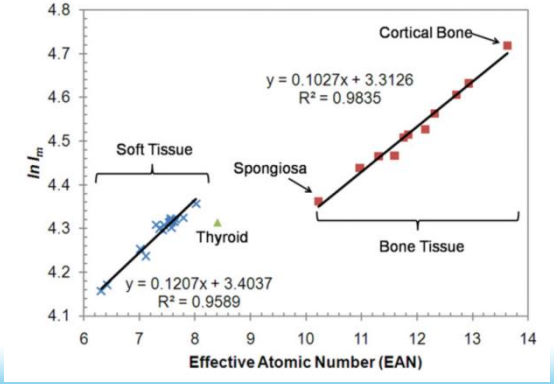
Radiother Oncol 119 (2016) 137

Imaging for treatment planning

- Dual Energy CT (DECT):
  - Several μ decomposition methods
  - Each method results into an ρ_ε and Z_{eff} calculation
  - For proton therapy we need RSP

$$\mathrm{RSP} \propto \boldsymbol{\rho_e} \frac{\ln\left(\frac{2m_e c^2\beta^2}{\boldsymbol{I}(1-\beta^2)}\right) - \beta^2}{\ln\left(\frac{2m_e c^2\beta^2}{I_{water}(1-\beta^2)}\right) - \beta^2}$$

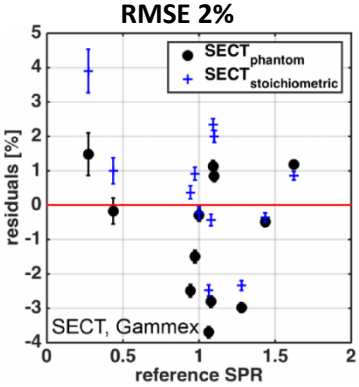
  - I value is derived from Z_{eff} via a calibration procedure

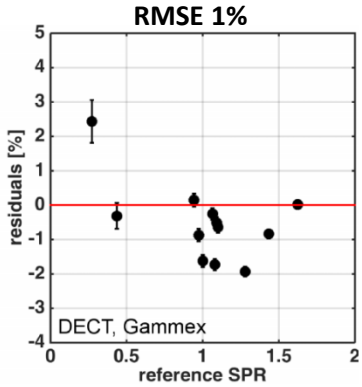


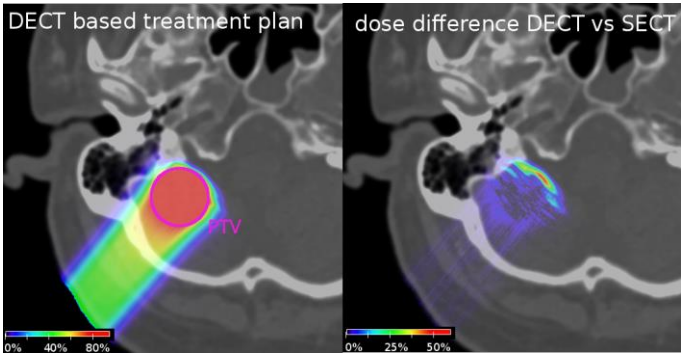
Phys Med Biol **55** (2010) 1343

Imaging for treatment planning

- Dual Energy CT (DECT):
  - Improved RSP calculation with respect to single energy CT





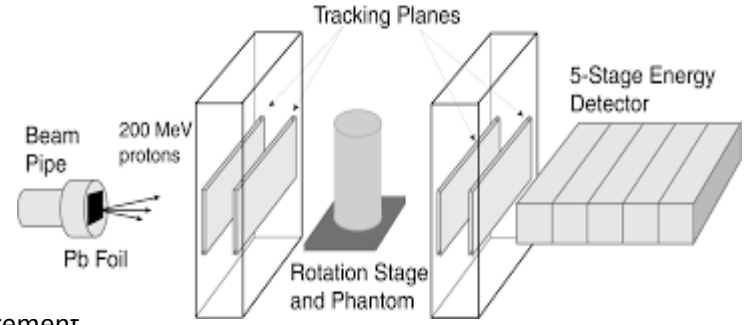


Med Phys **43** (2016) 495

Radiother Oncol 119 20016 137

Imaging for treatment planning

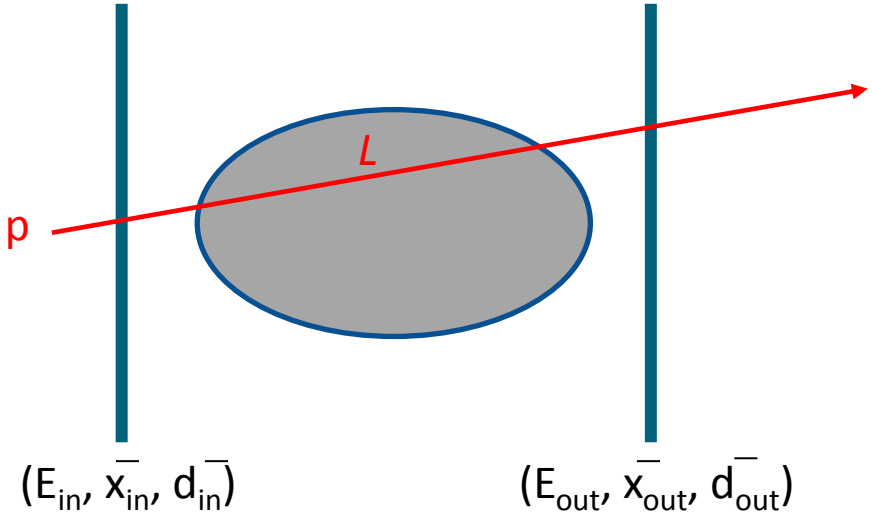
- Proton CT (pCT):
  - Position measurement at the entrance/exit
  - Direction measurement at the entrance/exit -> a second position measurement
  - Energy loss or residual energy or residual range measurement at the exit
  - Single proton tracking



NIM A **831** 394-399 (2016)

Imaging for treatment planning

- Proton CT (pCT):

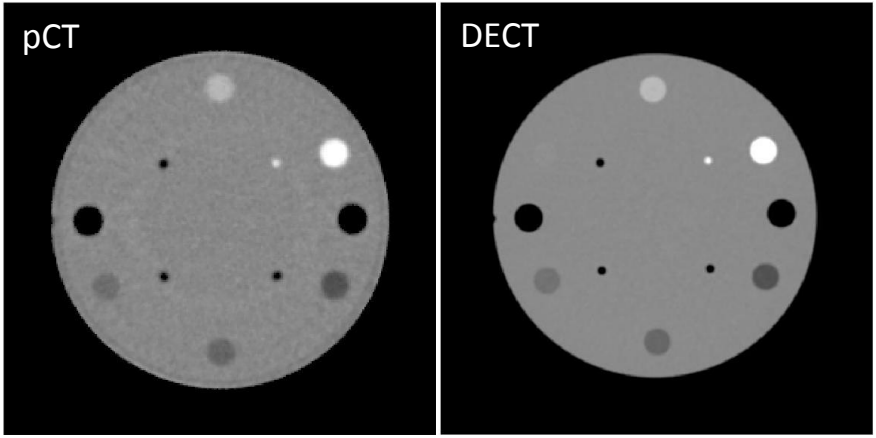


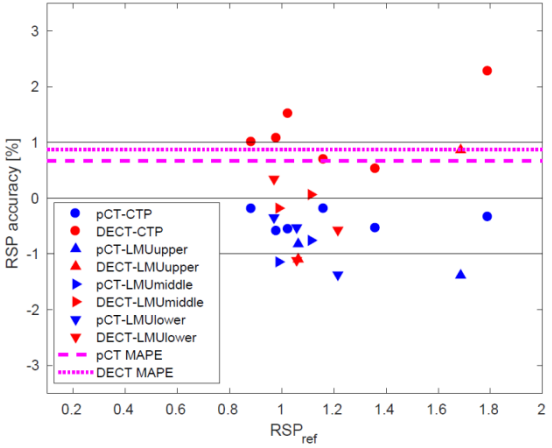
$$RSP = \left.\frac{\Delta E_m}{\Delta E_w}\right|_L$$

$$RSP = \frac{\Delta E_m}{\int_L \frac{\partial E}{\partial x}_w dl}$$

Imaging for treatment planning

- Proton CT (pCT):





Outline

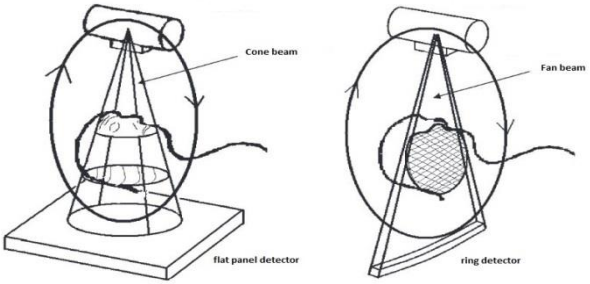
- Diagnostic (too broad to be covered in this talk)
- **Imaging for treatment planning**
- **Imaging for patient setup and plan adaptation**
- **Imaging for treatment verification**
- Reconstruction algorithms/techniques

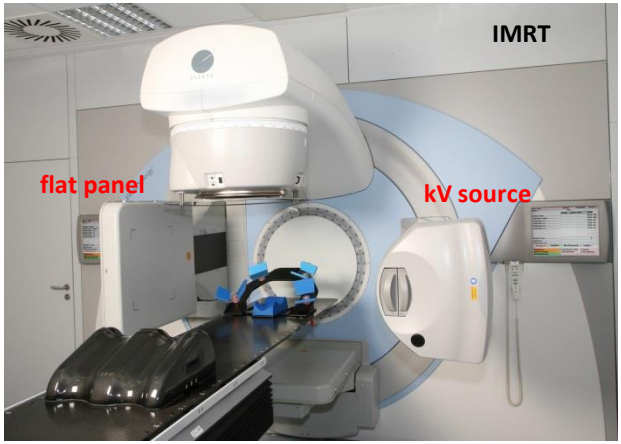
Imaging for patient setup and plan adaptation

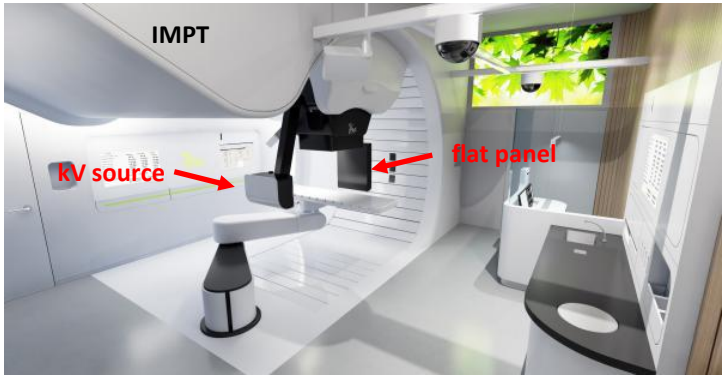
Equipment

Imaging for patient setup and plan adaptation

- CBCT:
  - Flat panel detector technology (scintillator + silicon detector array)
  - Cheaper than CT, compact, larger field of view, faster, lower imaging dose

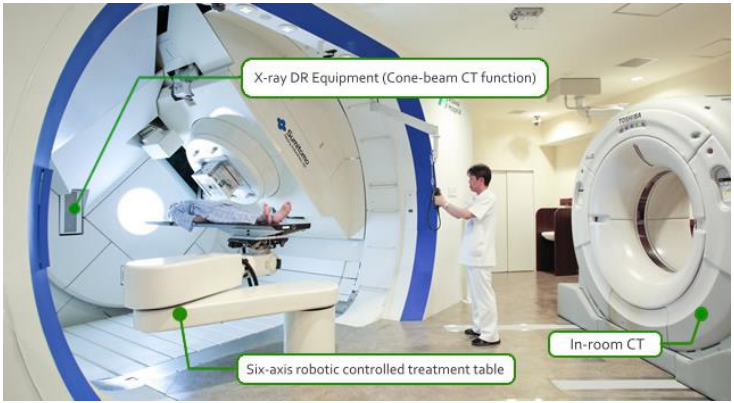






Imaging for patient setup and plan adaptation

- X-ray CT as for treatment planning:
  - In-room
  - Transfer to imaging room

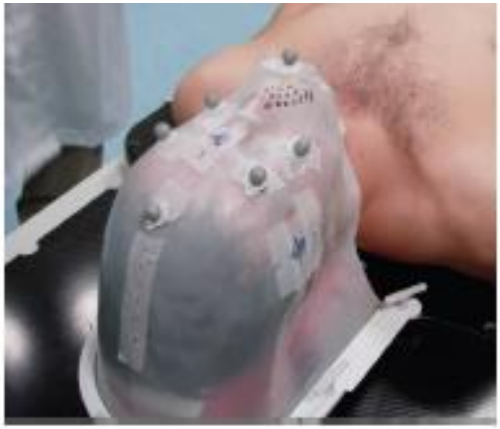


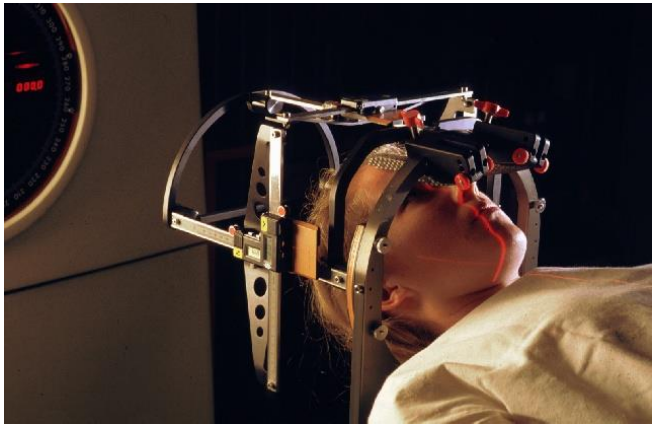
Imaging for patient setup and plan adaptation

Methods

Imaging for patient setup and plan adaptation

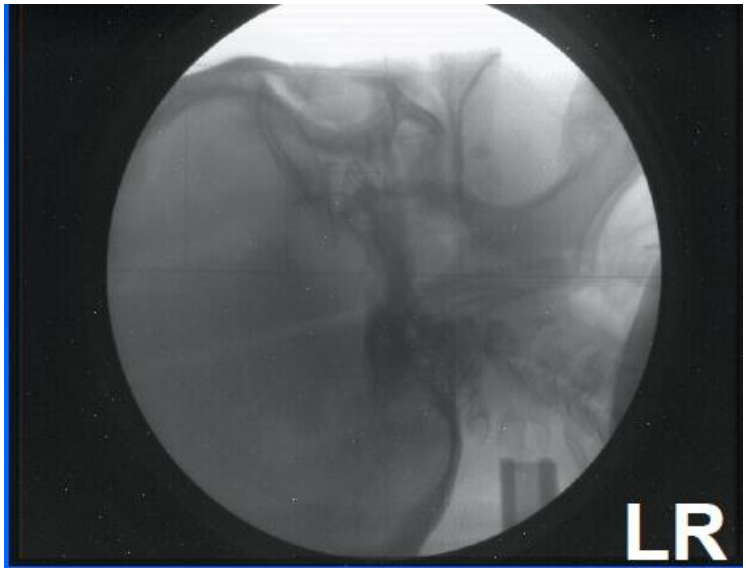
- Positioning:
  - Immobilization device and optical systems
  - Inner anatomy missing

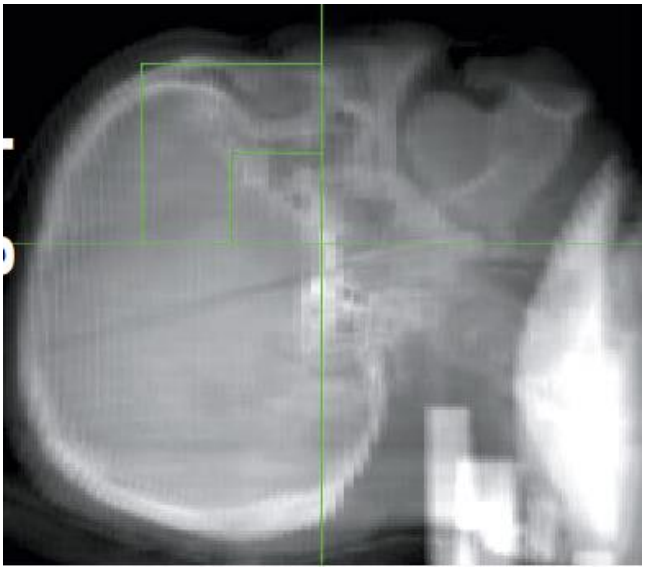




Imaging for patient setup and plan adaptation

- Positioning:
  - Planar X-ray images, compared to digitally reconstructed radiograph from planning CT

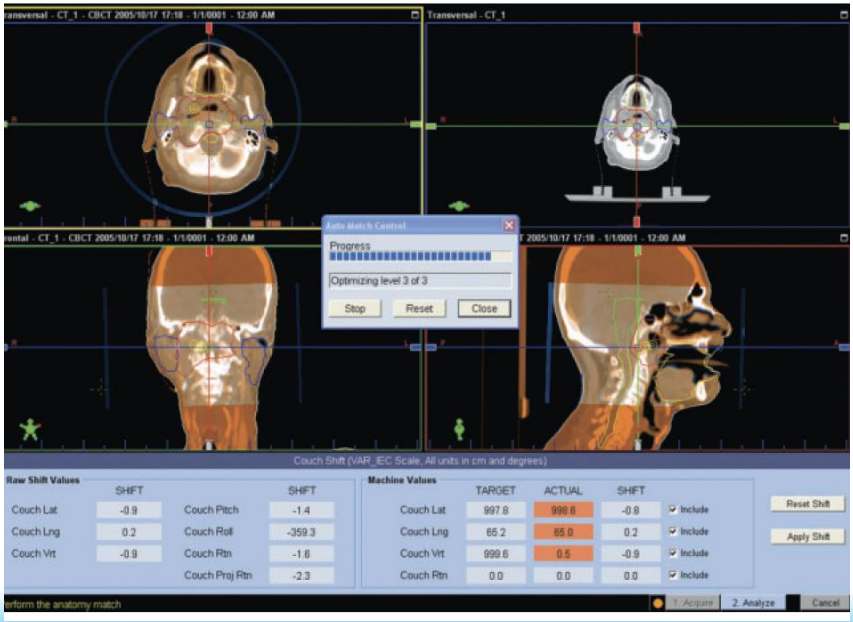




Imaging for patient setup and plan adaptation

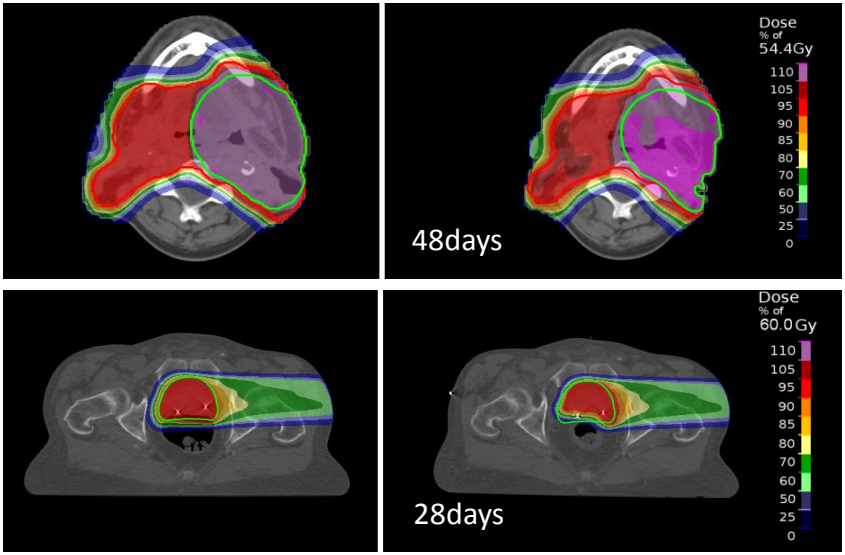
- Positioning:
  - Volumetric on iso-center imaging with CBCT
  - Registration with planning CT

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



Imaging for patient setup and plan adaptation

- Plan adaptation:
  - Proton treatment plan sensitive to anatomical changes



Head and neck:
Timescale:
days/weeks

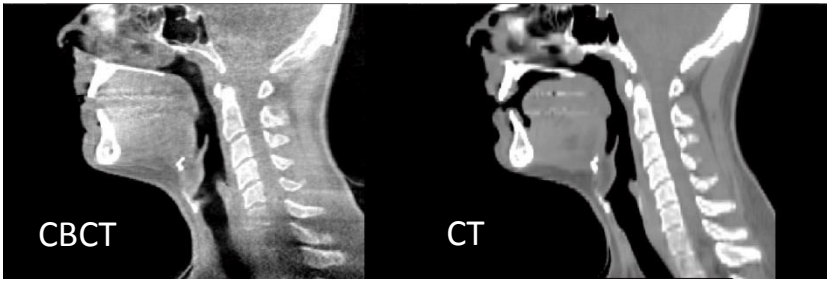
Prostate:
Timescale:
minutes/hours/days

Imaging for patient setup and plan adaptation

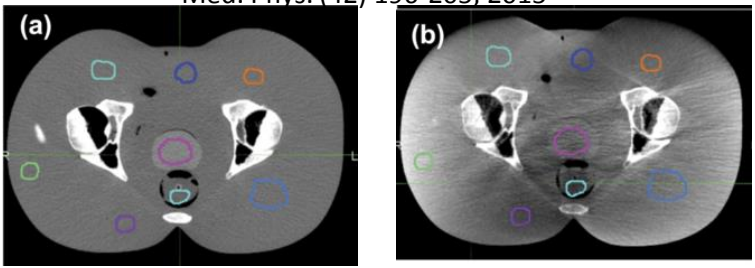
Challenges / Limitations

Imaging for patient setup and plan adaptation

- Limitations:
  - CBCT suffers from the same limitations as X-ray CT
  - In addition due to the beam/detector geometry: increased scattering, poor soft tissue contrast, limited field of view, spatial variation of HU



Med. Phys. (42) 196-205, 2015



CT CBCT

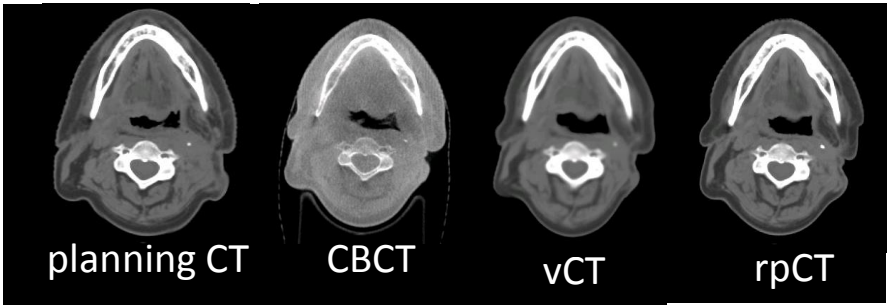
  - X-ray CT: expensive, high dose, bulky, patient needs to be moved

Imaging for patient setup and plan adaptation

New Approaches

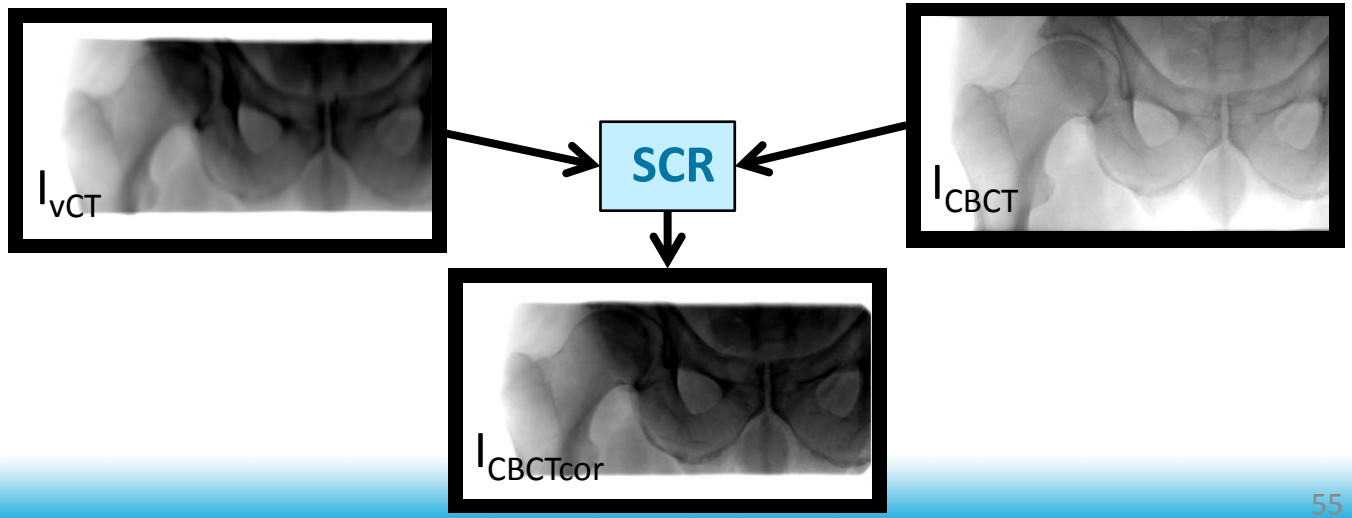
Imaging for patient setup and plan adaptation

- CBCT - anatomy of the day, CT – correct HU:
- For plan adaptation:
  - Deform planning CT to CBCT. This creates a virtual CT (vCT) which should match the rpCT ground truth (correct anatomy and HU)



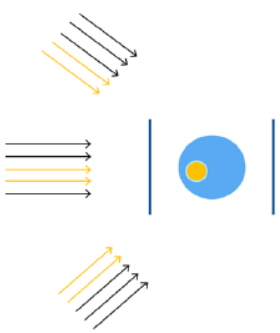
Imaging for patient setup and plan adaptation

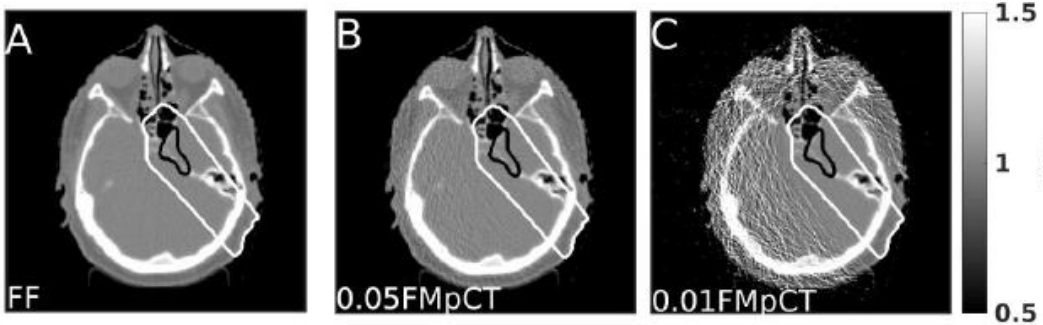
- CBCT - anatomy of the day, CT – correct HU:
- For plan adaptation:
  - Apply scatter correction to CBCT, using vCT as a prior



Imaging for patient setup and plan adaptation

- pCT with fluence modulation
  - Exploit the pCT accuracy in RSP estimation, with a spatially varying image quality to achieve a low dose imaging for positioning/plan adaptation



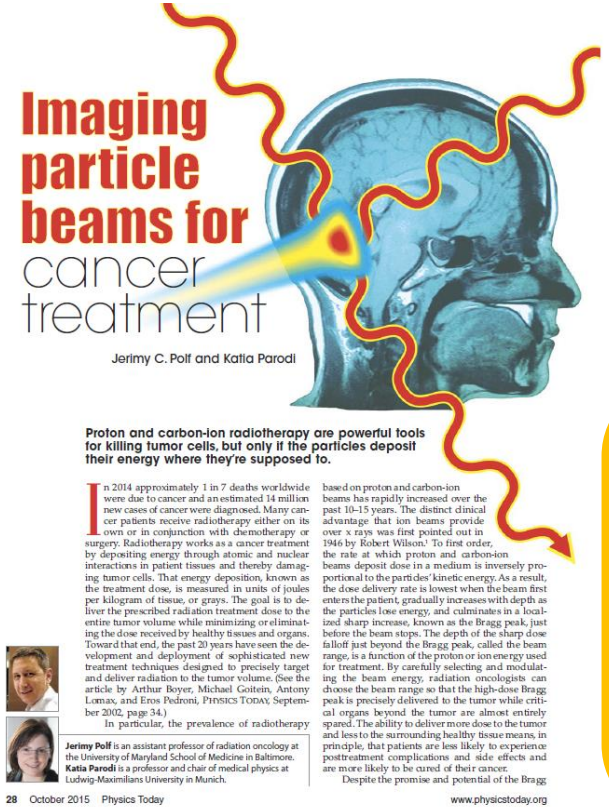


  - Dose savings up to 50% while retaining RSP accuracy in the ROI (beam path)

Outline

- Diagnostic (too broad to be covered in this talk)
- **Imaging for treatment planning**
- **Imaging for patient setup and plan adaptation**
- **Imaging for treatment verification**
- Reconstruction algorithms/techniques

Imaging for treatment verification



Imaging particle beams for cancer treatment

Jerimy C. Polf and Katia Parodi

Proton and carbon-ion radiotherapy are powerful tools for killing tumor cells, but only if the particles deposit their energy where they're supposed to.

In 2014 approximately 1 in 7 deaths worldwide were due to cancer and an estimated 14 million new cases of cancer were diagnosed. Many cancer patients receive radiotherapy either on its own or in conjunction with chemotherapy or surgery. Radiotherapy works as a cancer treatment by depositing energy through atomic and nuclear interactions in patient tissues and thereby damaging tumor cells. That energy deposition, known as the treatment dose, is measured in units of joules per kilogram of tissue, or grays. The goal is to deliver the prescribed radiation treatment dose to the entire tumor volume while minimizing or eliminating the dose received by healthy tissues and organs. Toward that end, the past 20 years have seen the development and deployment of sophisticated new treatment techniques designed to precisely target and deliver radiation to the tumor volume. (See the article by Arthur Boyer, Michael Goitein, Antony Lomax, and Eros Pedroni, PHYSICS TODAY, September 2002, page 34.)

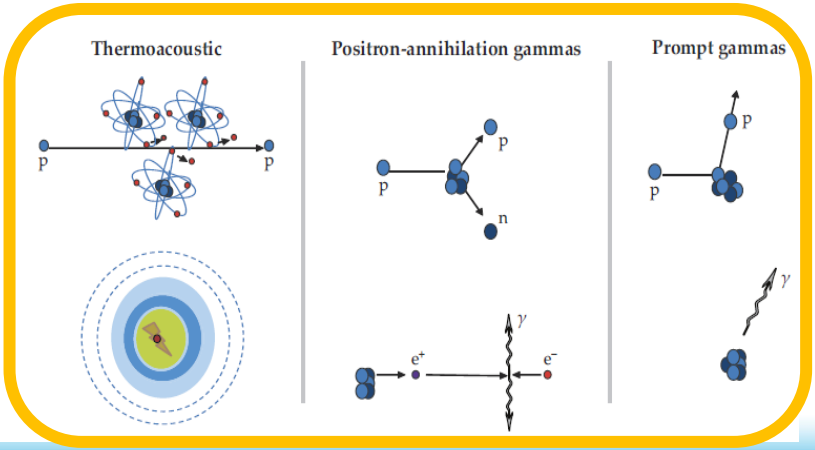
In particular, the prevalence of radiotherapy based on proton and carbon-ion beams has rapidly increased over the past 10–15 years. The distinct clinical advantage that ion beams provide over x rays was first pointed out in 1946 by Robert Wilson.[1] To first order, the rate at which proton and carbon-ion beams deposit dose in a medium is inversely proportional to the particles' kinetic energy. As a result, the dose delivery rate is lowest when the beam first enters the patient, gradually increases with depth as the particles lose energy, and culminates in a localized sharp increase, known as the Bragg peak, just before the beam stops. The depth of the sharp dose falloff just beyond the Bragg peak, called the beam range, is a function of the proton or ion energy used for treatment. By carefully selecting and modulating the beam energy, radiation oncologists can choose the beam range so that the high-dose Bragg peak is precisely delivered to the tumor while critical organs beyond the tumor are almost entirely spared. The ability to deliver more dose to the tumor and less to the surrounding healthy tissue means, in principle, that patients are less likely to experience posttreatment complications and side effects and are more likely to be cured of their cancer.

Despite the promise and potential of the Bragg

Jerimy Polf is an assistant professor of radiation oncology at the University of Maryland School of Medicine in Baltimore. **Katia Parodi** is a professor and chair of medical physics at Ludwig-Maximilians University in Munich.

- Beam particles do not escape the patient
- They can be detected indirectly

Different emission mechanisms



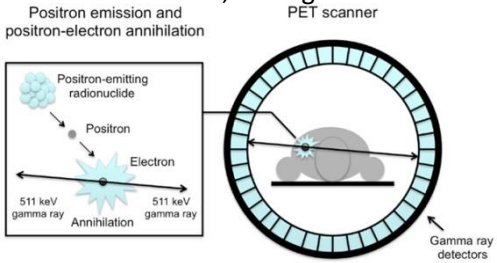
Imaging for treatment verification

Equipment

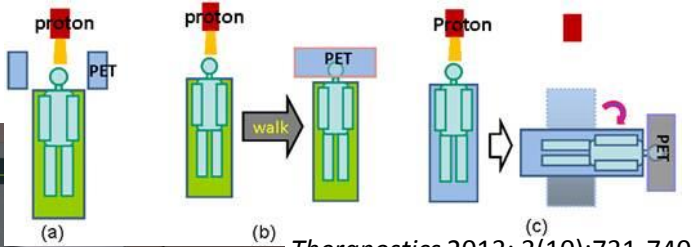
Imaging for treatment verification

- Use of positron emission tomography
  - Positron emitter induced by beam interaction with tissue

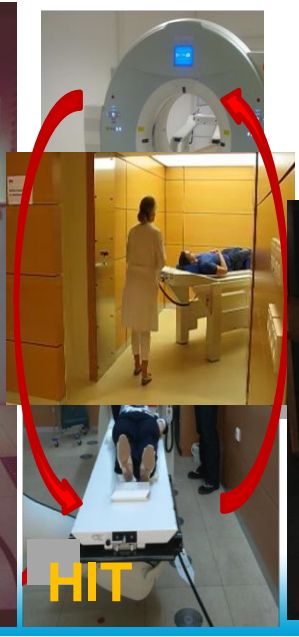
Front. Oncol., 13 August 2013

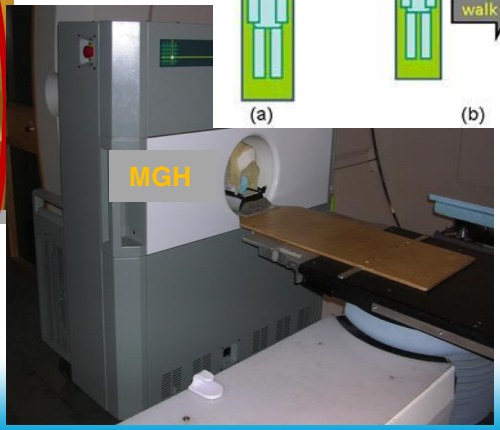


  - Can be in- beam (a), off-line (b) or in-room (c)



Theranostics 2013; 3(10):731-740



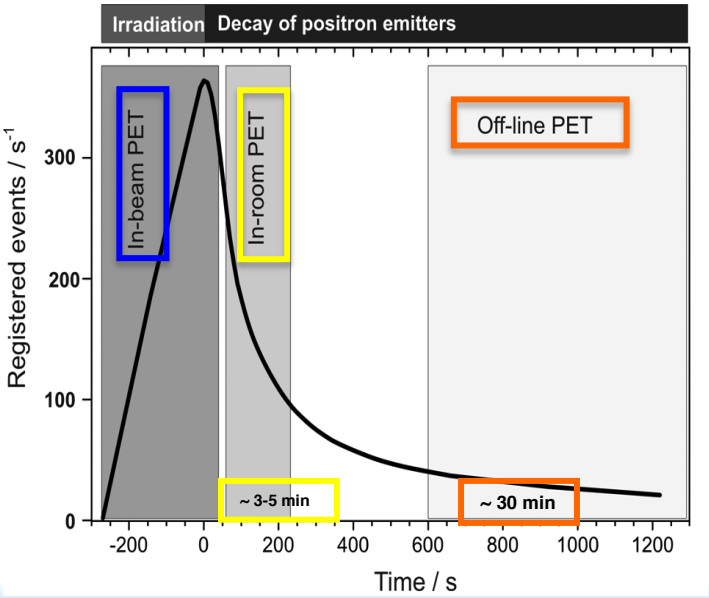


Imaging for treatment verification

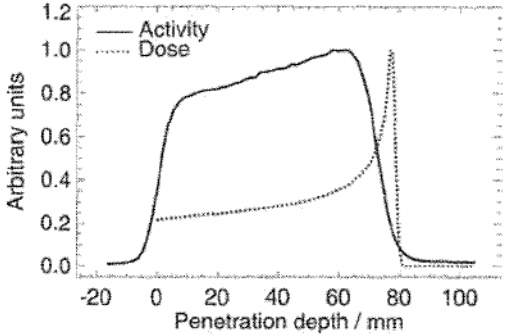
Methods

Imaging for treatment verification

- PET distribution correlated to proton/ion range
  - Not one-to-one correlation of PET profile to Bragg peak



Radiother. Oncol. 73, (2004), S96-S98

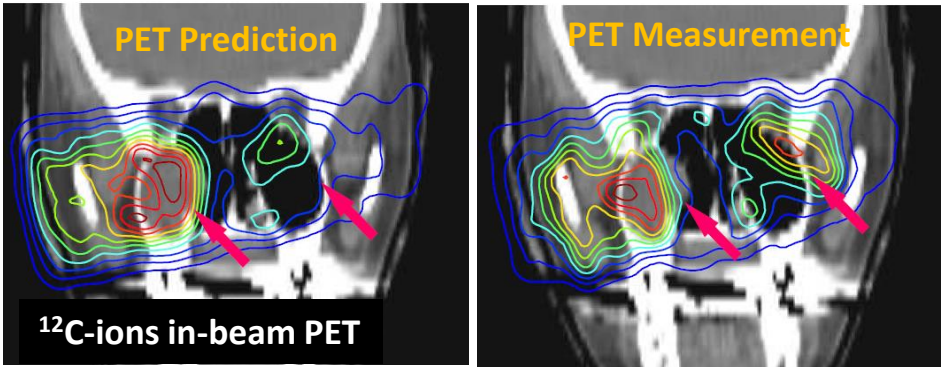


  - PET is a dynamic process depending on time of irradiation and acquisition

Phys Med Biol. 2011 Mar 7;56(5):1281-98

Imaging for treatment verification

- PET distribution correlated to proton/ion range
  - Calculate a PET prediction according to the treatment plan, compare it with the PET measurement



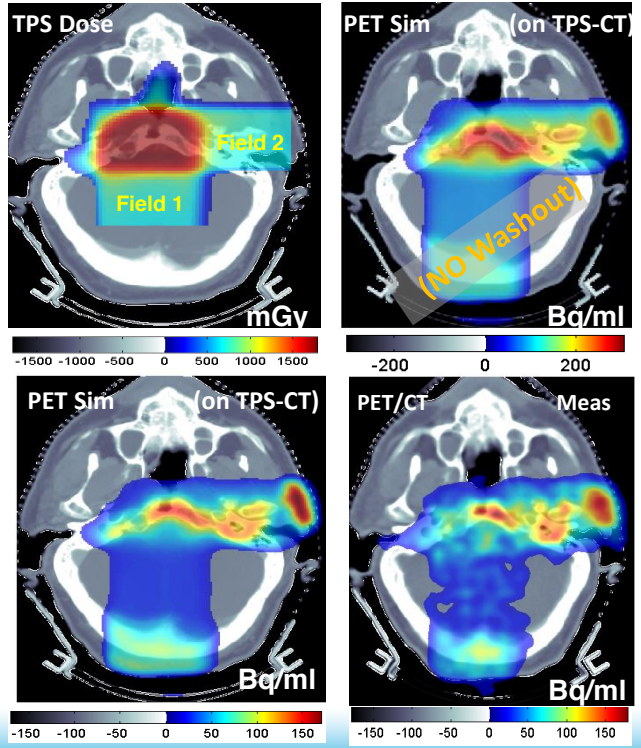
K. Parodi PhD Thesis 2004
Radiother Oncol 2004

Imaging for treatment verification

Challenges/Limitations

Imaging for treatment verification

- PET clinical application as treatment verification technique
  - Low SNR
  - Biological washout
  - Suboptimal hardware
    (adapted from clinical or small animal PET)
  - Need of fast & accurate model
  - In-house developed workflow



Parodi et al, IJROBP 68, 2007

Imaging for treatment verification

New Approaches

Imaging for treatment verification

- New detectors and scanner design for PET

INSIDE prototype at CNAO

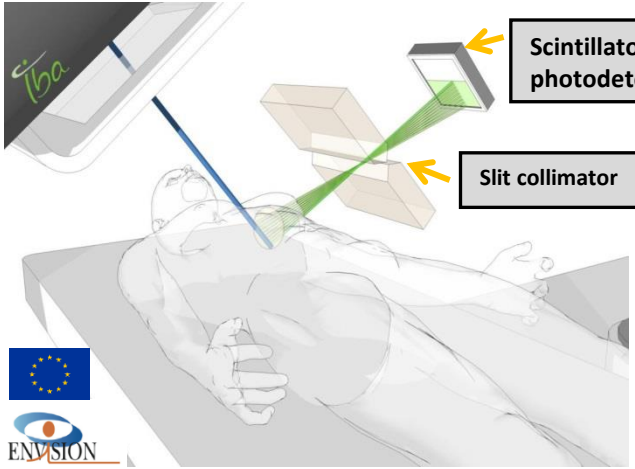
Bisogni et al, J Med Imag 2016

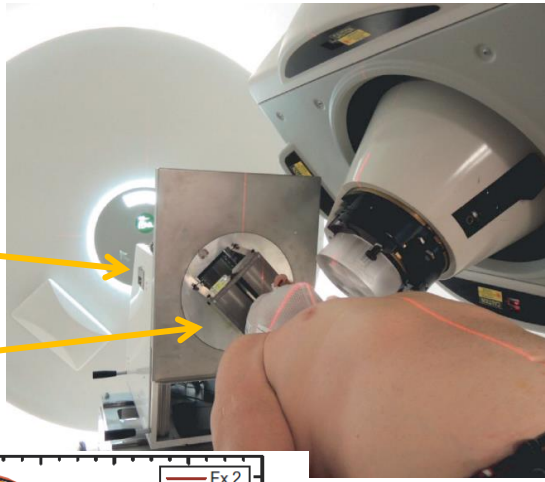
OpenPET at NIRS

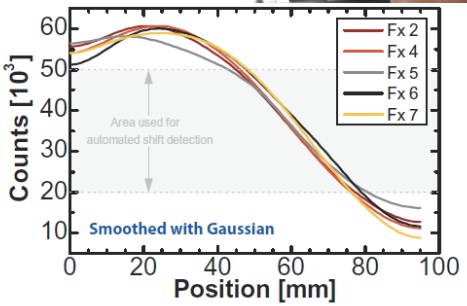
Tashima…Yamaya, PMB 2016

Imaging for treatment verification

- Exploiting the emission of prompt gamma
  - First clinical evaluation in Dresden (passive beam scattering)

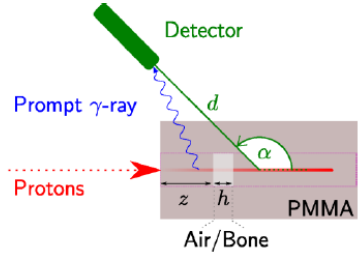


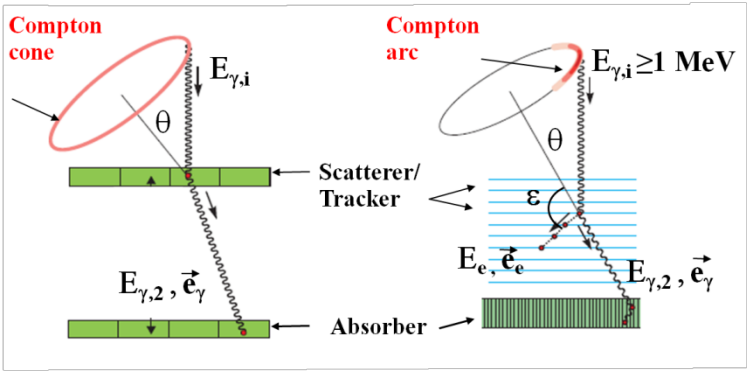




Imaging for treatment verification

- Exploiting the emission of prompt gamma
  - Compton camera's (no mechanical collimation + 3D imaging)
  - Prompt gamma timing
  - Prompt gamma spectroscopy
  - ….





Thank you for your attention