The use of imaging information in Monte Carlo simulations

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“Monte Carlo is perfect”

- But MC patient dose calculations require imperfect images as input
  ⇨errors/artifacts in images propagate in the dose calculation

  MC is more prone to this than other dose calculation methods

  In many MC papers hardly any mention is made of the tissue segmentation procedure
  ⇨including those that show few % difference between MC and other methods

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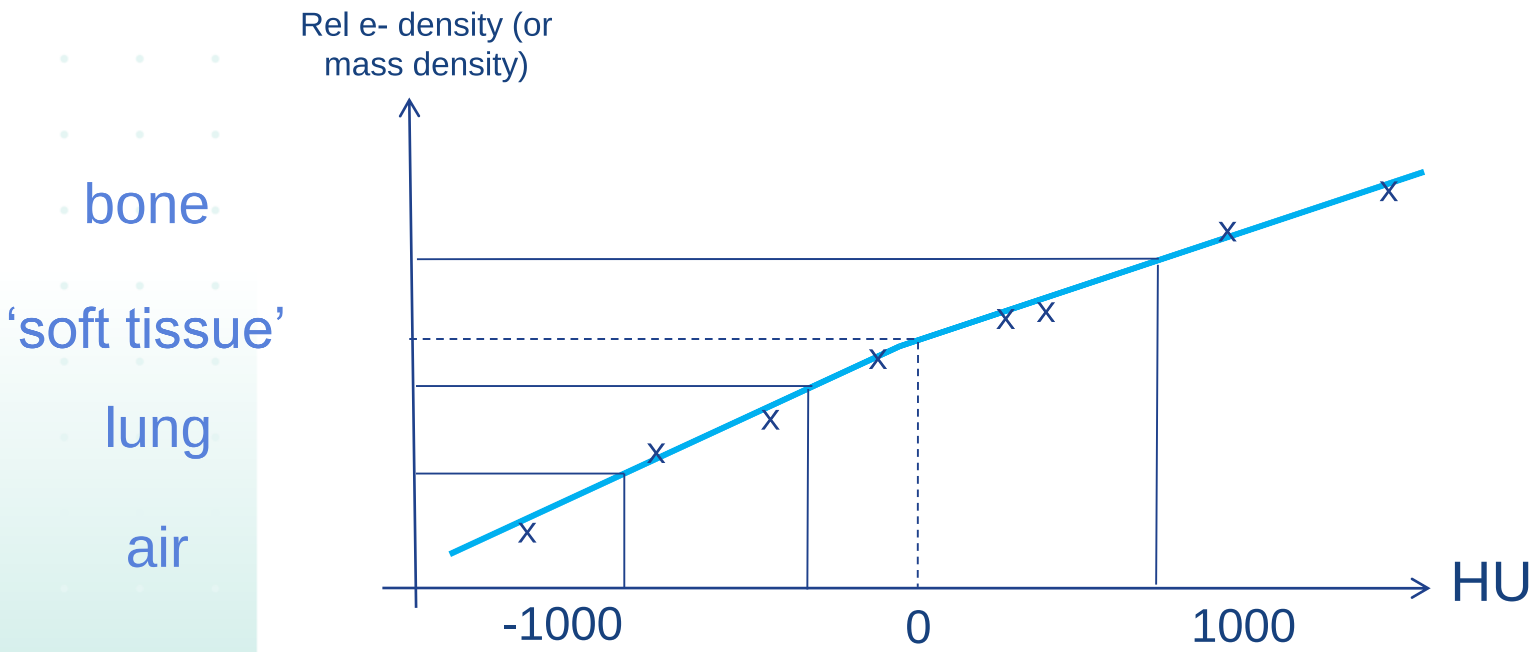
How does (nearly) everyone do MC dose calculations? Patient geometry segmentation



- Material segmentation (number, tissue types) somewhat arbitrary
- May influence dose calculation

Gammex electron density phantom

What can possibly go wrong?

- Pick wrong phantom for calibration
- Pick wrong kV of the CT scanner
- Pick wrong intervals for material assignment

Pick the wrong phantom

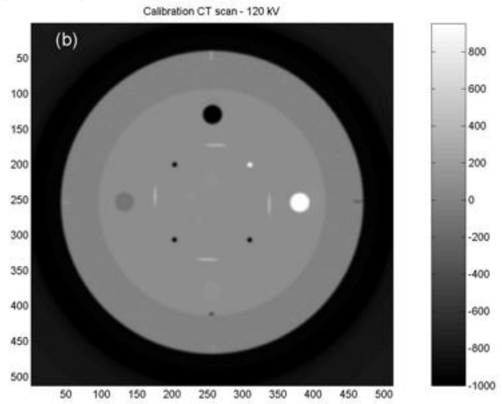
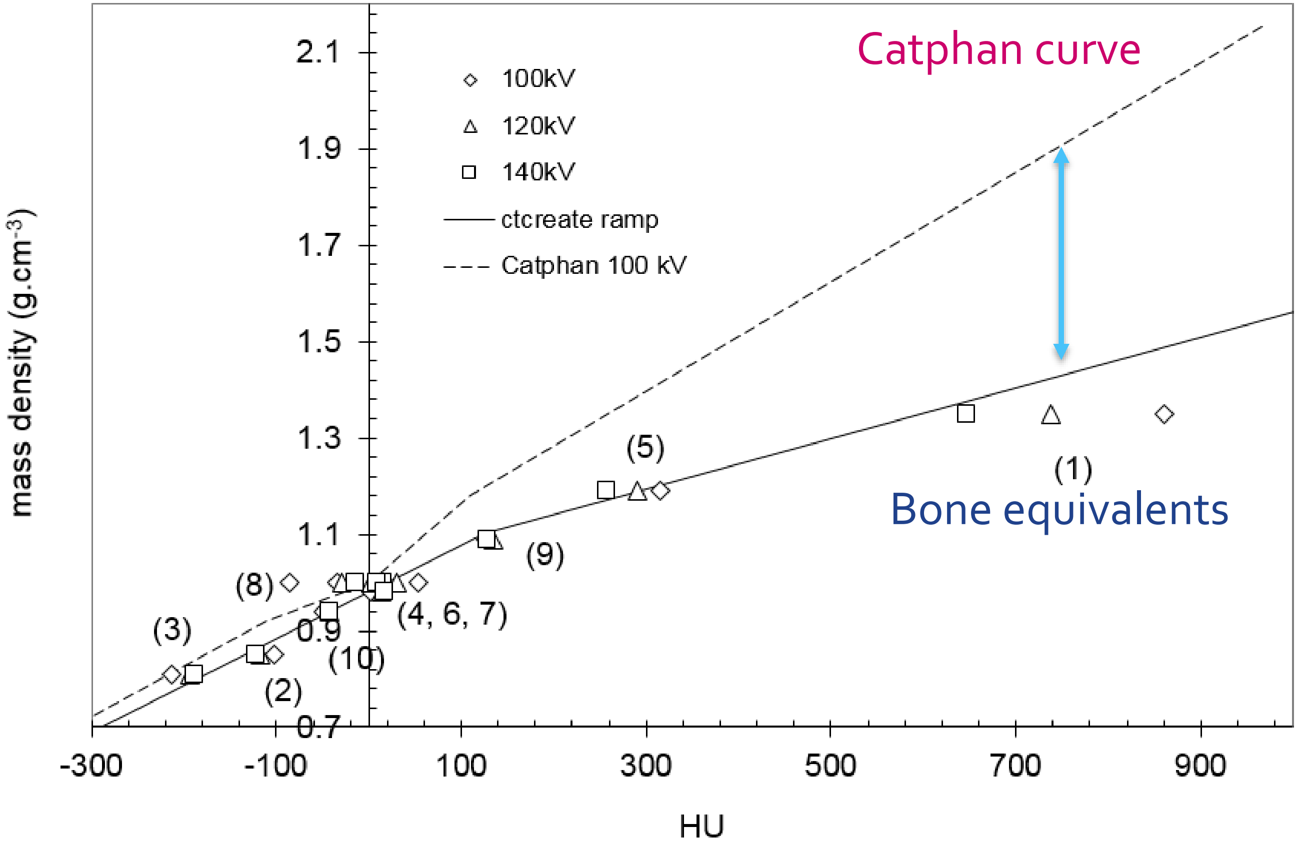


Table 3. Composition by fractional weight of the materials used in the *Catphan* calibration phantom and their mass densities.

		Fraction by weight						
#	Material	H	C	O	N	F	Ar	ρ (g cm^{-3})
1	Air			23.18	75.53		1.29	0.0012
2	C_2H_4	14.37	85.63					0.92
3	$C_5H_8O_2$	8.054	59.98	31.96				1.18
4	C_2F_4 (Teflon)		24.02			75.98		2.16

CatPhan 500 (The Phantom Laboratory)

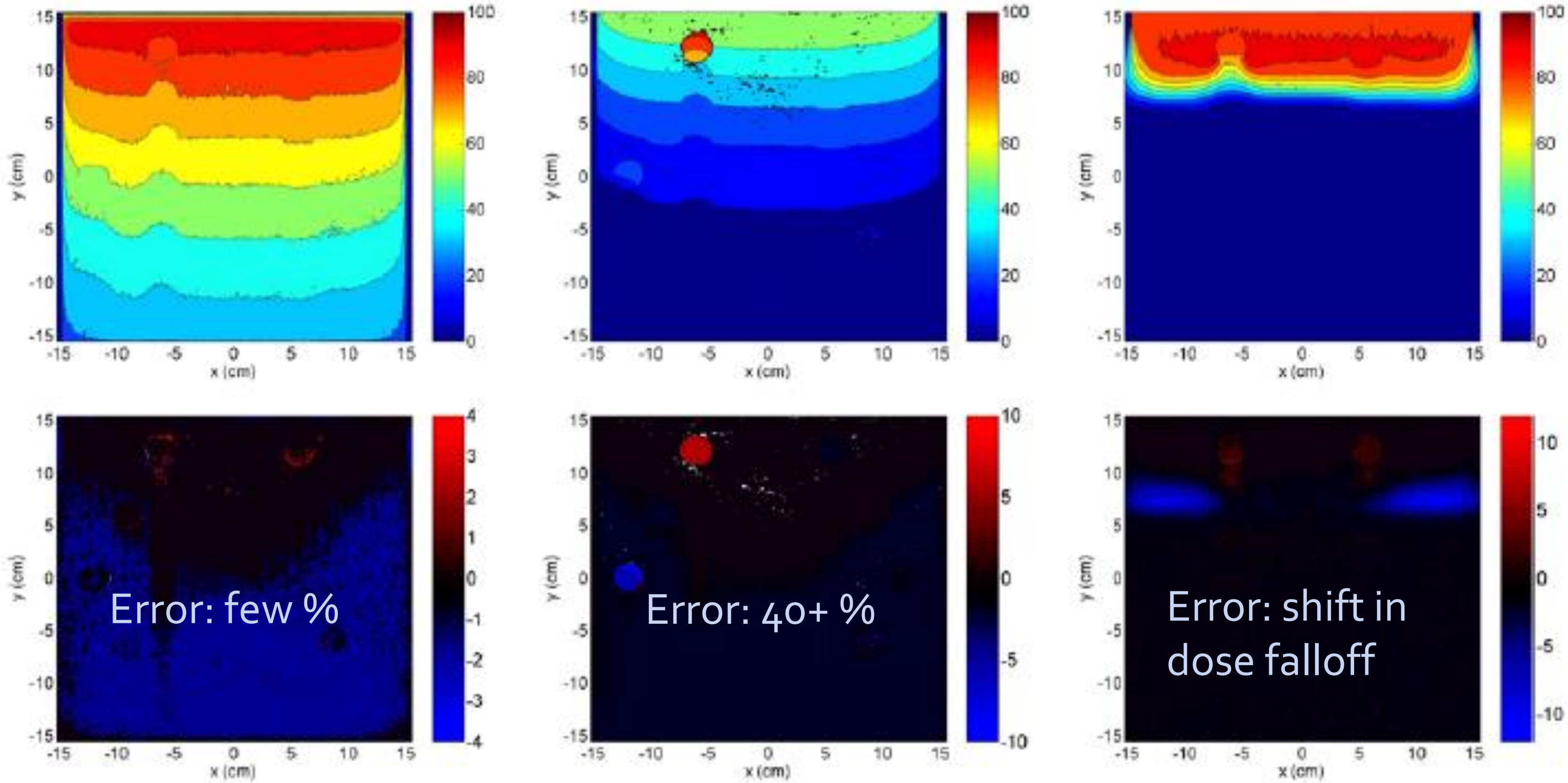
Improper HU – ρ calibration



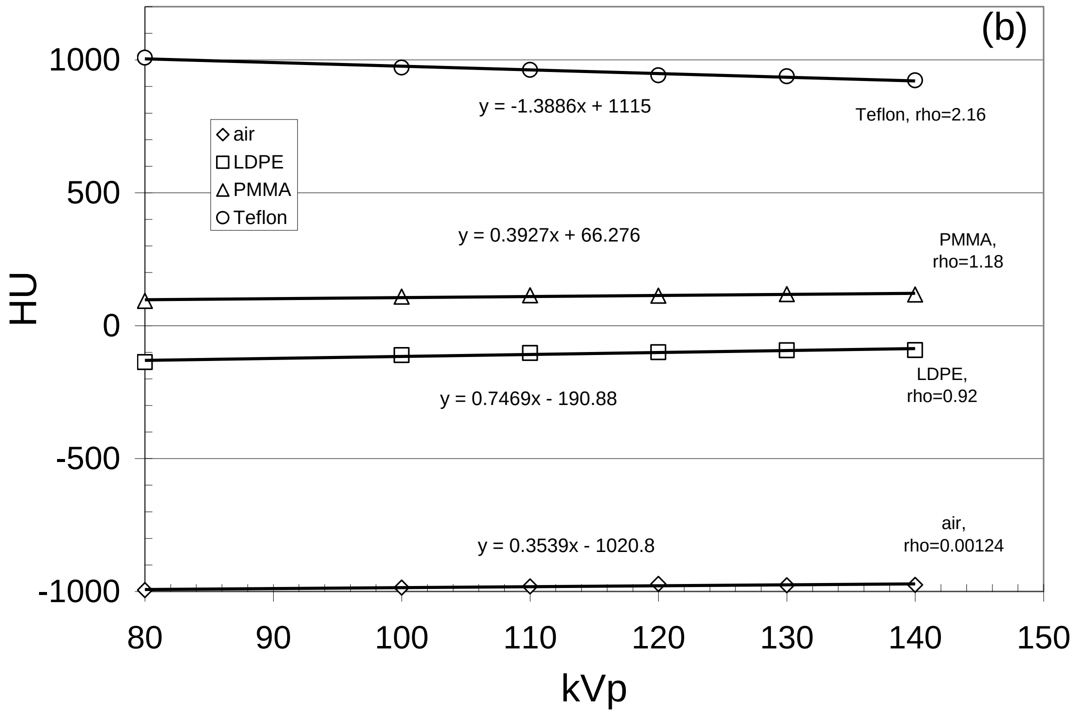
Verhaegen, Devic. *Sensitivity study for CT image use in Monte Carlo Treatment Planning.* Phys. Med. Biol., 50, 937-946, 2005

MC dose errors

6MV X-rays | 250 kVp X-rays | 18 MeV electrons

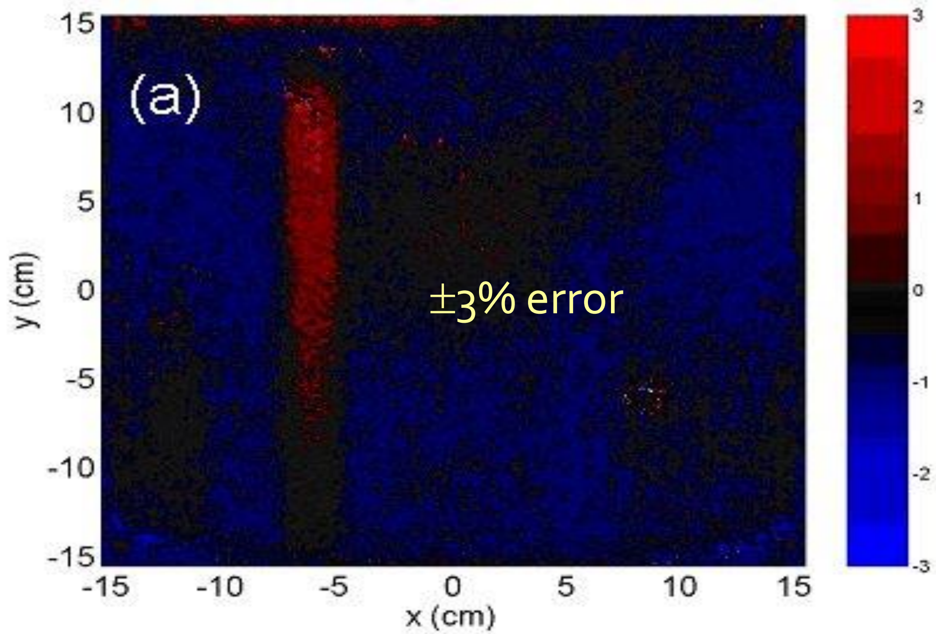


Pick wrong kV of the CT scanner:
HU depend on CT scanner kVp



Low HU: increase with kVp
High HU: decrease with kVp

$(D_{140kVp} - D_{100kVp}) / D_{100kVp}$



Common practice: use single 120 kVp calibration

Compare 6MV dose calculation in 100 kV and 140 kV CT image

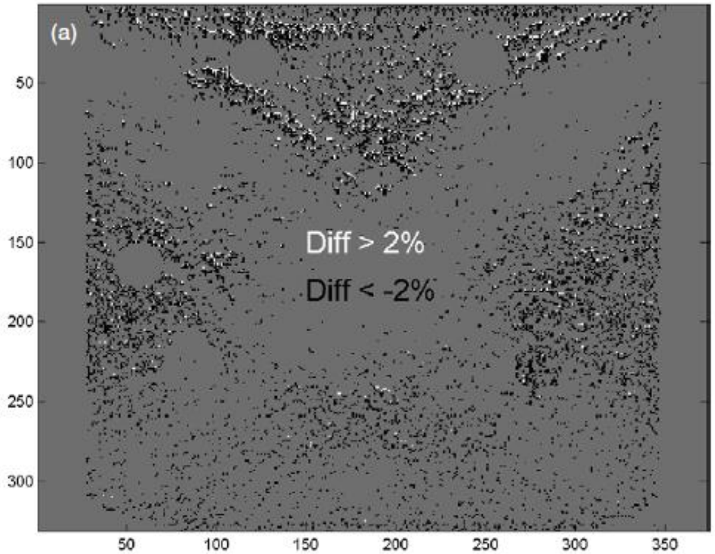
- 3% errors
- larger errors in kV photons

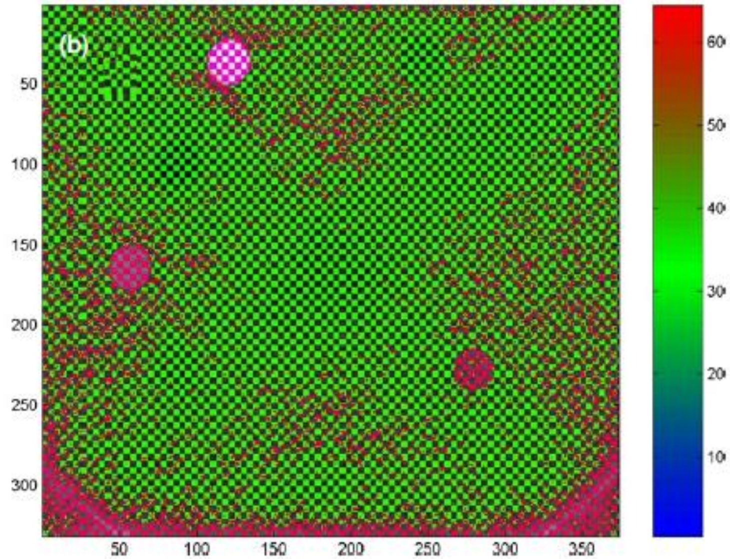
Errors can be larger if e.g. 140 kVp is used for calibration and 100 kVp for dose calculation

Pick wrong intervals for material assignment

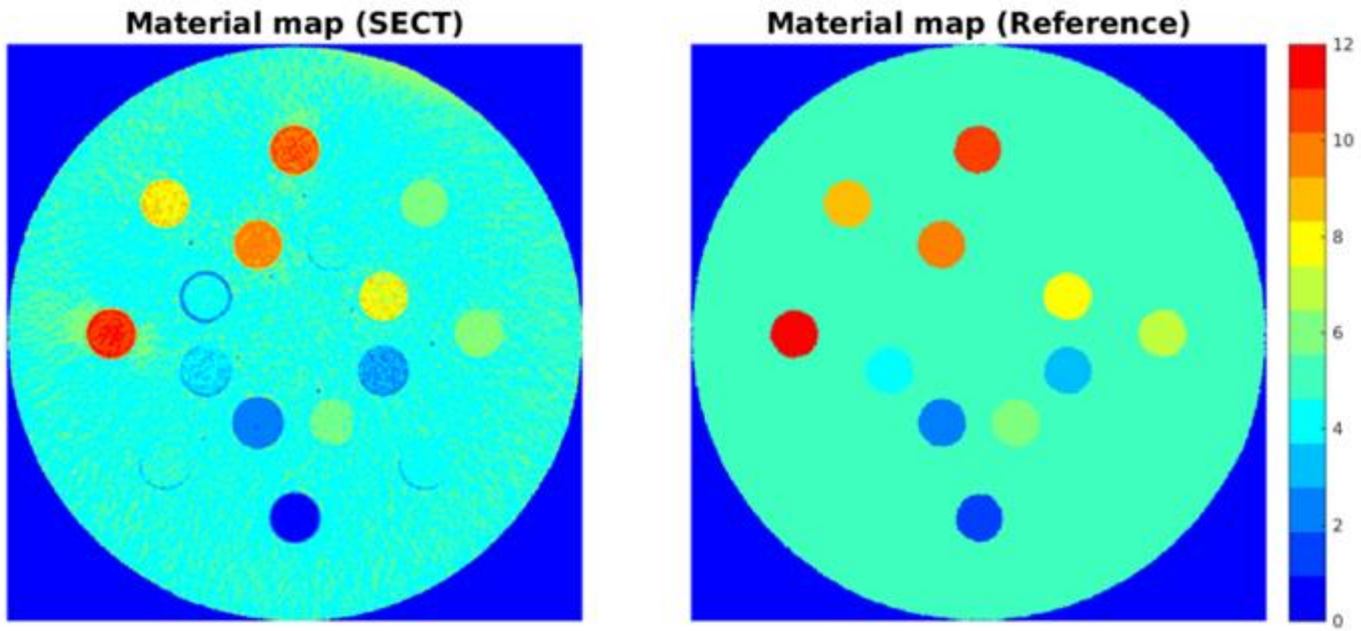
- Compare 6MV dose calculation with bone threshold set to 1.1 or 1.2 g/cm³

  CT artifacts can cause larger errors in MC than in other methods





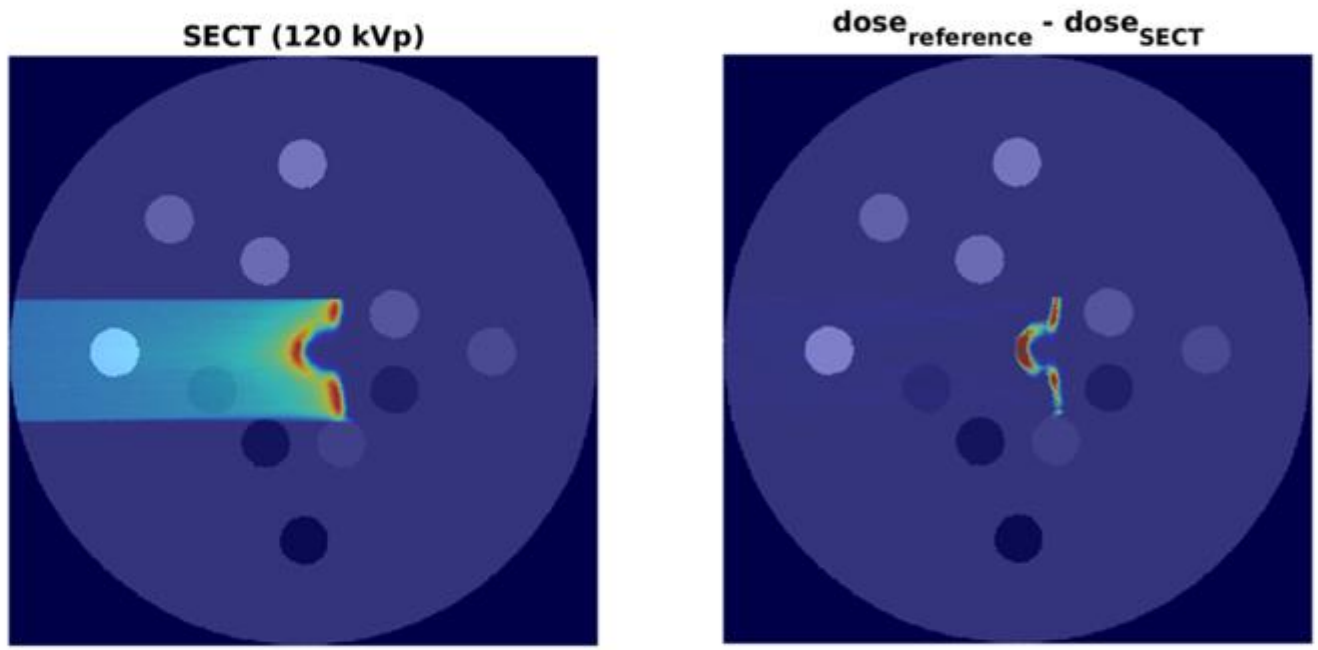
Protons: SECT vs absolute truth



RMI 467 phantom (Gammex)

Difficult to get all materials correctly identified based on density alone

Protons: Dose calculations based on stopping powers



175 MeV monoE protons

Errors in tissue assignment accumulate in Bragg peak position

Several mm shift of Bragg peaks ⇨ uncertainties in treatment margins

Conclusions: tissue assignment studies

- Mis-assignment of media and/or $\rho_{(e)}$ in calibration procedure can cause significant dose errors
  - Worst for kV photons, few% for MV photons
  - Significant range differences in protons
  - Need to explore this for kV therapy, kV imaging, brachytherapy, kV small animal radiotherapy

- Accurate calibration is essential
  - Assess commercial phantoms carefully
    - Teflon insert in Catphan phantom (older generation) inappropriate
  - In some cases assigning water (with correct density) is better than assigning wrong media

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Is there a better way to do dose calibration? The stoichiometric calibration (Schneider PMB 1996)

Method:

- Parametrize CT scanner (k1,k2) for set of materials (not necessarily tissue-equivalent)
- k1, k2: fit coefficients; importance of Rayleigh scatter and photo-electric effect wrt Compton scatter

$$\frac{\bar{\mu}}{\bar{\mu}_{\mathrm{w}}} = \frac{\rho}{\rho_{\mathrm{w}}} \frac{\sum_i \frac{w_i}{A_i}\left(Z_i + k_1 Z_i^{2.86} + k_2 Z_i^{4.86}\right)}{\frac{w_{\mathrm{H}}}{A_{\mathrm{H}}}(1 + k_1 + k_2) + \frac{w_{\mathrm{O}}}{A_{\mathrm{O}}}\left(8 + k_1 8^{2.86} + k_2 8^{4.86}\right)}$$

- Minimize expression to obtain k1,k2

$$\sum_j \left[\left(\frac{\bar{\mu}}{\bar{\mu}_{\mathrm{w}}}(k_1, k_2)\right)_j - \left(\frac{\mathrm{HU}}{1000} + 1\right)_j\right]^2$$

- Then calculate HU for any material ⇨ calibration curve

$$\mathrm{HU} = \left(\frac{\bar{\mu}}{\bar{\mu}_{\mathrm{w}}} - 1\right) \times 1000.$$

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Stoichiometric method

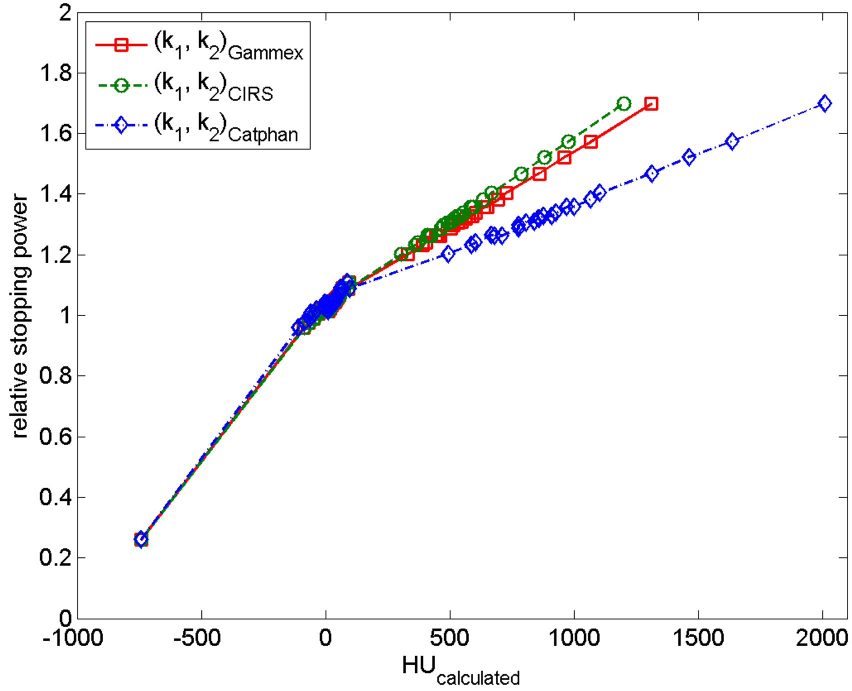
- Was intended to make the calibration curve independent of the calibration phantom

  Very commonly used in proton dose calculations

  However, no one seems to have verified this extensively
  - ❑ Recently it was shown that k1,2 characterization DOES depend on calibration phantom
  - ❑ Calibration with a well-chosen phantom (e.g.Gammex) is as good as the more complex stoichio method

  Gomà et al, in preparation, 2017

k1,2 depend on calibration phantom (Goma et al, in prep)



- Gammex, CIRS and Catphan phantom
- Differences in SPR of up to 5%
- Additional source of uncertainty in proton dosimetry
- Gammex phantom works best

Use the stoichiometric method with care

This method deserves thorough inspection after 20 yrs of clinical use

⇨Donate your CatPhan phantom to your Radiology Dept!

How sensitive are MC dose calculations to tissue composition?

The case of low-energy photons

What are human tissues made of?

Human tissues vary from one individual to the other
Data in literature is scarce and old
Most refs trace back to: (Woodard&White, BJR 1986)

Body tissue	Elemental composition (% by mass)					Densities		
						Mass	Electron	
	H	C	N	O	Elements with $Z > 8$	kg m^{-3}	el. kg^{-1} $\times 10^{26}$	el. m^{-3} $\times 10^{26}$
Adipose tissue 1	11.2	51.7	1.3	35.5	Na(0.1), S(0.1), Cl(0.1)	970	3.342	3241
Adipose tissue 2	11.4	59.8	0.7	27.8	Na(0.1), S(0.1), Cl(0.1)	950	3.347	3180
Adipose tissue 3	11.6	68.1	0.2	19.8	Na(0.1), S(0.1), Cl(0.1)	930	3.353	3118

Does any of this matter dosimetrically?

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Sensitivity of dose calcn to tissue composition:

Dose ratio for a breast case (Pd-103)

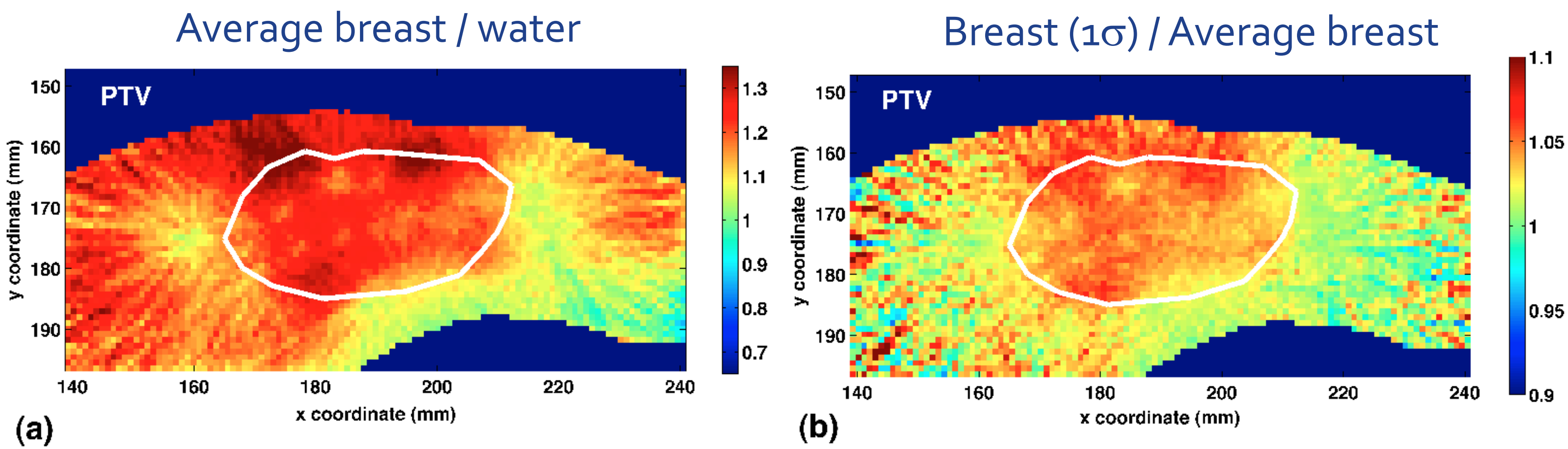

FIG. 7. (a) Ratio of *Breast mean-Z A70/G30* from a brachytherapy breast implant and $D_{TG\text{-}43}$. (b) Ratio of *Breast lo-Z* over *Breast mean-Z*.

- Left: From water to average breast, 30% ⇨largest effect!
- Right: Compositional uncertainty (1*σ) among patients, ±10%

This means most of the accuracy will be gained by replacing water ⇨ average breast tissue

(Landry et al. *Sensitivity of low energy brachytherapy Monte Carlo dose calculations to uncertainties in human tissue composition.* Med. Phys. 37, 5188-98, 2010)

A closer look at tissue compositions

D Mann-Krzisnik, F Verhaegen, S Enger. *The influence of tissue composition uncertainty on dose distributions in brachytherapy. Radiother Oncol, Submitted, 2017*

					for average dose to aorta.	
Siebert et al. (2013) [47]	HDR (^{192}Ir)	Floor of mouth, larynx and parotid	Target	D_{90}: -3.0%	$D_{w,m}$ model-based with CT density compared to TG-43 unit density water. GBBS Acuros module of BrachyVision for model-based calculation. Percent difference computed using median values.	CT densities mapped to materials. Elemental compositions from lung, adipose tissue, skeletal muscle, cartilage and bone taken from ICRP 23 [33].
Chibani et al. (2014) [48]	HDR (^{192}Ir)	Esophageal	Target	D_{90} (CTV): -3.2%	MC calculations with CT density compared to simulated TG-43 unit density water. Both calculations make use of HDRMC MC dose calculation engine.	ICRU-46
Hadad et al. (2015) [49]	HDR (^{192}Ir)	Nasopharynx	Target	D_{90}: -40%	MC calculations (DOSXYZ) with CT density compared to TG-43 unit density water (Oncentra^{TM} TPS)	Use of DOSXYZ/ctcreate [50] which maps CT densities to tissues. Compositions taken from ICRU-46.
		Mobile tongue, base of tongue, floor of mouth	Target (PTV)	D_{90}: -1.3%		

TG186 (2012) → ICRU 46 (1992) → W&W (1986) → ICRP23 (1975) *Reference man*

→ Studies from ORNL (50-60ies) classified!

→ Studies on HCNO (50-60ies)

150 cadavers
Lots of assumptions about tissue compositions
Spectrography by DC arc method for heavier atomic constituents
HCNO derived from evaporating water, dissolving fat, burning residue…
⇨derive Z

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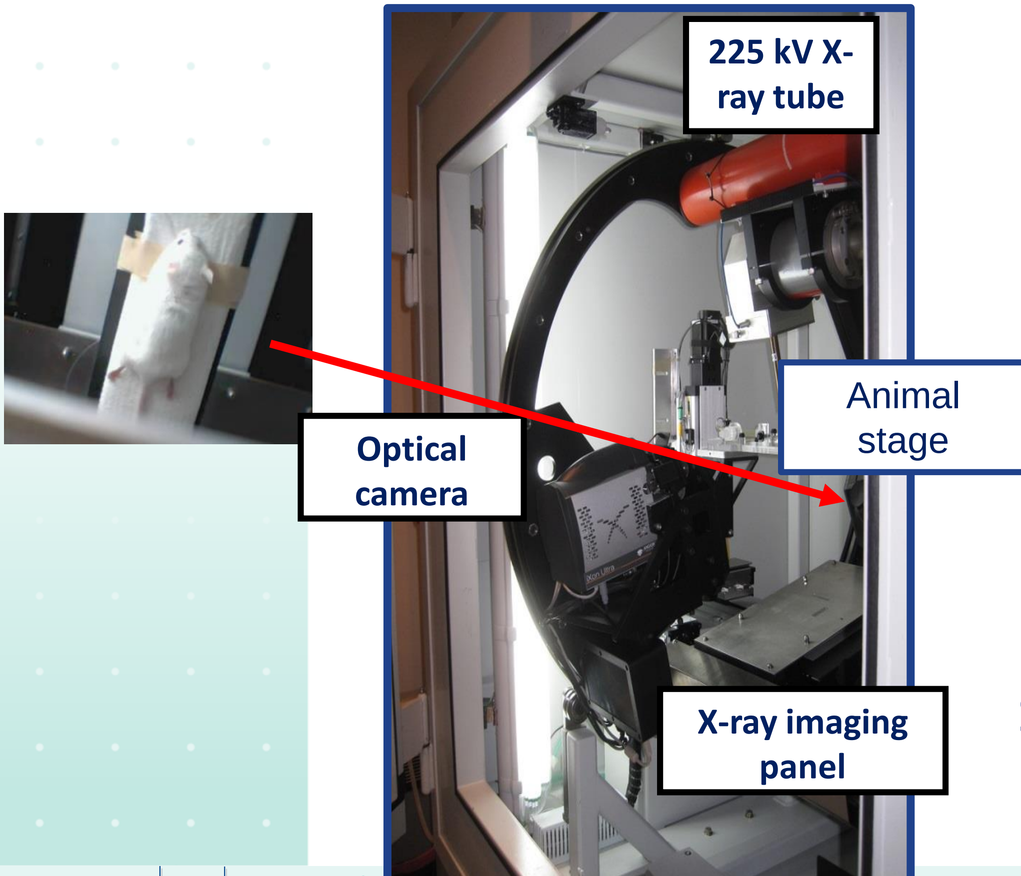
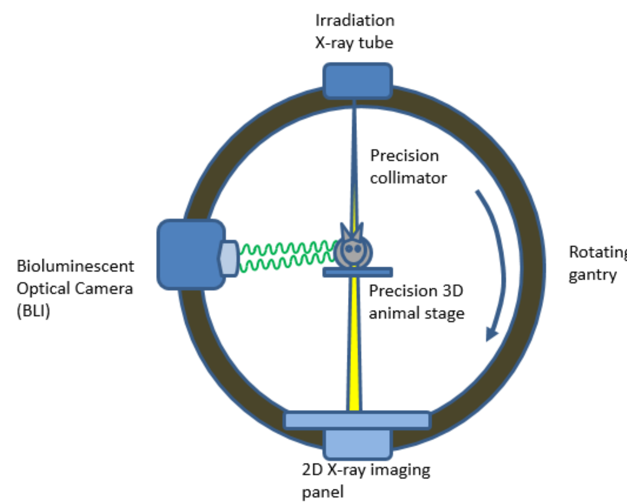
Need for accurate dose calculations in small animal radiotherapy

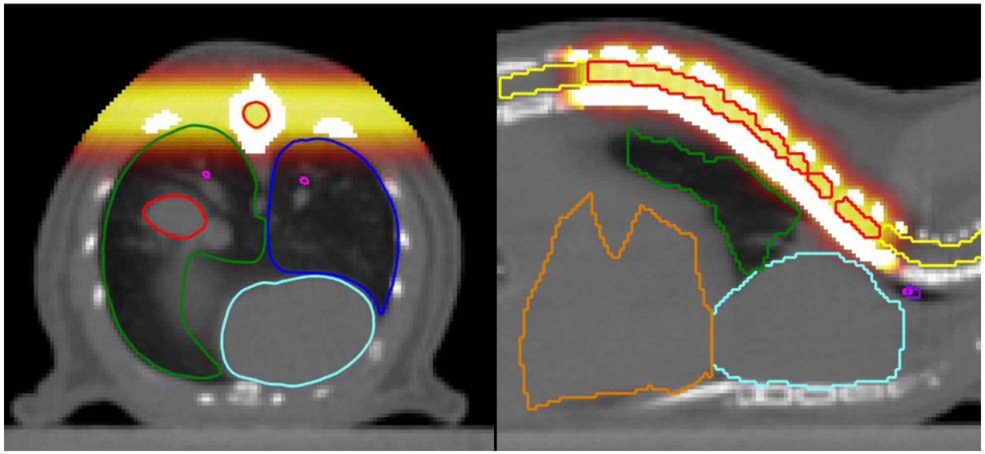




SmART: Small Animal RadioTherapy

Accurate kV photon dose calculations

'IMRT-like' dose painting in mice



Issues:

- Broad kV spectrum
- Very small beams + very small targets
- What are mouse tissues made of? No data
- How many different tissues should we assign for dose calculation?
- CT imaging can hardly distinguish any tissues at all

How will we improve this?
The need for more advanced imaging

- Different flavours of CT imaging
  - Single-energy CT
  - Dual-energy CT
  - Spectral CT
  - Cone Beam CT (for dose recalculation)
  - Proton CT
- MR imaging (as in e.g. MR-linac)
  - MR images not directly suitable for dose calculations
  - MR+overriding ρ could be reasonable approximation for MV photon beams, possibly also for proton beams
  - Not suitable for kV, brachytherapy

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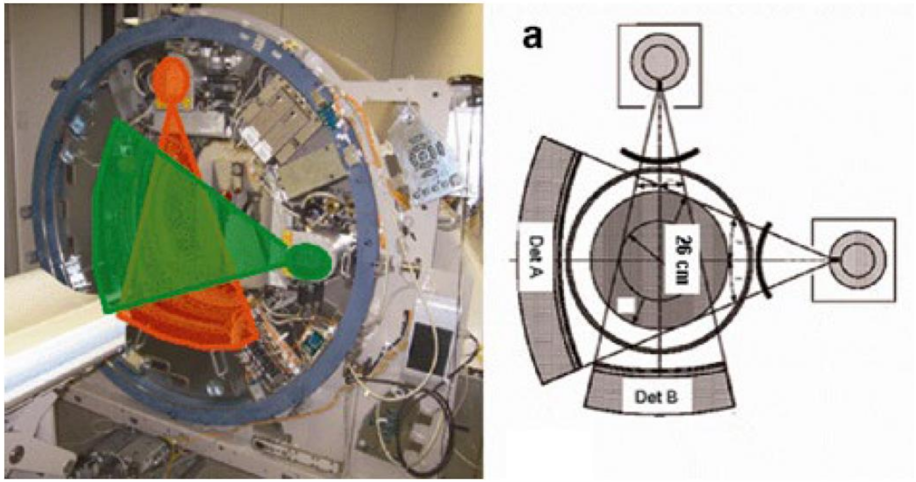
Current Dual-Energy CT scanners

Dual Source - Dual Detector

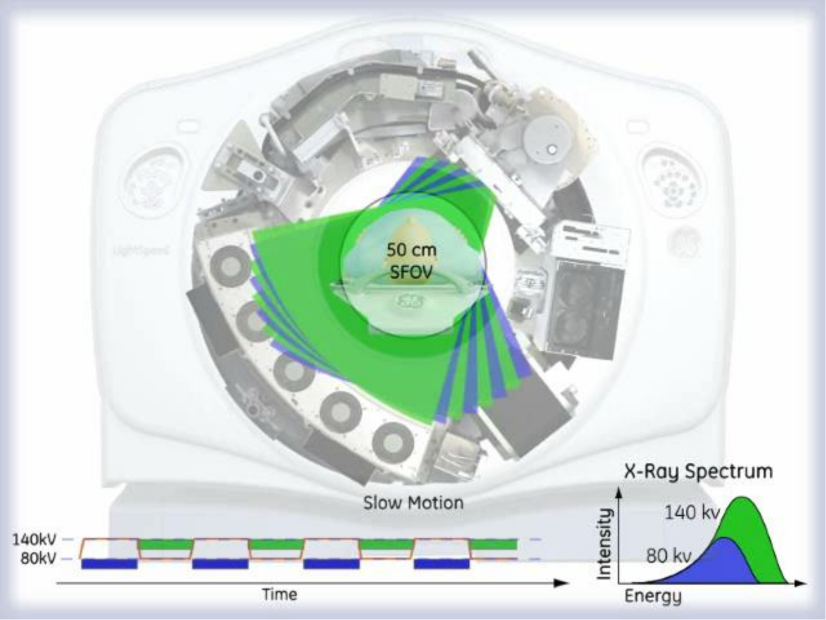
Siemens Definition Force CT

C.N. De Cecco et al. (eds.), *Dual Energy CT in Oncology*,
DOI 10.1007/978-3-319-19563-6_1

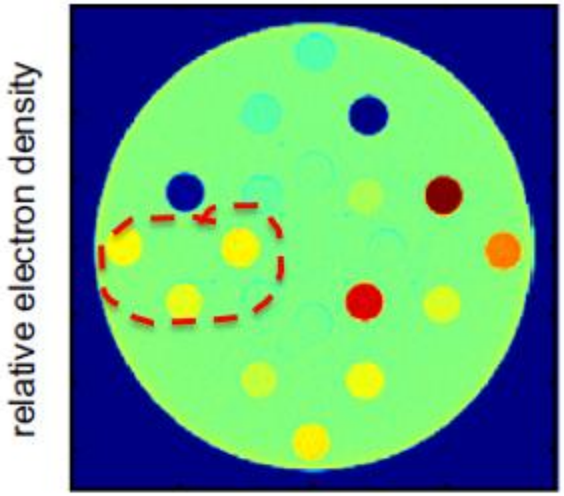


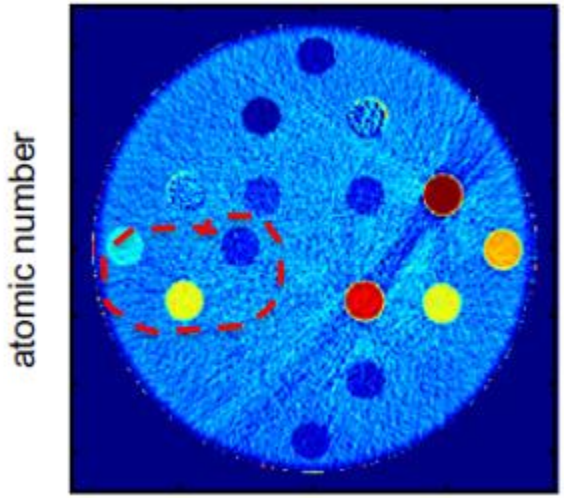
Rapid kV switching tube

GE Revolution GSI CT*



DECT yields density and atomic numbers





Atomic number images:
Bringing out differences in materials with similar densities

Z-images are noisy!

Review paper on DECT in 2016

Radiotherapy and Oncology 119 (2016) 137–144

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

ELSEVIER

Review: Dual Enrgi CT

Dual energy CT in radiotherapy: Current applications and future outlook

CrossMark

Wouter van Elmpt [a,*], Guillaume Landry [b], Marco Das [c], Frank Verhaegen [a,d]

Applications in:
- brachytherapy
- MV photons
- protons

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The type of CT scanner matters

EDGE: twinbeam

FLASH: dual-source

FORCE: dual-source

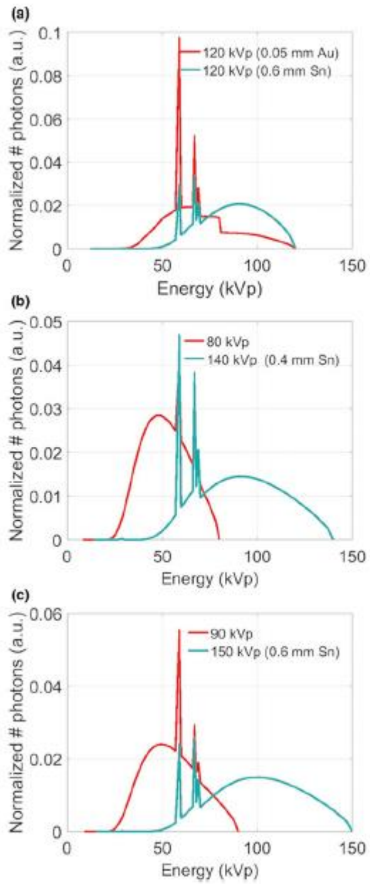

FIG. 1. Normalized X-ray photon spectra used in the EDGE (a), FLASH (b) and FORCE (c) scanners. All high energy spectra have a tin (Sn) filtration (0.6 mm for the EDGE and FORCE and 0.4 mm for the FLASH). The EDGE low energy spectrum has a gold (Au) filter of 0.05 mm.

Dual-energy CT quantitative imaging: a comparison study between twin-beam and dual-source CT scanners

Isabel P. Almeida, Lotte E. J. R. Schyns, Michel C. Öllers, and Wouter van Elmpt
Department of Radiation Oncology (MAASTRO), GROW – School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands

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Frank Verhaegen[a)]
Department of Radiation Oncology (MAASTRO), GROW – School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands

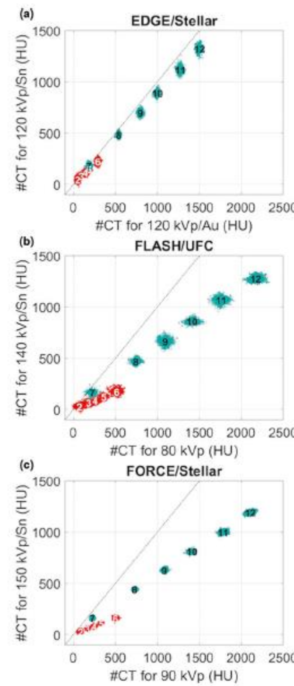

FIG. 3. Low and high energy #CT plots for the iodine (2, 2.5, 5, 7.5, 10, and 15 mg/ml) and calcium (50, 200, 300, 400, 500, and 600 mg/ml) inserts for $CTDI_{vol}$ of approximately 20 mGy for the EDGE (a), FLASH (b), and FORCE (c) scanners. Inserts are numbered from low to high density, in which the iodine inserts have numbers 1 to 6 (iodine 2 mg/ml and 2.5 mg/ml overlap) and the calcium inserts are numbered from 7 to 12. The identity line is plotted in black and each scatter point corresponds to one pixel from each insert's ROI.

EDGE has very poor separation of Hounsfield Units

DECT in low energy photons (brachytherapy)

Radiotherapy and Oncology 100 (2011) 375–379

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Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Dual energy CT

Extracting atomic numbers and electron densities from a dual source dual energy CT scanner: Experiments and a simulation model

Guillaume Landry [a], Brigitte Reniers [a], Patrick Vincent Granton [a], Bart van Rooijen [b], Luc Beaulieu [c,d], Joachim E. Wildberger [b], Frank Verhaegen [a,e,*]

[a] Department of Radiation Oncology (MAASTRO); [b] Department of Radiology, Maastricht University Medical Center (MUMC), The Netherlands; [c] Département de Physique, de Génie Physique et d'Optique, Québec, Canada; [d] Département de Radio-Oncologie et Centre de Recherche en Cancérologie, Université Laval, Québec, Canada; [e] Department of Oncology, McGill University, Montréal, Canada

IOP PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY

Phys. Med. Biol. **56** (2011) 6257–6278 doi:10.1088/0031-9155/56/19/007

Simulation study on potential accuracy gains from dual energy CT tissue segmentation for low-energy brachytherapy Monte Carlo dose calculations

Guillaume Landry[1], Patrick V Granton[1], Brigitte Reniers[1], Michel C Öllers[1], Luc Beaulieu[2,3], Joachim E Wildberger[4] and Frank Verhaegen[1,5]

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DECT in low energy brachytherapy dose calculations

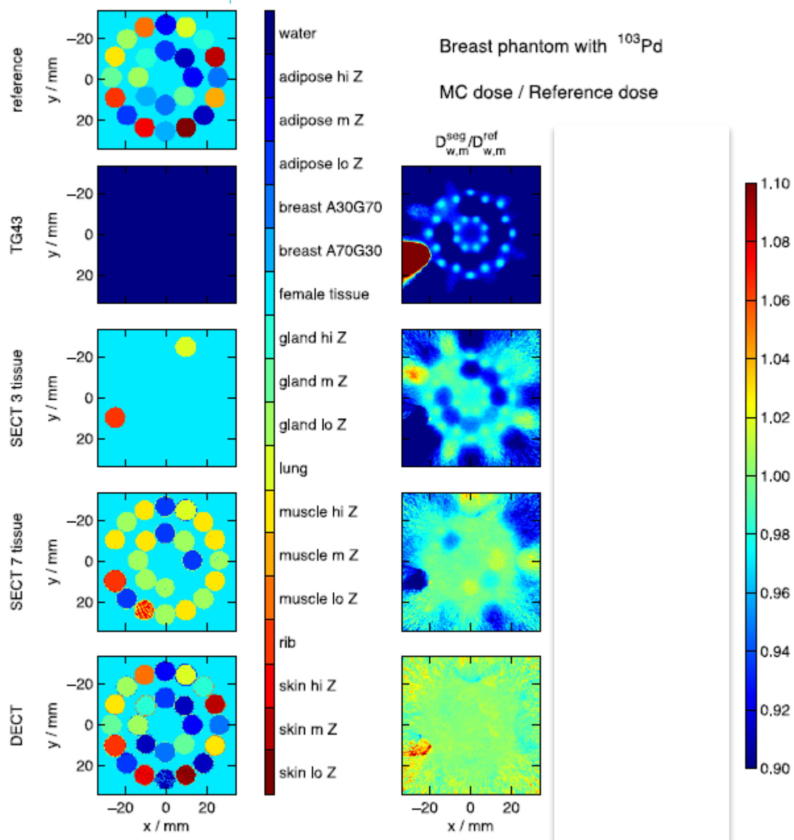


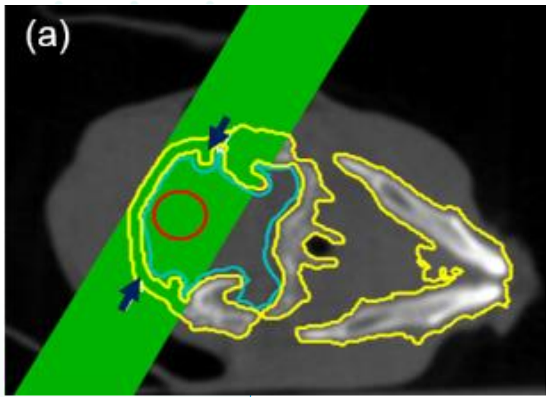
Figure 8. Left: representation of the performance of various segmentation schemes in assigning tissue composition. The top segmentation is the reference. Right: normalized to reference $D_{w,m}$ and $D_{m,m}$ distributions for each segmentation scheme. The radiation source is ^{103}Pd.

DECT leads to much beter tissue separation, which is essential for low-energy dose calcs

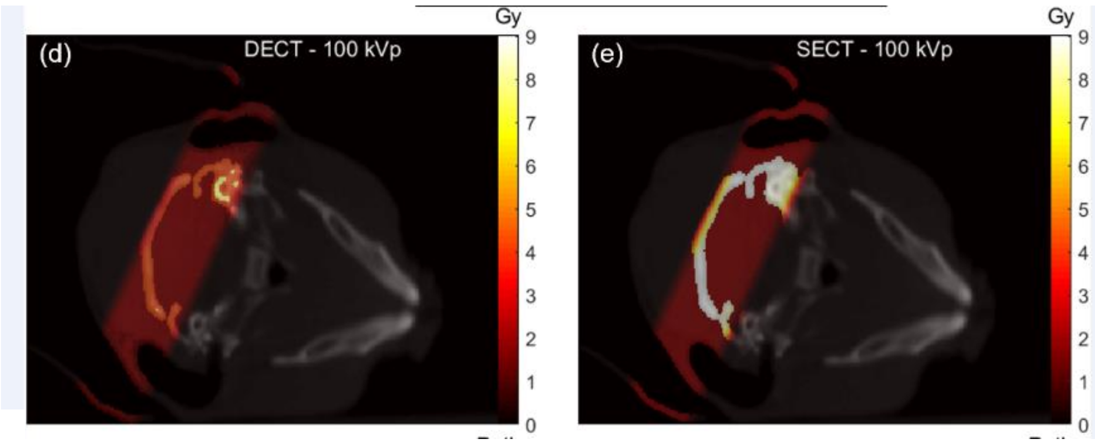
Landry et al. *Sensitivity of low energy brachytherapy Monte Carlo dose calculations to uncertainties in human tissue composition.* Med. Phys. 37, 5188-98, 2010.

Landry et al. *Simulation study on potential accuracy gains from dual energy CT tissue segmentation for low energy brachytherapy Monte Carlo dose calculations.* Phys. Med. Biol. 56, 6257-78, 2011.

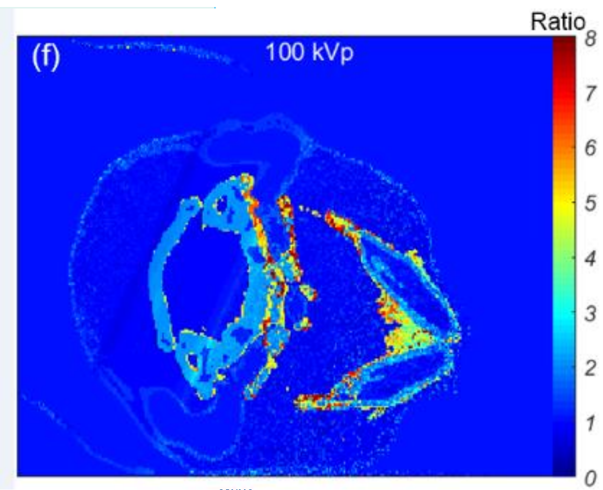
DECT in small animal irradiation



Parallel-opposed beams (100 kVp) mouse brain tumor treatment plan

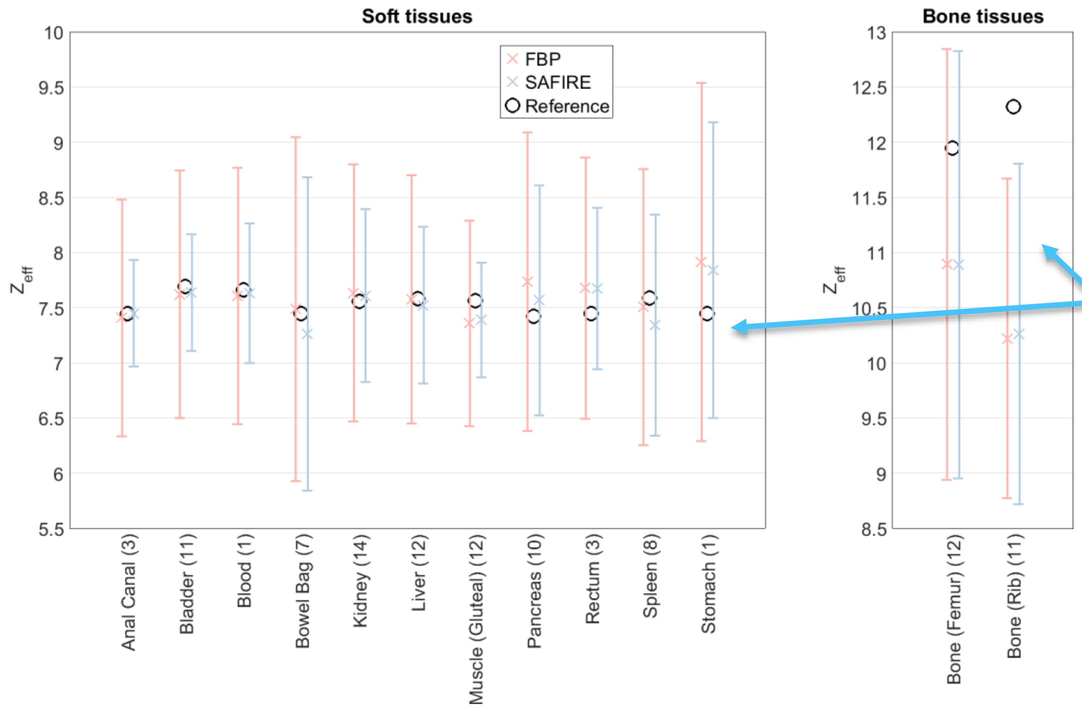


Dose distribution in SECT and DECT images for 100 kVp. SECT has only one type of bone.



Dose ratio (SECT/DECT) for 100 kVp: large dose differences in bone and adipose

DECT to determine human tissue composition: atomic number Zeff



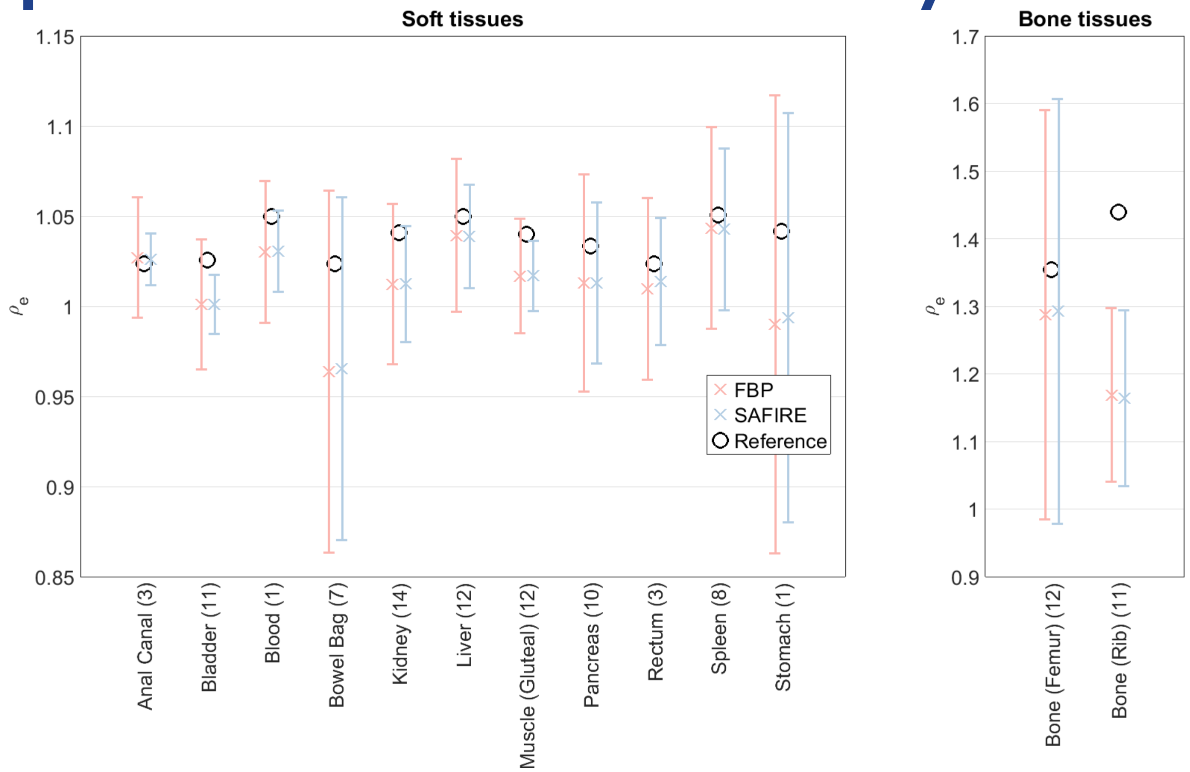
Large mean standard deviation over pts

- 26 patients, organs contoured
- DECT compared to W&W86: agrees reasonably
- DECT with different reconstruction methods:

  filtered backprojection

  Iterative reconstruction

DECT to determine human tissue composition: electron density



≈3-4% difference (DECT – W&W86) in soft tissues

Larger differences in bone

⇨you should take the ρ_e from the CT image, not from W&W86

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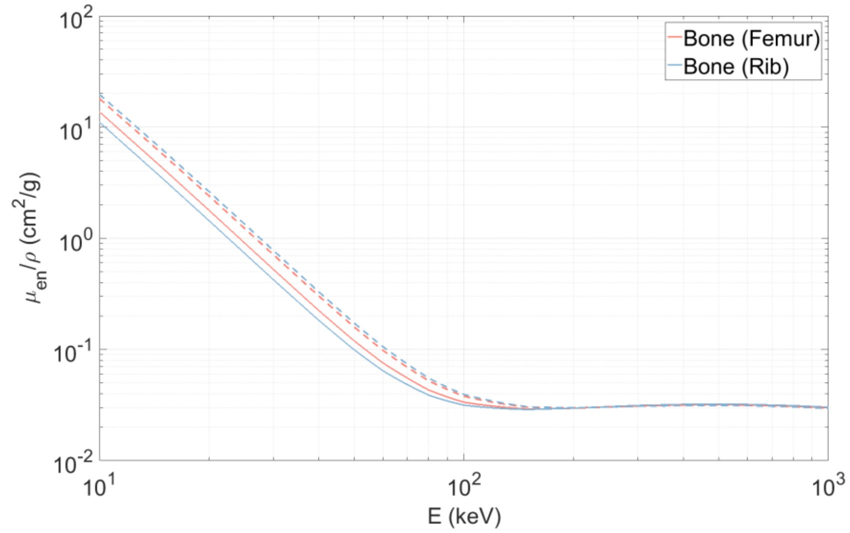
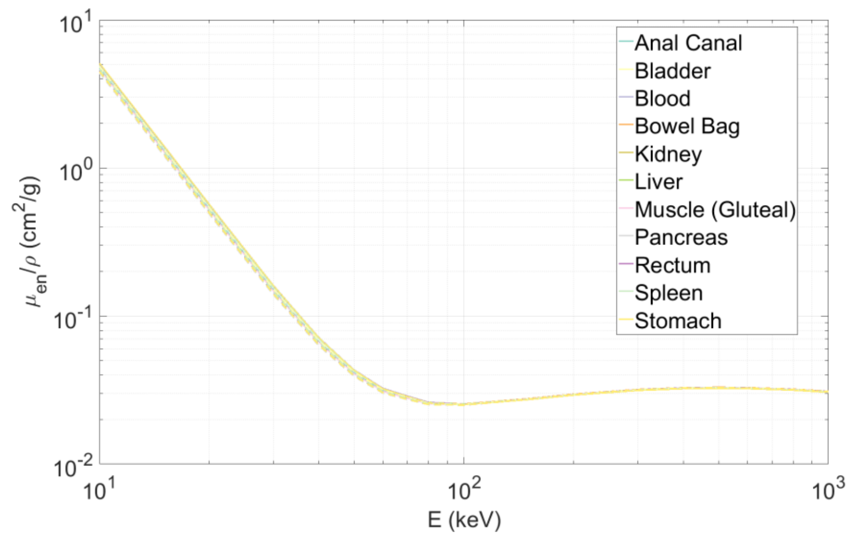
Dose differences (μ_{en}/ρ)





DECT extracted
W&W86

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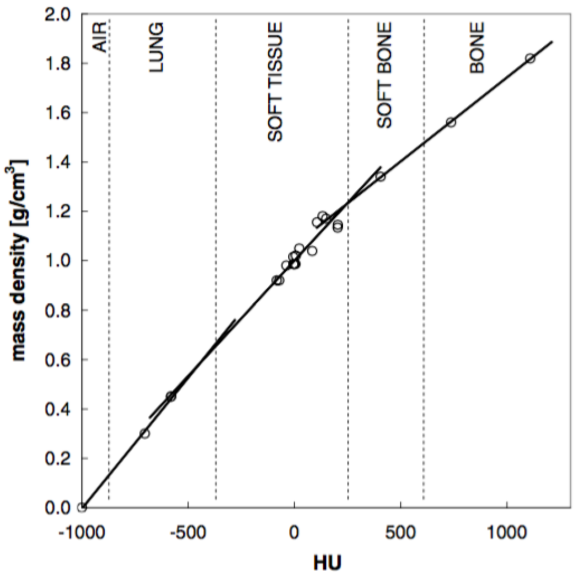
Improved dose calculation proton therapy: SECT based Stopping Power Ratio

Bethe-Bloch formula

$$\mathrm{SPR} = \frac{\varrho_{\mathrm{e,medium}}}{\varrho_{\mathrm{e,water}}} \cdot \frac{\ln\left(\frac{2m_e c^2 \beta^2}{(I_{\mathrm{medium}}/\mathrm{eV})(1-\beta^2)}\right) - \beta^2}{\ln\left(\frac{2m_e c^2 \beta^2}{(I_{\mathrm{water}}/\mathrm{eV})(1-\beta^2)}\right) - \beta^2}$$



- CT Calibration curve
  - ρ_e
  - Material ⇨ Ionization potential
- Choices to be made:
  - how many linear segments should be used?
  - which tissue-equivalent materials are suitable for calibration?
  - where should the boundaries between tissue types be set?

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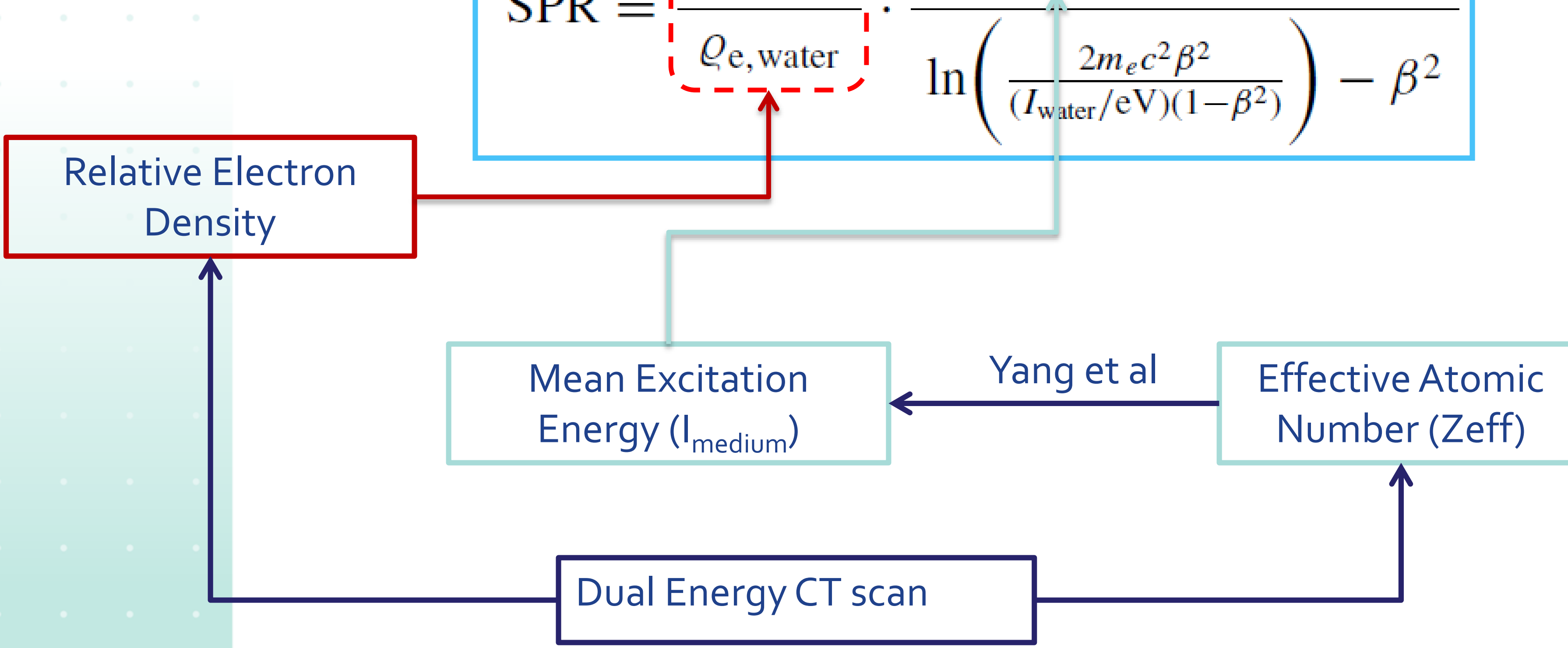
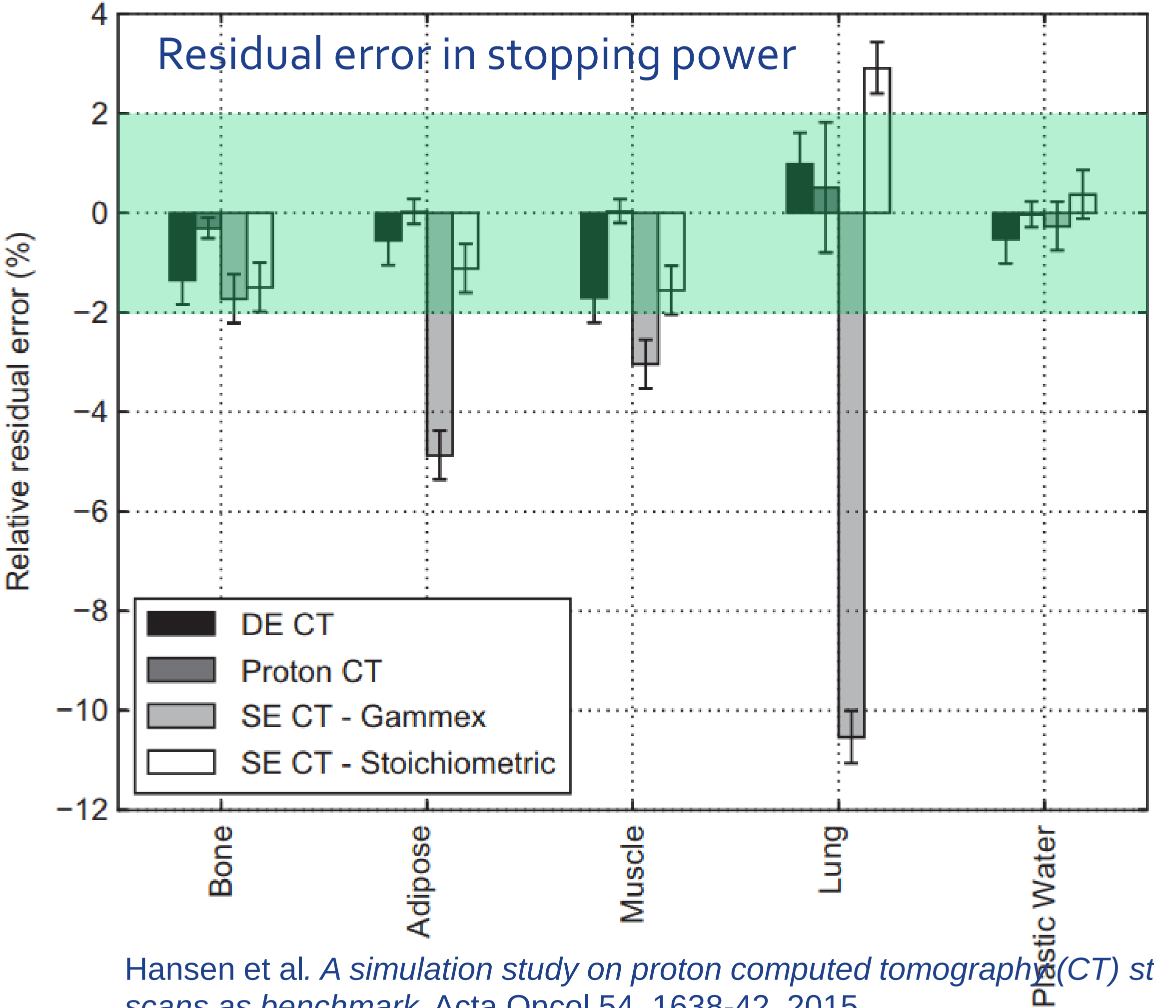
DECT based estimation of Stopping Power Ratio

Bethe-Bloch formula

$$\mathrm{SPR} = \frac{\varrho_{\mathrm{e,medium}}}{\varrho_{\mathrm{e,water}}} \cdot \frac{\ln\left(\frac{2m_e c^2 \beta^2}{(I_{\mathrm{medium}}/\mathrm{eV})(1-\beta^2)}\right) - \beta^2}{\ln\left(\frac{2m_e c^2 \beta^2}{(I_{\mathrm{water}}/\mathrm{eV})(1-\beta^2)}\right) - \beta^2}$$



Comparison different approaches for SPR estimation: SECT vs DECT vs proton CT

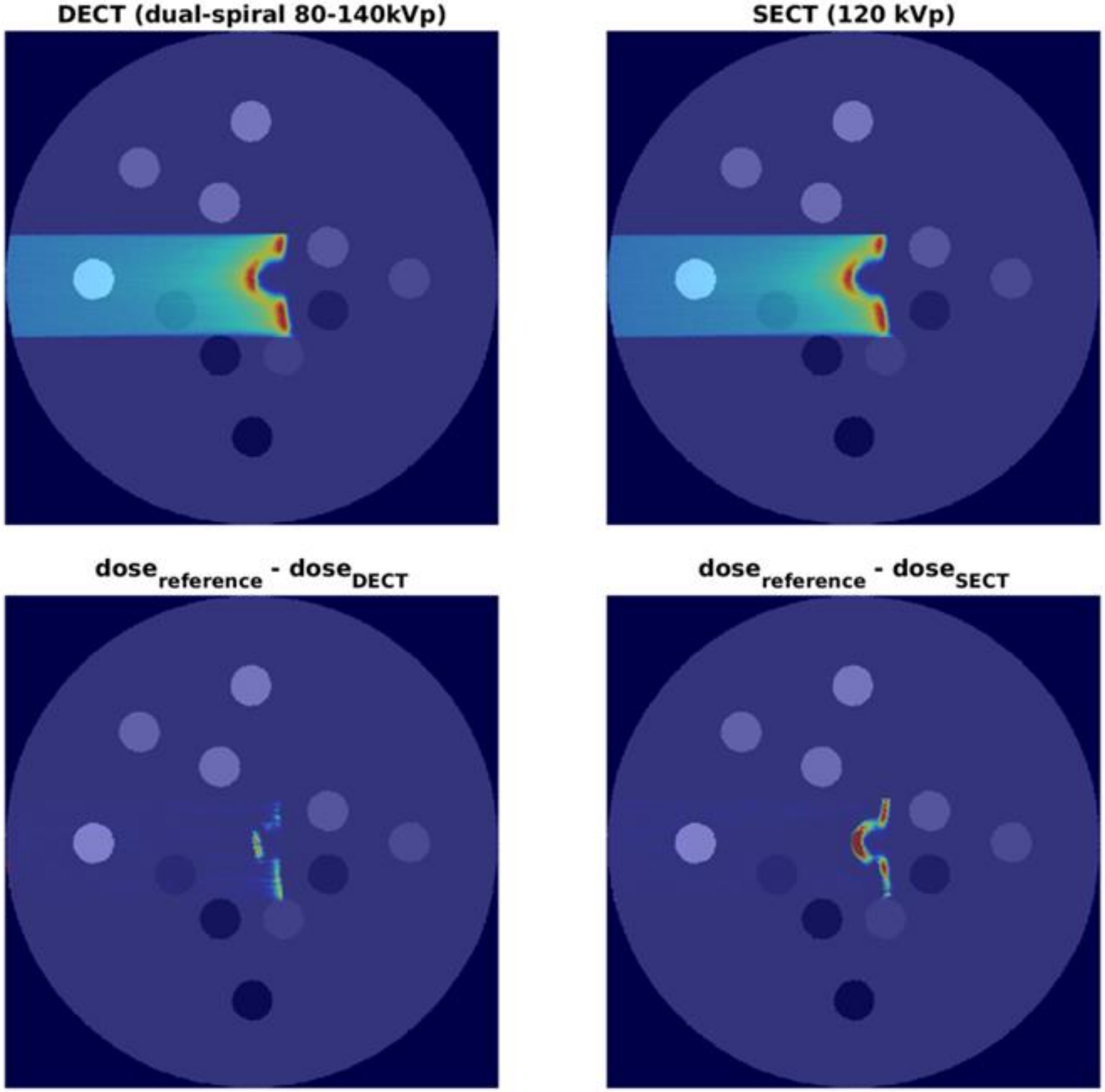


Conversion of SECT into stopping power results in ~3-4% range uncertainty

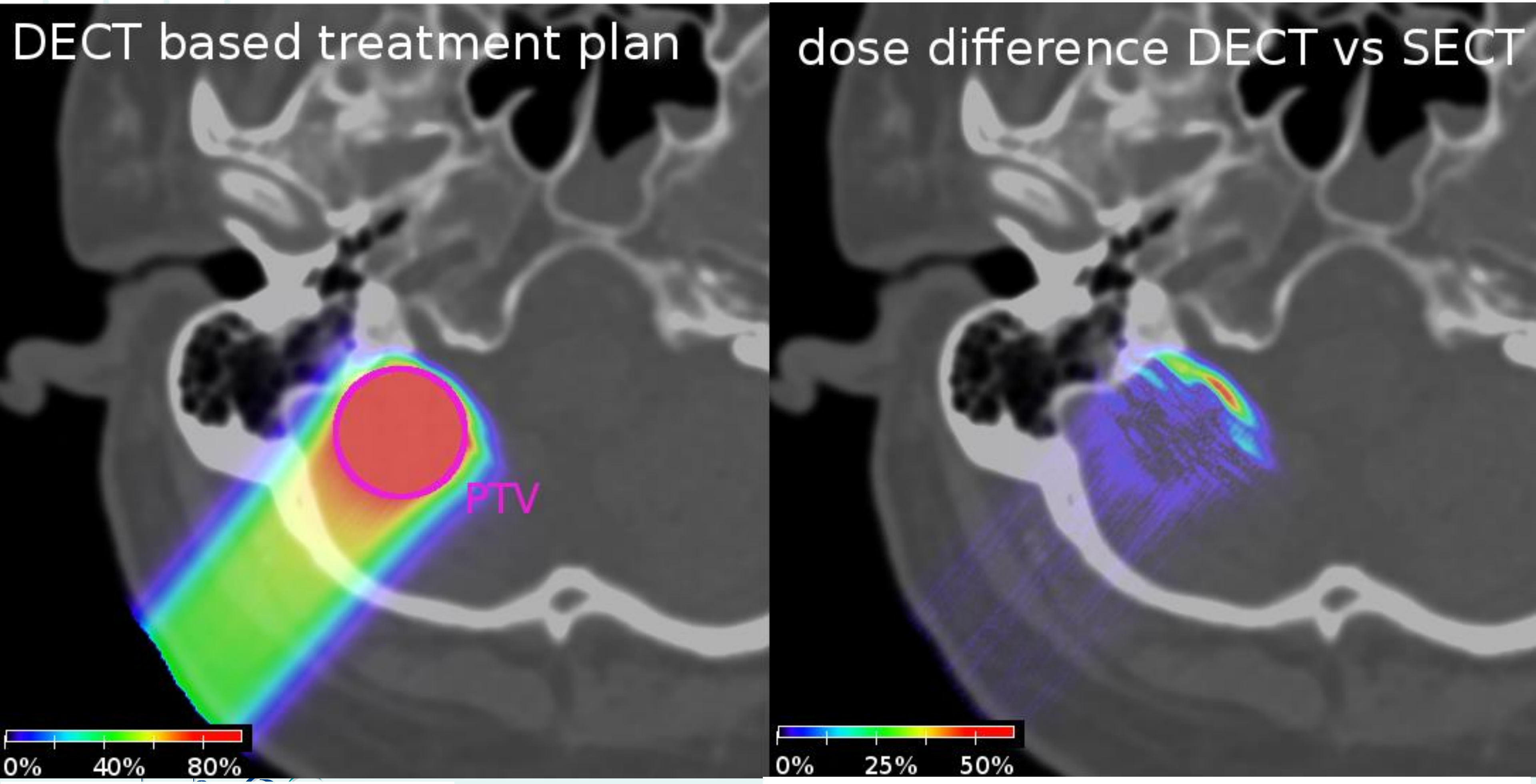
DECT allows for a reduction in this uncertainty → smaller safety margins

Hansen et al. *A simulation study on proton computed tomography (CT) stopping power accuracy using dual energy CT scans as benchmark.* Acta Oncol 54, 1638-42, 2015

DECT vs SECT proton range



DECT vs SECT: Proton therapy plan



Courtesy: Guillaume Landry, LMU

Hudobivnik et al. Med Phys 2016

Remark

- No treatment planning system can currently handle DECT images directly
  - Varian/Siemens, RaySearch, … are thinking about it
- Can already use the improved electron density from DECT
- Atomic number info / tissue segmentation can only be used indirectly currently
- Pseudo-monochromatic images could be used e.g.for contouring

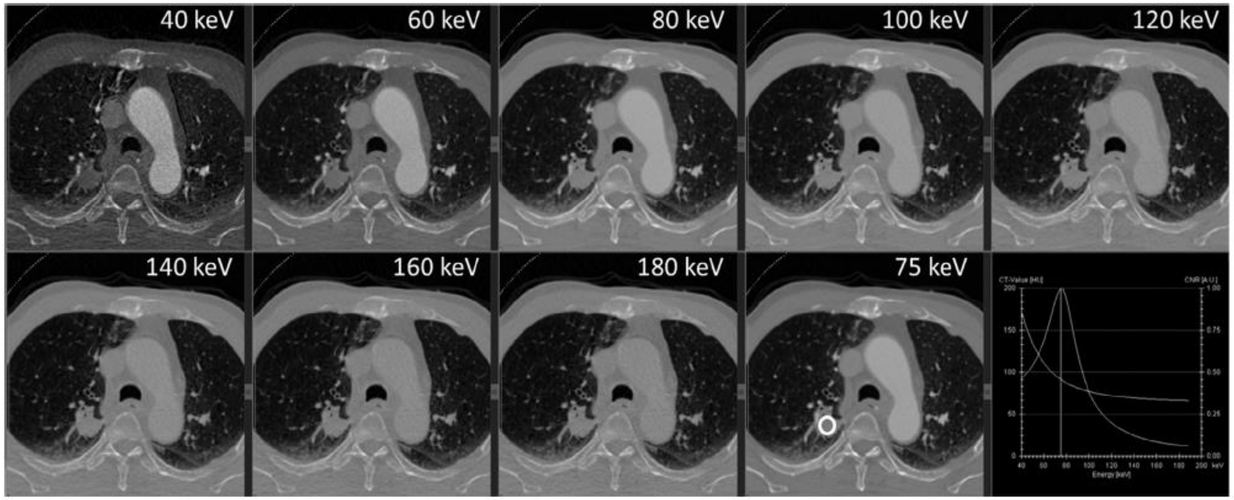


Fig. 2. Example of a mono-energetic reconstruction of a lung cancer patient. Various keV energy levels are reconstructed ranging from 40 keV to 180 keV. The bottom right panel shows the average Hounsfield Unit inside the region of interested together with an estimate of contrast-to-noise ratio, showing that 75 keV was optimal for this patient.

Noise reduction in Z-images with iterative reconstruction

Improved dose calculation accuracy for low energy brachytherapy by optimizing dual energy CT imaging protocols for noise reduction using sinogram affirmed iterative reconstruction

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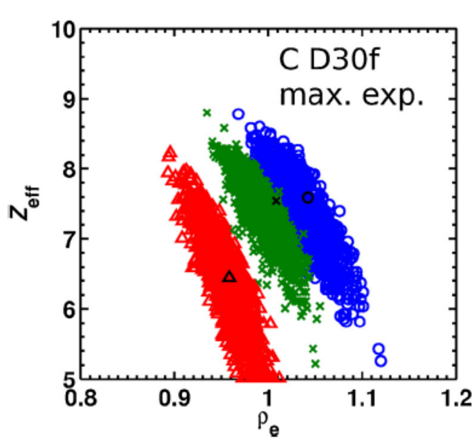
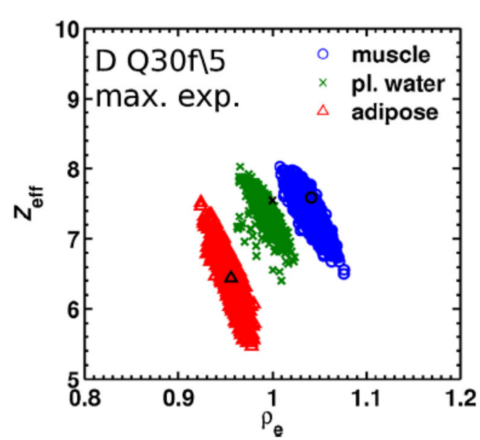
[f] Medical Physics Unit, Department of Oncology, McGill University, Montréal, Québec, Canada

Filtered backprojection



Iterative reconstruction



Applications of DECT in-vivo range measurements in ion therapy

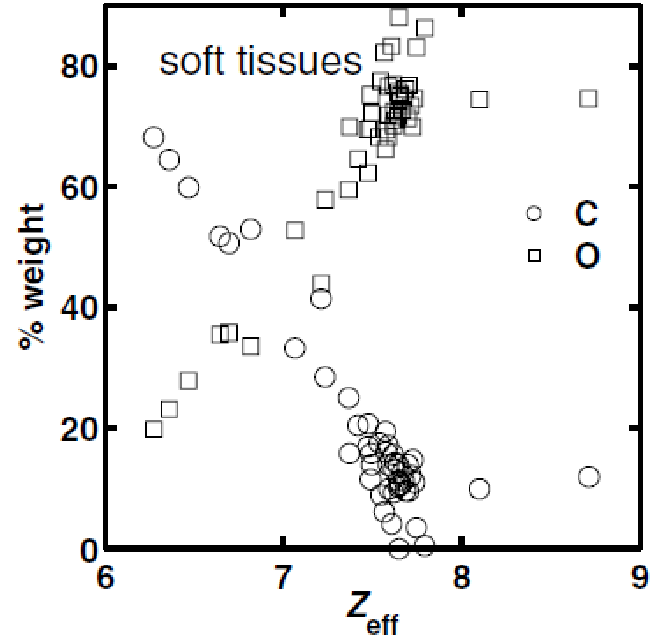
C, O emit positrons (+annihilation photons) or prompt gammas

- Determine Zeff from DECT
- Determine C, O concentrations from Zeff

IOP Publishing | Physics in Medicine and Biology
Phys. Med. Biol. 58 (2013) 5029–5048 | doi:10.1088/0031-9155/58/15/5029

Deriving concentrations of oxygen and carbon in human tissues using single- and dual-energy CT for ion therapy applications

Guillaume Landry[1], Katia Parodi[2], Joachim E Wildberger[3] and Frank Verhaegen[1,4]



% weight for C, O vs Zeff

Conclusions: What have we learned from all these studies

- DECT gives better estimates of ρ_e: good for all dose calculations
- DECT gives Z-maps: good for low energy photons and protons
- DECT gives better estimates for proton SPR
- It matters which CT scanner you're using
- Tissue compositions are uncertain ☹
  - Both in academic sense & in how you derive them from imaging
  - Human tissues need more study
  - Animal tissues completely unknown

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Future work

- Do we need individual tissue compositions?
  - How?
- Or are averages (with age?) sufficient?

- Do we need spectral CT to characterize tissues

Acknowledgments

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- Dr Wouter van Elmpt (Maastro Clinic)

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  - Varian Medical Systems
  - Siemens Healthineers
  - IBEX
  - Eurostars (EU) research program

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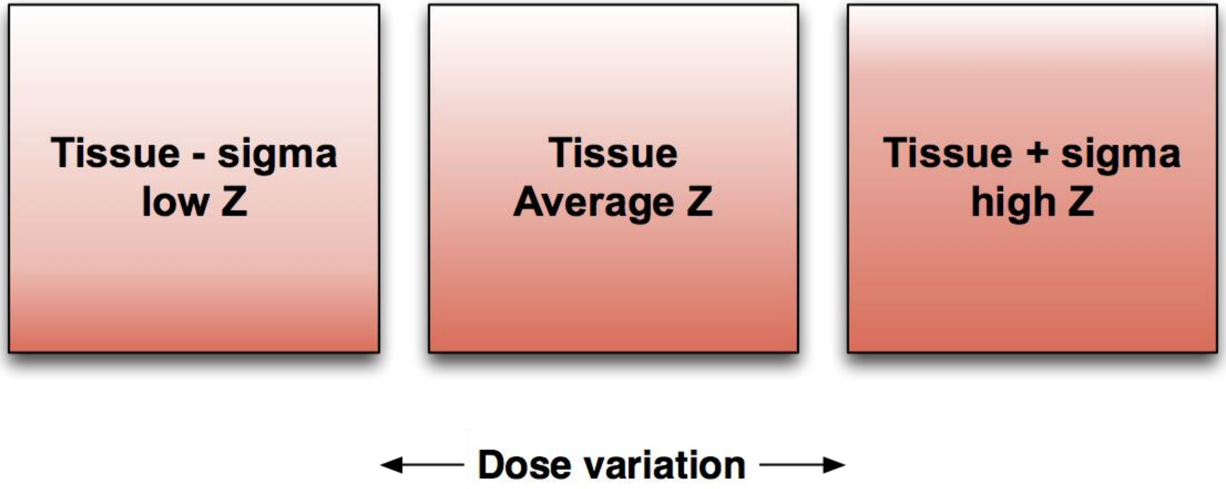
Backup slides

“Dead mouse moving”

Sensitivity of dose calcs to tissue composition

- Assess the influence in tissue composition and its variation across the population on dose calculations
- Compare everything to water (commonly used for low-energy photons (brachytherapy))



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A good way to misassign densities

- For tissue compositions everyone refers to W&W86
- In clinical practice ρ(e) is commonly deduced from CT scan
  - We have seen the calibration is critical
- If one would get ρ from W&W86
  ⇨additional 2% uncertainty

Moreover, ρ depends on temperature, so make sure you use the 37° density values!

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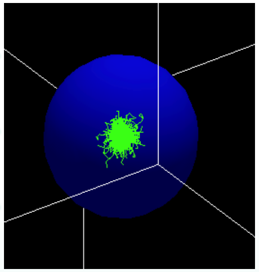
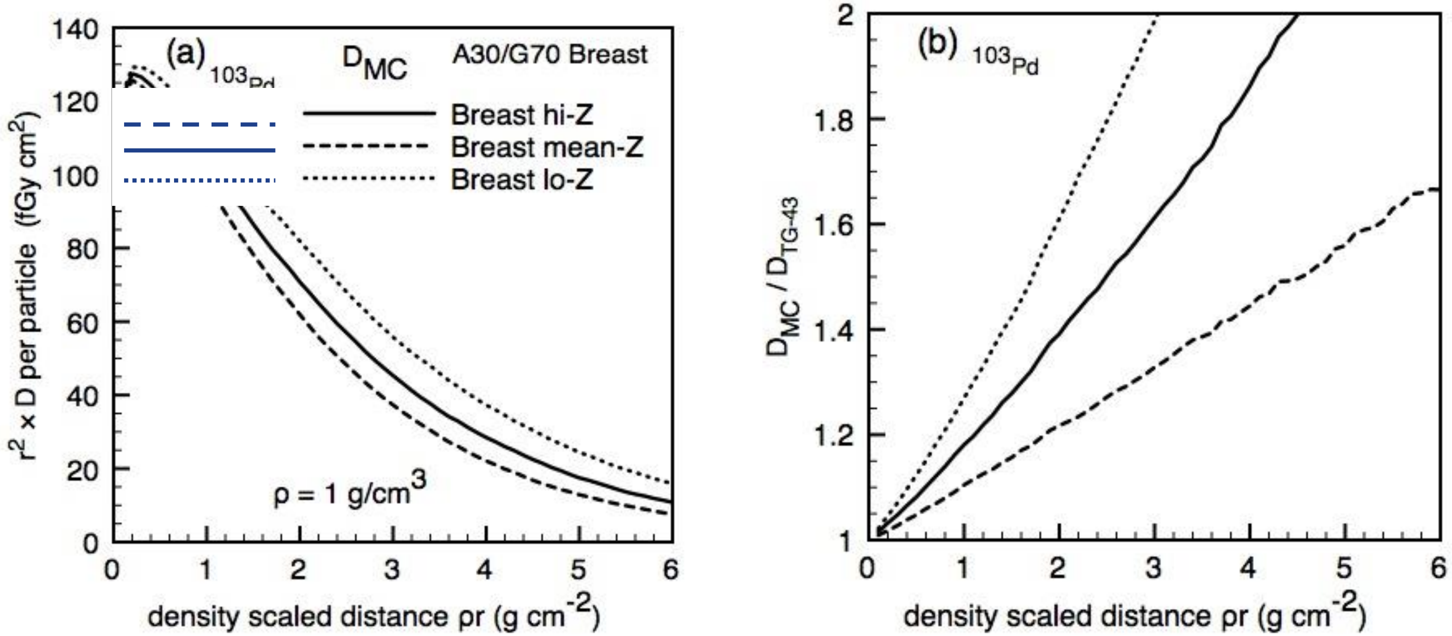
Simulation - breast tissue (adipose + gland)



Point source in infinite geometry



- D can differ from D_{water} by >80% in 3cm
- Difference due to variation in breast composition
- Different low energy sources behave differently

(Landry et al. *Sensitivity of low energy brachytherapy Monte Carlo dose calculations to uncertainties in human tissue composition.* Med. Phys. 37, 5188-98, 2010)

Even trace elements influence the dose

TABLE III. Material definitions. Water is given for comparison.

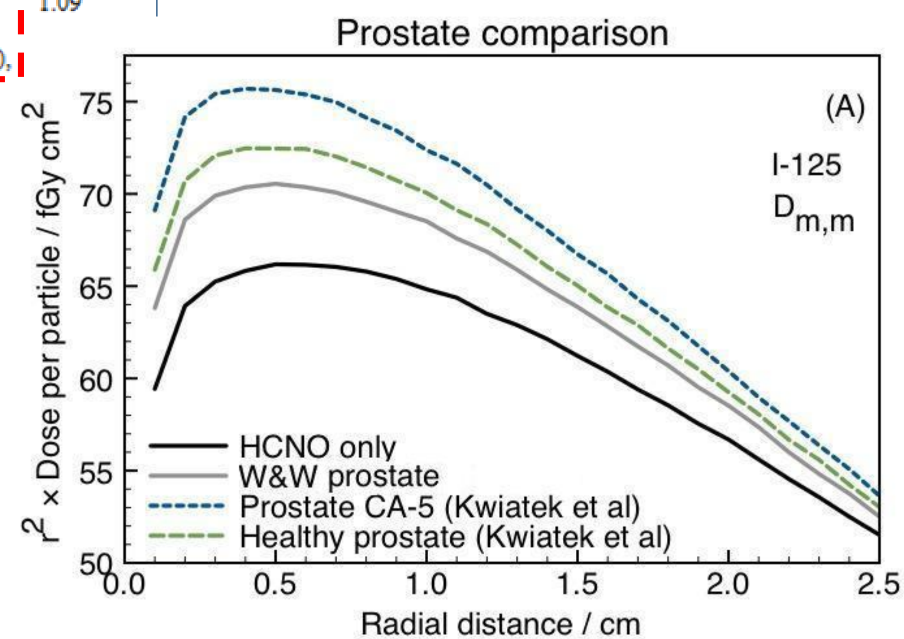
Tissue	H	C	N	O	Z > 8	Mass densit
	% by weight					g·cm^{-3}
Prostate[105]	10.5	8.9	2.5	77.4	Na(0.2), P(0.1), S(0.2), K(0.2)	1.040
Mean adipose[105]	11.4	59.8	0.7	27.8	Na(0.1), S(0.1), Cl(0.1)	0.95
Mean gland[105]	10.6	33.2	3.0	52.7	Na(0.1), P(0.1), S(0.2), Cl(0.1)	1.02
Mean soft tissue[104]	10.1	11.1	2.6	76.2		1.00
Mean skin[104]	10.0	20.4	4.2	64.5	Na(0.2), P(0.1), S(0.2), Cl(0.3), K(0.1)	1.09
					Na (0.1), Mg (0.2), P (10.3), S (0.3),	

Woodard and White, 1986

- > 10% difference compared to pure HCNO
- Dependence on distance

⇨photo-electric effect is to blame!

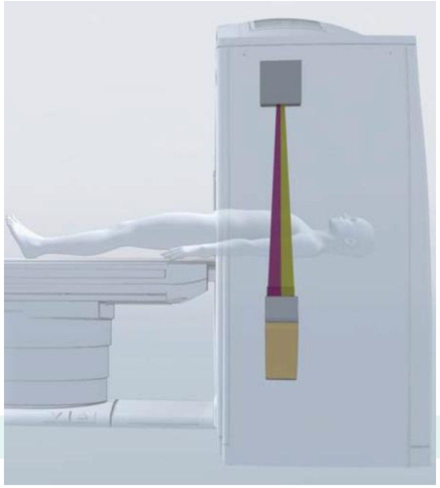
What about prostate calcifications?
Difference between healthy/cancerous tissue?

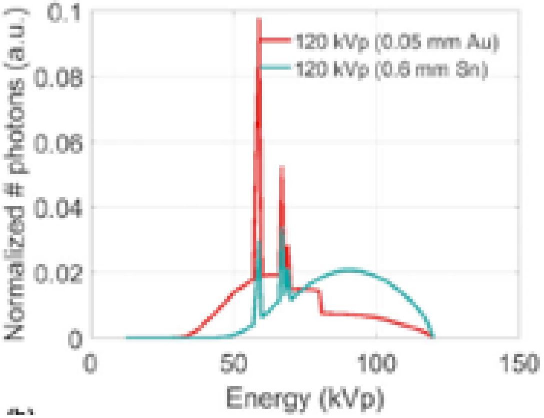


(White et al. *Influence of trace elements in human tissue in low energy photon brachytherapy dosimetry*. Phys Med Biol 57, 3585–3596, 2012)

Imaging technology for Dual Energy CT

- Rotate-Rotate DECT: two sequential helical CT scans at different kVp (‘poor man’s DECT’)
- Dual Source – Dual Detector approach (Siemens)
- Rapid kV switching (GE)
- Dual-layer detector technology (Philips)
- Single Source – sequential rotations with different kVp (Toshiba)
- Split-beam (Siemens)

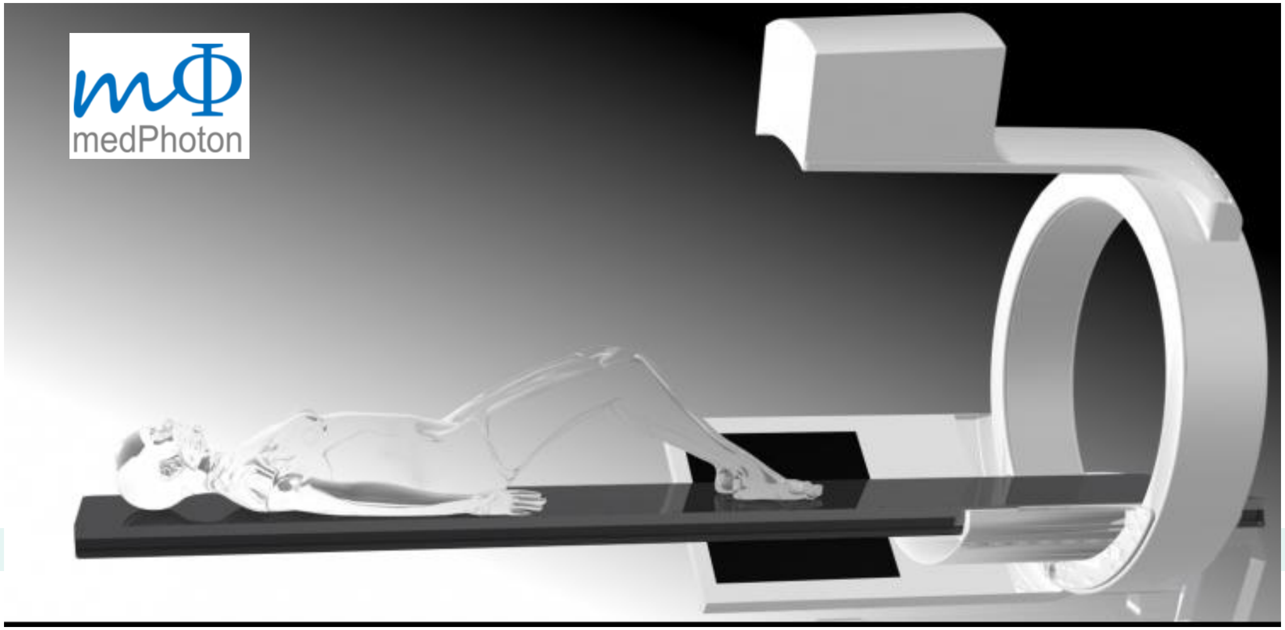




Split filter: Au and Sn

Dual energy Cone Beam CT: Imaging Ring System (medPhoton)

- CBCT with Rapid-switching dual-energy system
- Independent x-ray source and imaging panel
- Many more degreesof freedom compared to conventional CBCT
- Project to develop multi-energy imaging system for photon and proton radiotherapy



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MC dose calculation is perfect, but it requires imperfect images as input
Sensitivity study 2005
CT artifacts exaggerated in MC (due to material assignment, artifacts can be set to bone)
Stoechiom method + problems with different phantoms
Sensitivity of low energy photon dose calculations
Trace elements
Where to get data on human tissues? (story of ORNL)
Mostly CT, sometimes MRI (look up papers MR based dose calculations – would be very logical for MR-linac)
CT comes in many flavors: CT/DECT/ spectral CT/ CBCT
Using different CT scanners can lead to different results: some CT scanners especially made for radiotherapy are not doing all that well
DECT works for brachy (esp low energy)!
No TPS can handle DECT
Small animal systems, a kV application where it matters
-DECT, spectral CT
Protons: seems to be consensus SPR are better estimated, but by how much?
"Dead mouse moving"
Lotte's tissue overview
TG186 recommendations
Is there an advantage for MV? Perhaps contouring
General DECT info (PMI, Zeff, …)

Radiomics
Overview TPS: which imaging data can they handle?