Dual Energy Computed Tomography For Proton Dose Calculation

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Disclosure

- **Research funding: Varian Medical Systems**

Learning Objectives

1. Understand the different implementations of dual energy CT in commercial scanners.
2. Understand the methods for processing DECT for estimating material composition properties: Zeff, electron density and proton SPR
3. Understand methods to validate DECT derived SPR and its clinical impact

What is Dual-Energy (Spectral) CT?

What: Acquiring 2 CT images with different kVp

How: Exploit differential response of materials to different X-ray spectra

- Compton effect → low kV dependence, ~ electron density
- Photoelectric effect ~Z^3/E^3 ← High Z dependence

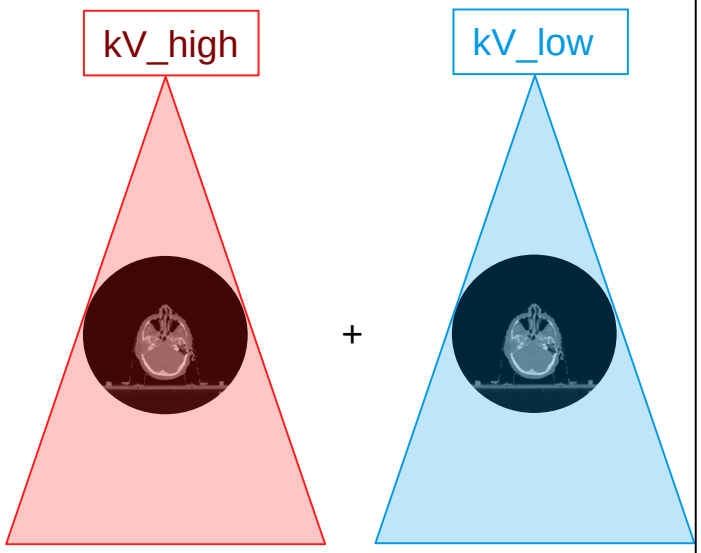
Use:

- Calculate material properties: electron density, Z_{eff}
- Quantify Iodine (Z=53) and Calcium (Z=20) concentrations
- Reconstruct virtual monochromatic images at any kV
- More accurate proton Stopping Power Ratio (SPR) calculation for dose calculation

* Yang et al 2000, Phys Med Biol 55 1343

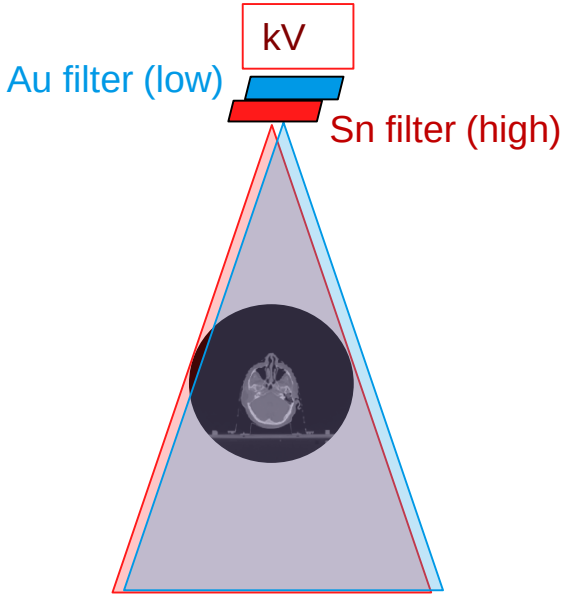
Dual Energy CT Acquisition Modes

Single Source, Sequential scans



- Widely available
- **Time delay**: Motion between scans
- Deformable Image Registration step may be required

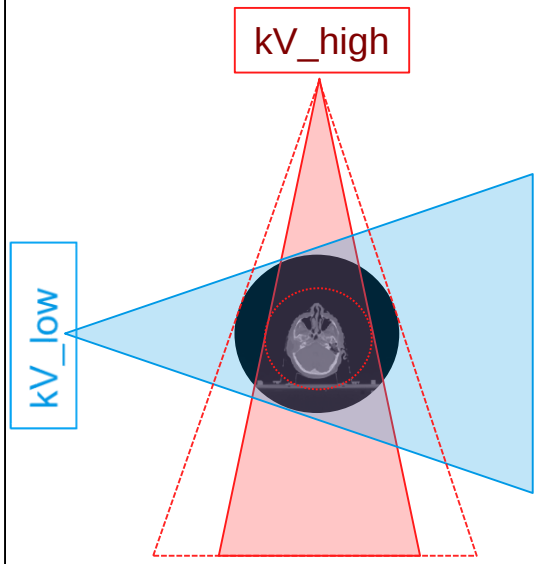
Single Source, eg Split filter (TwinBeam), Photon counting detector



- Single acquisition
- Other implementations:

1. Multi-layer energy sensitive detector (Spectral CT, Photon Counting CT)
2. Rapid kVp switching

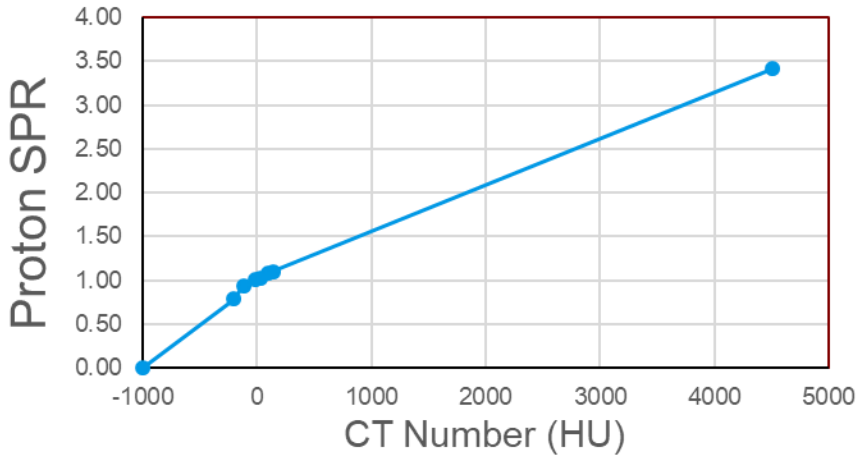
Dual Source



- Near simultaneous acquisition
- One detector has smaller field of view (FOV)
- Higher cost
- Potential for cross-scatter contamination

kV_high typically 140kVp with or without filter eg Sn or up to 150 kVp
kV_low typically 70 to 90 kVp

SECT Calibration for Proton Therapy



Traditional SECT calibration:

- Assume one to one correspondence between CT number (HU) and SPR- **not true for human tissue**
- Use tissue surrogate phantom with known SPR

Either

(a) Tabulate HU vs SPR directly

OR

(b) Use Stoichiometric method *Schneider PMB 14 111-24 1996, Ainsley JACMP 15 202-220 2014*

(minimize impact of use of nonhuman tissue)

SECT has a tissue-dependent uncertainty- up to ~3-4% error

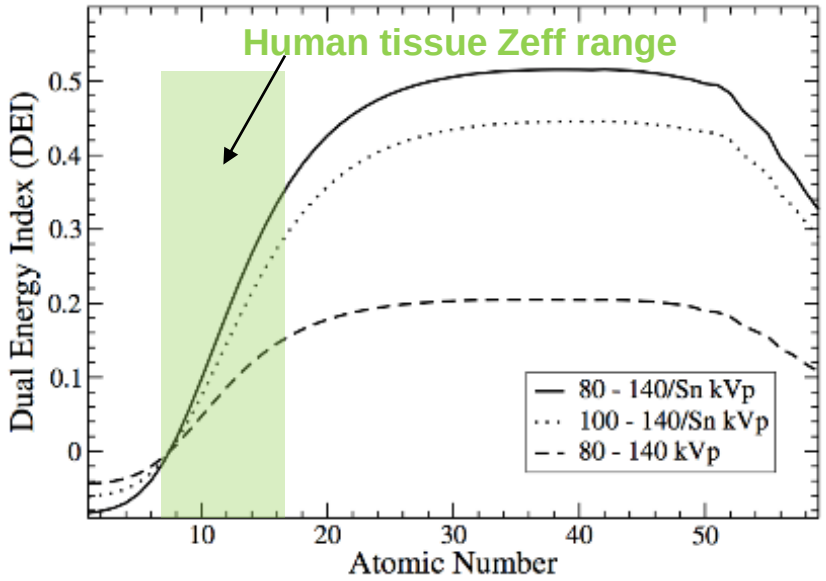
Dual-energy CT (DECT) has been predicted to be superior to SECT (~1% accuracy)

Proton Stopping Power Ratio from DECT

Stopping Power Ratio (SPR) can be calculated using Bethe-Bloch eqn:

$$SPR = \rho_e \frac{\log\left[\frac{2m_e c^2 \beta^2}{I_m(1-\beta^2)}\right] - \beta^2}{\log\left[\frac{2m_e c^2 \beta^2}{I_{water}(1-\beta^2)}\right] - \beta^2}$$

$$lnI_m \equiv h(Z_{eff}) = \sum_{m=0}^{M} c_m Z_{eff}^m$$



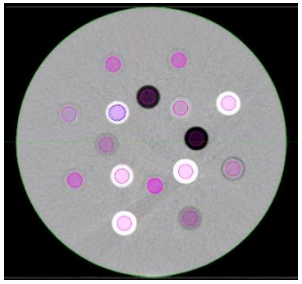
Bourque et al Phys. Med. Biol. 59 (2014) 2059

ρ_e : electron density

I_m : excitation energy of the medium, calculated from Zeff: effective atomic number

- **DECT can remove the degeneracy by defining new variable, eg DEI = $(u_L-u_H)/(u_L+u_H)$**
- **Mapping between DEI and Z_{eff} is bijective for human tissues**
- **DECT can be used to calculate ρ_e and Zeff to derive SPR**

Calculating ρ_e and Z_{eff} from DECT



1. **Scan tissue density phantom** $u_{L/H} = (HU_{L/H} + 1000)/1000$
2. **Compute Dual energy Index (DEI) or Dual energy ratio (DER)**

$$\Gamma \equiv \begin{cases} \dfrac{u_L - u_H}{u_L + u_H} & \text{for} \quad \Gamma = \text{DEI} \\ \dfrac{u_L}{u_H} & \text{for} \quad \Gamma = \text{DER}. \end{cases}$$

3. **Fit known ρ_e and Z_{eff} values of tissue surrogates to power functions of** Γ

$$Z_{\text{eff}} = \sum_{i=0}^{K} \overline{a}_i \Gamma^i,$$

$$\rho_{e,L/H} = \frac{u_{L/H}}{\sum_{l=0}^{L} \overline{b}_{l,L/H} Z_{\text{eff}}^l}$$

$$\ln I_m = \sum_{m=0}^{M} c_m Z_{\text{eff}}^m$$

Phys. Med. Biol. 59 (2014) 2059 A E Bourque et al

Other Methods to Extract ρ_e and Z_{eff}

- **The relative electron density can be expressed by the weighted differences of HU_H and HU_L (Saito Med Phys (39) 4 2012):**

$$\rho_e = a \cdot \frac{(1+\alpha)\mathrm{HU_H} - \alpha \mathrm{HU_L}}{1000} + b$$

a, b, α are fit parameters

- **The effective atomic number (eg Almeda Med Phys (44) 171 2017, Landry PMB (58) 6851 2013, several other parameterization methods available):**

$$\mu^{\text{Low kVp}}_{\text{High kVp}} = \frac{\mathrm{A} + \mathrm{B}Z_{\text{eff}}^{n-1} + \mathrm{C}Z_{\text{eff}}^{m-1}}{\mathrm{D} + \mathrm{E}\,Z_{\text{eff}}^{n-1} + \mathrm{F}\,Z_{\text{eff}}^{m-1}}$$

μ=is attenuation coeff from HU. A, B, C, D, E, F are fit parameters

Summary of DECT Methods

E Bar et al Med. Phys. 44 (6), June2017 pp 2332-2344 Tables 1 and 2

TABLE I. Summary of the theoretical foundation of different DECT formalisms.

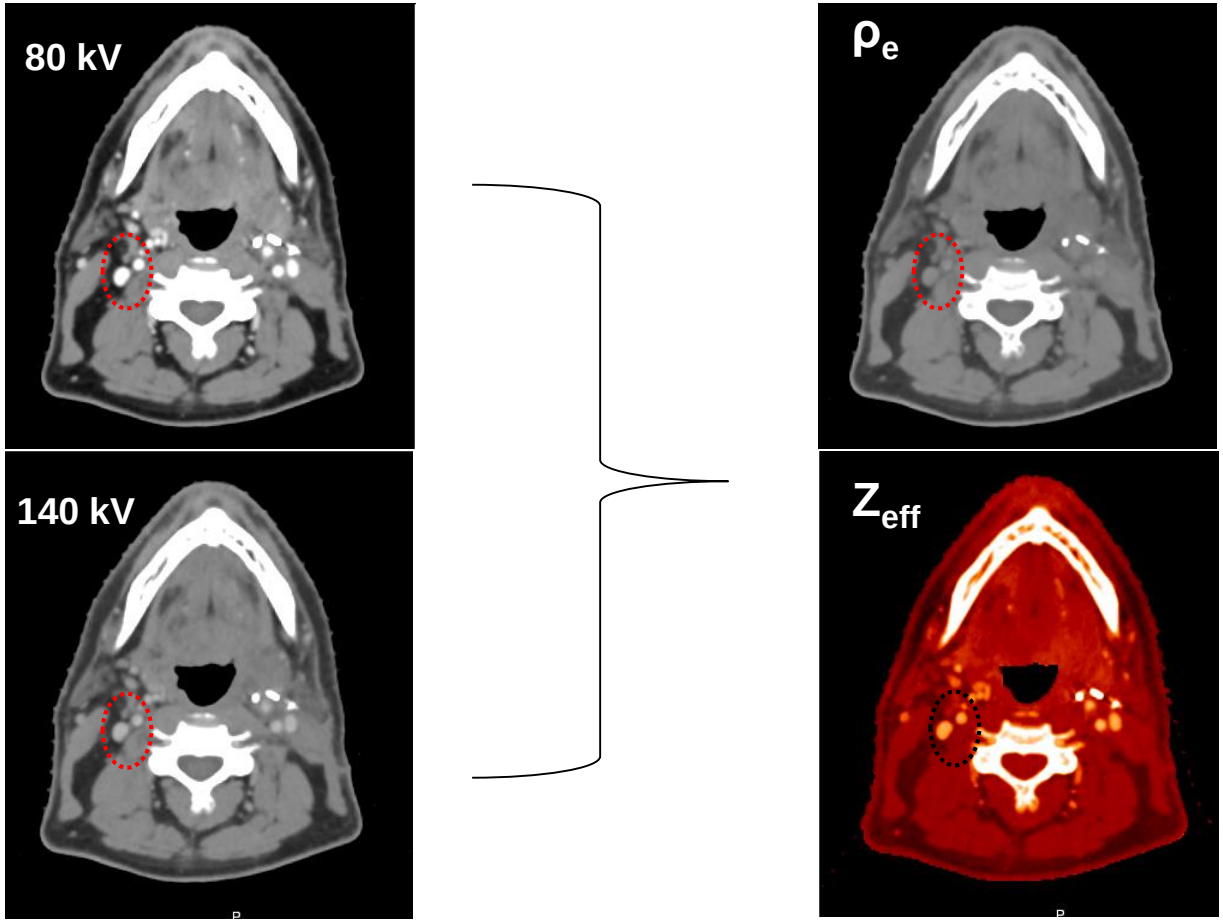
	μ parametrization	Z definition	Requires CT calibration
Bazalova et al.	$\mu = \rho_e \sum_i w_i (Z^4 F(E_i, Z) + G(E_i, Z))$	Mayneord (m = 3.5)	No
Landry et al. #1 and #2	$\mu = \rho_e (A + BZ^m + CZ^n)$	Mayneord (m = 3.3)	Yes
Hünemohr et al. #1 and #2	$\mu = \rho_e (\alpha \frac{Z^m}{E^l} + \beta)$	Mayneord (m = 3.1)	Yes
Bourque et al.	$\mu/\mu_w = \rho_e \sum_{m=1}^{M} b_m Z^{m-1}$	Behavior of electronic cross sections for elements	Yes
Van Abbema et al.	$\mu = \int_0^\infty w(E)_e \sigma^{tot}(E, \widehat{Z}) dE$	Behavior of $\frac{\mu_L}{\mu_H}$ for mixtures	No
Han et al.	$\mu = c_1 \mu_1 + c_2 \mu_2$	None	Yes
Lalonde and Bouchard	$\mu/\mu_w = \overline{y}_0 f_0 + \sum_{k=1}^{K} y_k f_k$	None	Yes

TABLE II. Summary of different formalisms to predict tissue parameters with DECT.

	EAN	I-value	ED
Bazalova et al.	solve $\frac{\mu_L}{\mu_H}$ numerically	Yang et al.	substitute $\widehat{Z}$
Landry et al. #1 and #2	solve $\frac{\mu_L}{\mu_H}$ for Z	Yang et al. Bragg additivity rule	$\widehat{\rho}_e = \frac{\Delta HU}{1000} + 1$
Hünemohr et al. #1 and #2	substitute $\widehat{\rho}_e$	Yang et al. Bragg additivity rule	$\widehat{\rho}_e = \frac{1}{\beta} \frac{g_L \mu_H - g_H \mu_L}{g_L - g_H}$
Bourque et al.	$\widehat{Z}_{eff} = \sum_{k=1}^{K} c_k \Gamma^{k-1}$	5th-order fit with Z_{med}	$\widehat{\rho}_{e,L/H} = \frac{u_{L/H}}{\sum_{m=1}^{M} b_{m,L/H} Z_{eff}^{m-1}}$
Van Abbema et al.	solve $\frac{\mu_L}{\mu_H}$ numerically	Yang et al.	substitute $\widehat{Z}$
Han et al.	None	$\widehat{I}_x = f_I (\frac{c_1}{c_1 + c_2}) \exp(\frac{c_1 \rho_{e1} \ln(I_1) + c_2 \rho_{e2} \ln(I_2)}{c_1 \rho_{e1} + c_2 \rho_{e2}})$	$\widehat{\rho}_{ex} = c_1 \rho_{e1} + c_2 \rho_{e2}$
Lalonde and Bouchard	None	Bragg additivity rule	$\widehat{\rho}_e = \overline{y}_0 + \sum_{k=0}^{K} y_k$

CT Scanner: ρ_e and Z_{eff}

- Commercial CT scanners have software that outputs ρ_e and Z_{eff} images
- User needs to independently verify accuracy



Location with contrast media- higher HU on low kV image

Using DECT SPR with TPS

Given ρ_e and Z_{eff} :

$$SPR = \rho_e \frac{\log\left[\frac{2m_e c^2 \beta^2}{I_m(1-\beta^2)}\right] - \beta^2}{\log\left[\frac{2m_e c^2 \beta^2}{I_{water}(1-\beta^2)}\right] - \beta^2}$$

$$lnI_m \equiv h(Z_{eff}) = \sum_{m=0}^{M} c_m Z_{eff}^m$$

$$SPR = \begin{cases} \rho_e & ;\ 0 \le Z_{\text{eff}} < 0.5 \\ \left(1.1114 - 0.0148\, Z_{\text{eff}}\right) \rho_e & ;\ 0.5 \le Z_{\text{eff}} < 8.5 \\ 0.9905\, \rho_e & ;\ 8.5 \le Z_{\text{eff}} < 10 \\ \left(1.1117 - 0.0116\, Z_{\text{eff}}\right) \rho_e & ;\ Z_{\text{eff}} \ge 10 \end{cases}$$

Hunemohr *et al*
Phys Med Biol. 59 (2014) 83-96

1. **Import calculated SPR image to TPS and create unity look up table**
2. **Convert SPR image to HU using inverted SECT HU to SPR table.**

TPS

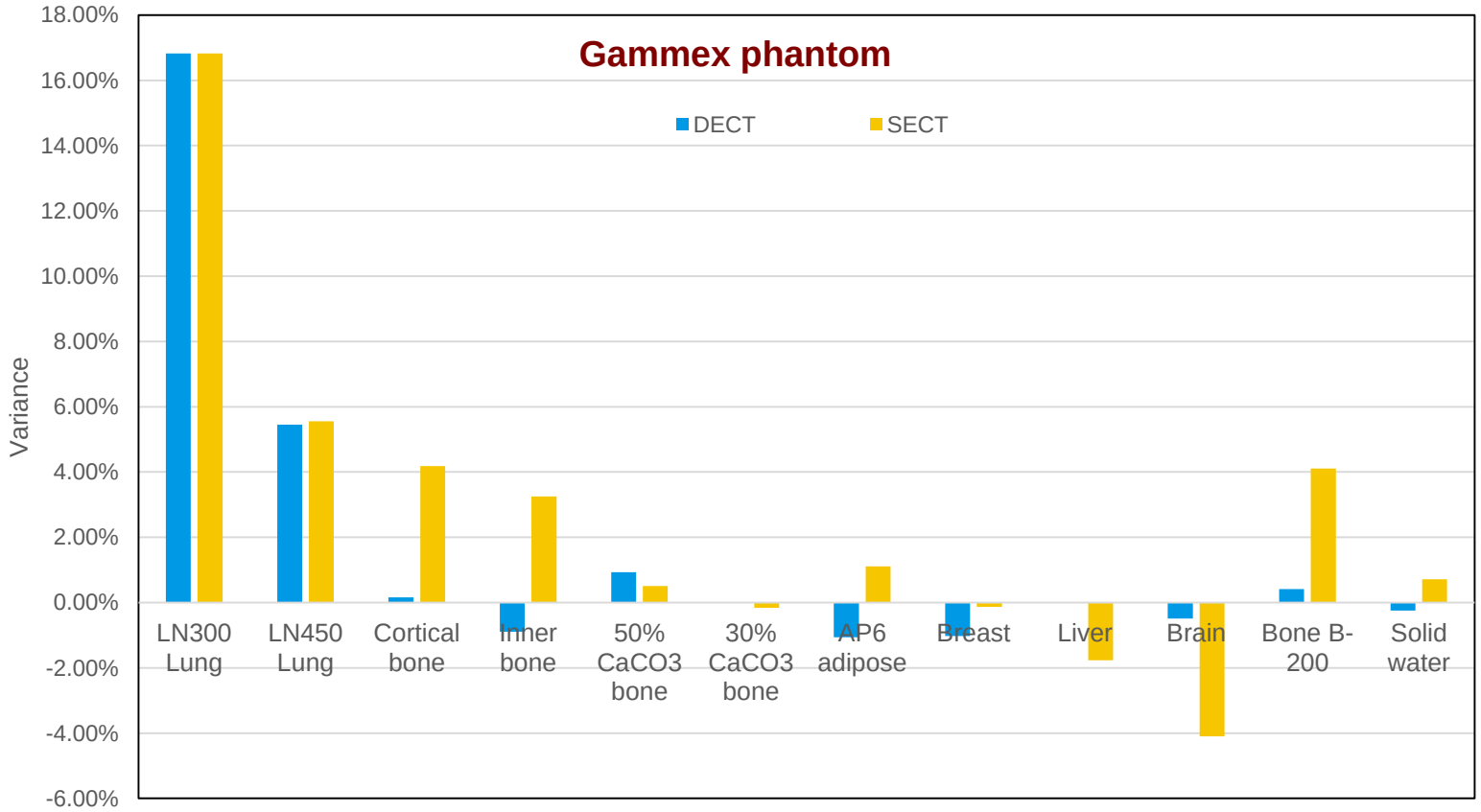
DECT SPR → HU (inverted SECT HU-SPR table) → DECT SPR (SECT HU-SPR)

Imported SPR CT will be converted back from HU to DECT SPR in TPS

3. **Import ρ_e and Z_{eff} images into TPS which computes SPR (eg scripting)**

Validating Accuracy of DECT SPR

1. **Comparison with tissue surrogates (known composition)**
2. **Comparison with proton beam measurements (animal tissue)**



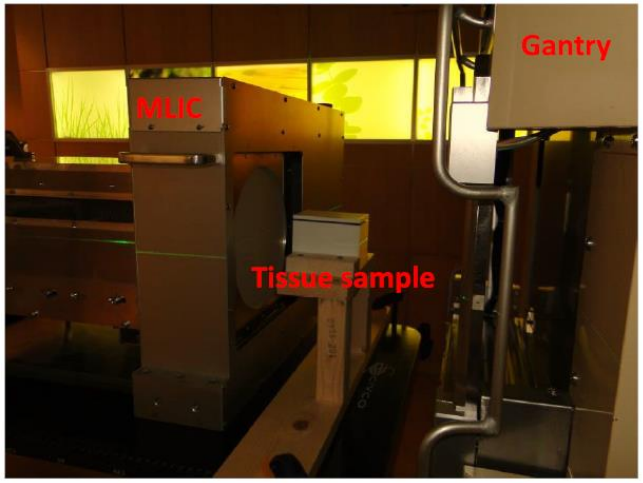
Variance of SPR is below 1% for DECT for most plugs except lung

Validating Accuracy of DECT SPR

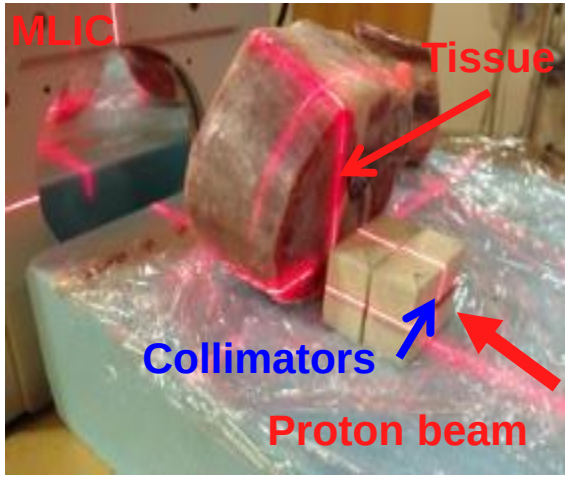
1. Comparison with tissue surrogates (known composition)
2. **Comparison with proton beam measurements (animal tissue)**

Irradiate sample and evaluate water equivalent thickness to deduce SPR

A. Multi-Layer Ion Chamber (MLIC) – residual range measurement

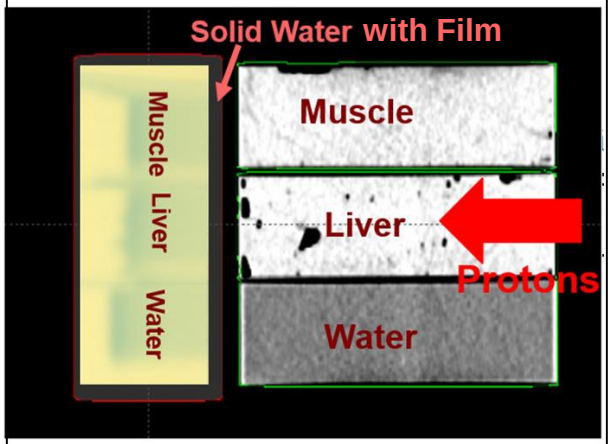


Taasti et al 2018
Phys. Med. Biol. **63** 015012



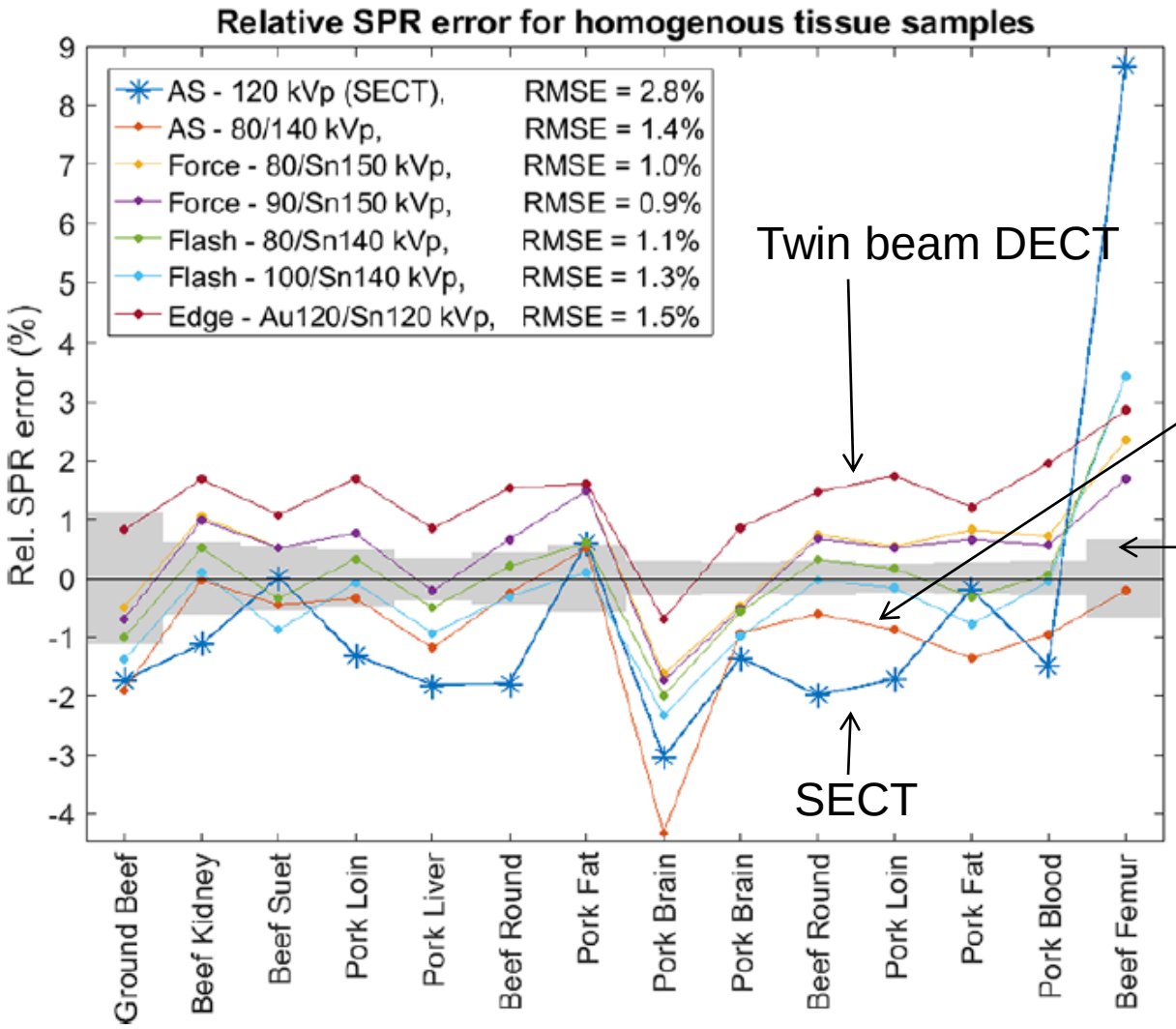
Xie et al 2018
Phys. Med. Biol. **63** 055016

B. Film



Xie et al 2018 *Phys. Med. Biol.* **63** 055016

Validation: Animal Tissue (MLIC)



Twin beam DECT

Sequential DECT

Uncertainty

SECT

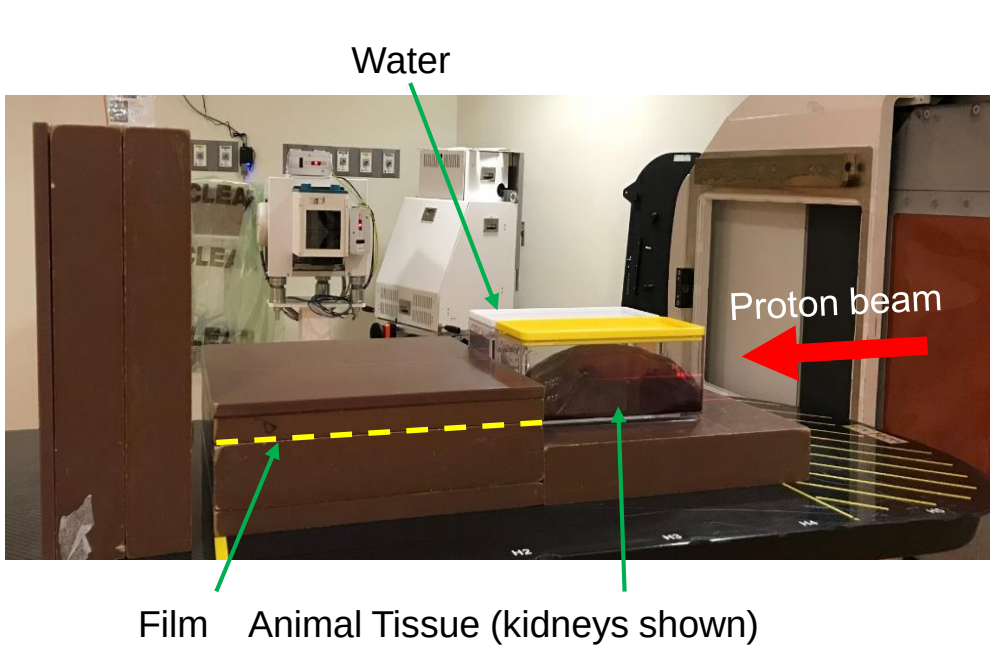
Note:
Twin beam DECT SPR is worse than sequential CT or dual source CT

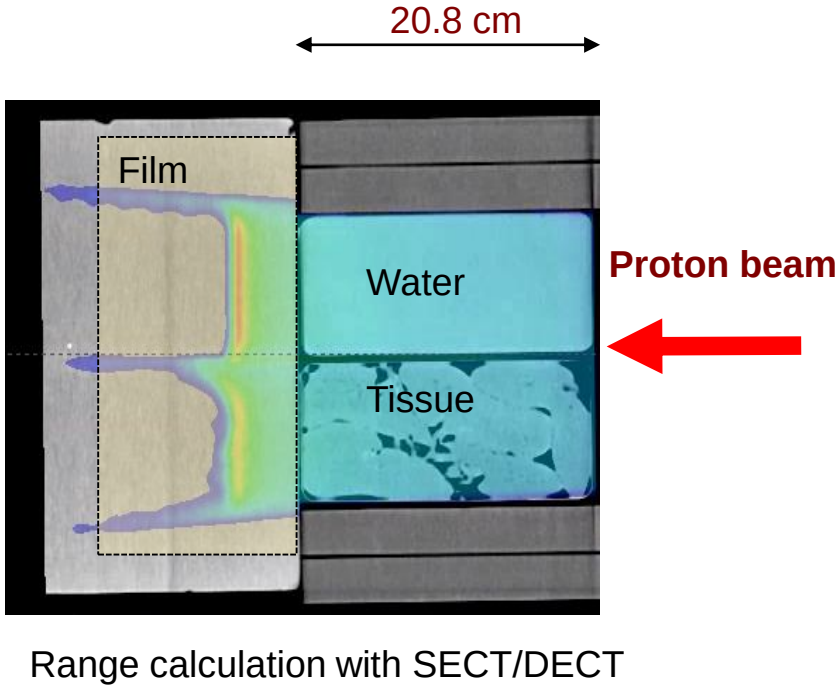
RMSE: 0.9% to 1.5% for DECT vs 2.8% for SECT , Taasti 2018 PMB

Validation: Animal Tissue (Film)

1. Comparison with tissue surrogates (known composition)
2. **Comparison with proton beam measurements**

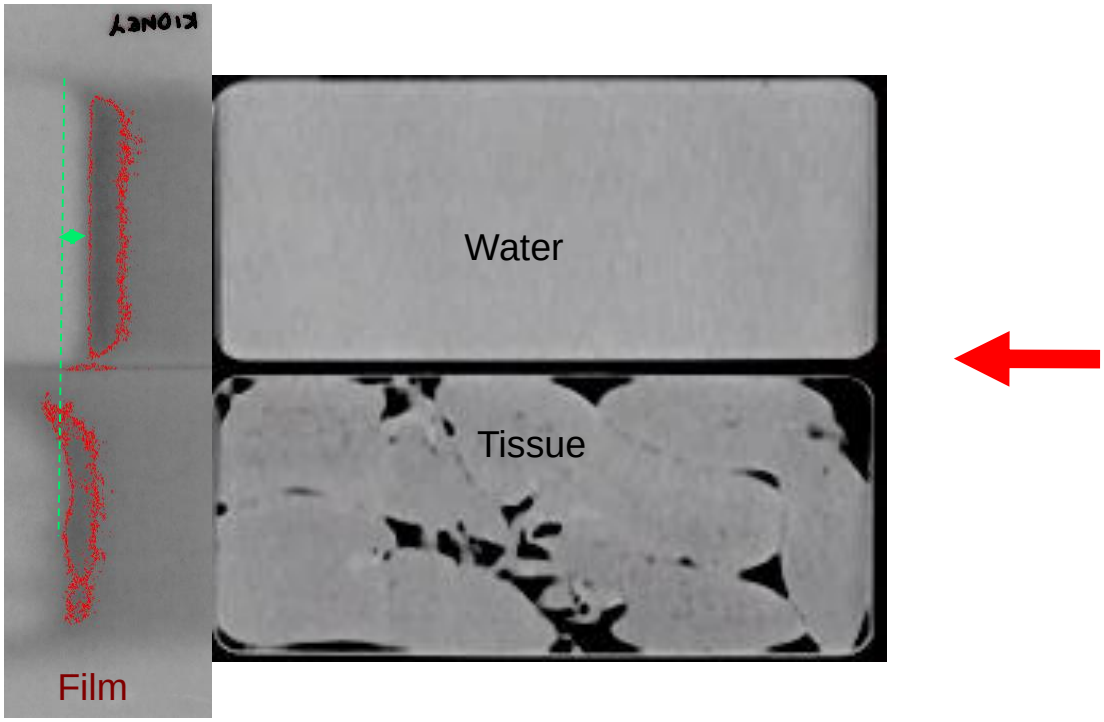
- ***Frozen Tissue Samples:***
  - **Ribs, Pork, Liver, Heart, Brain, Kidney**
- ***Delivery:***
  - **Single energy layer (192MeV proton) broad beam**
  - **Relative distal falloff to water measured with GafChromic film**





Range calculation with SECT/DECT

Range Analysis: Film Measurement



- Evaluate iso-intensity curves
- Absolute Bragg peak position on film not reliable (quenching)

→Compare **Relative** range in Tissue to Water

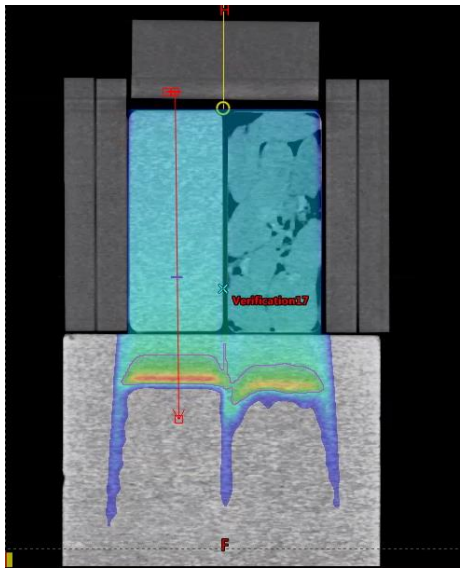
Advantages:

- Insensitive to film position and alignment errors
- Air pockets and tissue heterogeneity taken into account
- **End to End test** for comparison with dose calculation

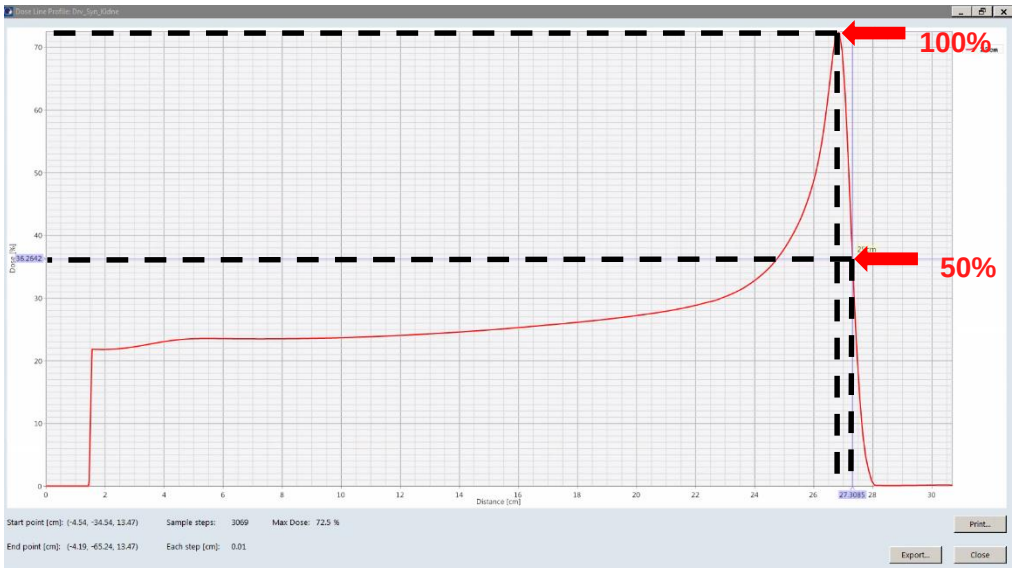
Range Analysis: SECT and DECT Prediction

Treatment Planning System (TPS) Range measurement:

- Dose calculated using SECT and DECT
- Relative range differences between water and animal tissue (ΔR) measured at 50% Isodose fall-off of Bragg peak.

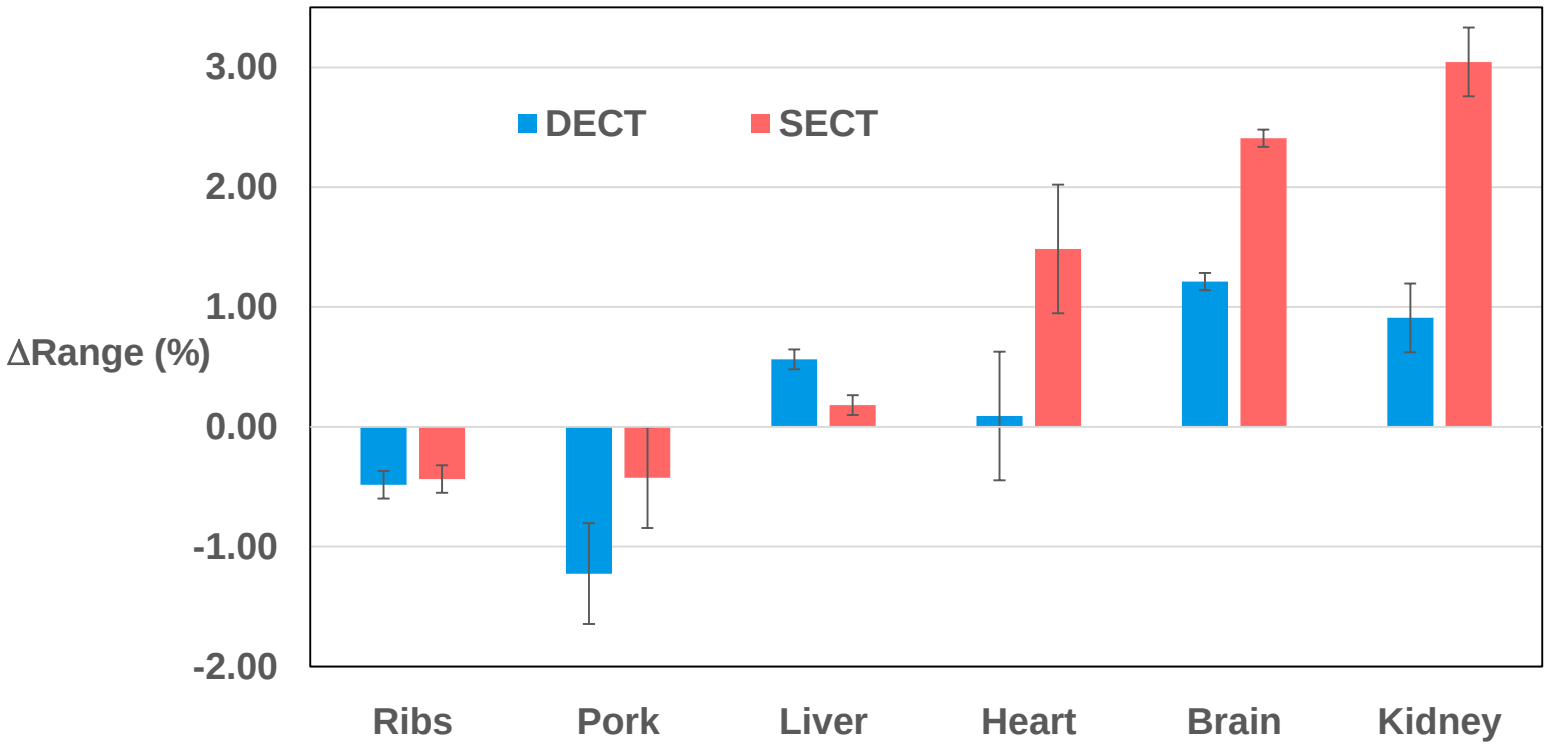


Dose distribution in TPS



50% Isodose line of dose fall-off of Bragg Peak

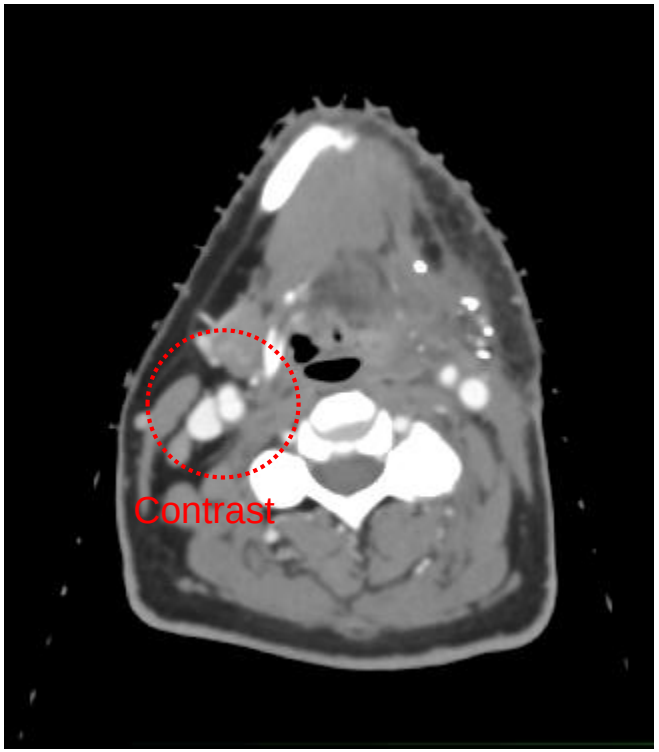
Range Comparison (SECT vs DECT)



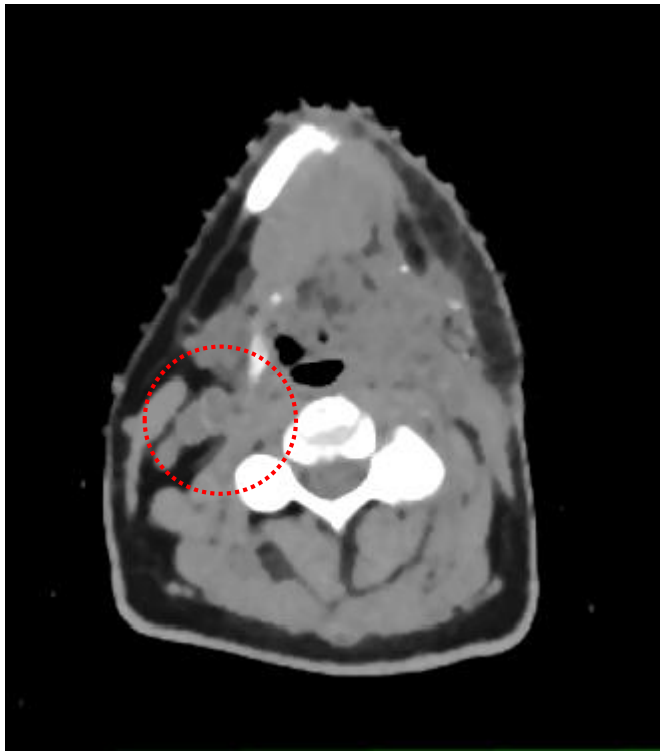
- SECT range deviation up to 3.0%
- DECT range deviation up to 1.2%

Impact of CT Contrast Media

Mixed Image (70% 140kV + 30% 80kV)=SECT

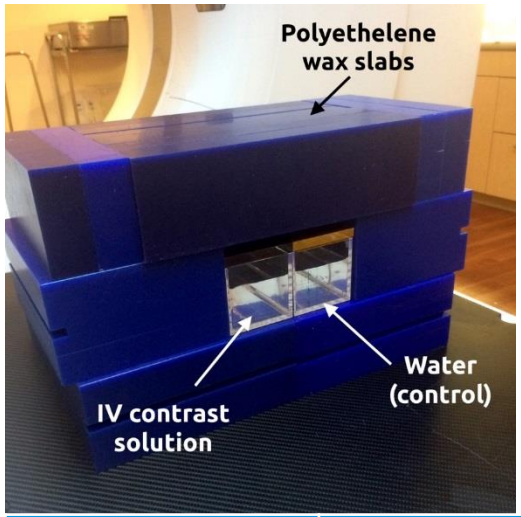


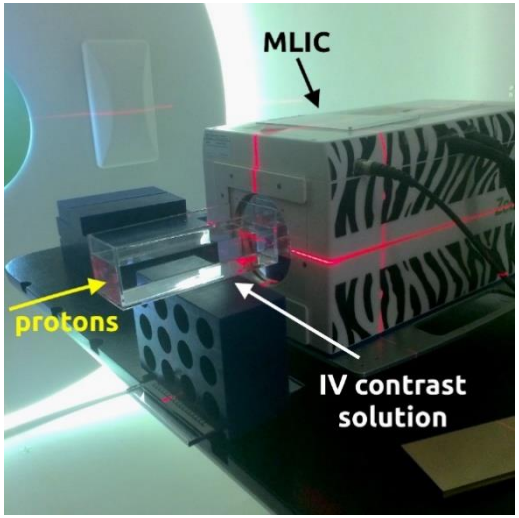
DECT SPR Image



- **Iodinated contrast SPR is approximately 1.0**
- **SECT shows incorrect SPR**
- **DECT predicts SPR correctly for iodinated contrast**

Measurements of Contrast Agent SPR





Vol. fraction of contrast agent [%]	SPR Error (%) SECT	DECT ρ_e / Z_{med} Sequential	Measured SPR
0.5	2.7	1.3	1.001
1	5.2	2.1	1.003
2	9.1	1.0	1.006
4	16.6	0.0	1.010
6	23.2	-0.2	1.014

Lalonde et al Phys Med Biol. 2019 Jun 21;64(12):125024

DECT predicted SPR of contrast is close to water

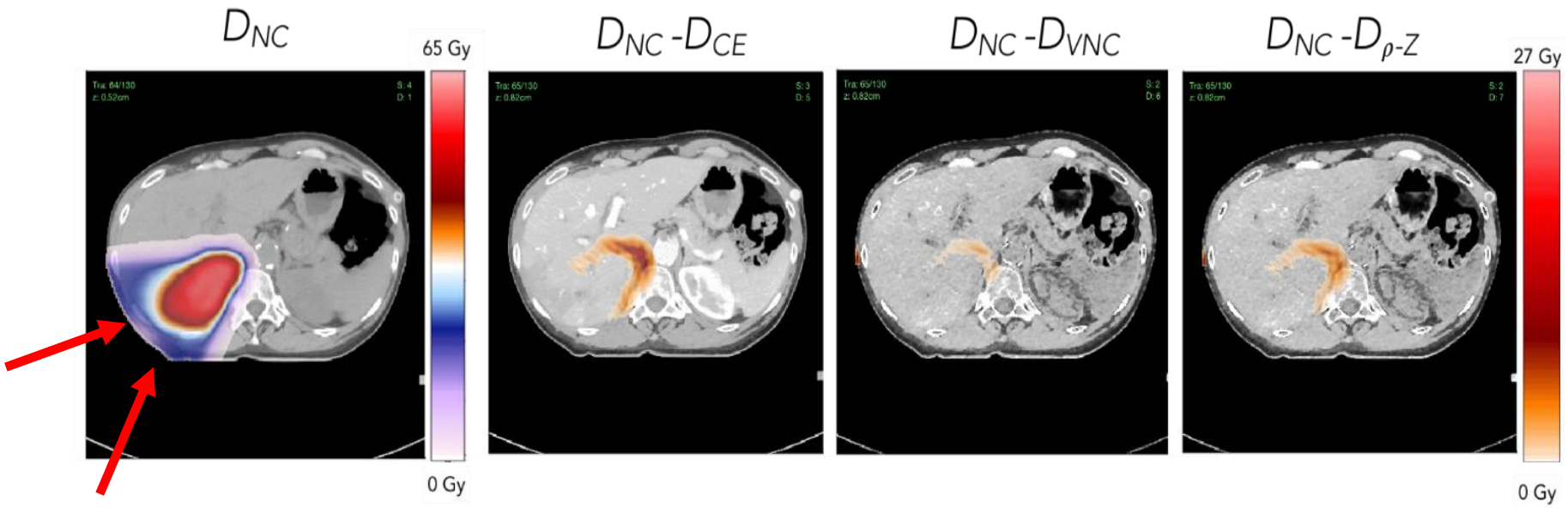
Large SPR error ~20% in SECT, < 2% for DECT

Dose Calculation with Contrast Agent

Non Contrast CT Dose Distribution

Large range error from contrast

Dose Differences using DECT SPR CT with contrast



DECT SPR CT may be used directly for proton dose calculation (if spatial and temporal registration errors are small)

Lalonde et al Phys Med Biol. 2019 Jun 21;64(12):125024

What SPR Uncertainty Should We Use?

Table 9. Uncertainties (1σ) in SPR estimation caused by different uncertainty sources.

Uncertainty source	SPR estimation uncertainties (1σ) Lung (%)	Soft (%)	Bone (%)
DECT imaging uncertainty	3.6	0.9	1.8
DECT modeling uncertainty	1.3	0.6	0.4
DECT inherent uncertainty	0.1	0.3	0.2
Uncertainty in the determination of I	0.2	0.2	0.6
Uncertainty due to ignorance of SPR change with proton energy by most commercial treatment planning systems	0.2	0.2	0.4
Total (RSS)	**3.8**	**1.2**	**2.0**

← Largest source

Uncertainty depends on tissue type

Table 10. Percentile (90th and 95th) of composite range uncertainties estimated for prostate, lung and head-and-neck tumor sites, respectively.

Tumor site	Range uncertainty: 90th percentile %	90th percentile g cm^{-2}	95th percentile %	95th percentile g cm^{-2}
Prostate	1.7	0.4–0.5	2.1	0.5–0.6
Lung	1.8	0.1–0.3	2.2	0.2–0.4
Head and neck	1.8	0.1–0.4	2.1	0.1–0.4

Phys. Med. Biol. **62** (2017) 7056–7074

~2 % is feasible

Proton Planning Workflow with DECT

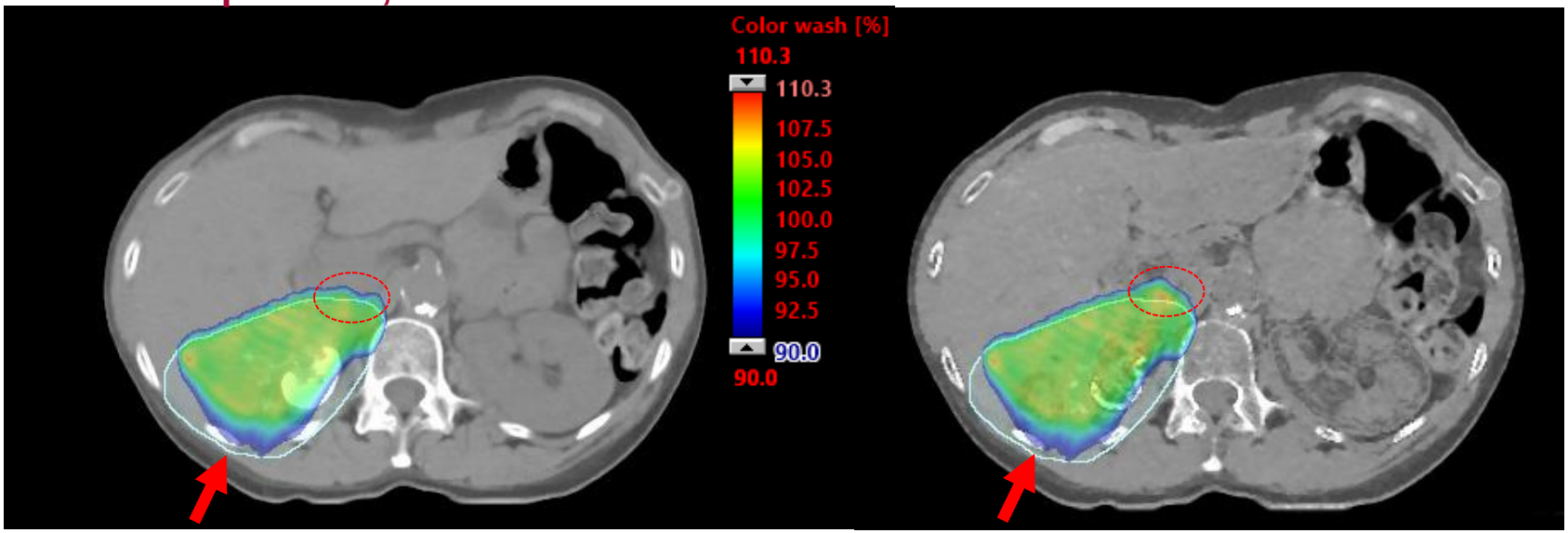
Use of DECT SPR is still new, precautions and safety checks need to be implemented

1. **Optimize with SECT image, forward calculate on DECT SPR for final dose distribution**

2. **Optimize with DECT SPR image, forward calculate on SECT for dose check**

Workflow 1: Optimize with SECT

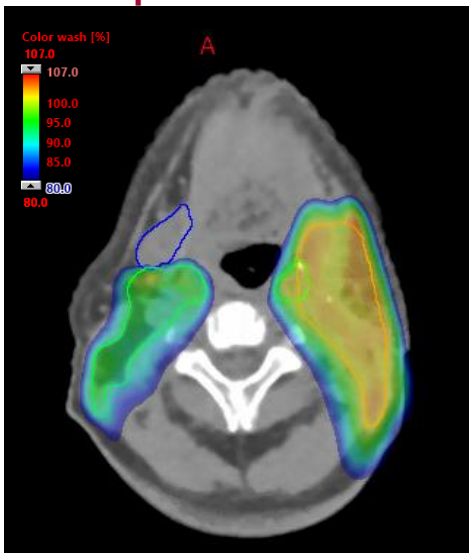
SECT optimized, RPO field dose | **Forward calculation: DECT SPR final dose**



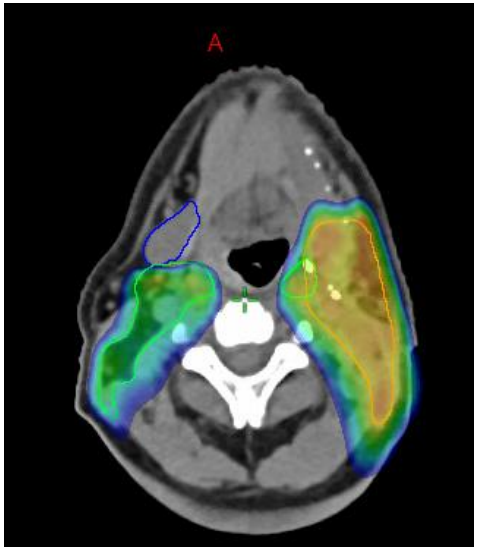
- SPR of lipiodol (contrast agent, not IV injected) over-estimation in SECT
- Over-ranging seen in RPO field with DECT dose
- Real liver dose higher than reflected in SECT plan

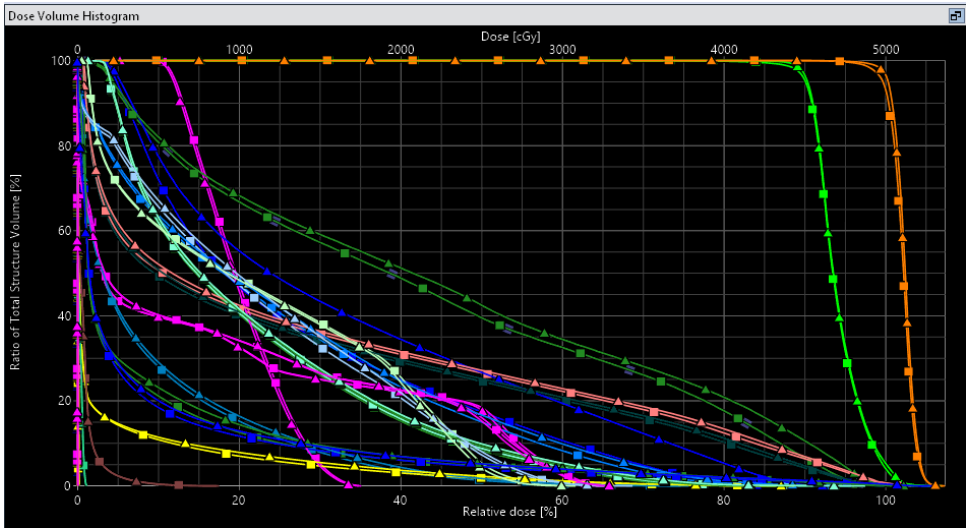
Workflow 2: Optimize with DECT

DECT optimization



Forward calculation on SECT: dose check





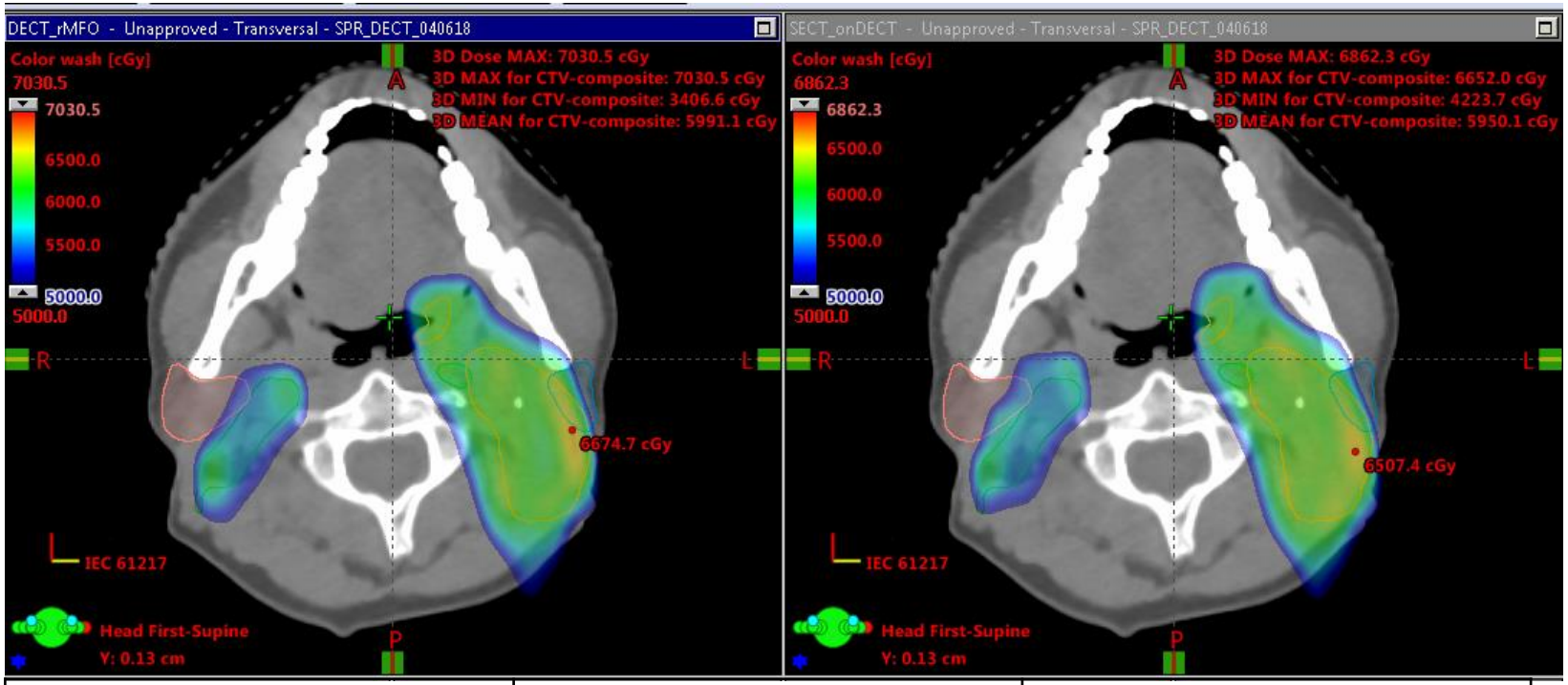
- Small dose differences observed
- Review regions of SPR/dose deviation

Impact of Reduced Range Uncertainty Margins

1. Head and neck, MFO 3 fields (2 posterior obliques + 1 anterior)
2. Optimized with DECT (2%, 3mm) compare with SECT (3.5%, 3mm)
3. 30 fxs, CTV 5400 and CTV 6000

DECT optimization

SECT plan forward calculated on DECT

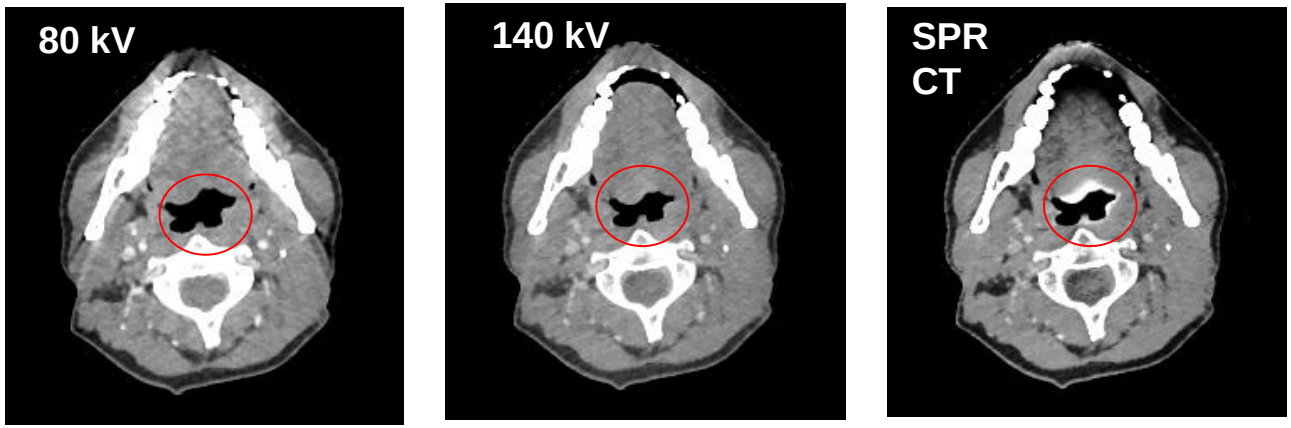


	SECT	DECT
5200cGy isodose volume	1241cc	863cc
Right Parotid mean dose	1478cGy	1240cGy

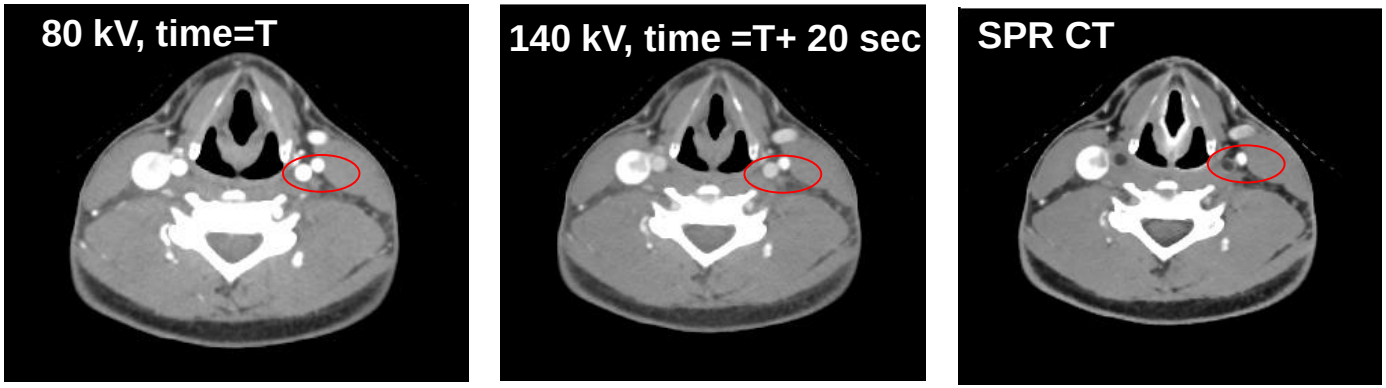
Reduced range uncertainty margin of 2% leads to slightly smaller volume of high dose

Errors from DECT calculated SPR

1. **Spatial registration error (motion between sequential scans)**



2. **Temporal registration error (dynamic change in IV contrast conc., sequential scans)**



3. **Image artifacts: streaking from metal, CT number clipping**

Spatial and temporal registration errors may be reduced with dual source or single source spectral DECT

Clinical Use of DECT SPR in Proton Therapy

1. **Feasible to use contrast scans for proton dose calculation (dual source DECT or spectral CT preferred)**
2. **Feasibility of reduced margins (2%) for some sites eg brain, head-neck, some abdominal cases**
3. **Not likely to benefit for lung or abdominal sites with large motion or change in organ filling (anatomic uncertainty >> CT-SPR uncertainty)**
4. **Even if margins are not reduced, DECT dose more likely to reflect delivered dose → especially to OARs**