Assessment of the impact of CT calibration procedures for proton therapy planning on paediatric patients

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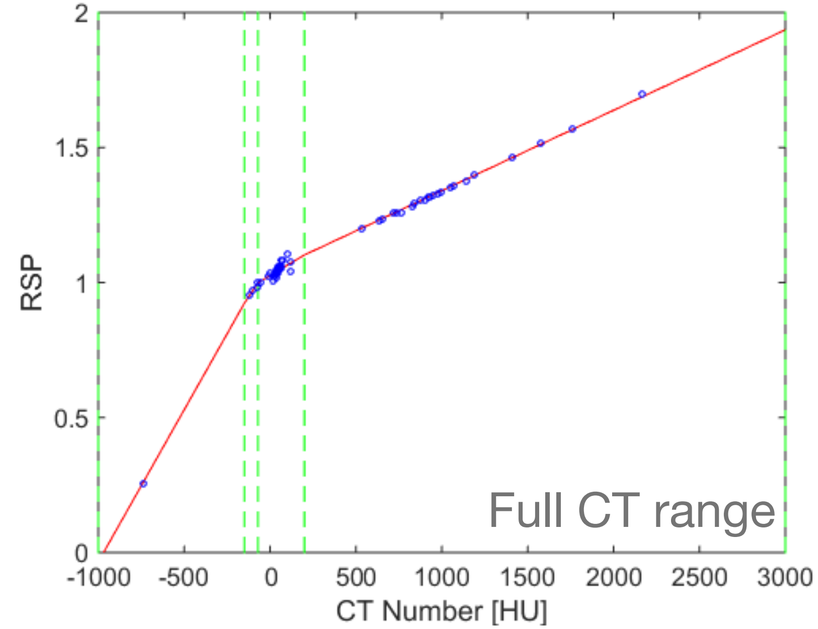
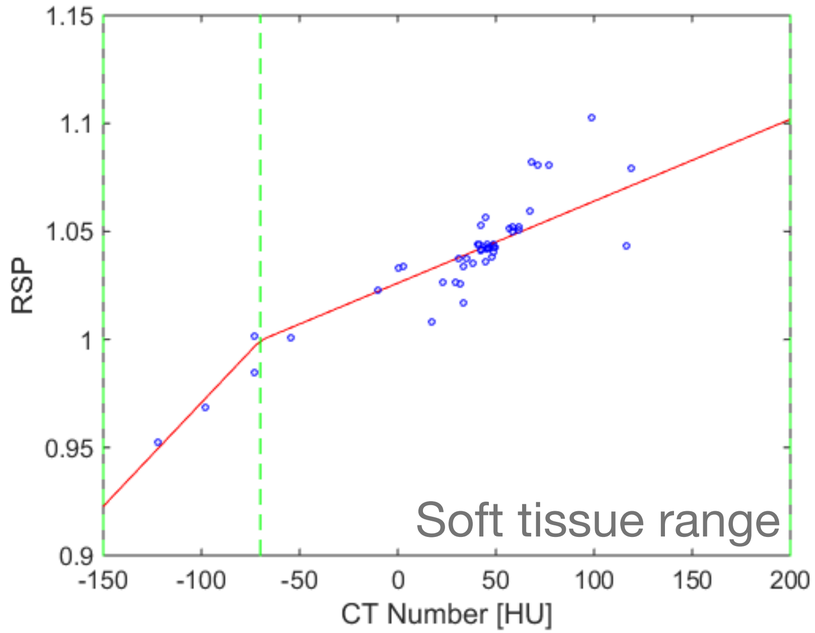
CT calibration: A one size fits all approach

- RSP estimation from CT images is currently done using either **tissue substitutes** or the **stoichiometric calibration** [1,2]





[1] Schneider, U., Pedroni, E. and Lomax, A., 1996. The calibration of CT Hounsfield units for radiotherapy treatment planning. *Physics in Medicine & Biology*, *41*(1), p.111.
[2] Taasti, V.T., et al., 2018. Inter-centre variability of CT-based stopping-power prediction in particle therapy: survey-based evaluation. *Physics and imaging in radiation oncology*, *6*, pp.25-30.

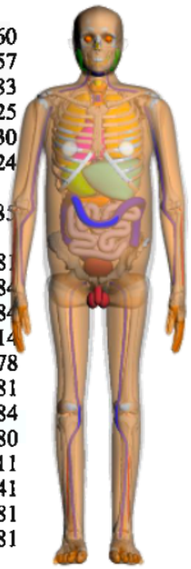
CT calibration: A one size fits all approach

- RSP estimation from CT images is currently done using either **tissue substitutes** or the **stoichiometric calibration** [1,2]
- Stoichiometric calibration is based on **reference tissues** from an **adult population** [3,4]

TABLE III

THE ELEMENTAL COMPOSITIONS OF THE BODY TISSUES

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
Adrenal gland	10.6	28.4	2.6	57.8	P(0.1), S(0.2), Cl(0.2), K(0.1)	1030	3.324	3424
Aorta	9.9	14.7	4.2	69.8	Na(0.2), P(0.4), S(0.3), K(0.1), Ca(0.4)	1050	3.304	3469
Blood—erythrocytes	9.5	19.0	5.9	64.6	P(0.1), S(0.3), Cl(0.2), K(0.3), Fe (0.1)	1090	3.291	3588
Blood—plasma	10.8	4.1	1.1	83.2	Na(0.3), S(0.1), Cl(0.4)	1026	3.330	3417
Blood—whole	10.2	11.0	3.3	74.5	Na(0.1), P(0.1), S(0.2), Cl(0.3), K(0.2), Fe(0.1)	1060	3.312	3511
Brain—cerebrospinal fluid	11.1	—	—	88.0	Na(0.5), Cl(0.4)	1010	3.339	3373
Brain—grey matter	10.7	9.5	1.8	76.7	Na(0.2), P(0.3), S(0.2), Cl(0.3), K(0.3)	1040	3.327	3460
Brain—white matter	10.6	19.4	2.5	66.1	Na(0.2), P(0.4), S(0.2), Cl(0.3), K(0.3)	1040	3.324	3457
Connective tissue	9.4	20.7	6.2	62.2	Na(0.6), S(0.6), Cl(0.3)	1120	3.288	3683
Eye lens	9.6	19.5	5.7	64.6	Na(0.1), P(0.1), S(0.3), Cl(0.1)	1070	3.295	3525
Gallbladder—bile	10.8	6.1	0.1	82.2	Na(0.4), Cl(0.4)	1030	3.330	3430
Gastrointestinal tract—small intestine (wall)	10.6	11.5	2.2	75.1	Na(0.1), P(0.1), S(0.1), Cl(0.2), K(0.1)	1030	3.325	3424
Gastrointenstinal tract—stomach	10.4	13.9	2.9	72.1	Na(0.1), P(0.1), S(0.2), Cl(0.1), K(0.2)	1050	3.319	348
Heart 1	10.3	17.5	3.1	68.1	Na(0.1), P(0.2), S(0.2), Cl(0.2), K(0.3)	1050	3.315	348
Heart 2	10.4	13.9	2.9	71.8	Na(0.1), P(0.2), S(0.2), Cl(0.2), K(0.3)	1050	3.318	348
Heart 3	10.4	10.3	2.7	75.6	Na(0.1), P(0.2), S(0.2), Cl(0.2), K(0.3)	1050	3.318	348
Heart—blood filled	10.3	12.1	3.2	73.4	Na(0.1), P(0.1), S(0.2), Cl(0.3), K(0.2), Fe(0.1)	1060	3.315	351
Kidney 1	10.2	16.0	3.4	69.3	Na(0.2), P(0.2), S(0.2), Cl(0.2), K(0.2), Ca(0.1)	1050	3.312	3478
Kidney 2	10.3	13.2	3.0	72.4	Na(0.2), P(0.2), S(0.2), Cl(0.2), K(0.2), Ca(0.1)	1050	3.315	3481
Kidney 3	10.4	10.6	2.7	75.2	Na(0.2), P(0.2), S(0.2), Cl(0.2), K(0.2), Ca(0.1)	1050	3.318	3484
Liver 1	10.3	15.6	2.7	70.1	Na(0.2), P(0.3), S(0.3), Cl(0.2), K(0.3)	1050	3.315	3480
Liver 2	10.2	13.9	3.0	71.6	Na(0.2), P(0.3), S(0.3), Cl(0.2), K(0.3)	1060	3.312	3511
Liver 3	10.1	12.6	3.3	72.7	Na(0.2), P(0.3), S(0.3), Cl(0.2), K(0.3)	1070	3.309	3541
Lung—parenchyma	10.3	10.1	2.9	75.5	Na(0.2), P(0.2), S(0.3), Cl(0.3), K(0.2)	1050	3.315	3481
Lung—blood-filled	10.3	10.5	3.1	74.9	Na(0.2), P(0.2), S(0.3), Cl(0.3), K(0.2)	1050*	3.315	3481



[3] Woodard, H.Q. and White, D.R., 1986. The composition of body tissues. *The British journal of radiology*, *59*(708), pp.1209-1218.

[4] White, D.R., Woodard, H.Q. and Hammond, S.M., 1987. Average soft-tissue and bone models for use in radiation dosimetry. *The British journal of radiology*, *60*(717), pp.907-913.

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- RSP estimation from CT images is currently done using either **tissue substitutes** or the **stoichiometric calibration** [1,2]
- Stoichiometric calibration is based on **reference tissues** from an **adult population** [3,4]
- Paediatric tissues: ‘Both soft tissues and skeletal tissues exhibit a **reduction in water content with increasing age**.’ (ICRP report 46) [5,6]

Body tissue	Elemental composition (% by mass)										Densities
											Mass
	H	C	N	O	Na	P	S	Cl	K	Others	kg m^{-3}
Adipose tissue[a]											
Newborn 1		20.5	0.9	67.2				0.1			1000
Newborn 2		29.7	0.9	58.0				0.1			990
Newborn 3		39.0	0.9	48.6				0.1			980
Infant (2 days–10 months) 1		31.0	1.1	56.5				0.1			990
Infant (2 days–10 months) 2		39.2	0.9	48.4				0.1			970
Infant (2 days–10 months) 3		47.3	0.6	40.4				0.1			960
Child (1–18 years) 1		34.7	0.8	53.0				0.1			980
Child (1–18 years) 2		44.5	0.6	43.3				0.1			960
Child (1–18 years) 3		54.3	0.5	33.4				0.1			950
Adult 1		51.7	1.3	35.5				0.1			970
Adult 2		59.8	0.7	27.8				0.1			950
Adult 3		68.1	0.2	19.8				0.1			930
Blood—whole											
Fetus (20 weeks)	10.5	7.3	2.2	79.2	0.1	0.1	0.1	0.2	0.2	Fe (0.1)	1040
Newborn	10.0	13.1	4.0	72.0	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1070
Infant (1 week)	10.1	12.2	3.7	73.1	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1070
Infant (6–12 months)	10.4	9.1	2.8	76.8	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1050
Adult	10.2	11.0	3.3	74.5	0.1	0.1	0.2	0.3	0.2	Fe (0.1)	1060
Brain—whole											
Fetus (14 weeks)	10.9	3.3	0.7	84.2	0.2	0.2		0.3	0.2		1020
Newborn	10.8	5.5	1.1	81.6	0.2	0.3	0.1	0.2	0.2		1030
Infant (18 months)	10.7	9.1	1.6	77.6	0.2	0.3	0.1	0.2	0.2		1030
Adult	10.7	14.5	2.2	71.2	0.2	0.4	0.2	0.3	0.3		1040

[5] White, D.R., Widdowson, E.M., Woodard, H.Q. and Dickerson, J.W.T., 1991. The composition of body tissues.(II) Fetus to young adult. *The British journal of radiology*, *64*(758), pp.149-159.
[6] White, D.R., Griffith, R.V. and Wilson, I.J., 1992. Report 46. *Journal of the International Commission on Radiation Units and Measurements*.

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- RSP estimation from CT images is currently done using either **tissue substitutes** or the **stoichiometric calibration** [1,2]
- Stoichiometric calibration is based on **reference tissues** from an **adult population** [3,4]
- Paediatric tissues: ‘Both soft tissues and skeletal tissues exhibit a **reduction in water content with increasing age**.’ (ICRP report 46) [5,6]
- We aim to evaluate **dose and range errors in paediatric proton therapy** arising from a calibration curve created with reference tissues representing an adult population.

Body tissue	Elemental composition (% by mass)										Densities
											Mass
	H	C	N	O	Na	P	S	Cl	K	Others	kg m^{-3}
Adipose tissue[a]											
Newborn 1		20.5	0.9	67.2				0.1			1000
Newborn 2		29.7	0.9	58.0				0.1			990
Newborn 3		39.0	0.9	48.6				0.1			980
Infant (2 days–10 months) 1		31.0	1.1	56.5				0.1			990
Infant (2 days–10 months) 2		39.2	0.9	48.4				0.1			970
Infant (2 days–10 months) 3		47.3	0.6	40.4				0.1			960
Child (1–18 years) 1		34.7	0.8	53.0				0.1			980
Child (1–18 years) 2		44.5	0.6	43.3				0.1			960
Child (1–18 years) 3		54.3	0.5	33.4				0.1			950
Adult 1		51.7	1.3	35.5				0.1			970
Adult 2		59.8	0.7	27.8				0.1			950
Adult 3		68.1	0.2	19.8				0.1			930
Blood—whole											
Fetus (20 weeks)	10.5	7.3	2.2	79.2	0.1	0.1	0.1	0.2	0.2	Fe (0.1)	1040
Newborn	10.0	13.1	4.0	72.0	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1070
Infant (1 week)	10.1	12.2	3.7	73.1	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1070
Infant (6–12 months)	10.4	9.1	2.8	76.8	0.1	0.1	0.2	0.2	0.2	Fe (0.1)	1050
Adult	10.2	11.0	3.3	74.5	0.1	0.1	0.2	0.3	0.2	Fe (0.1)	1060
Brain—whole											
Fetus (14 weeks)	10.9	3.3	0.7	84.2	0.2	0.2		0.3	0.2		1020
Newborn	10.8	5.5	1.1	81.6	0.2	0.3	0.1	0.2	0.2		1030
Infant (18 months)	10.7	9.1	1.6	77.6	0.2	0.3	0.1	0.2	0.2		1030
Adult	10.7	14.5	2.2	71.2	0.2	0.4	0.2	0.3	0.3		1040

[5] White, D.R., Widdowson, E.M., Woodard, H.Q. and Dickerson, J.W.T., 1991. The composition of body tissues.(II) Fetus to young adult. *The British journal of radiology*, *64*(758), pp.149-159.
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Methods: Paediatric composition and density data

- We use recently published composition and density data for paediatric tissues (ICRP publication 143) [7].

Table B.1. List of media, their elemental compositions (percent by mass), and their mass densities for the newborn male phantom.

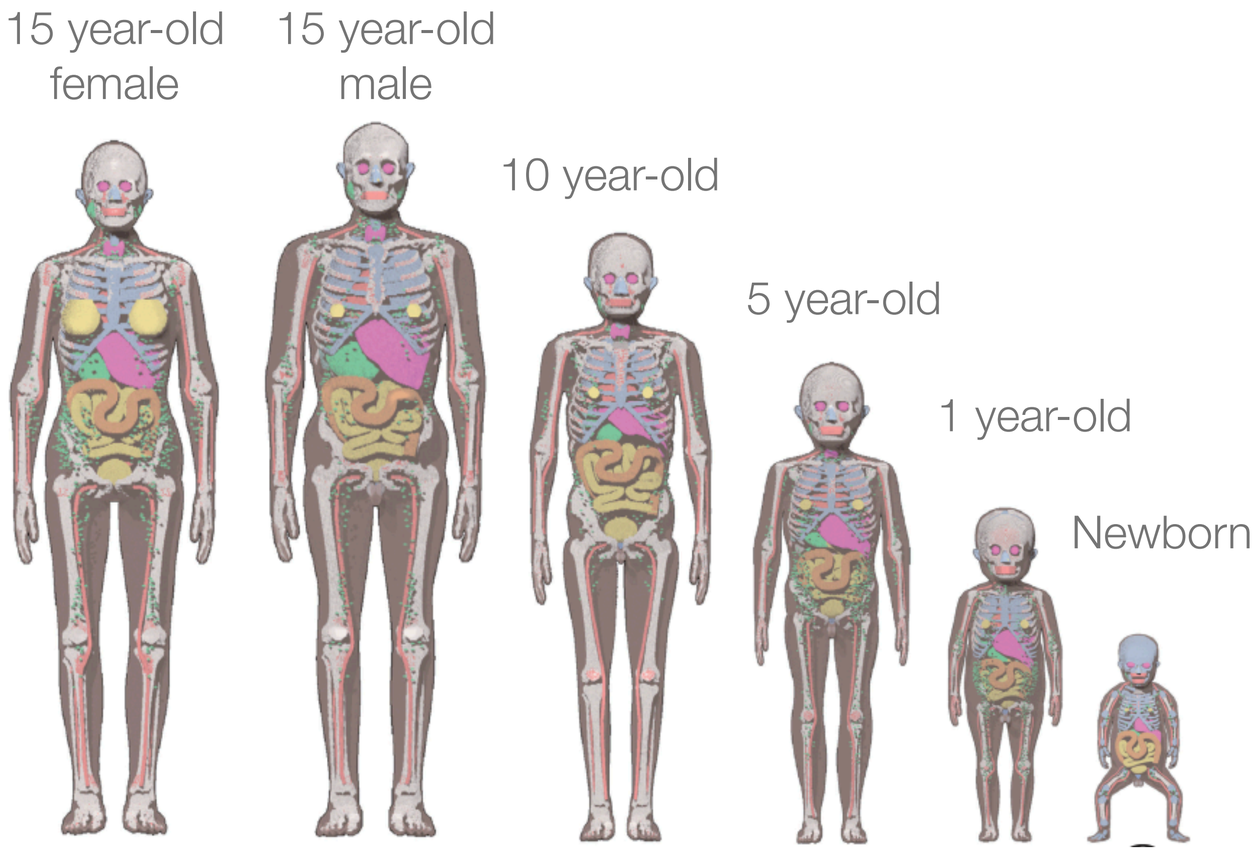
Medium		H_1	C_6	N_7	O_8	Na_{11}	Mg_{12}	P_{15}	S_{16}	Cl_{17}	K_{19}	Ca_{20}	Fe_{26}	I_{53}	Density (g/cm^3)
1	Teeth	2.2	9.5	2.9	42.1	0.0	0.7	13.7	0.0	0.0	0.0	28.9	0.0	0.0	1.65
2	Mineral bone	4.5	15.8	4.5	51.4	0.0	0.3	7.5	0.3	0.0	15.6	0.0	0.0	0.0	1.65
3	Humeri, upper half, spongiosa	7.3	23.1	4	52.8	0.1	0.2	4	0.3	0.0	8.1	0.1	0.0	0.0	1.307
4	Humeri, lower half, spongiosa	10.4	34	3.5	51.2	0.1	0.1	0.2	0.2	0.1	0.0	0.1	0.1	0.0	1.307
5	Ulnae and radii, spongiosa	10.4	34	3.5	51.2	0.1	0.1	0.2	0.2	0.1	0.0	0.1	0.1	0.0	1.307
6	Wrists and hand bones, spongiosa	10.4	34	3.5	51.2	0.1	0.1	0.2	0.2	0.1	0.0	0.1	0.1	0.0	1.244
7	Clavicles, spongiosa	6.9	21.8	4.1	53	0.1	0.2	4.5	0.3	0.0	9.1	0.1	0.0	0.0	1.257
8	Cranium, spongiosa	6.3	19.4	4.2	53.4	0.0	0.2	5.3	0.3	0.0	10.8	0.0	0.0	0.0	1.433
9	Femora, upper half, spongiosa	7.3	23.1	4	52.8	0.1	0.2	4	0.3	0.0	8.1	0.1	0.0	0.0	1.307
10	Femora, lower half, spongiosa	7.3	23.1	4	52.8	0.1	0.2	4	0.3	0.0	8.1	0.1	0.0	0.0	1.307
11	Tibiae, fibulae, and patellae, spongiosa	7.6	24	4	52.7	0.1	0.2	3.7	0.3	0.0	7.4	0.1	0.0	0.0	1.306
12	Ankles and foot bones, spongiosa	7.3	23.1	4	52.8	0.1	0.2	4	0.3	0.0	8.1	0.1	0.0	0.0	1.244
13	Mandible, spongiosa	7.9	25.3	3.9	52.5	0.1	0.2	3.2	0.2	0.0	6.5	0.1	0.1	0.0	1.244
14	Pelvis, spongiosa	7.3	23.1	4	52.8	0.1	0.2	4	0.3	0.0	8.1	0.1	0.0	0.0	1.257
15	Ribs, spongiosa	7.9	25.2	3.9	52.5	0.1	0.2	3.3	0.3	0.0	6.5	0.1	0.0	0.0	1.244
16	Scapulae, spongiosa	7.1	22.2	4.1	52.9	0.1	0.2	4.3	0.3	0.0	8.8	0.1	0.0	0.0	1.257
17	Cervical spine, spongiosa	7.9	25.3	3.9	52.5	0.1	0.2	3.2	0.2	0.0	6.5	0.1	0.1	0.0	1.338
18	Thoracic spine, spongiosa	7.8	24.8	3.9	52.5	0.1	0.2	3.4	0.3	0.0	6.8	0.1	0.0	0.0	1.351
19	Lumbar spine, spongiosa	7.8	24.8	3.9	52.5	0.1	0.2	3.4	0.3	0.0	6.8	0.1	0.0	0.0	1.307
20	Sacrum, spongiosa	7.8	24.8	3.9	52.5	0.1	0.2	3.4	0.3	0.0	6.8	0.1	0.0	0.0	1.307
21	Sternum, spongiosa	7.3	23.1	4	52.8	0.1	0.2	4	0.3	0.0	8.1	0.1	0.0	0.0	1.245
22	Humeri and femora, upper half, medullary cavity	7.3	23.1	4	52.8	0.1	0.2	4	0.3	0.0	8.1	0.1	0.0	0.0	1.03
23	Humeri and femora, lower half, medullary cavity	7.9	25.3	3.9	52.5	0.1	0.2	3.2	0.2	0.0	6.5	0.1	0.1	0.0	1.03
24	Ulnae and radii, medullary cavity	10.4	34	3.5	51.2	0.1	0.1	0.2	0.2	0.1	0.0	0.1	0.1	0.0	1.03
25	Tibiae, fibulae, medullary cavity	7.3	23.1	4	52.8	0.1	0.2	4	0.3	0.0	8.1	0.1	0.0	0.0	1.03
26	Cartilage	9.6	9.9	2.2	74.4	0.5	0.0	2.2	0.9	0.3	0.0	0.0	0.0	0.0	1.1
27	Skin	10.4	10.6	2.9	75.3	0.2	0.0	0.1	0.2	0.3	0.0	0.1	0.0	0.0	1.1
28	Blood vessels	10.2	11	3.3	74.5	0.1	0.0	0.1	0.2	0.3	0.0	0.2	0.1	0.0	1.07
29	Oral mucosa	10.4	10.3	2.4	76.1	0.1	0.0	0.1	0.1	0.2	0.0	0.2	0.0	0.0	1.03
30	Liver	10.2	12.8	3.1	72.9	0.1	0.0	0.2	0.2	0.2	0.0	0.3	0.0	0.0	1.04
31	Pancreas	10.5	16	2.6	70	0.2	0.0	0.2	0.1	0.2	0.0	0.2	0.0	0.0	1.03

(continued on next page)

[7] ICRP, 2020. Paediatric reference computational phantoms. ICRP Publication 143. Ann. ICRP 49(1)

Methods: Paediatric composition and density data

- We use recently published composition and density data for paediatric tissues (ICRP publication 143) [7].
- Data covers 57 paediatric tissues ranging from newborn to 15-year old.



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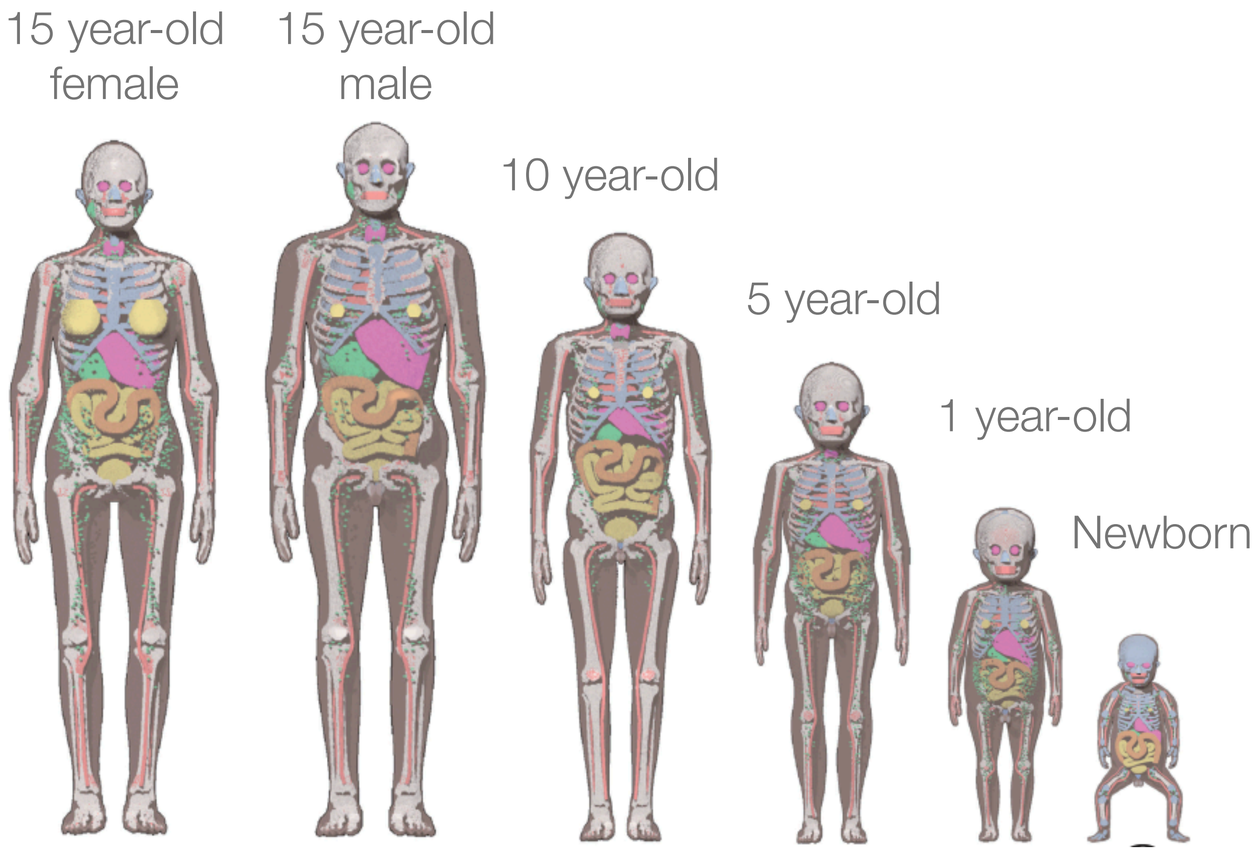
Methods: Paediatric composition and density data

- We use recently published composition and density data for paediatric tissues (ICRP publication 143) [7].
- Data covers 57 paediatric tissues ranging from newborn to 15-year old.
- Use tissue information and CT spectral information to calculate **CT numbers** and **reference RSPs** for the tissues.



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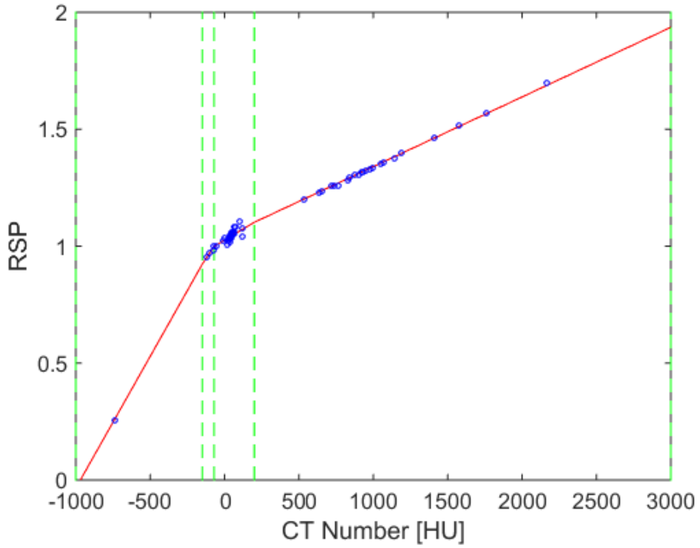
Methods: CT calibration methods

(1) Stoichiometric calibration



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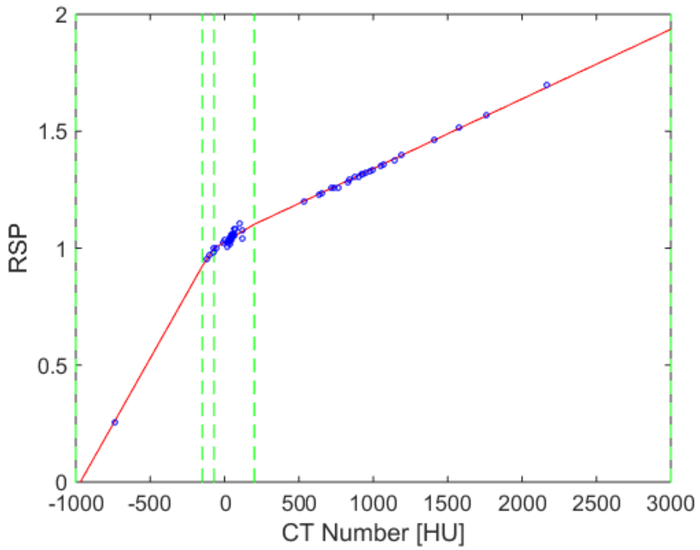
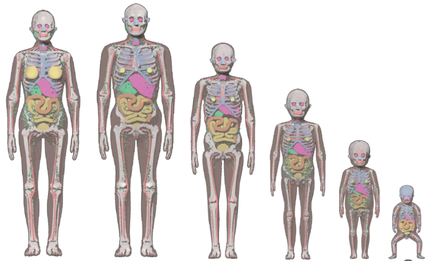
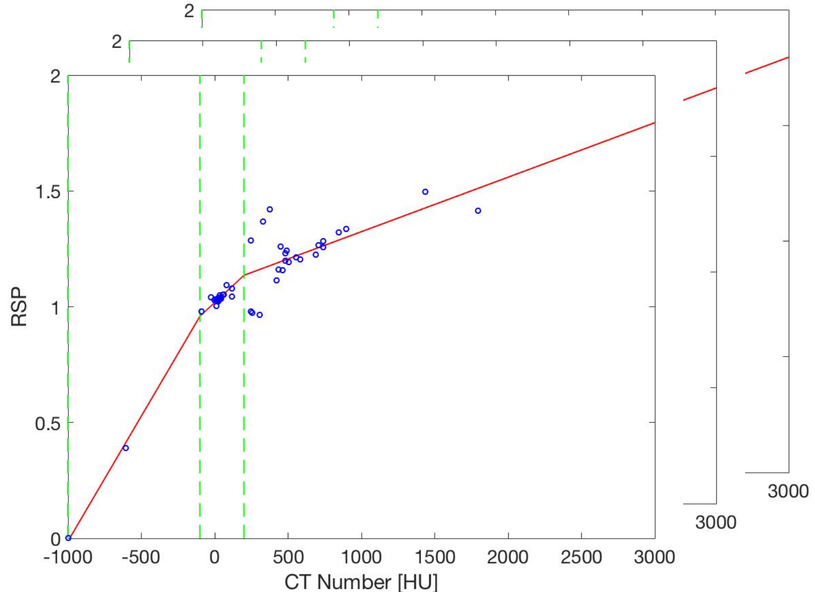


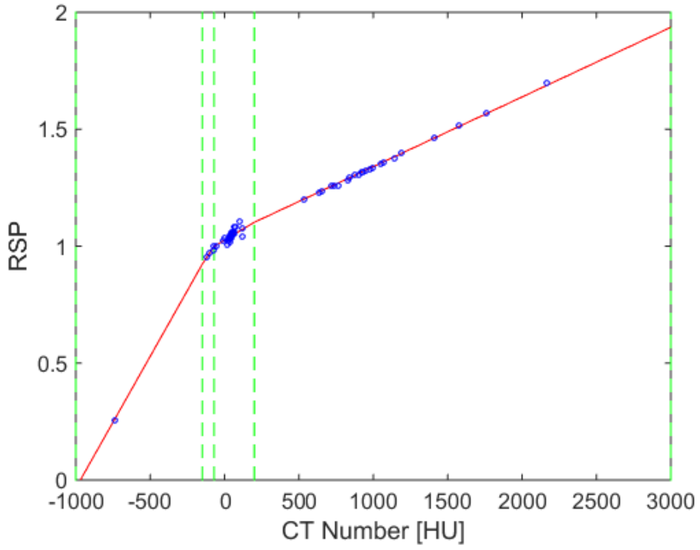
(2) Age-specific stoichiometric calibration



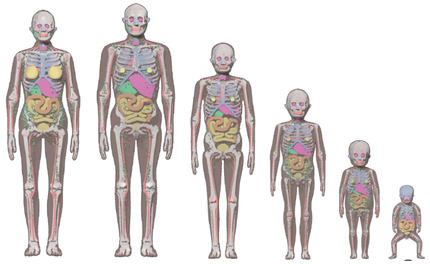


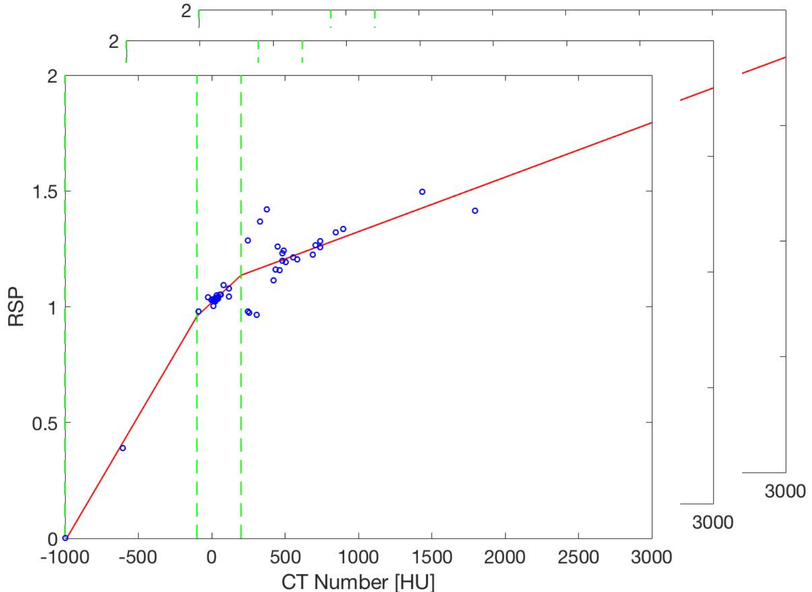
Methods: CT calibration methods

(1) Stoichiometric calibration

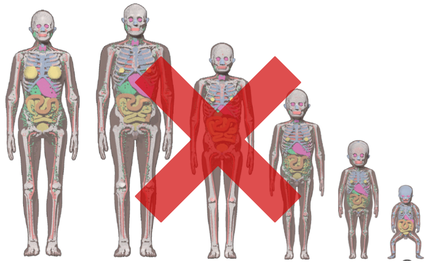


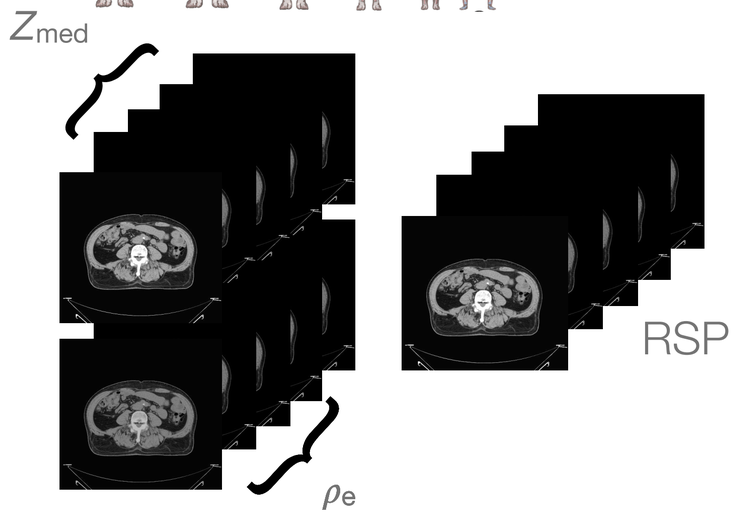
(2) Age-specific stoichiometric calibration





(3) Dual-energy stoichiometric calibration [8]



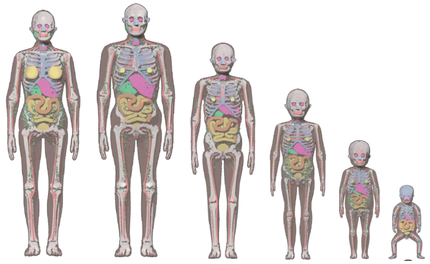


[8] Bourque, A.E., Carrier, J.F. and Bouchard, H., 2014. A stoichiometric calibration method for dual energy computed tomography. *Physics in Medicine & Biology*, *59*(8), p.2059.

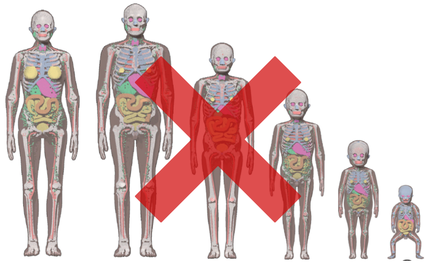
Methods: CT calibration methods

(1) Stoichiometric calibration

(2) Age-specific stoichiometric calibration



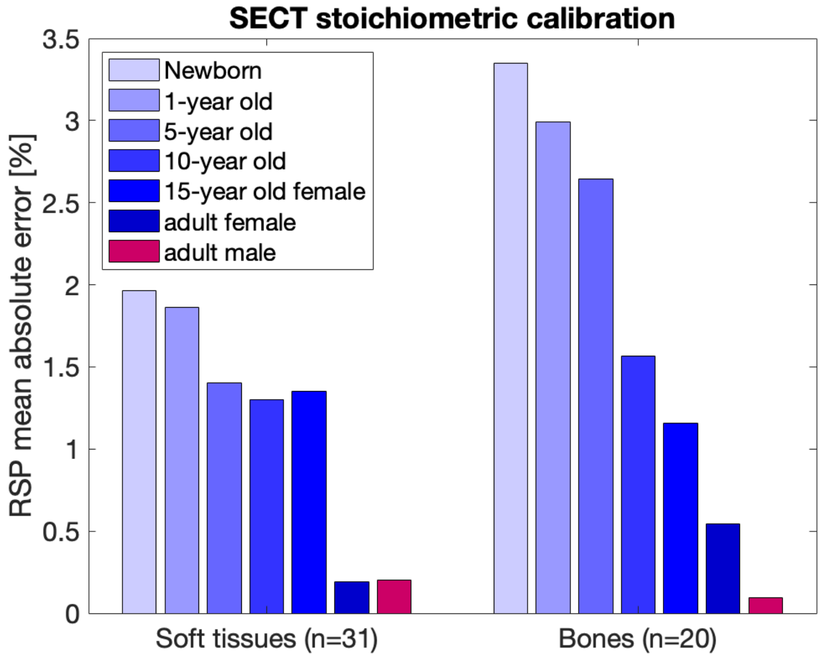
(3) Dual-energy stoichiometric calibration



- Q1: How well can three CT calibration methods estimate the RSPs of paediatric tissues?

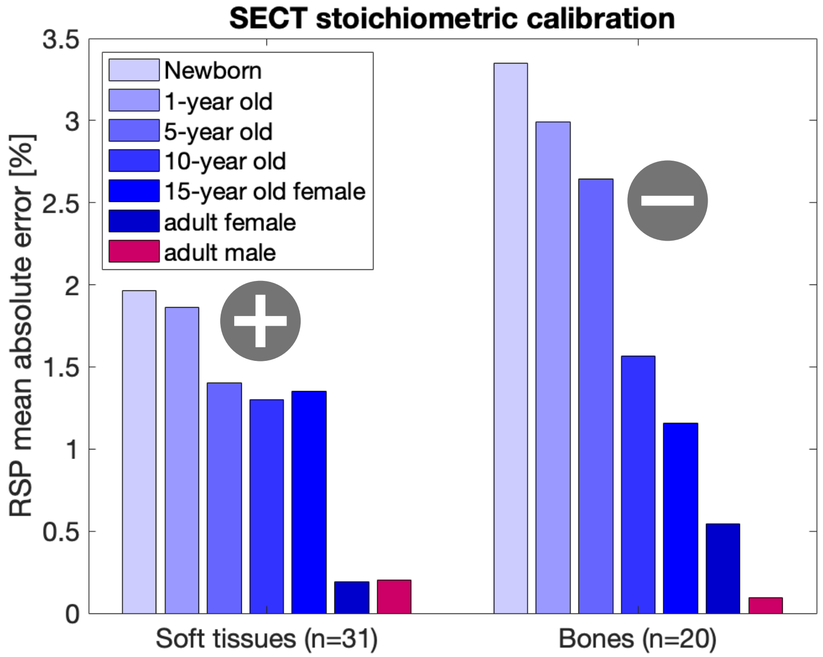
Results: Accuracy of RSP predictions

(1) Stoichiometric calibration



Results: Accuracy of RSP predictions

(1) Stoichiometric calibration

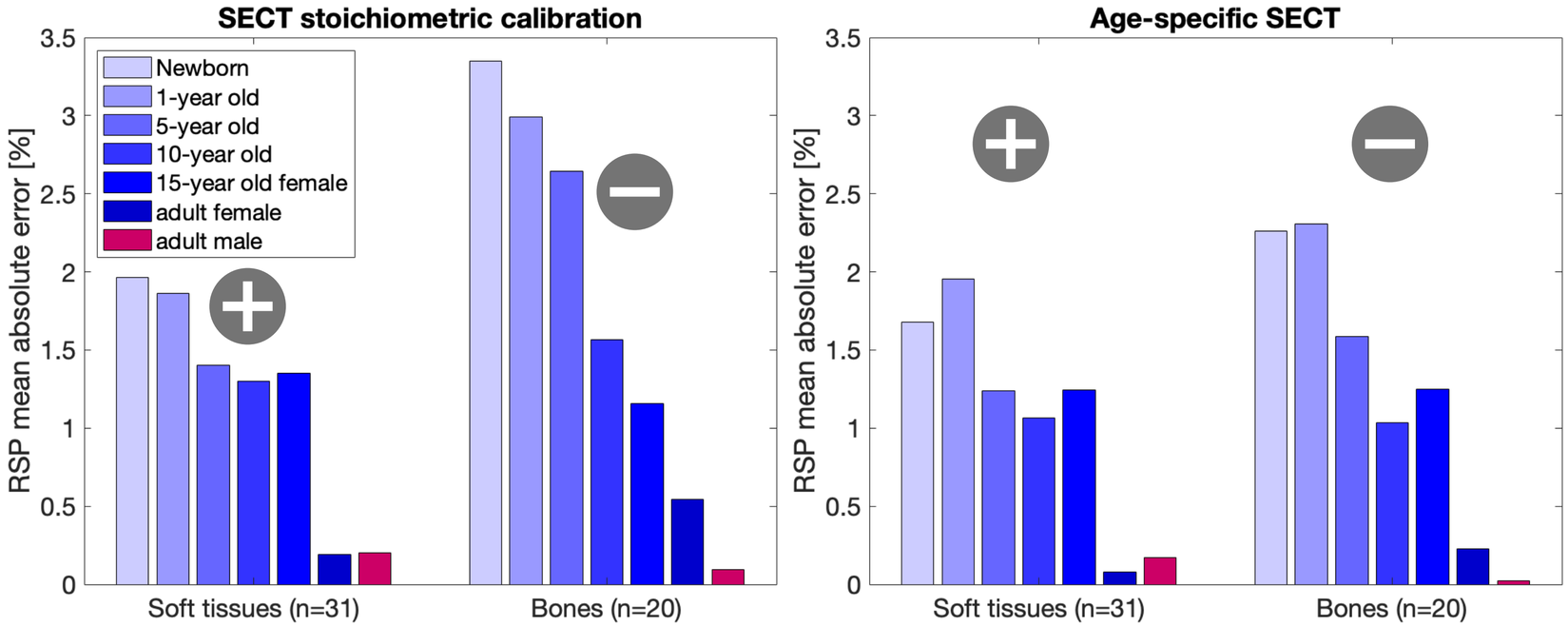


Min error: -18.65% (spongy bones)
Max error: 17.80% (medullary cavity tissue)

Results: Accuracy of RSP predictions

(1) Stoichiometric calibration

(2) Age-specific stoichiometric calibration



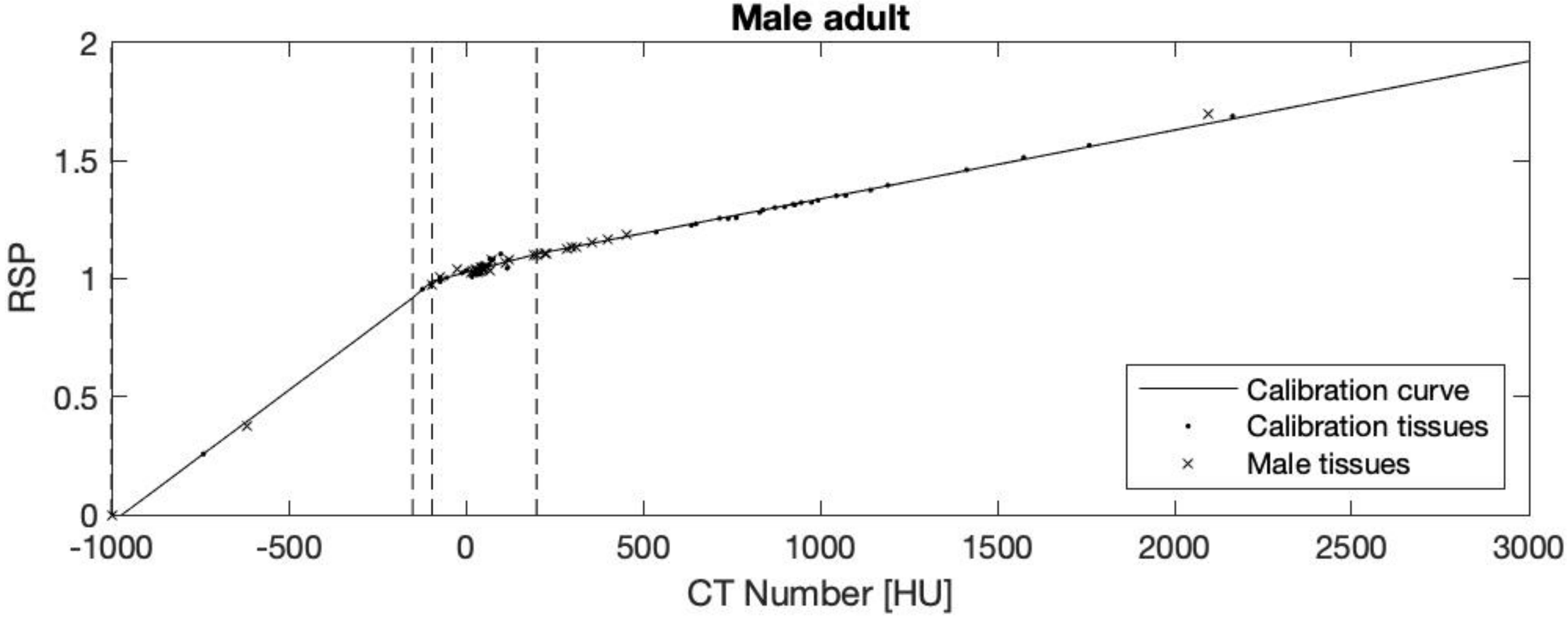
Min error: -18.65% (spongy bones)
Max error: 17.80% (medullary cavity tissue)

Min error: -17.08%
Max error: 20.24%

Results: Accuracy of RSP predictions

(1) Stoichiometric calibration

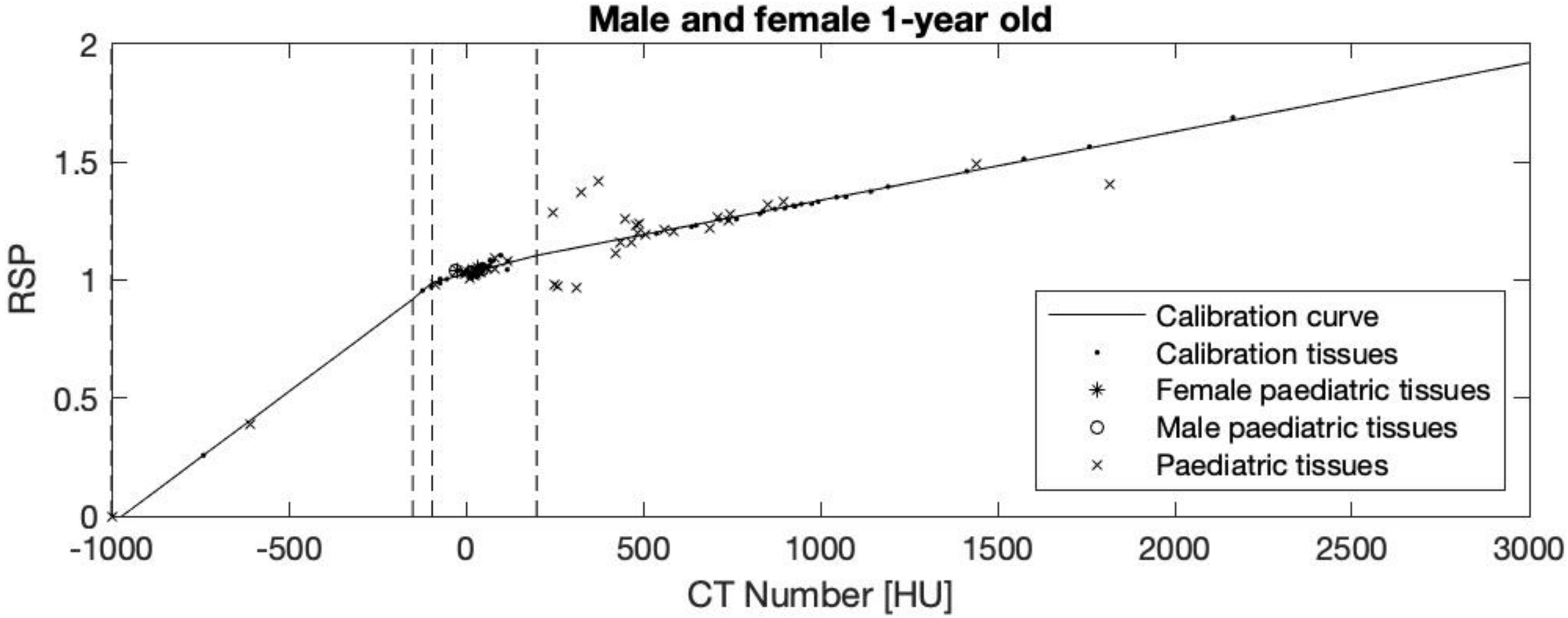
(2) Age-specific stoichiometric calibration



Results: Accuracy of RSP predictions

(1) Stoichiometric calibration

(2) Age-specific stoichiometric calibration

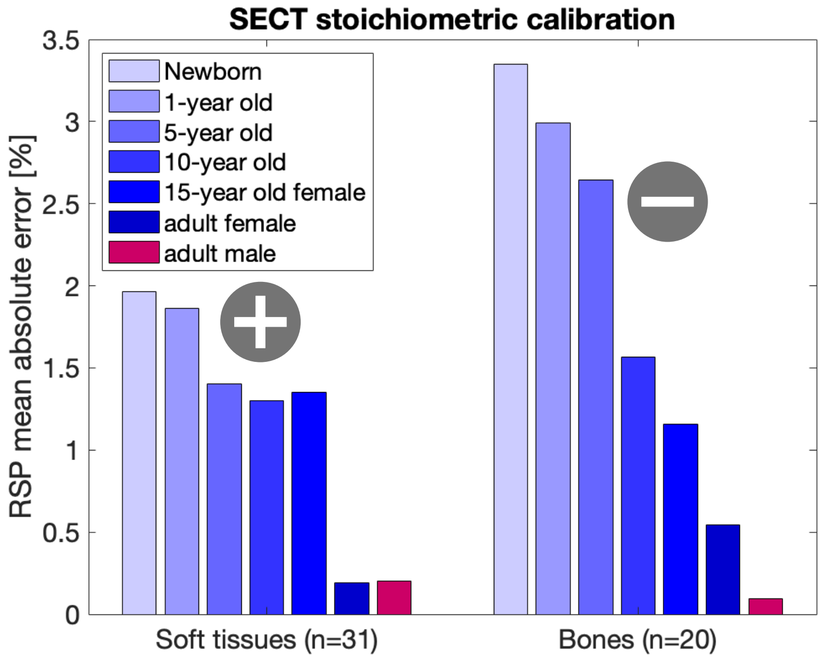


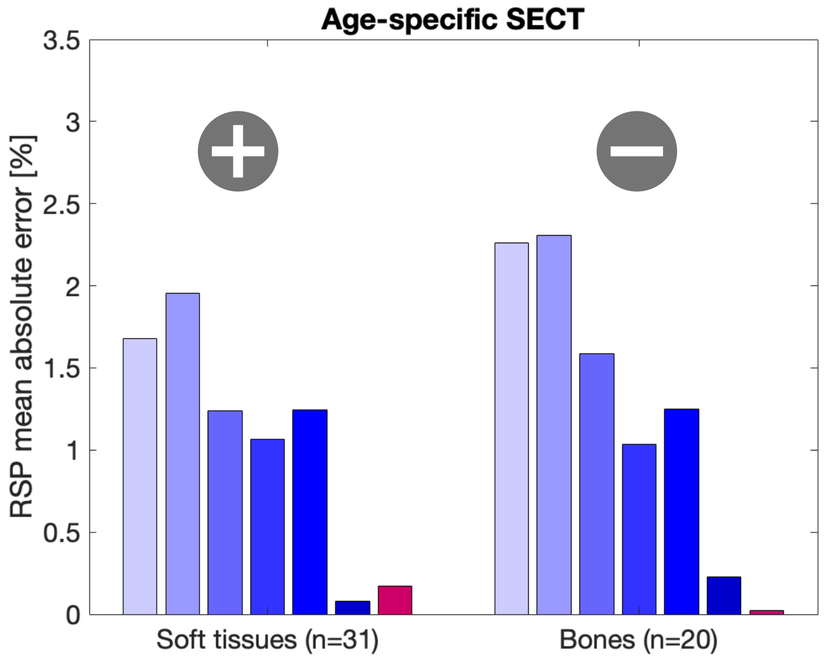
Results: Accuracy of RSP predictions

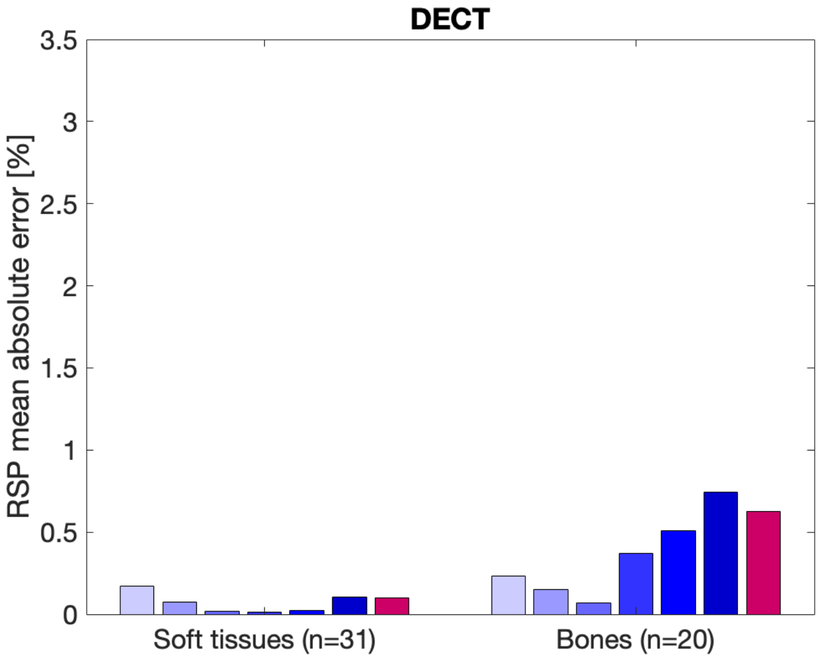
(1) Stoichiometric calibration

(2) Age-specific stoichiometric calibration

(3) Dual-energy stoichiometric calibration







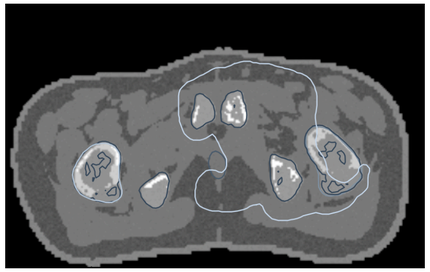
Min error: -18.65% (spongy bones)
Max error: 17.80% (medullary cavity tissue)

Min error: -17.08%
Max error: 20.24%

Min error: -1.36%
Max error: 0.76%

Methods: Computational phantoms

- To assess dose and rage errors from RSP prediction errors, we construct three computational phantoms from CT images of paediatric proton therapy patients



	Ewing's sarcoma	Salivary sarcoma	Glioma
Tissue assignment	10-year old	15-year old	5-year old
RSP maps	1) Theoretical 2) Stoichiometric 3) DECT	1) Theoretical 2) Stoichiometric 3) DECT	1) Theoretical 2) Stoichiometric 3) DECT
Treatment plan	IMPT, 50.4 Gy	IMPT, 64.8 Gy	IMPT, 54 Gy

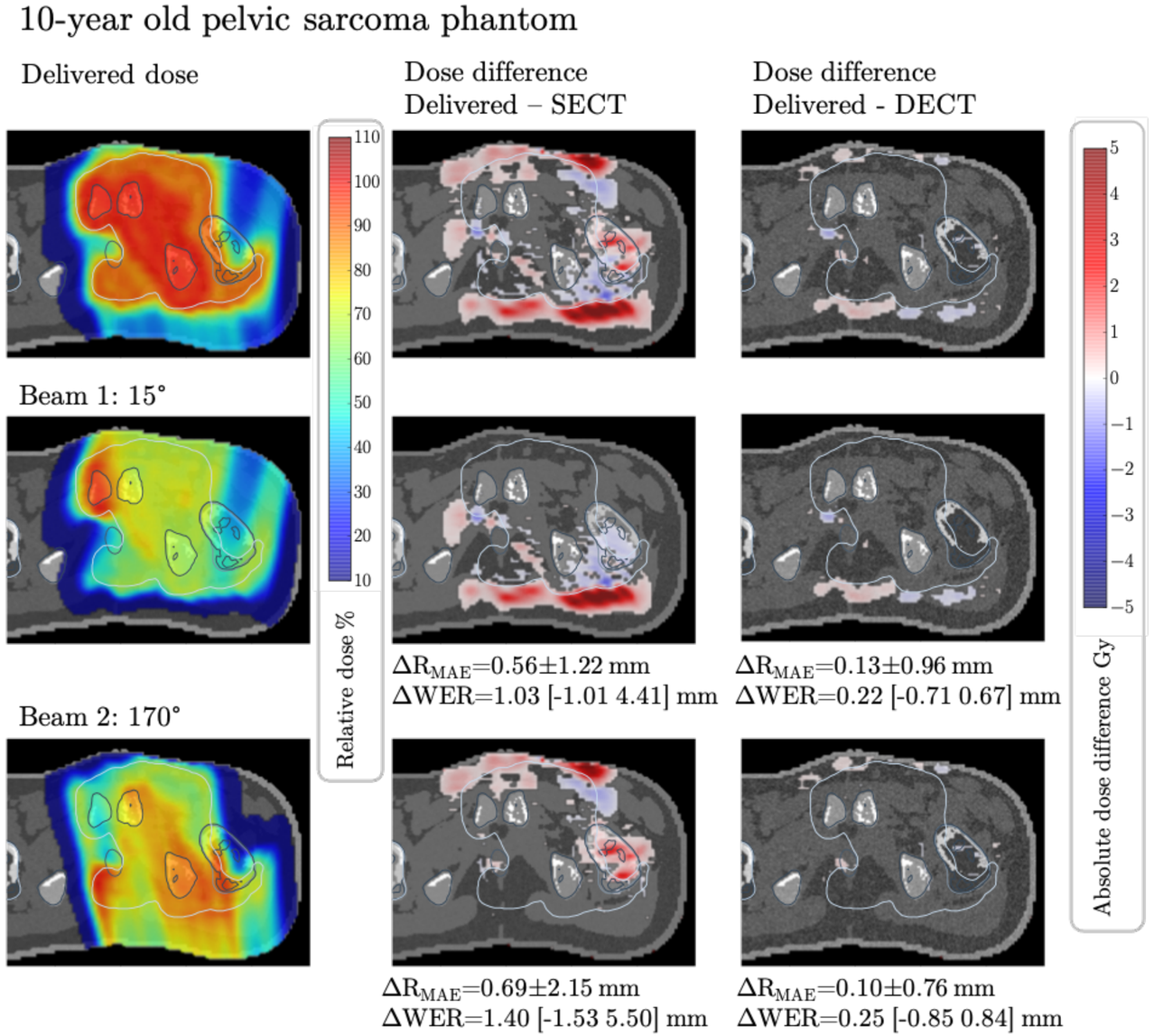
K-means clustering

Plan optimisation on stoichiometric RSP maps, recalculated on theoretical and DECT maps

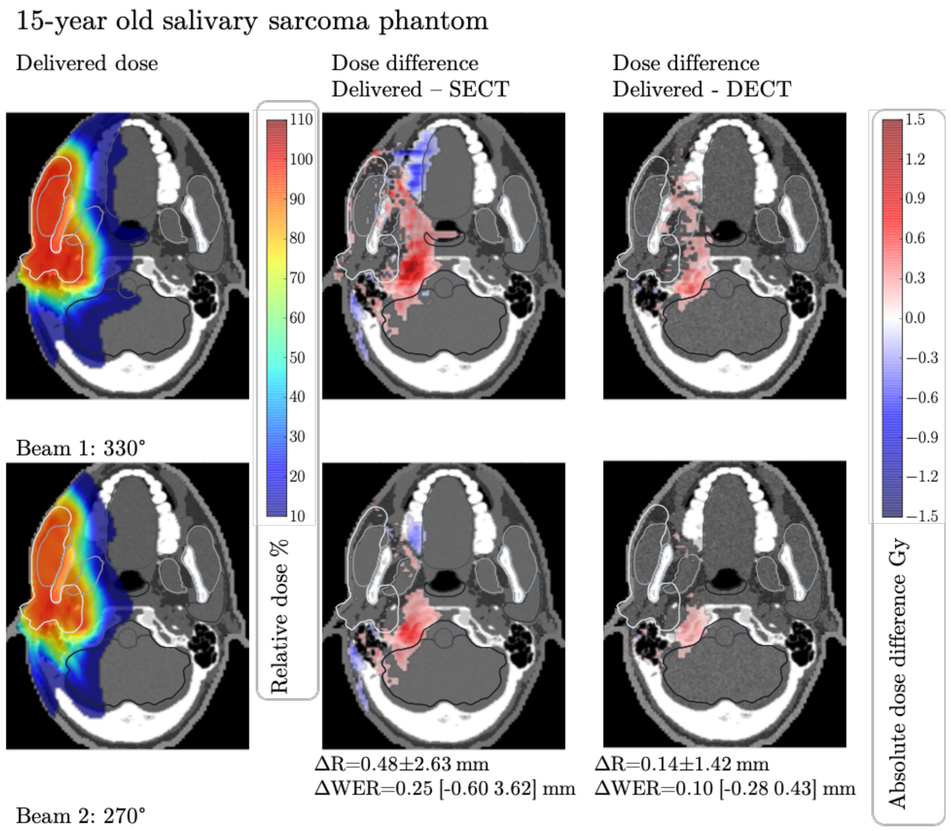
- Q1: What are the dose/range errors caused by erroneous RSP predictions?

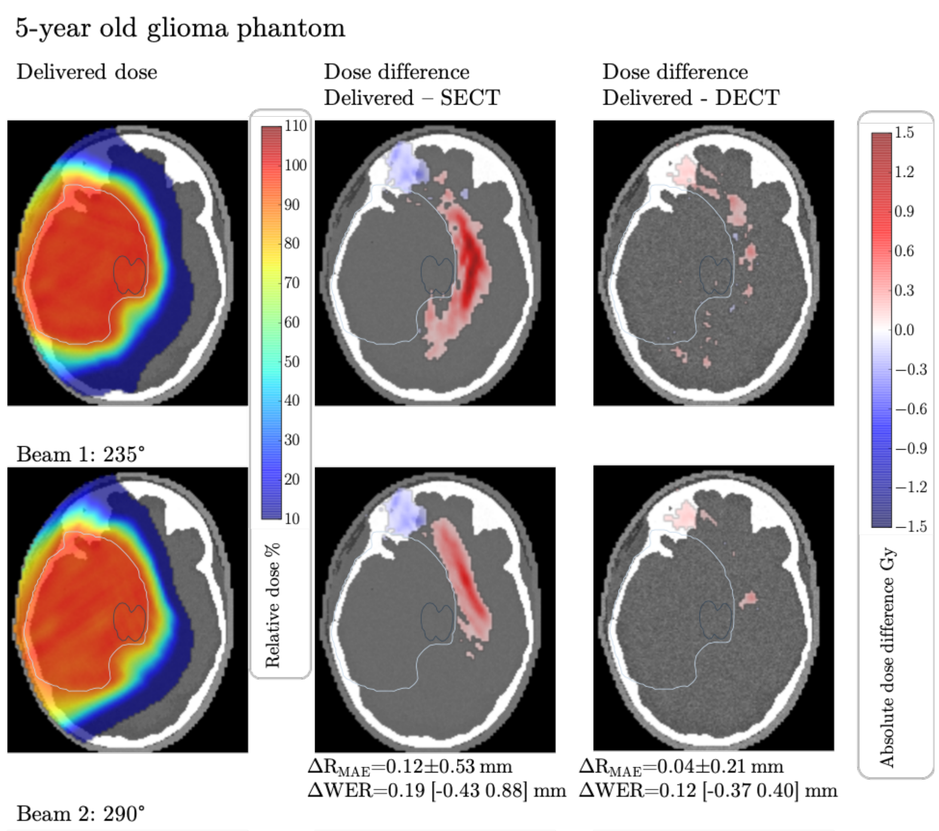
Results: Dose and range errors in Ewing's sarcoma phantom

- Stoichiometric calibration: Water equivalent range overshoots of up to **5.5 mm**, overdose distal to the target exceeding **5 Gy** (~10% of prescribed dose).
- DECT: range overshoots **<1 mm**, dose errors **<1 Gy**.

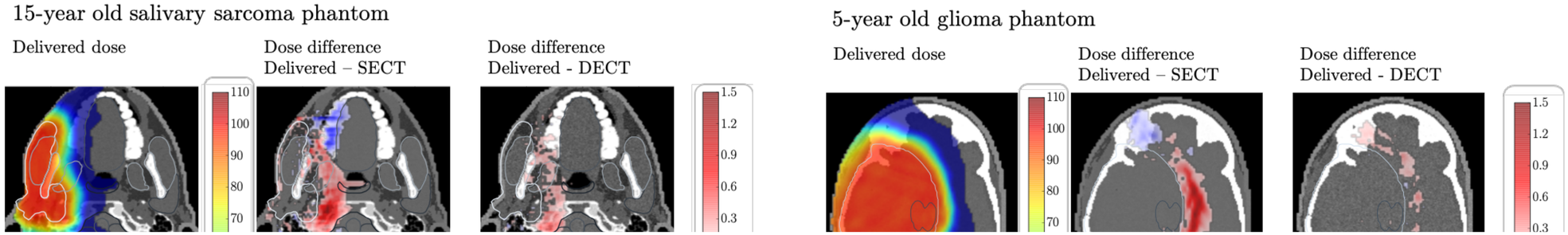


Results: Dose and range errors in the head and neck phantoms





Results: Dose and range errors in the head and neck phantoms



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RESEARCH ARTICLE

MEDICAL PHYSICS

Assessment of the impact of CT calibration procedures for proton therapy planning on pediatric treatments

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Next steps

- All investigations so far were theoretical
- Children's tissue compositions and densities need to be verified
  - Work in progress to do elemental analysis on few tissues
- DECT will be implemented at UCLH - initiating a patient study comparing DECT vs SECT
- Future outlook: Reduction of treatment-related side effects?

Take-home message

- Children's tissues are different from adult tissues in composition and density
- A **single-energy CT** calibration curve is **not sufficient** to represent paediatric tissues
- RSP errors lead to **dose errors larger than 5 Gy, range errors larger than 5 mm**
- DECT better represents differences in tissues, in fact **DECT reduces the dose errors to <1 Gy and the range error <1 mm** in the three here demonstrated cases.
- Range differences only represent errors from CT-to-RSP conversion and do not include other sources of range uncertainties (e.g., *I*-value, biology, CT grid size,…).

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