

Dosimetry & treatment planning for Ac-225 and other alpha-emitters

Disclosures

- Consultant
 - Abdera Therapeutics, Bayer, Clovis, Precirix, RayzeBio
- Scientific Advisory Board
 - Orano Med
- Founder, Stakeholder
 - Radiopharmaceutical Imaging and Dosimetry, LLC (Rapid)

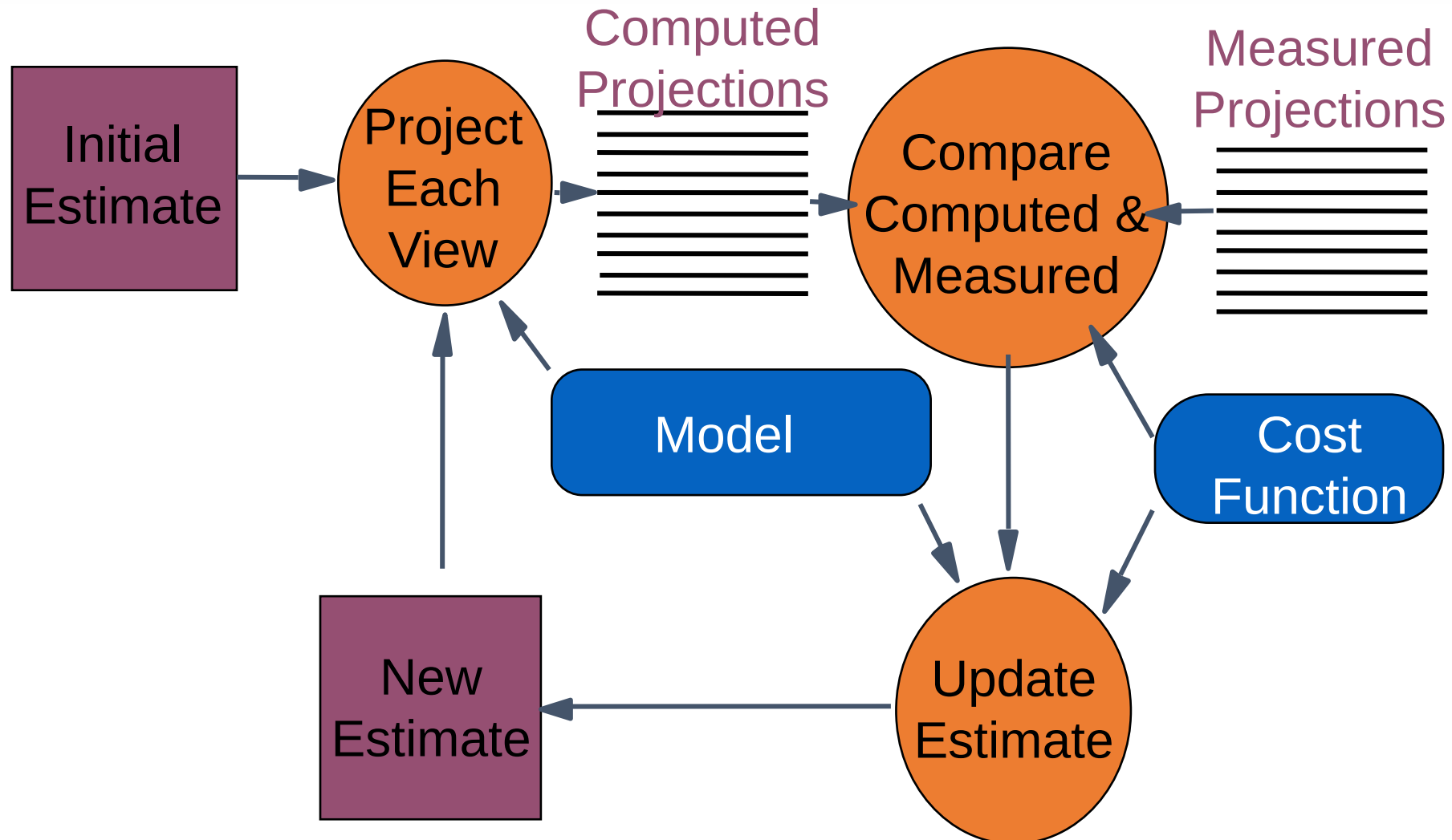
**Radioactive
chemo**



**Imaging,
dosimetry-
based delivery**

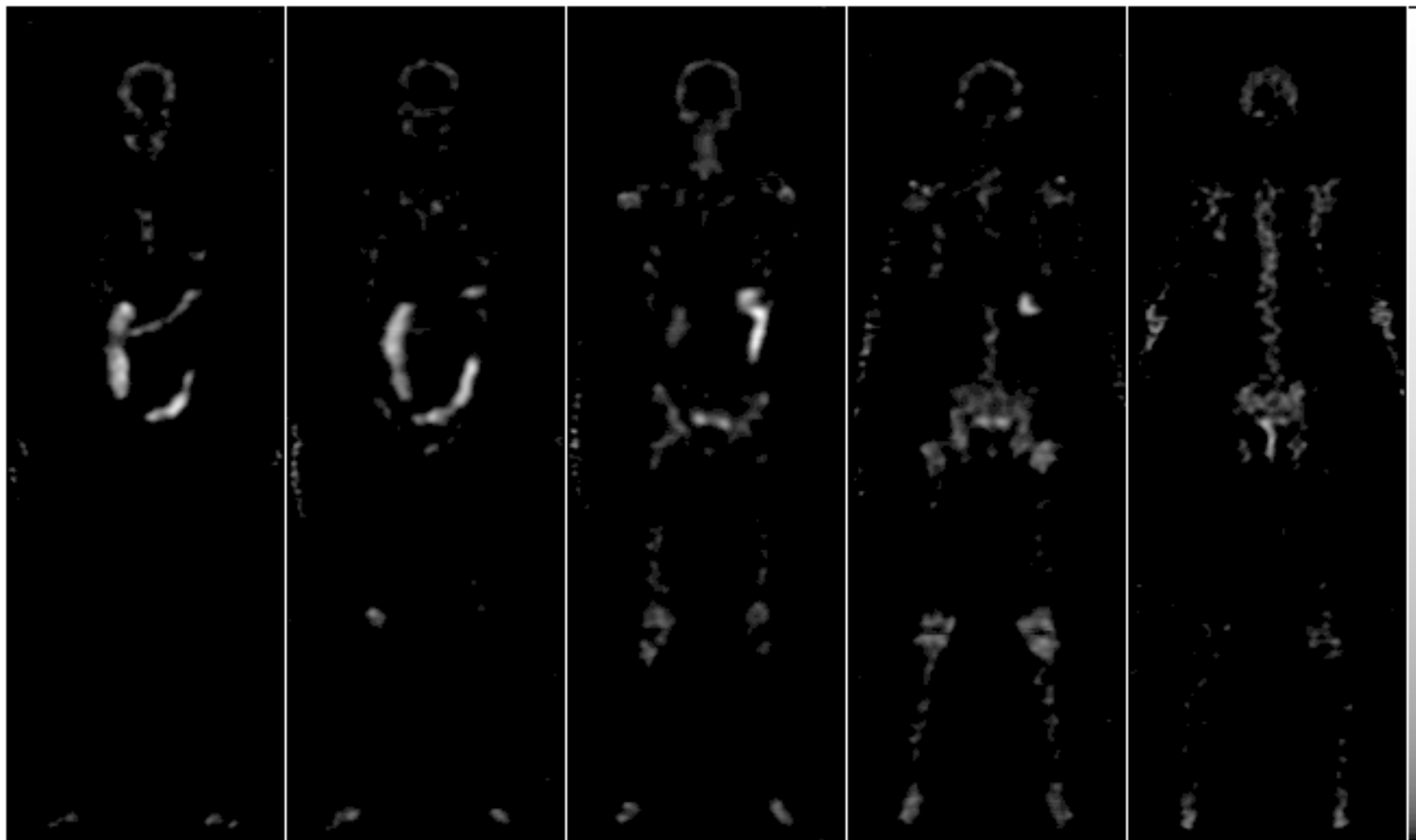
- Imaging
 - Advanced recon
 - New instruments
- Macro to micro (M2 μ)
 - Microscale S values
 - Microscale apportionment factors
- RBE
 - In vitro, In vivo
- Treat canine OS

Imaging – Advanced reconstruction



Imaging – Advanced reconstruction

5 coronal slices, 144 h, 5 iterations, 12 subsets per iteration, logarithmic grayscale



Imaging – Advanced reconstruction

Ra-223 Errors in Organ Activity Estimates

	4 h	24 h	72 h	144 h
Small intestine	$-3.8 \pm 0.6\%^1$	-	-	-
Upper large intestine	-	$9.7 \pm 0.6\%$	$8.4 \pm 0.8\%$	$6.5 \pm 1.7\%$
Lower large intestine	-	$11.4 \pm 1.7\%$	$12.8 \pm 1.7\%$	$12.6 \pm 1.8\%$
Bones	$-7.3 \pm 0.5\%$	$-7.0 \pm 0.7\%$	$-9.0 \pm 0.7\%$	$-12.9 \pm 1.0\%$

20 iterations, 12 subsets

Uncertainties are COVs over 50 simulated noise realizations

True VOIs are assumed known

Imaging – build a new instrument

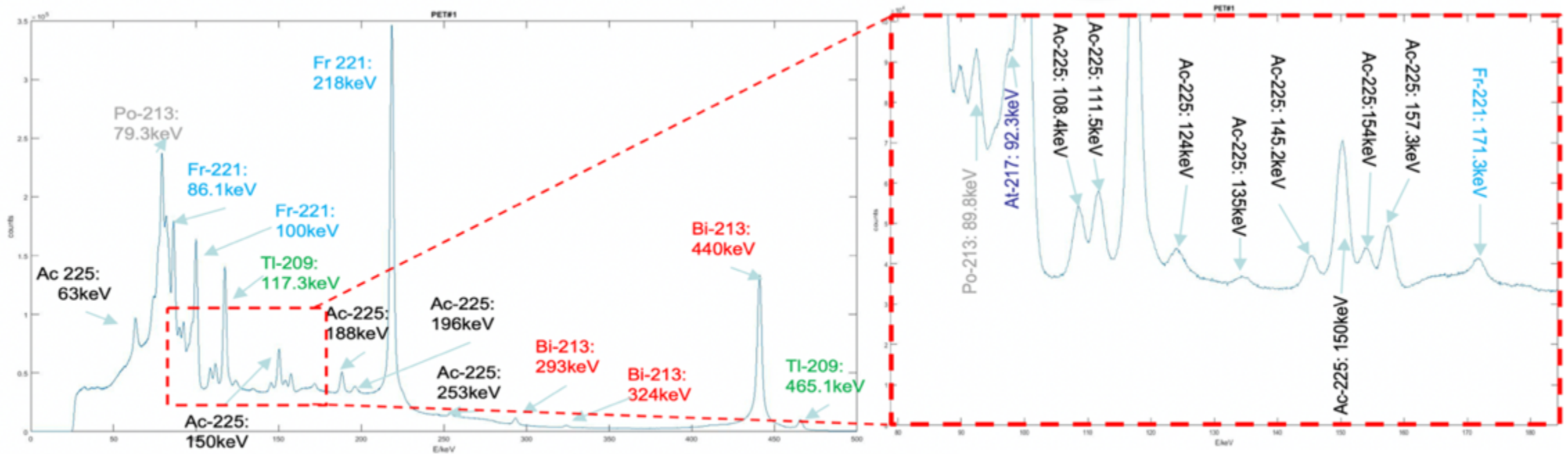


Fig. 4: An energy spectrum collected with an Ac-225 solution and a 3-D CZT imaging spectrometer having an active detector volume of 4 cm x 4 cm x 1 cm in size. Note that the spectrum includes all types of interactions (single photoelectric, Compton scattering, charge-sharing etc.) physically happened inside the detector.

Macro 2 micro – S values

Wesley Bolch UFL, Rob Hobbs

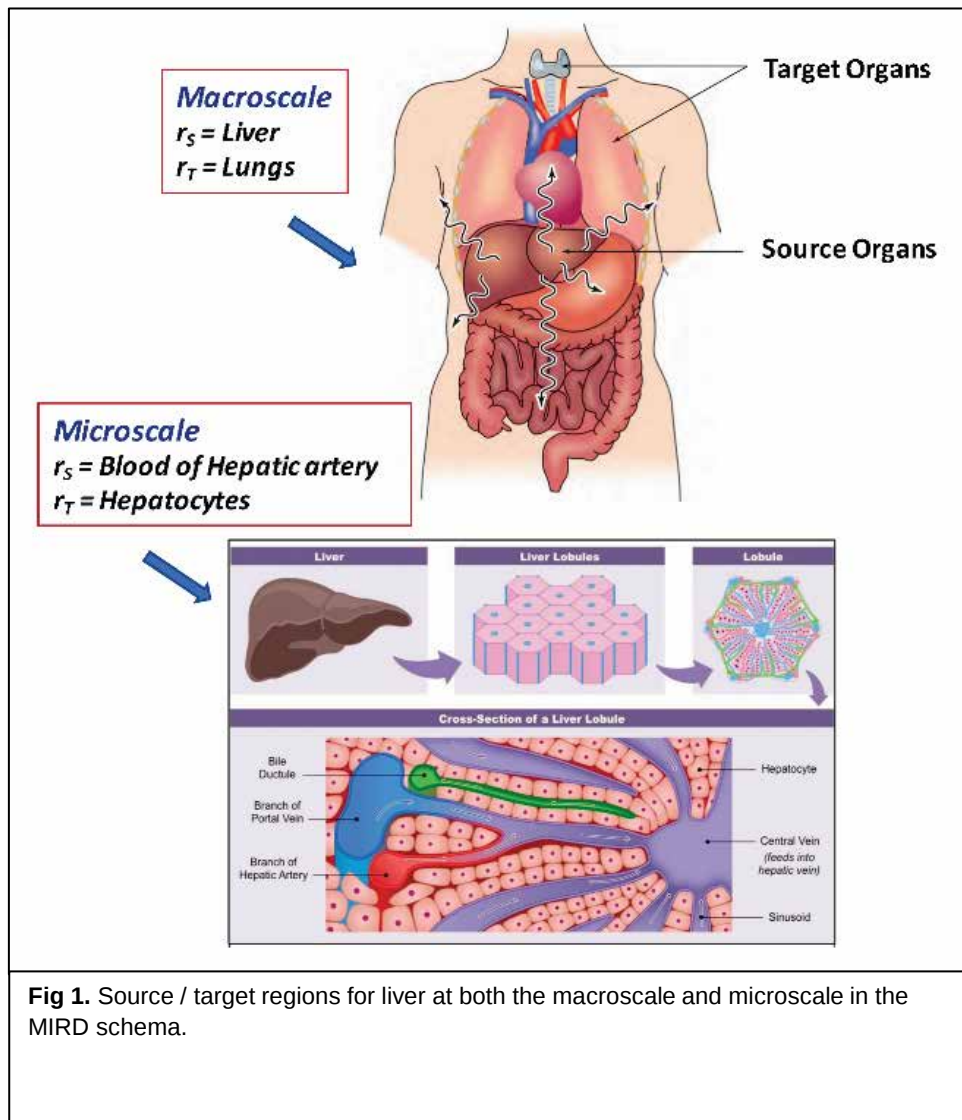


Table 1. Murine microscale S values for the ^{225}Ac decay chain for both the unit and compartmental nephron model.

^{225}Ac	S-value (unit) (Gy/Bq-s)	Absorbed energy (MeV/decay)	Absorbed Fraction	S-value (compartment) (Gy/Bq-s)
glc $\leftarrow$ glc	5.74E-04	4.29	0.721	1.53E-07
glc $\leftarrow$ prt	5.20E-06	1.12	0.188	1.39E-09
prtc $\leftarrow$ glc	2.33E-04	0.05	0.009	1.86E-09
prtc $\leftarrow$ prtc	6.82E-04	4.37	0.734	5.44E-09
prtc $\leftarrow$ prtl	6.85E-04	4.39	0.737	5.46E-09
prtc $\leftarrow$ prts	6.84E-04	4.38	0.736	5.45E-09
kid $\leftarrow$ kid	-	5.94	0.998	3.22E-09
cor $\leftarrow$ cor	-	5.40	0.908	4.44E-09

Table 2. Human microscale S values for the ^{225}Ac decay chain for both the unit and compartmental nephron model.

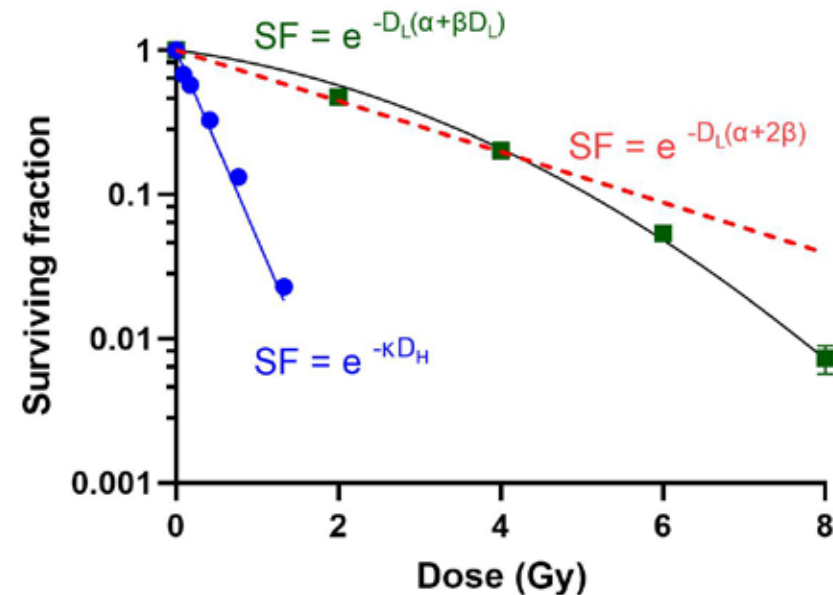
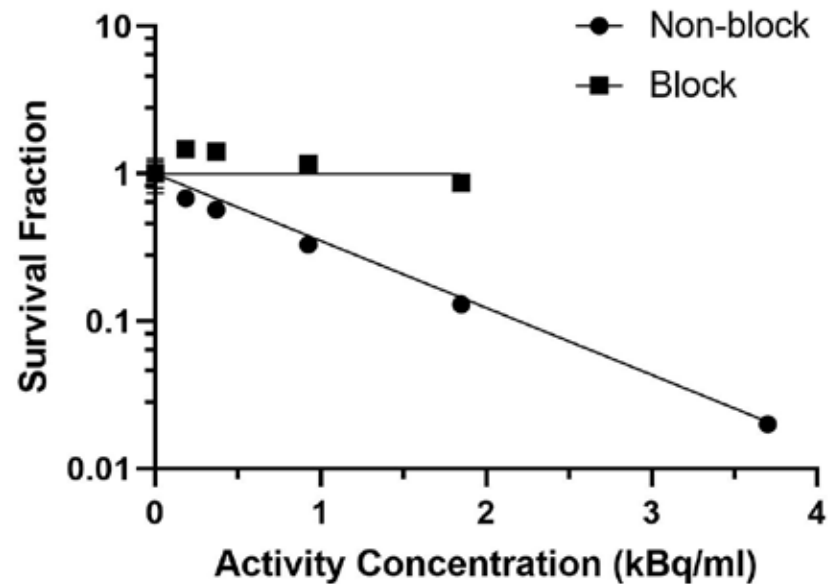
^{225}Ac	S-value (unit) (Gy/Bq-s)	Absorbed energy (MeV/decay)	Absorbed Fraction	S-value (compartment) (Gy/Bq-s)
glc $\leftarrow$ glc	5.70E-05	5.24	0.881	1.85E-10
glc $\leftarrow$ prt	5.39E-06	0.75	0.126	6.08E-13
prtc $\leftarrow$ glc	3.02E-05	0.096	0.016	3.12E-12
prtc $\leftarrow$ prtc	4.54E-05	1.28	0.215	4.69E-12
prtc $\leftarrow$ prtl	4.49E-05	1.76	0.296	4.64E-12
prtc $\leftarrow$ prts	4.52E-05	1.53	0.257	4.66E-12
kid $\leftarrow$ kid	-	5.95	1.000	3.17E-12
cor $\leftarrow$ cor	-	5.95	1.000	4.82E-12

Macro 2 micro – Apportionment factors

Rob Hobbs, Anders Josefsson

Fig 4. Schema of the apportionment paradigm. Whole organ activity coefficients are measured as a function of time for the whole organ, or portion (blue line). Concurrently,

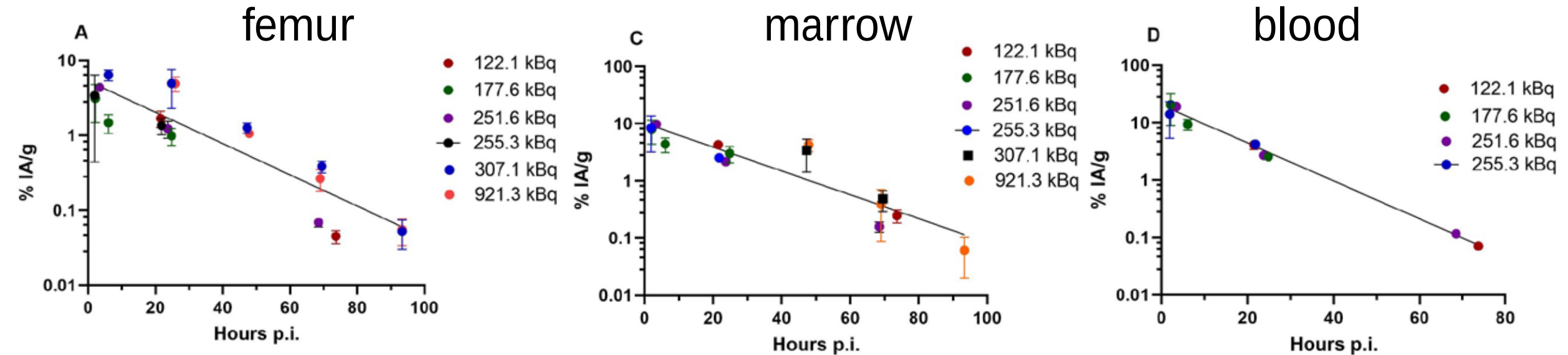
RBE – In Vitro (for $^{212}\text{Pb}/^{212}\text{Bi}$)



RBE for 37% survival = 8; RBE2 = 10

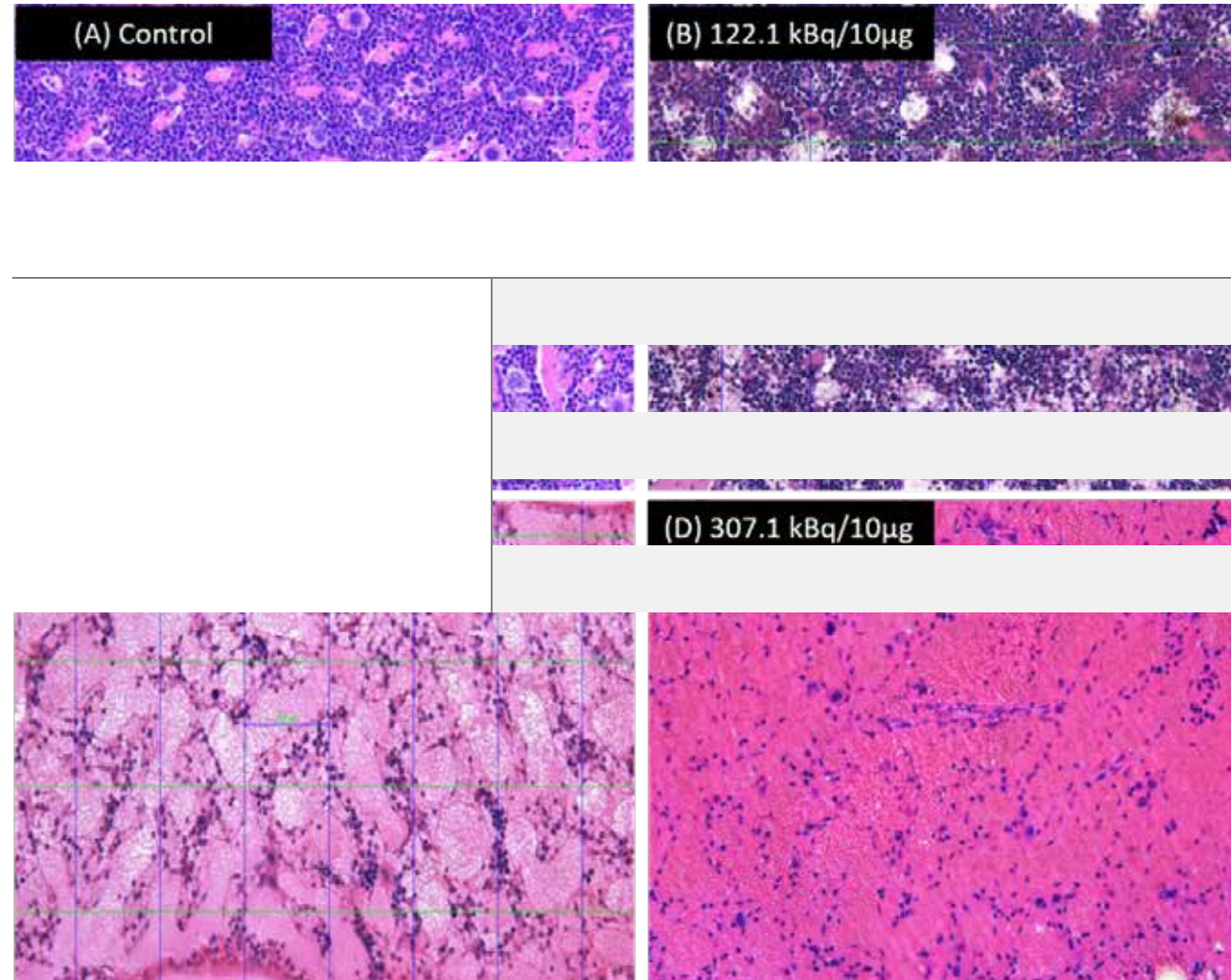
Ioanna Liatsou, Remco Bastiaannet, Rob Hobbs

RBE – In Vivo (for $^{212}\text{Pb}/^{212}\text{Bi}$)



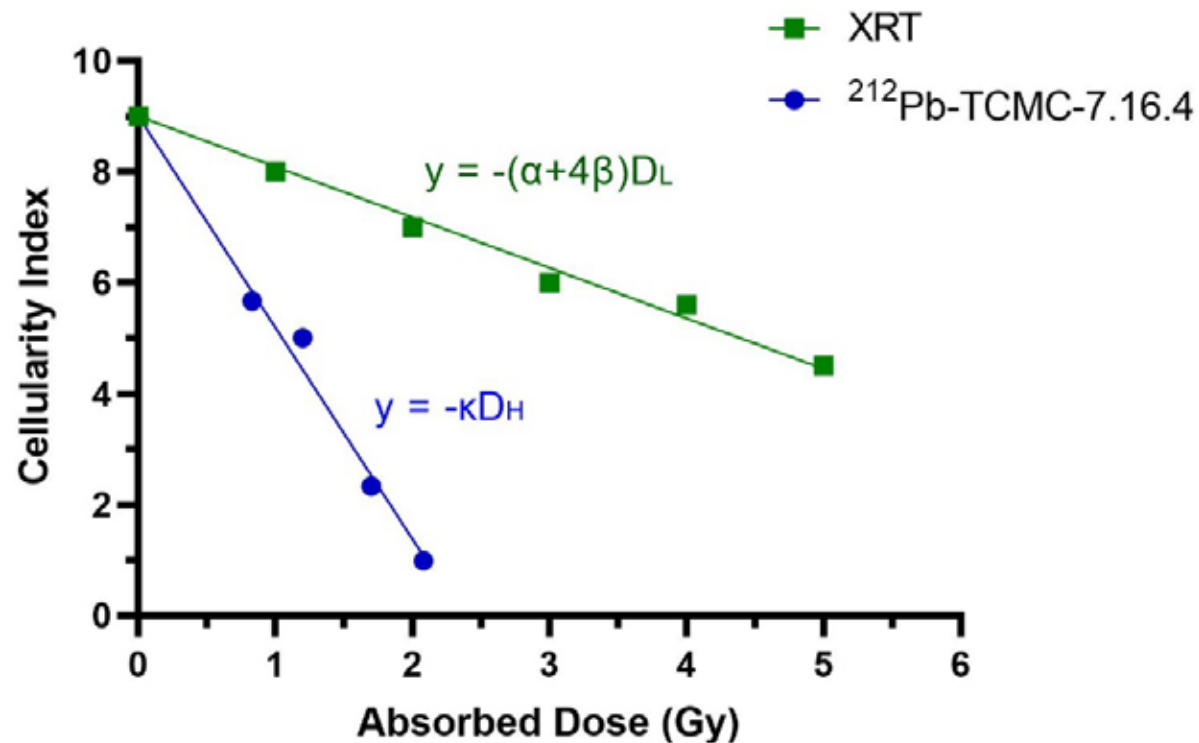
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RBE – In Vivo (for $^{212}\text{Pb}/^{212}\text{Bi}$)



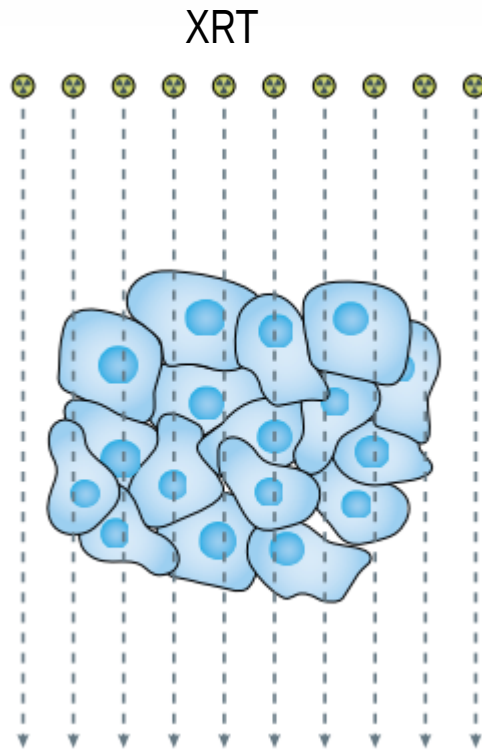
Ioanna Liatsou, Remco Bastiaannet, Anders Josefsson, Rob Hobbs

RBE – In Vivo (for $^{212}\text{Pb}/^{212}\text{Bi}$)

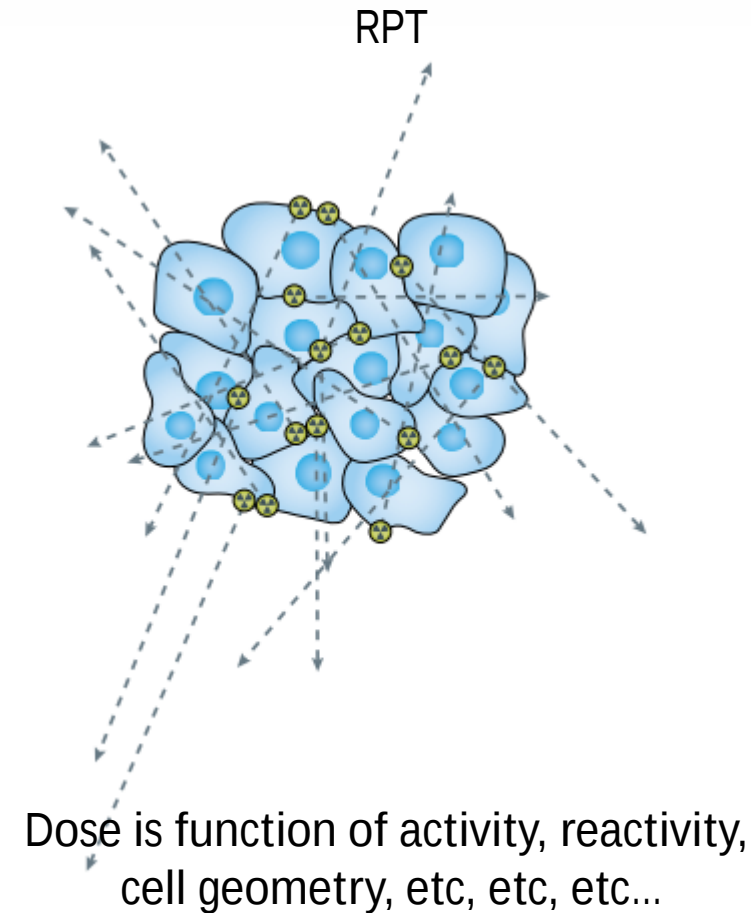


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RBE – In Vitro (for $^{212}\text{Pb}/^{212}\text{Bi}$)

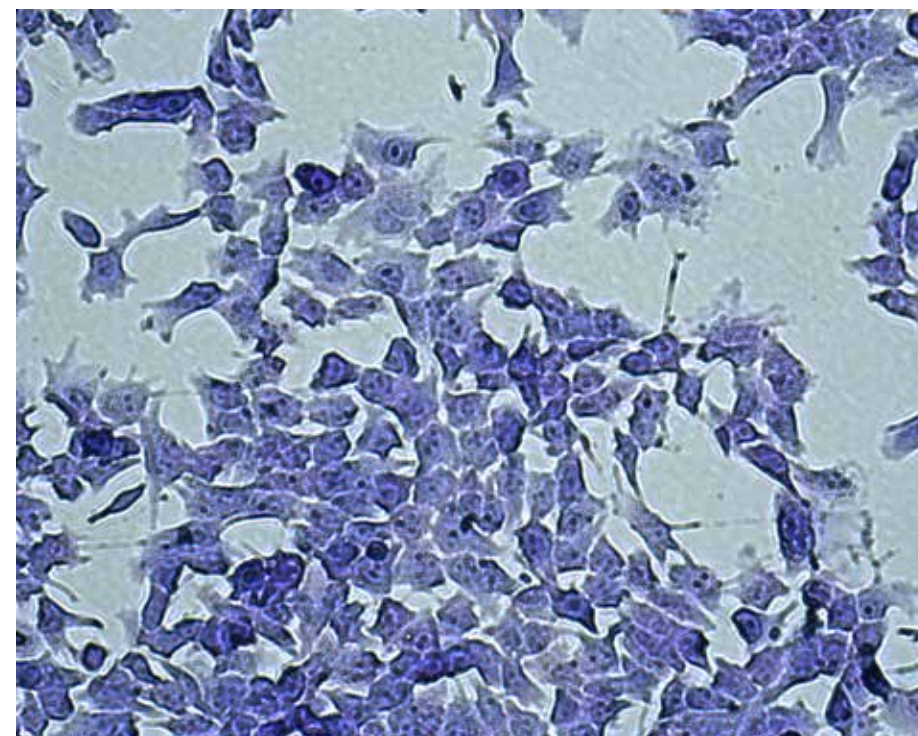
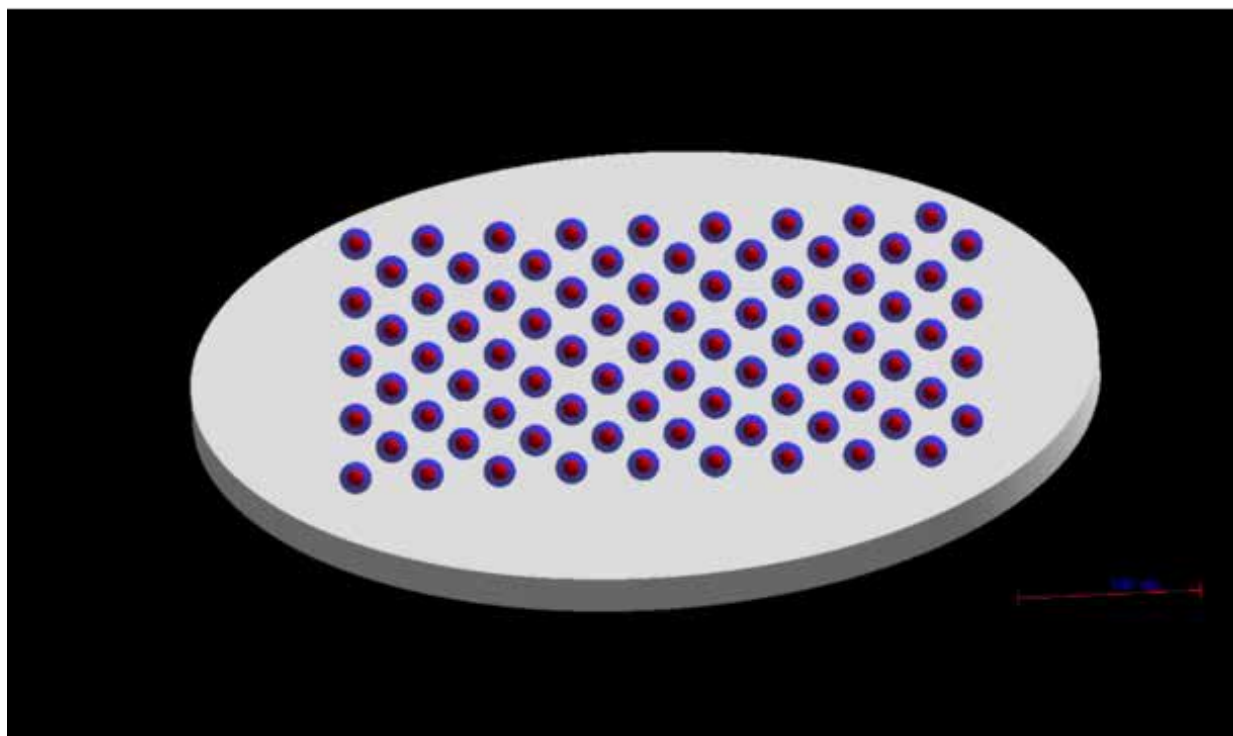


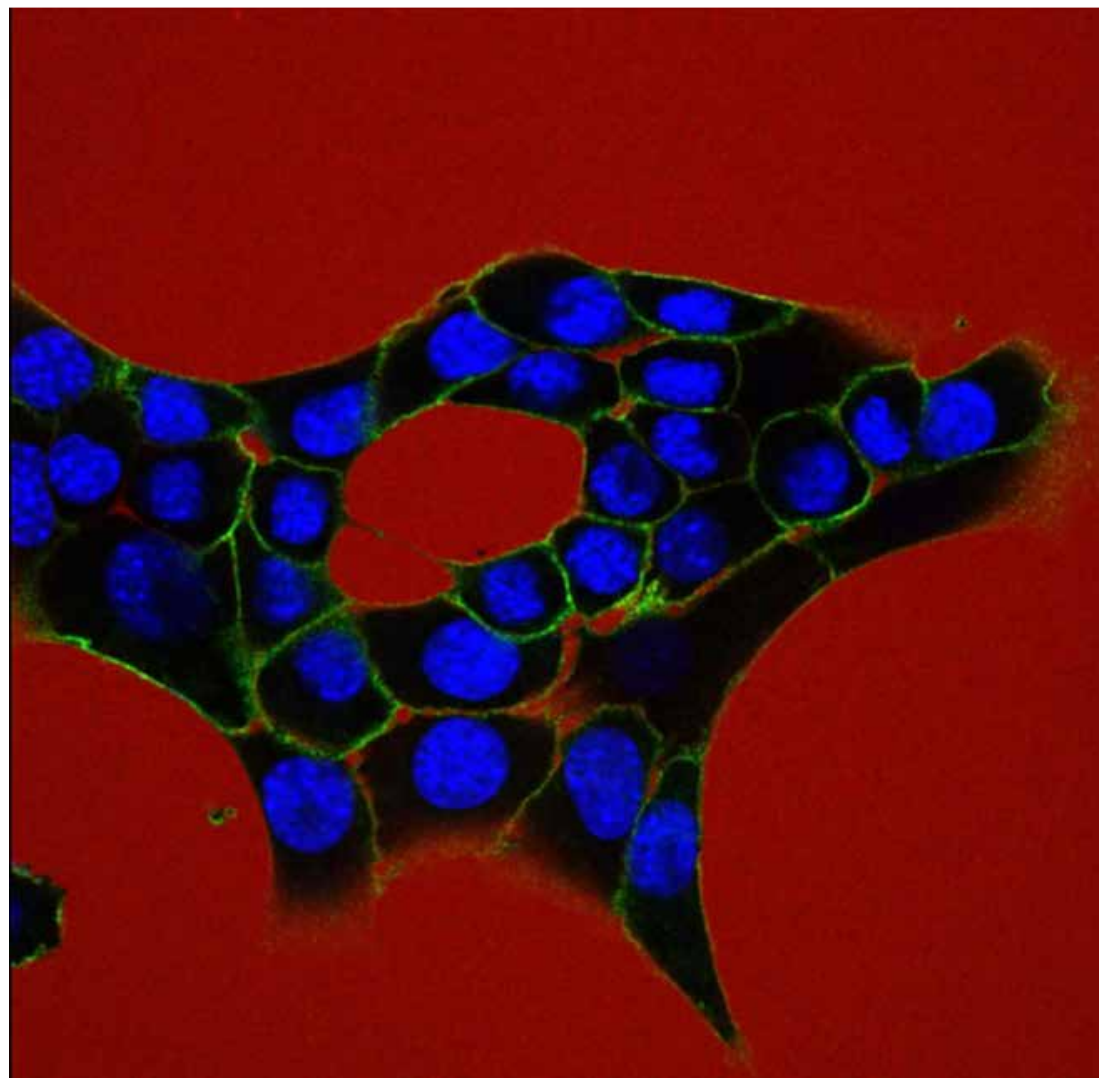
Dose is "set"

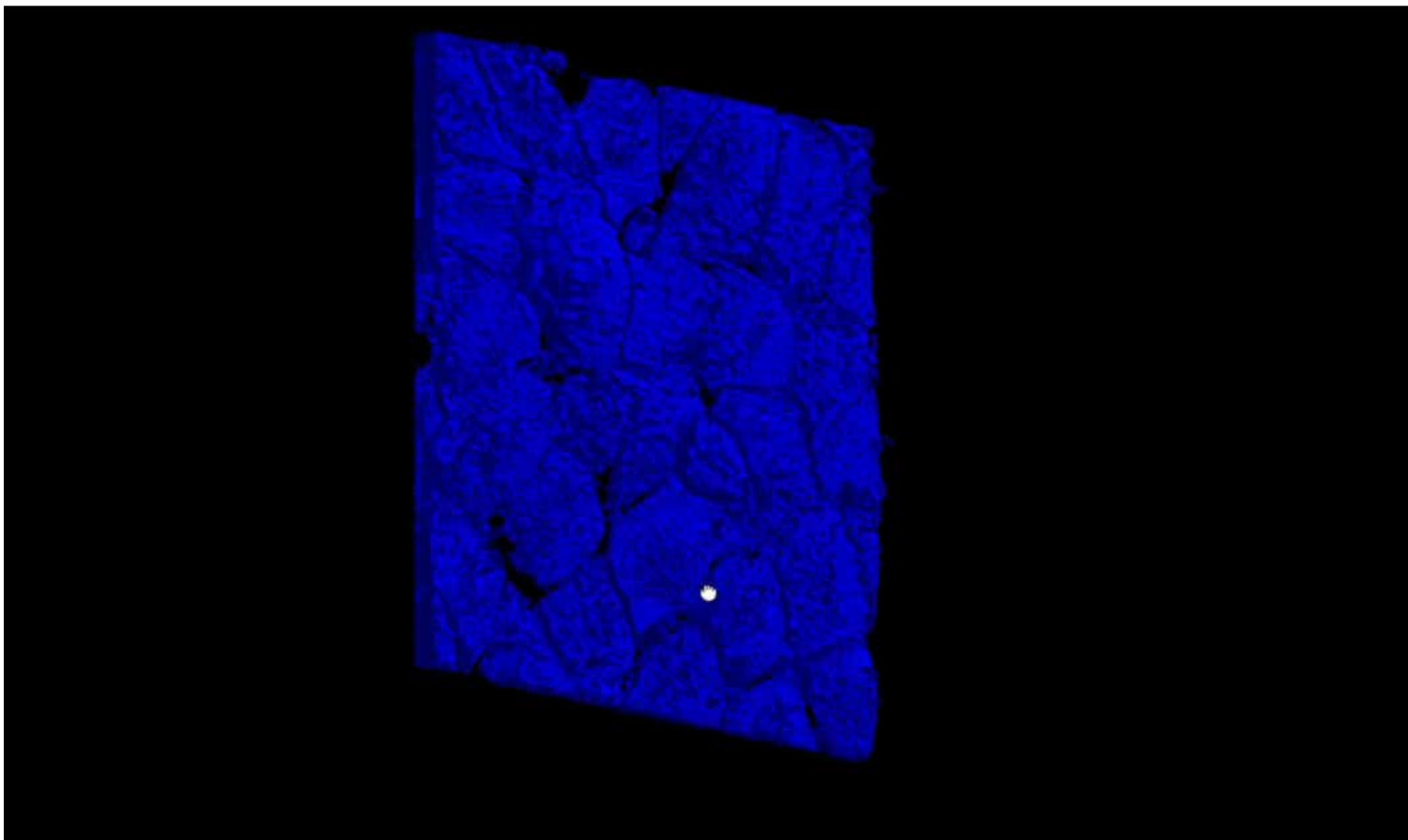


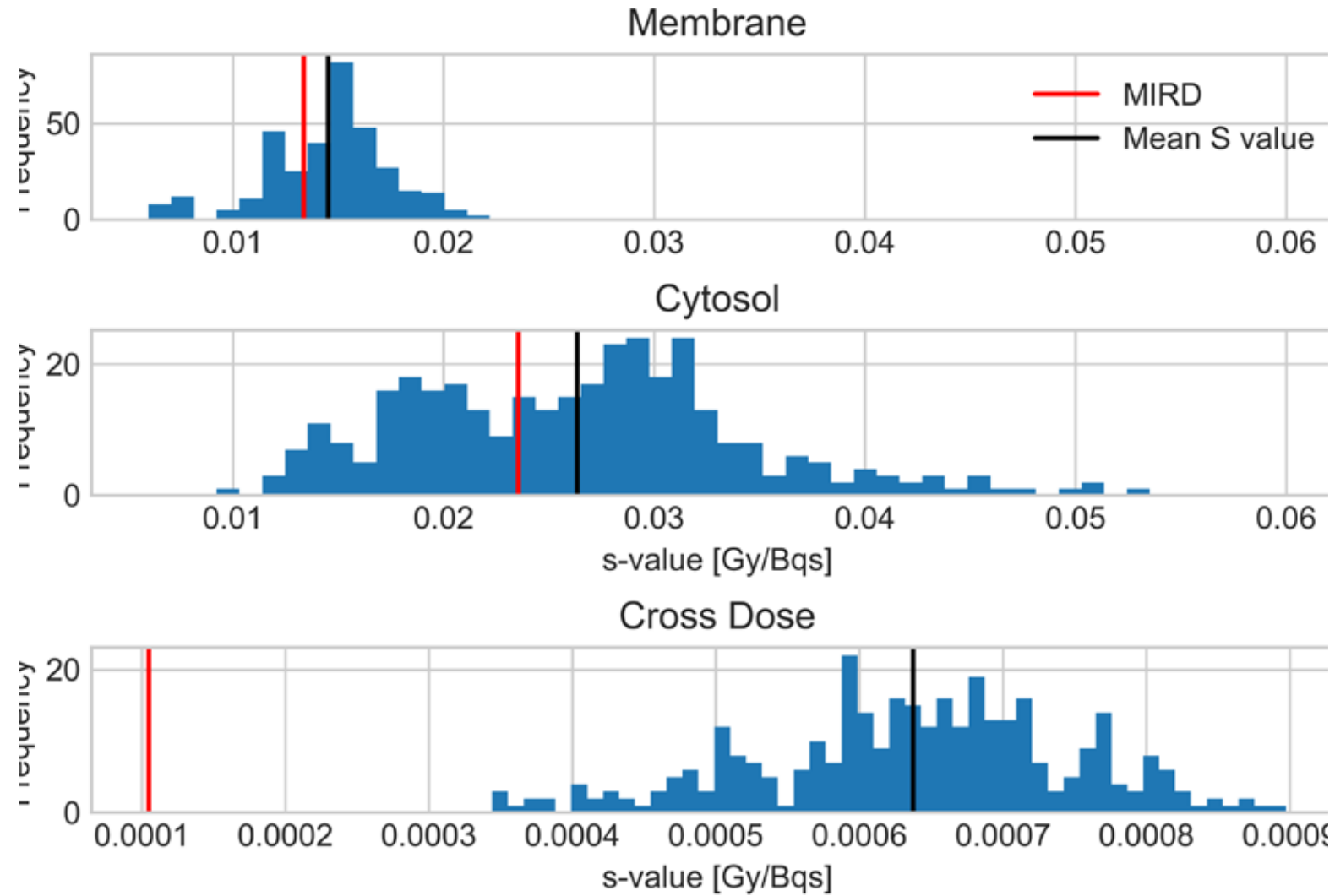
Sgouros et al. 2020

Ioanna Liatsou, Remco Bastiaannet, Rob Hobbs

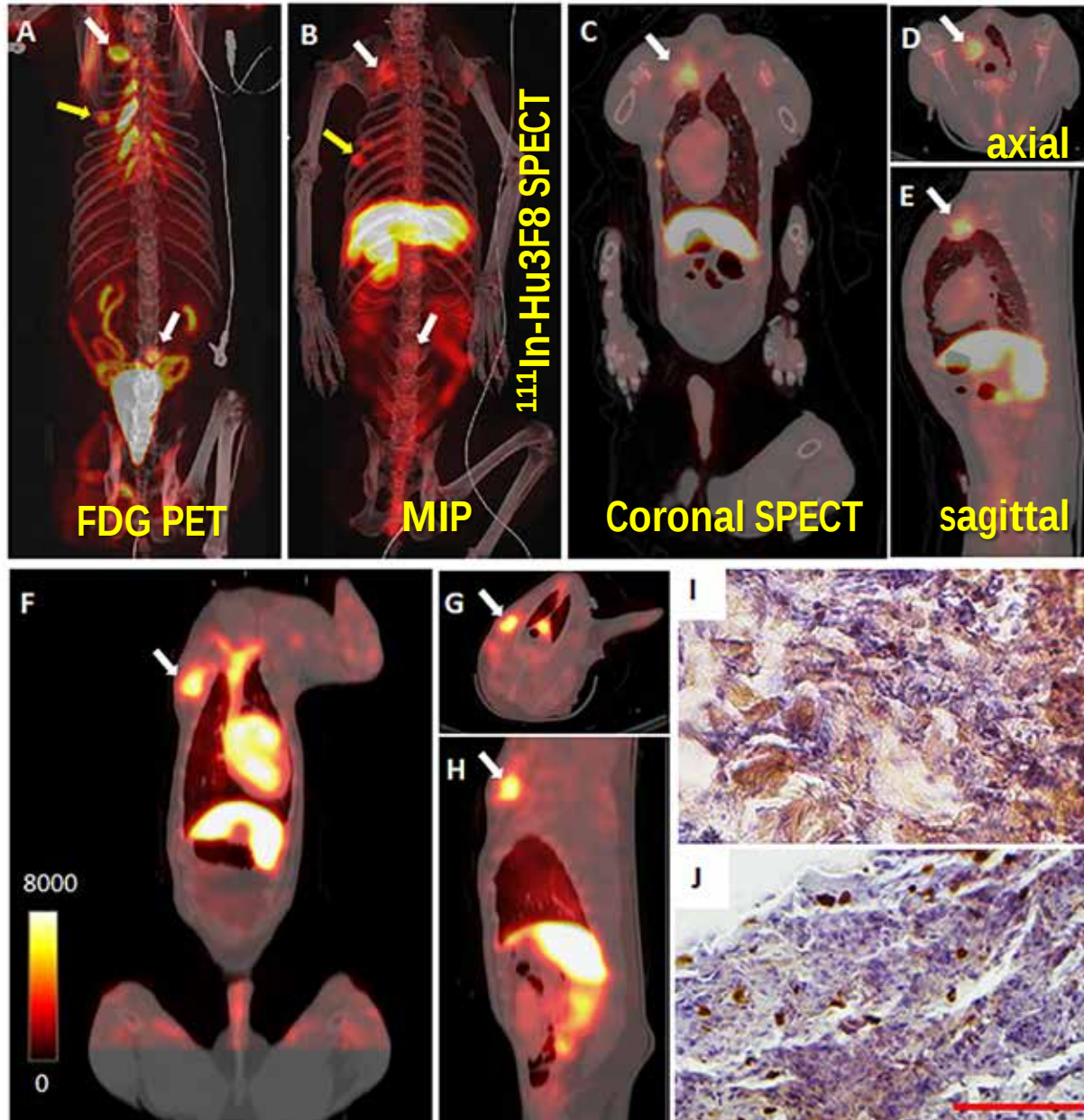








Canine Osteosarcoma

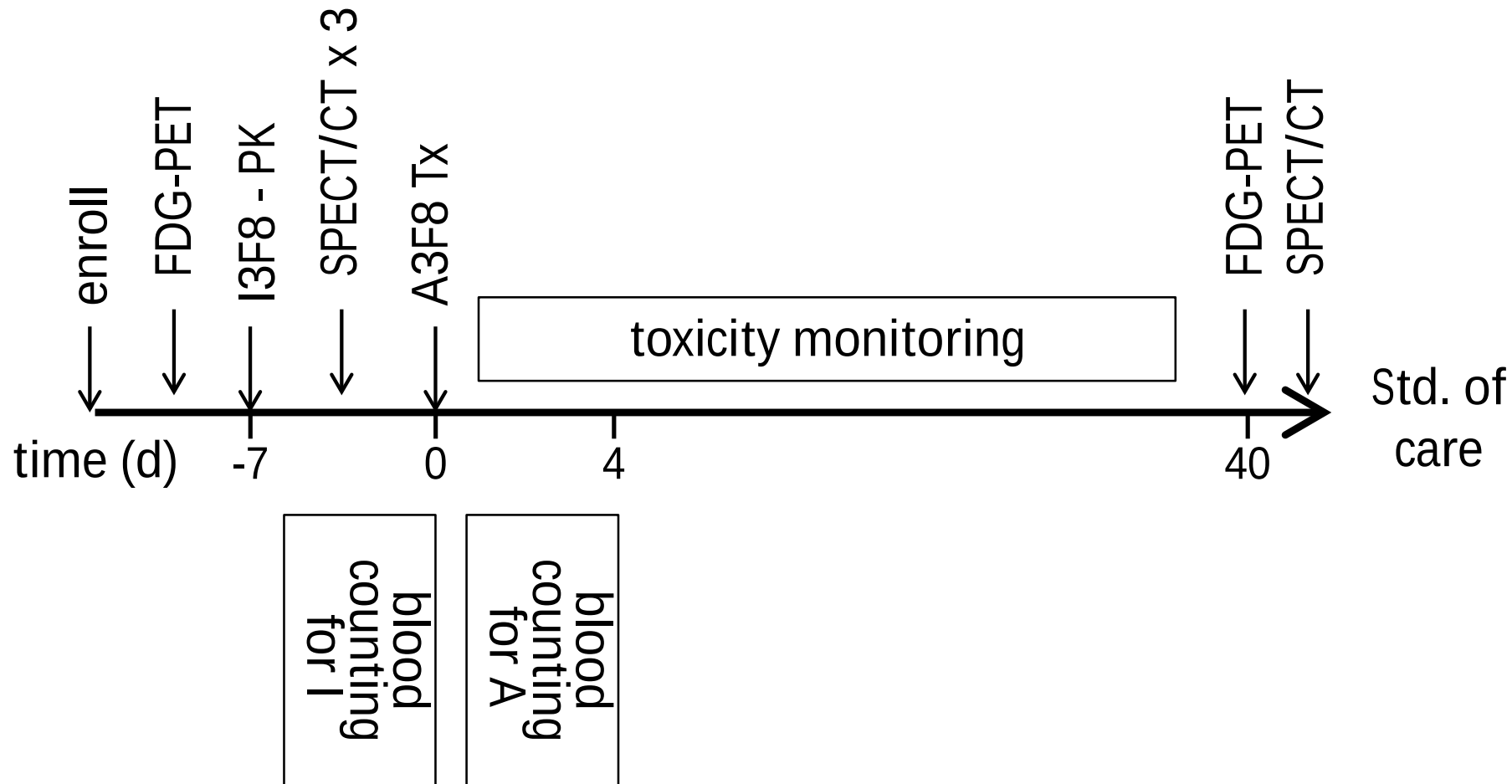


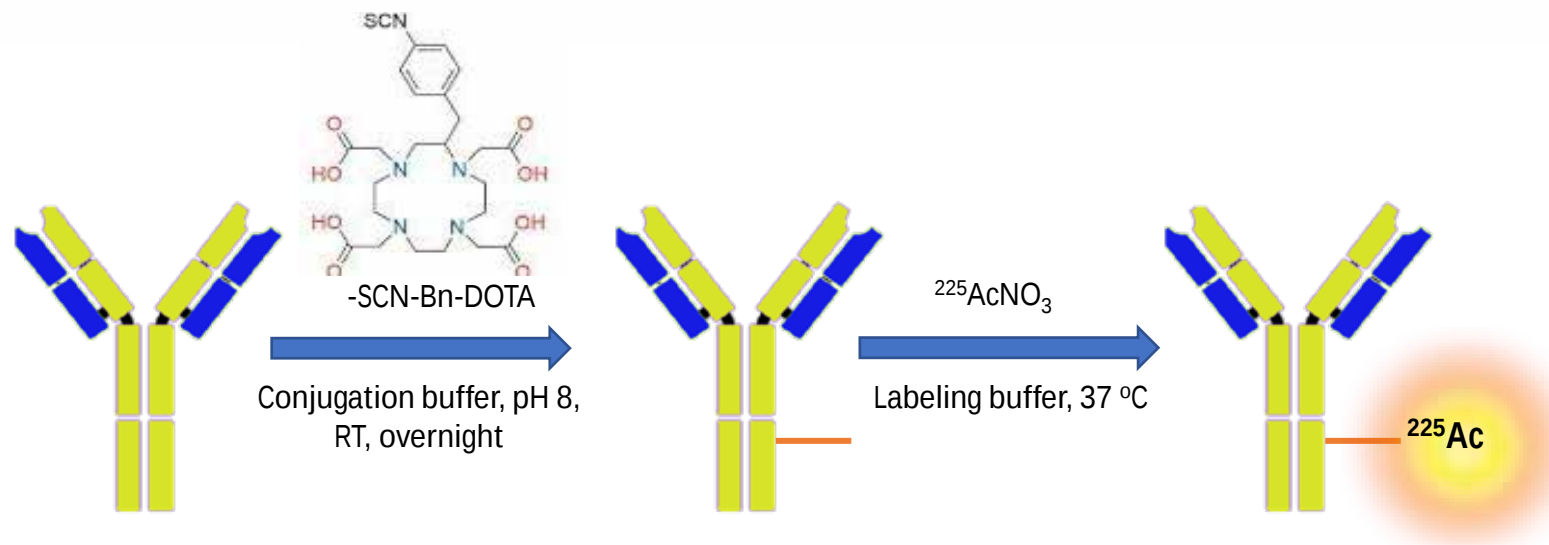
(A) FDG-PET/CT image of an OS-bearing dog shows three metastatic tumors with two in the ribs and one in the fourth lumbar vertebra (arrows). (B) SPECT/CT image of the same dog as shows avid uptake of ^{111}In -DTPA-hu3F8 (IV-administered 36 MBq) in all the OS lesions (arrows) 48 hours after injection. (C-E) Coronal (C), axial (D), and sagittal (E) views of SPECT/CT images of one OS lesion from the same dog as (A). (F-H) Coronal (F), axial (G), and sagittal (H) views of SPECT/CT images of the second dog show avid uptake of ^{111}In -DTPA-hu3F8 (IV-administered 100 MBq) in metastatic lesions close to previous amputation site in the right thoracic limb (arrow). (I-J) Immunohistochemical staining of postmortem shoulder (I) and pulmonary (J) metastatic tissues shows the detection of ^{111}In -DTPA-hu3F8 within both shoulder and lung lesions of the dog shown in F. Bar represents 100 μm .

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Canine Osteosarcoma





	Isotope to Conjugate Ratio	Labeling Buffer, pH	Duration of Labeling at 37 °C (mins)	*iTLC Yield (%)	Purification w/ PD-10 column	Purity (%)	Specific Activity (kBq/ g)
Anti-HER2/neu Ab (7.16.4)	-11	3M NaOAc, pH: 7-7.5	60	>95	NO	>>95	3.4
Anti-GD2 Ab (Hu3F8)		3M NaOAc/0.2 N HCl, pH: 6.5-7	80	60-77	YES	>95	2.8

*iTLC moving phase: EDTA (10mM) or NaOH (10mM), NaCl (150mM)

Acknowledgments

- Remco Bastiaannet
- Mahmood Hasan
- Rob Hobbs
- Zhi Li
- Jing Yu
- Ioanna Liatsou



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Master's in Medical Physics



The program is designed for full-time students who wish to pursue a career as a medical physicist either as a researcher, as a certified clinical profession or in industry. The program, set to commence in fall 2021, will require successful completion of a minimum of 38 credits for Master's degree and completion of a research thesis (in conjunction with one or more of the faculty). Full-time master's students will complete the program in two years.

- Yong Du
- Eric Frey
- Yingli Fu
- Dara Kraitchman
- Jeffrey Bryan (Mizzou)
- Nai-Kong Cheung (MSKCC)

