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

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# 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

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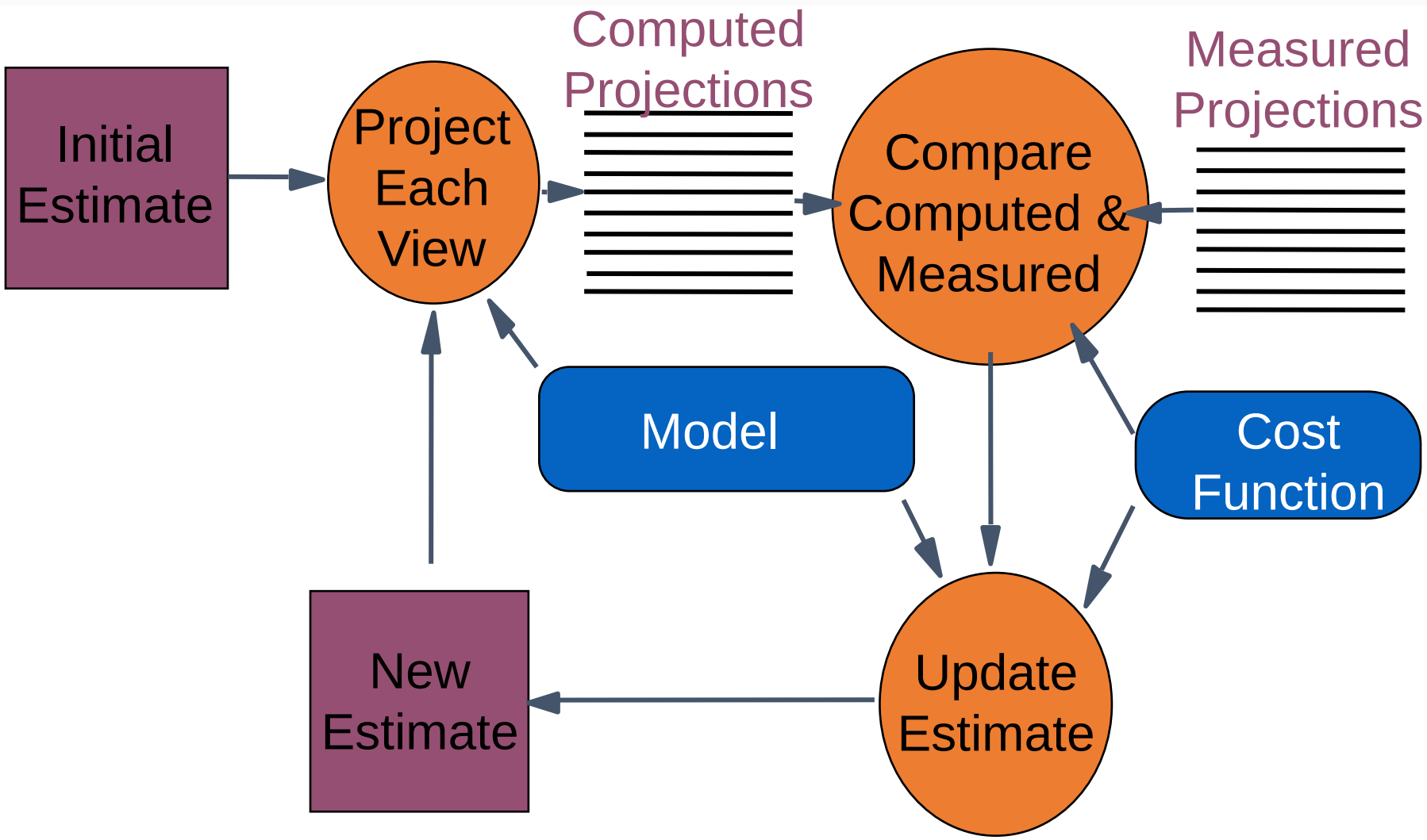
- Imaging
  - Advanced recon
  - New instruments
- Macro to micro (M2µ)
  - Microscale S values
  - Microscale apportionment factors
- RBE
  - In vitro, In vivo
- Treat canine OS

# Imaging – Advanced reconstruction




Eric Frey, Rapid & Hopkins

# Imaging – Advanced reconstruction

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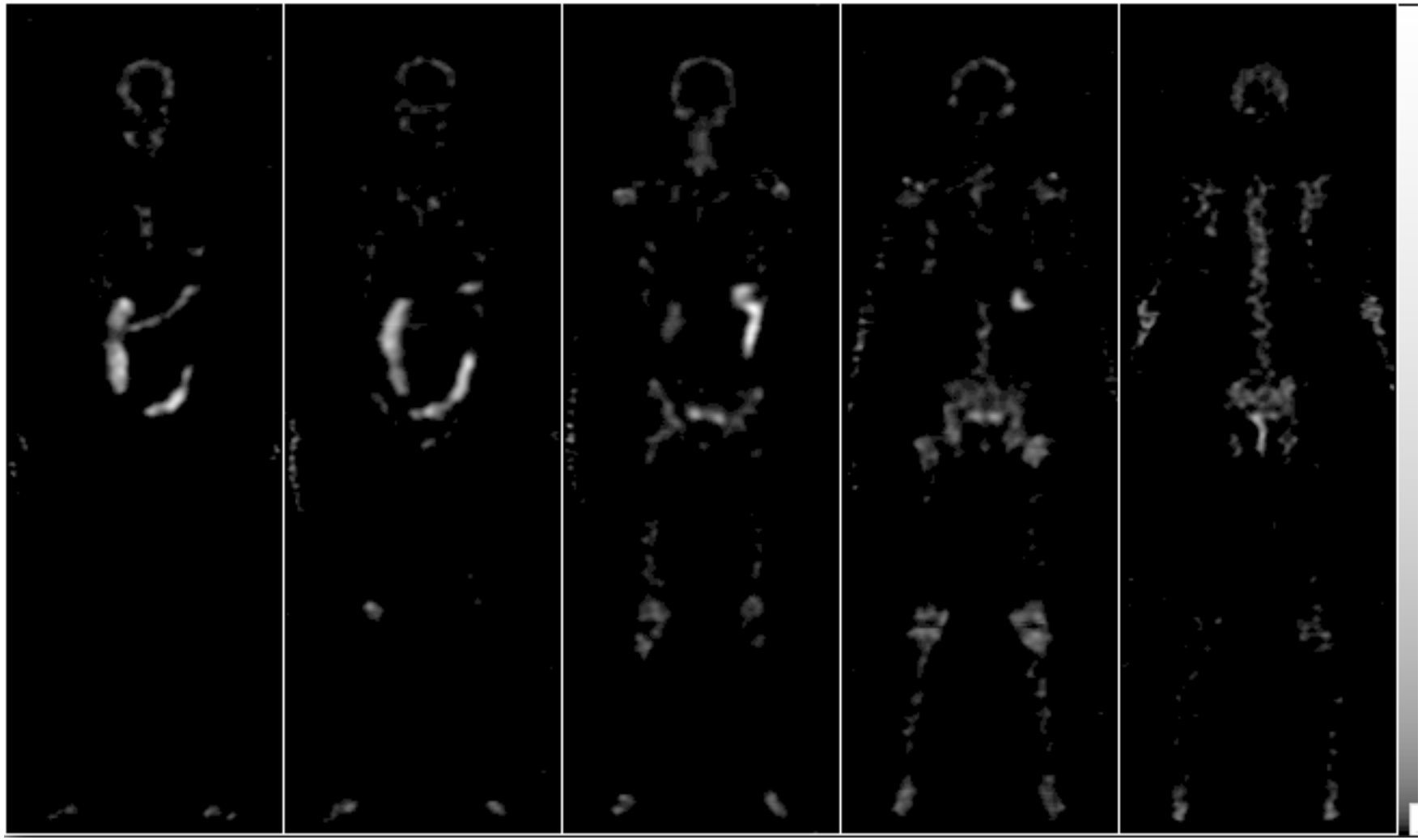
5 coronal slices, 144 h, 5 iterations, 12 subsets per iteration, logarithmic grayscale



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# Imaging – Advanced reconstruction

## Ra-223 Errors in Organ Activity Estimates

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

20 iterations, 12 subsets
Uncertainties are COVs over 50 simulated noise realizations
True VOIs are assumed known

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# Imaging – build a new instrument

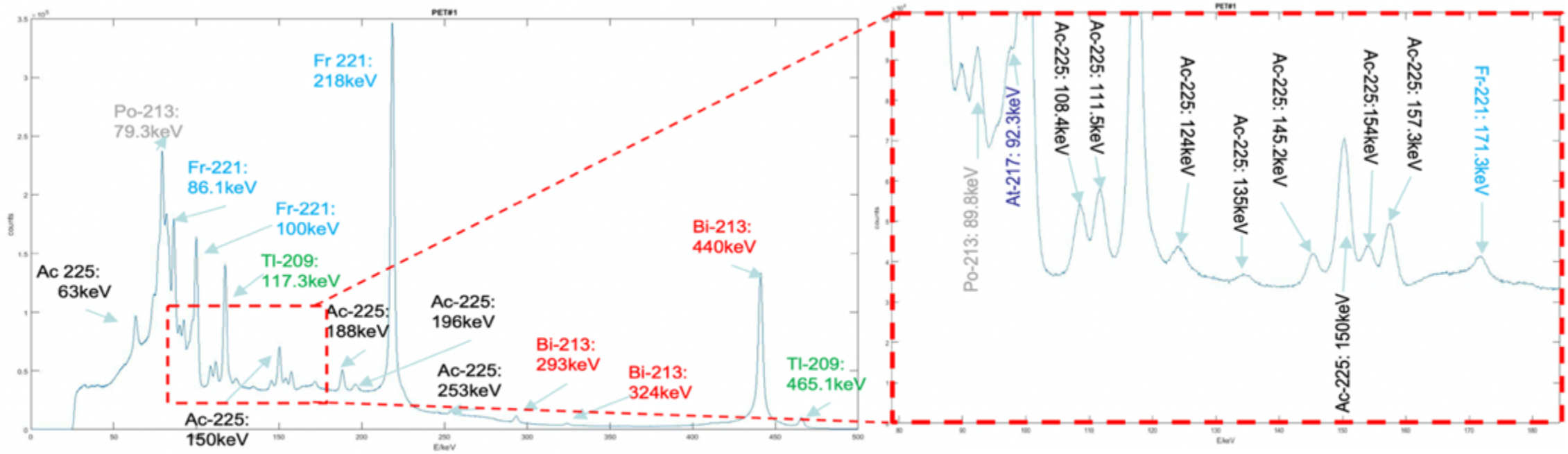



**Fig. 4:** An energy spectrum collected with an Ac-225 solution and a 3-D CZT imaging spectrometer having an active detector volume of 4 cm x 4 cm x 1 cm in size. Note that the spectrum includes all types of interactions (single photoelectric, Compton scattering, charge-sharing etc.) physically happened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

**Ling-Jian Meng, UIUC**

# Macro 2 micro – S values

Wesley Bolch UFL, Rob Hobbs

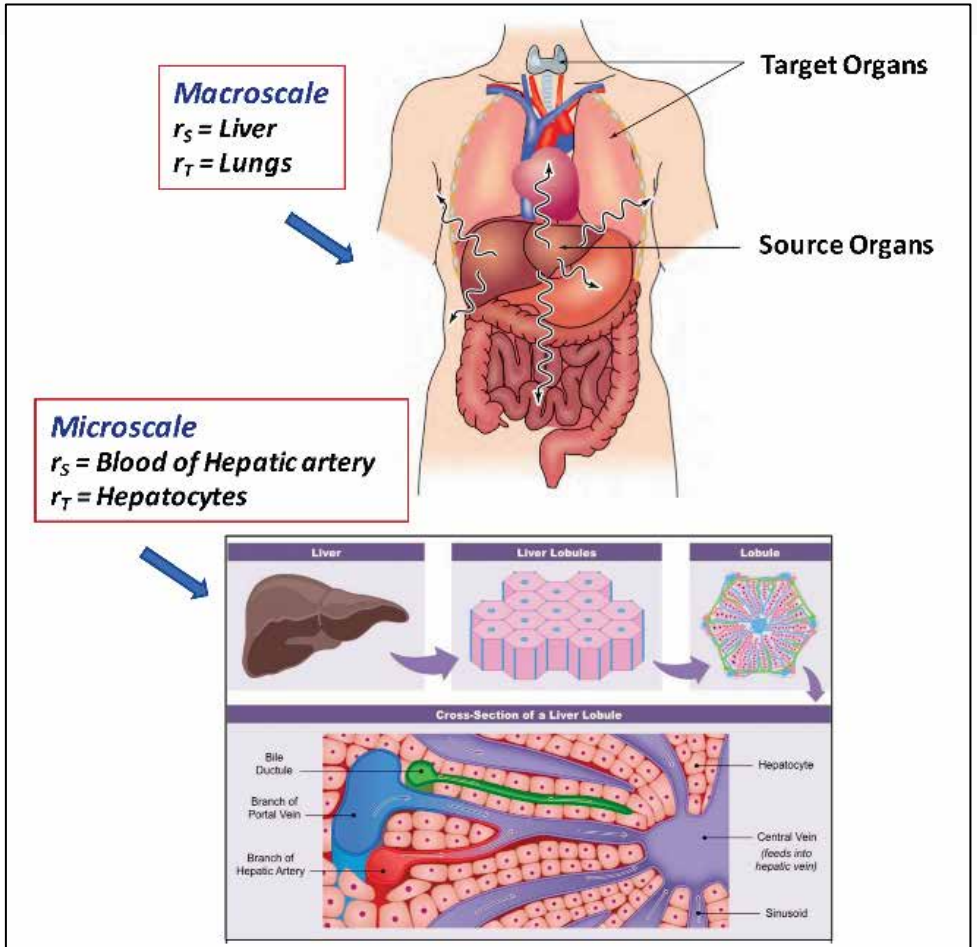



**Fig 1.** Source / target regions for liver at both the macroscale and microscale in the MIRD schema.

**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 ← glc | 5.74E-04 | 4.29 | 0.721 | 1.53E-07 |
| glc ← prt | 5.20E-06 | 1.12 | 0.188 | 1.39E-09 |
| prtc ← glc | 2.33E-04 | 0.05 | 0.009 | 1.86E-09 |
| prtc ← prtc | 6.82E-04 | 4.37 | 0.734 | 5.44E-09 |
| prtc ← prtl | 6.85E-04 | 4.39 | 0.737 | 5.46E-09 |
| prtc ← prts | 6.84E-04 | 4.38 | 0.736 | 5.45E-09 |
| kid ← kid | - | 5.94 | 0.998 | 3.22E-09 |
| cor ← 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.

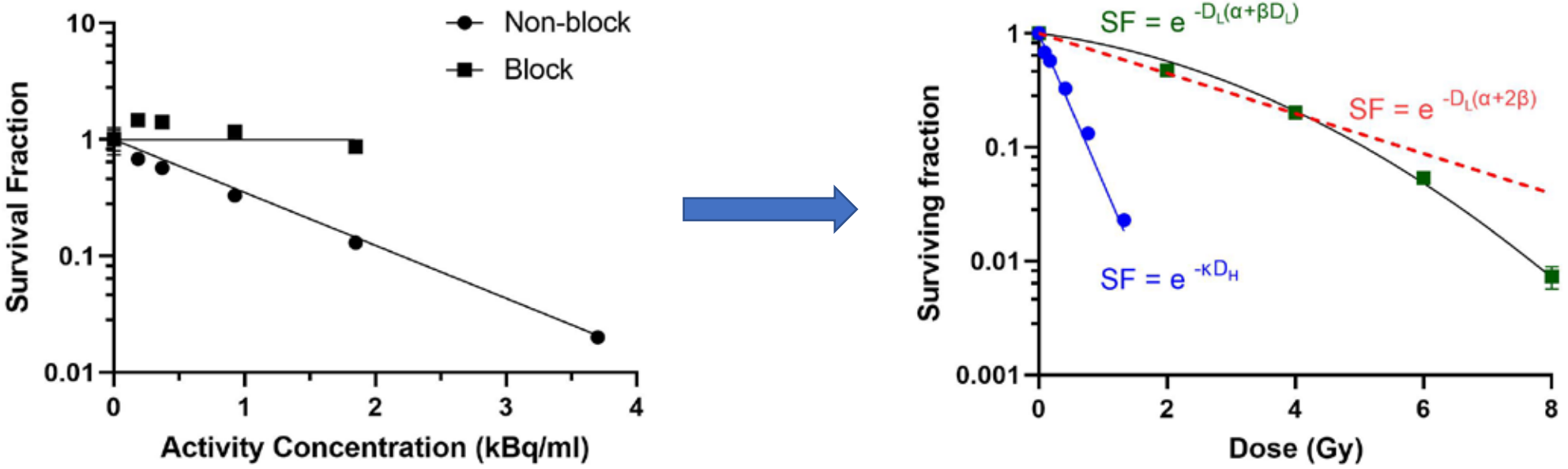
| $^{225}$Ac | S-value (unit) (Gy/Bq-s) | Absorbed energy (MeV/decay) | Absorbed Fraction | S-value (compartment) (Gy/Bq-s) |
|---|---|---|---|---|
| glc ← glc | 5.70E-05 | 5.24 | 0.881 | 1.85E-10 |
| glc ← prt | 5.39E-06 | 0.75 | 0.126 | 6.08E-13 |
| prtc ← glc | 3.02E-05 | 0.096 | 0.016 | 3.12E-12 |
| prtc ← prtc | 4.54E-05 | 1.28 | 0.215 | 4.69E-12 |
| prtc ← prtl | 4.49E-05 | 1.76 | 0.296 | 4.64E-12 |
| prtc ← prts | 4.52E-05 | 1.53 | 0.257 | 4.66E-12 |
| kid ← kid | - | 5.95 | 1.000 | 3.17E-12 |
| cor ← 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 $^{212}Pb/^{212}Bi$)




RBE for 37% survival = 8; RBE2 = 10

**Ioanna Liatsou, Remco Bastiaannet, Rob Hobbs**

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

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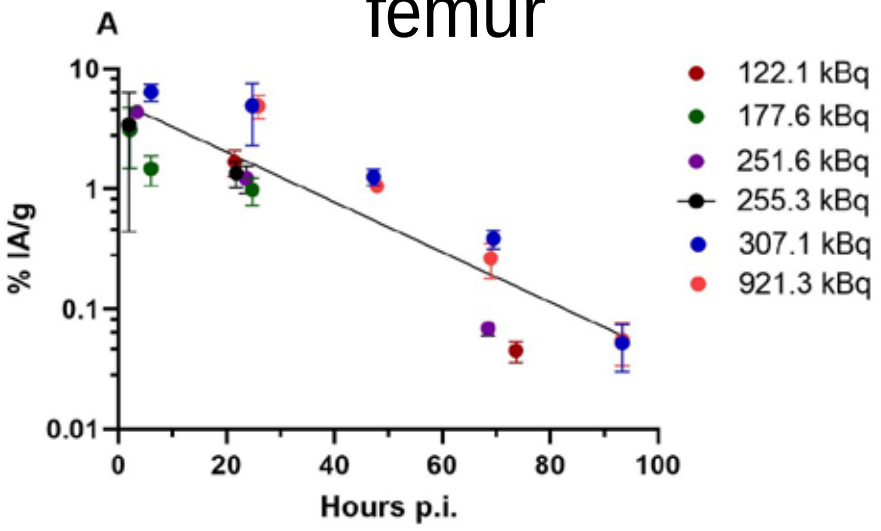
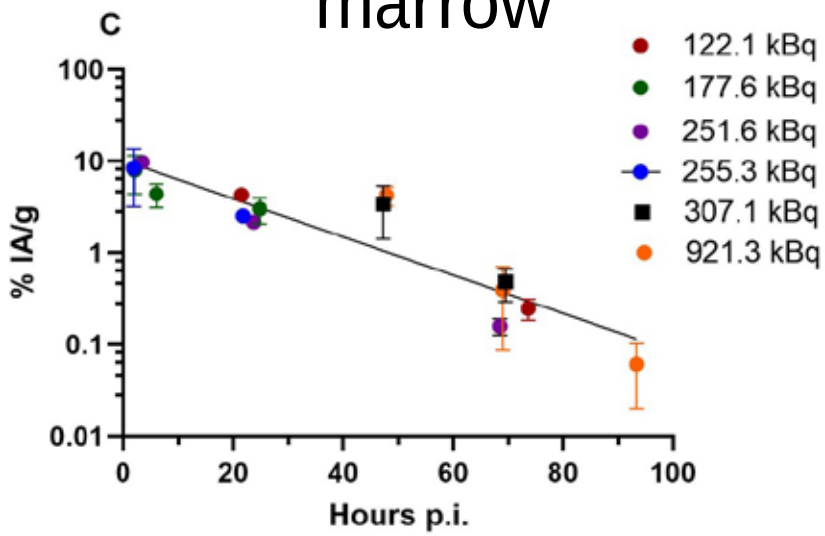
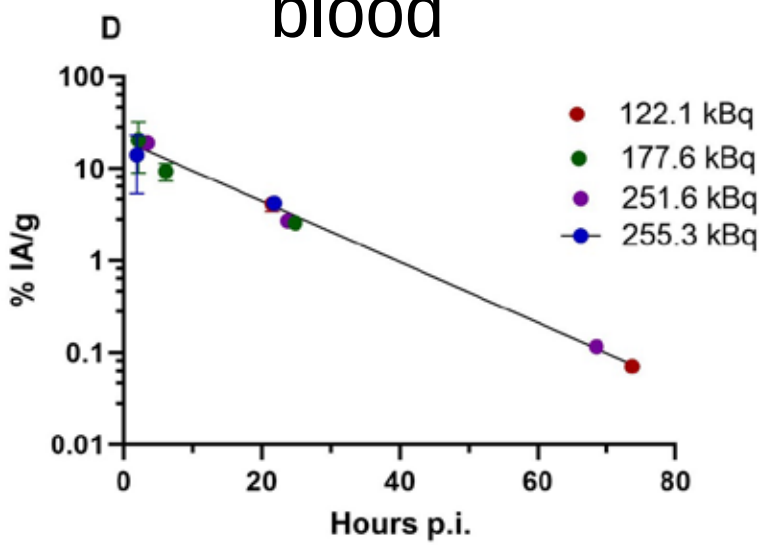
femur




marrow




blood

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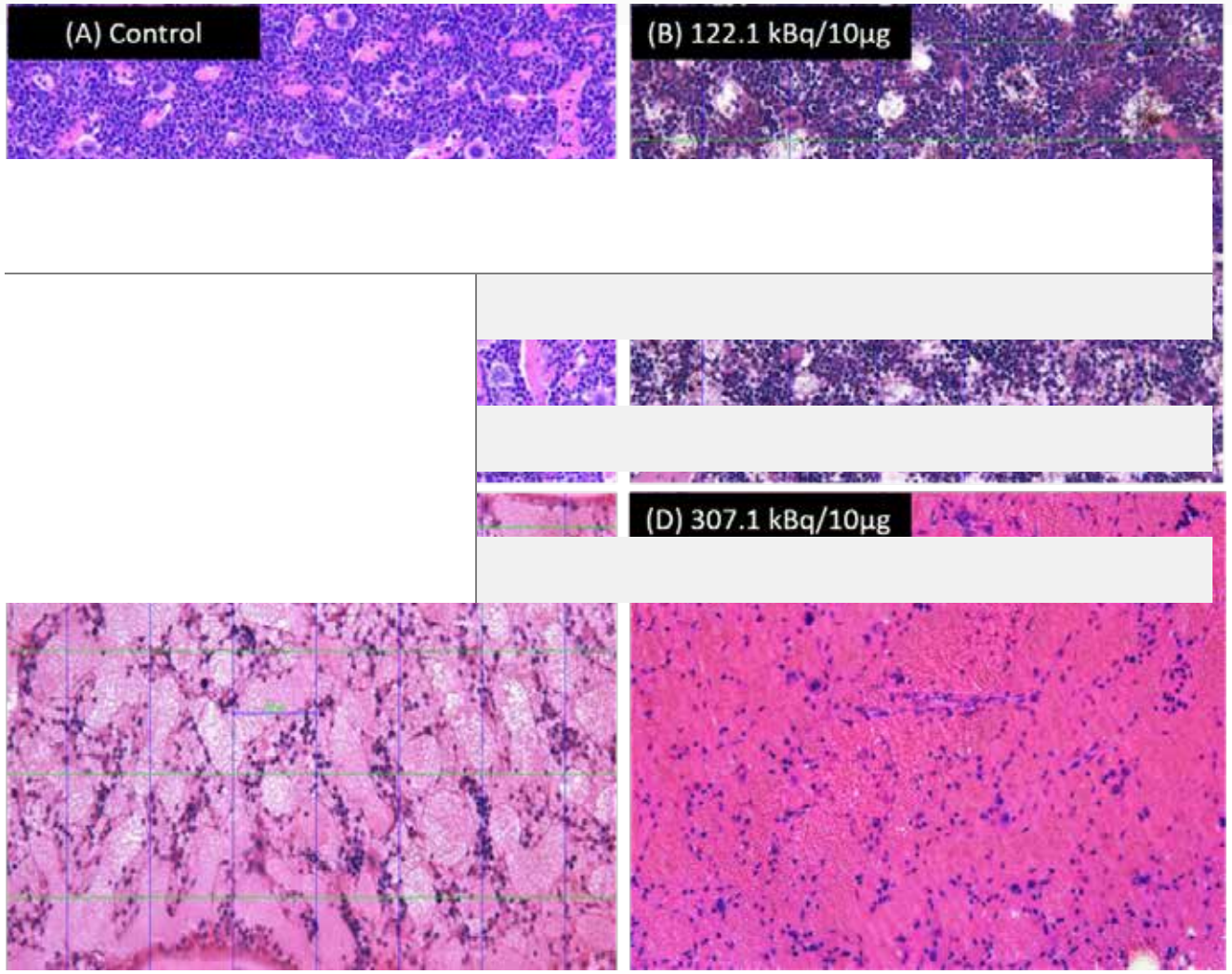
# RBE – In Vivo (for $^{212}Pb/^{212}Bi$)

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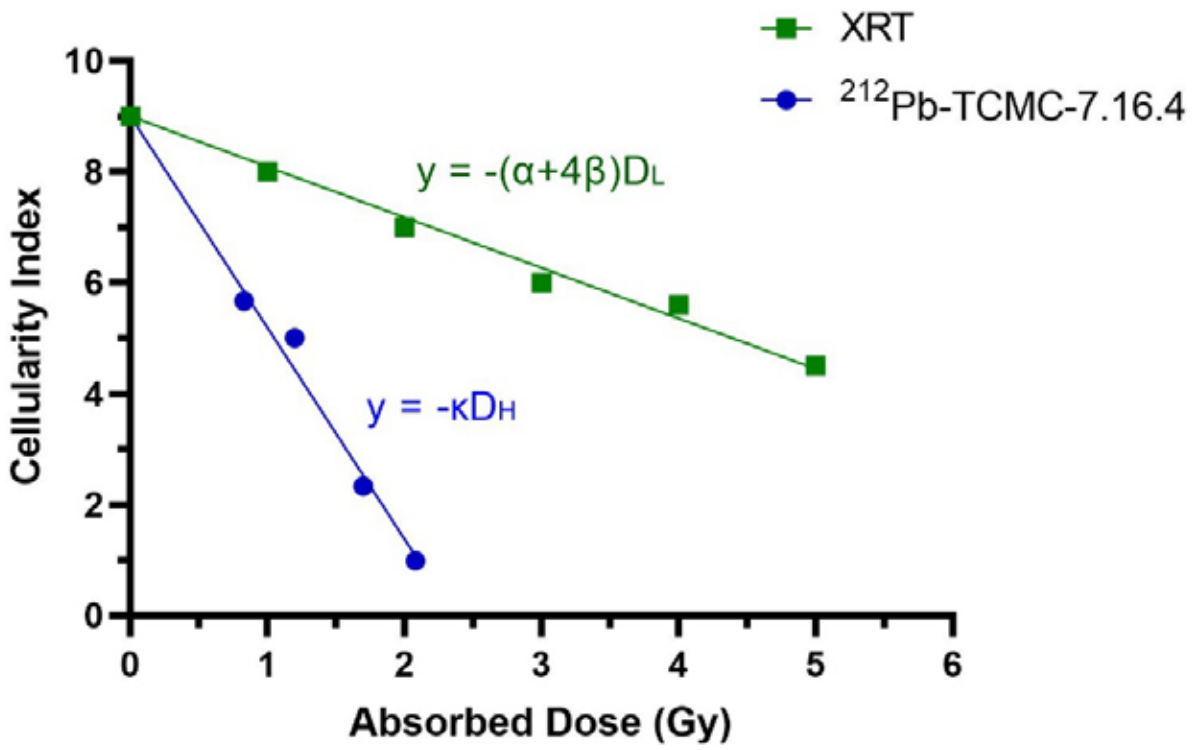
# RBE – In Vivo (for $^{212}Pb/^{212}Bi$)

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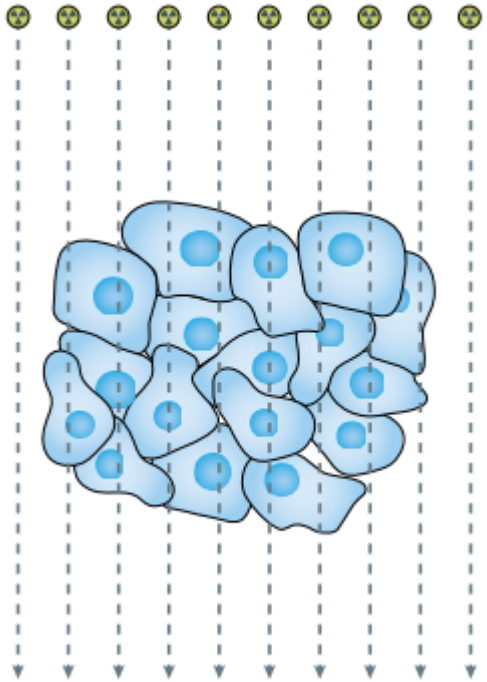
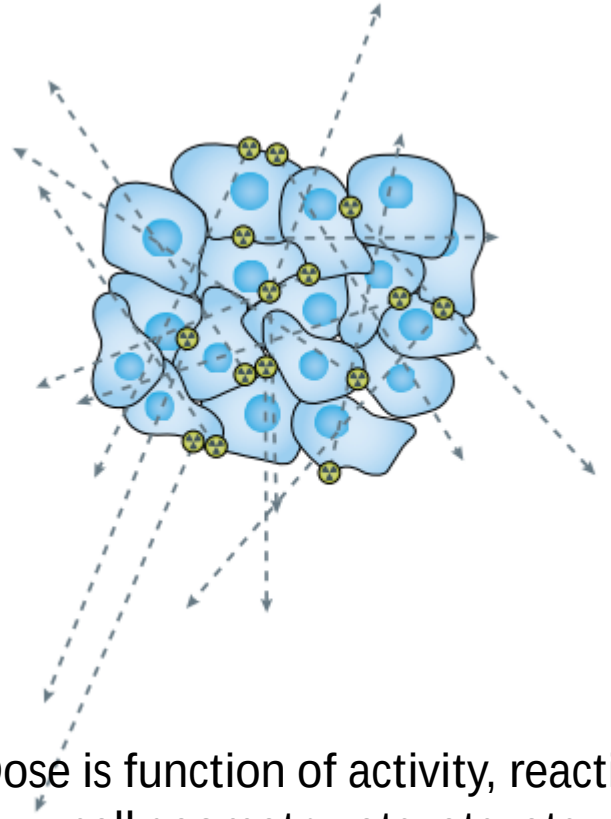
# RBE – In Vitro (for $^{212}Pb/^{212}Bi$)

XRT



Dose is ”set”

RPT



Dose is function of activity, reactivity, cell geometry, etc, etc, etc…

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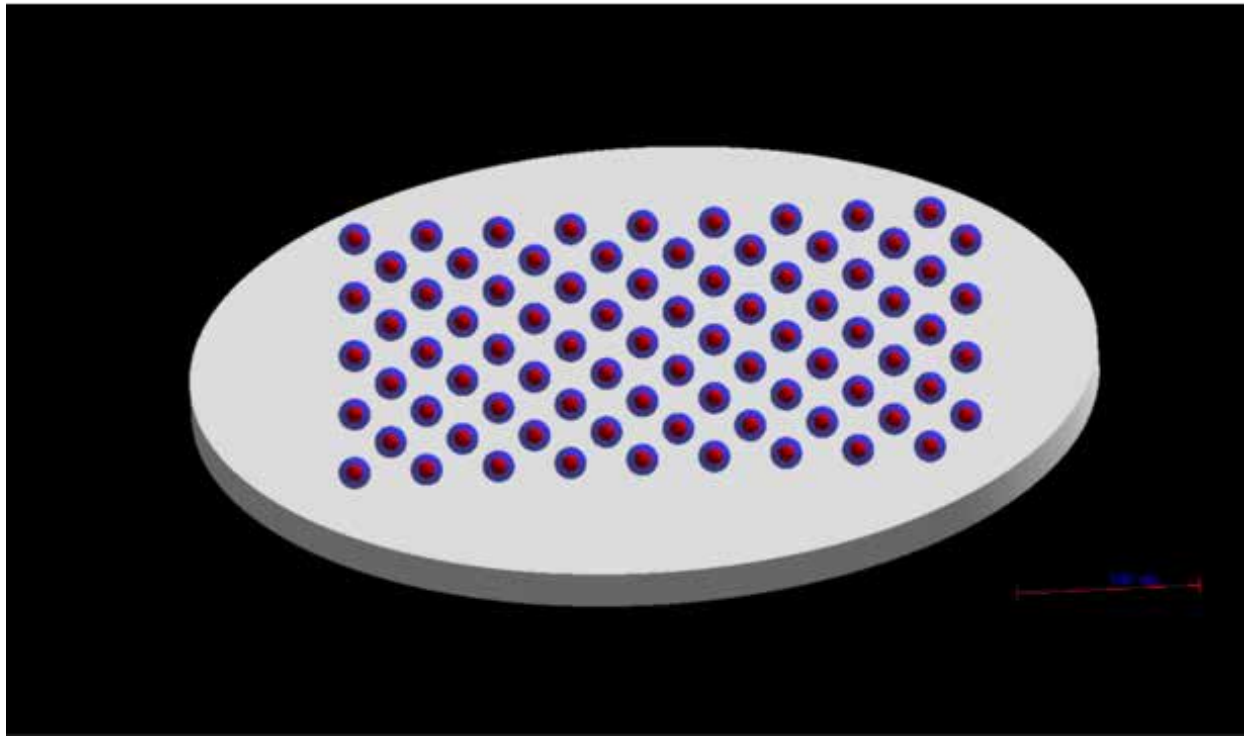

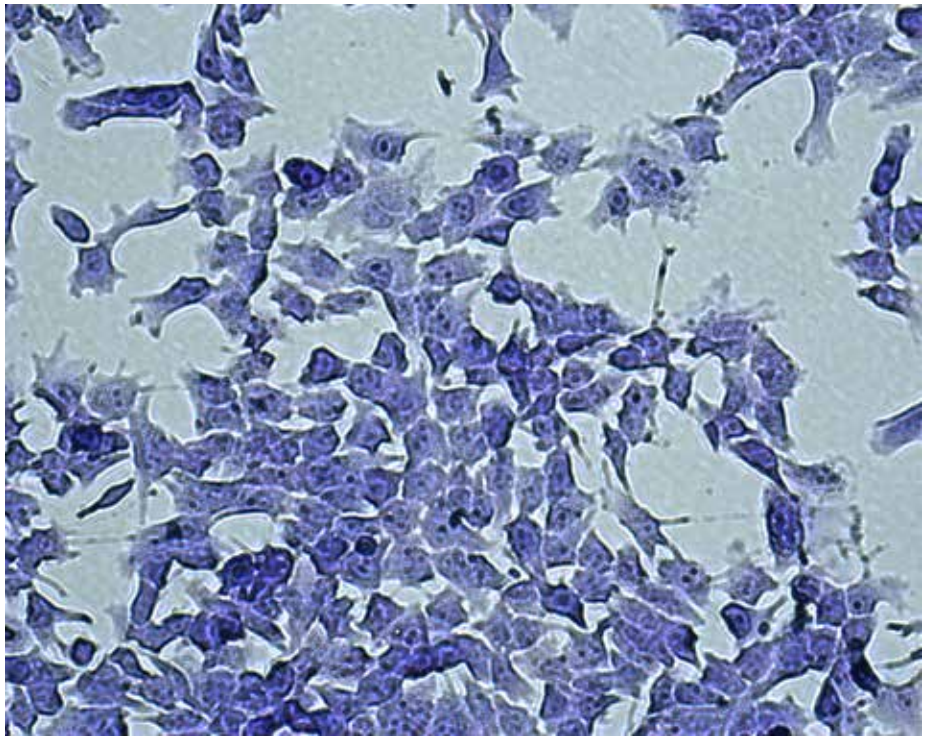

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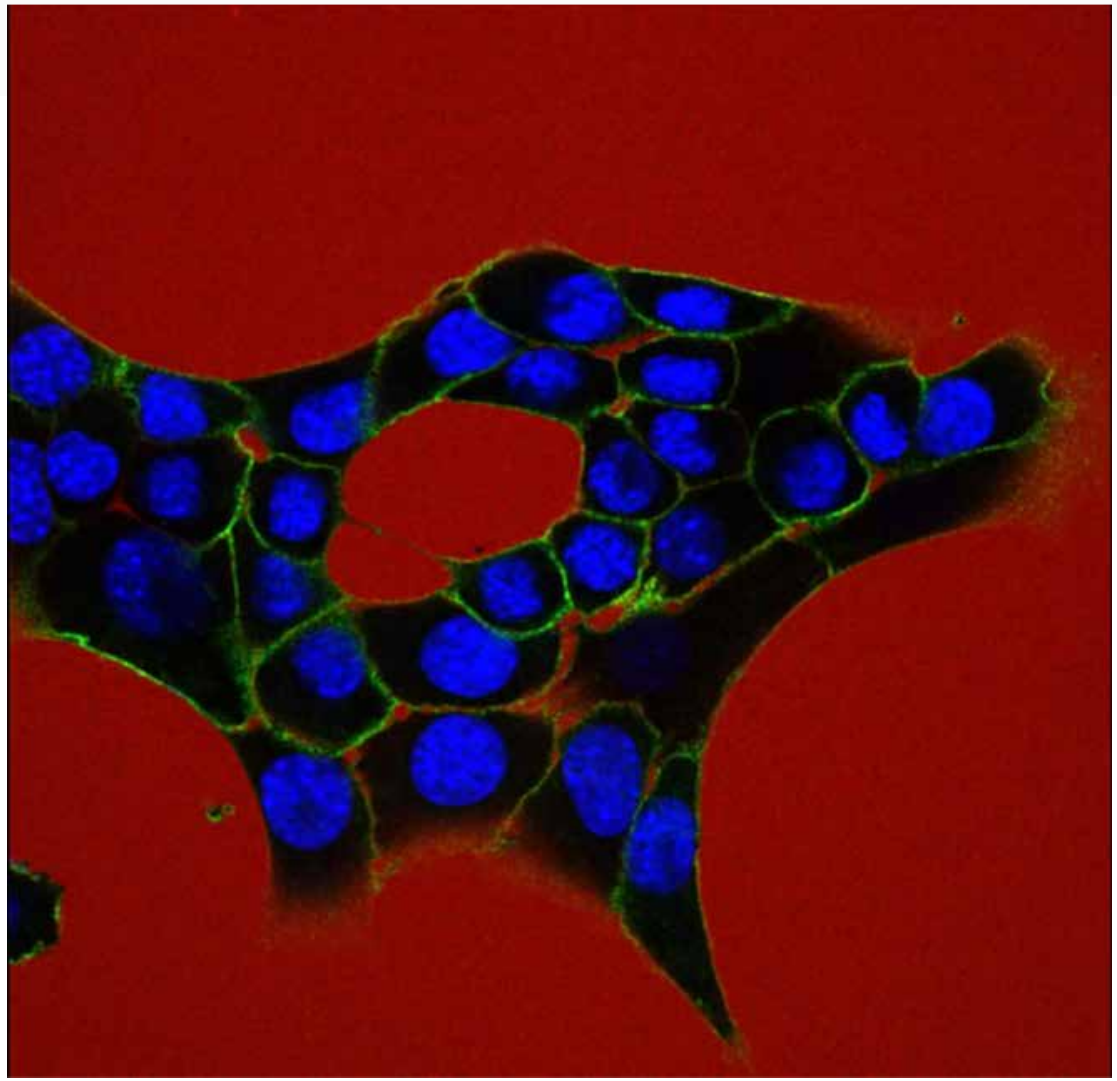

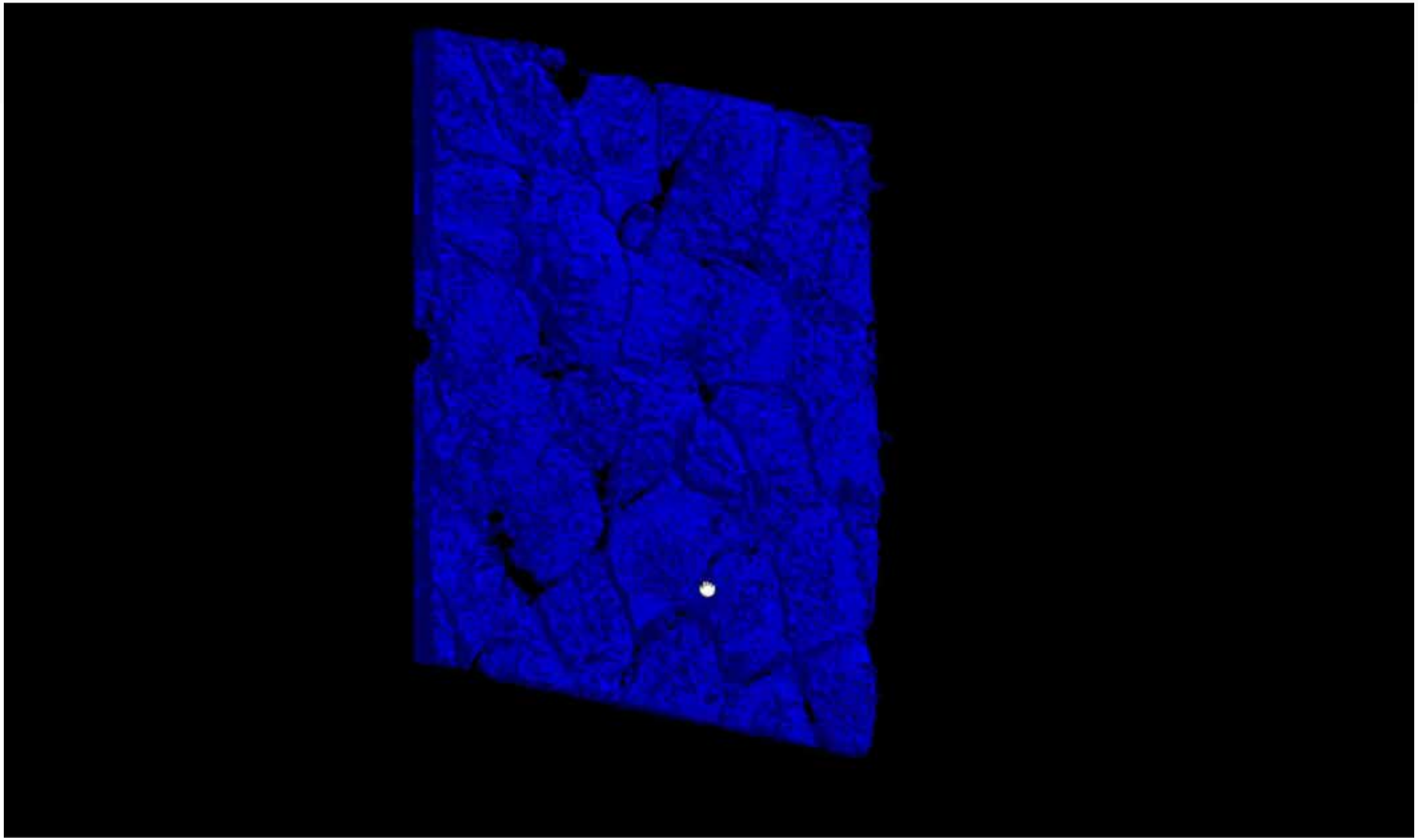

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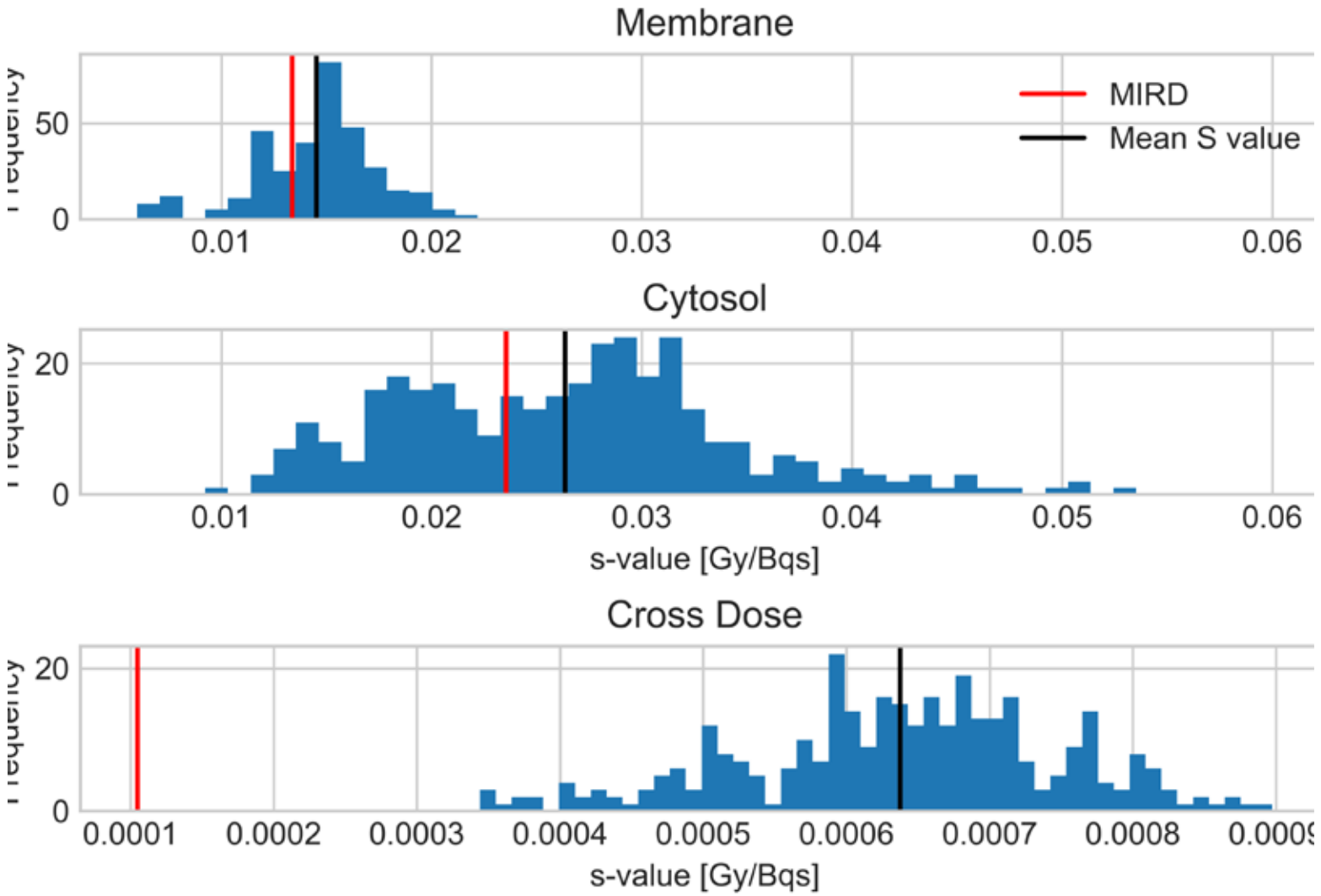
Membrane
Frequency
50
0
0.01
0.02
0.03
0.04
0.05
0.06
MIRD
Mean S value
Cytosol
Frequency
20
0
0.01
0.02
0.03
0.04
0.05
0.06
s-value [Gy/Bqs]
Cross Dose
Frequency
20
0
0.0001
0.0002
0.0003
0.0004
0.0005
0.0006
0.0007
0.0008
s-value [Gy/Bqs]

# Canine Osteosarcoma

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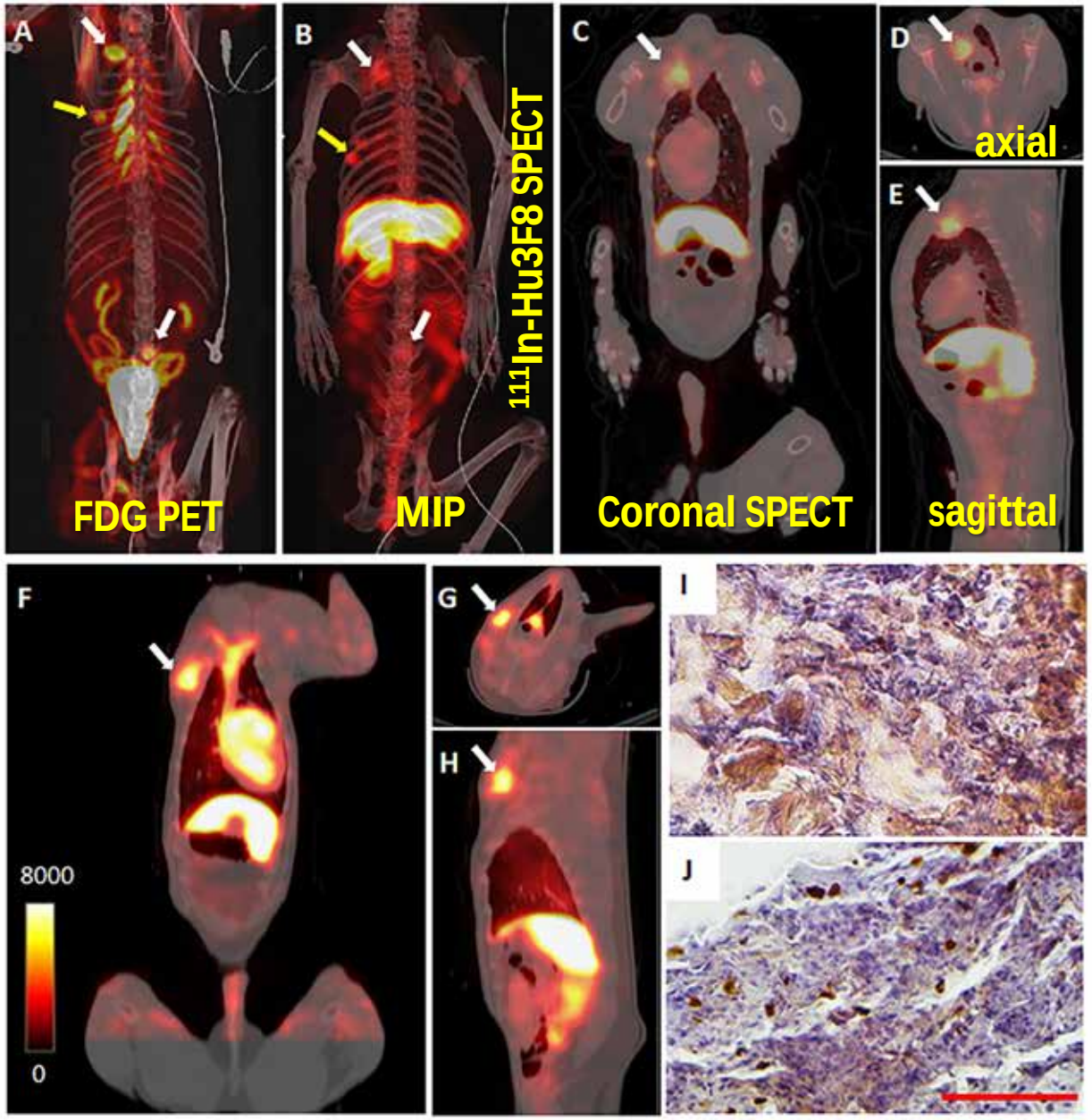


(A) FDG-PET/CT image of an OS-bearing dog shows three metastatic tumors with two in the ribs and one in the fourth lumbar vertebra (arrows). (B) SPECT/CT image of the same dog as shows avid uptake of [$^{111}$In]In-DTPA-hu3F8 (IV-administered 36 MBq) in all the OS lesions (arrows) 48 hours after injection. (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]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]In-DTPA-hu3F8 within both shoulder and lung lesions of the dog shown in F. Bar represents 100 μm.

**Yingli Fu, Jing Yu, Ioanna Liatsou, Yong Du, Jeffrey Bryan, Dara Kraitchman**

# Canine Osteosarcoma

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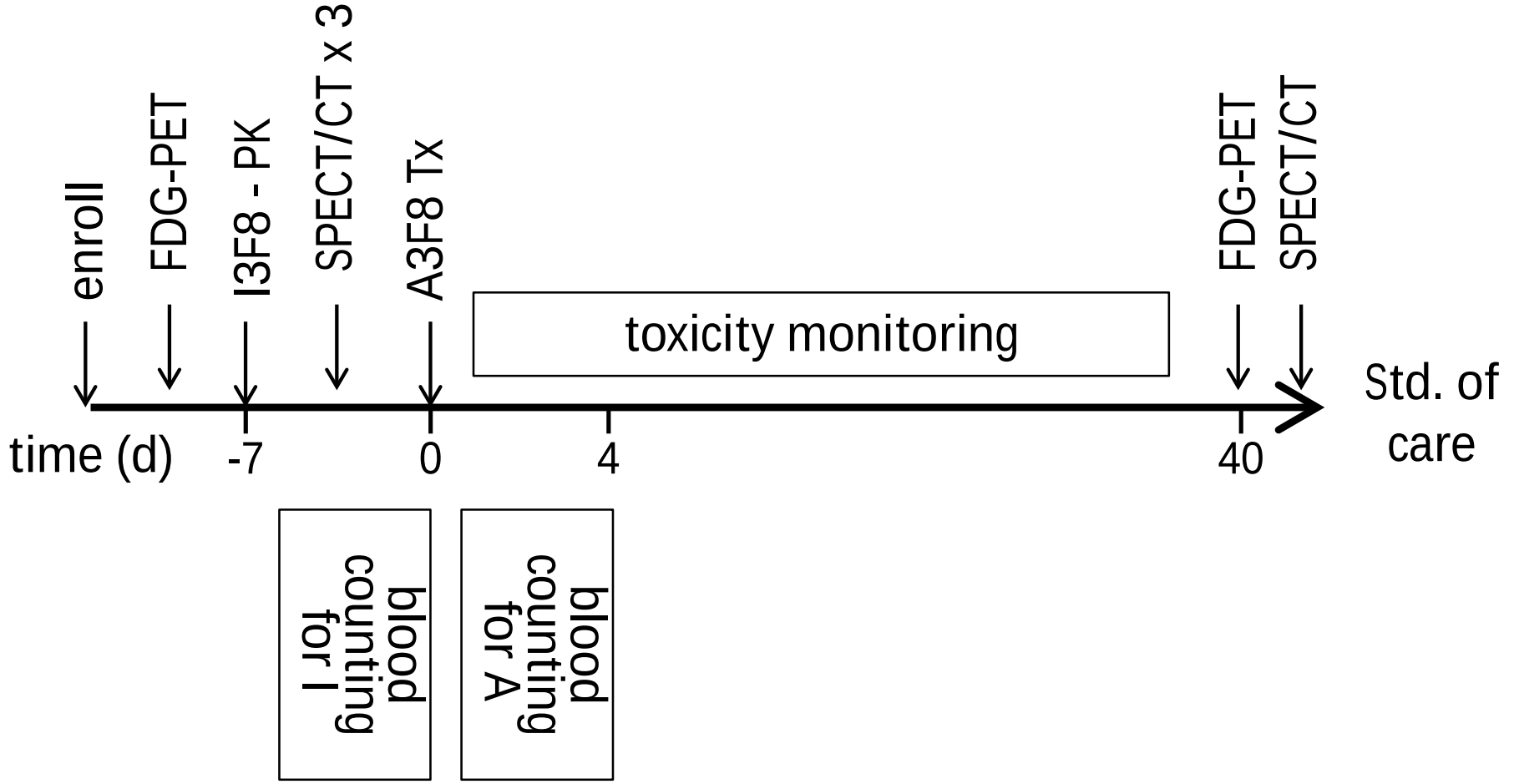


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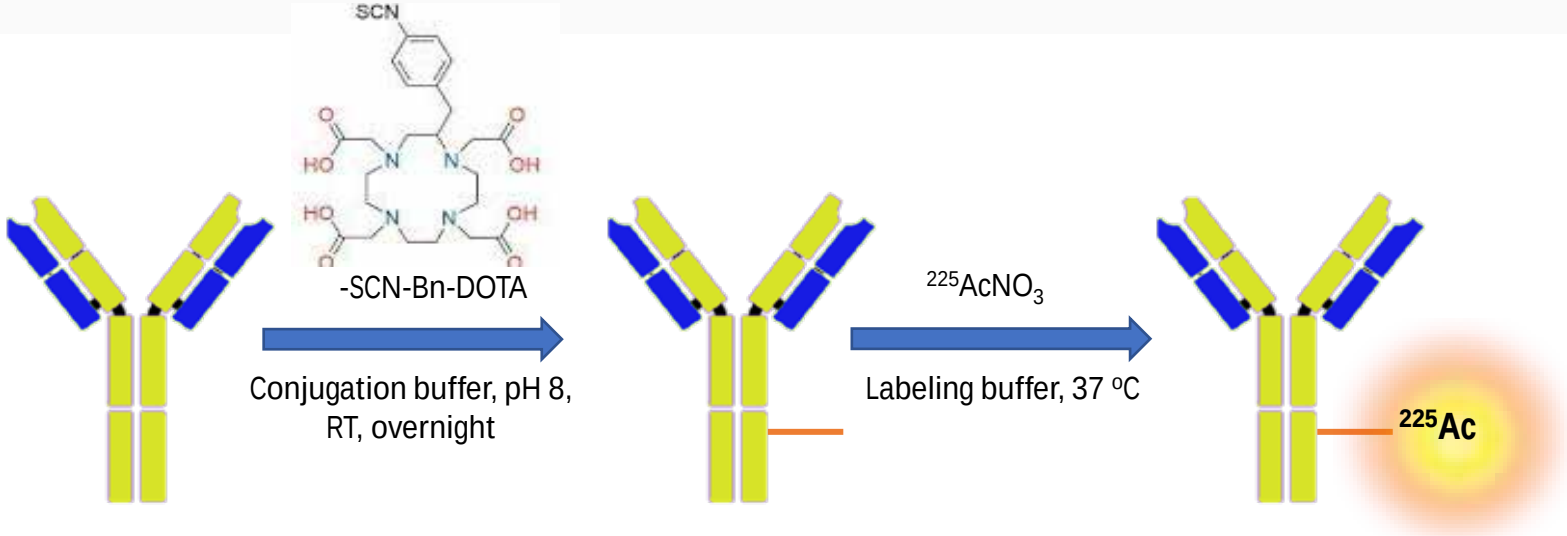


| | Isotope to Conjugate Ratio | Labeling Buffer, pH | Duration of Labeling at 37 °C (mins) | *iTLC Yield (%) | Purification w/ PD-10 column | Purity (%) | Specific Activity (kBq/ g) |
|---|---|---|---|---|---|---|---|
| **Anti-HER2/neu Ab (7.16.4)** | -11 | 3M NaOAc, pH: 7-7.5 | 60 | >95 | NO | >>95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


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

Radiology and Radiological Science > Education > ms_medical_physics

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.