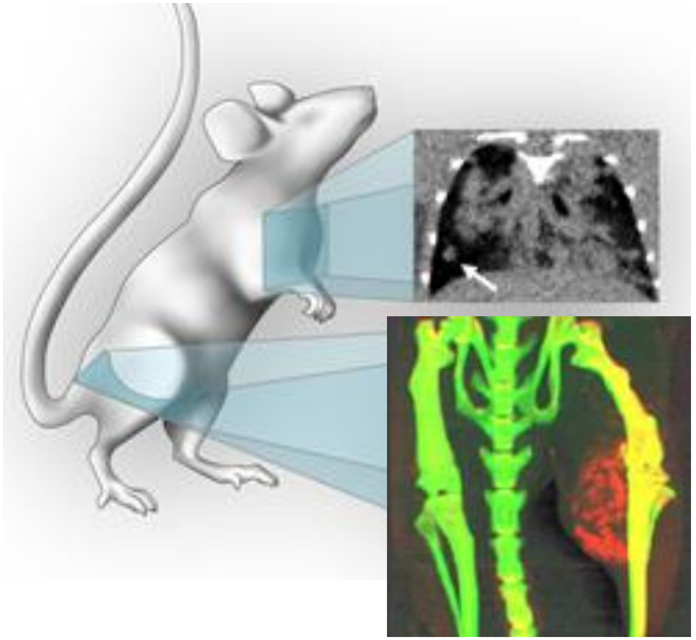


Spectral Micro-CT and Preclinical Applications

C. T. Badea, PhD

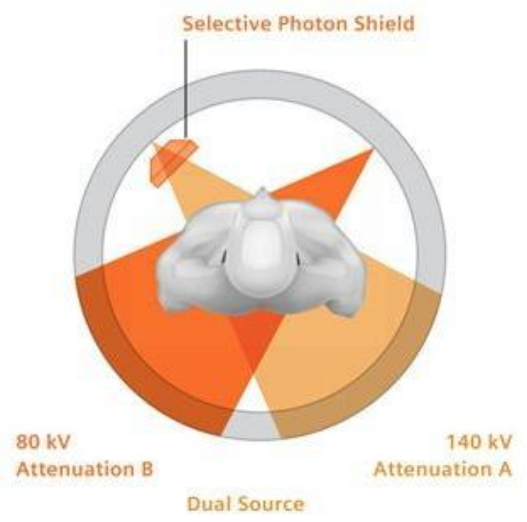
Quantitative Imaging and Analysis Lab

Dept. of Radiology

Duke University

https://sites.duke.edu/qial/

Dual Energy micro-CT



80 kVp

40 kVp

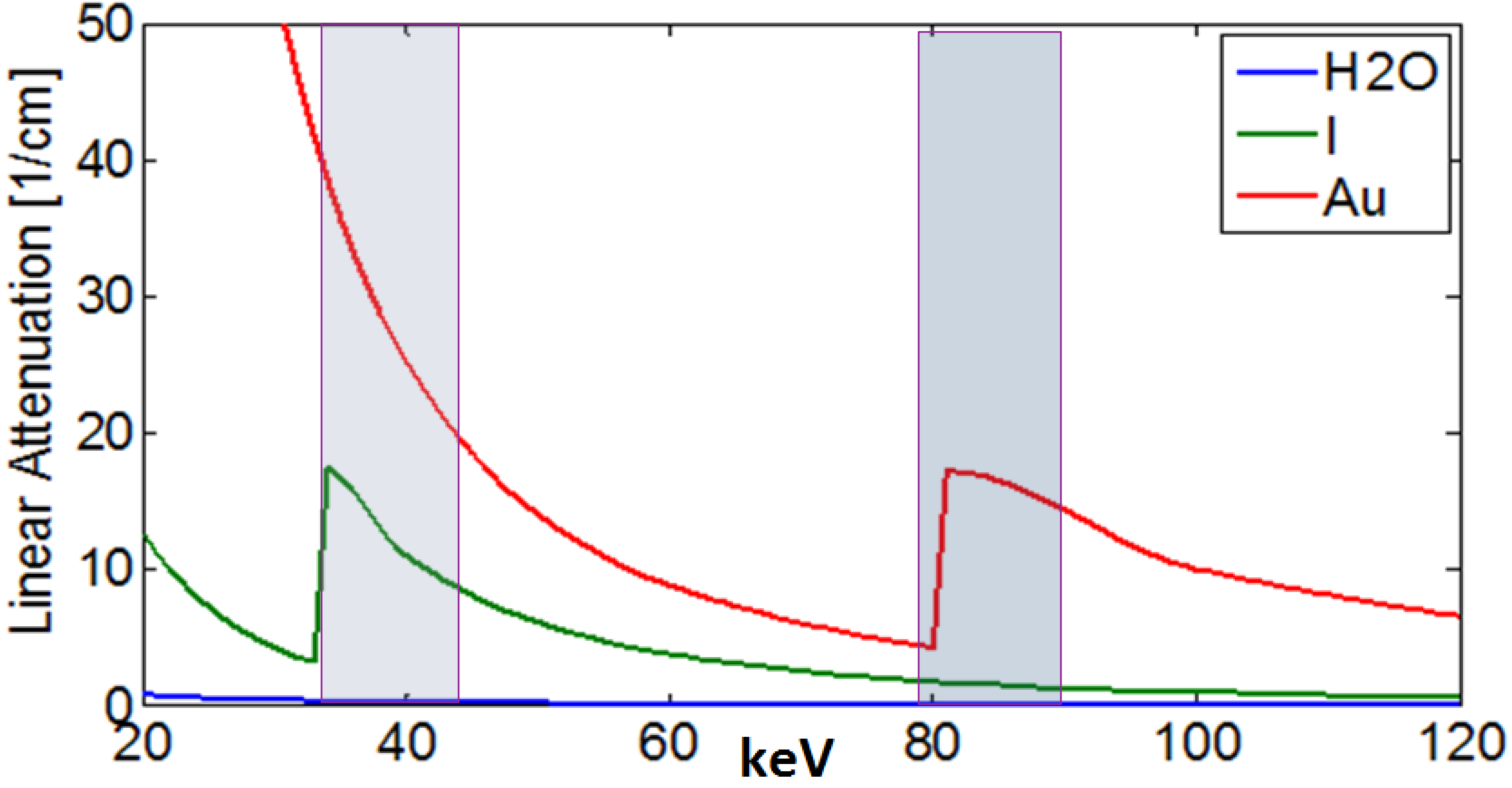
CT signal and contrast:

$$I = I_o \exp\{-\mu(E)t\}$$

- t = thickness
- μ = linear attenuation
- μ depends on energy, E

CT signal can be ambiguous!

Iodine vs Gold



Dual Energy (DE) CT: Decomposition

- Post Reconstruction Method
- 2 materials (Au and I mixed with water)

CT measurements @ E1 and E2

$$\begin{aligned} e_{I,E1}c_I + e_{Au,E1}c_{Au} &= \mathrm{CT}_{E1} \\ e_{I,E2}c_I + e_{Au,E2}c_{Au} &= \mathrm{CT}_{E2} \end{aligned} \Rightarrow \begin{bmatrix} c_I \\ c_{Au} \end{bmatrix} = \begin{bmatrix} e_{I,E1} & e_{Au,E1} \\ e_{I,E2} & e_{Au,E2} \end{bmatrix}^{-1} \begin{bmatrix} \mathrm{CT}_{E1} \\ \mathrm{CT}_{E2} \end{bmatrix}$$

Sensitivity Matrix [HU/mg/ml]

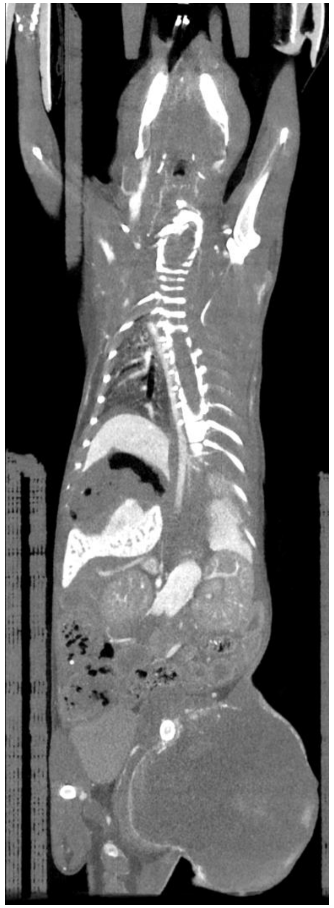
Enhancement for I or Au @E1, E2

Concentrations of I and Au [mg/ml]

DE micro-CT

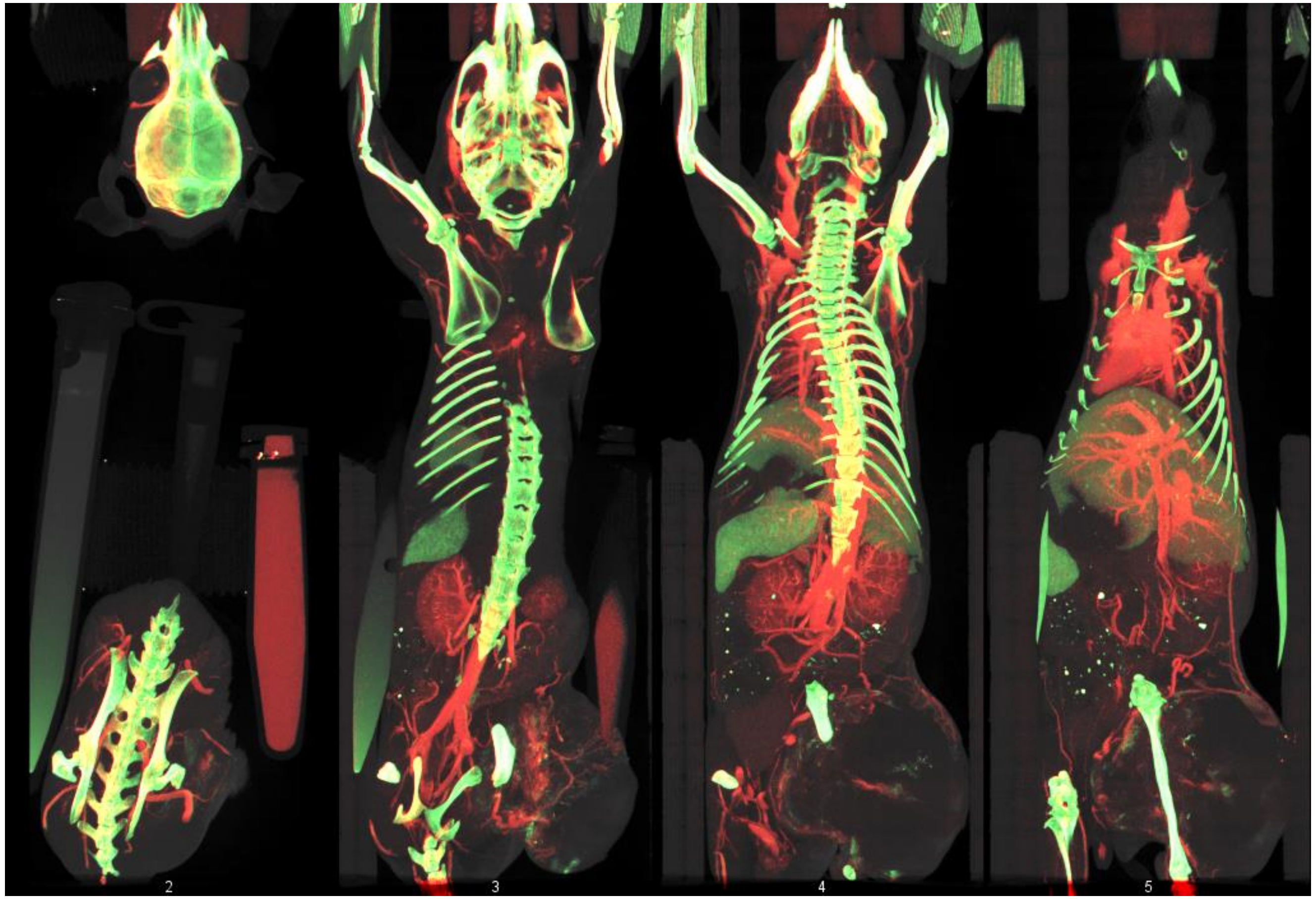
DE acquisitions

80 kVp



40 kVp

Material decompositions

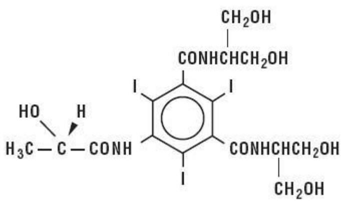


Iodine, Gold + calcium

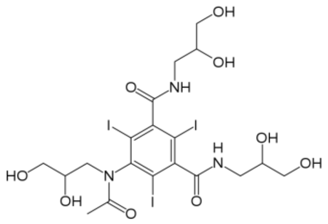
Contrast Agents

1) Low Molecular Weight

Iodine

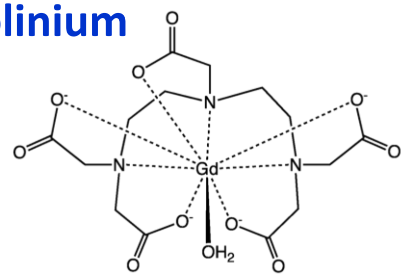


Isovue
(Bracco Diagnostic Inc.)



Omnipaque
(GE Healthcare)

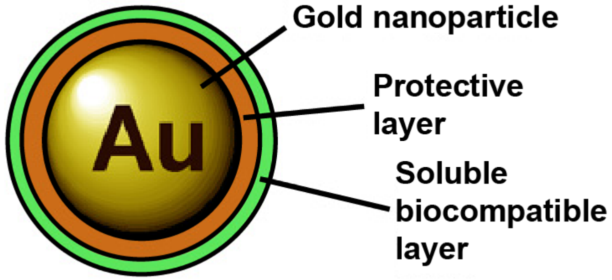
Gadolinium



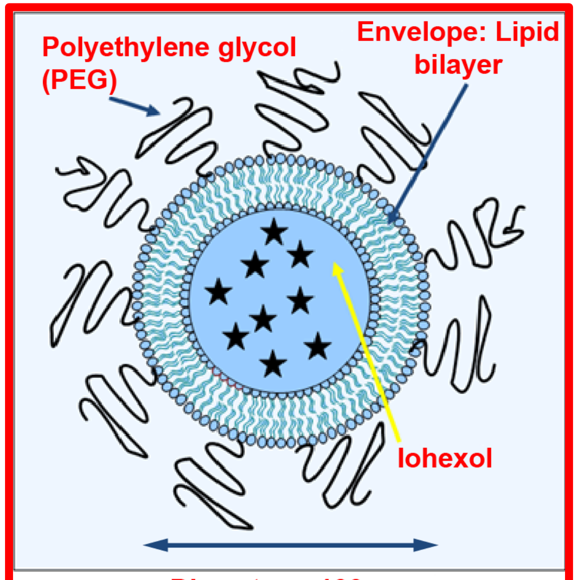
Magnevist
(Bayer Schering Pharma AG)

2) Nanoparticle (NP)

Gold



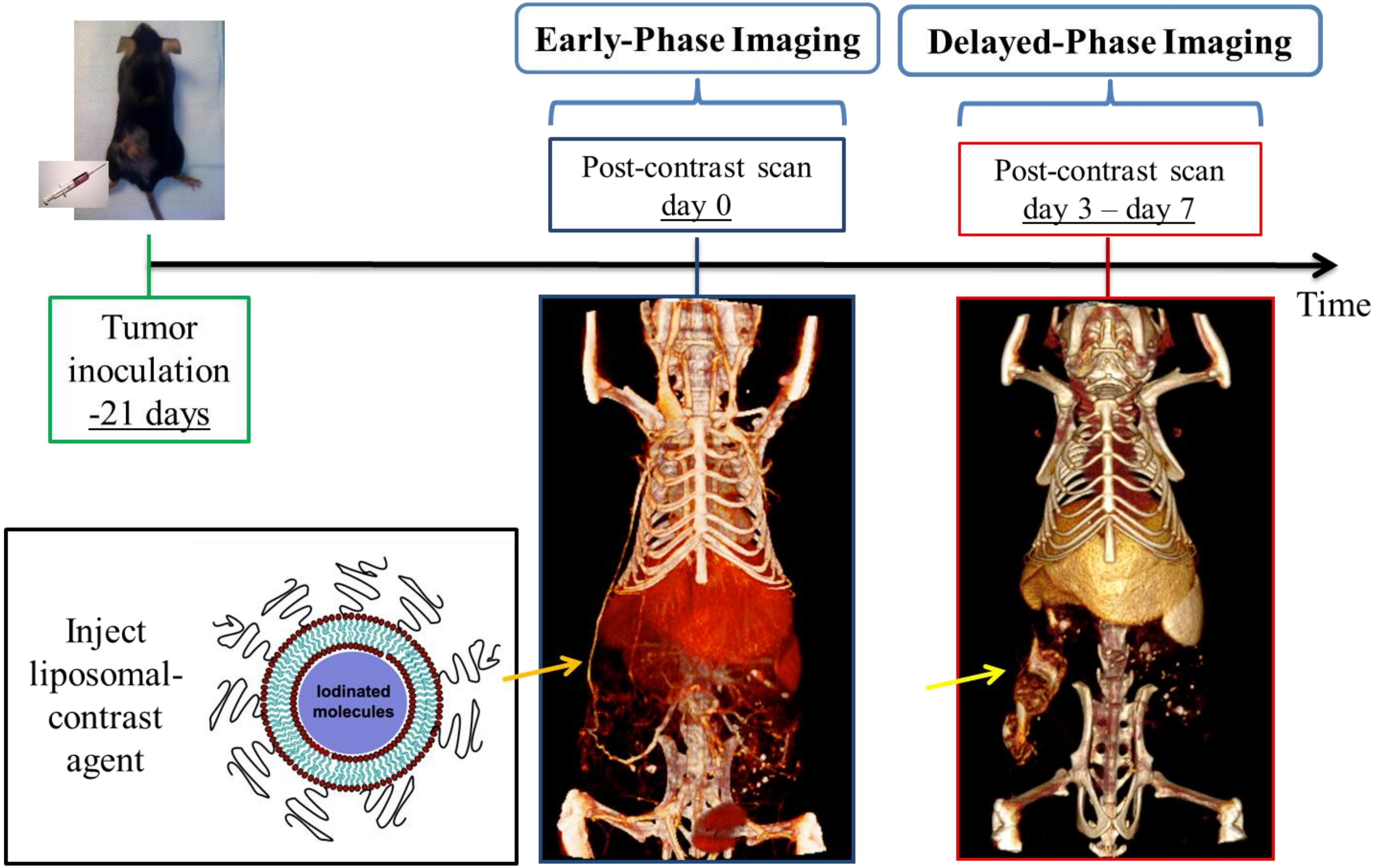
Iodine



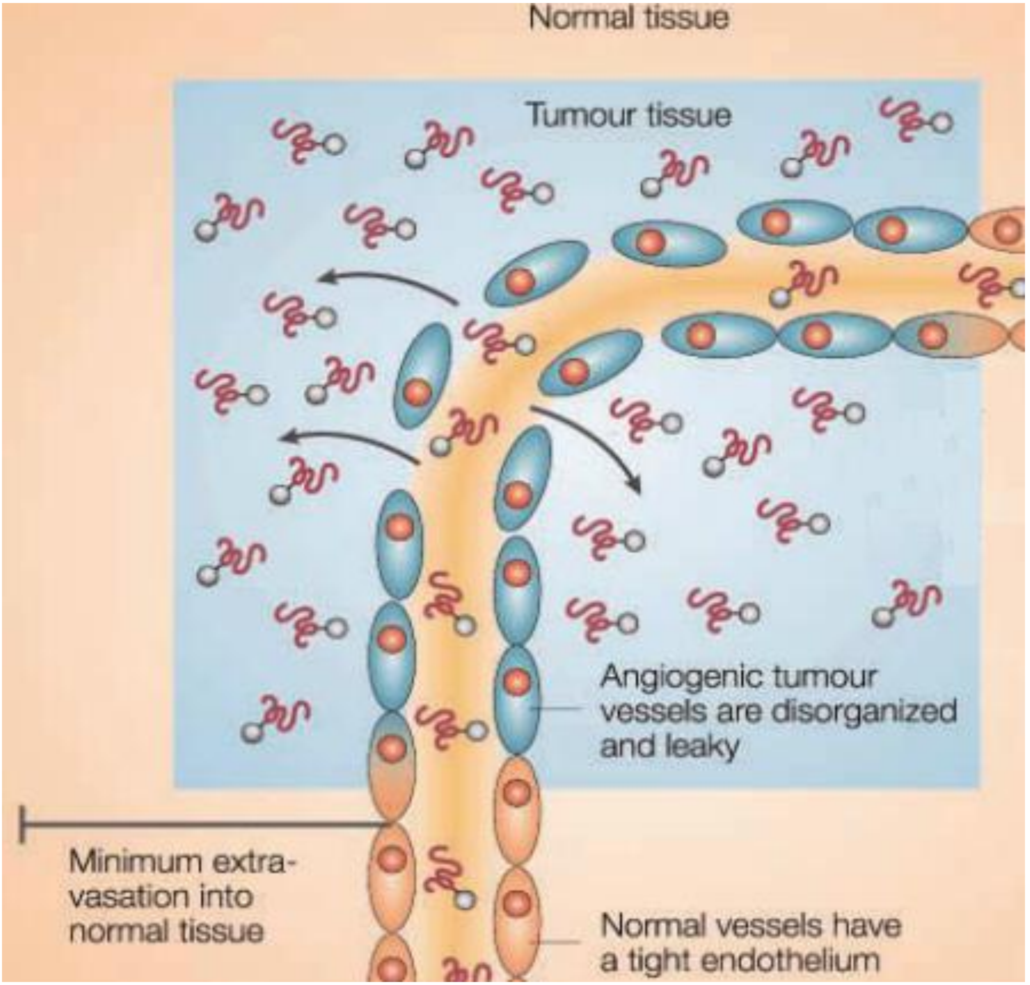
S. Mukundan et al , "A liposomal nanoscale contrast agent for preclinical CT in mice," AJR Am J Roentgenol **186**, 300-307 (2006).

Tumor Imaging using NPs

Dr. K. Ghaghada



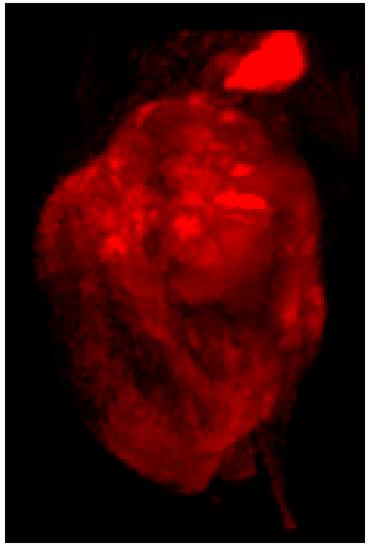
Enhanced Permeability and Retention (EPR)



James W. Burns, *Nature Materials* **8**, 441 – 443 (2009)

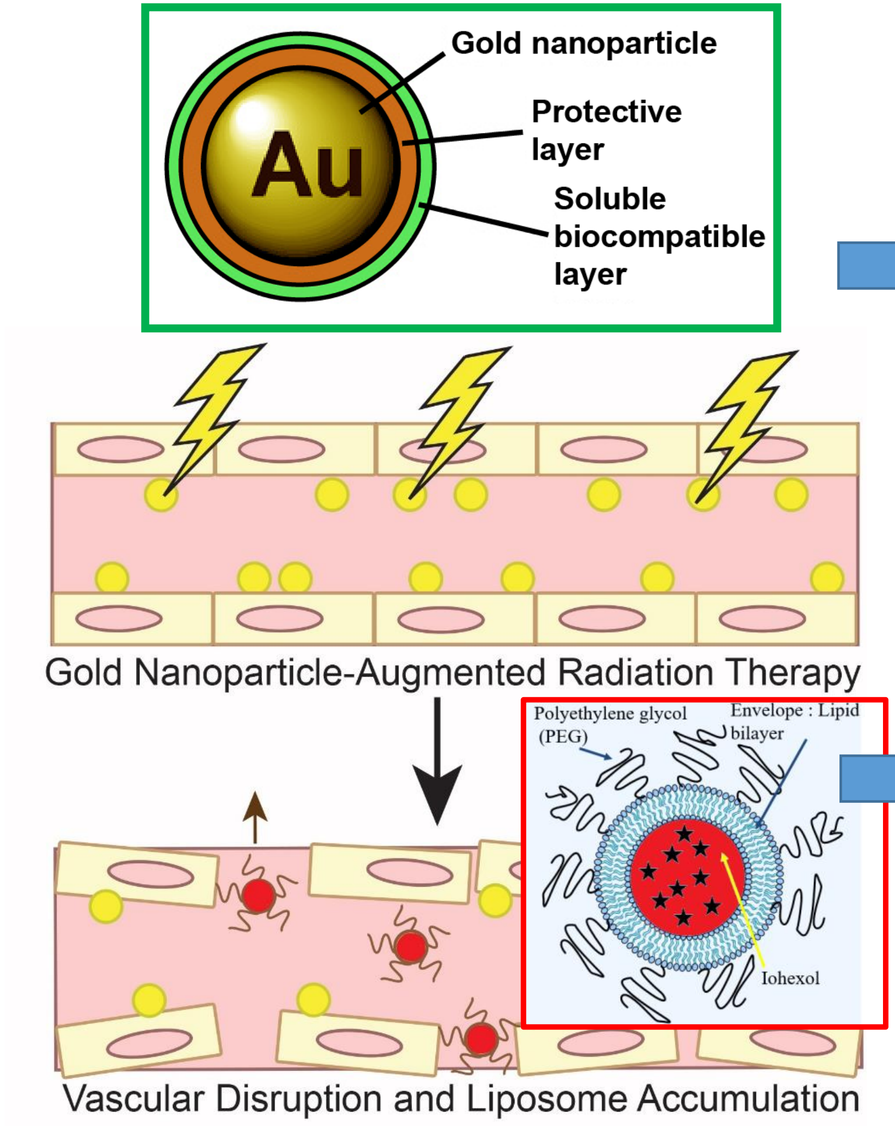
Tumor Vasculature

2 hours after injection: Iodine in the blood pool

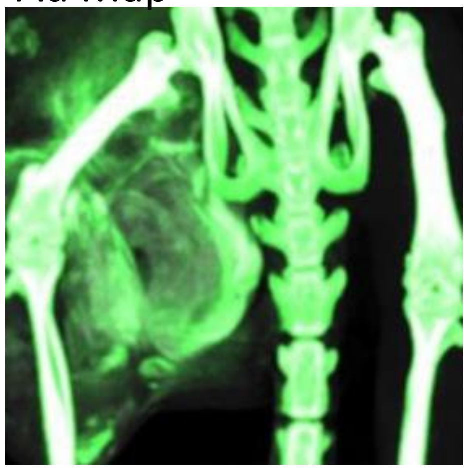


48 hours after injection: extravasated Iodine

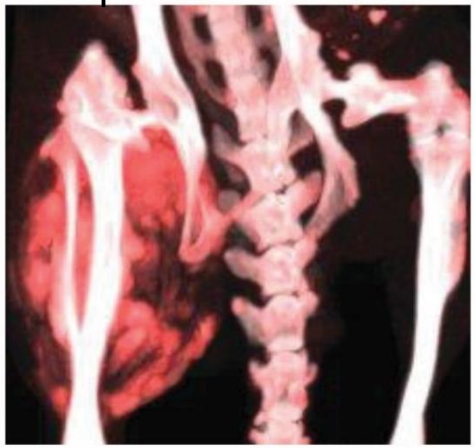
THERANOSTICS: AuNP augmentation of RT



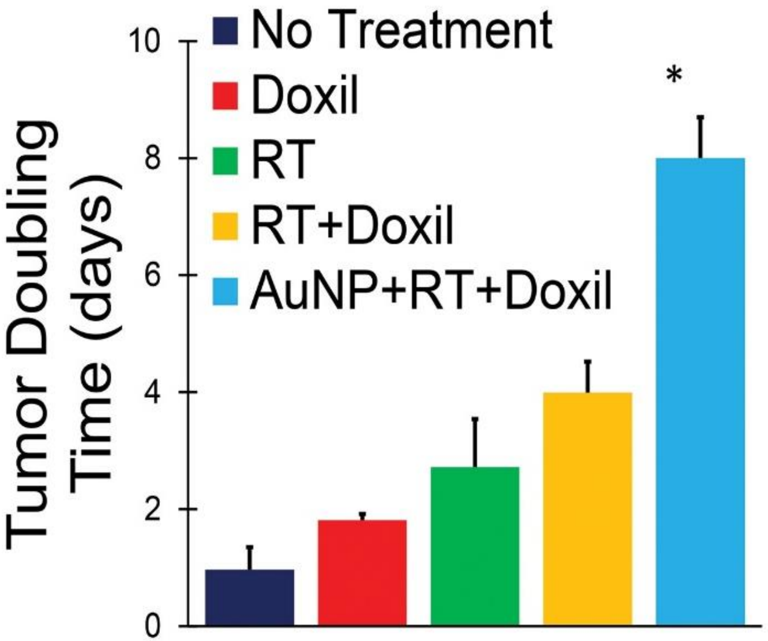
Au Map



I Map



DE micro-CT



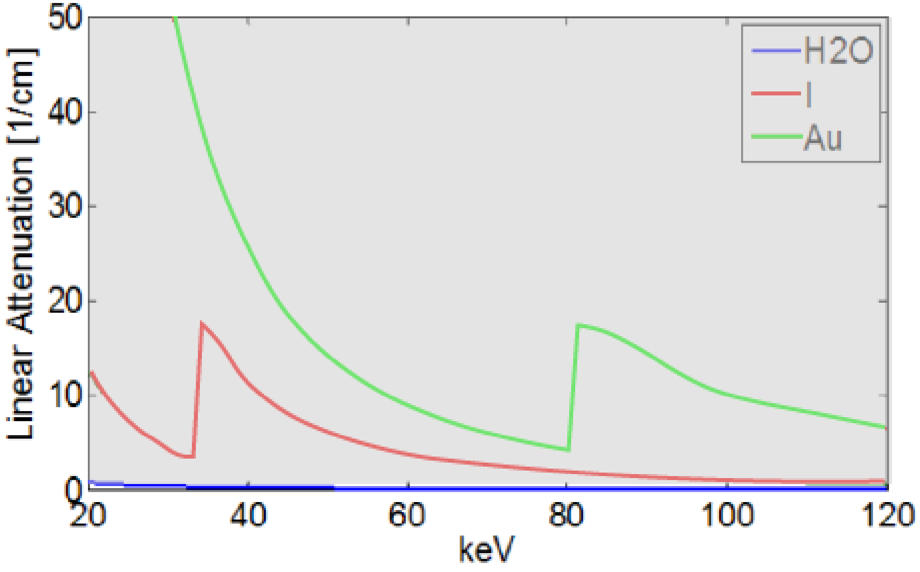
Ashton et al, Theranostics 2018

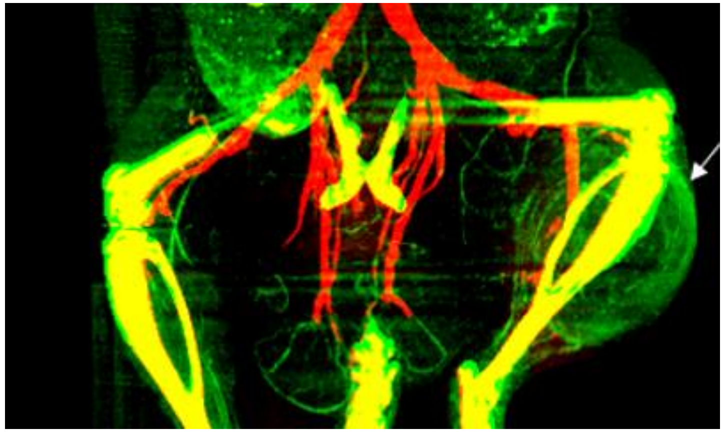
Energy Integrating vs Photon Counting Detectors

Energy integrating detector (EID):

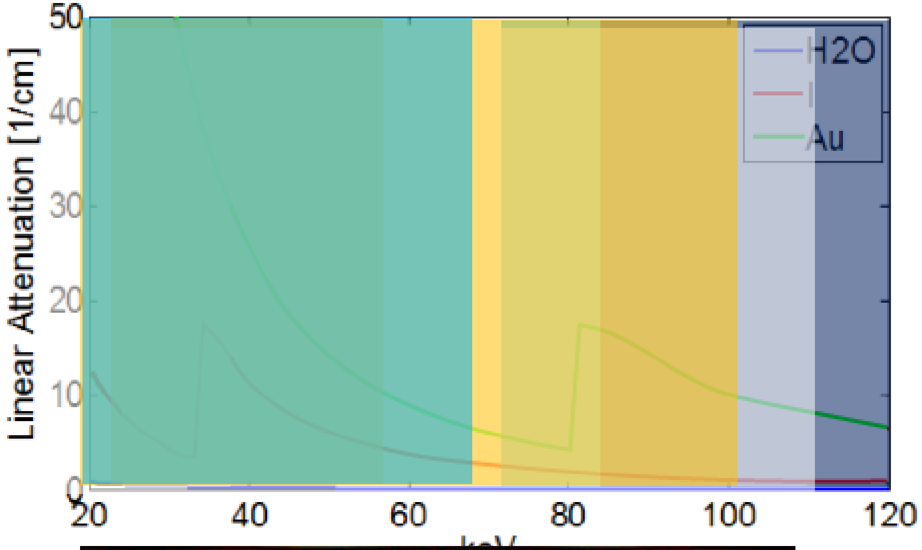
- Sum up pixel charge
- “Blind” to energy of incoming photons

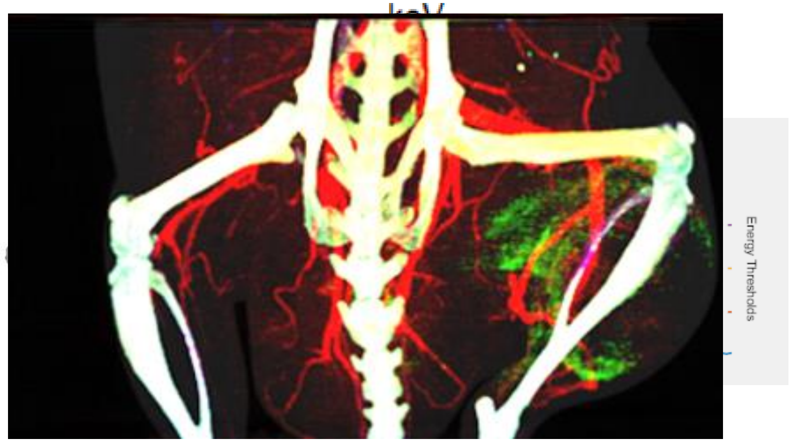
DE CT: Energy Integrating detector





Photon counting detector





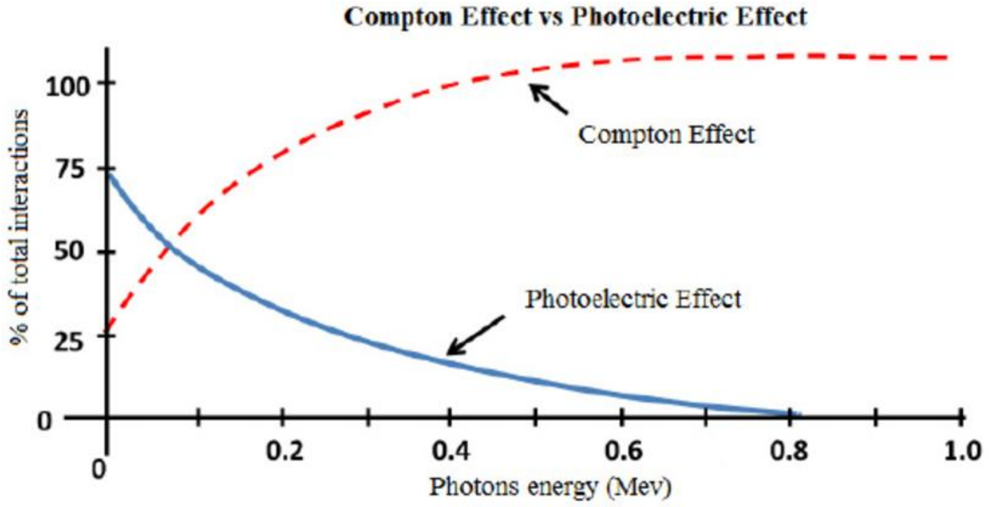
PC CT: Material Decomposition

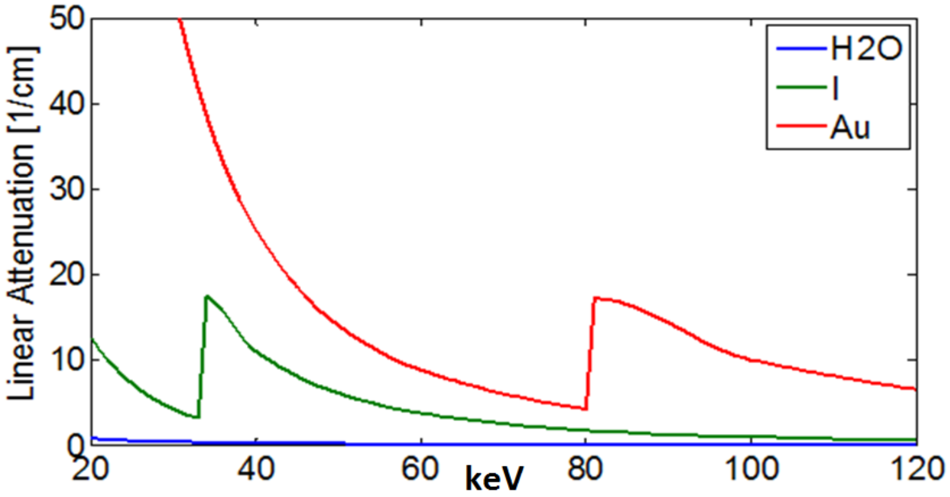
- Post-reconstruction decomposition method*:

$$\mathbf{X}(\mathbf{E}) = \boxed{\boldsymbol{C}_{\boldsymbol{PE}}\boldsymbol{e}_{\boldsymbol{PE}}(\mathbf{E}) + \boldsymbol{C}_{\boldsymbol{CS}}\boldsymbol{e}_{\boldsymbol{CS}}(\mathbf{E})} + \boxed{\boldsymbol{C}_{\mathbf{I}}\boldsymbol{e}_{\mathbf{I}}(\mathbf{E}) + \boldsymbol{C}_{\mathbf{Au}}\boldsymbol{e}_{\mathbf{Au}}(\mathbf{E})}$$

K-edge materials

- $\mathbf{X}(\mathbf{E})$ are the CT measurements
- $\boldsymbol{e}_{\mathbf{i}}(\mathbf{E})$ are material sensitivity measurements
- Solve for material maps $\boldsymbol{C}_{\boldsymbol{i}}$

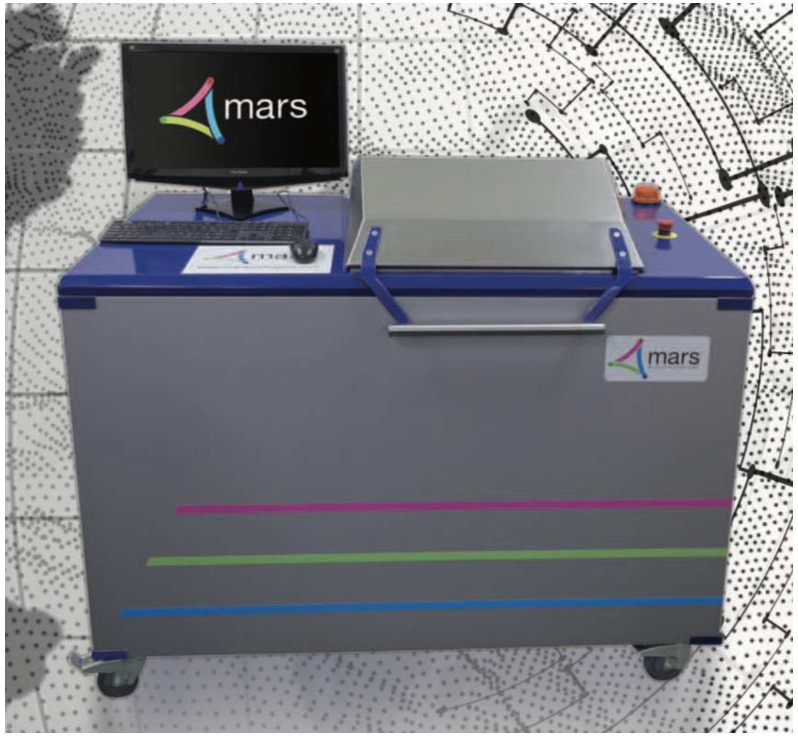


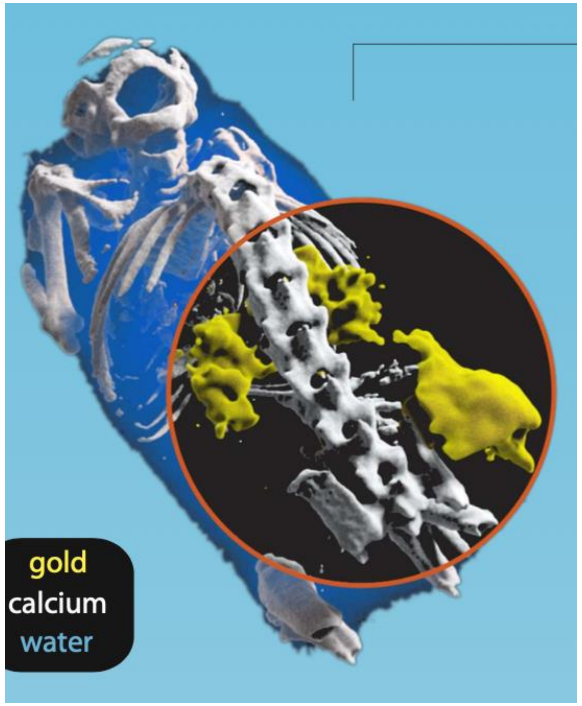


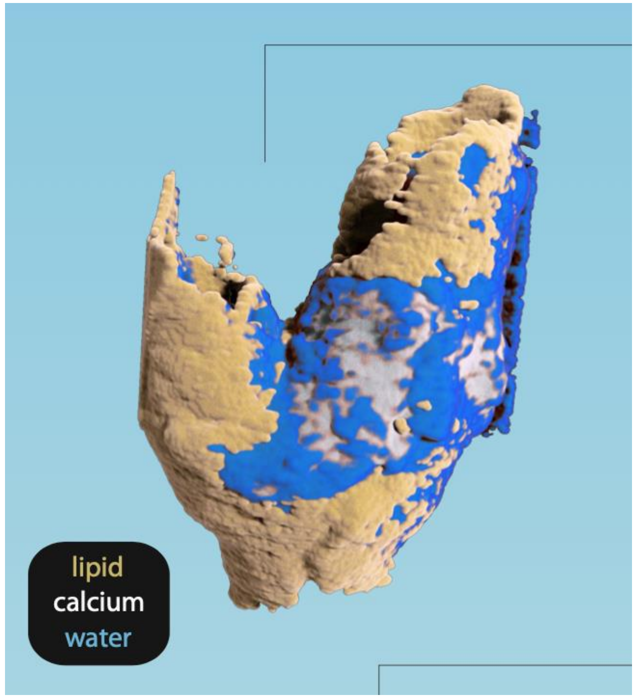
* R. E. Alvarez and A. Macovski, *Phys. Med. Biol*.

Mars Preclinical PC CT

Scanner	Diameter FOV (mm)	Length (mm)	Spatial Res.	kV	Scanning Time	Gating	Other Characteristics
Mars Preclinical Spectral CT System	100 mm	280 mm	30 -100 µm (user selects)	30-120 keV	8 mins for 30 x 15 mm volume	-Not available	-Uses photon counting detector with 8 energy bins -Detector constructed from CZT-Medipix3RX detector modules with 110-µm^2 pixels -Charge summing mode improves spectral measurement accuracy -Radiation dose: 20-80 mGy

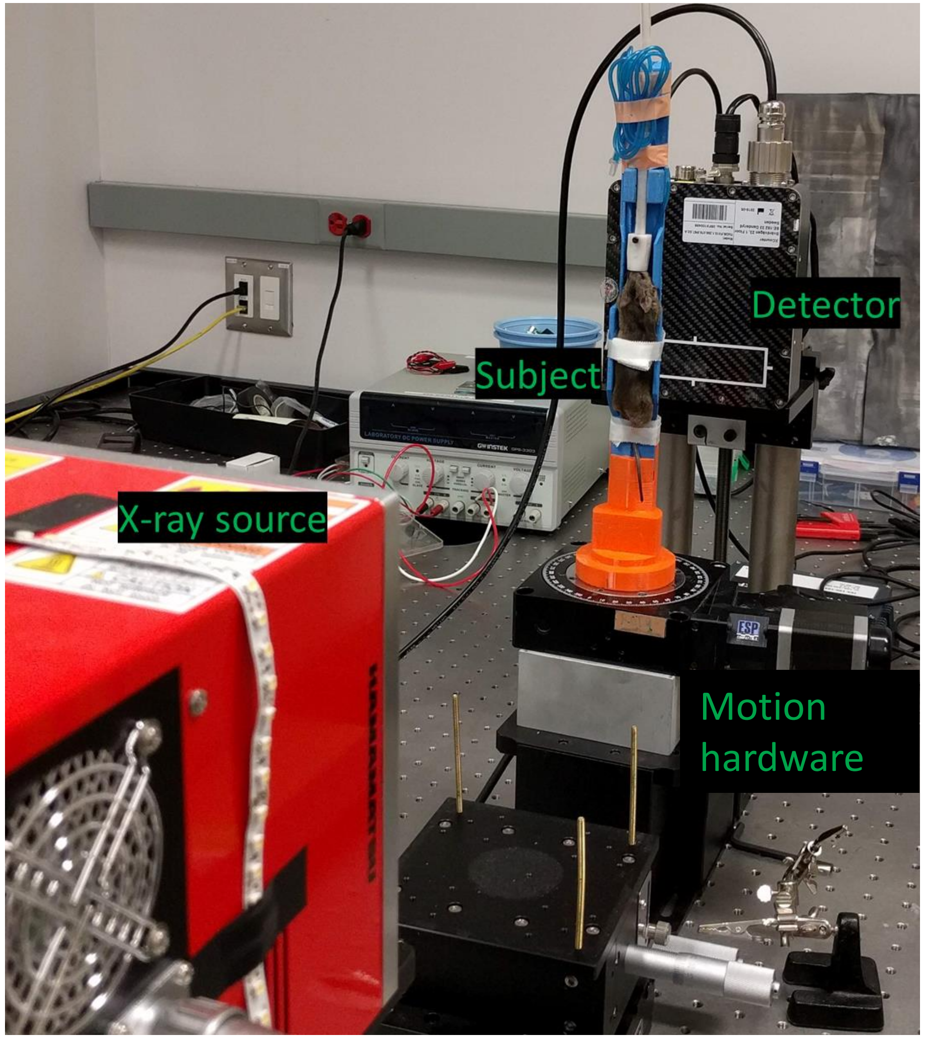






https://www.marsbioimaging.com/mars/wp-content/uploads/2018/07/MARS_Electronic.pdf

Ex Vivo PC Micro-CT System with Anti-Coincidence Corrections



Detector:

- XC-Thor from Direct Conversion
- 2 energy thresholds
- 100 µm pitch
- Anti-coincidence correction
- 2 x 4 cm detector area

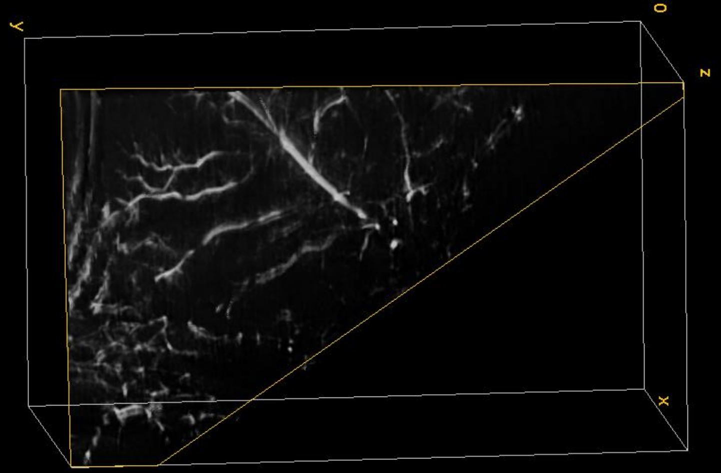
Source:

- Hamamatsu L9181-02 microfocus
- Tungsten anode
- Focal spot: 16 – 50 µm

High Resolution *Ex Vivo* PC micro-CT

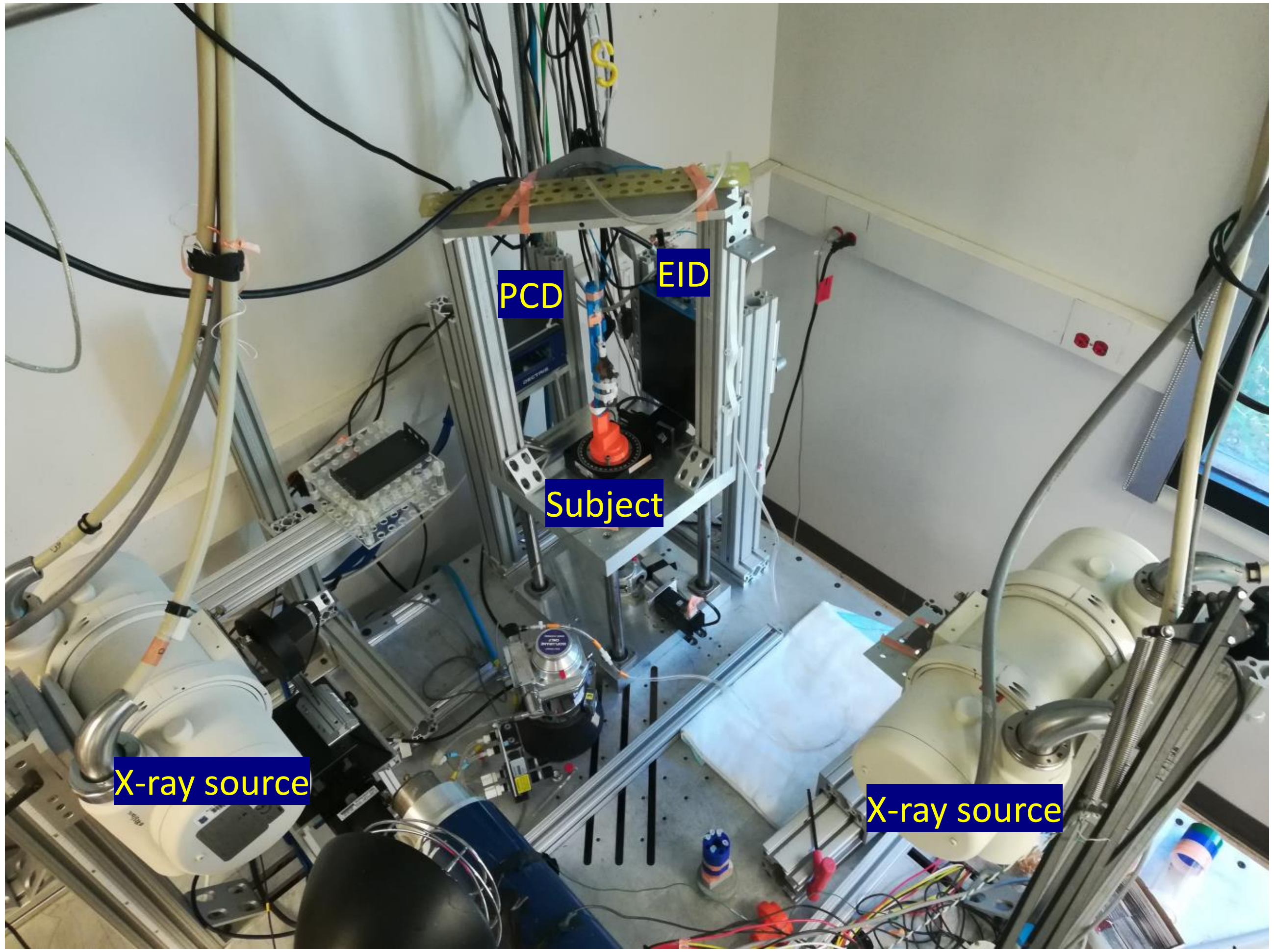
Vascular Casting using a Barium-based contrast agent BriteVu (*ScarletImaging*)

Voxel Size : 30 microns



Holbrook et.al SPIE Medical Imaging 2020: Physics of Medical Imaging 11312, 356-365

Duke Hybrid Spectral micro-CT



Dual source EID + PCD system

- PCD:
  - Santis 0804 CdTe by Dectris
  - 4 energy thresholds
  - 150 µm pitch
- EID:
  - Dexela 1512 CMOS with CsI
  - 75 µm pitch

Holbrook M, et al. Physics in Medicine & Biology 65 (20), 205012, 2020

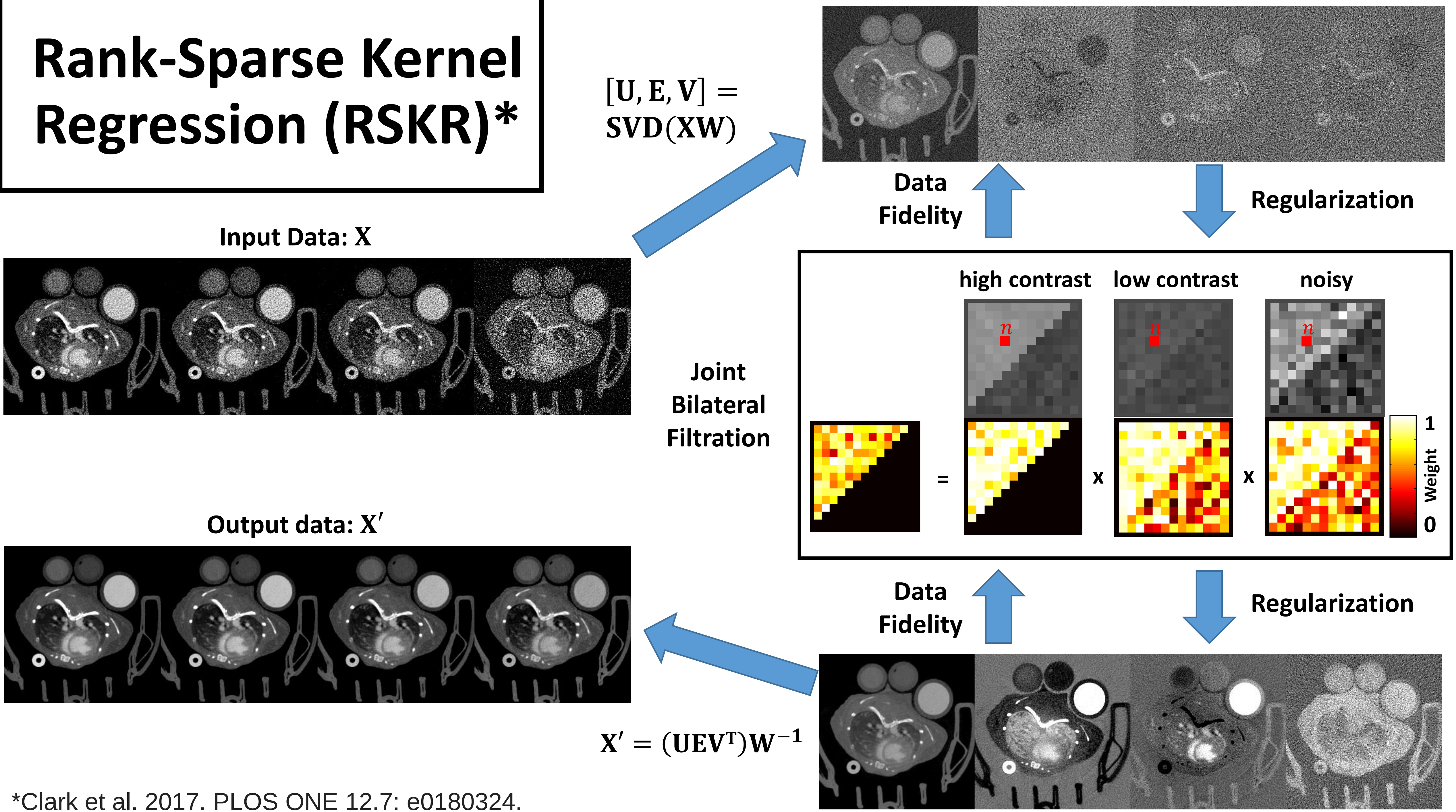
Multi-Channel Iterative Reconstruction

Dr. D. Clark

Solve: $\mathrm{X} = \underset{\mathrm{X}}{\mathrm{argmin}} \frac{1}{2}\sum_c \|\mathrm{RX}_c - \mathbf{y}\|_{\mathrm{Q}_c}^2 + \lambda\|\mathrm{X}\|_{\mathrm{Reg}},$ where $\mathrm{X} = \mathrm{X}_\mathrm{L} + \mathrm{X}_\mathrm{S}$	Robust PCA cost function.
Inputs: $\mathbf{Q}, \mathbf{y}, \boldsymbol{\alpha}, \mathrm{h}$	Parameters.
Initialization: 1: $\mathrm{X} = \underset{\mathrm{X}}{\mathrm{argmin}} \frac{1}{2}\sum_c \|\mathrm{RX}_c - \mathbf{y}\|_{\mathbf{Q}_c}^2$	<u>Initialization</u>: Algebraic reconstruction.
2: $\boldsymbol{\mu}_c = \boldsymbol{\alpha}_c \frac{\|\mathrm{R}^\mathrm{T}\mathrm{Q}_c\mathbf{y}\|_2}{\|\mathrm{X}_c\|_2}$	Data-adaptive scaling.
While not converged … 3: $\mathrm{D} = \mathrm{RSKR}(\mathrm{X} + \mathrm{V})$	<u>Iterative reconstruction</u>: Denoising with RSKR.
4: $\mathrm{V} = \mathrm{X} + \mathrm{V} - \mathrm{D}$	Residual tracking.
5: $\mathrm{X} = \underset{\mathrm{X}}{\mathrm{argmin}} \sum_c \left[\frac{1}{2}\|\mathrm{RX}_c - \mathbf{y}\|_{\mathbf{Q}_c}^2 + \frac{\boldsymbol{\mu}_c}{2}\|\mathrm{X}_c + \mathrm{V}_c - \mathrm{D}_c\|_2^2\right]$ **End While**	Data fidelity update.

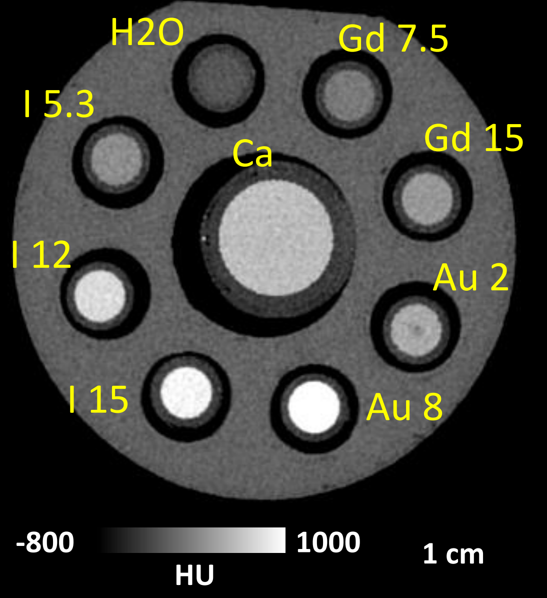
Goldstein, T., & Osher, S. (2009). The split Bregman method for L1-regularized problems. *SIAM journal on imaging sciences, 2*(2), 323-343.
Clark et al. 2018. Data-efficient methods for multi-channel x-ray CT reconstruction. *SPIE Medical Imaging*.

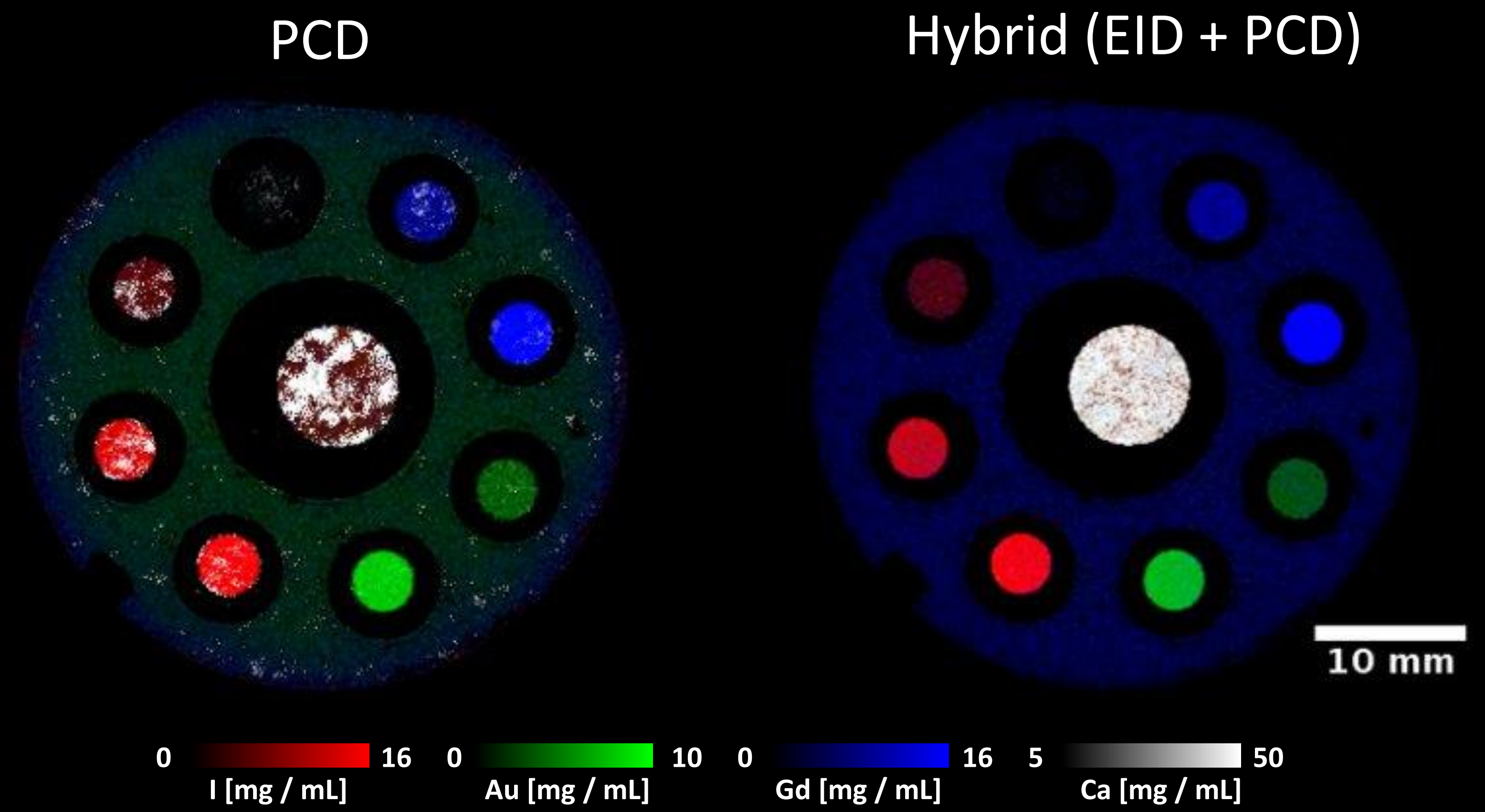
Rank-Sparse Kernel Regression (RSKR)*



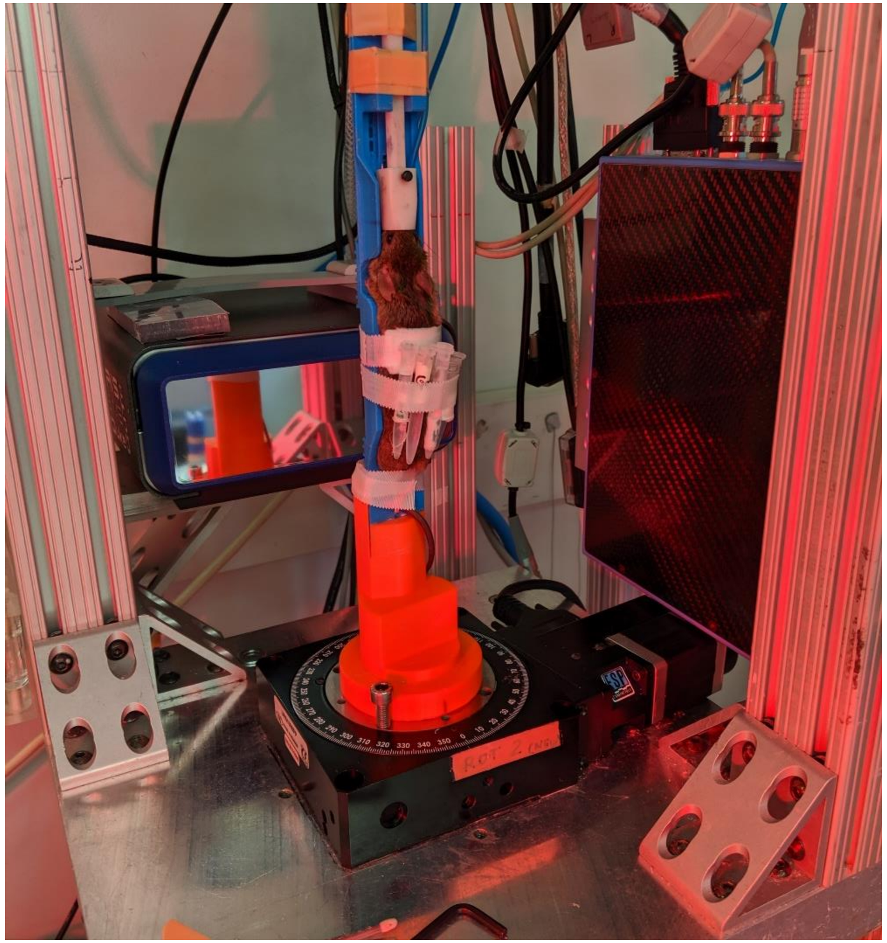
*Clark et al. 2017. PLOS ONE 12.7: e0180324.

Phantom decompositions





Cancer Studies: *In Vivo* Experiments



Subject:

- *p53*$^{fl/fl}$ mouse model [1]
- Hind limb sarcoma generated by delivery of Adeno-Cre followed by carcinogen 3-methylcholanthrene

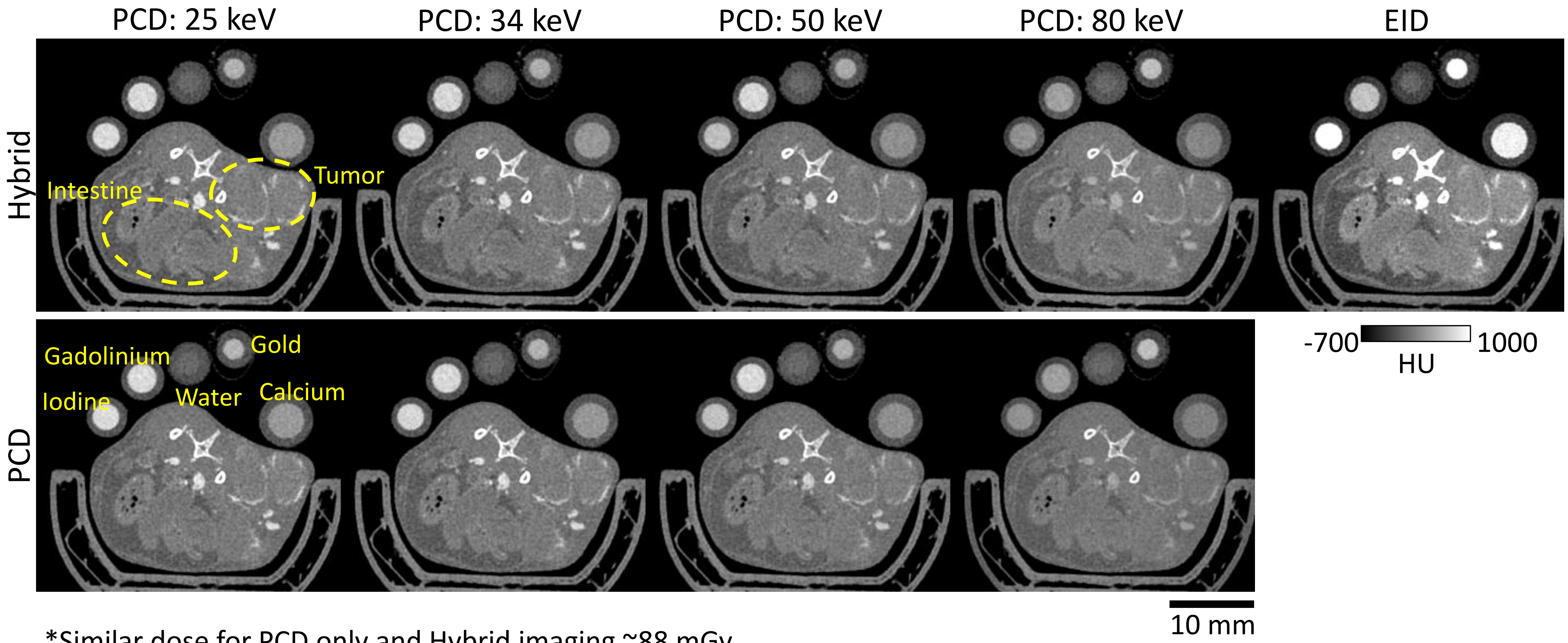
Contrast agents:

- Day 0: targeted RGD-Gold nanoparticles
- Day 1: Liposomal Gadolinium
- Day 2: Liposomal Iodine

Imaging (PCD-only and hybrid) was performed on **day 2**.

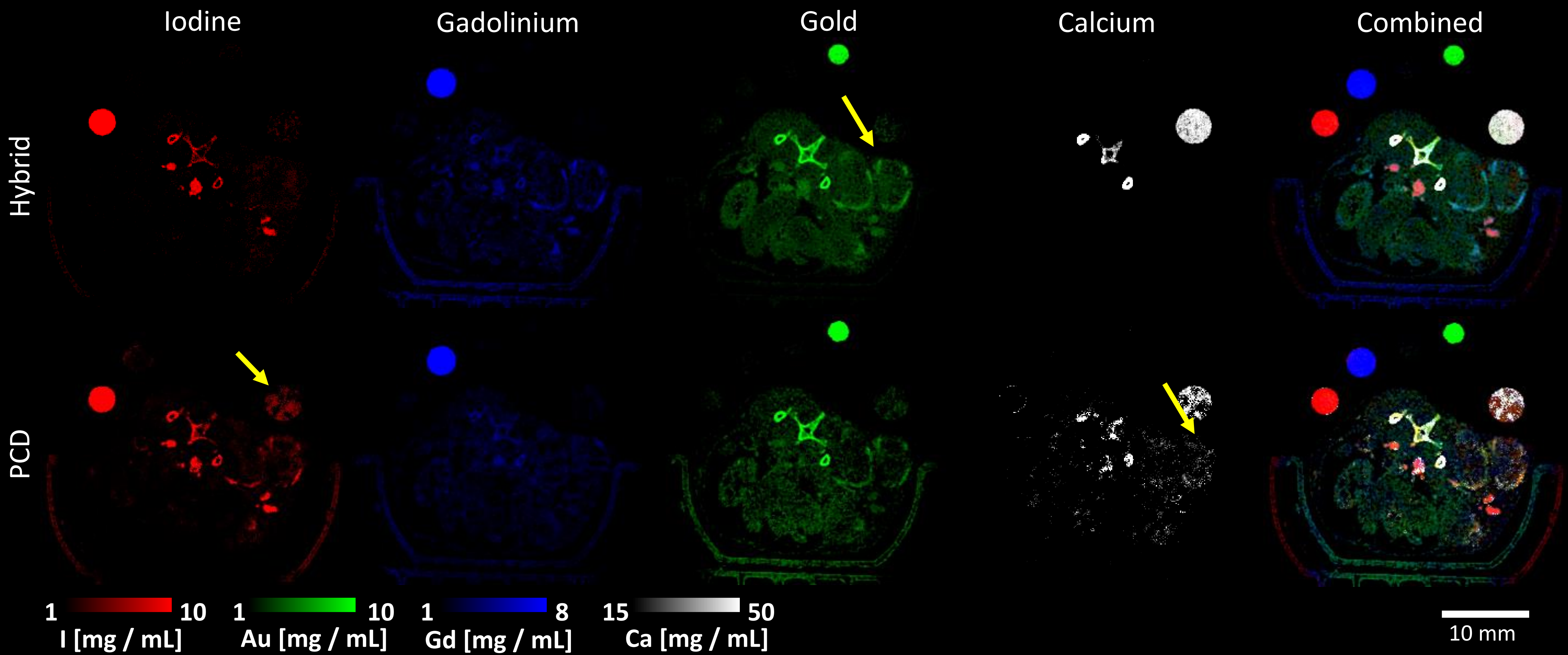
Holbrook M, et al. Physics in Medicine & Biology 65 (20), 205012, 2020

PC micro-CT: Reconstructions

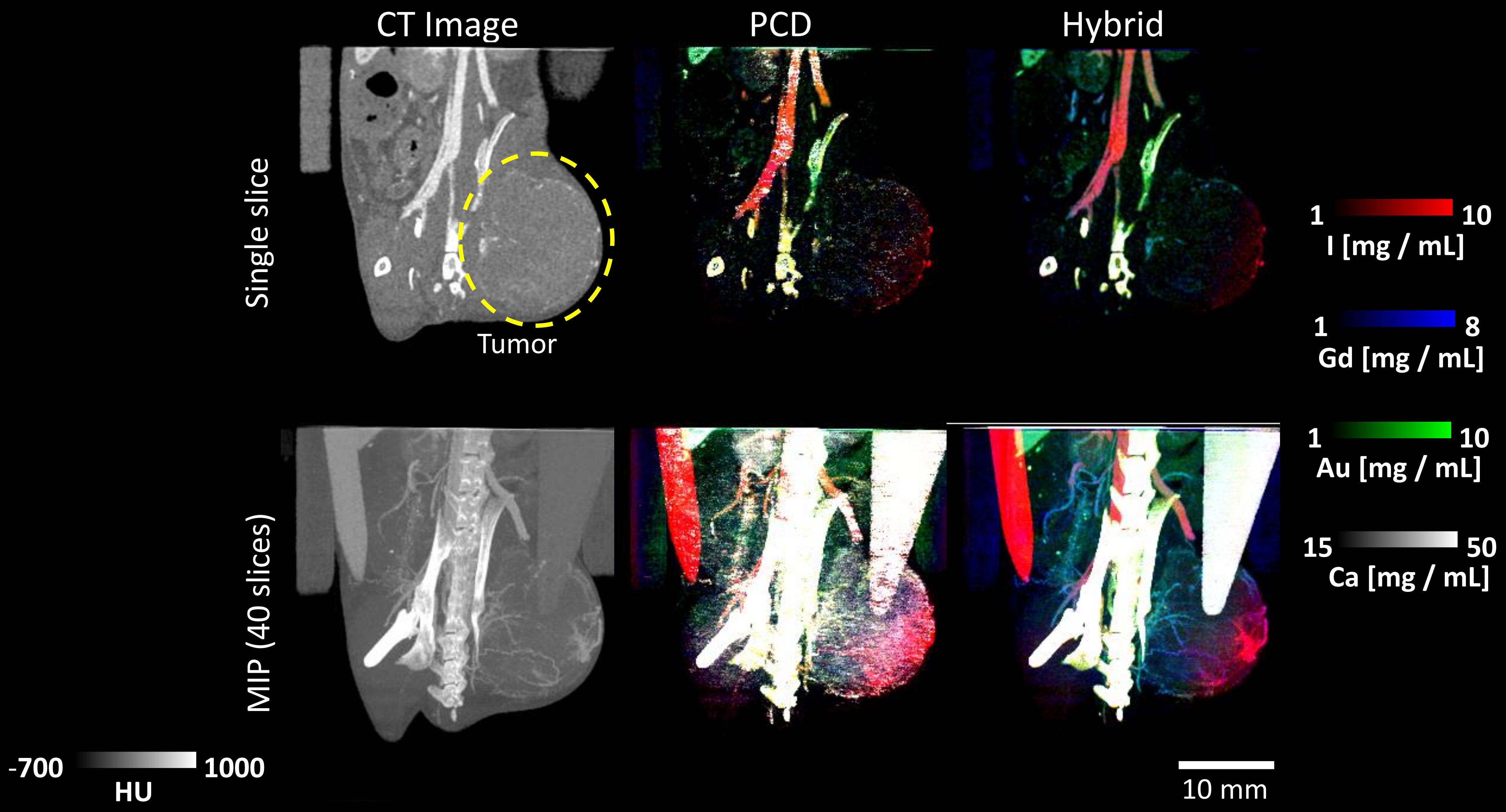


*Similar dose for PCD only and Hybrid imaging ~88 mGy

Material Decompositions



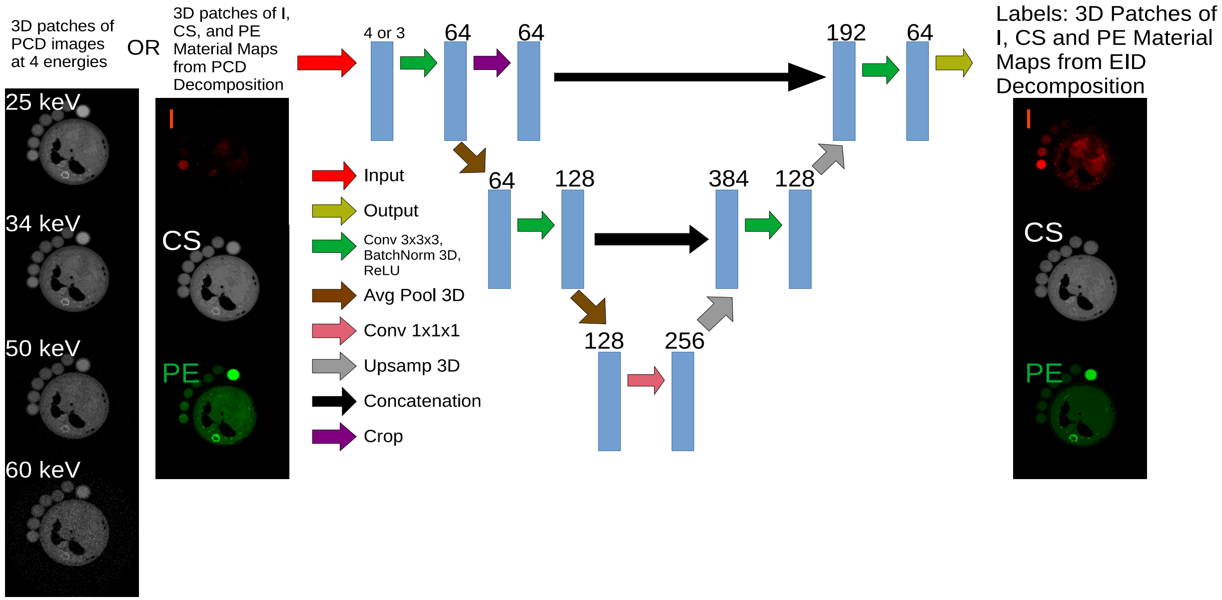
Material Decompositions

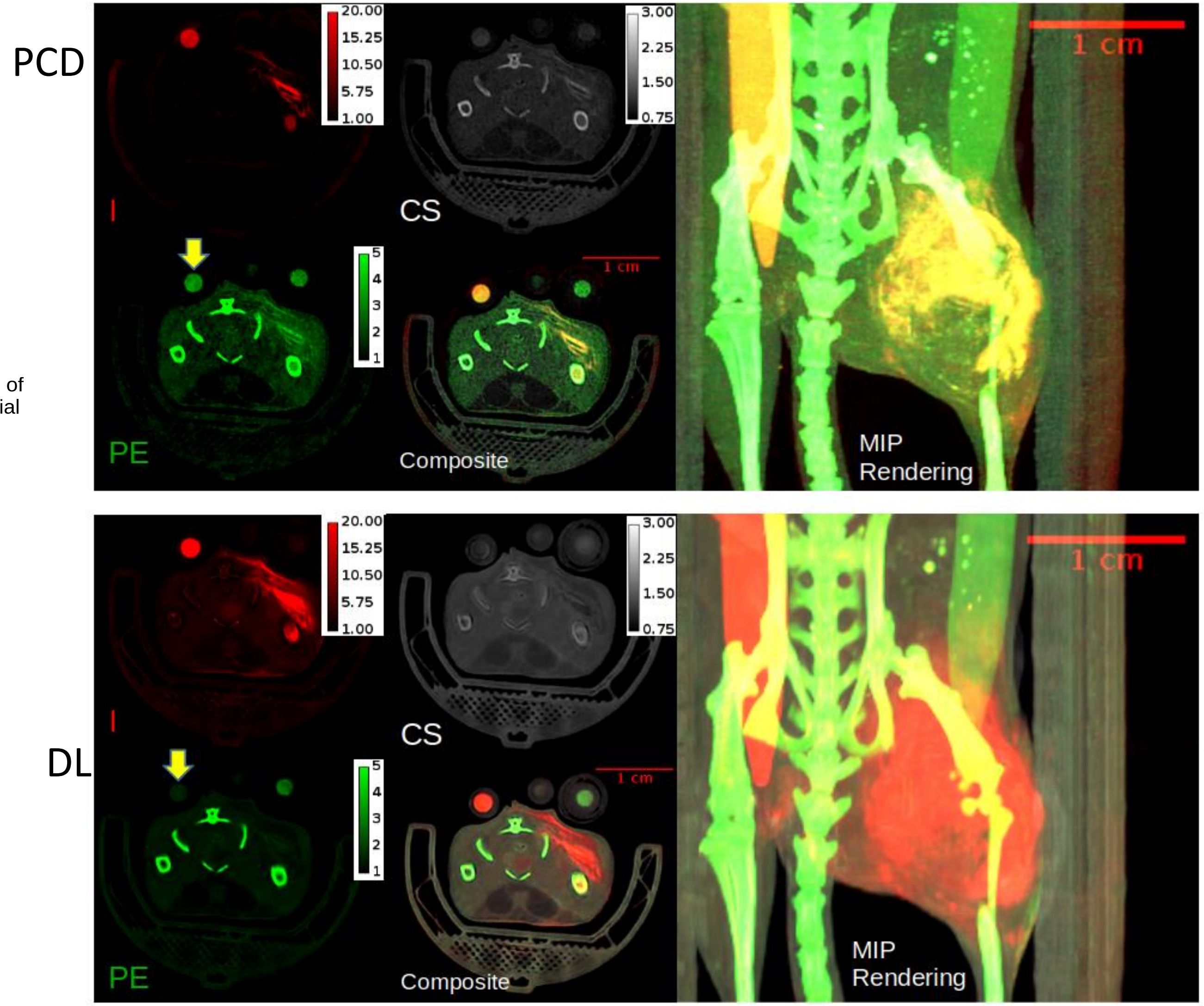


Material Decomposition from PC CT using Deep Learning and Energy-Integrating CT Training Labels

R. Nadkarni

- 3D U-net
- high-dose multi-EID data for training
- 27.50% lower RMSEn in the I map and 59.87% lower RMSE in the PE map

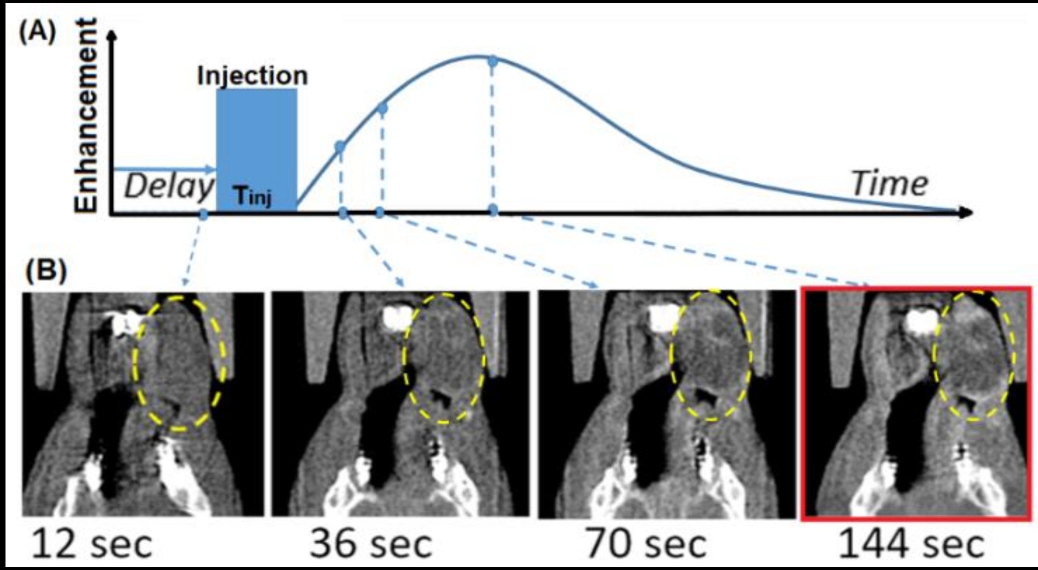


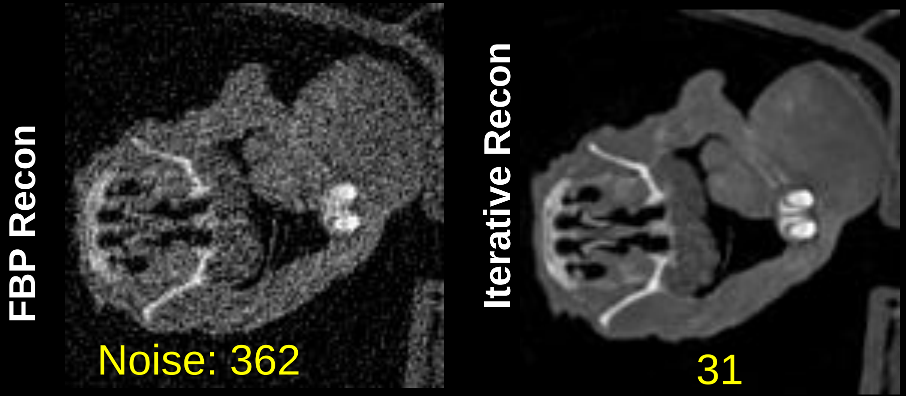


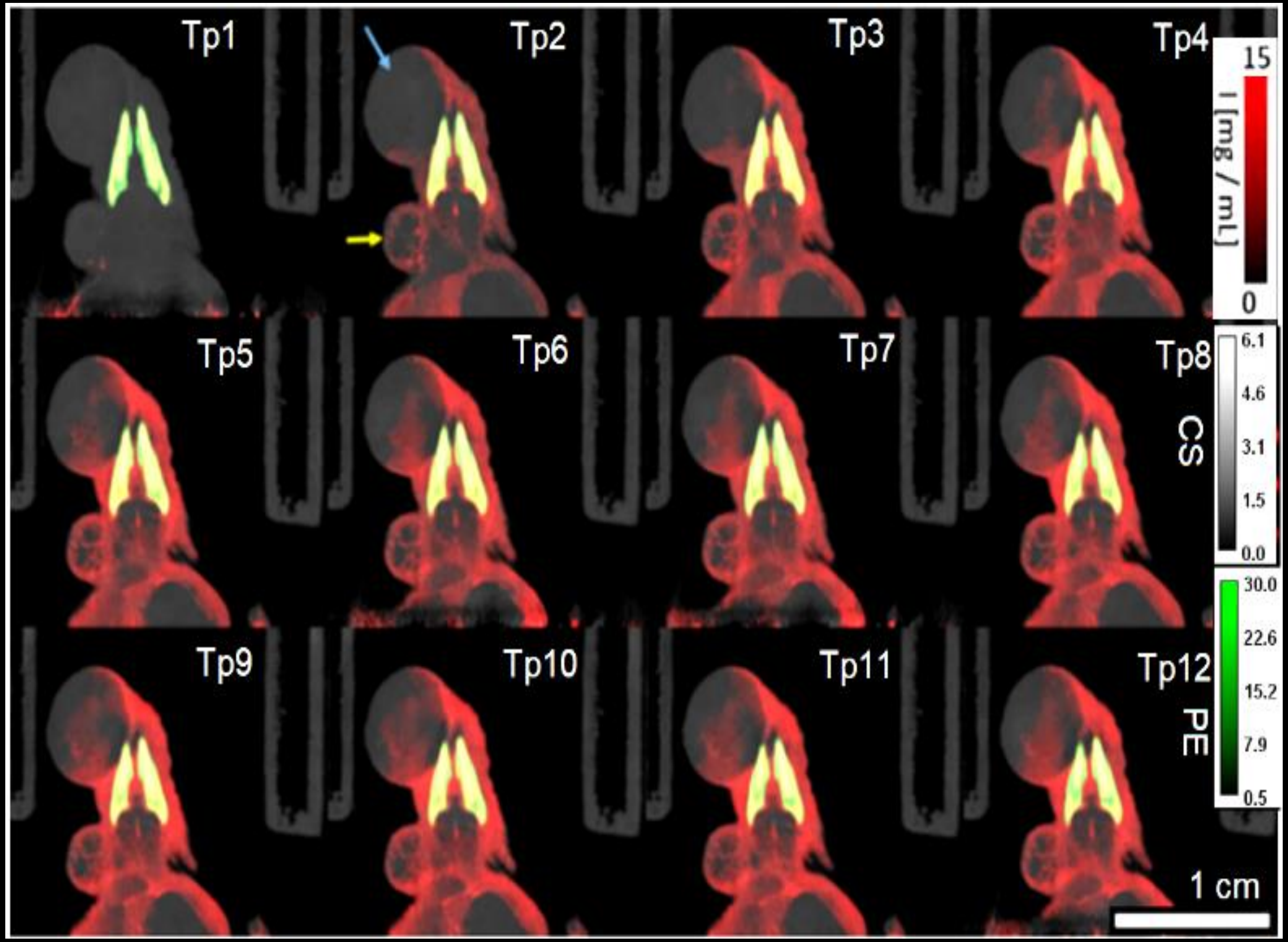
Nadkarni R *et al*. Phys. Med. Biol., under revision, 2022

PC micro-CT Perfusion

- Using a single injection of Isovue
- 5D (3D + Time + Energy) reconstruction
- Material decomposition (PE, CS, I map)

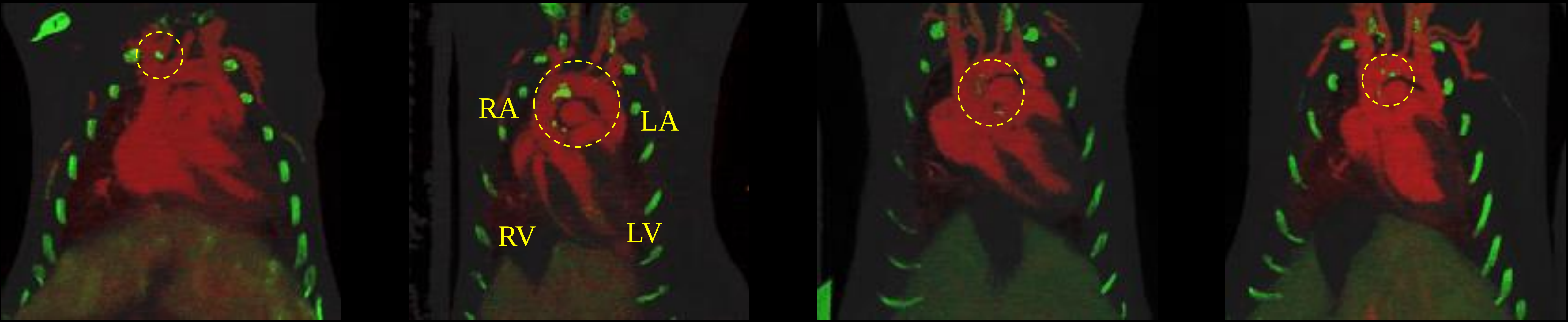






* See poster: Clark D et al.

Dynamic Cardiac PC micro-CT



Materials: Iodine, Photoelectric Effect, Compton Scattering

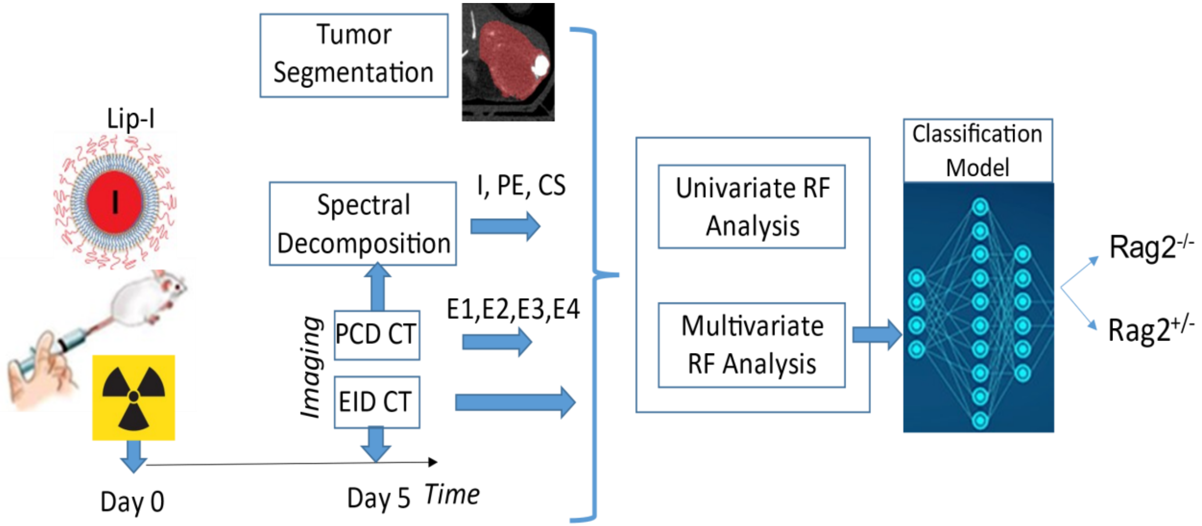
1 cm

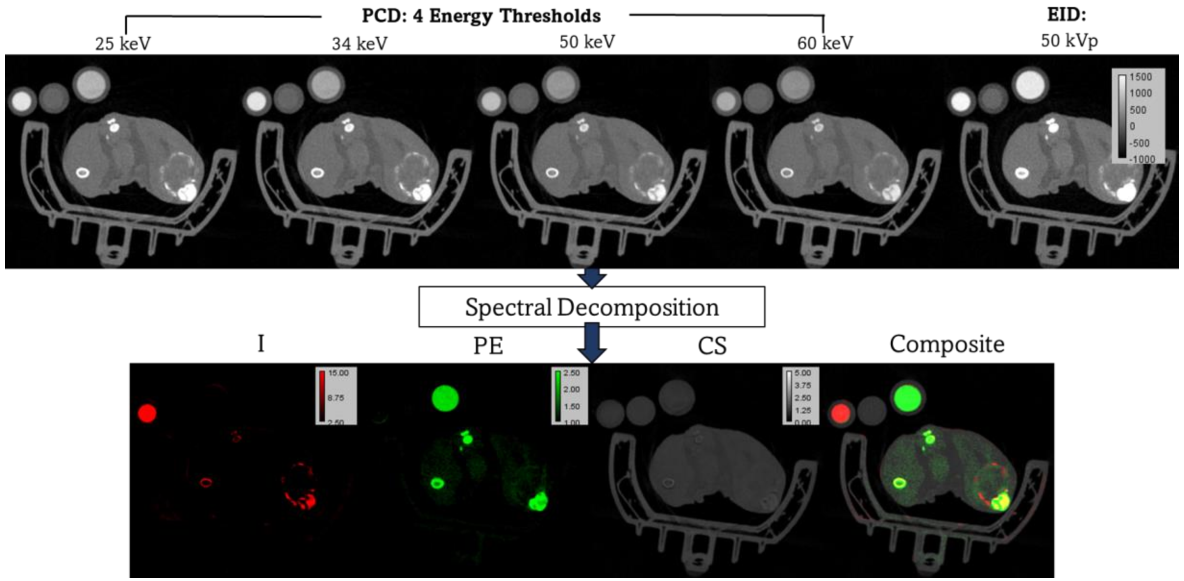
Clark et al. 2019, “Photon-counting cine-cardiac CT in the mouse”

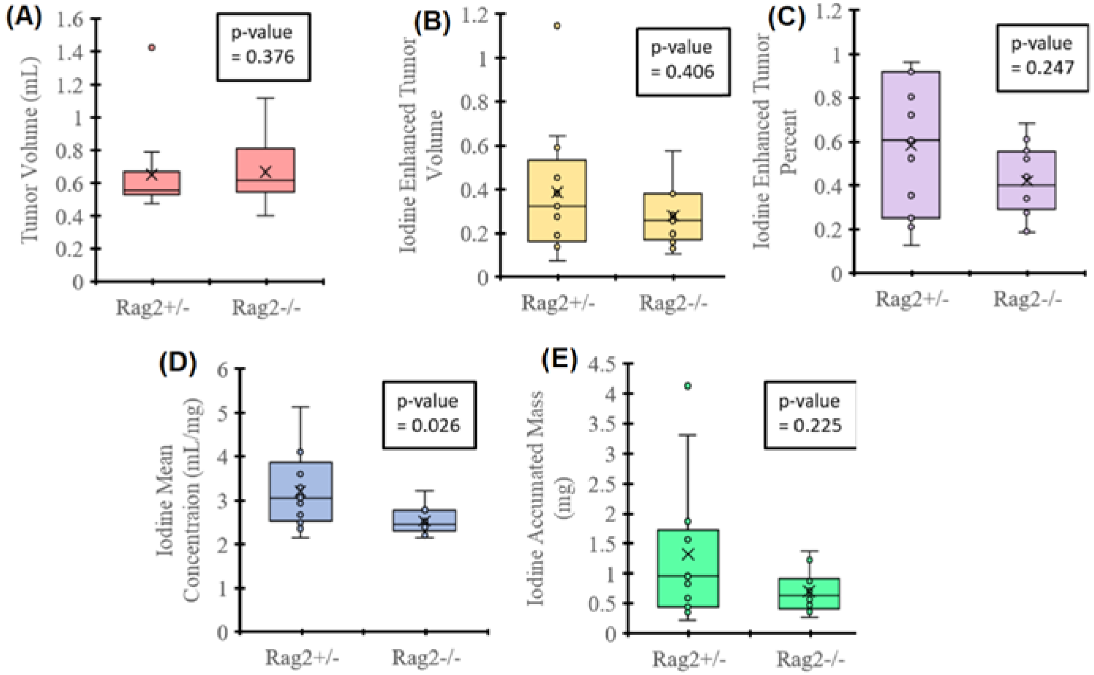
Dose: ~190 mGy

Photon Counting CT and Radiomic Analysis for Detection of Lymphocytic Infiltrate

A. Allphin and Dr. Y. Mowery







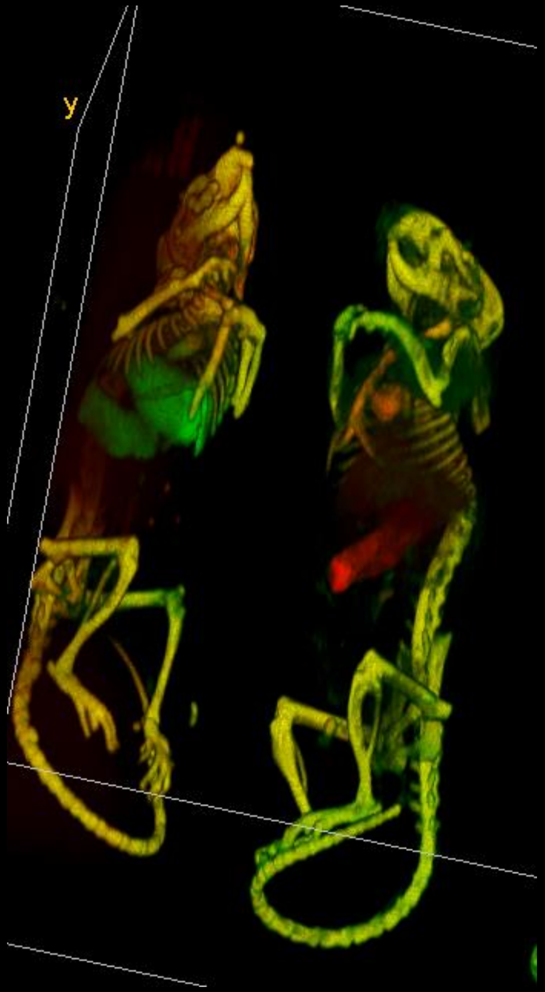
Radiomics

Feature Source	Accuracy	Precision/Recall Intersection	AUC
EID	0.656	0.648	0.693
PCD	0.840	0.833	0.897
Material Maps	0.782	0.788	0.842

A. Allphin et al. Tomography **8**(2): 740-753 (2022).

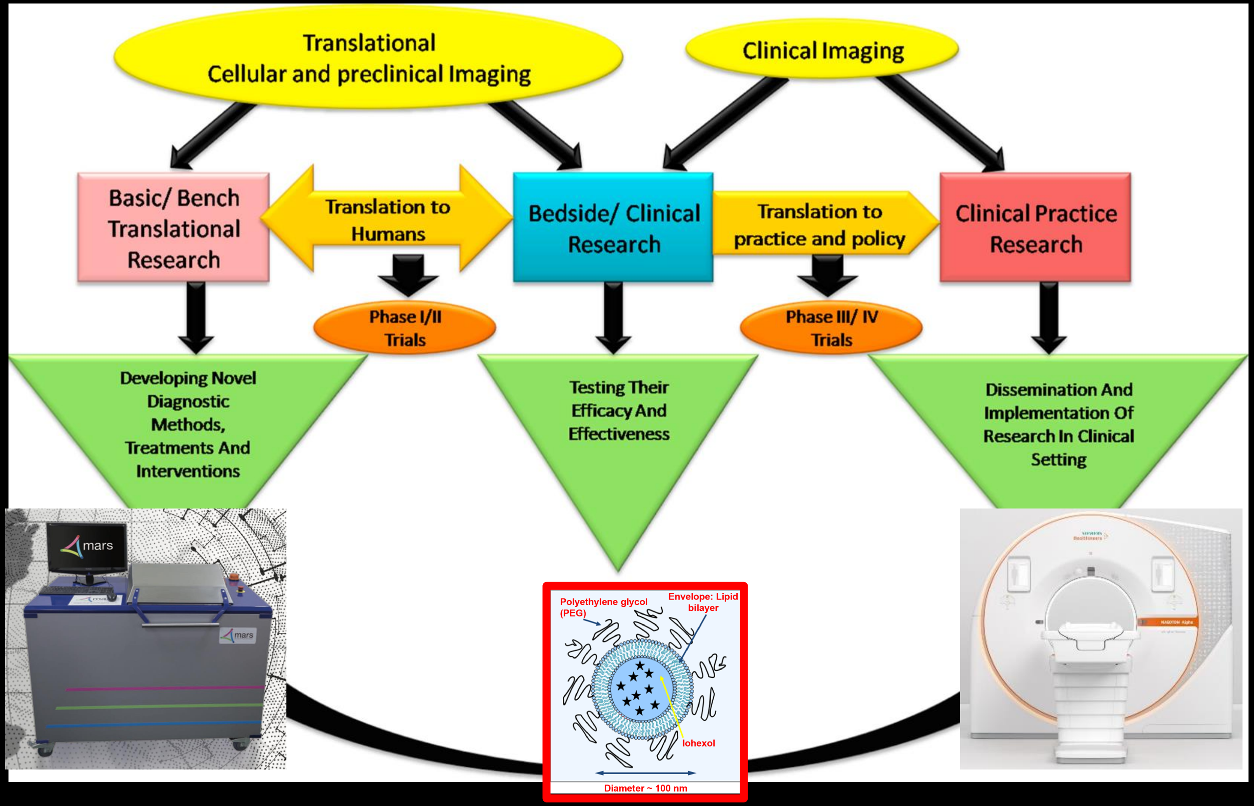
Clinical PC CT: Siemens NAEOTOM Alpha

High-resolution mono-energy images (~150 µm in plane)



Lower resolution spectrally resolved images (~300 µm in plane)

Road map to practice-based translational research.



Mahajan A et al. Clinical Radiology, Volume 71, Issue 3, 2016, Pages 304-305

Summary and Conclusions

- Spectral PC micro-CT promises improved contrast resolution and lower dose
- Nanoparticle contrast agents can serve well preclinical studies with PC micro-CT.
- PC CT may provide more functional and molecular imaging information
- Co-Clinical PC CT studies may bridge the translational gap

NIH

U24 CA220245

1RF1AG070149-01

Our Team and Collaborators

- Dr. C.T. Badea

- Dr. D. Clark

- A. Allphin

- R. Nadkarni

- Dr. A. Badea

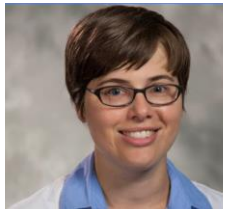
- Dr. M. Holbrook

- Dr. Y. Qi

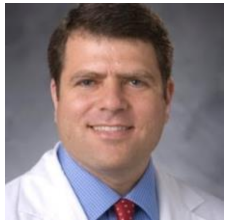
- Dr. K. Ghaghada
Texas Children's Hospital

- Dr. R. Patel

- Dr. Y. Mowery



- Dr. D. Kirsch



- Dr. J. West
University of Virginia