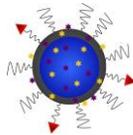


Novel contrast agents for multi-energy CT imaging

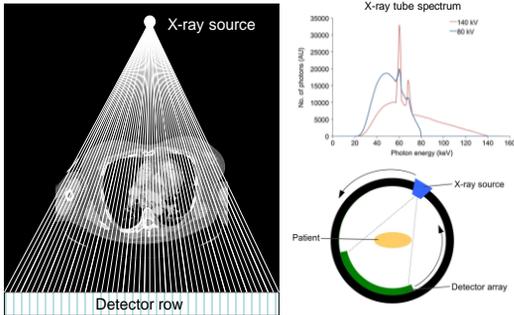
David P. Cormode
Radiology, Cardiology, Bioengineering
University of Pennsylvania



Disclosures

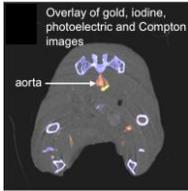
- Research grant from Philips Healthcare
- Research grants from the NIH, AHA, NSF, Fulbright, etc
- Stock owner of PolyAurum

CT scanning



DP Cormode et al Contrast Media Mol. Im. 2014, 9(1):37-52

Photon counting CT in CV imaging



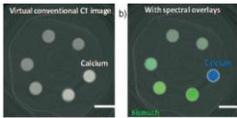
- Imaging three materials simultaneously – in vivo?
- No – whole mouse took 24 hours
- Low count rate detectors

DP Cormode et al, *Radiology*, 2010, 774-782

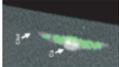
Thrombus imaging

Bismuth nanoparticle, targeted to fibrin

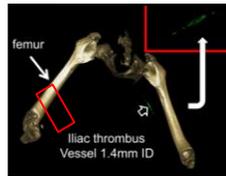
Phantom



Ex vivo, carotid endarterectomy

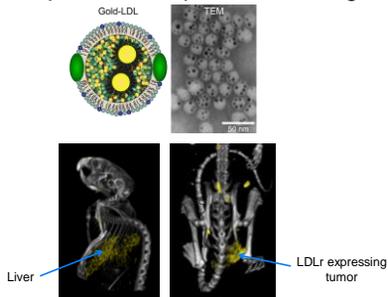


Ex vivo



D Pan et al, *Angewandte Chemie*, 2010, 9635-9639

Gold nanoparticles for photon counting CT



- Gold labeled low density lipoprotein
- Accumulates in tumors that overexpress the LDL receptor

IE Ailijn et al, *ACS Nano*, 2013, 7(11):9761-70

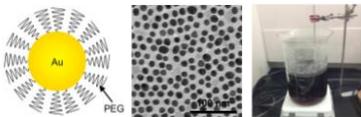
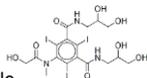
Results from prototype clinical photon counting CT



- Built by Philips (Haifa, Israel)
- Located at the Douek Lab (Lyon)
- Fast temporal resolution: 1s scan time
- High spatial resolution: 0.25 mm
- Low radiation dose (~50% of conventional CT)
- Limited field of view (168 mm)
- 4 slices, 2 mm z-coverage

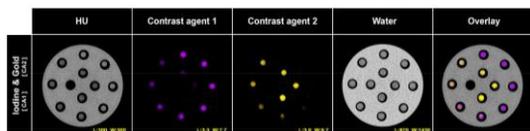
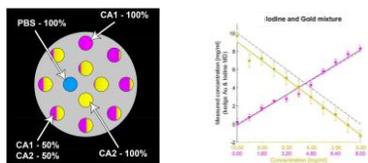
Experimental parameters

- Scans were done at 120 kV and 100 mA
- Thresholds: 30, 51, 78, 83, 98 keV
- Contrast agent 1: iodinated small molecule
- Contrast agent 2: PEG-coated gold nanoparticles: 12.5±2.4 nm core (TEM), 18.3±0.5 nm (DLS)



- Synthesized 'conventional CT' images formed
- Material decomposition into gold, iodine and water images

Distinguishing mixed contrast agents

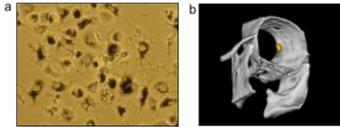


DP Comode et al. Sci Reports. 2017, 7, 4784

Benefits of photon counting CT for cell tracking

- Eliminate laborious & error prone pre/post image analysis
- Specific determination that contrast is due to labeled cells
- More precise quantification of uptake

Use of AuNP to track cells in treatment of stroke with SPCCT



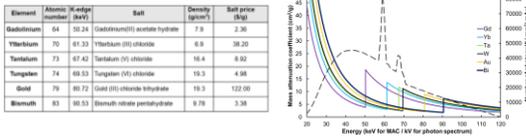
E Cuccione et al, in preparation

Novel SPCCT-specific contrast agent development

- What is the effect of element on contrast generation?

□ Element selection criteria

- Elements with k-edge in high x-ray flux region
- Non-toxic, non-radioactive, affordable



□ Analysis: high attenuation rate, high CNR, and low noise level in SPCCT

J Kim et al, submitted

Phantom scanning

SPCCT scanner (University of Lyon):

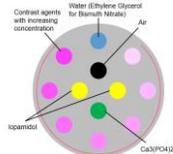
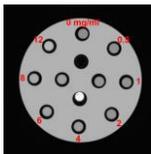
- A prototype SPCCT system
- FOV: 168 mm in-plane, z-coverage: 2 mm
- Gantry rotation time: 1 second (2400 projections per rotation)

Range of concentrations:

- 0.5, 1, 2, 4, 6, 8, 12 mg/ml

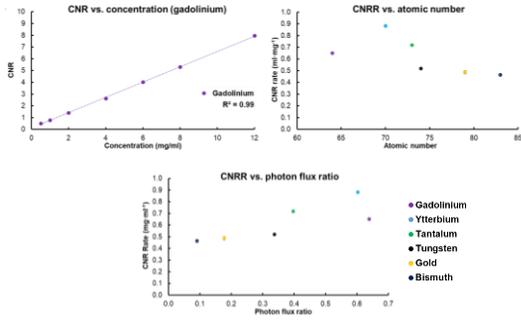
Scanning conditions:

- 5 axial scans (120kVp, 100mA)
- 5 different energy thresholds (e.g. 30, 51, 78, 83, 98 keV for Au)



J Kim et al, submitted

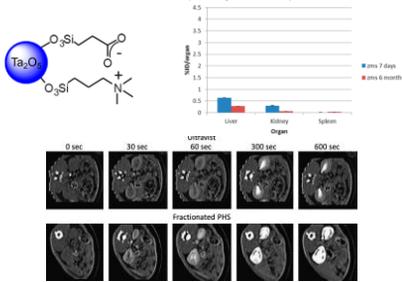
Element specific contrast



J Kim et al, submitted

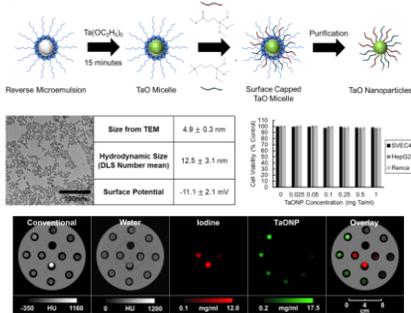
Tantalum CT contrast agents

- Coming out of GE research labs
- Around 5 nm (renally excreted)



PJ Bonitatibus et al. *Chem. Commun.* 46, 8956-8958
 PJ Bonitatibus et al. *ACS Nano*, 2012, 6, 6650-6658
 AS Torres et al. *Investigative Radiol.* 2012, 47, 578-587

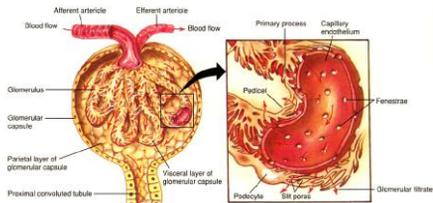
Tantalum SPCCT contrast agent



J Kim et al, submitted

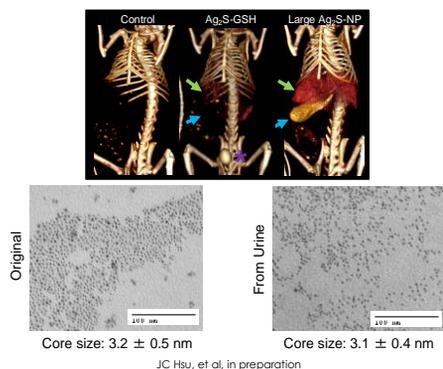
Criteria for translation of x-ray contrast agents

- Excretion
- Excretion
- Excretion

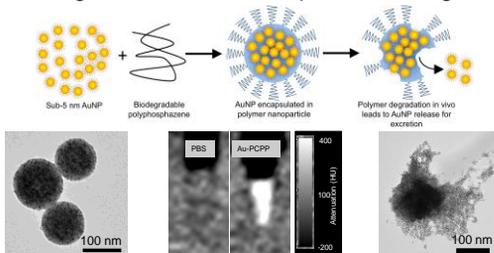


- NP less than ~6 nm can be excreted via the kidneys

Silver sulfide NP for renal excretion



Biodegradable metal nanoparticle CT agents



> These are translational nanoparticles since degradation allows for excretion

R Chehelhiani et al, *Biomaterials*, **2014**, 102, 87-97
 P Naha et al, *J. Mater. Chem.*, **2014**, 2, 46, 8239-8248
 AL Brown et al, *Chem. Mater.*, **2014**, 26, 2266-2274
 E Swy et al, *Nanoscale*, **2014**, 6(21):13104-12

Conclusions

- 1) Agent specific imaging is possible with high-count rate photon counting CT scanners
- 2) Can allow multi-agent imaging
- 3) Photon counting CT may prove beneficial for CT cell tracking
- 4) Alternative elements such as tantalum can produce greater contrast than gold in photon counting CT
- 5) Clearance of paramount importance for translation

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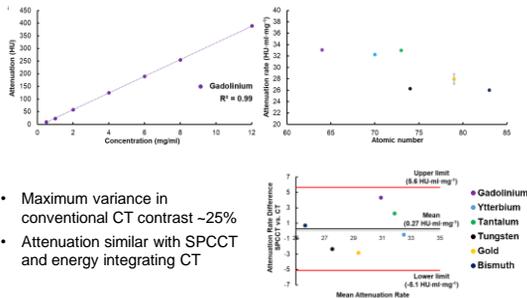


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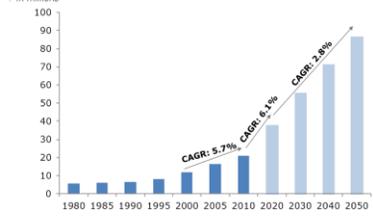
'Conventional' CT contrast



- Maximum variance in conventional CT contrast ~25%
- Attenuation similar with SPCCT and energy integrating CT

Rise in iodine contraindicated patients

Historical and Projected US Cases of Type II Diabetes
For the Years Ended and Ending December 31, 1980 - 2050P
± in millions



Source: CDC Population Health Metrics, Projection of the year 2050 burden of diabetes in the US population: dynamic modeling of incidence, mortality, and prediabetes prevalence

- Diabetics commonly develop kidney disease
- Iodinated contrast agents damage their kidneys further
- Diabetics also at risk of CVD and need CT/fluoroscopy
