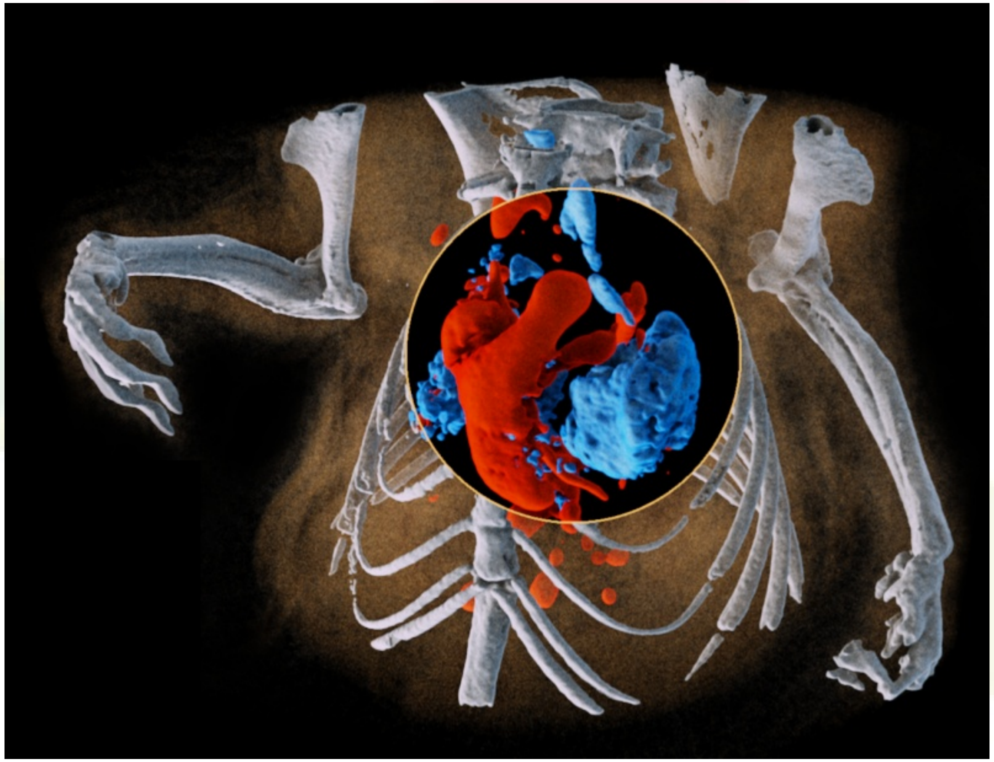
MARS Spectral Imaging:

From High Energy Physics, To a Biomedical Business



Anthony Butler

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Medipix All Resolution System

UC UNIVERSITY OF CANTERBURY Te Whare Wānanga o Waitaha CHRISTCHURCH NEW ZEALAND

CERN

UNIVERSITY OF OTAGO Te Whare Wānanga o Otāgo

Overview

- **Timeline of HEP to Biomedical Imaging**
- **Computed Tomography**
  - Where did it start and where is it going?
- **NZ MARS Spectral CT programme**
  - Why we want to develop new imaging tools
  - MARS technology
  - Several potential areas of clinical impact
- **Conclusions**

NZ History

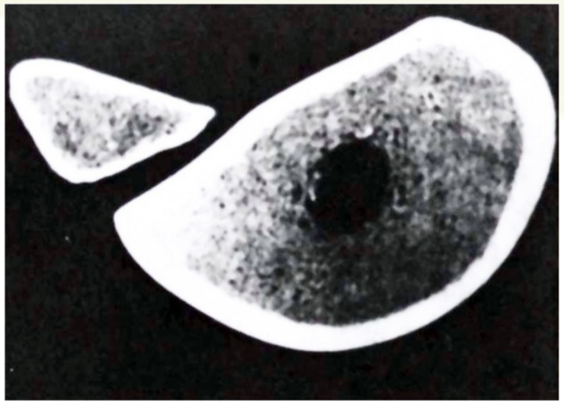
Ernest Rutherford

Early work at University of Canterbury

Bates and Peters

1971 First use of Fourier transform in CT

1972 First CT of biological tissue

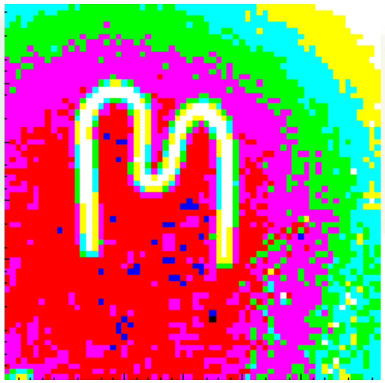


CT of sheep bone, 1972

CERN History

Early ’80s, direct Si detectors – Erik Heijne

His role is recognized be recent European Physical Society prize



Mid ’90s, Medipix – Michael Campbell

“Various application like Medical Imaging should be profit”

Timeline

2000

- NZ scientists collaborate with CERN scientists
- NZ joins CERN and CMS
- Funding for NZ detector development – HEP + medical

2005

- I came to CERN and met Michael Campbell
- 1.5m NZD grant to do HEP and tools for MedTech students
- Canterbury Uni joins Medipix3
- MARS CT-1 proof of principal
- MARS Bioimaging Ltd Formed

2010

- 4.5 NZD grant + private equity *(research plan with business plan)*
- Scientific release of scanners to partners *(Mayo, Charles Uni, KIT)*
- Research partnership with GE Healthcare
- 12m NZD grant + VC funding *(Taking MARS to humans)*

2015

- Human translatable scanner sold to reference sites (ND, RPI)
- Human scanner under construction

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The Team

30 People in Christchurch

NZ university team

Canterbury, Otago, Lincoln, Auckland

International Partners

Incl. CERN, Mayo Clinic, RPI, Notre Dame, OHSU, plus many others

The commercial partners

MARS Bioimaging Ltd

ILR Ltd, Shamrock, etc

GE Healthcare

Where did CT start?

and…

Where is it going?

Wilhelm Röntgen

8 Nov 1895 “X”-rays

Week to demonstration,

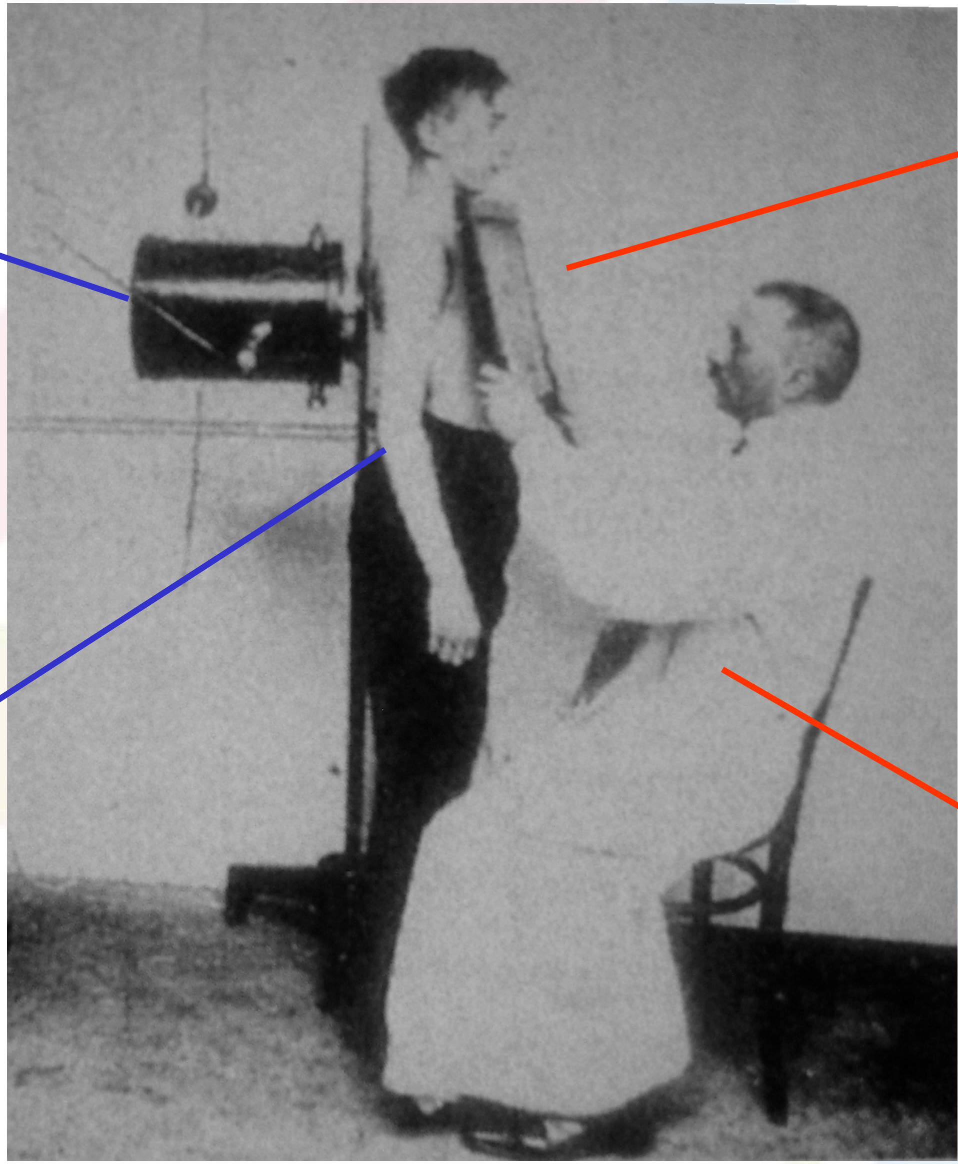
then rapid clinical adoption

Nobel physics 1901

X-ray systems

X-ray source

Object



Detector

Pattern Recognition System

Godfrey Hounsfield

Oct 1, 1971
First clinical scan

Nobel Prize 1979

Commercialised as
EMI scanner

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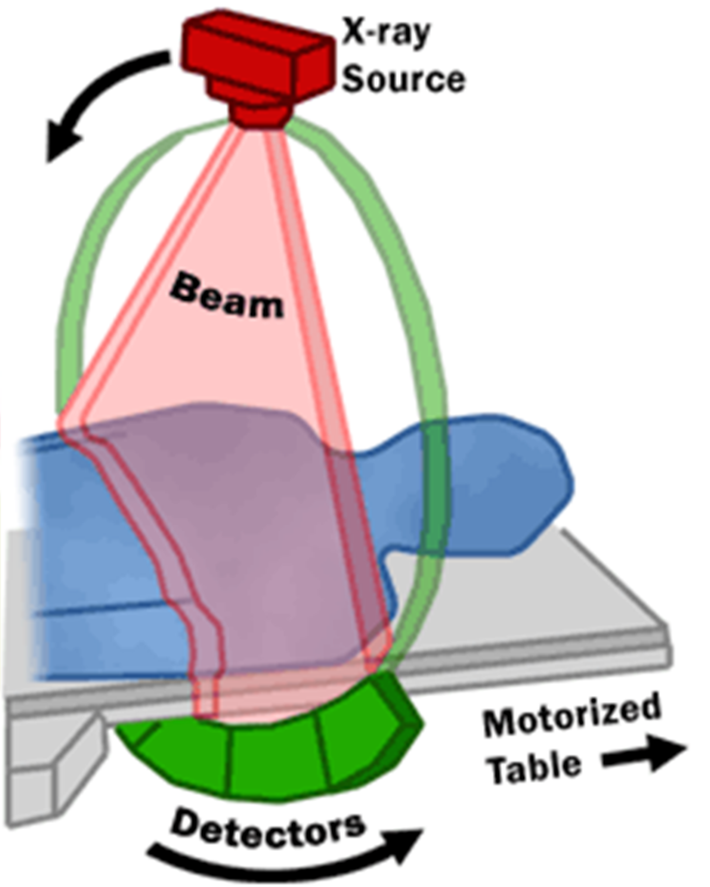
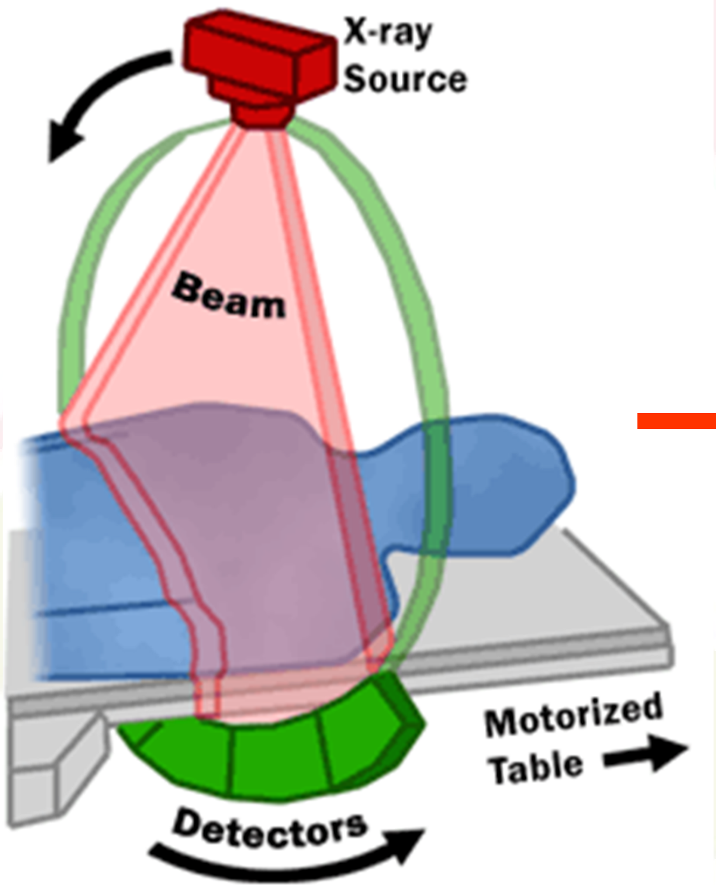
CT – Computed Tomography

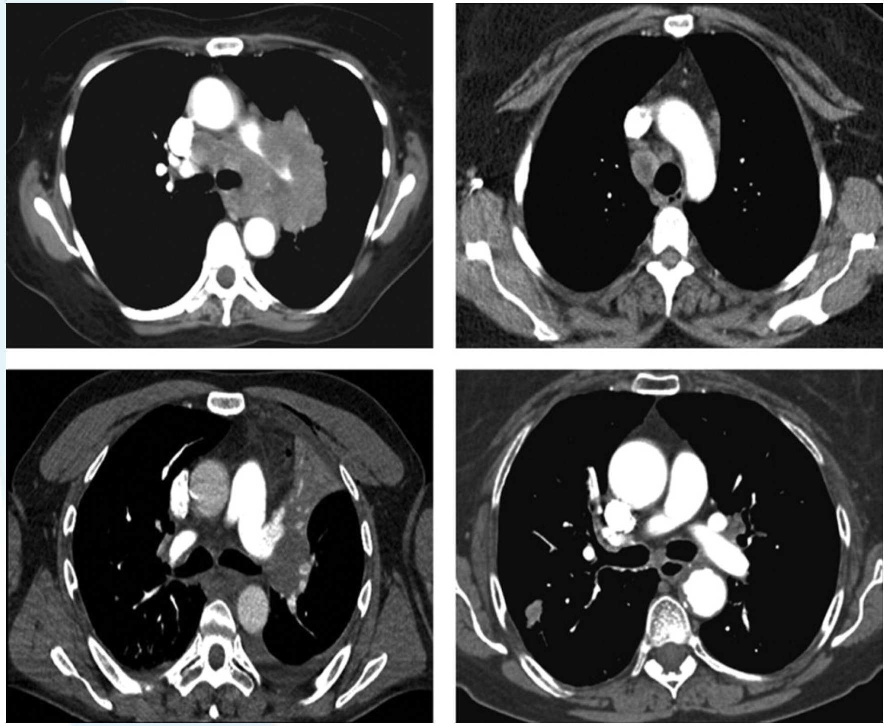
"3d X-rays"



CT – Computed Tomography

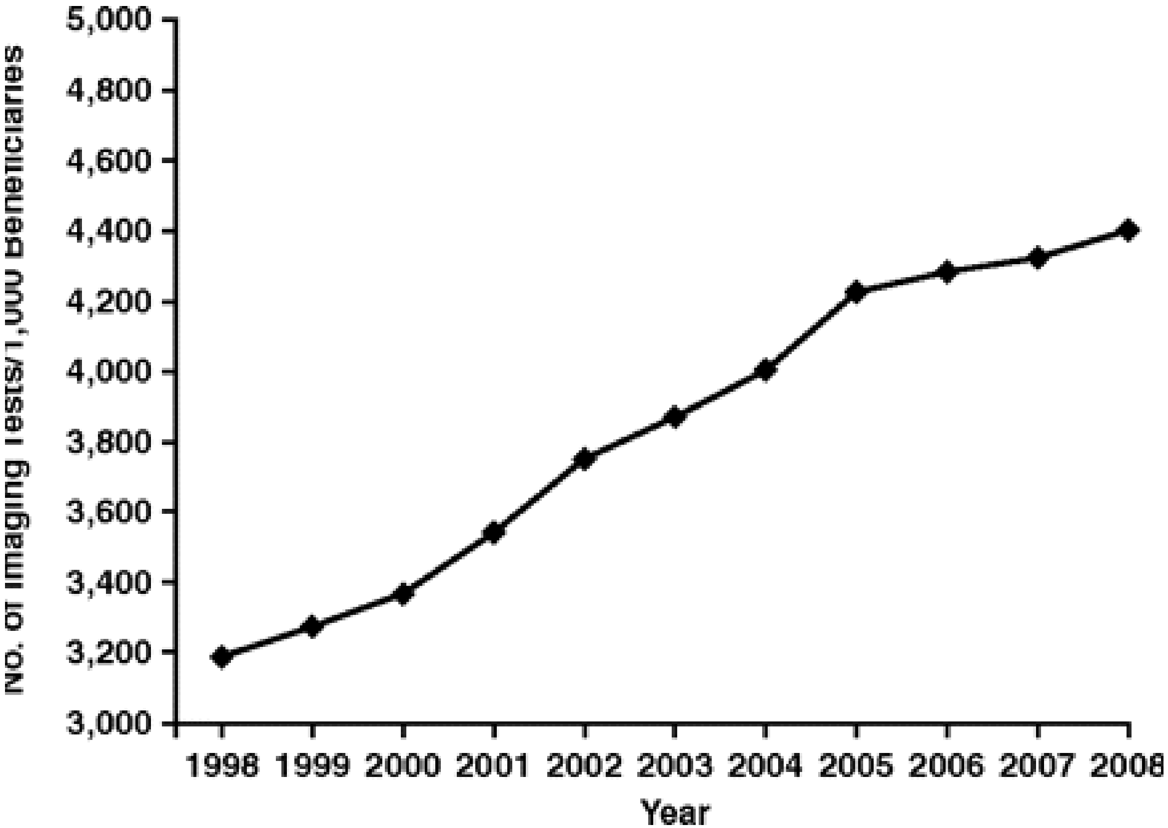
"3d X-rays"





Data processed, transmitted,
and stored digitally

Change in radiology utilisation



1998-2005 => 4.5% /year

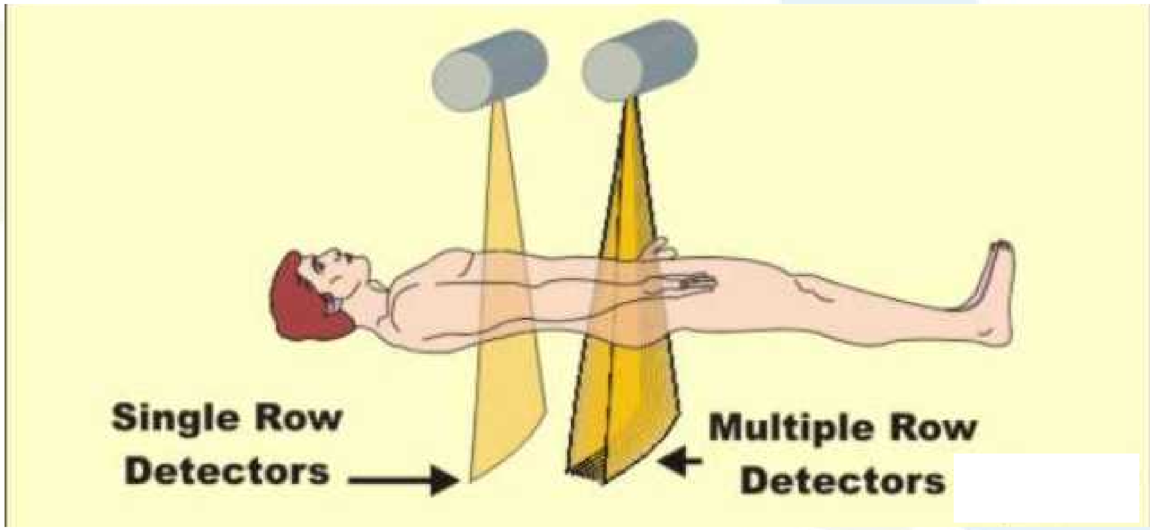
2006-2008 => 1.4% /year

Bending the Curve: The Recent Marked Slowdown in Growth of Noninvasive Diagnostic Imaging
American Journal of Roentgenology, Jan. 2011

Drivers of change

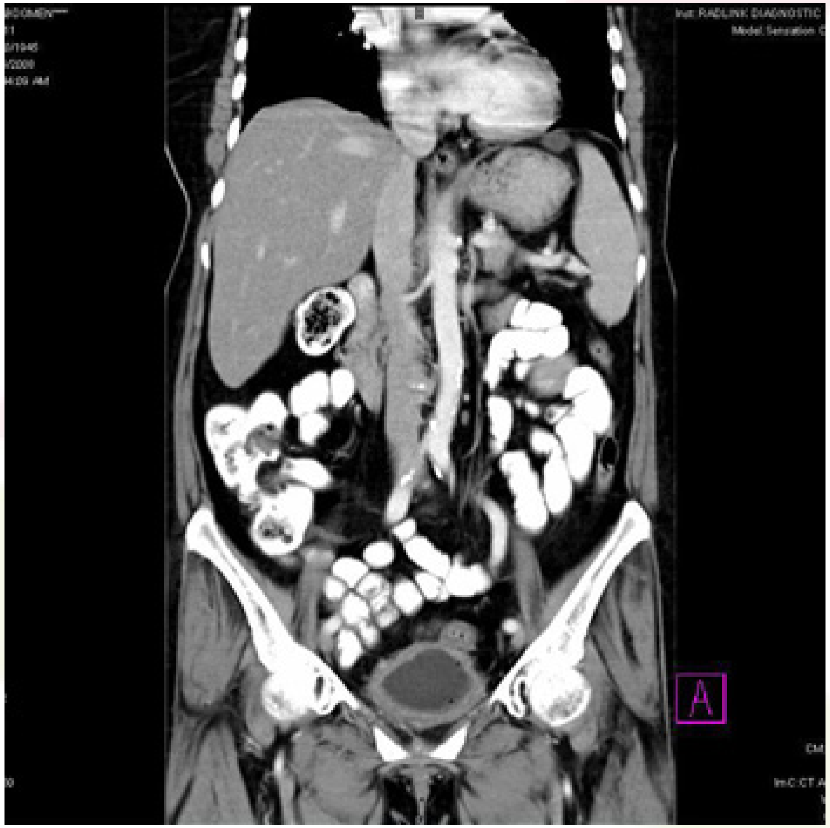
2000-2008 “CT Slice War”

- *CT became very fast with small voxel / pixels*
  - 2000: acquire a single transverse slice per rotation
  - 2012: acquire up to 64-500 slices per rotation



Anatomical imaging is now really good

Very little benefit in more speed or resolution



Anatomical imaging is now really good

Molecular imaging is the future

What is the tissue?

What is its behaviour?

Is the treatment working?

(not just size, shape, location)

What the researcher wants to know

- *Constituents (fat, water, calcium, iron)*
- *Cancer and pathogen labels*
- *Physiological markers*
- *etc*

Anatomical imaging is now really good

Molecular imaging is the future

What is the tissue?

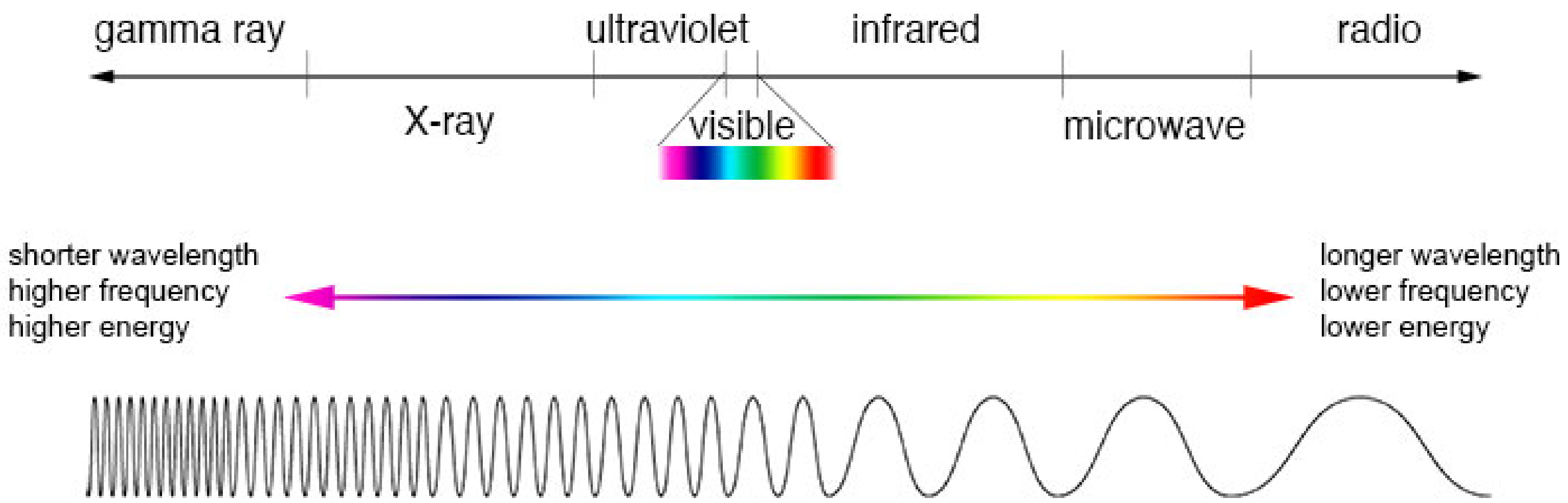
What is its behaviour?

We need a fundamental change in the information provided by x-rays

- *Cancer and pathogen labels*
- *Physiological markers*
- *etc*

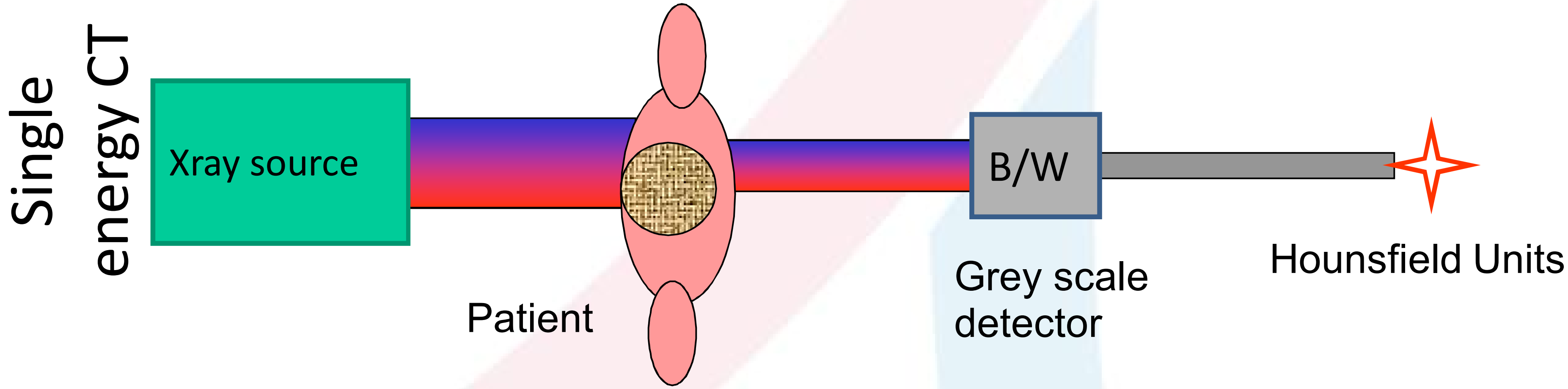
X-rays come in different colours

Also called: Wavelength, Frequency, or Energy

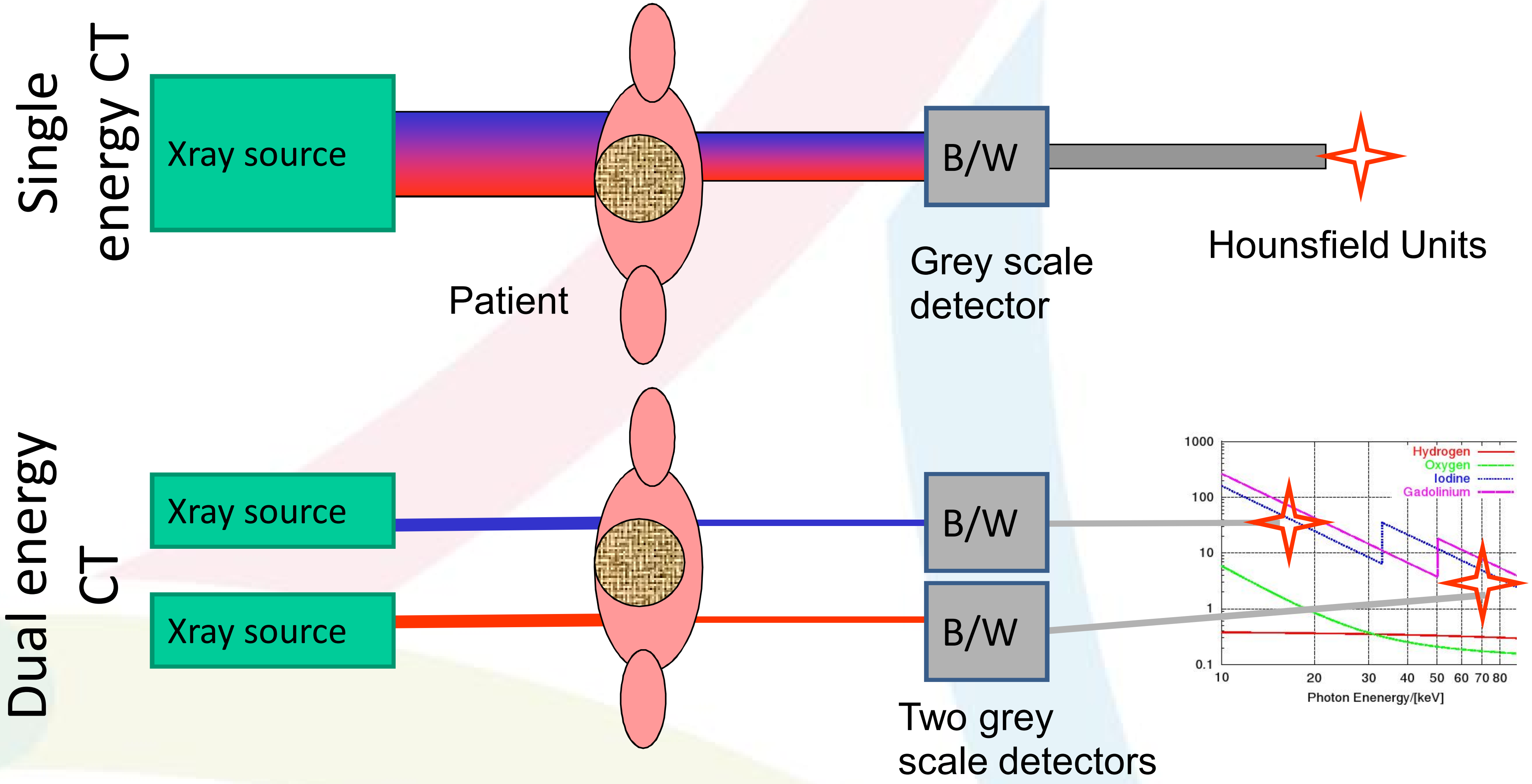


The electromagnetic spectrum

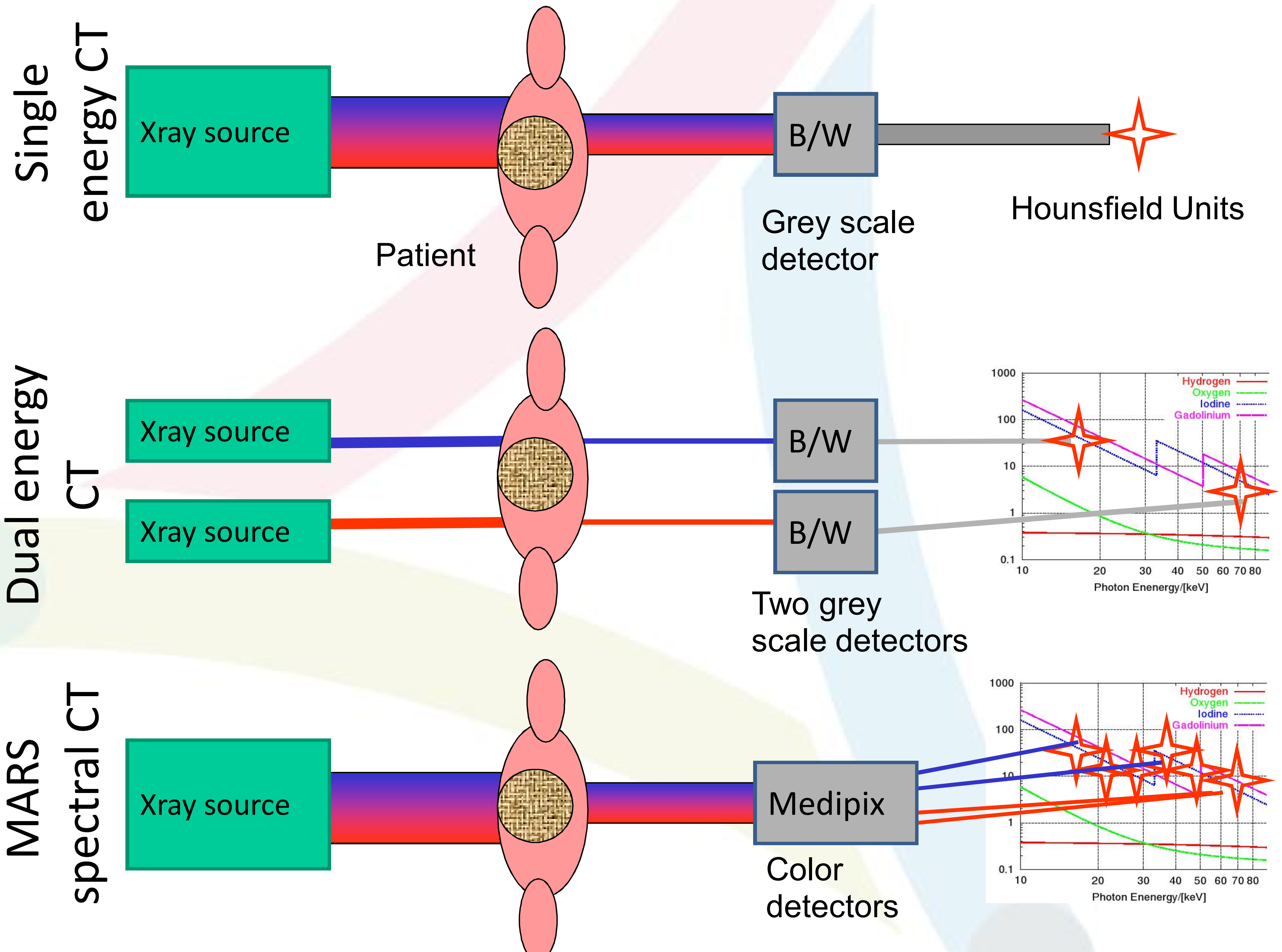
Single- , dual-, and spectral CT



Single- , dual-, and spectral CT



Single- , dual-, and spectral CT



New Zealand's
MARS Spectral CT program

Goals

- To provide new information about tissues
- To have a route to human imaging

Spectral CT is now possible

Medipix **A**ll **R**esolution **S**ystem

- **Energy resolution**
- Spatial resolution
- Temporal resolution

Single-energy CT provides

- Brightness only (grey scale)
- Spatial resolution
- Temporal resolution

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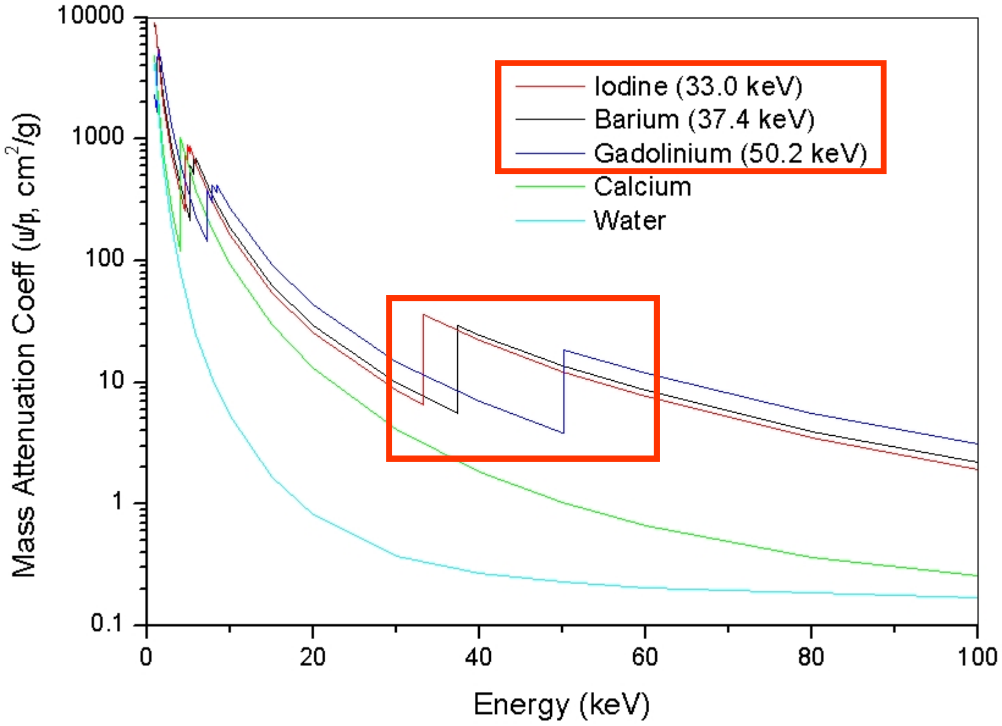
Medipix All Resolution System

Example of spectral information

"Heavy atom" imaging



Better diagnosis because

- can use in combination
- can have new pharmaceuticals (functional imaging)

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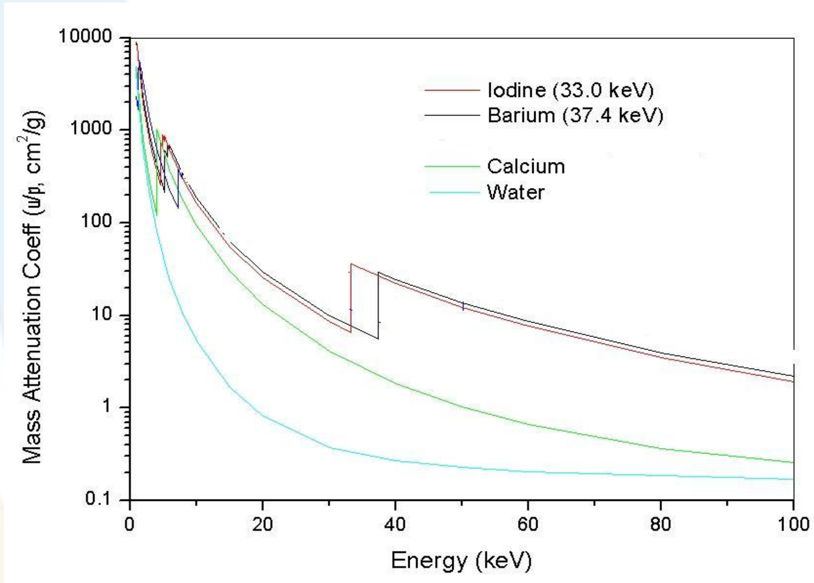
Measure individual materials

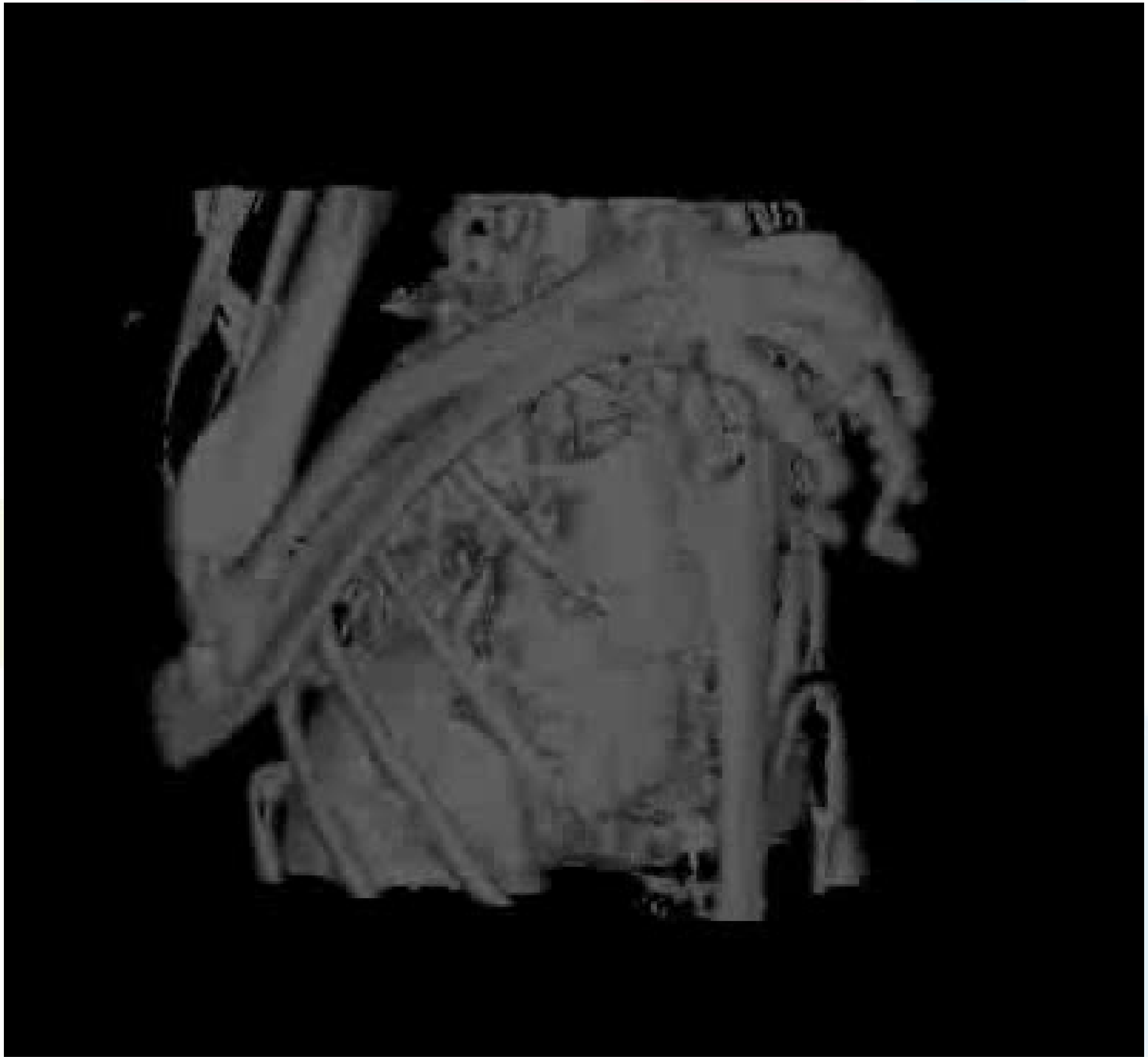
Iodine: Pulmonary circulation

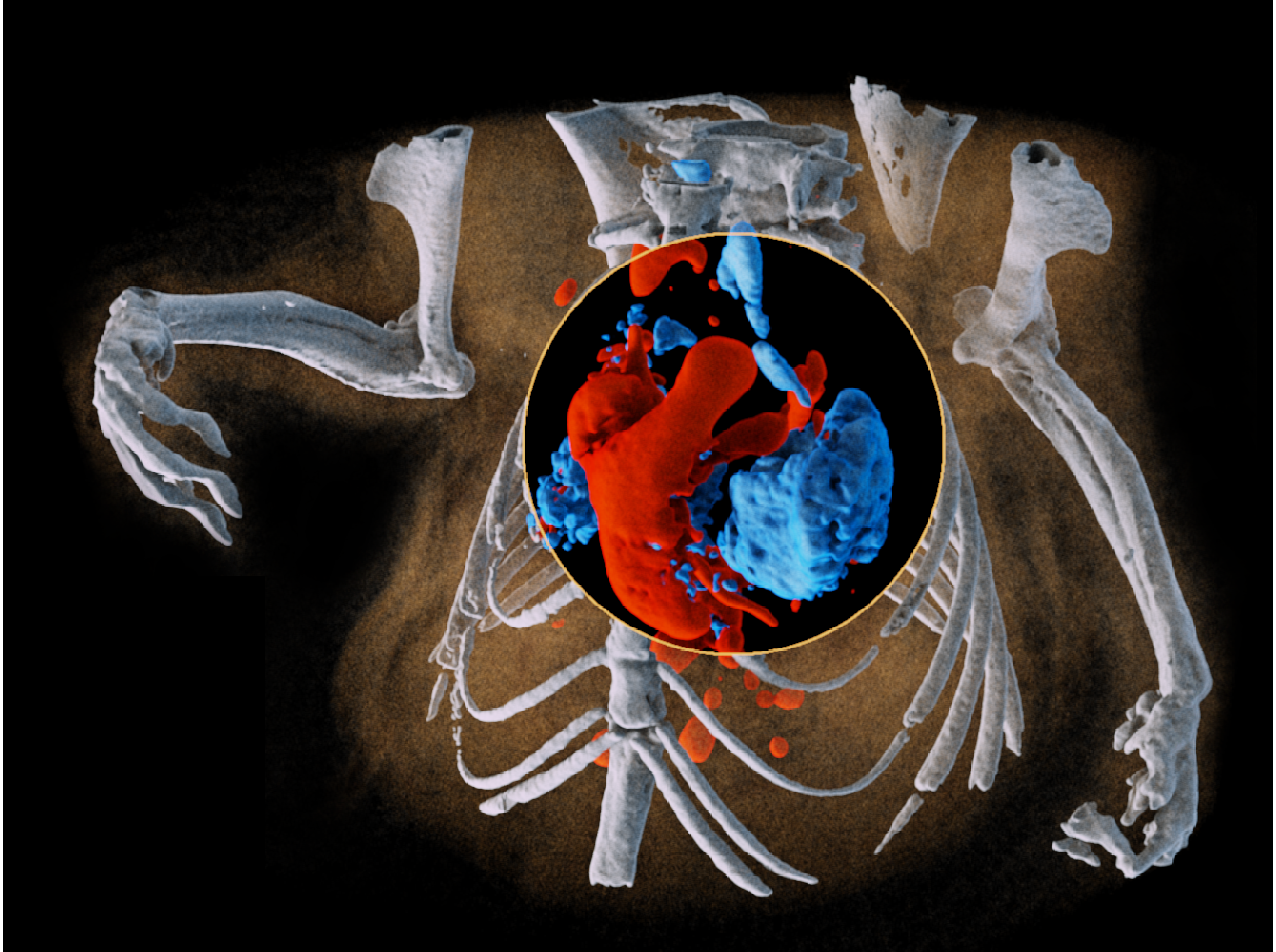
Barium: Lung

Calcium: normal bone



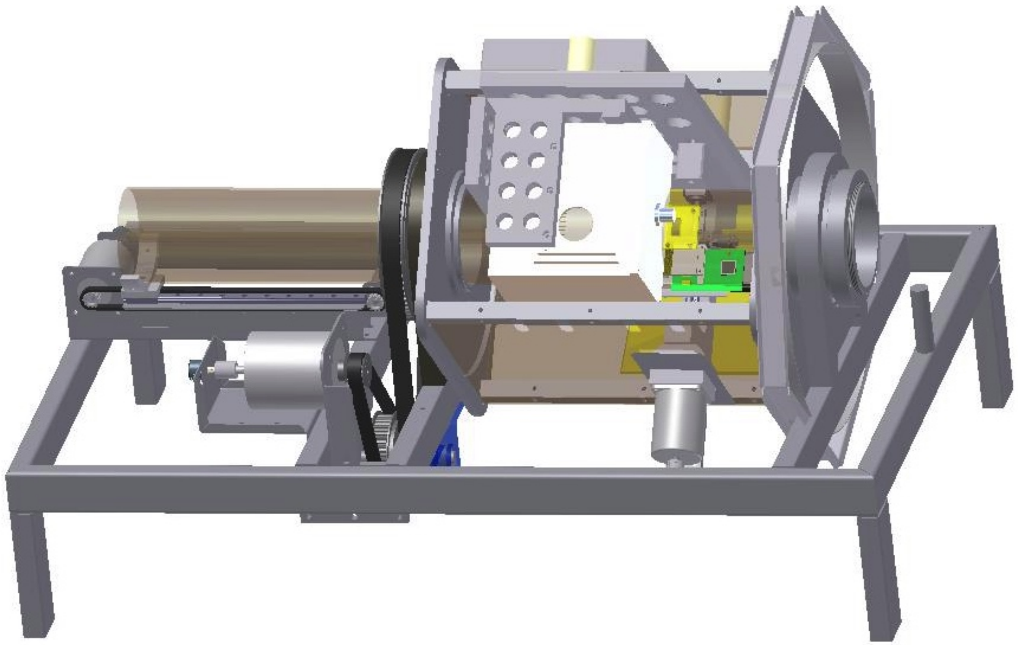
Traditional "broad spectrum" CT



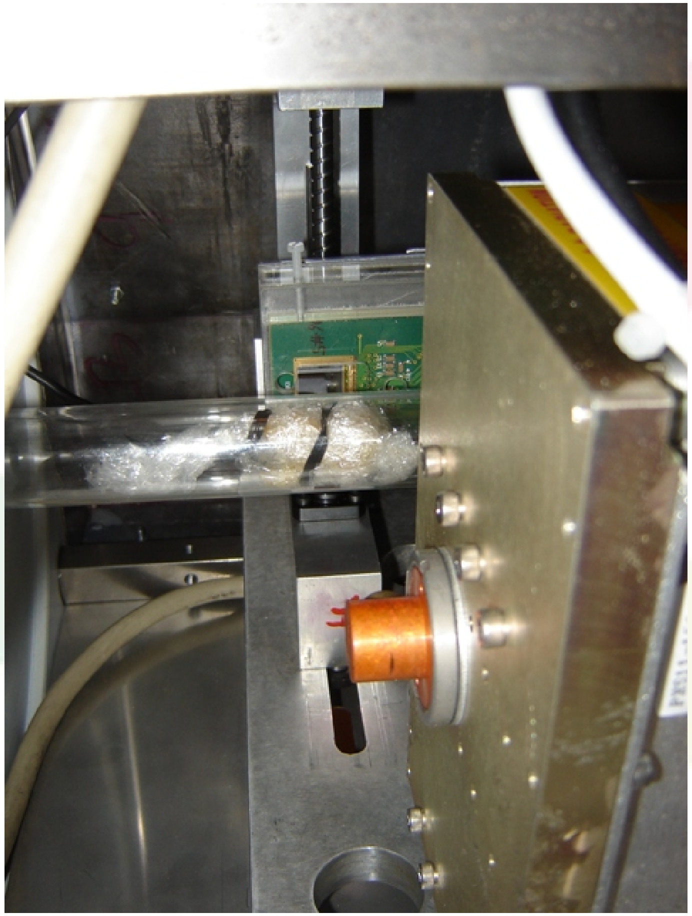


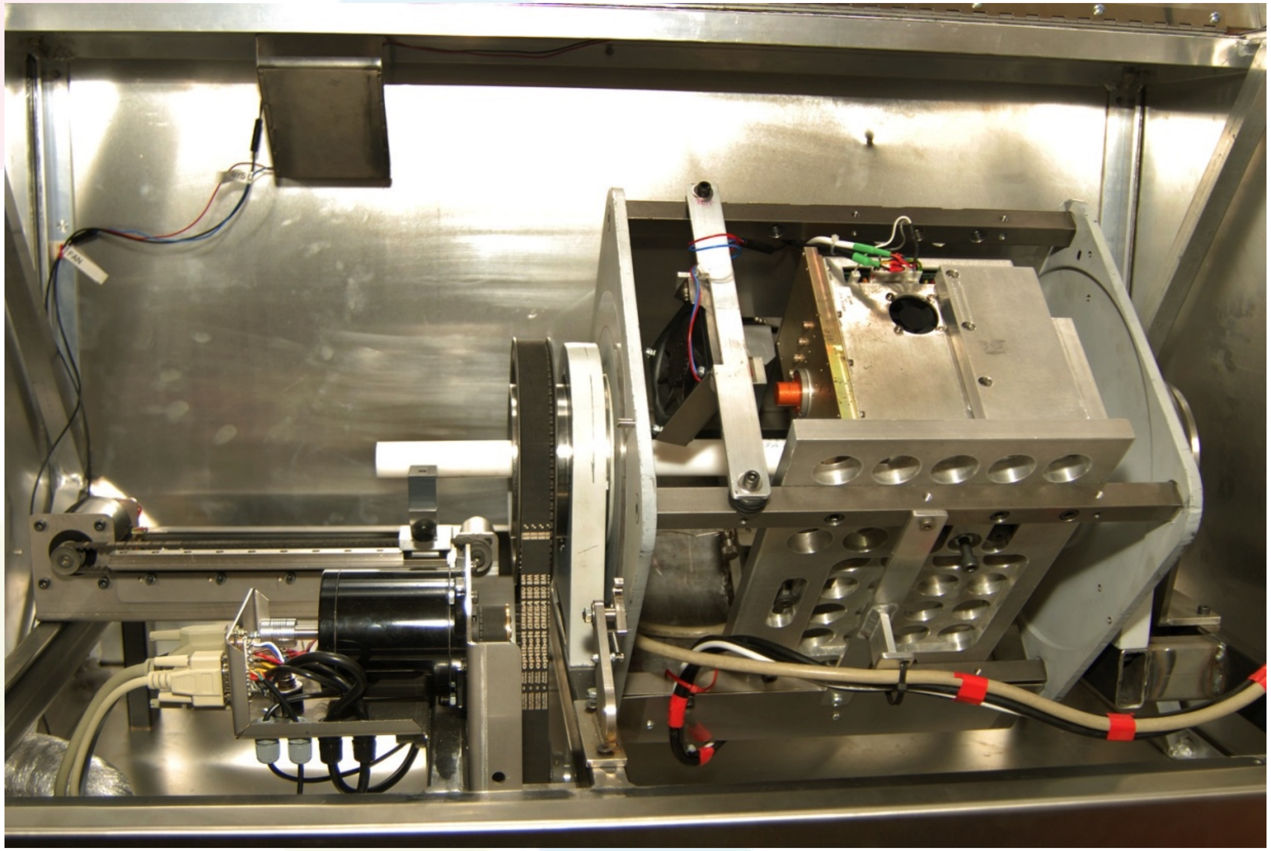
Our MARS scanners

MARS v1 – physics lab



MARS v2
physics lab to medical school





MARS v3 #1
to Mayo Clinic

Medipix **A**ll **R**esolution **S**ystem

- **Energy resolution**
- Spatial resolution
- Temporal resolution

v3, v4 – pre-commercial systems

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Medipix All Resolution System

Unpacking the Mayo scanner

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v5 – Commercial release

Human ready system

- X-ray energy is 30-120 kVp
- High efficiency CZT
- Continuous motion spiral scans
- Modular readout for scalability

Designed for biomedical users

- Automated detector set-up
- Green-button acquisition
- Automated recon and MD
- Visualisation and analysis tools

Reference sites at ND, UOC, and RPI

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Visualization Tools

Hybrid 2d/3d viewer

- 3d for orientation

- 2d for detail

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v5 – Commercial release

Notre Dame imaging lab

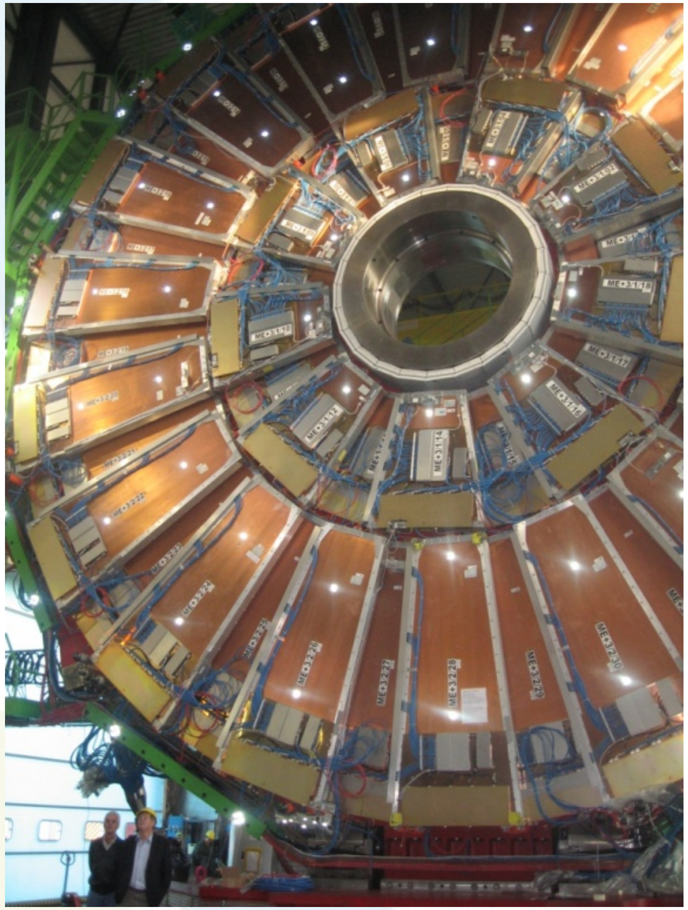
Microchips for X-rays

CERN

High energy physics lab generating new technology

NZ works with detector groups

- CMS, and in particular BRIL
- Medipix collaboration



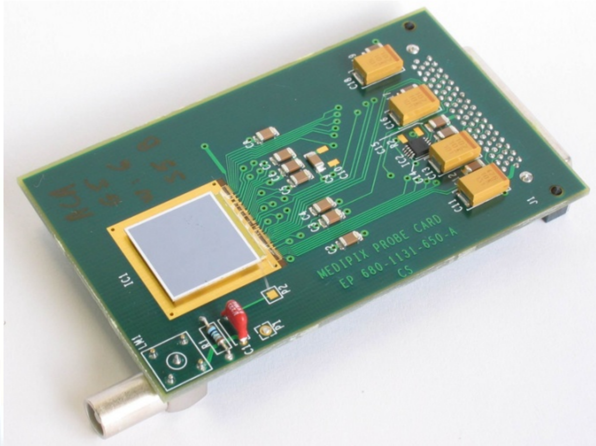
Medipix neutron system in CMS

Medipix 3/4 Collaborations

Transferring CERN's high energy physics technology into medicine

NZ provides

- **Test-bed for technology**
- **Application development**
- **First clinical experiments**



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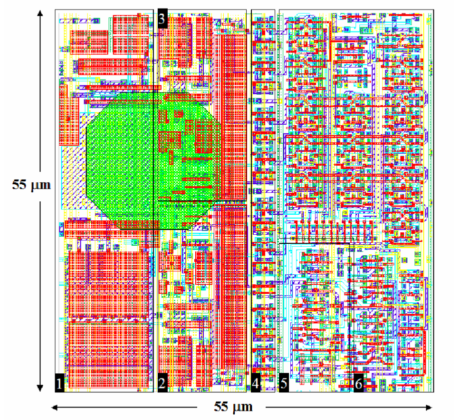
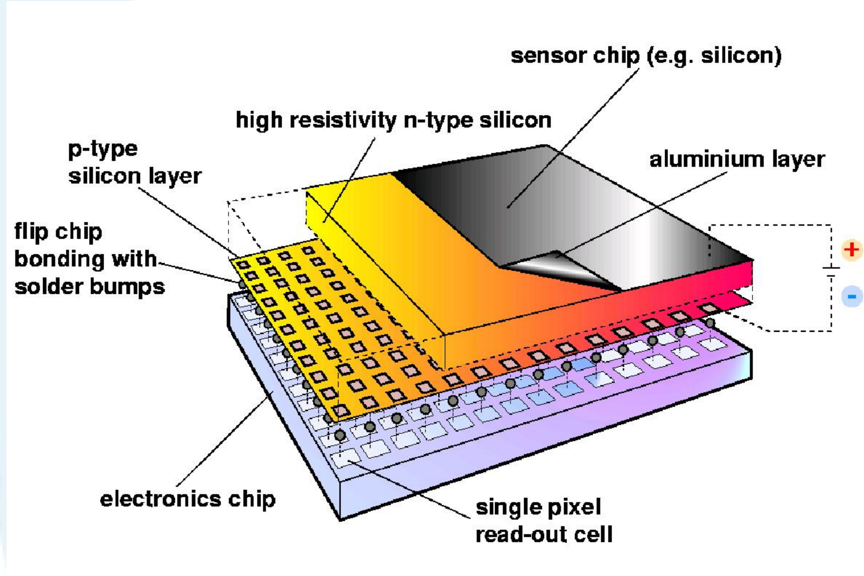
Medipix3





Up to 8 Simultaneous energies

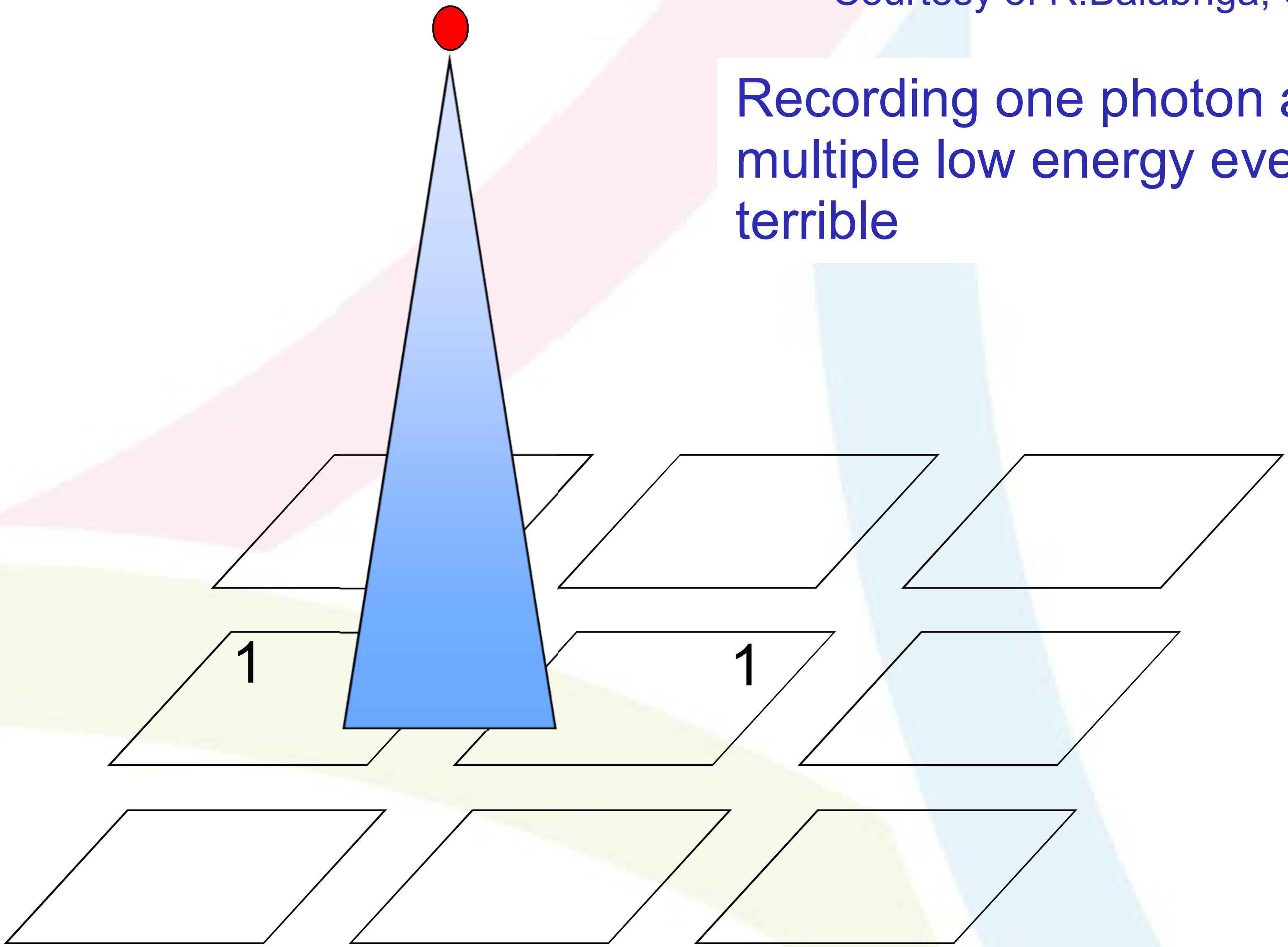
- 5000 transistors per 110um pixel
- Each pixel communicates with its neighbour

128 x 128 pixel array per chip

Medipix3 Charge Summing

Courtesy of R.Balabriga, CERN

Recording one photon as multiple low energy events is terrible



Medipix3 Charge Summing

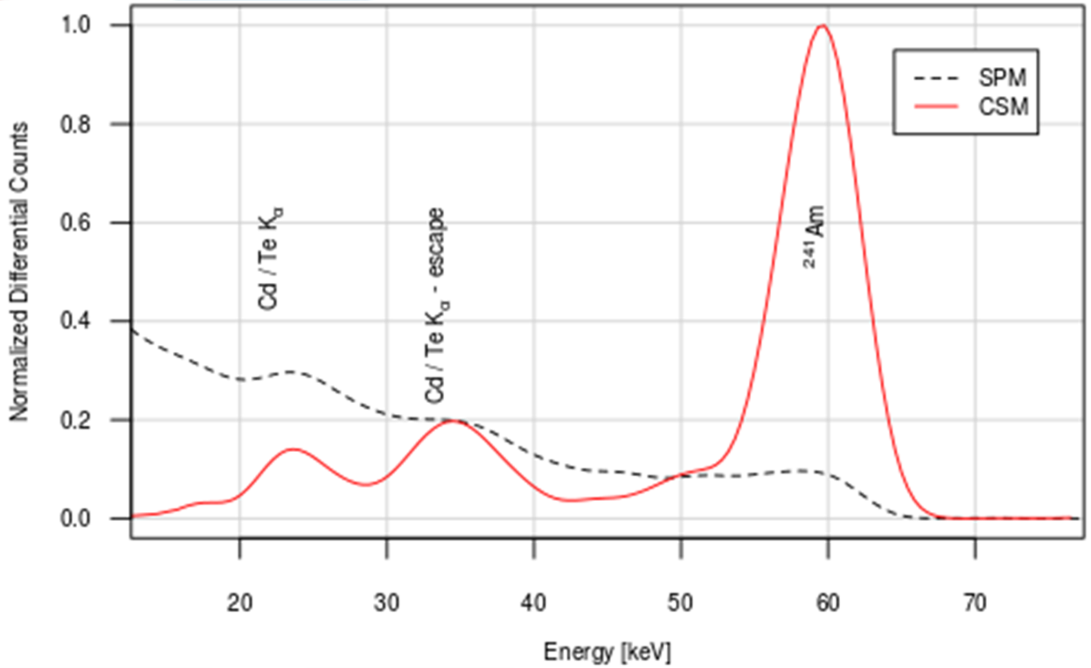
Energy resolution is the key determinate of sensitivity and specificity

Charge Summing Mode

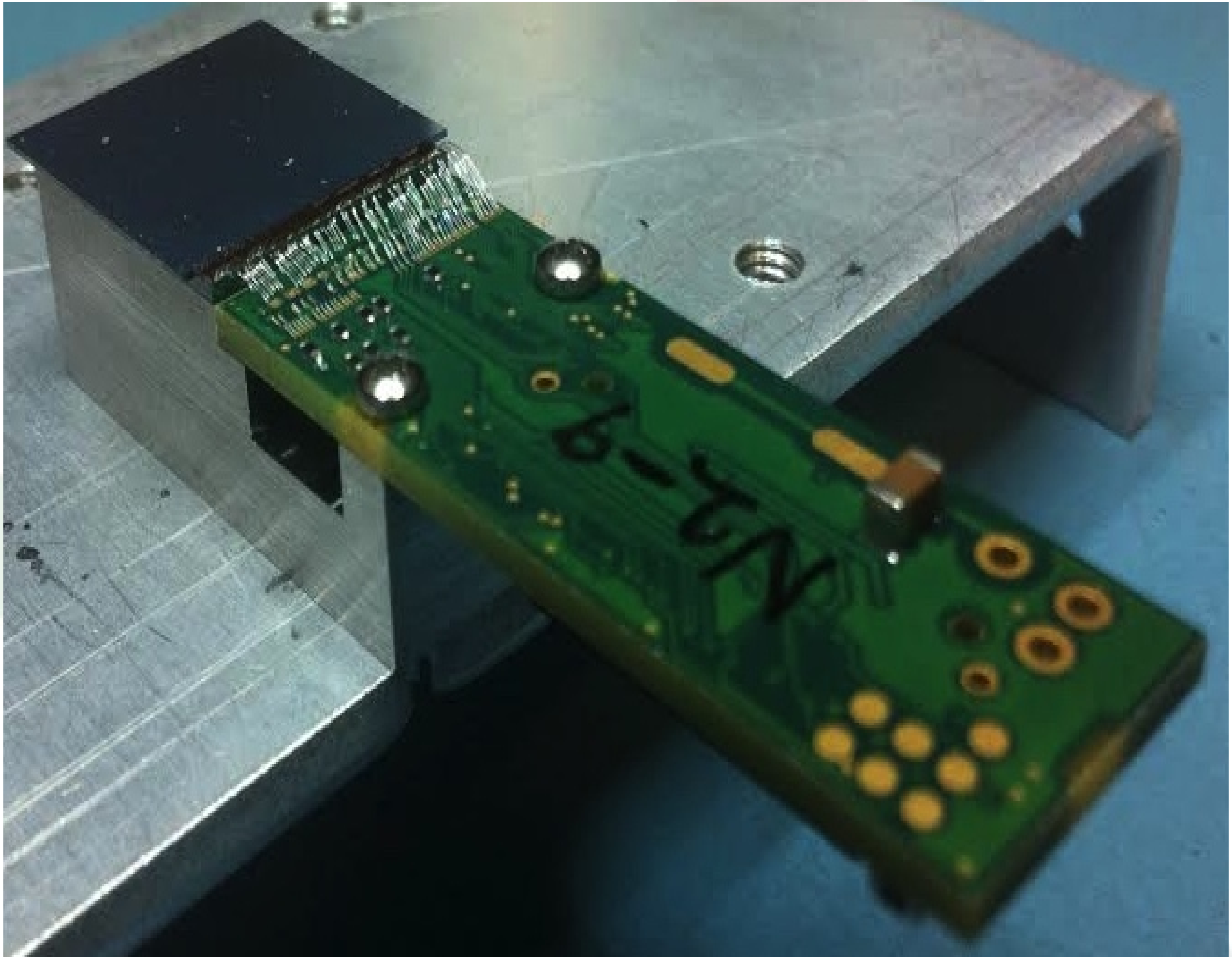
- *Pixel communicate*

Benefits

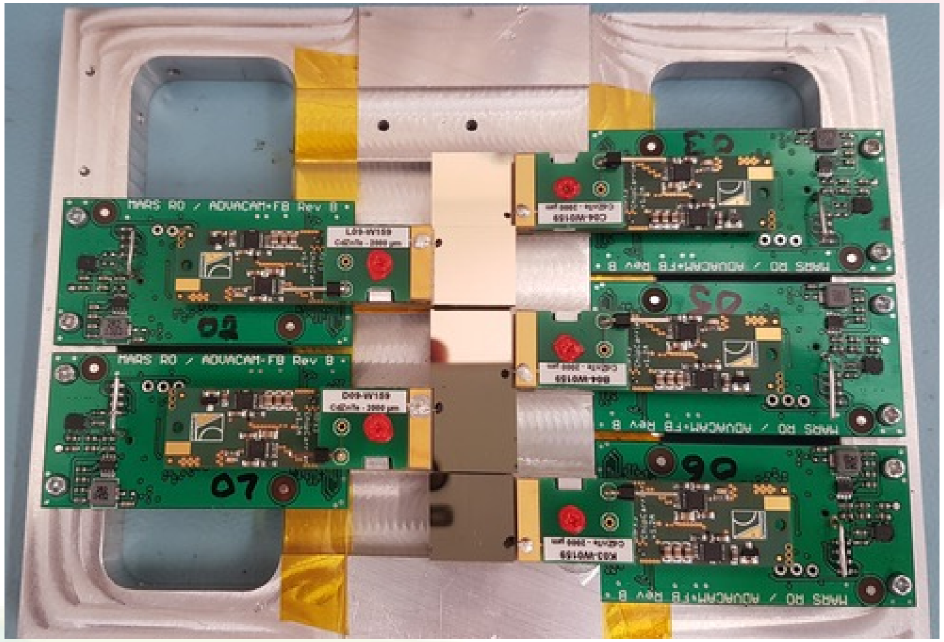
- *Improves energy resolution*

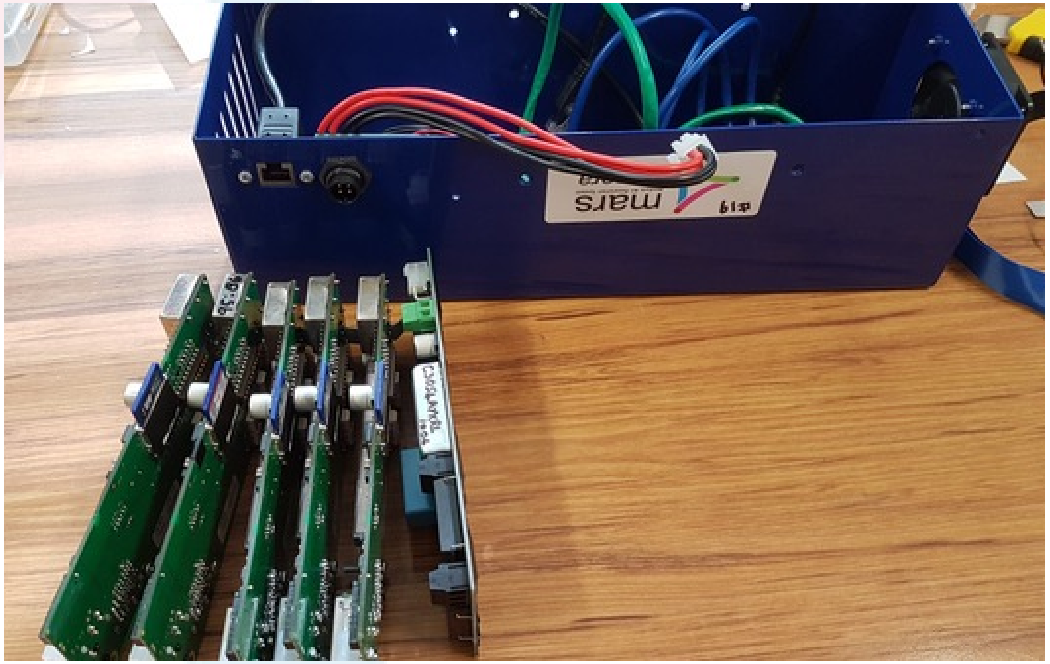


MARS Medipix3RX detector



Multi-chip MARS camera





Multichip cameras at UC, ND, RPI, soon UOC

- Parallel readout allows us to scale-up as required
- Each ASIC has 1 ethernet readout (FPGA,SDRAM,CPU)
- Single HV per camera
- Hardware synchronisation of shutter

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Clinical impact of Spectral CT:

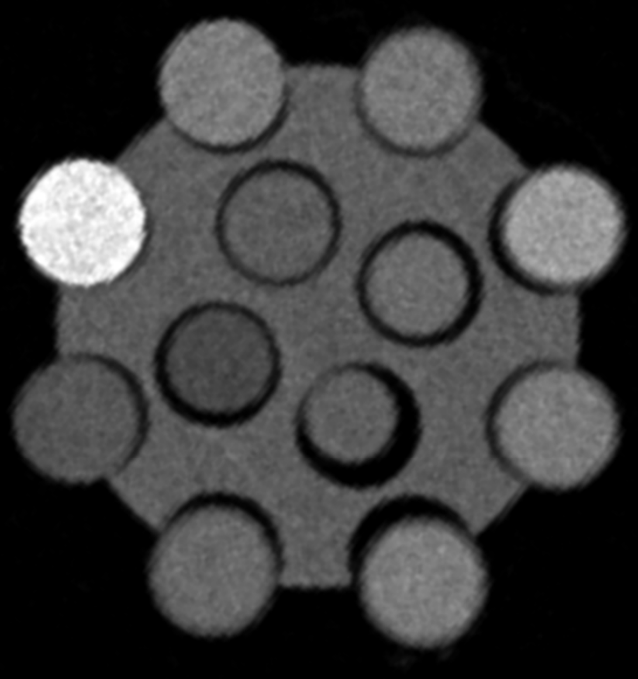
Current achievements, and the where they may lead

Greyscale to Material Imaging

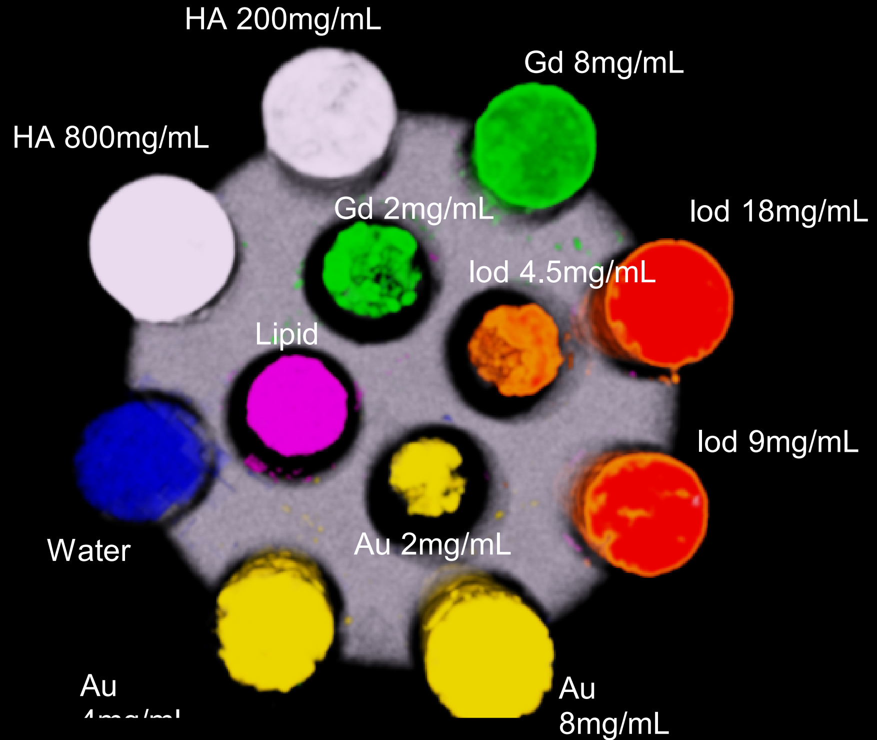
Spectral imaging allow to you identify and quantify different materials

- a separate map (data channel) is made for each materials
- each map give the partial density (g/cm^3) for the material
- each material is then assigned a colour for easy visualisation

A phantom containing Au, Gd, iodine, Lipid, water and hydroxyapatite



Grey scale CT image

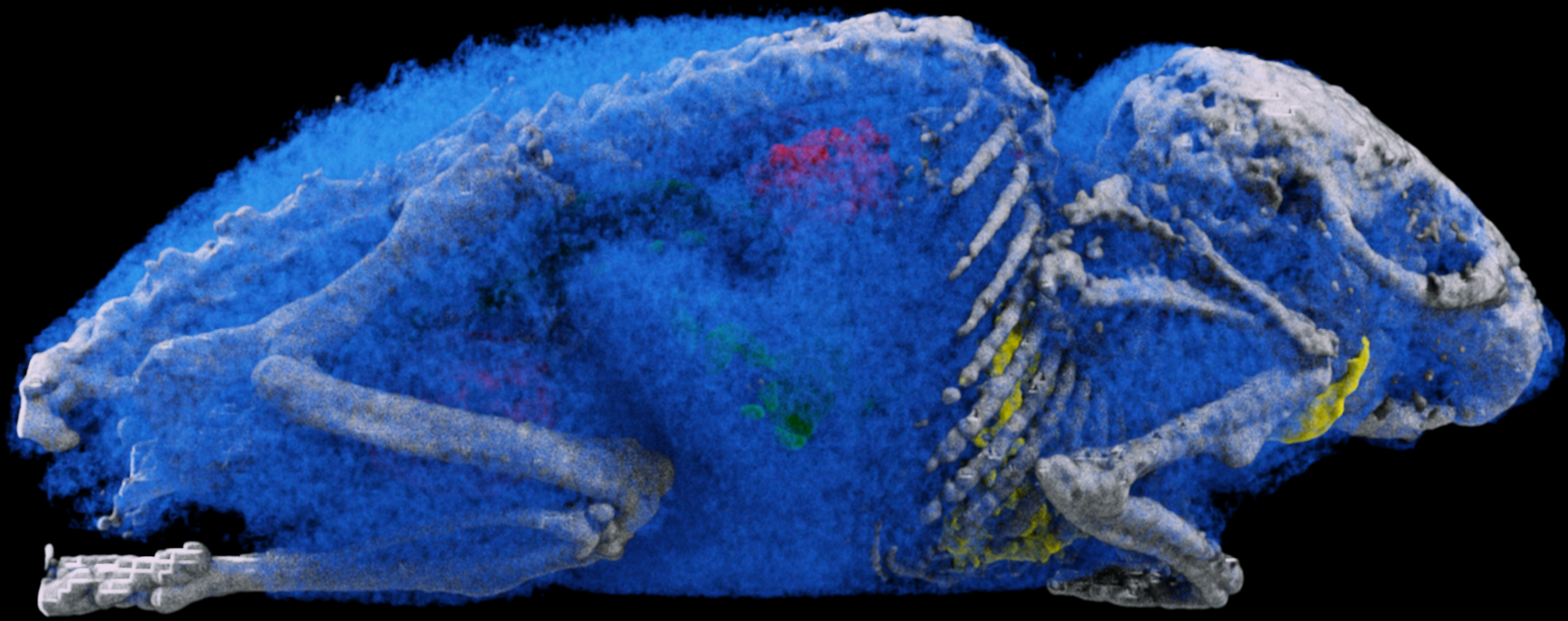


MARS image

Similar data has been made publically available for people interested in doing their own analysis.
Moghiseh et al, JSM Biomed Imaging Data Pap 3(1): 1007. (2016)
Discrimination of Multiple High-Z Materials by Multi-Energy Spectral CT– A Phantom Study.

Greyscale to Material Imaging

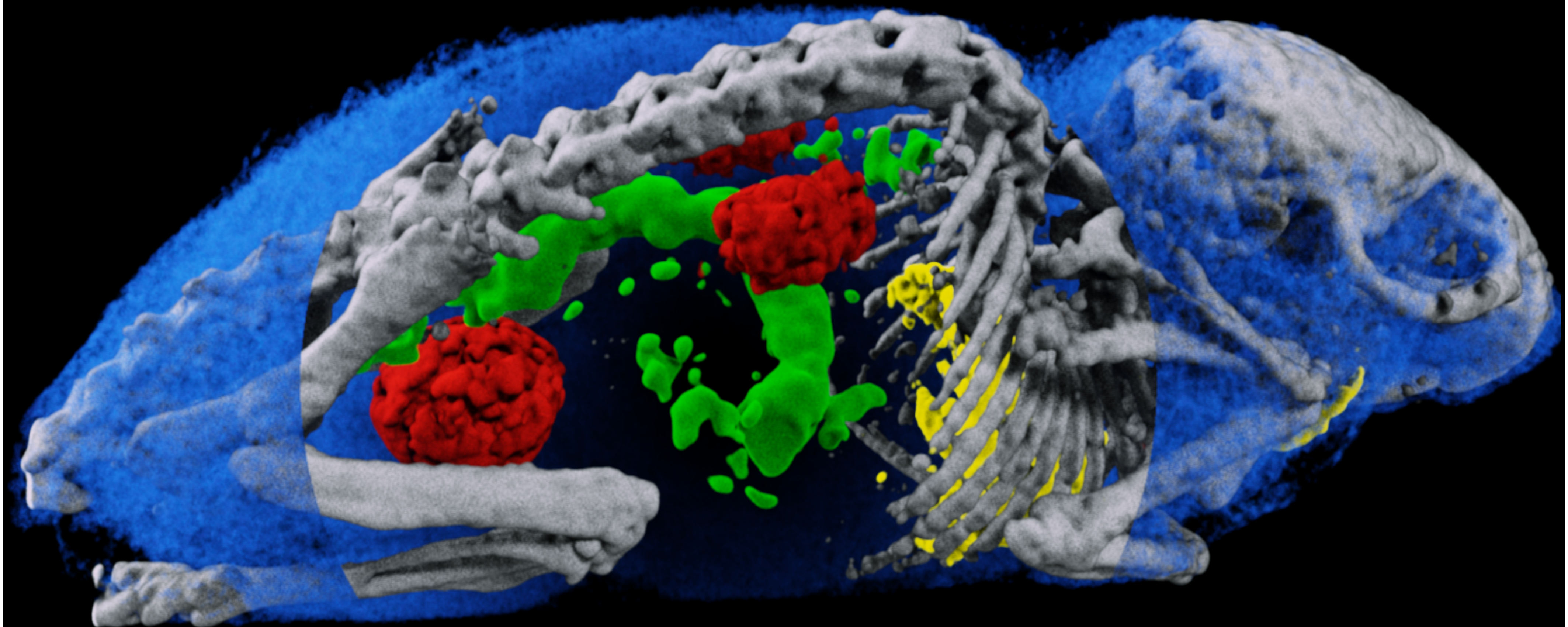
A mouse containing, gold, gadolinium, and iodine



All materials are shown in this image

Images presented and the European Congress of Radiology, Vienna, March 2017.

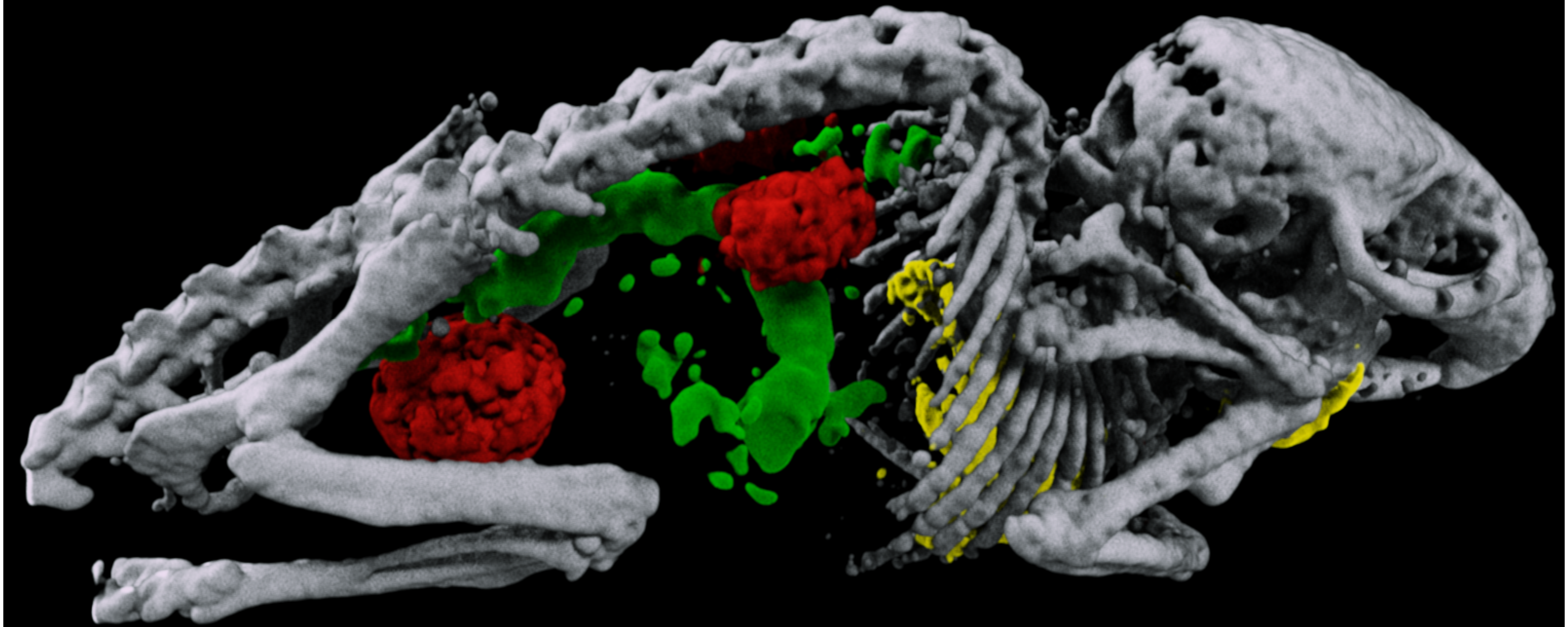
Greyscale to Material Imaging



The water has been partly cut away to reveal the bone, gold, gadolinium and iodine

Images presented and the European Congress of Radiology, Vienna, March 2017.

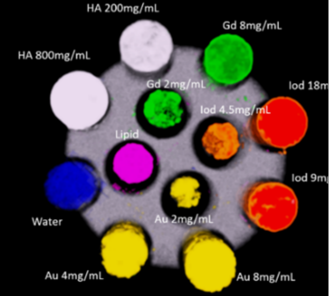
Greyscale to Material Imaging

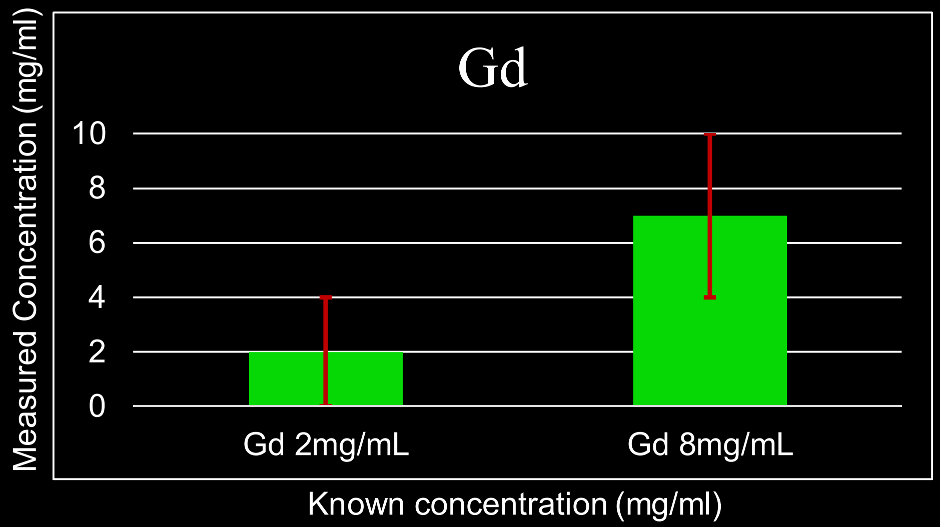


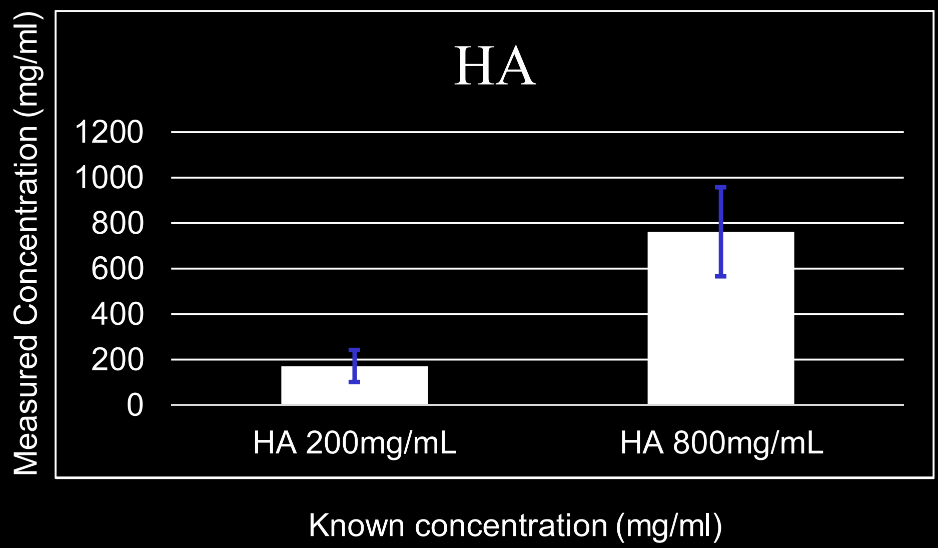
The water has been completely removed leaving just bone, gold, gadolinium and iodine vissible

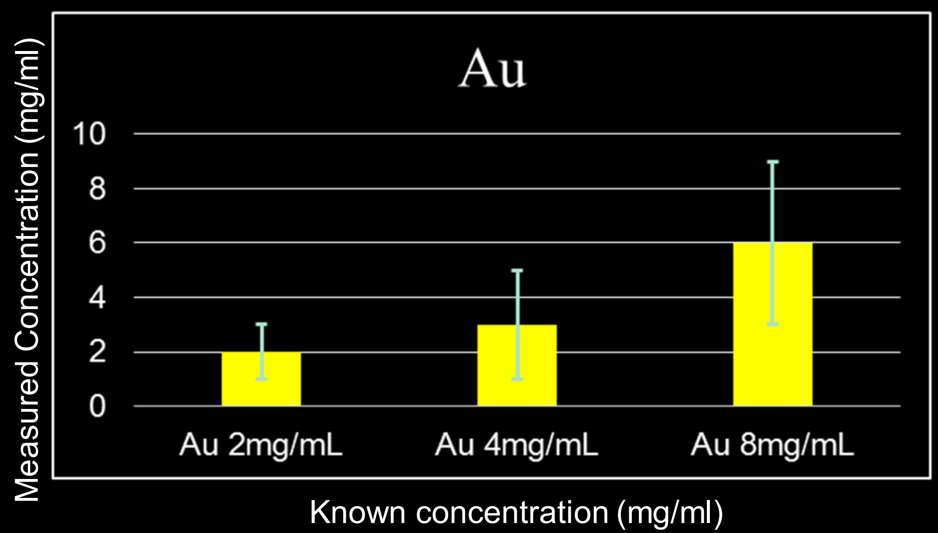
Images presented and the European Congress of Radiology, Vienna, March 2017.

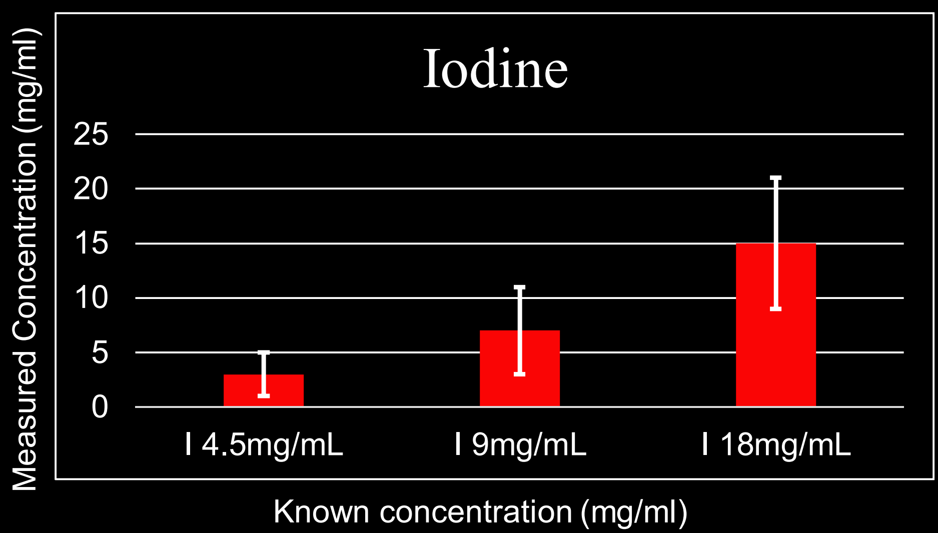
Identification and Quantification Accuracy











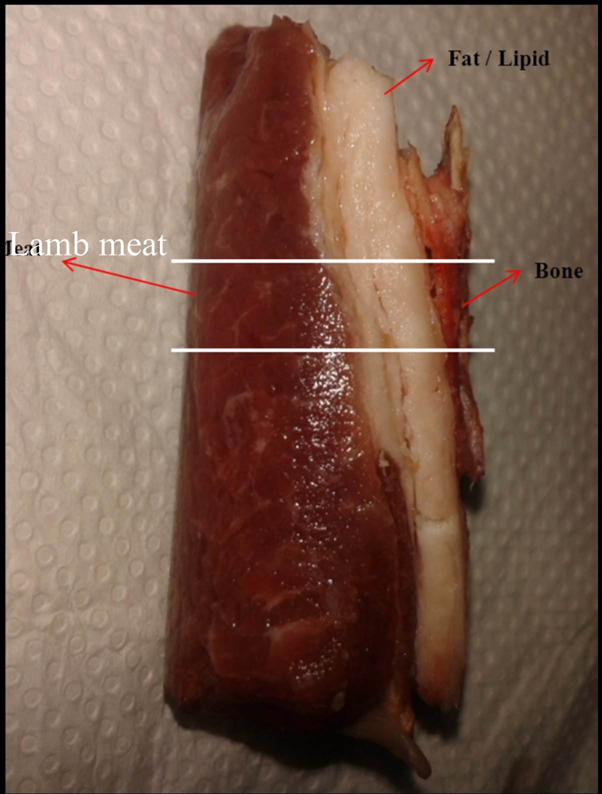
NZ Clinical projects

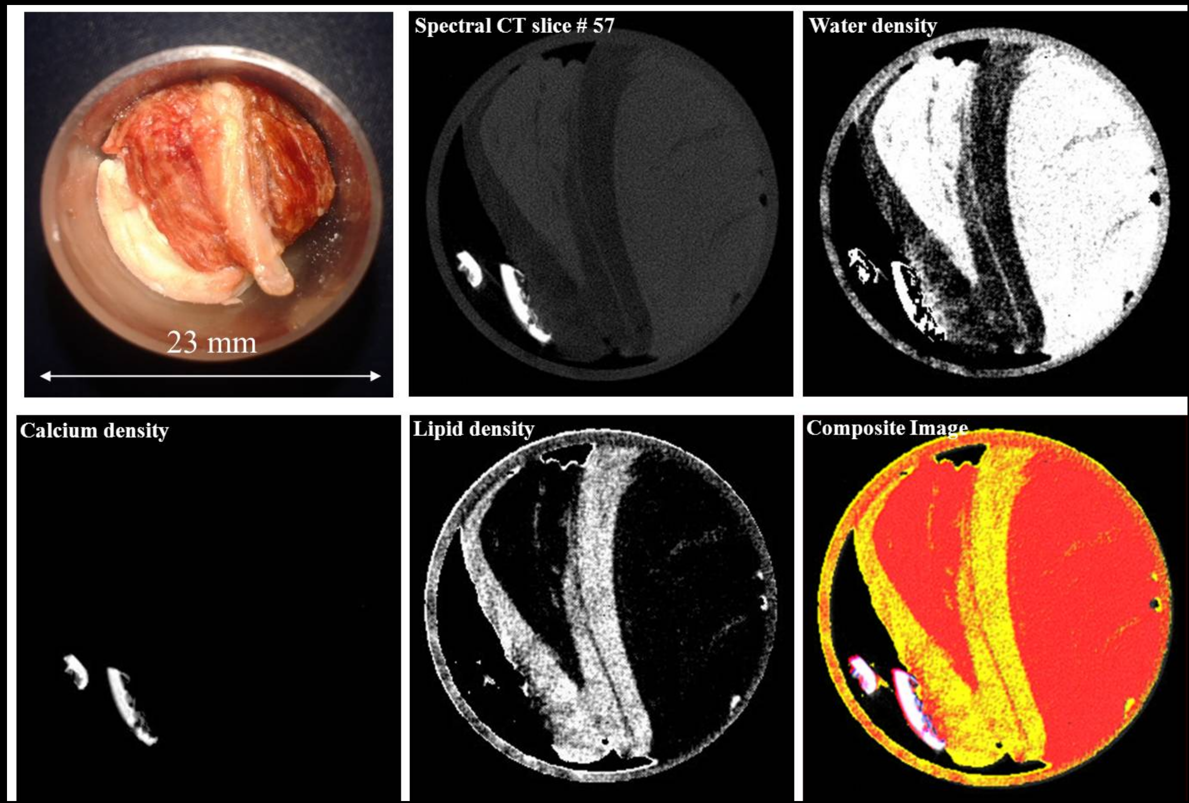
Areas of pre-clinical research in NZ:

- Soft tissue quantification
- Bone and cartilage health
- Atheroma characterisation
- Cancer research
- Reduced metal artefacts in implants
- X-ray dosimetry

Quantification of soft tissues

MARS enables identification and quantification of fat, water, and Ca



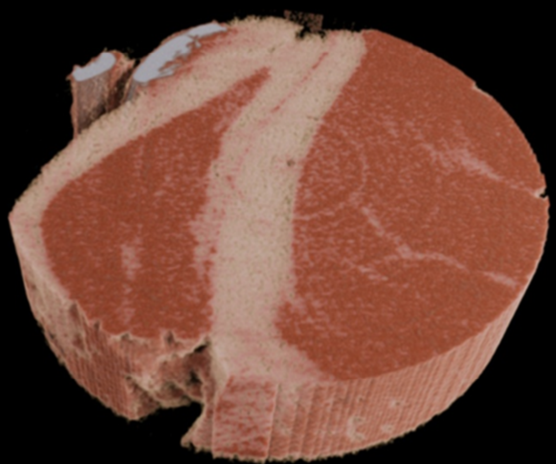


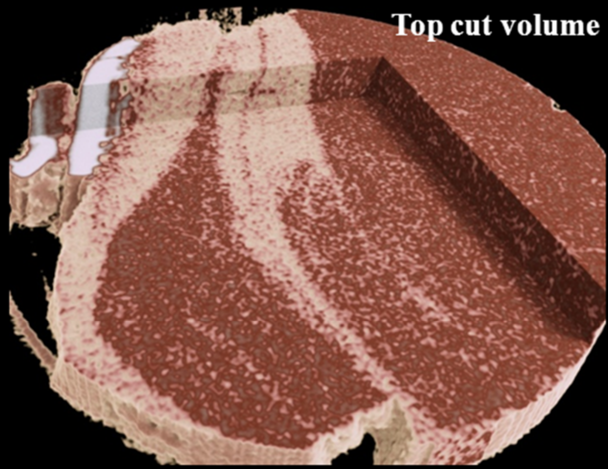
R. Aamir et al., Journal of Instrumentation, 2014. 9 P02005.
Raw, partial and fully processed data is publically available at http://hdl.handle.net/10092/8531

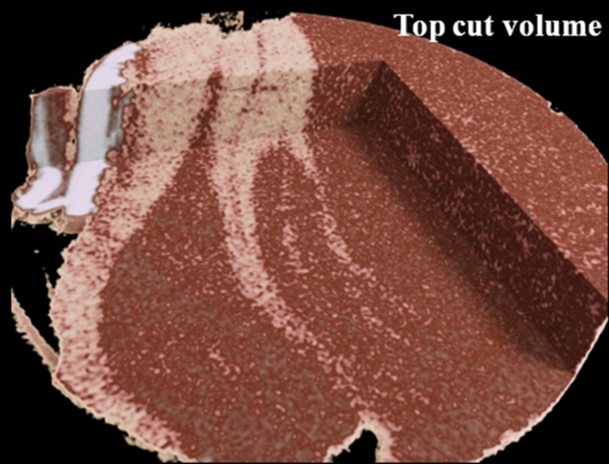
Quantification of soft tissues

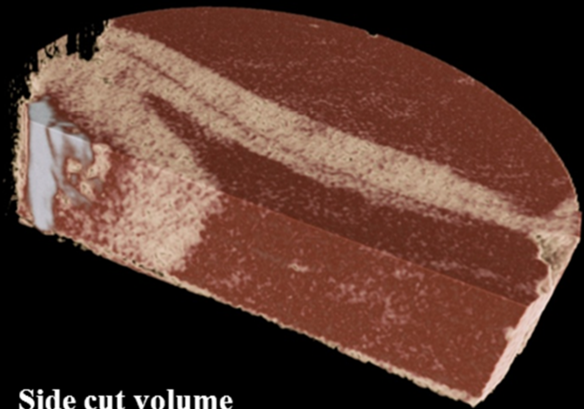
MARS enables identification and quantification of fat, water, and Ca

Whole volume









Side cut volume

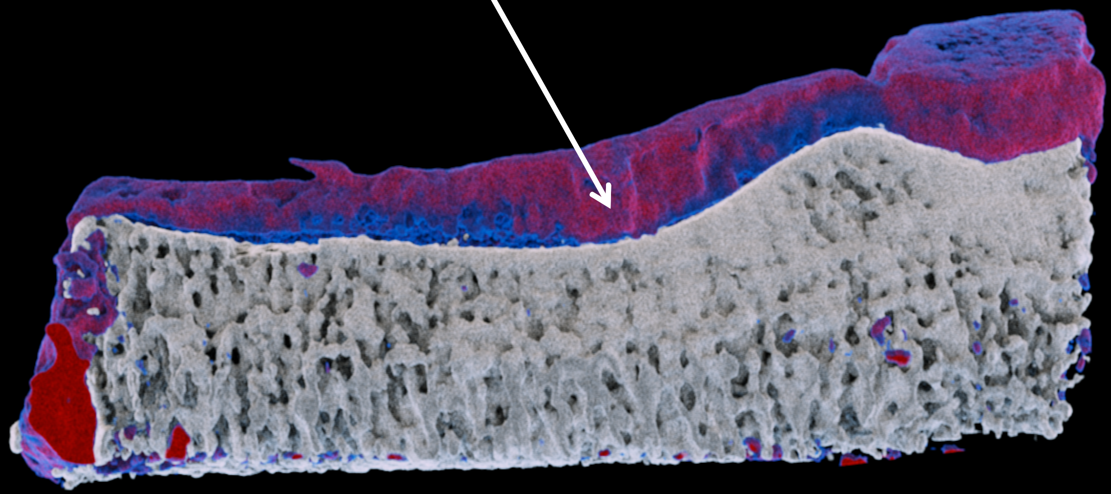
3D rendering of lamb meat scanned using MARS

R. Aamir et al., Journal of Instrumentation, 2014. 9 P02005.

Raw, partial and fully processed data is publically available at http://hdl.handle.net/10092/8531

Osteoarthitis biochemistry

Measurement of cartilage health in excised human tibial cartilage

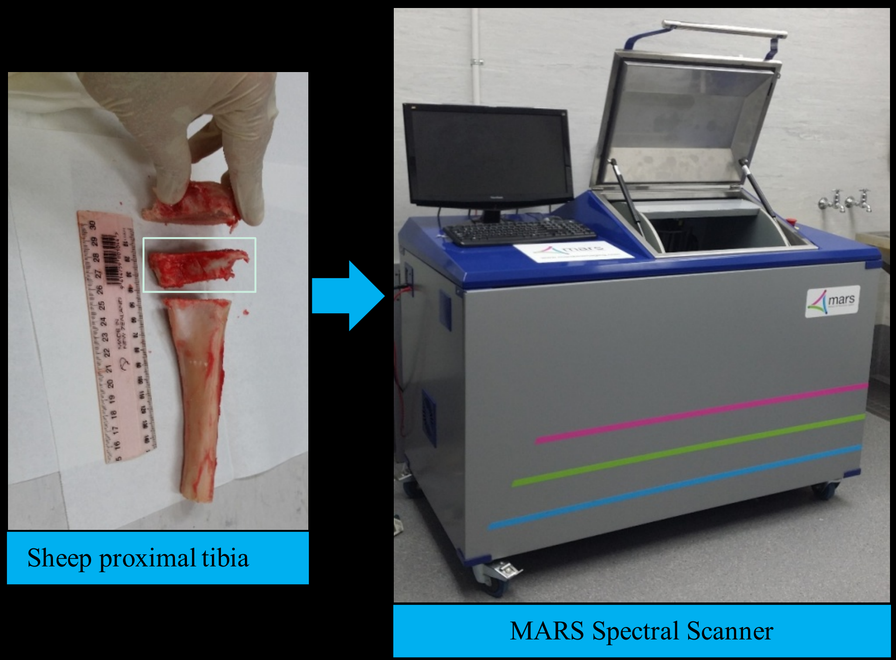


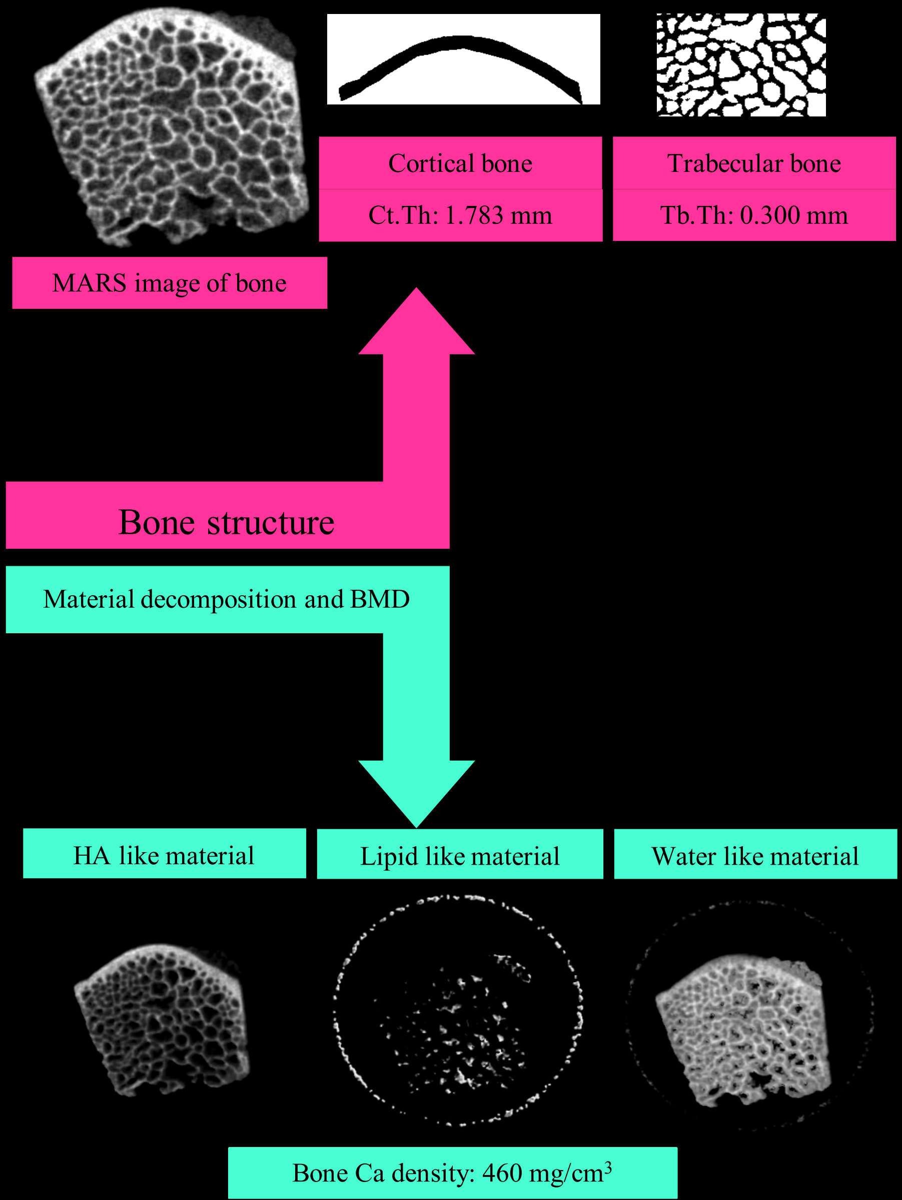
The early biochemical changes of osteoarthritis can be quantified

Quantitative imaging of excised osteoarthritic cartilage using spectral CT.
Rajendran *et al,* European Radiology, 2017 Jan; 27(1):384-392.

Bone Health

Bone structure and calcium density can be measured simultaneously

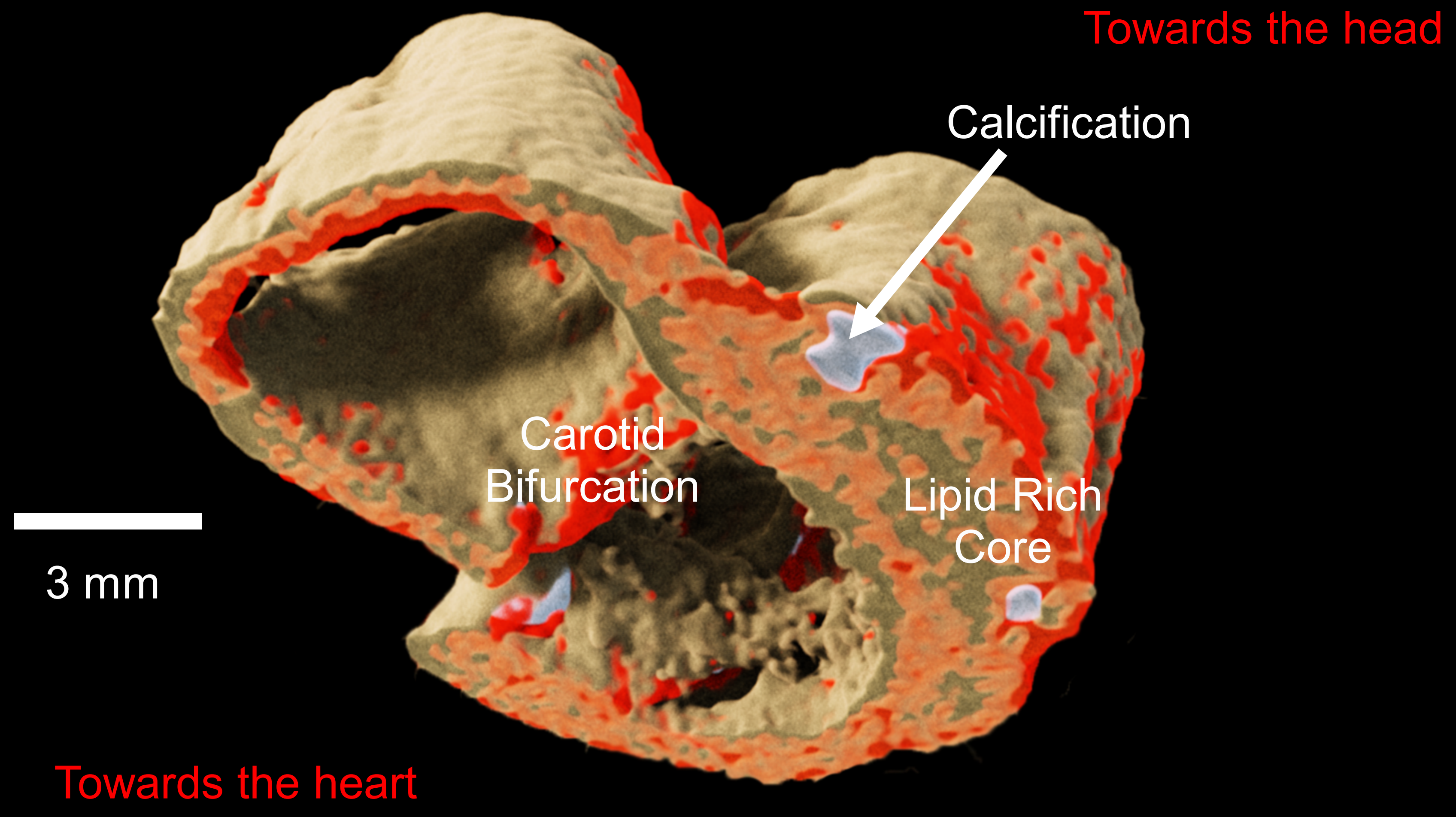




Presented at SPIE Medical Imaging, January 2017.

Spectral imaging of blood vessels

The components of an atherosclerotic plaque can be measured



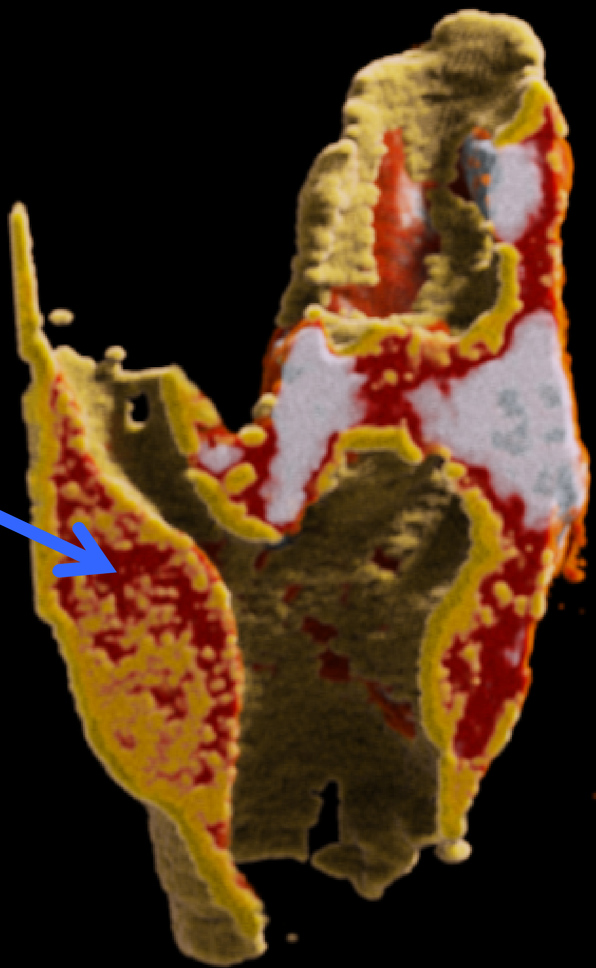
R Zainon et al, Spectral CT of carotid atherosclerotic plaque: comparison with histology. European Radiology, 2012, Vol 22 (12), 2581-2588pp.

Spectral imaging of blood vessels

The components of an atherosclerotic plaque can be measured

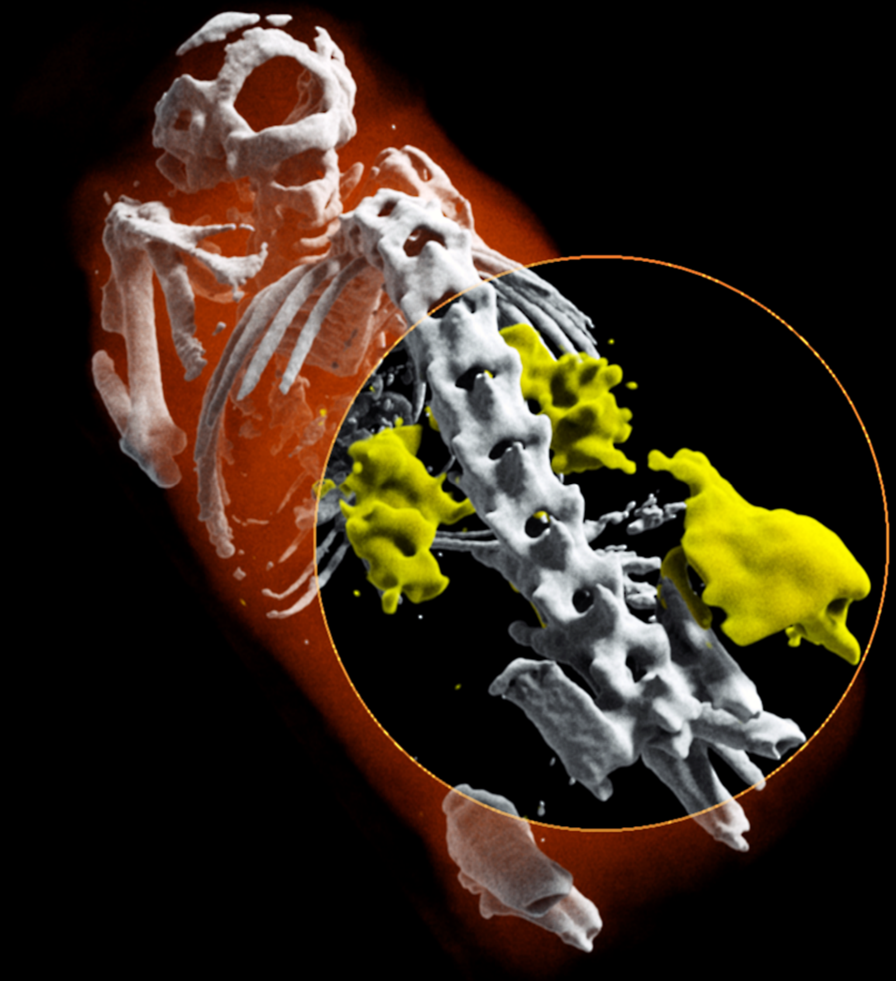
Key
Lipid,
water
calcium

Necrotic lipid core



Cancer Imaging

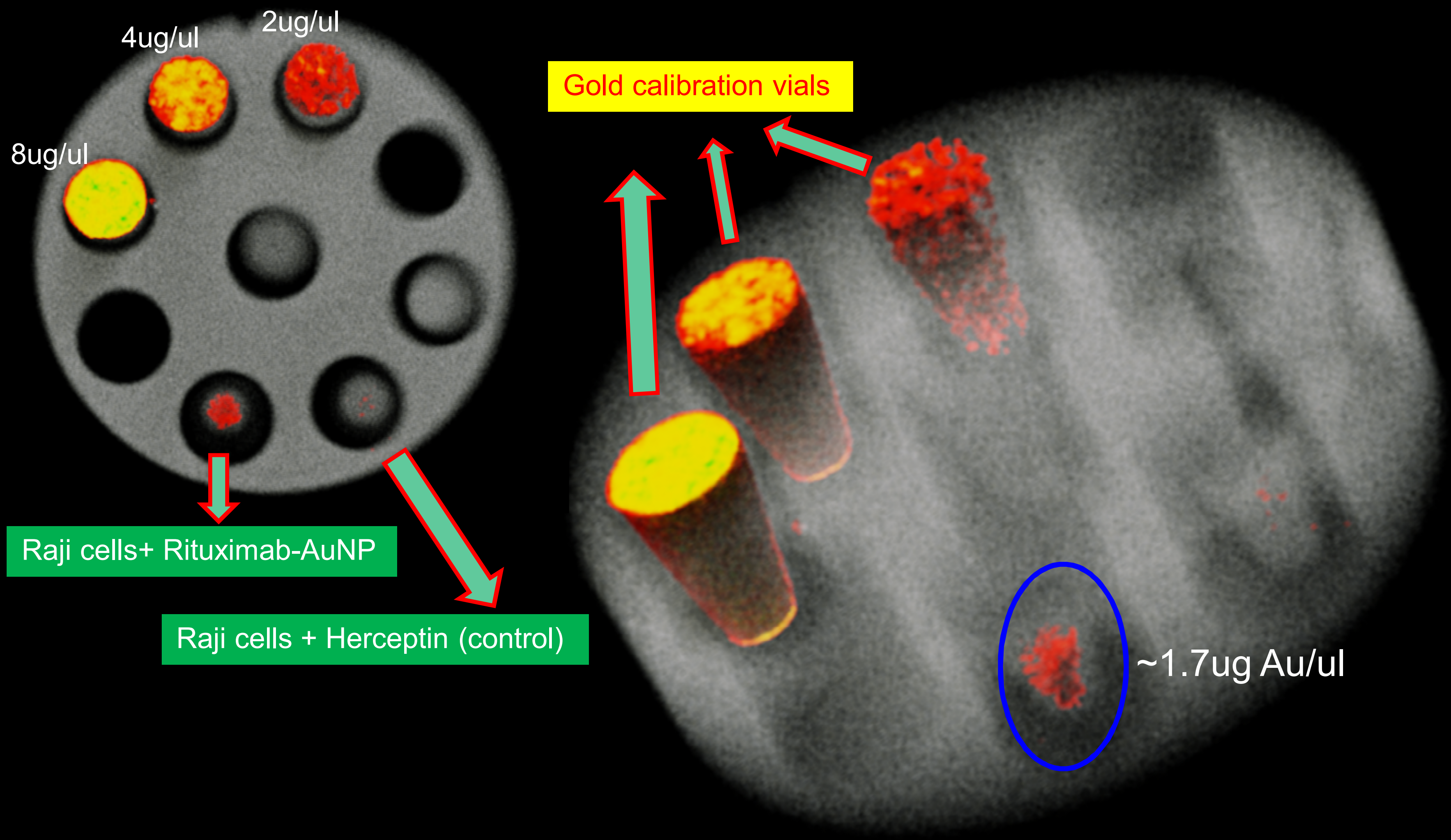
Better characterisation and better drug delivery



Poof Concept:
Au-nano probes measured in Lewis Lung cancer model

Cancer Imaging

Labelling of individual cell lines

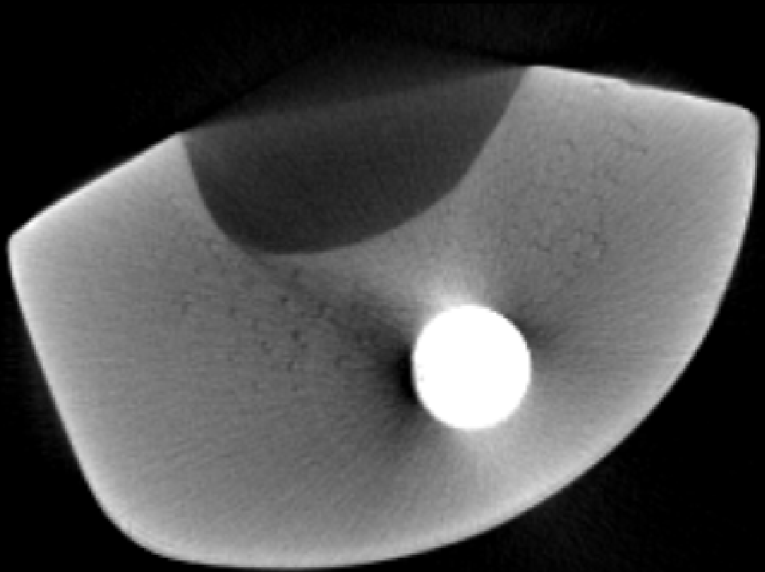


Reducing metal artifacts in bone

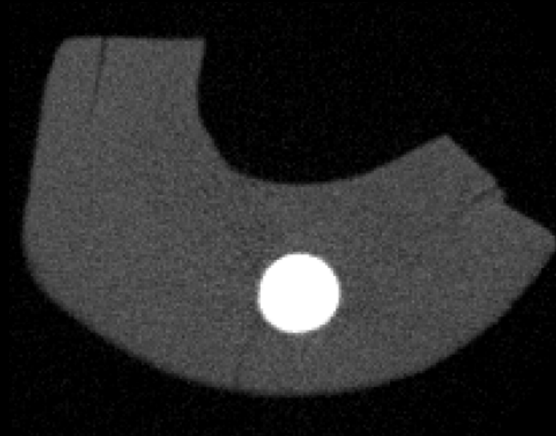
Ti locking screw in bone

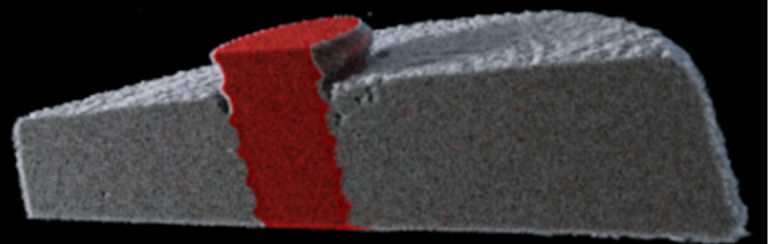
Titanium screw

Standard CT Image



MARS Image



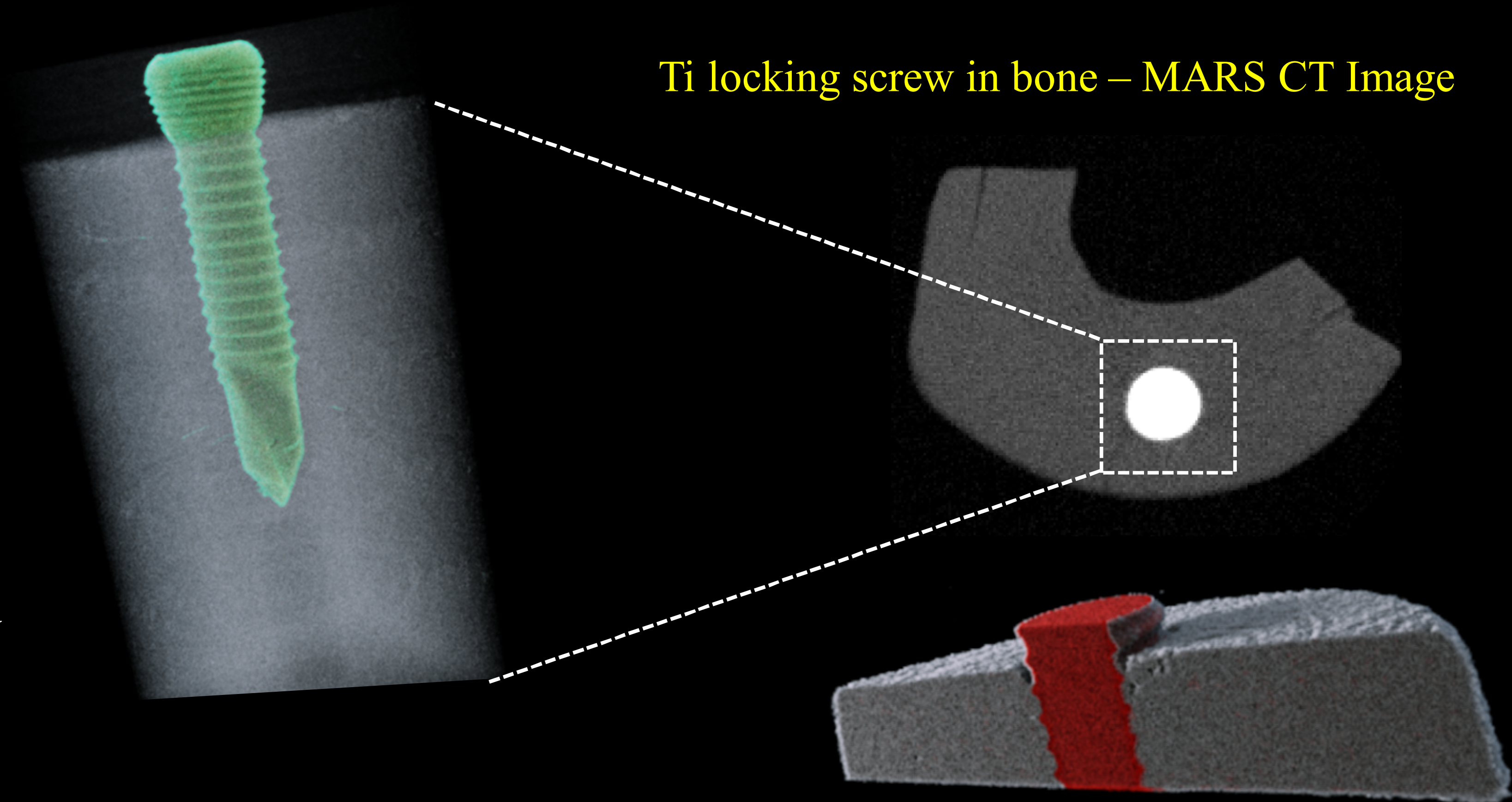


K. Rajendran et.al, Reducing Beam hardening and metal artefacts in spectral CT using Medipix3RX, Journal of Instrumentation, Vol. 9 P03015, March 2014.

Reducing metal artifacts in bone

Titanium screw

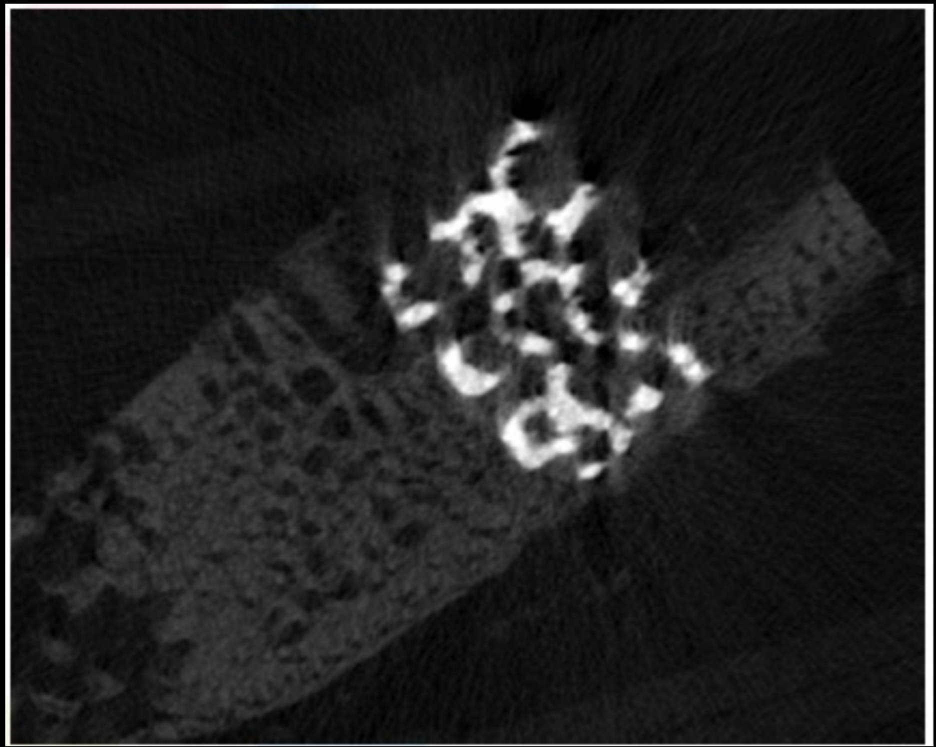
Ti locking screw in bone – MARS CT Image



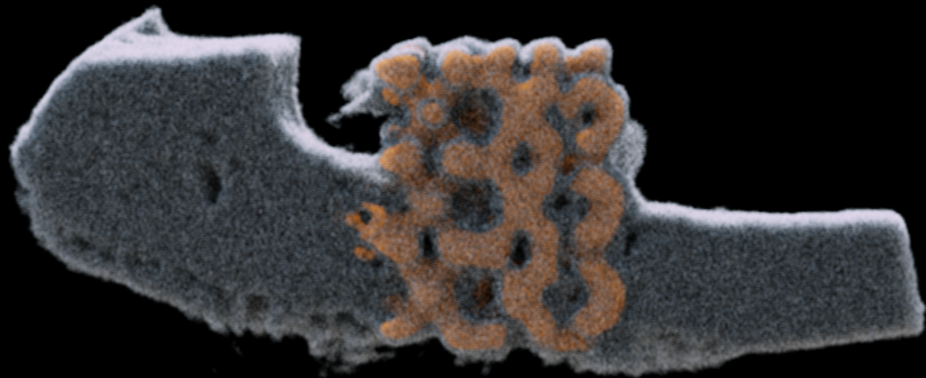
K. Rajendran et.al, Reducing Beam hardening and metal artefacts in spectral CT using Medipix3RX, Journal of Instrumentation, Vol. 9 P03015, March 2014.

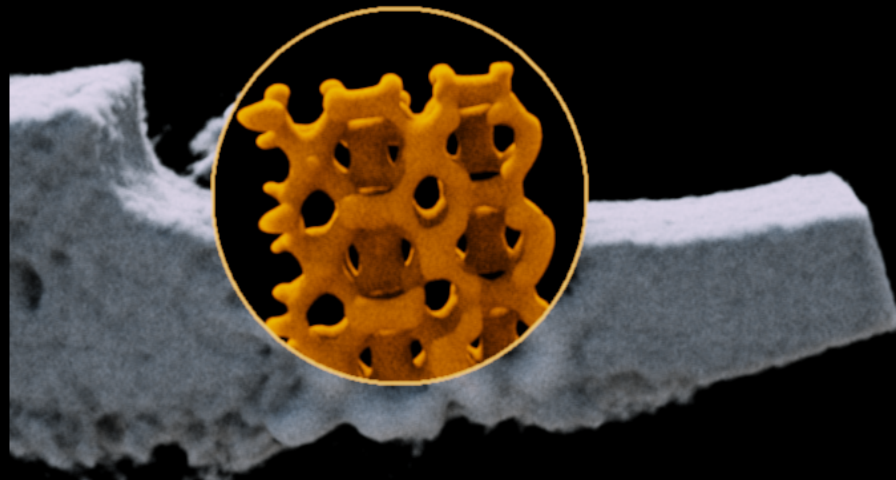
Reducing metal artifacts in bone

Ti scaffold in bone – Standard CT Image



Ti scaffold in bone – MARS CT Image



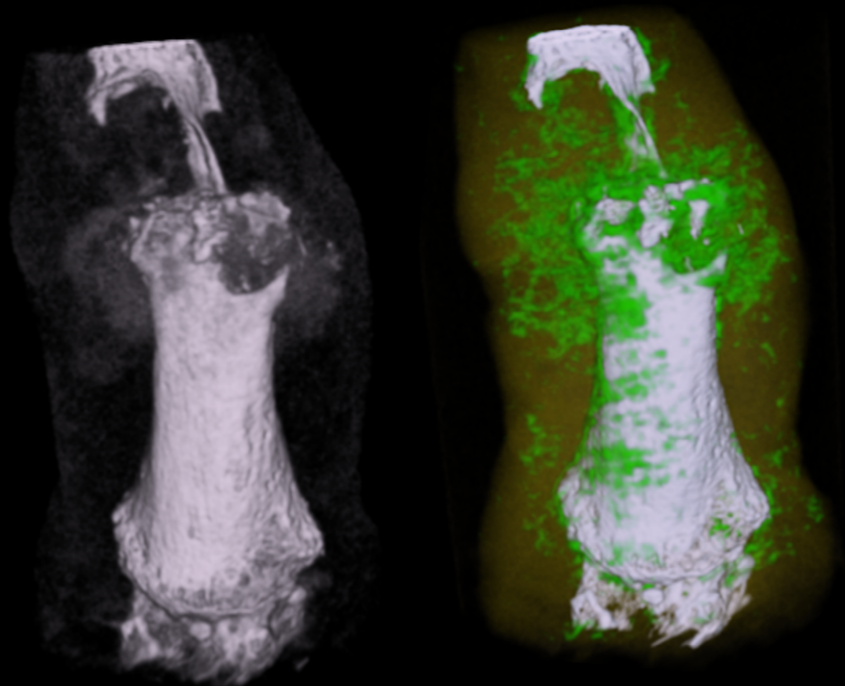


Better imaging of gout

Gout crystal can be measured more accurately

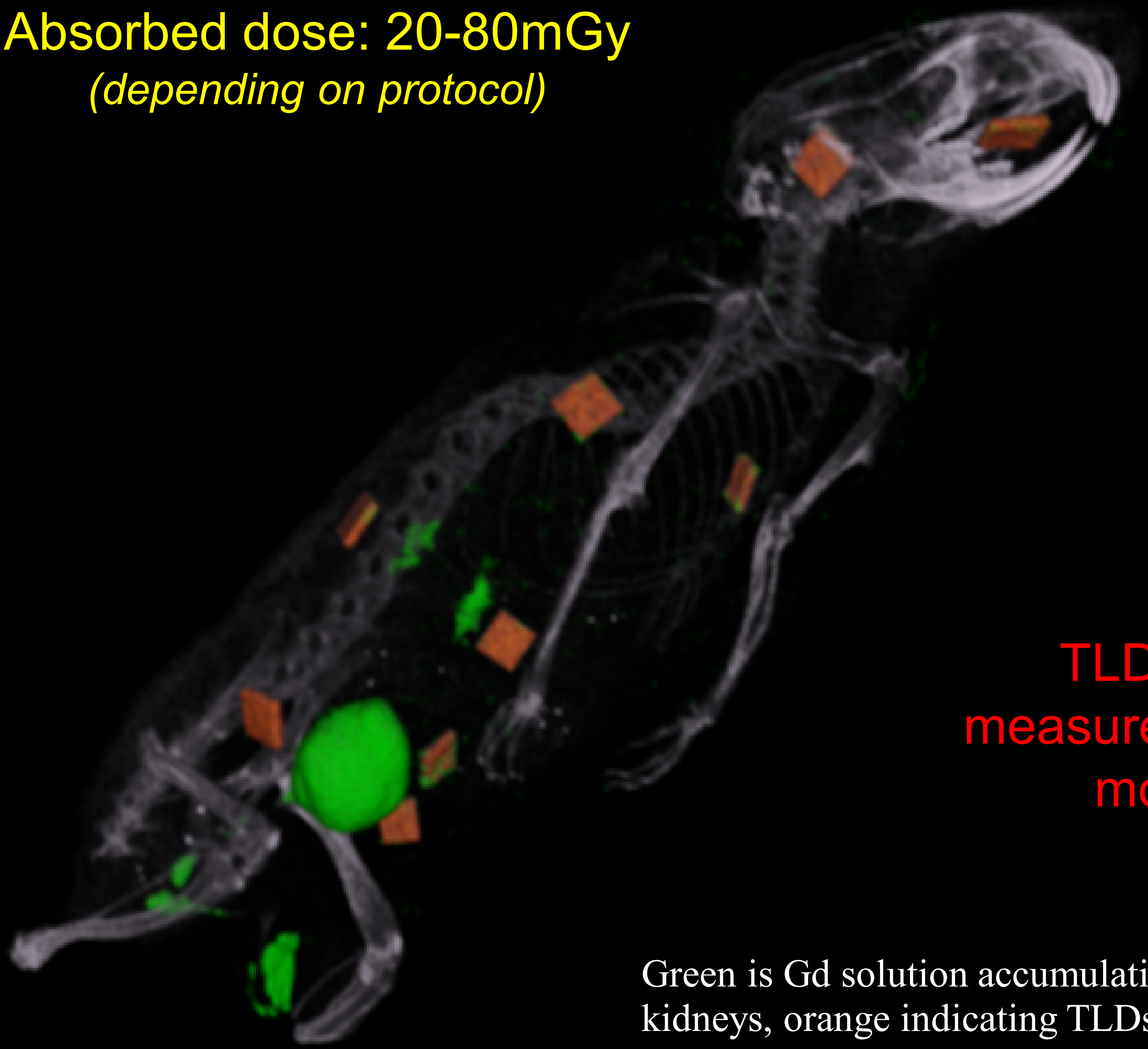
Dual-Energy CT

MARS



X-ray dose comparable with micro CTs

Absorbed dose: 20-80mGy
(depending on protocol)



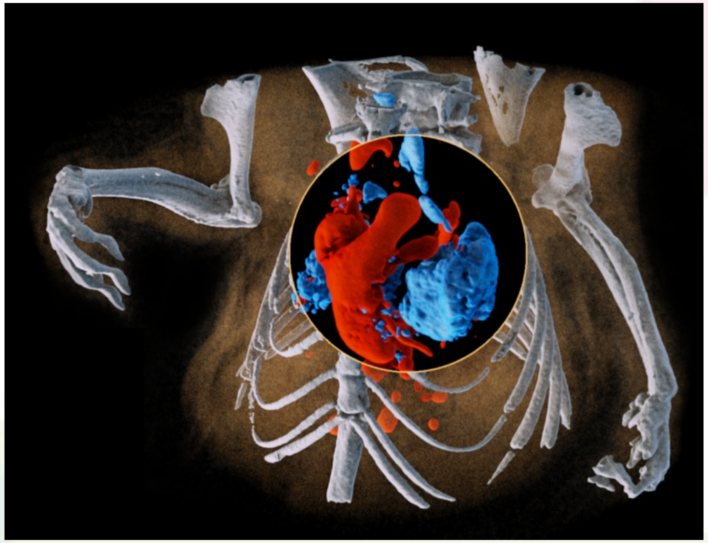
TLD dose measurement in a mouse

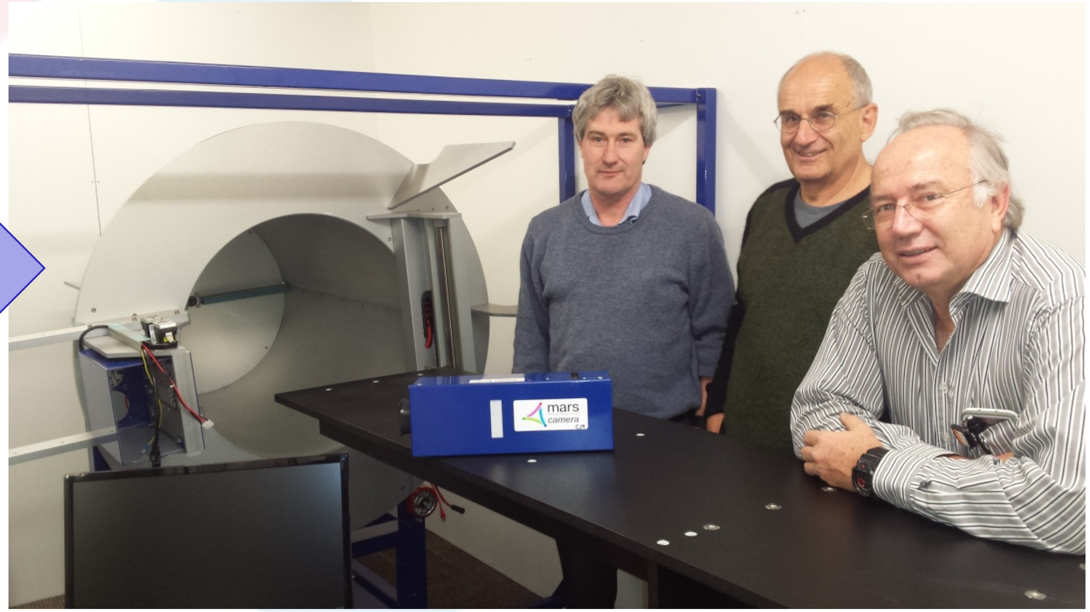
Green is Gd solution accumulation in the bladder and kidneys, orange indicating TLDs.

Current work:

Taking MARS to humans

Taking MARS to humans





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Medipix All Resolution System

Why take MARS to humans

To grow the NZ spectral CT industry

- funding from High Value Manufacturing portfolio

(part of Ministry for Business Innovation and Employment)

To enable clinical trials of spectral CT

- ie. funded to first human scans

- assist NZ MedTech companies

(both imaging companies and implant manufacturers)

Timeline

2000

- NZ scientists collaborate with CERN scientists
- NZ joins CERN and CMS
- Funding for NZ detector development – HEP + medical

2005

- I came to CERN and met Michael Campbell
- 1.5m NZD grant to do HEP and tools for MedTech students
- Canterbury Uni joins Medipix3
- MARS CT-1 proof of principal
- MARS Bioimaging Ltd Formed

2010

- 4.5 NZD grant + private equity *(research plan with business plan)*
- Scientific release of scanners to partners *(Mayo, Charles Uni, KIT)*
- Research partnership with GE Healthcare
- 12m NZD grant + VC funding *(Taking MARS to humans)*

2015

- Human translatable scanner sold to reference sites (ND, RPI)
- Human scanner under construction

Timeline

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NZ is an example of doing HEP research….

… leading to development of a high-tech industry

- Research partnership with GE Healthcare
- 12m NZD grant + VC funding *(Taking MARS to humans)*

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Conclusions

- Colour (Spectral) X-rays are the next step in CT

Anthony Butler

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Conclusions

- Colour (Spectral) X-rays are the next step in CT
- Partnership with CERN is mutually beneficial

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Conclusions

- Colour (Spectral) X-rays are the next step in CT
- Partnership with CERN is mutually beneficial
- NZ is building a human scanner
  - Providing health and economic benefit

Anthony Butler

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