MARS Spectral Imaging:
From High Energy Physics,
To a Biomedical Business

Anthony Butler
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
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
- 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

2005

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
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
- Detector
- Object
- Pattern Recognition System
Godfrey Hounsfield

Oct 1, 1971
First clinical scan

Commercialised as
EMI scanner

Nobel Prize 1979
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

- X-ray source
- Patient
- Grey scale detector
- Hounsfield Units
Single-, dual-, and spectral CT

Single energy CT
- X-ray source
- Patient
- Grey scale detector
- Hounsfield Units

Dual energy CT
- X-ray source
- Two grey scale detectors
Single-, dual-, and spectral CT

- **Single energy CT**
  - X-ray source
  - Grey scale detector
  - Hounsfield Units

- **Dual energy CT**
  - Two grey scale detectors

- **MARS spectral CT**
  - Medipix
  - Color detectors
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 All Resolution System**

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

Single-energy CT provides

- Brightness only (grey scale)
- Spatial resolution
- Temporal resolution
Example of spectral information

“Heavy atom” imaging

Better diagnosis because
- can use in combination
- can have new pharmaceuticals
  (functional imaging)
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 All Resolution System

Energy resolution
Spatial resolution
Temporal resolution
v3, v4 – pre-commercial systems
Unpacking the Mayo scanner
**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
Visualization Tools

Hybrid 2d/3d viewer
- 3d for orientation
- 2d for detail
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
Medipix3

Up to 8 Simultaneous energies
- 5000 transistors per 110um pixel
- Each pixel communicates with its neighbour

128 x 128 pixel array per chip
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
Clinical impact of Spectral CT:

Current achievements,
and the where they may lead
Greyscale to Material Imaging

Spectral imaging allow you to identify and quantify different materials
- a separate map (data channel) is made for each material
- each map gives 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 publicly available for people interested in doing their own analysis.
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

Greyscale to Material Imaging

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

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

Identification and Quantification Accuracy

**Gd**

- **Gd 2mg/mL**
  - Known concentration: 2 mg/mL
  - Measured concentration: 4 mg/mL

- **Gd 8mg/mL**
  - Known concentration: 8 mg/mL
  - Measured concentration: 8 mg/mL

**HA**

- **HA 200mg/mL**
  - Known concentration: 200 mg/mL
  - Measured concentration: 180 mg/mL

- **HA 800mg/mL**
  - Known concentration: 800 mg/mL
  - Measured concentration: 800 mg/mL

**Au**

- **Au 2mg/mL**
  - Known concentration: 2 mg/mL
  - Measured concentration: 2 mg/mL

- **Au 4mg/mL**
  - Known concentration: 4 mg/mL
  - Measured concentration: 4 mg/mL

- **Au 8mg/mL**
  - Known concentration: 8 mg/mL
  - Measured concentration: 6 mg/mL

**Iodine**

- **I 4.5mg/mL**
  - Known concentration: 4.5 mg/mL
  - Measured concentration: 4.5 mg/mL

- **I 9mg/mL**
  - Known concentration: 9 mg/mL
  - Measured concentration: 9 mg/mL

- **I 18mg/mL**
  - Known concentration: 18 mg/mL
  - Measured concentration: 18 mg/mL
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
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3D rendering of lamb meat scanned using MARS
Osteoarthritis 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.
Bone Health

Bone structure and calcium density can be measured simultaneously

Sheep proximal tibia

MARS Spectral Scanner

Bone structure and calcium density can be measured simultaneously

Cortical bone
Ct.Th: 1.783 mm
Trabecular bone
Tb.Th: 0.300 mm

MARS image of bone

Material decomposition and BMD

HA like material
Lipid like material
Water like material

Bone Ca density: 460 mg/cm³

Presented at SPIE Medical Imaging, January 2017.
Spectral imaging of blood vessels

The components of an atherosclerotic plaque can be measured

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

- Raji cells + Rituximab-AuNP
- Raji cells + Herceptin (control)
- Gold calibration vials

Concentrations:
- 1.7ug Au/ul
- 2ug/ul
- 4ug/ul
- 8ug/ul
Reducing metal artifacts in bone

Ti locking screw in bone

Standard CT Image

MARS Image

Titanium screw

Reducing metal artifacts in bone

Reducing metal artifacts in bone
Better imaging of gout

Gout crystal can be measured more accurately
X-ray dose comparable with micro CTs

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

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

Taking MARS to humans
Taking MARS to humans
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)
NZ scientists collaborate with CERN scientists

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NZ is an example of doing HEP research…

…leading to development of a high-tech industry

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Conclusions

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

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- Partnership with CERN is mutually beneficial
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- 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

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