INNOVATIVE HEALTH SOLUTIONS USING NUCLEAR TECHNIQUES

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Department of Nuclear Medicine • Royal North Shore Hospital
Professor in Medical Radiation Sciences • University of Sydney
Sydney • AUSTRALIA
Ionising Radiation in Medicine

Australian annual per capita radiation dose from natural and medical sources

- Radon progeny 0.2 mSv (9%)
- Cosmic rays 0.3 mSv (13%)
- Terrestrial 0.6 mSv (26%)
- Uranium/Thorium in the body 0.2 mSv (8%)
- Potassium-40 in the body 0.2 mSv (9%)
- Medical diagnostic 0.8 mSv (35%)

Source: ARPANSA
Where is Ionising Radiation Used in the Hospital?

DIAGNOSTIC IMAGING
Where is Ionising Radiation Used in the Hospital?

MONITORING TREATMENT

Pre-Tx +3 months
Pre-Tx Lymphoma +9 months
Pre-Tx
Lung Cancer
+4 months
Where is Ionising Radiation Used in the Hospital?

THERAPY
Where is Ionising Radiation Used in the Hospital?

INTERVENTIONAL PROCEDURES
Where is Ionising Radiation Used in the Hospital?

GUIDING SURGERY & BIOPSY
Where is Ionising Radiation Used in the Hospital?
Fig. 1.3 A diagrammatic plot of the spectrum of electromagnetic radiation with frequency and wavelength shown vertically on logarithmic scales. The various phenomena shown to the right include the two main absorption regions due to electric dipole (E1) resonances. These are indicated by heavy arrows. The one in the ultraviolet region (UV) is associated with electronic motion. The other in the infrared (IR) is due to the motion of nuclei and atoms.

From Fundamental Physics for Probing and Imaging. Wade Allison (Oxford)
What is Nuclear Medicine?

Nuclear medicine uses very small amounts of unsealed radioactive materials (radiopharmaceuticals) to diagnose and treat disease.

- Diagnostic imaging
- Radionuclide therapy
What is Nuclear Medicine? (aka “Molecular Imaging”)

<table>
<thead>
<tr>
<th>Type of Diagnostic Scan</th>
<th>Used for:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone scan</td>
<td>Bone pain, musculo-skeletal problems, metastatic cancer (lung, breast, prostate, <em>etc</em>)</td>
</tr>
<tr>
<td>Lung scan</td>
<td>Blood clots in lungs, lung function</td>
</tr>
<tr>
<td>Renal scan</td>
<td>Individual kidney function, obstruction, post-transplant function of implanted organ</td>
</tr>
<tr>
<td>Thyroid scan</td>
<td>Goitre, thyroid function (hypo- &amp; hyper-), thyroid cancer</td>
</tr>
<tr>
<td>Gastric emptying</td>
<td>Measure transit of food through stomach – gastric motility disorders</td>
</tr>
<tr>
<td>PET FDG scan</td>
<td>Mostly staging cancer – lung, colon, brain, head &amp; neck, uro-gynae, lymphoma</td>
</tr>
<tr>
<td>Myocardial perfusion scan</td>
<td>Detecting compromises in blood flow (perfusion) at rest and during exercise</td>
</tr>
<tr>
<td>Liver scan</td>
<td>Measure liver function – bile duct obstruction?, hepatic failure?</td>
</tr>
<tr>
<td>Adrenal scan</td>
<td>Distinguish between hyperactive adrenal gland(s) and functioning tumour</td>
</tr>
<tr>
<td>PET DOTATATE scan</td>
<td>Assess function of tumours of neuro-endocrine origin</td>
</tr>
<tr>
<td>Cardiac function</td>
<td>Measures pumping ability of heart – often compromised by some chemotherapy (<em>e.g.</em>, Herceptin)</td>
</tr>
</tbody>
</table>
PET FDG – NSC Lung Cancer with Lymph Node involvement
Right occipito-temporo-parietal glioblastoma (GBM), 3 weeks following right temporal craniotomy and biopsy
## What is Nuclear Medicine?
(aka “Molecular Imaging”)

### Type of Therapy

<table>
<thead>
<tr>
<th>Type of Therapy</th>
<th>Used for:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radioiodine ($^{131}$I) – NaI ($\beta^-$)</td>
<td>Thyroid cancer (after surgery for completion thyroidectomy), hyperactive thyroid</td>
</tr>
<tr>
<td>mIBG ($^{131}$I) ($\beta^-$)</td>
<td>Metabolically active neuro-endocrine tumours</td>
</tr>
<tr>
<td>SIR-Spheres ($^{90}$Y) ($\beta^-$)</td>
<td>Liver cancer treatment by direct implantation of radiolabelled microspheres</td>
</tr>
<tr>
<td>Peptide Receptor Radionuclide Therapy (PRRT) - ($^{177}$Lu &amp; $^{90}$Y) ($\beta^-$)</td>
<td>Treatment of neuro-endocrine tumours (Octreotate)</td>
</tr>
<tr>
<td>$^{223}$RaCl$_2$ ($\alpha^{++}$)</td>
<td>Treatment of bone pain from prostate cancer metastases</td>
</tr>
<tr>
<td>$^{90}$Y colloid ($\beta^-$)</td>
<td>Alternative to surgical synovectomy (knees, etc)</td>
</tr>
<tr>
<td>Bexxar ($^{131}$I) and Zevalin ($^{90}$Y) ($\beta^-$)</td>
<td>Treatment of refractory lymphoma</td>
</tr>
</tbody>
</table>

**Nuclear Medicine = Physiological Imaging + Targeted Therapy**
How does Nuclear Medicine differ from Radiology?

<table>
<thead>
<tr>
<th>Source of radioactivity</th>
<th>Nuclear Medicine</th>
<th>Radiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>unsealed</td>
<td>sealed</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Method of detection</th>
<th>Nuclear Medicine</th>
<th>Radiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>emission</td>
<td>transmission</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rapid changes over time</th>
<th>Nuclear Medicine</th>
<th>Radiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>usual</td>
<td>less common</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Nuclear Medicine</th>
<th>Radiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>physiological</td>
<td>anatomical</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radiation dose</th>
<th>Nuclear Medicine</th>
<th>Radiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>dose injected, biodistribution &amp; elimination of radiopharmaceutical</td>
<td>dose settings, area to be irradiated</td>
<td></td>
</tr>
</tbody>
</table>

Slice courtesy of Dr Bill MacDonald, Royal Perth Hospital
Transmission vs Emission Imaging

Transmission image
  e.g. CT scan

Emission image
  e.g. SPECT, PET scan

Slice courtesy of Dr Bill MacDonald, Royal Perth Hospital
Radiopharmaceuticals

• They’re pharmaceuticals – and they’re radioactive!
  – Usually given in homeopathic doses (nanogram)

• Short half-life (typically mins – hours)
  – specialised manufacture
  – production & distribution
    • need to deploy quickly (half-life, radiochemical stability)
  – small volume markets (esp. Australia)

• GMP QA issues
  – no or limited ability to complete exhaustive stability & sterility testing on every batch prior to dispatch
Why do we need different radiopharmaceuticals?
Theranostics

Diagnostic evaluation
$^{68}$Ga-DOTATATE

Therapy
$^{177}$Lu-DOTATATE

Slice courtesy of Dr Bill MacDonald, Royal Perth Hospital
AAEC (1953-1983)
MEDICAL ISOTOPE PRODUCTION WITHOUT HIGHLY ENRICHED URANIUM

Committee on Medical Isotope Production Without Highly Enriched Uranium
Nuclear and Radiation Studies Board
Division of Earth and Life Studies
NATIONAL RESEARCH COUNCIL OF THE NATIONAL ACADEMIES
THE NATIONAL ACADEMI E PRESS
Washington, D.C.
www.nap.edu

Summary

This report is the product of a congressionally mandated study\(^1\) to examine the feasibility of eliminating the use of highly enriched uranium (HEU\(^2\)) in reactor fuel, reactor targets, and medical isotope production facilities. The report focuses primarily on the use of HEU for the production of the medical isotope molybdenum-99 (Mo-99), whose decay product, technetium-99m\(^7\) (Tc-99m), is used in the majority of medical diagnostic imaging procedures in the United States, and secondarily on the use of HEU for research and test reactor fuel.

This summary is organized around the four study charges provided by Congress and a fifth study charge negotiated between the National Academies and the study sponsor, the Department of Energy’s National Nuclear Security Administration (DOE-NNSA). The fifth charge was formally approved by the sponsor and the National Academies prior to the start of the study. The complete study charge is given in Sidebar 1.2.

\(^1\)The study was mandated by Section 630 of the Energy Policy Act of 2005 (Public Law 109-58). See Appendix A.

\(^2\)HEU is uranium enriched in uranium-235 (U-235) to concentrations greater than or equal to 20 weight percent. Uranium enriched in U-235 to concentrations less than 20 weight percent is low enriched uranium (LEU); see Sidebar 1.1.

\(^7\)The “m” denotes that this radionuclide is metastable.
ACHIEVEMENTS - Radiopharmaceuticals

• “Skeltec”: AAEC Radioisotopes Division -1972
  • One of the first $^{99m}$Tc labelled bone scanning agents
  • Revolutionised bone scanning in nuclear medicine

• “Technegas” – $^{99m}$Tc labelled “carbon soot”
  • <200 nm nanoparticle – Tc in a carbon cage
  • Developed by William ‘Bill’ Burch at ANU Curtin School of Medicine - 1984
  • To date over 3,000,000 ventilation scans performed world-wide

Lung Ventilation Scan
Yttrium-90:
- Half-life: 64 hrs
- $\beta$- emitter (0.93 MeV average energy)
[\textsuperscript{90}Y]-SIR-Spheres Treatment

CORONAL  SAGITTAL  TRANSAXIAL

BASELINE FDG

SIR-Spheres

FOLLOW-UP FDG  11 weeks after SIRT
ACHIEVEMENTS – Image Reconstruction

- Mathematician, physicist & radio-astronomer
- University of Sydney: BSc (1941) ME (1943)
- Cambridge University: DPhil (1949)
- Tomographic image reconstruction from projections
- Fellow Royal Astronomical Society
- U.S. National Academy of Sciences in 1992 honoured Bracewell with foreign membership to its Institute of Medicine - the first Australian to achieve the distinction

Ron Bracewell (1921-2007)

Illustration of the 2D central-section theorem.
Maximum Likelihood Reconstruction for Emission Tomography

L. A. SHEPP AND Y. VARDI

1982 – Bell Labs

Accelerated Image Reconstruction using Ordered Subsets of Projection Data

H. Malcolm Hudson, Richard S. Lackin

Abstract: We define ordered subset processing for standard algorithms (such as Expectation Maximization EM) for image restoration from projections. Ordered subsets methods group projection data into an ordered sequence of subsets (or blocks). An iteration of ordered subsets EM is defined as a single pass through all the subsets, in each subset using the current estimate to initialize application of EM within that data subset.

This approach is similar in concept to block-Kaczmarz methods introduced by Kaczmarz et al. [1] for iterative reconstruction. Simultaneous iterative reconstruction (SIRT) and multiplicative algebraic reconstruction (MARM) techniques are well known special cases. Ordered subsets EM (OS-EM) provides a restoration imposing a natural positivity condition and with close links to the EM Algorithm.

OS-EM is applicable in both single photon (SPECT) and positron emission tomography (PET). In simulation studies in SPECT the OS-EM algorithm provides an order-of-magnitude acceleration over EM, with restoration quality maintained.

Keywords: EM algorithm, emission tomography, MART, OSL algorithms.
ACHIEVEMENTS – ‘Hybrid’ Imaging

• ANSTO produced $^{153}$Gd in HIFAR for SPECT transmission source – 1984
• First simultaneous measurement of body density ("low quality CT") and radionuclide distribution

ACHIEVEMENTS – ‘Hybrid’ Imaging

Development of a cost-effective modular SPECT/CT scanner

Dale L. Bailey · Paul J. Roach · Elizabeth A. Bailey · James Hewlett · Ronnie Keijzers

CT: 130kVp, 30mA, 4mm slices
SPECT: 30 min acq
Post left adrenalectomy $[^{131}I]$-mIBG
2008

Quantitative SPECT reconstruction using CT-derived corrections

Kathy Willson¹,², Dale L Bailey¹,²,³ and Clive Baldock¹

¹ Institute of Medical Physics, School of Physics, University of Sydney, Camperdown, NSW 2006, Australia
² Department of Nuclear Medicine, Royal North Shore Hospital, St Leonards, NSW 2065, Australia
³ Faculty of Medicine and Discipline of Medical Radiation Sciences, Faculties of Health, University of Sydney, Lidcombe, NSW 2141, Australia

2013

An Evidence-Based Review of Quantitative SPECT Imaging and Potential Clinical Applications

Dale L. Bailey¹,² and Kathy P. Willson³

¹Department of Nuclear Medicine, Royal North Shore Hospital, St. Leonards, Australia; ²Discipline of Medical Radiation Sciences, University of Sydney, Sydney, Australia; and ³School of Physics, University of Sydney, Sydney, Australia

Learning Objectives: On successful completion of this activity, participants should be able to (1) review the current status of SPECT imaging, with an emphasis on clinical applications for quantitative interpretations; (2) consider the requirements for quantitative SPECT imaging—instrumentation, software, and image calibration; and (3) acquire knowledge of the capabilities of quantitative SPECT with a view to developing new clinical applications.
ACHIEVEMENTS – Education & Training

FOUNDATIONS OF PET-CT
Sixth annual comprehensive training course for nuclear medicine professionals

2013
ACHIEVEMENTS – Education & Training

IAEA African Training Course 2009

IAEA Latin American Training Course 2011

Department of Technical Cooperation (TC)
End-of-Mission Report

Title: Fact finding mission on current status of clinical practice of Nuclear Medicine and Diagnostic Imaging

Project Number: OMA600302

Project Title: Urgent Needs for Diagnostic Imaging & Therapeutic Oncology services in Oman

Name of Expert: (1) Dale Bailey (Sydney) (2) Giuliano Mariani (Pisa)

Dates of Mission: Dec 5-9, 2009

Counterpart:
Professor Hadj Slimane Cherif
Head-Peaceful Nuclear Technology Office
Ministry of Foreign Affairs
Sultanate of Oman

Please provide full contact details for the Institute and main counterpart.
Meeting the Challenges of Global Nuclear Medicine Technologist Training in the 21st Century: The IAEA Distance Assisted Training (DAT) Program

Heather E. Patterson, CNMT,
Margarita Nunez, PhD, CNMT,
Geraldine M. Philotheou, MSc,
and Brian F. Hutton, PhD

Table 2: Number of Students and Locations Participating in the DATOL Program (Estimated Mid 2012)

<table>
<thead>
<tr>
<th>Regions/Countries</th>
<th>Part 1</th>
<th>Part 2</th>
<th>Part 1 Off-line</th>
<th>Completed Off-line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia-Pacific</td>
<td>~20</td>
<td>298</td>
<td>60</td>
<td>37</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>7</td>
<td>2</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>India</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaysia</td>
<td>17</td>
<td>2</td>
<td>6</td>
<td></td>
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<tr>
<td>Philippines</td>
<td>26</td>
<td>2</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td></td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Australasia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TRAINING & SERVICE PROVISION
- Medical Training – second-to-none, often complemented by overseas training
- Physics training – improving, always strong in R&D
- Allied health technologists – world-leading in education; have exported our training programmes throughout SE Asia and continue to do so
- Pharmaceutical and radiochemical sciences – historically not university based, built around ANSTO (not CSIRO) or research institutes

RESEARCH OUTPUT
- “punching above our weight”

IMAGING EQUIPMENT AND FACILITIES
- generally good but, due to the capital sums involved, can be left wanting when solely funded by State Governments

REGIONAL VARIATIONS
- state-based funding means very different treatments can be offered between states (e.g., NSW vs VIC); geography imposes further constraints (e.g., NT)

ACCESS TO DIAGNOSTIC IMAGING AGENTS
- trailing rest of world
Are we slipping behind in Australia?

September 2013 issue of Journal of Nuclear Medicine:

- 24 scientific and review articles
Australia is starved of contemporary practice in radiopharmaceuticals:

- Many diagnostic imaging tests are tightly restricted *even for approved radiopharmaceuticals*
  
  - *e.g.*, cannot currently use FDG PET in breast cancer where indications are very strong

- Extremely difficult & expensive process for Medicare funding (TGA, Medical Services Advisory Committee approval usually takes many years)

- Demand to replicate expensive randomised clinical trials in Australia when product already approved in USA and Europe (often impossible due to small population)

- No training programme or accreditation for radiopharmacy practitioners
We Need to be SMART

› **S**elect the most appropriate radiopharmaceutical available to answer the clinical question – not just the one that has the Medicare approval

› **M**ove to a funding model that allows cost savings in downstream areas (e.g., planned surgery that would be futile) to be incorporated into overall cost analysis of the imaging study

› **A**llow collection of data for potential new indications with partial funding under agreements to contribute to larger data collection exercise

› **R**eview high-level clinical data with solid evidence as it becomes available from overseas studies without requiring replication in local clinical trials

› **T**rain the next generation of radiopharmaceutical scientists
To introduce new radiopharmaceuticals for diagnostic tests and therapies
  - May already be in use overseas
To be a key supplier of radiopharmaceuticals for use in medicine in the region
To develop an indigenous programme of radioligand development
To collaborate with the nuclear medicine community to capitalise on the expertise at ANSTO to address basic science & clinically relevant questions using nuclear techniques (AINSE)
Serve as a training ground for next-generation radiopharmaceutical scientists (regional role)
Explore new approaches to radionuclide production (e.g., cyclotron-based)