



Joint submission from the Australian & New Zealand Society of Nuclear Medicine & the Australasian Association of Nuclear Medicine Specialists on behalf of their Australian memberships



NATIONAL RESEARCH INFRASTRUCTURE ROADMAP

National Research Infrastructure Capability Issues

EXECUTIVE SUMMARY

- The ANZNM & AANMS are the organisations representing the majority of clinical, scientific and technical staff providing nuclear medicine imaging and therapy services in Australia & New Zealand;
- As such, the membership of these professional bodies are the gatekeepers to extensive resources for access to nuclear medicine facilities in hospitals, universities, private practices and research institutions as available. This includes state-of-the-art equipment, experienced medical and scientific staff and, significantly, large cohorts of a variety of clinical patient groups;
- The existing NIF programme has, to date, predominantly focused on preclinical imaging and animal models;
- The opportunity exists to greatly expand the capability of both of the aforementioned imaging infrastructures, which have had little previous interaction, by expanding the reach of NIF to include research-oriented clinical facilities containing PET and SPECT imaging systems, medical cyclotrons and radiopharmaceutical production facilities;
- This expansion would involve four tasks:
 - undertaking a national audit of the existing infrastructure and identifying gaps or deficiencies (particularly in the area of radiopharmaceutical production);
 - providing resources for the members of the expanded program to meet to establish a coordinated and standardised program across multiple centres irrespective of their location to rapidly disseminate advances in radiopharmaceutical developments, imaging technology and novel therapeutics;
 - establishing a national imaging biobank based on NBN technology which would provide disease-coded image access to all researchers in Australia and potentially abroad;
 - to further enhance engagement with industry, especially for the purpose of conducting clinical trials where the ANZSNM and AANMS have already established an imaging trials network (ARTnet);
- This proposal seeks to capitalise on the pre-existing resources available by expanding the NIF programme to incorporate clinical sites as part of a research matrix, and by standardising procedures and rationalising the production of novel radiopharmaceuticals in a programme which predominately facilitates collaboration between existing researchers and clinicians, as well as working to respond to any gaps or deficiencies identified that are impacting on the ability to produce high level translational research in imaging.

BACKGROUND

At the present time Australia is regarded internationally as an increasingly desirable location for conducting clinical trials (Phase 0-III) of new nuclear medicine diagnostics and therapeutics, particularly in the areas of neuroscience and managing advanced cancer. This is being driven by a number of factors including:

- rapid developments in radiochemistry which are bringing a number of new functional imaging radioligands to the clinical environment far more rapidly than has historically occurred;
- the radiopharmaceutical/radiochemistry and imaging infrastructure¹ we have is of a comparable high standard to anywhere else in the world. *NB: the majority of the imaging-associated equipment being used in these trials is located in the tertiary referral hospitals around the country;*
- high levels of well-educated staff with national accreditation and credentialing, with ready access to large patients cohorts via our public/private health system;
- a sensible regulatory and ethical environment to investigate new radiopharmaceuticals and therapies without the large overheads that are required by many other jurisdictions;
- a sensible, measured approach to the issues of radiation safety and protection of patients, carers, staff and the general public.

Recent examples of advances in the field include the investigation of the value of functional imaging of amyloid deposits in dementia, new radiopharmaceutical theranostics for the staging and treatment of metastatic prostate cancer, and advances in the understanding and biology of metastatic neuroendocrine tumours.

Until now, the National Imaging Facility (NIF) operating under NCRIS has been predominantly focused on pre-clinical developments, animal models and implementation of new imaging equipment. The translation of NIF developments into the clinical domain has not, though, generally speaking, occurred to date.

In parallel with this the nuclear medicine community has been self-organising into a formalised structure to undertake multicentre clinical imaging and radionuclide therapy trials. The ANZSNM and the AANMS in a joint venture have established the Australasian Radiopharmaceutical Trials network² (ARTnet) to coordinate research-capable hospital facilities & researchers around the country. ARTnet has identified 3 primary types of clinical trials it anticipates being involved in which would use imaging or radionuclide-based therapies: (i) for self-initiated studies from members of the nuclear medicine imaging and therapy community, (ii) as an imaging trials expertise network to identify, initiate and co-ordinate multicentre trials using functional imaging as an endpoint for other trials groups in Australia and New Zealand (*e.g.*, AGITG, ALTG), and (iii) as an entry portal for external organisations and industry to engage with Australian sites to participate in clinical trials. ARTnet has recently been accepted as an associate member of the Australian Clinical Trials Alliance (ACTA), an umbrella organisation for all active clinical trials groups in Australia.

ARTnet will play a key role in the recently funded (\$1.3m) Movember/PCFA multicentre clinical trial of [⁶⁸Ga]-PSMA PET/CT imaging in primary staging of high risk prostate cancer (the “proPSMA” study), thereby demonstrating the value of a collaborative clinical trials network to attract funding for clinical trials in Australia which would be less likely to occur if only a single site were to be involved. Australia therefore has an excellent opportunity to build on the coordinated, national activities of the NIF program by complementing this with ARTnet’s reach to tap into the advanced clinical facilities that exist in our hospital environment, with their access to large patient pools, and to enhance the capability of both NIF and ARTnet in a national program of radiopharmaceutical development and rapid translation to the clinic for novel therapies. This will lead to earlier access to effective new diagnostics and therapies and help to define the appropriate therapeutic pathway for differing disease phenotypes which will, in itself, lead to better targeted therapies in an attempt to contain health costs and generate income from clinical trials which can be used to supplement further developments of the imaging and therapies.

¹As proposed by Dr Alan Finkel and the EWG panel at the NISA briefing session in Sydney in August 2016 we understand “infrastructure” to include personnel

²<http://www.artnet.org.au>

PROPOSAL

The ANZSNM and the AANMS jointly propose that the remit of NIF be expanded (referred to here as “ENIF” – *Expanded NIF*) to include appropriate imaging infrastructure for human imaging into the program, wherever it may be housed (*e.g., hospitals*), which would greatly enhance the capability of the current NIF consortium. The funding required for this activity would be relatively modest, as it would not be funding new equipment or a large number of salaries, but would rather focus on enabling the network of academics and clinician researchers to collaborate effectively. A key feature of the ENIF would be to have a mechanism to fund the exchange of knowledge between the multidisciplinary groups by supporting meetings, workshops, training, short term scientific exchanges and outreach activities.

Task 1 - National Audit of Existing Infrastructure

The first task for ENIF would be to undertake a national audit of existing capabilities and identifying gaps, including:

- radiopharmaceuticals in routine production at individual locations;
- radionuclide production capabilities including OPAL and medical cyclotrons;
- documentation of all relevant imaging equipment (*e.g., PET/CT, SPECT/CT, PET/MRI, Pre-Clinical imaging*);
- research-available staff resources;
- training programs in molecular imaging, “hybrid” multi-modality imaging, radiopharmaceutical sciences and medical physics. One of the most pressing areas of workforce deficiency currently is that of appropriately trained radiochemists and radiopharmaceutical scientists. An ENIF-co-ordinated programme of supported training should be created by collaborating and complementing current certified training (*i.e., ACPSEM*);
- available animal models of disease matched with suitable imaging probes;
- capabilities and areas of interest of all research-available staff;
- Expressions of Interest from parties not currently involved in NIF to explore expanding the scope (*e.g., metabolism, endocrine, etc*);
- A wish-list for future radiopharmaceuticals which may have general applicability for a particular metabolic/transmitter/hormonal pathway (*e.g., [¹⁸F]-Fluoro-DOPA*).

Task 2 – Coordination, Standardisation & Rapid Dissemination of IP

Having conducted the initial national audit (Task 1), the ENIF would then establish working groups dedicated to filling the gaps and assigning them to specific tasks required to achieve a national matrix of imaging and radionuclide therapy access portals. These would include:

- Molecular imaging probe standardisation and development of a roadmap for future labelled tracers and innovative radiochemical processes (*e.g., microfluidics*). The group would also coordinate dissemination of the intellectual property (IP) required to transfer routine production of the different labelled tracers to imaging sites or regional distribution centres for use under currently permitted regulations (CTN/CTX for clinical trials or SAS for patient administration);
- enhancing capabilities for PET radiopharmaceutical production at sites with established facilities and track record in research and collaboration (particularly hospital-based), by supporting infrastructure upgrades, and by supporting personnel to enable distribution of novel PET radiopharmaceuticals to trial sites. This aligns with other applications, addresses a key issue for current hospital-based cyclotron facilities, and also places appropriate emphasis on supply of PET radiopharmaceuticals at reasonable cost to researchers;
- imaging & protocol standardisation to allow multi-centric imaging trials to be undertaken rapidly in a manner whereby results from different institutions may be pooled (in collaboration with ARTnet);
- an industry engagement working group that would develop national collaborations with the pharmaceutical industry and medical imaging equipment vendors;
- a multidisciplinary clinical/outreach group that would provide a link between ENIF and the variety of medical specialties that may benefit from access to imaging trials (*e.g., cancer, neurosciences, cardiovascular, metabolism, infection/inflammation & autoimmunity, musculoskeletal, etc*).

Task 3 - Establishing a National Imaging Biobank

The ENIF should investigate the establishment (potentially with an IT/imaging partner, *e.g.*, CSIRO/Data61 or a vendor) of an anonymized, diagnostic category-linked national image biobank of all ENIF acquired image data for ethics-approved access by all validated researchers. This would greatly enhance the capability for image analysis beyond those groups which currently “own” or control the data. The value of any biobank is ultimately dependent upon the disease definition, quality of the samples, available knowledge of the genetics/phenotype and subject-specific outcomes related to each data set and these would be of prime importance for any national archive.

A further option for the national biobank might be to accumulate anonymized medical images (*e.g.*, from participating imaging facilities in the private or public sectors) with the aim of permitting population-based analysis of normal and abnormal morphology and physiology as a surrogate for anatomical pathology autopsies, recognising that the “routine post-mortem examination” is rapidly disappearing and, thus, access to population estimates of organ morphology, normal variants, disease incidence and anomalies is increasingly difficult to obtain due to changing social, cultural, religious and ethnic mores.

The establishment of a National Imaging Biobank would also capitalise on and be enhanced by one of the Federal Government’s current major projects, the National Broadband Network. State-of-the-art connectivity and communications would be an essential element of this task.

Task 4 - Engagement with Industry

ENIF should also take a leading role in coordinating the efforts of its research & clinical community with industry to expedite approvals for new imaging agents and devices, and to allow industry to gain rapid answers to their research questions by utilising the national matrix of imaging facilities. This would likely garner interest from international organisations and industry partners who would be attracted to the high quality of medical imaging practice in Australia combined with a favourable environment in which to participate. ARTnet is a pre-existing portal for such organisations seeking to partner with Australian institutions.

CONCLUSIONS

- Current imaging infrastructure is good due to previous investment. However, it must be recognised that to maintain this position a continuous programme of renewal and upgrading is required, which can be sustained from a diverse range of funding sources;
- Identifying and addressing areas of deficiency in national capabilities, individual site limitations, and in the workforce is critical to be able to enhance capability, and this may be through targeted funding strategies, national linkages or structured training opportunities;
- To improve the sharing and data mining capabilities a National Imaging Biobank based on NBN technology should be investigated;
- To maximise the existing expertise and infrastructure the NIF programme should be expanded to include appropriate research-capable imaging facilities and NIF capability expanded by introducing a programme of co-ordination of targeted working groups to address generic questions of standardisation and harmonisation to greatly expand the resources available nationally. An expanded NIF could be readily incorporated into the existing network established by AANMS/ANZSNM/ARTnet for clinical translational research. Such a programme would ensure that both preclinical and clinical research would be more likely to lead to significantly greater opportunity to support further world-leading research, particularly in the development and validation of novel tracers and therapies.

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ABOUT THE ORGANISATIONS

The Australian & New Zealand Society of Nuclear Medicine (ANZSNM) is the main professional organisation for all those involved in the practice of Nuclear Medicine in Australia and New Zealand. The Society includes physicians/specialists, physicists, radiochemists, radiopharmaceutical scientists, technologists, nurses and others interested in the practice of Nuclear Medicine. It has close ties with other professional groups in nuclear medicine, most notably the Australasian Association of Nuclear Medicine Specialists (AANMS). The ANZSNM membership also includes radiologists, cardiologists and oncologists who have a particular interest in functional imaging and are involved in this increasingly multidisciplinary area of healthcare.

The Australasian Association of Nuclear Medicine Specialists (AANMS) is the peak body representing nuclear medicine and molecular imaging medical specialists in Australia and New Zealand. The AANMS has a range of objectives that include: promotion and advancement of the practice of nuclear medicine and molecular imaging, the development and delivery of practice and training site accreditation programs, research coordination, training and CPD program development, trainee support, referrer education, representation of the specialty at Commonwealth and State levels and close involvement in all matters concerning the sustainability of nuclear medicine and molecular imaging, including liaison with a range of organisations such as ANSTO and the ANZSNM.