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The Importance of Training, Accreditation and Guidelines for The Practice of Theranostics: The Australian Perspective

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Abstract

Theranostics is a burgeoning development in nuclear medicine which is being rapidly implemented worldwide. There is an increasing need to provide a multidisciplinary framework to the practice of theranostics, to ensure that patients receive this treatment in a safe manner and are provided with security in the knowledge that the health practitioners providing the service are adequately trained. Nuclear medicine experts in Australia have taken the initiative to produce a set of Theranostic guidelines relevant to Australian medical practice. These guidelines encompass specialist qualifications, patient care, radiopharmaceutical production, radiation safety and dosimetry. We propose these guidelines could be adapted for other countries, and promote standards of practice leading to optimal clinical outcomes for patients receiving theranostic treatments.

Noteworthy:

- The rapid expansion of Theranostic services requires guidelines for safe practice (page 3)
- The practice of Theranostic requires a multidisciplinary approach, involving the referrer and service providers, including dosimetry and radiopharmacy (page 4-6)
- Medical practitioners providing theranostic services should be appropriately trained and credentialled (page 6-7)

Theranostics is the buzz word of the century in nuclear medicine, denoting cell targets with paired imaging and therapeutic radionuclides. Theranostic imaging is used to guide subsequent therapy by demonstrating a cellular target expressed at sufficient concentration for a targeted radionuclide. The concept embodies precision medicine, targeting the right treatment for the right patient at the right time. While most often utilised in oncology, it also has potential applications in neurology and cardiovascular disease.

A number of landmark theranostic papers have been published in recent years[1-4]. The success of these trials and subsequent implications on patient management of these radionuclide treatments have driven increasing demand for this form of treatment, not just from treating oncology specialists, but from the patients themselves, especially in this digital age with patients connecting via social media. The other consequence of this success is increasing involvement of small to large pharmaceutical companies in theranostics research and development.

Although this treatment approach is being rolled out in both developed and developing countries around the world, there are few consensus statements with regards to the overall safe practice of theranostics. There are individual 'best practice' statements and guidelines[5,6], and the IAEA has developed a "Training Curriculum for Nuclear Medicine Physicians"[7]. This technical document states that there should be an understanding of the general principles of treatment using radiopharmaceuticals and unsealed radioactive sources, including the theranostics approach for personalised medicine. Unfortunately, it was not within the scope of that document to expand on the specifics required in order to be accredited for the practice of theranostics. The SNMMI Nuclear Medicine Global Initiative on Theranostics is currently working on a universal approach to the practice of theranostics.

In Australia, the peak body of nuclear medicine medical practitioners – AANMS, The Australasian Association of Nuclear Medicine Specialists – have produced a *Position Statement on the Practice of Theranostics in Australia*[8]. This statement was produced in conjunction with representatives from the multidisciplinary membership of the Australia and New Zealand Society of Nuclear Medicine (ANZSNM), including medical physicists, radiopharmaceutical scientists, nurses and nuclear medicine technologists. This position statement provides a consensus on recommendations regarding the care of patients receiving theranostic therapy and to support the provision of safe, high quality, targeted care by qualified professionals in this area. These recommendations include, but are not limited to: identifying the optimal workplace and facility requirements for the production and administration of a radiopharmaceutical; specialist training requirements; patient workflow and multidisciplinary team requirements. It covers some essential prerequisites for the practice of theranostics, including the qualifications of a Theranostics Specialist, appropriate patient selection for theranostics treatment, individualising treatment plans and departmental requirements, including radiopharmaceutical production and quality control, radiopharmaceutical administration and discharge requirements.

This position statement outlines the common concepts which need to be understood by theranostic specialists. There are a wide range of theranostic therapies which are currently available with more on the horizon. The most important components of theranostics considered

in the development of these guidelines include acknowledging the differences and complexities involved in managing patients, developing a good understanding of the breadth of treatments available, and the need for a strong multidisciplinary approach to patient management. There is also an inherent need to understand the patient's objectives in regards to treatment and to ensure that patient consultation is an essential component of determining optimal patient management.

Synopsis of AANMS Position Statement

1) The Theranostics Specialist

In the AANMS Position statement, a Theranostics Specialist is defined as a qualified Nuclear Medicine Specialist trained in the practice of theranostics by the Committee for Joint College Training in Nuclear Medicine, which oversees Nuclear Medicine training in Australia with representation from the Royal Australasian College of Physicians (RACP) and Royal Australian and New Zealand College of Radiologists (RANZCR). In order to obtain accreditation in theranostics, a qualified Nuclear Medicine specialist in Australia will need to meet specified accreditation and training requirements as outlined below. PET and SPECT interpretation is fundamental to determining suitability for treatment, dosimetry and response assessment for theranostics practice, and Nuclear Medicine provides this expertise. In Australia, Nuclear Medicine training includes a wide range of adult and paediatric imaging with radiopharmaceuticals, radionuclide therapy experience including thyroid cancer, and radiation protection principles and legislative requirements for administering radiopharmaceuticals. The requirement for sub-accreditation in Theranostics within our specialty group recognises the importance of advanced training and experience in this emerging area, and the lead role of Nuclear Medicine in this field.

2) The Patient

Clinical consultation is an essential step for proper evaluation of a patient's suitability for radionuclide therapy, including a full clinical assessment of the patient's medical condition and evaluation of the appropriate molecular imaging studies for the theranostic agent to be given. Careful imaging assessment underpins the decision making process regarding the appropriateness of radionuclide therapy for each patient. This imaging must also be performed in an appropriate time frame relevant to the condition being treated in order to minimise disease progression/transformation which may impact on treatment efficacy. Again, this should be performed in a multidisciplinary setting which enables accurate and shared discussion of all imaging and clinical aspects of patient care. If treatment is recommended, the patient must be provided with the practical aspects and logistics of treatment, including any potential side effects and complications, management of the side effects and long term complications. The radiation protection issues relevant for the patient and family members must be provided. Once fully informed the patient can decide if he/she will proceed with treatment and written informed consent must be obtained.

Post-treatment, there should be follow up assessment with the treating theranostics specialist according to local institutional practice, with assessment of toxicities, imaging and pathology results as needed, to determine whether the patient remains suitable for further cycles of

radionuclide therapy, and if so, whether any dose modifications are required. There should be ongoing multi-disciplinary involvement with shared care between the referring oncology specialist and the theranostics specialists through treatment to ensure optimal holistic disease management. This is particularly important in patients with more aggressive disease and pain control requirements. Shared care can involve alternating visits between the oncology and theranostics specialists (such as at 3 weekly intervals). A multi-disciplinary team (MDT), also known as a "tumour board" may also be of value, not only at treatment onset but at seminal stages of treatment (particularly premature cessation and any complications), and to consider and/or co-ordinate other therapies if appropriate.

3) Radiopharmaceutical Production

Depending on the relevant local regulations, radiopharmaceuticals may be produced by a central radiopharmacy or a local hospital-based radiopharmaceutical laboratory. The AANMS guidelines does cover the specific requirements, and in alignment with our local regulatory requirements in Australia, the radiopharmaceutical can be manufactured in a departmental radiopharmacy by a trained radiopharmaceutical scientist using appropriate standard operating procedures (SOP) under Good Laboratory Practice (GLP) adopted for continued process control and high quality standards. Where applicable, radiopharmaceuticals should be prepared according to regulatory and monograph guidelines. The entire manufacturing process should be documented on a batch record or worksheet, and staff training and compliance to this procedure should be recorded. Deviations to this procedure should be documented according to site protocols. A risk-based approach to process validation should be completed prior to preparing radiopharmaceuticals for human use.

Equipment used in the manufacturing and quality control testing of radiopharmaceuticals should be certified at installation and routine checks to ensure reliability in operation, and ongoing maintenance and use logs for critical equipment is also recommended. Radiopharmaceutical production in commercial radiopharmacies is performed under Good Manufacturing Practice (GMP) guidelines.

The final review of product quality remains the responsibility of the administering theranostic specialist.

4) Medical Radiation and Dosimetry

Good radiation safety practice both within the department and in the general population must be maintained according to local regulations. This would commonly involve medical physicist and radiation safety officers, in the development of the SOP. For treatments that are given as outpatients, the medical physicist's advice is used to decide when the patient can be released from the treating facility to either their home, another residence or back to the hospital ward. Once released, the patient needs to be aware of the radiation protection guidelines that they should follow and for the period of time that these apply. This advice can be given by a theranostics medical specialist, a trained medical physicist or nuclear medicine technologist. Any departure from normal procedures, such as a spill or an extravasated injection, will require an objective assessment of the likely implications and expert knowledge of the procedures that

should be undertaken to mitigate the effect on patients. The medical physicist also plays a critical role in assisting with dosimetry and individual dose planning, as required.

Sites should have specific guidelines for each radiotherapeutic administration, with site specific medical, nursing and technologist protocols, as each group will often have important roles in supervising the patient before, during and after treatment and may coordinate necessary care arrangements. Nursing staff will also administer required pre-medications for the specific radionuclide therapy and any necessary preparatory infusions (*e.g.*, amino acids).

All departments should have SOP guidelines for delivery of therapeutic radiopharmaceuticals, to ensure absolute safety of staff, patients and the general public.

All SOPs developed should be endorsed by both the Medical Physicist involved in the delivery of care at that site and the theranostics medical specialists directly responsible for care at the treatment facility. In Australia, a qualified Nuclear Medicine Medical Physics Specialist accredited with the Australasian College of Physical Scientists and Engineers in Medicine (ACPSEM) must oversee this, either actively or through the use of SOP.

Training and Accreditation

All medical specialists seeking to establish proficiency in theranostics are required to achieve the following skills during their training program:

- Understanding of the physiology and radiation physics employed in Theranostics, including understanding of the radiobiology of therapeutic nuclear medicine
- Patient selection (including molecular imaging assessment and correlation) and preparation
- Understanding standard of care therapies for different cancer subtypes
- Understanding of how theranostics treatments fit optimally with other cancer treatment options and when it is most appropriate for theranostics to be administered in each patient journey (right treatment for the right patient at the right time) based on existing evidence.
- Understanding the indications, contraindications, and management of adverse events
- Radiation protection of patient, staff and general public

The AANMS document has provided some requirements for the two-level accreditation which can be provided. Both include a variety of 'live' and case-based learnings, with a range of therapies and documentation for both prospective and retrospective training. In recognition of prior practice, a "legacy provision" category has been developed for current nuclear medicine specialists to apply to be credentialled according to their appropriate level over the last 3 years. The accreditation levels are as follows:

General Accreditation
Completion of the minimum additional training requirements and/or Legacy Provisions for specialists in nuclear medicine will qualify the applicant for *General Accreditation* allowing for participation in providing theranostic services. These requirements are:
1. Experience with >50 therapies by initial consultations and/or administrations within the last 3 years
2. Participation in multidisciplinary discussion of >50 cases
3. Ongoing participation in relevant CPD activities (e.g. conferences, courses)

Advanced Accreditation
Practitioners who have extensive experience may apply for *Advanced Accreditation*.
Advanced accredited specialists will be allowed to provide training and are a requirement for site accreditation. These requirements are:
1. Clinical experience which encompasses >120 therapy initial consultations and/or administrations within the last 3 years
2. Participation in multidisciplinary discussion of >100 cases
3. Ongoing Participation in relevant CPD activities (e.g. conferences, courses)
4. Participation in recognised research in the field

The training site requirements are also outlined, but the minimum level includes the presence of an accredited theranostics specialist onsite during the delivery of the therapy, and other necessary staff. There should be updated protocol manual including general provisions for administration of radionuclide therapies and for each specific therapy offered, including roles of medical, radiopharmaceutical scientist, physicist, nursing and administrative staff, protocols for radiopharmaceutical dispensing, labelling and disposal (as required). Regular multidisciplinary team meetings which encompass all theranostic applications employed at the site is also important.

Theranostics Committee

The committee will aim to promote a collaborative and consistent model of theranostic training and service delivery, with a multidisciplinary representation from ANZSNM, the relevant Colleges/stakeholders and patient representative. The Committee's role is to formulate and review guidelines for training in theranostics, provide and review suitable training courses, advice on theranostic research initiatives, and advice to government regarding theranostics. It should be noted that the training courses in theranostics do not necessarily supplant the need for experiential training, which is the most important aspect in the provision of theranostics.

Conclusion
Whilst theranostics has increasing importance in the future of nuclear medicine there is a constant need to ensure that this is delivered by the most qualified specialists in the field, which in Australia is the appropriately trained Nuclear Medicine Specialists. The AANMS Position Statement is the first local foray into addressing this issue but can be adapted to the requirements of any jurisdictions across the world.

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