**Radiopharmaceutical Sciences**

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Topic cover: Introduction of Radio pharmaceutics, **Radiopharmaceutical Sciences Council,** Characteristics of radiopharmaceuticals, Conflicts between radiation and aseptic regulations, Personnel monitoring, Opportunities

**1.1 Introduction:**

Radiopharmacy (= Nuclear pharmacy) is a branch of pharmacy, which deals with the preparation, characterization and quality of radioactive materials for use in nuclear medicine procedures A Radiopharmaceutical (radiotracer, tracer) is a radioactive compound for diagnosis and therapy of human diseases.

Radiopharmaceutical science is a multidisciplinary field encompassing chemistry, physics and biology. It is the science of incorporating a suitable radionuclide into a pharmaceutical biologically active molecule in vivo physiological or biochemical processes.

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The resulting radiopharmaceuticals are used in diagnostic imaging or therapy of patients. A Radiopharmaceutical Scientist (RPS) is a specialist professional with a chemistry, pharmacy or sciences background and is involved in the design, manufacture and analysis of radiopharmaceuticals.

By utilising their scientific knowledge and analytical skills, RPS also provide knowledge and guidance on the safe and efficacious use of these products to ensure their suitability for clinical application.

A qualified RPS has postgraduate qualifications and suitable experience such that they are eligible for admission to the Register of Radiopharmaceutical Scientists administered by the Australian College of Physical Scientists and Engineers in Medicine (ACPSEM). The RPS training, education and assessment program (TEAP), also administered by ACPSEM, guides a new university graduate through the required mentored work experience to become eligible for professional certification as a qualified RPS.

**1.2 Radiopharmaceutical Sciences Council** :

The **Radiopharmaceutical Sciences Council** is made up of members of the SNMMI who have a common interest in the radiopharmaceutical sciences. It has been set up for the purpose of providing a forum to; discuss and disseminate information relating to radiopharmaceutical sciences, promote and encourage basic research and applied technology in the radiopharmaceutical sciences, and provide the SNMMI information relating to the radiopharmaceutical sciences.

The mission of the Radiopharmaceutical Sciences Council is to: provide a forum for members with similar interests; provide expertise in the field of interest to the membership; foster education in research and application of radiopharmaceutical sciences; provide outreach to other professionals and organizations; nurture new membership into the Society and serve as a resource to SNMMI Leadership.

The Radiopharmaceutical Sciences Council encourages all professionals within SNMMI to consider being members, as your input is needed to help promote and develop the many aspects of the Radiopharmaceutical Sciences.

**1.3 Characteristics of radiopharmaceuticals:**

A radiopharmaceutical is a pharmaceutical that, when ready for use, incorporates one or more radionuclides (radioactive isotopes).

There is no dose-response relationship in this case, which thus differs significantly from conventional drugs. Radiation is an inherent characteristic of all radiopharmaceuticals, and patients always receive an unavoidable radiation dose. In the case of therapeutic radiopharmaceuticals, radiation is what produces the therapeutic effect.

A radiopharmaceutical can be as simple as a radioactive element such as 133Xe, a simple salt such as 131I-NaI, or a labelled compound such as 131I-iodinated proteins and 99mTc-labeled compounds.

Usually, radiopharmaceuticals contain at least two major components:

• A radionuclide that provides the desired radiation characteristics.

• A chemical compound with structural or chemical properties that determine the in vivo distribution and physiological behaviour of the radiopharmaceutical.

Radiopharmaceuticals should have several specific characteristics that are a combination of the properties of the radionuclide used as the label and of the final radiopharmaceutical molecule itself.Radiopharmaceuticals are used for diagnosis or therapeutic treatment of human diseases; hence nearly 95% of radiopharmaceuticals are used for diagnostic purposes, while the rest is used for therapy.

Radiopharmaceuticals usually have no pharmacologic effects, as they are used in tracer quantities.

**1.4 Conflicts between radiation and aseptic regulations:**

There can be conflicts between the requirements of different regulatory systems. However, there are also areas of agreement.

Specialist trained staff are required and meticulous record keeping is important. However, even within these areas, there are conflicts.

Radioprotection requires handwashing facilities at the perimeter of the controlled area, while the medicines inspectors don’t want a sink anywhere near a cleanroom. Radiopharmacy managers must find a delicate balance to satisfy both sets of inspectors.

For example, segregation of activities, with change of apparel and dedicated equipment, minimises cross contamination with both radioactivity and microbes, as does a separate air handling system and the use of containment hoods/glove boxes.

For radioprotection, the production area should be at negative pressure relative to the outside world (containment of gaseous or aerosol discharge), while pharmaceutical aseptic units are at positive pressure to minimise ingress of microbes.

The compromise is a negative pressure isolator within a positive pressure room. From a pharmaceutical point of view, there should be a minimum number of trained staff, whereas for radioprotection there should be a rotation of staff to share the radiation dose.

**1.5 Personnel monitoring**

All staff classified as radiation workers must wear a personal dosimeter (TLD, film badge, electronic dosimeter). In addition to their regular whole body dosimeter, staff preparing and handling radioactive materials should wear a finger TLD to monitor extremity dose.

Prior to each use, the TLD should be wiped, using an alcohol wipe, and worn inside the glove. Upon leaving the preparation area, the finger TLD should be removed and appropriately stored.

Protective clothing Prior to commencing work in the radiopharmacy, staff should ensure that they wash their hands thoroughly. Before a person enters an area where radioactive substances are handled, any cut or break in the skin should be covered.

Dressings should incorporate a waterproof adhesive strapping. Protective coats or gowns should be worn for preparation and dispensing of radiopharmaceuticals. Disposable gowns offer benefits in terms of maintaining sterility.

 Gloves worn in the LAFC or contained workstation must be powder free in order to prevent clogging of the air filters within the cabinet. Alcohol rub should be rubbed onto gloves and allowed to evaporate before entering the LAFC.

After handling radioactive materials, gloves must always be removed and disposed of as radioactive waste before handling/touching any other materials/surfaces within the radiopharmacy. Hands should be washed again after removal of gloves.

Upon leaving the radiopharmacy, disposable gowns should be removed. Prior to disposal, they should be stored as radioactive waste until monitoring confirms that they are at background radiation levels.

Protective equipment The use of protective equipment, when handling radioactive materials, can have a significant impact on reducing staff dose.

Laboratories and other work areas for manipulation of unsealed radioactive substances should be provided with equipment kept specifically for this purpose, and should include the following.

1. tools for maximising the distance from the source, for example tongs and forceps,

2. syringe shields,

3. vial shields,

4. drip trays for minimising the spread of contamination in the case of spillage,

5. shielded syringe carriers and

6. decontamination kit

Unshielded syringes or vials should never be used during manipulation of radiopharmaceuticals. Equipment should be stored outside the laminar flow cabinet when not in use and should be cleaned regularly in accordance with local recommendations.

**1.6 Regulation**

As radiopharmaceutical sciences produces radioactive materials, the facility requires authorization from the [Canadian Nuclear Safety Commission (CNSC)](https://nuclearsafety.gc.ca/eng/).

Finally, in addition to federal regulatory agencies oversight, the Radiopharmaceutical Sciences Program has attracted highly qualified experts (i.e. cyclotron engineer, medical physicist, radiochemist, radiopharmacists, quality assurance professional and technologists) who are committed to providing a safe and quality service.

These extensive regulatory processes must be followed during the construction of the facility, the installation of the cyclotron and during operation. Following authorization to operate, the CNSC periodically audits the facility to ensure it is following the guidelines and is operating safely.

In addition, the radiopharmaceuticals prepared at the facility are regulated by [Health Canada](https://www.canada.ca/en/health-canada.html) providing oversight of the manufacturing and quality of the medical isotopes and radiopharmaceuticals produced onsite.

**1.7 Opportunities:**

 1. Commonwealth funding exists for training positions for Radiation Oncology Medical Physicists (ROMPs) and Diagnostic Imaging Medical Physicists (DIMPs). For NSW to take advantage of that opportunity, more of a coordinated approach is required.

2. Assist the development of online training modules for the Masters of Radiopharmaceutical Science course – to provide for distance educations and less time off the job.

3. Succession management. Retiring practitioners must be able to prepare successors. Availability of experienced certified practitioners for mentoring will impact on the availability of training.

3. Increasing intake into the Masters Degree in Radiopharmaceutical Science at Macquarie University with incentives.

4. Establishing and strengthening relationships between health services and educational institutions.

**Summary & Conclusion**:

Radiopharmacy and radiopharmaceutical preparation is multi-disciplinary endeavor. There is a clear trend from decentralized to centralized radiopharmaceutical production with qualified personnel in qualified environment due to increasing regulations Pharmaceutical, (radio)chemical and radiophysical radiation protection know-how is essential Education of radiopharmacists is necessary at the University level (master or higher) to cope with complexity International standards have to be achieved to shape the future of radiopharmacy.

**Refrences:**

1. Marcu, L.; Bezak, E.; Allen, B.J. Global Comparison of Targeted Alpha vs. Targeted Beta Therapy for Cancer: In Vitro, in Vivo and Clinical Trials. Crit. Rev. Oncol. Hematol. 2018, 123, 7–20. [CrossRef] [PubMed]

2. Allen, B.J.; Huang, C.-Y.; Clarke, R.A. Targeted Alpha Anticancer Therapies: Update and Future Prospects. Biologics 2014, 8, 255–267. [CrossRef] [PubMed]

3. Knapp, F.F.; Dash, A. Therapeutic Radionuclides Decay with Particle Emission for Therapeutic Applications. In Radiopharmaceuticals for Therapy; Springer: New Delhi, India, 2016; pp. 25–35.

4. Holik, H.A.; Uehara, T.; Nemoto, S.; Rokugawa, T.; Tomizawa, Y.; Sakuma, A.; Mizuno, Y.; Suzuki, H.; Arano, Y. CoordinationMediated Synthesis of 67 Ga-Labeled Purification-Free Trivalent Probes for In Vivo Imaging of Saturable Systems. Bioconjugate Chem. 2018, 29, 2909–2919. [CrossRef]

5. Kruijff, R.M.; Ht, W.; Ag, D. A Critical Review of Alpha-Radionuclide Therapy-How to Deal with Recoiling Daughters? Pharmaceuticals 2015, 8, 321–336. [CrossRef]

6. Wick, R.R.; Nekolla, E.A.; Gaubitz, M.; Schulte, T.L. Increased Risk of Myeloid Leukaemia in Patients with Ankylosing Spondylitis Following Treatment with Radium-224. Rheumatology 2008, 47, 855–859. [CrossRef]

7. Vanpouille-Box, C.; Hindré, F. Nanovectorized Radiotherapy: A New Strategy to Induce Anti-Tumor Immunity. Front. Oncol. 2012, 2, 136. [CrossRef]

8. Murshed, H. Radiation Biology. In Fundamentals of Radiation Oncology; Elsevier: Amsterdam, The Netherlands, 2019; pp. 57–87.

10. Zukotynski, K.; Jadvar, H.; Capala, J.; Fahey, F. Targeted Radionuclide Therapy: Practical Applications and Future Prospects: Supplementary Issue: Biomarkers and Their Essential Role in the Development of Personalised Therapies (A). Biomark. Cancer 2016, 8 (Suppl. S2), 35–38. [CrossRef]

11. Kassis, A.I. Therapeutic Radionuclides: Biophysical and Radiobiologic Principles. Semin. Nucl. Med. 2008, 38, 358–366. [CrossRef] 13. Boros, E.; Packard, A.B. Radioactive Transition Metals for Imaging and Therapy. Chem. Rev. 2019, 119, 870–901. [CrossRef] [PubMed]

12. Al-Suqri, B.; Al-Bulushi, N. Gallium-67 Scintigraphy in the Era of Positron Emission Tomography and Computed Tomography: Tertiary Centre Experience. Sultan Qaboos Univ. Med. J. 2015, 15, e338–e343. [CrossRef] [PubMed]

13. Othman, M.F.B.; Verger, E.; Costa, I.; Tanapirakgul, M.; Cooper, M.S.; Imberti, C.; Lewington, V.J.; Blower, P.J.; Terry, S.Y.A. In Vitro Cytotoxicity of Auger Electron-Emitting [67Ga]Ga-Trastuzumab. Nucl. Med. Biol. 2020, 80–81, 57–64. [CrossRef] [PubMed]

 14. Velikyan, I. 68Ga-Based Radiopharmaceuticals: Production and Application Relationship. Molecules 2015, 20, 12913–12943. [CrossRef]

15. Meisenheimer, M.; Saenko, Y.; Eppard, E. Gallium-68: Radiolabeling of Radiopharmaceuticals for PET Imaging—A Lot to Consider. In Medical Isotopes; IntechOpen: London, UK, 2021.

16. Frigerio, B.; Franssen, G.; Luison, E.; Satta, A.; Seregni, E.; Colombatti, M.; Fracasso, G.; Valdagni, R.; Mezzanzanica, D.; Boerman, O.; et al. Full Preclinical Validation of the 123I-Labeled Anti-PSMA Antibody Fragment ScFvD2B for Prostate Cancer Imaging. Oncotarget 2017, 8, 10919–10930. [CrossRef]

17. Bajaj, N.; Hauser, R.A.; Seibyl, J.; Kupsch, A.; Plotkin, M.; Chen, C.; Grachev, I.D. Association between Hoehn and Yahr, MiniMental State Examination, Age, and Clinical Syndrome Predominance and Diagnostic Effectiveness of Ioflupane I 123 Injection (DaTSCANTM) in Subjects with Clinically Uncertain Parkinsonian Syndromes. Alzheimer’s Res. Ther. 2014, 6, 67. [CrossRef]

18. Stevens, L.A.; Claybon, M.A.; Schmid, C.H.; Chen, J.; Horio, M.; Imai, E.; Nelson, R.G.; Van Deventer, M.; Wang, H.-Y.; Zuo, L.; et al. Evaluation of the Chronic Kidney Disease Epidemiology Collaboration Equation for Estimating the Glomerular Filtration Rate in Multiple Ethnicities. Kidney Int. 2011, 79, 555–562. [CrossRef]

19. Schwarz, S.B.; Thon, N.; Nikolajek, K.; Niyazi, M.; Tonn, J.C.; Belka, C.; Kreth, F.W. Iodine-125 Brachytherapy for Brain Tumours-a Review. Radiat. Oncol. 2012, 7, 30. [CrossRef]