Radiopharmacy: a scarce and specialised skill

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Introduction
Radiopharmacy is a specialisation that is recognised by the South African Pharmacy Council (SAPC). In 2009, it was identified as a scarce skill by the Nuclear Technologies in Medicine and the Biosciences working group.

Radiopharmaceuticals are used in the diagnosis and treatment of life-threatening conditions in nuclear medicine, which uses administered radiopharmaceuticals as a source of radioactivity, e.g. gamma rays, positron emission and beta particles. The radiopharmaceuticals are used in a safe, painless and cost-effective way to target body processes and thus to diagnose and/or treat a wide variety of diseases through scintigraphic image interpretation. Radiopharmaceuticals can be used in every major organ system. The images are of body function (through scintigraphy of radiation emission from the organs i.e. ‘hot’ or ‘cold’ areas) as opposed to structure (as in the case of X-rays, which are images of rays transmitted through the body).

Handling of radiopharmaceuticals requires strict pharmaceutical management processes, quality assurance approaches, specific skills (aseptic and radiation safety) and specialised knowledge of radionuclides and related organ targeting. Radiopharmaceuticals localise in the target tissues through a range of physiological mechanisms. They may bind to receptors, be attached to blood cells or simply mimic common elements (for example, 201thallium mimics potassium). Hence the radionuclide can be used alone or linked to a ligand that will transport the radionuclide to a target site. The radiation levels in diagnostic radiopharmaceuticals are fairly low.

There are approximately 40 different radioactive elements that are used alone, or with ligands, to target a specific organ or cell type.

Technetium-99m (Tc-99m) is the most widely used radionuclide as it has ideal imaging properties (γ = 140 keV), is easily available via a molybdenum/technetium generator, and has a relatively short half-life of six hours which allows for adequate imaging time, and yet relatively short patient exposure time.

It is versatile, though difficult, in its chemistry, and will bind to a wide range of molecules or ligands.

The following applies:
- $^{99m}$TcO$_4^-$ (pertechnetate) is taken up by thyroid and salivary glands
- $^{99m}$Tc–MDP (methylene diphosphonate) is a bone tracer
- $^{99m}$Tc–DTPA (diethylenetriaminepenta-acetic acid) is a renal tracer
- $^{99m}$Tc – MIBI (methoxy-isobutyl isonitrile) is a cardiac tracer

The aim of the presentation described in this paper was to provide “snapshots” of the role of the radiopharmacist. The examples used were postgraduate projects from our Department of Pharmacy at Medunsa Campus, which illustrate how a pharmacist who is skilled in this special area can contribute to patient care and research. The projects were conducted with the co-supervision of subject specialists.

The examples cover the following areas of radiopharmacy:
- Radiopharmaceuticals management (quality control, aseptic services and radiation safety)
- Radiochemistry (drug development and stability)
- Radionuclides and organ targeting (clinical).

Radiopharmaceuticals management
The Department of Nuclear Medicine at Dr George Mukhari Academic Hospital, previously called Ga-Rankuwa Hospital, had no radiopharmacy involvement up to 2009. Therefore, our first postgraduate radiopharmacy project (Qatyana, MSc, 2010) addressed the basic principles of radiopharmacy management using the 2008 International Atomic Energy Agency hospital radiopharmacy audit as a data collection tool.
The radiopharmacy audit highlighted shortcomings, which resulted in three follow-on projects to address:

- Radiopharmaceuticals quality control (Kanga, MSc, current)
- Aseptic services (Maringa, MSc, 2012)
- Radiation safety (Tshitake, MSc, 2012).

All of the above projects were addressed by surveys, focus group discussions and the collaborative development of standard operating procedures to promote improved services.

Radiochemistry

**131I-metaiodobenzylguanidine stability and radiochemical purity**

131I-metaiodobenzylguanidine (MIBG) emits destructive radiation (β-) and is used in ablation therapy, e.g. for hyperthyroidism or thyroid cancer.

When linked to MIBG, a norepinephrine analogue, 131I is taken up in adrenergic tumours, e.g. phaeochromocytoma, which are then destroyed by the β- radiation (a short range of activity).

Currently the registration of the 131I-MIBG is for a shelf life of 6 hours, which limits its use to areas within a few hours travel of the production site (Pelindaba). Extending the duration of stability to 48 hours would promote wider geographical availability for use in the ablation of neuroendocrine tumours and phaeochromocytoma malignancy (du Plessis – current MSc).

**Infection and inflammation targeting: immunoglobulin G**

Currently, the choices for infection imaging are expensive (67Ga or 18F-fluorodeoxyglucose positron emission tomography), or require complex processes (radiolabelling of white blood cells).

Infection and inflammation diagnosis would be facilitated through the formulation of a Tc-99m kit to simplify radiolabelling of immunoglobulin G. A freeze-dried, tricine-based formulation has been prepared (Mtshali, MSc, 2013). Currently, it is a two-step kit, but further development work is possible to formulate a one-step kit for easy in-house use in nuclear medicine departments.

**Radionuclides and organ targeting**

**Technetium-99m-ethylenedicysteine-metronidazole in cervical cancer**

Metronidazole (MN) metabolites are trapped inside hypoxic tissue. Tc99m-ethylenedicysteine (EC)-MN will enter the tissue and the radioactive metabolite will be trapped there. Tc99m-EC-MN has previously been studied with regard to strokes, but not cervical cancer. Hypoxic cervical cancer is resistant to chemo- and radiotherapy. A diagnosis of tissue hypoxia would aid clinical decisions (Mdlophane, MSc, 2011).

**Biliary atresia**

Biliary atresia is a neonatal condition which requires a liver transplant. Time can be “bought” with early diagnosis and surgical insertion of a shunt in the bile duct to prevent bile accumulation and hepatic damage. Currently, biliary atresia is diagnosed at our hospital with Tc-99m disopropyl iminodiacetic acid. (When taken up into the liver, the excretion mimics that of bile). Alternative approaches may give faster and more reliable results (Ekosse, MSc, 2013).

**Technetium-99m-methoxyisobutylisonitrile myocardial insufficiency**

Myocardial perfusion is imaged using Tc-99m-MIBI, which accumulates in myocardial mitochondria. The difference between rest and stress scans is used to diagnose myocardial “hibernation”, ischaemia or infarction. The “stress test” scan is performed with dipyridamole, a vasodilator, as a pharmacological stressor in those who cannot exercise.

Patient preparation (the cessation of some drugs, fasting and limited drink intake), as well as drug-related factors (preparation method, relative times of administration of dipyridamole and Tc-99m-MIBI), all affect scan quality and hence accuracy of diagnosis. This study investigated scan quality and related variables in 50 “stress tests”. Optimisation of the process at Dr George Mukhari Academic Hospital will lead to better quality diagnostic scans (Teffu, MSc, current).

**Conclusion**

Radiopharmacy is as challenging and varied as other specialist pharmacy disciplines.

There are only two SAPC-registered radiopharmacy specialists. Radiopharmacists are needed in the public and private sector hospital, nuclear medicine, as well as industry. The estimated current local need is 25 and rising.

Nuclear medicine teams are eager to have pharmacists as part of the group. They realise that the specialised handling of radiopharmaceuticals for advanced therapy and research can only be achieved using pharmacists as part of the team.

Hence progress in nuclear medicine in South Africa, and Africa as a whole, will be facilitated by postgraduate education and training in radiopharmacy.

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