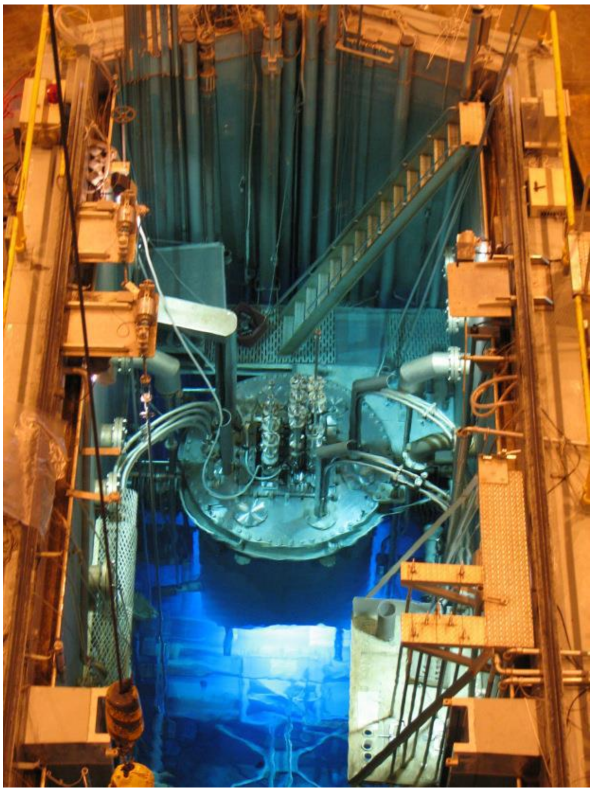
Cancer Association of South Africa (CANSA)

Report on the Importance of Nuclear Medicine for Cancer Patients

Background

The recent shutdown of SAFARI-1, South Africa's only research nuclear reactor at Pelindaba outside Pretoria, drew attention to the importance of Molybdenum-99 for Cancer patients worldwide.

SAFARI-1 is an acronym for South Africa Fundamental Atomic Radiation Installation. The number '1' attached to the name indicates that this was the first nuclear reactor installed in South Africa. SAFARI-1 was originally installed as part of South Africa's nuclear physics programme and was commissioned on 18 March 1965. Today SAFAR-1 is exclusively used for the benefit of mankind with providing products and services both locally and internationally to various industrial and institutional sectors, proving that nuclear technology does, indeed, offer many beneficial applications.



[Picture Credit: SAFARI-1]

The picture of SAFARI-1 shows a view of looking down into the special "pool" where the radioactive rods are stored. The pool is typically at least 12 metres deep, with the bottom at least 4.3 metres below the end of the nuclear rods. The quality of the water in the pool is tightly controlled to prevent the nuclear fuel or its cladding from degrading. The water surrounding the rods actually glows bright blue as can be seen in the photograph. The blue glow is due to a phenomenon called Cherenkov Radiation which is the electromagnetic radiation emitted when a charged particle moves through a dielectric medium at a speed faster than the velocity of light.

Nuclear Medicine

Nuclear medicine is a medical specialty that utilises radioactive isotopes, referred to as *radionuclides,* to diagnose and treat disease. These radionuclides are incorporated

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into *radiopharmaceuticals* and introduced into the body by injection, swallowing, or inhalation. Physiologic/metabolic processes in the body concentrate the different tracers in specific tissues and organs. The radioactive emissions from the tracers are then used to non-invasively image these processes or kill cells in regions where radionuclides have concentrated.

Other types of non-invasive diagnostic procedures - for example, computed tomography (CT) and magnetic resonance imaging (MRI) - can detect anatomical changes in tissues and organs as the result of disease, for example different cancers. Nuclear medicine procedures, however, can often detect the physiological and metabolic changes associated with disease long before any anatomical changes occur. Such procedures can be used to identify disease at very early stages and can also evaluate patients' early responses to therapeutic interventions (treatment of their cancer).

The South African Nuclear Energy Corporation (Necsa) is a producer of a range of medical isotopes that are used for diagnostic purposes and therapeutic treatment of cancer. Many millions of people have reaped the benefits of medical isotopes originating from SAFARI-1. Patients are diagnosed and treated annually in South Africa and internationally with isotopes of which the target material is irradiated within SAFARI-1.

Molybdenum-99 (99Mo)

Molybdenum-99 (99Mo), the radioisotope used extensively as a raw material for Technitium-99, the most important diagnostic nuclear medicine isotope, originally had to be imported into South Africa on a weekly basis. The reason that 99Mo had to be imported weekly is because its half-life is only 66 hours. The half-life of an isotope tells one that the isotope loses half of its power within a certain time – in the case of 99Mo, the half-life is only 66 hours.

Since 1993 SAFARI-1 has become the sole local, and an important international, provider of 99Mo. The nuclear production cycle is initiated with enriched uranium, a fuel fabricated for the manufacture of 99Mo. SAFARI-1 is currently one of the four largest producers of 99Mo and medical isotopes in the world. Other countries that produce 99Mo include Canada, Australia, Belgium and the Netherlands. The United States of America uses 50% of all 99Mo produced in the world.

Because of its relatively short half-life (66 hours), 99Mo cannot be stockpiled for use. It must be made on a weekly or more frequent basis to ensure continuous availability. The processes for producing 99Mo and Technetium generators and delivering them to customers are tightly scheduled and highly time dependent. An interruption at any point in the production, transport, or delivery of 99Mo or Technitium generators can have substantial impacts on patient care.

Technetium-99m Use in Nuclear Medicine

Molybdenum-99 is the radioisotope used extensively as a raw material for technetium-99m (Tc-99m), which is the most important nuclear medicine isotope for diagnostic imaging. Tc-99m is used for the detection of disease and for the study of organ structure and function.

Tc-00m is especially useful for nuclear medicine procedures because it can be chemically incorporated into small molecule ligands and proteins that concentrate in specific organs or tissues when injected or taken into the body. Tc-99m has a half-life of about 6 hours and is used in approximately 80 percent of all nuclear medicine procedures performed worldwide each year.

Tc-99m is a particularly useful imaging radionuclide because it:

- Can be chemically incorporated into radiopharmaceuticals that have affinities for different tissue and organ systems.
- Has a sufficiently long half-life (~6 hours) to be usable in nuclear medicine procedures.
- Emits energetic gamma rays (140 kiloelectron volts [keV]) that can be detected efficiently with widely available camera technologies.
- Can be supplied efficiently to hospitals and clinics using *technetium generators*.
- Provides low patient doses for some procedures because of its short half-life and lack of alpha or beta radiations.

Tc-99m-based radiopharmaceuticals are used to diagnose disease in a large number of tissue and organ systems, including bone, brain, heart, kidneys, liver, and lungs. About 50 percent of Tc-99m utilisation in the United States is in nuclear cardiology, predominantly for myocardial perfusion imaging which images blood flow through heart muscle.

I-131 and Xe-133

I-131 and Xe-133 are products of Uraneum (U-235) fission and are coproduced with 99Mo when U-235 is irradiated with neutrons. I-131 and Xe-133 also have important nuclear medicine applications.

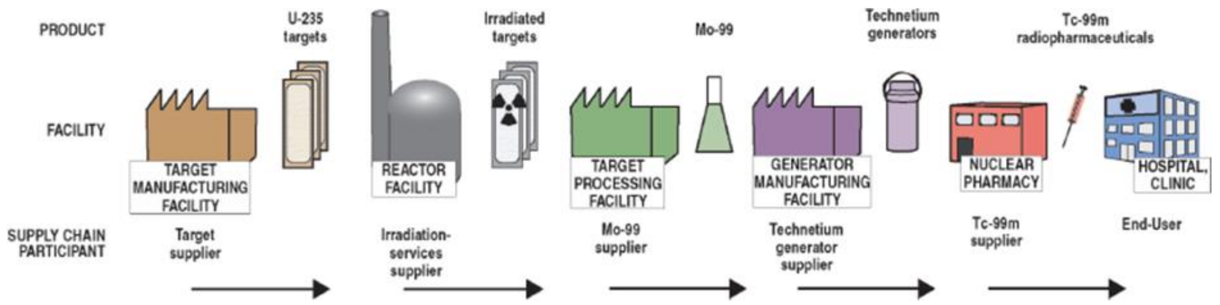
Xe-133 is used to image the distribution and rate of exchange of air in the lungs. It decays with a half-life of ~5.2 days and emits 81 keV gamma rays, which can be detected using existing camera technologies. Xe-133 is the only approved tracer for this application in the United States. Other countries use Technegas™, a radiopharmaceutical containing a dispersion of Tc-99m-labelled carbon, for lung imaging.

I-131 is used as a therapeutic agent to treat several types of disease. Its ~8-day half-life and emission of high-energy beta particles (mean energy ~190 keV) make it effective for killing cancer cells. The most commonly used I-131 therapeutic agents are:

- I-131-labeled sodium iodide, used in the treatment of hyperthyroid disorders and thyroid cancer. Iodine-based therapies are effective for treating these diseases because iodine is naturally taken up by the thyroid.
- I-131-labeled metaiodobenzylguanidin, used in the treatment of neuroblastomas[4] and some cancers of the adrenal glands—for example, pheochromocytoma.

Overview of 99Mo/Tc-99m Supply Chain

Almost all 99Mo for medical use is produced by irradiating targets containing U-235 in research reactors. The supply chain for this production process is graphically illustrated graphically below:



This supply chain is designed to deliver 99Mo/Tc-99m on a weekly or more frequent basis. Such "just-in-time" delivery is essential to the successful operation of the supply chain because 99Mo and Tc-99m have short half-lives (~66 and 6 hours, respectively) and, therefore, cannot be stockpiled. The activity of 99Mo declines by about 1 percent per hour because of radioactive decay. It must be moved through the supply chain quickly to minimise decay losses. The elapsed time from production of 99Mo in a reactor to the delivery of a Tc-99m dose to a hospital or clinic can be as short as 4-5 days.

The quantity of 99Mo in the supply chain is time-dependent because of radioactive decay. The quantity of supply is conventionally measured in *6-day curies*, that is, the amount of 99Mo available 6 days after the point of measurement. The point of measurement is not fixed in the supply chain but is instead determined by supply chain participants to suit their particular needs.

Tc-99m is supplied to hospitals and clinics for use in medical isotope procedures. Tc-99m may be supplied as bulk sodium pertechnetate or as single doses of Tc-99m-labelled radiopharmaceuticals for administration to specific patients. End users can receive Tc-99m one or more times per day depending on their patient loads.

The production of 99Mo from irradiated uranium targets produces four waste streams:

- Solids containing uranium.
- Processing off-gases, primarily the noble gases xenon (Xe-131m, Xe-133, Xe-133m, and Xe-135) and krypton (Kr-85).
- Process liquids from target dissolution.
- Other solid wastes produced during target processing: for example, radioactively contaminated processing equipment.

All of these waste streams are generated in Mo-99 supplier facilities and requires specialised management.

Shortage of Technitium-99m Threatens Cancer and Other Patients
Each year more than 20 million people in the US, two million in Canada, 10 million in Europe, and 14 million in the rest of the world benefit from nuclear medicine tests involving medical isotopes, especially Tc-99m.

Worldwide, there are only five old, high-energy Uranium 235 reactors that produce virtually all of the raw material from which Tc-99m is made. They are in Canada, Belgium, South

Africa, the Netherlands and France. These high-energy nuclear reactors run on Uranium 235, are 40 to 50 years old, and between them have been closed down several times over the last few years.

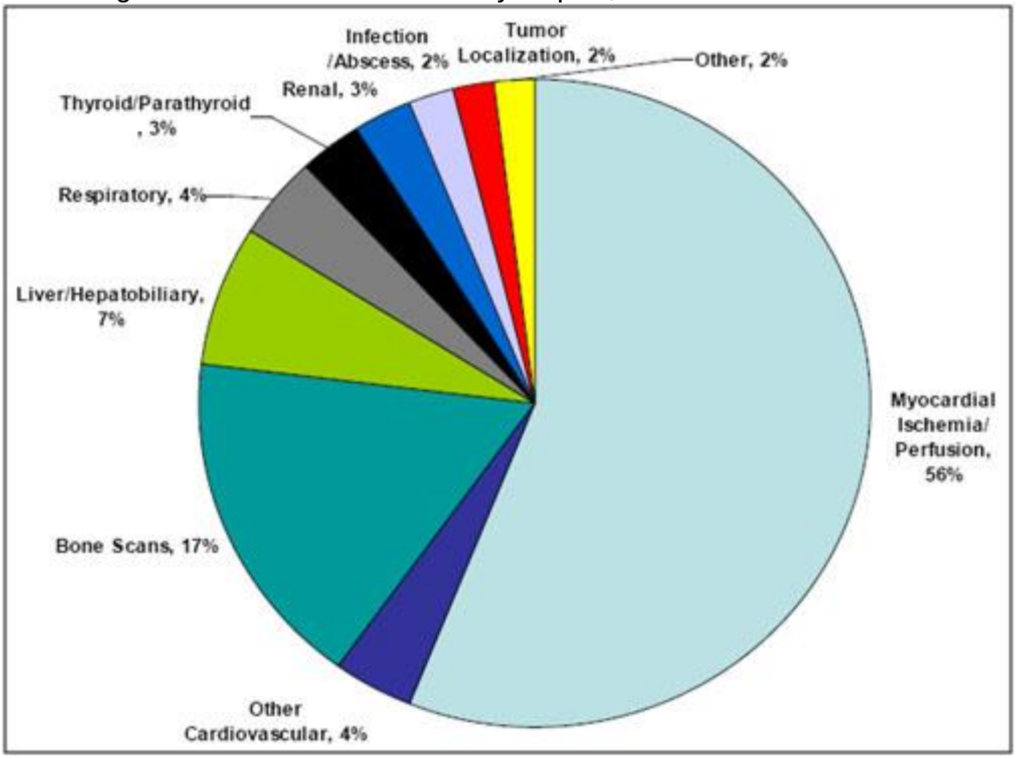
The closure of just one of these reactors can disrupt the security of the global medical isotope supply.

It is now time to add a new phrase to the dictionary of disasters: **Technetium-99m** - also known as Tech-99 or Tc-99m. A shortage of Tc-99m could be life-threatening to anyone who suffers from cancer, heart disease, or a score of other medical conditions. Tc-99m is the radioactive material used in four out of every five nuclear medicine procedures performed.

Tc-99m cannot be stockpiled because it has a short half-life. Doctors and hospitals that use this material must be re-supplied every 67 hours to have a continuous supply.

An example of the critical value of Tc-99m: If the 41st president of the United States of America, George H.W. Bush, had not been tested using Tc-99m, his diagnosis of Grave's Disease (a type of autoimmune problem that causes the thyroid gland to produce too much thyroid hormone) might have come very later, after significant medical problems had progressed.

According to a Canadian Parliamentary Report, Tc-99m is utilised in Canada as follows:



(Parliament of Canada).

<u>The importance of the availability of Tc-99m</u>:

The nuclear medicine procedures that are most affected by shortages in Tc-99m include, cardiac imaging, bone scintigraphy (including tumour metastases), lung investigations, and thyroid, parathyroid and kidney function and analysis imaging. Each of these procedures uses Tc-99m as the preferred isotope.

If the Tc-99m dose is too low when conducting tests, it will result in both false-negative and false-positive results that could potentially lead to less effective imaging scans

To minimize the effect on patient care, the nuclear medicine community has employed a number of mitigation strategies.

Common approaches include:

- Prioritising patients - Priority cases include sentinel lymph nodes, paediatric cases, situations in which other imaging modalities are specifically contraindicated (e.g., patients in renal failure where intravenous contrast may not be given for computed tomography [CT] scan or magnetic resonance imaging [MRI])
- Treating only priority patients
- Rescheduling non-urgent scans
- Referring patients to alternate diagnostic modalities where possible
- Delaying procedures
- Cancellation of procedure
- For some procedures where there really is no alternative, such as hepatobiliary scanning for suspected gall bladder cancer and disease, sentinel lymph node determination for cancer surgery, and kidney function investigations, a shortage of Tc-99m may be critical.

(Brozaks & Jindra, 2009; CADTH).

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