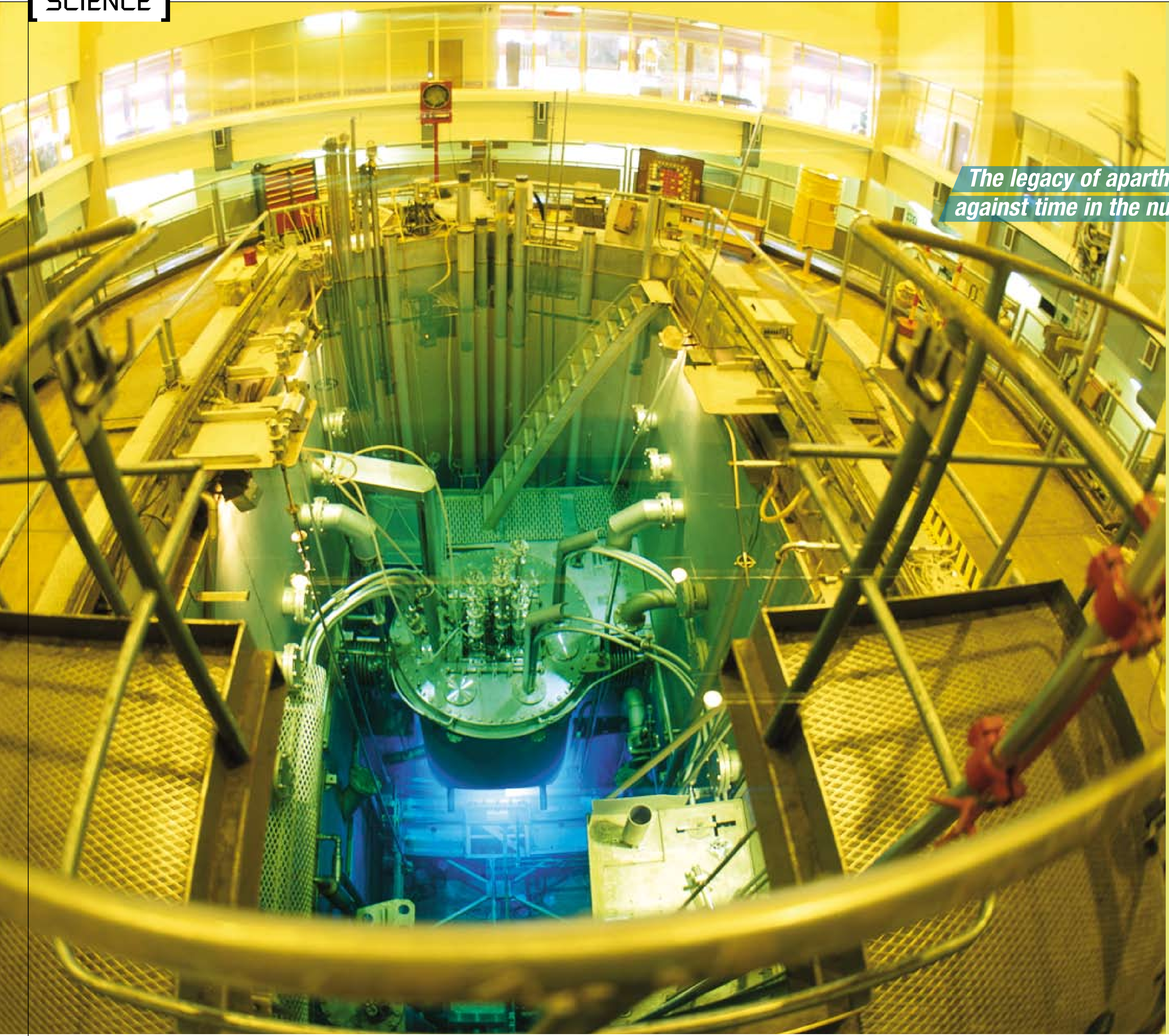


Isotopes, Inc.

The legacy of apartheid's atomic bombs: it's a race against time in the nuclear medicine business

Top: Radiochemical production hot cells. Above: Sealed radioactive source (Ir-192) production. All of these operations take place behind massively thick walls and lead glass. Opposite: The eerie blue glow of the SAFARI-1 nuclear reactor at Pelindaba.

Every night, international flights out of Johannesburg's OR Tambo airport carry about half a dozen anonymous-looking metal canisters the size and shape of small milk churns. But these are no ordinary containers.

For one thing, they're heavy. Very heavy.

More importantly, they're marked with the distinctive *Danger: Radioactive* logo. That's because they hold radioactive isotopes that are on their way to medical technologists around the world.

Here's the thing: by the time the aircraft touch down, a big slice of the volatile cargo has already died off. That's the nature of highly radioactive material, some of it with a half-life of just hours. In fact, the deterioration starts the moment the raw material is produced. And the clock keeps ticking relentlessly.

"The big thing with this isotope game," says NTP Radioisotopes (Pty) Ltd boss Don Robertson, "is that there is no bloody shelf life."

From bombs to medicine

Robertson heads an organisation that's quietly established itself as a major player in the highly competitive isotope business: NTP, a division of the South Africa's nuclear custodians, the Nuclear Energy Corporation of SA. NTP's job is to supply raw materials worldwide for everything from silicon chip doping to molecular imaging.

And it all began within a massive organisation, secluded in the valleys of Pelindaba about 30 km west of Pretoria, that was focused on "national strategic objectives" that included, among a host of other nuclear technology-related activities, the making of highly enriched uranium (>90 per cent U-235) for nuclear bombs.

Today the SAFARI-1 nuclear reactor uses fuel that was produced as part of the nuclear weapons programme. And the critically important medical isotopes that NTP makes and distributes worldwide are made by first bombarding plates of highly enriched uranium with intense beams of neutrons in the reactor.

Several scientists working on the bomb and other "strategic" programs (such as uranium enrichment for commercial nuclear reactors – about 4,5 per cent U-235 – and nuclear fuel assembly prioduction for Koeberg nuclear power station) are now those running the large and growing radio-isotope business at Pelindaba.

Nuclear physicist Robertson himself was one of those who faced a jobless future when the weapons programme was canned in the early 1990s. "Historically, this place had about 8 000 people working here. One of the options would have been to close it down," he says.

Last year, thanks to the increasingly successful and lucrative production of isotopes for NTP, SAFARI-1 was the world's most effectively used reactor.

Of the 15 million nuclear medicine procedures performed worldwide annually, about one-fifth use radiopharmaceuticals produced from NTP radiochemicals. Over 150 000 of these are done locally.

"Our business is export-oriented. Easily 95 per cent is in forex," says Robertson.

The company is riding the crest of a wave. "Nuclear is the flavour of the month – the energy as well as new science."

In fact, its biggest trading partner is also its biggest competitor: MDS Nordion of Canada. NTP is a big player in yttrium-90, which it supplies to MDS for use in radioimmunotherapy, a promising new area of cancer treatment. This involves specially engineered "cancer-seeking" antibodies carrying radiation payloads to destroy malignant cells.

Because of their products' volatility, the big 4 international suppliers of Moly-99 provide mutual backup to ensure a steady supply.

"There will be times when you can't produce," says Robertson. "The patient has to have the product. You are obliged to have a network." If there's a problem, it's bad enough for the likes of NTP that radiation gets a bad name. "What's worse is that the patient suffers."

Cooking up an isotope

Of course, getting the product to market is only one aspect of the operation. Manufacturing is a finicky business. How finicky? Well, you try picking up tiny scraps of material on the other side of a lead-brick wall a metre and a half thick, looking through lead glass nearly a metre thick. Irradiated material is manipulated and processed in a row of shielded "hot cells", to extract the desired quantities and types of radioisotopes.

In effect, these are miniature chemical factories more or less capable of creating the entire periodic table.

Once purified, the resulting material, mostly molybdenum-99 (see "Isotopes and what they do"), is sent on its way in tablet, liquid or powder form. At its destination, a medical technologist processes the radioisotope in a "generator" – basically a vial of the isotope in a shielded enclosure. To create a specific concentration of isotopes, a certain amount of chemical solution is passed through the generator and mixes with any "daughter" isotope (technetium-99) present. The resulting isotope-containing fluid is ready for use.

In case you were wondering, no, there haven't been any unpleasant incidents in transit. And even if there were, the precautions include several centimetres of shielding containing depleted uranium (nearly twice as dense as, and no more toxic than, lead). The canister itself is NTP's own design, subject to rigorous nuclear industry and air transport testing. Among other things, the container needs to remain intact when dropped from 9 metres on to a spike.

In the world of specialised radiation-based products for healthcare and industrial markets NTP says it is now counted amongst the top companies of its kind. It serves customers in more than 50 countries on five continents.

Medical technology is not the only field to benefits from NTP's expertise, either. For instance, the tritium generated at Pelindaba is used in luminous equipment for everything from signage to gun sights.

Their product portfolio consists of five main areas:

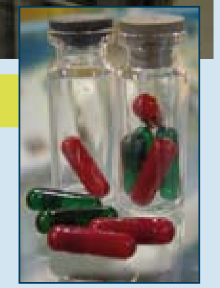
- Radiopharmaceuticals for diagnostic (imaging) and therapeutic purposes.
- Irradiation: Neutron Transmutation Doping of Silicon crystals, used in microchips, and other neutron irradiation services.
- Radiochemicals such as molybdenum-99 and iodine-131, produced in bulk for the manufacture of various radiopharmaceutical products.
- Radioactive sealed sources for industry to be used in non-destructive testing or industrial gauging, and process control applications such as crack testing.
- Radiation technology products, including radioluminescent light sources and safety signage.

"When we started out, I was travelling the world," Robertson says. "Nobody knew me. And they could not believe that we could be making these isotopes." So they started supplying the little guys – China, India, Australia – in an effort to establish a track record.

Clearly, it's working. And, although NTP is located far away from world markets, it has one big advantage: "We control the logistics," says Robertson. They've designed transport containers and established reliable transport.

"Over there, reactors are usually situated far from where they are needed," he says. "In Belgium, the reactor is 350 km from the chemical plant. Here, we're right next door." PM

Top: Checking radiation levels in the container closure area. Middle: Preparing chemicals (cold) for use in radiochem production. Above: The radioisotope payload nestles in the centre of the protective container at right; the blue-and-white plastic container at the left is the "generator" that medical technologists use to derive technetium-99 from the molybdenum-99 parent on site.



Above: Here's where luminous light sources start their lives at the tritium facility. Right, capsules of iodine-131, used in the diagnosis and treatment of thyroid disease.

Isotopes and what they do

An imbalance in the number of neutrons versus protons in an atom's nucleus results in an isotope. In Nature these are stable – an element can have various isotopes – but unstable isotopes can be produced artificially. What makes these unstable isotopes so useful is that they emit radiation.

The two main ways of making radioisotopes are by means of a nuclear reactor or a particle accelerator.

Inside a nuclear reactor, radioisotopes are created by subjecting selected elements to the neutron flux inside the reactor core. They can also be produced in a particle accelerator such as a cyclotron. The accelerated particle collides with target, resulting in radionuclides. Cyclotron reactions are less productive and predictable than those performed in a reactor, and the isotopes produced differ in type. (Incidentally, the acquisition of a cyclotron has put NTP in a position to provide an even wider range of radioisotopes.)

The isotope technetium-99m, used in the vast majority of medical applications, has a half-life of 6 hours. Fortunately, there's a way to buy more time: technetium-99m is produced in the decaying process of a parent isotope, molybdenum-99 – which has a half-life of a little over 2¾ days. So, molybdenum-99 is sent out as the raw material.

Nuclear medicine, which dates back to the 1950s, uses radiation to provide information about the functioning of a person's specific organs. Radiotherapy has been found to be useful in treating many medical conditions, especially cancer.

So what's the big deal? Well, instead of a radiation source looking into the body (X-rays), nuclear medicine uses a radiation source on the inside, looking out. Both bone and soft tissue can be imaged.

Essentially, diagnostic techniques in nuclear medicine are based on radioactive tracers that emit gamma rays.

Radioisotopes are also used as a tracer in conjunction with a carrier that is attracted to cancerous cells. Originally, a gamma camera was used to detect and build up an image taken from various points. Computer-enhanced, the image shows a trained operator whether there are any abnormalities.

Subsequently, Positron Emission Tomography (PET) has improved diagnoses dramatically, notably in cancer treatment. PET uses isotopes in a carrier that targets specific tissue. It produces extremely precise images, thanks to gamma ray reactions resulting from its decay – particularly in combination with computed X-ray tomography (CT) scans. This technique is shedding new light on ailments such as dementia.

In radiotherapy, radiation is used to weaken or destroy particular targeted cells. Its oldest function was the use of iodine-131 to diagnose and treat thyroid disease.

In cancer treatment, radiotherapy makes use of the principle that rapidly dividing cells – cancer cells, for instance – are easily damaged by radiation. The process involves incorporating a radio-isotope into a molecule that has a chemical affinity with the targeted part of the body. The molecule "seeks out" the selected site in the body and the radio-active particle damages the surrounding cells; normal cells recover, but the cancer cells aren't as tough.

The shining lights

Reactor-made

Molybdenum-99 (66-hour half life): The "parent" in a generator that results, after decay, in technetium-99m.

Technetium-99m (6-hour half life): Used for imaging the skeleton and heart muscle in particular. Also used for imaging liver, spleen, kidney (structure and filtration rate), gall bladder, bone marrow, salivary and lacrimal glands.

Cyclotron-made

Carbon-11, nitrogen-13, oxygen-15, fluorine-18: Positron emitters used in PET for studying brain physiology and pathology. Useful in epilepsy, dementia, psychiatry and neuropharmacology.

Source: *www.uic.com.au*