The revolution in nuclear medicine in the 21st century

About the author

Guy Turquet de Beauregard

Honorary President of Nuclear Medicine Europe

Highlights

- **Theragnostic Revolution:** Nuclear medicine has advanced through theragnostics, using the same biological vector for both cancer diagnosis and therapy, with different radioactive tracers.

- **Key Advances in NM:** Progress in molecular biology, radioelement production, AI-enhanced imaging, and hybrid cameras has driven a new era of precision in nuclear medicine diagnostics and treatments.

- **Success in Cancer Treatment:** nuclear medicine has shown promising results in treating cancers like prostate, attracting major investments and expanding research in oncology.

- **Challenges:** nuclear medicine faces logistical and regulatory hurdles, including complex radiopharmaceutical production, short shelf life, and opaque reimbursement processes.

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The renowned journal *Nature* recently published several review articles showing how nuclear medicine (NM) offers a new way of treating cancer.

The aim of this article is to explain how and why this discipline, which dates back to 1940, has been reborn with a new revolution in medicine, thanks in particular to theragnostic, a particular method which uses the same biological vector for both imaging diagnosis and therapy, but with different radioelements as tracer.

The unique role of biology and nuclear physics

The principle of nuclear medicine is based on the substitution of a stable isotope (e.g. Iodine 127) by its radioactive isotope (e.g. Iodine 131), called a tracer, within a chemically or biologically pathology-specific molecule (e.g. a protein or an antibody), called the vector. The combination of vector and tracer forms a radiopharmaceutical. Once injected into the patient, the radiation emitted by this radioactive atom is used, either to diagnose the patient by means of a 3D tomographic image (using the gamma radiation emitted by the tracer), or to treat the patient by means of internal radiotherapy, known as vectorized radiotherapy, using aggressive radiation targeting malignant cells (e.g. beta electron radiation on a cancer cell).
Thus, the unique aspect of nuclear medicine research requires both mastery of the latest molecular or cellular biology, and nuclear physics for the choice and production of radioelements as tracers.
In 2023, almost 2 million NM procedures were carried out in France, and 50 million worldwide, 90% for imaging diagnosis and 10% for internal radiotherapy. While the main applications of NM are in oncology (almost 50%) and cardiology (around 40%), NM covers more than 100 metabolic indications, including neurology.

New factors in the renaissance of nuclear medicine

The major advance in NM is linked to the recent concomitance of 4 factors:

- Current advances in molecular and cellular biology now offer an exceptional range of molecules for new vectors (antibodies, peptides or proteins) that are highly specific to a particular pathology,

- Active research into new radioelements has progressed, particularly for internal vectorized radiotherapy, thanks to new means of large-scale production (reactors and cyclotrons),

- Fast computing and artificial intelligence are now making possible to considerably improve, the productivity of imaging diagnosis times, the reliability of NM imaging procedures and the associated R&D,

- The advent of hybrid cameras combining simultaneous imaging by the same camera, using an X-ray scanner and a 3D gamma emission tomograph, has been a major advance for nuclear physicians and radiologists. These cameras offer a precise morphological image with the scanner and a functional and metabolic image with the NM. This is the case for over 200 PET scans* in France, which now routinely offer oncologists a unique diagnostic tool.

An emblematic application of theranostics to the prostate

The potential of theragnostic in the treatment of certain cancers is illustrated by the recent example of prostate cancer.
This can be seen in the image below, which shows in “a” , a PET scan* of a patient undergoing follow-up treatment for prostate cancer with multiple metastases. The biological vector for imaging is an antibody to a membrane protein overexpressed by prostate cells (PSMA). The associated radioactive tracer is Gallium 68, a gamma emitter. Image “b” is an equivalent PET scan* after 4 months of internal radiotherapy using the same biological vector (PSMA), but labelled with the radioactive tracer Lutetium 177. Image “b” shows the disappearance of metastases by radiotherapy with beta electrons emitted by Lutetium 177.

The success of two treatments (for prostate and neuroendocrine tumors) has prompted the “big pharma” to invest in NM: five acquisitions have been closed for over $10 billion in the past year.
In addition to the radiopharmaceuticals that already have marketing authorization (8 for internal radiotherapy and over 30 for NM imaging), there are currently some twenty treatments under development worldwide, solely for oncology.

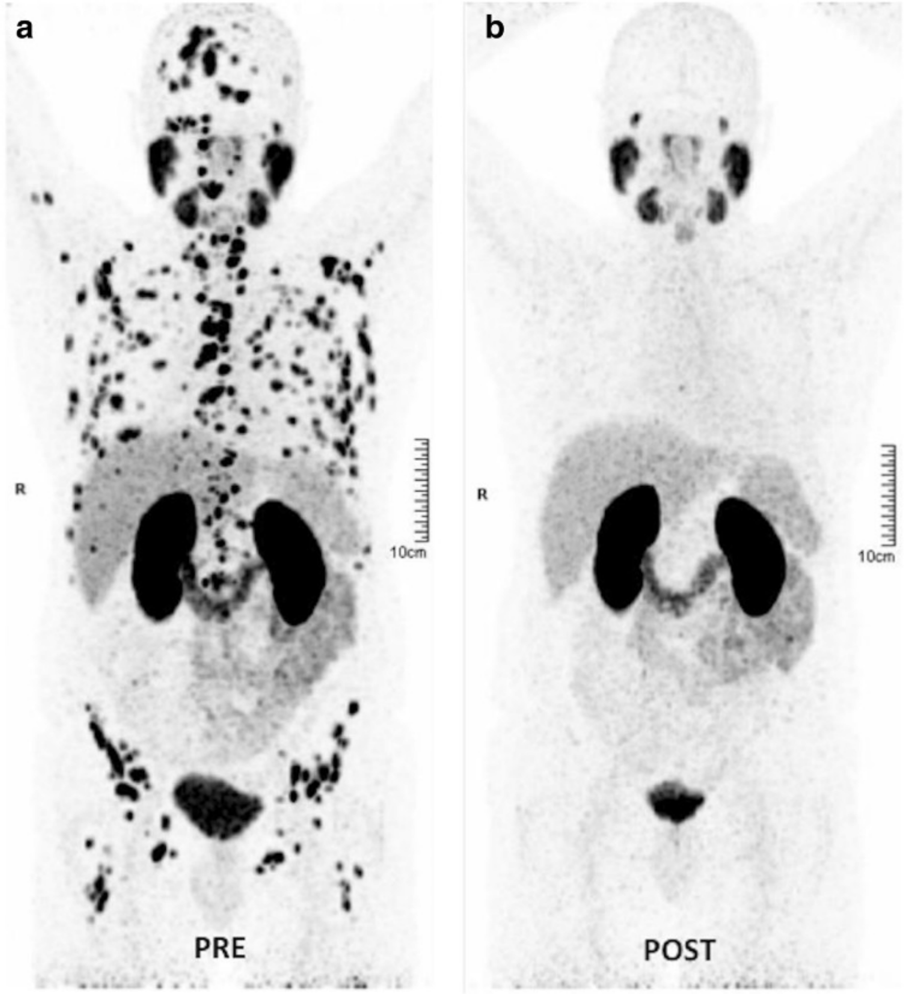

Fig. 11 Theranostic in oncology with PSMA. ^{177}Lu-PSMA radioligand therapy in a 67-year-old man with metastatic castration-resistant prostate cancer. **a** Pretherapy. PET image evidenced a difuse metastatic involvement. PSA value 50 ng/ml. **b** 4 months following the treatment with ^{177}Lu-PSMA radioligand therapy (8000 MBq), PET showed a complete metabolic response. PSA value 0 ng/ml

Nuclear medicine: innovationversusconservatism

The above-mentioned example of theragnostic reveals the strengths, but also the constraints, of nuclear medicine.
Its advantages, apart from its efficacy, are the simplicity of the treatment protocol (typically 6 injections over 8 months for internal radiotherapy) and reduced toxicity, both of which mean a better quality of life for the patient than with other conventional treatments.

Its handicaps are of two types. The first, operational, is the complexity of radiopharmaceutical production and distribution logistics (due to radioactivity and its rapid decay). The other, organizational and regulatory ones, arise in the hospital, in the necessary but demanding multidisciplinary coordination between oncology, nuclear medicine and radiology departments. Finally, there's the fact that radiopharmaceuticals, which are non-storable and have a very short shelf-life, do not pass through the hospital's central pharmacy, and therefore do not follow its usual management. Also, historically, reimbursements for nuclear medicine in Europe generally relate to the overall NM procedure itself, and not, as usual, on the one hand to the drug alone, and on the other to the therapeutic act. As a result, the economic negotiation of reimbursement is highly "opaque", to the detriment of the radiopharmaceutical and its future R&D.

More generally, the many well-established regulations and procedures for non-radioactive drugs need to be adapted to the specificities of NM, so that its potential can be deployed more widely.

*PET scan: imaging technique for simultaneous 3D tomography using positron emission (functional image) from a radioactive tracer and radiation from an X-ray scanner (morphological image).

References

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