

The Rising Role of Radiotheranostics Supported by the Oncidium Foundation

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Recent research and developments have brought forward the pivotal role of Radiotheranostics for cancer care. Whether you refer to them as Radiotheranostics, Theranostics, Theragnostics, Radioligand therapy or Radionuclide therapy, they all describe an innovative approach to cancer care through a beneficial application of radioisotopes, within the Nuclear Medicine field.

State of Play

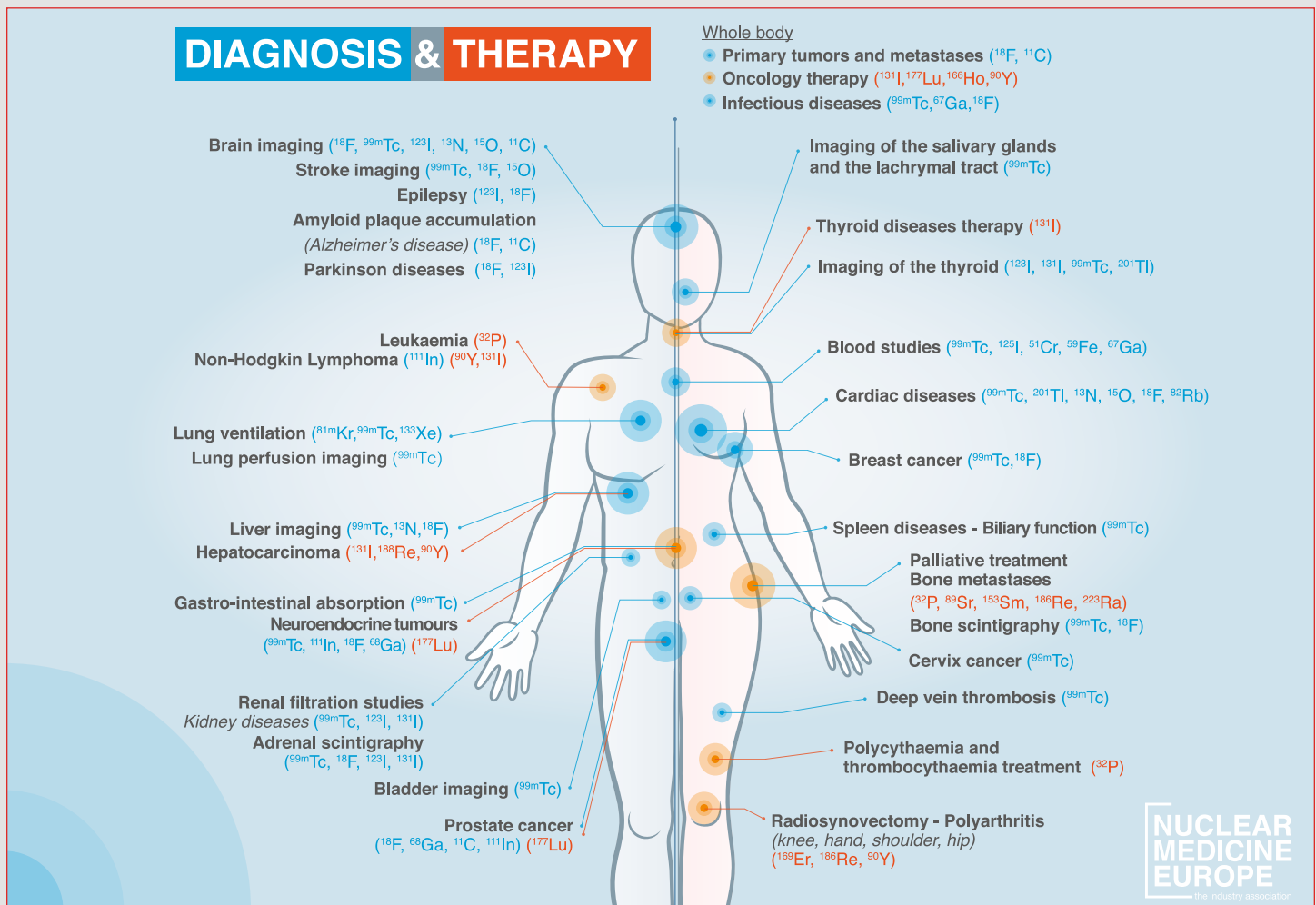
The pandemic situation did not slow down interest for radiotheranostics.

As a matter of fact, over the past 15 months, investment in new radiolabeled compounds pursued an almost exponential growth. This is not only a consequence of the very high amounts of funds presently available from investors looking for rewarding opportunities worldwide but is also proportional to the increasing awareness about the potential of radiolabeled compounds for therapy. Present decisions to invest in this area are based on the past 10 years of successful advancements. Stakeholders look at growing revenues

for therapeutic drugs, certainly more attractive than for diagnostics ones.

Interest in radiotheranostics has grown over the past 20 years in the same way it did for biologics and particularly antibodies between the years 1980 and 2000. At that time, the pharmaceutical industry preferred to observe the technology evolution led by startups and smaller companies which resulted in some company shutdowns but also acquisition of the remaining ones for

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billions of dollars, when technology maturity was reached.

Radiotherapeutics are now mature, but therapeutic development implies much higher funds than diagnostics. During the past 50 years, the radiopharmaceutical industry did not have the budget to develop such drugs in the way expected by the authorities. Only 'conventional' pharmaceutical companies had the sufficient capital to bring such drugs onto the market. In addition to their financial capacities, they also have access to a broader customer target which includes all oncologists.

As such, Bayer and Novartis became the precursors. The success of their drugs (^{223}Ra -Xofigo, ^{177}Lu -Lutathera) is limited by their generic character and for this reason did not (yet) reach the blockbuster status (sales above US\$1B/year). Nevertheless, the next generation of drugs will all be based on proprietary assets. The first one is expected to reach the market by next year (^{177}Lu -PSMA-617, prostate cancer – Novartis).

Besides Novartis which invested again in new therapeutic areas (FAP target, solid tumors, with iTheranostics/Sofie Biosciences -2021 or alphatherapy with Aktis Oncology), there has been a flurry of acquisitions of drugs to increase strengths of portfolios, notably the collaborations between Astellas/Actinium Pharma, Jubilant/Sofie Biosciences, Lantheus/Noria Therapeutics, Bracco/Blue Earth Diagnostics/Scintomics, Fusion Pharma/Ipsen and very recently EZAG/Pentixapharm (2021). At the same time (2020), new names of startups dedicated to radiotherapeutics have appeared on the scene, such as Abscint, Abdera Therapeutics, Precirix, RayzeBio and others.

It is only recently that dedicated radiotheranostic companies have

emerged. These new companies were able to raise hundreds of millions of US\$ following successful IPO's. Telix Pharmaceutical (a company developing radiolabeled drug pairs for prostate cancer, glioblastoma, kidney cancer, bladder cancer) was a precursor, but creation of similar dedicated radiotheranostic companies was also observed such as Fusion Pharmaceuticals (solid cancers, company specialized in alpha therapies based on ^{225}Ac), Point Biopharma (created in 2020, for NET and prostate cancer, based on ^{177}Lu), RayzeBio (created in 2020, with a pipeline based on ^{225}Ac) or Precision Molecular Inc. (created in 2019 for prostate and various cancer treatments).

More than 60 radiotherapeutics have presently entered clinical trials, among which 6 are already recruiting patients in Phase III. These molecules address more than 20 different cancer indications. Unfortunately, 27 of them are targeting the very crowded areas of NET (9) and prostate cancer (18) and only a small fraction of those will reach the market. Future development should now aim at targeting alternatives indications and the choices are quite large. In oncology, radiotheranostics are not far from becoming a viable alternative to surgery, external radiotherapy, hormone therapy, or chemotherapy, and may soon be used as second- or even first-line treatments.

The concept of radiotheranostics is generating a lot of interest, namely as it shifts from an approach where every patient is treated in the same way, to a more personalized and systemic approach, with specific radiotheranostics developed for each target. However, there is a lot of work still to be done. Next to the logistical, regulatory, financial accessibility challenges and convincing conventional pharmaceutical companies to invest in the industry,

there remains an important lack of knowledge and several apprehensions among the non-nuclear physicians and the general public about their potential.

Accelerating Radiotheranostics Development

It is towards this goal that the Oncidium foundation was created, a non-profit, public benefit organization that would bring to light and illustrate the benefits of this technology. Based in Belgium but acting globally, the mission of the foundation is to support, promote and accelerate the development of radiotheranostics for cancer care with the aim of enhancing access for people living with cancer, regardless of origin, technology access or financial situation.

To be able to enhance *Access*, the foundation is determined to identify all the centers worldwide that provide radiotherapeutics for cancer care. Nuclear Medicine Practitioners can register their centers to help patients find them and evaluate therapy options. Also, through a precise and up-to-date work on *Education*, the foundation helps bring a better understanding of the functioning and benefits of such therapies, list marketed and under-development molecules and clear up common misconceptions. Furthermore, to build *Hope*, support regarding clinical developments is provided, namely with its ongoing international collaboration "Noble Registry", to enable prostate cancer patients, regardless of origin or financial situation, to access PSMA-SPECT imaging when PSMA-PET is not an option and thus, with Nobody Left Behind.

Additionally, the foundation cannot act alone and be efficient. With already 18 recognized experts on board representing 11 countries, a

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worldwide network is emerging with Oncidium Ambassadors that endeavor to raise awareness through education campaigns, local collaborations, liaison with national cancer organizations and shared knowledge. Finally, a scientific board regrouping key opinion leaders in the field is set up to guarantee an accurate and precise communication and to identify developments and recommend projects advancing the technology.

Because radiotheranostics represent a new approach to cancer care, it comes with its set

of practical challenges. Along with the development of new diagnostics and therapeutics for even more indications, the aim in the coming years will be to bring together the different actors and enable a more global use and access, so that every person living with cancer can be offered the right diagnosis and therapy, wherever and whenever they need it.

1. To register your therapy center: www.oncidiumfoundation.org/register
2. To access the education page: www.oncidiumfoundation.org/education



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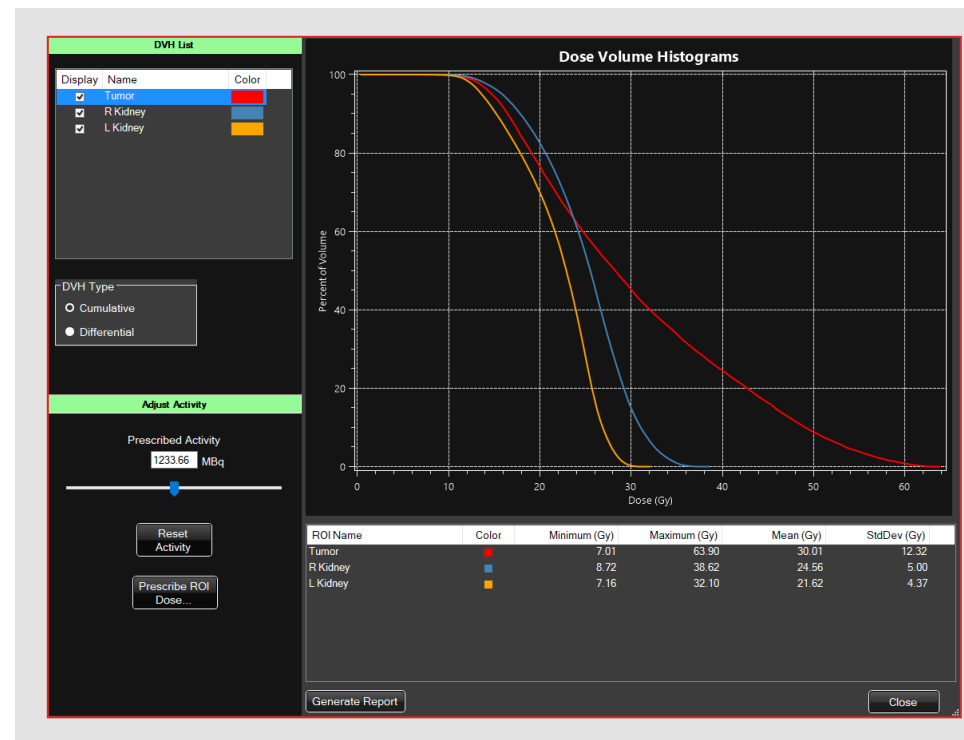


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\$15,000 - \$50,000⁴ per patient when side-effects are reduced. This is a strong indicator that personalized RPT savings will easily outweigh the additional cost of two incremental SPECT/CT or PET/CT images.

In addition, some physicians are uncomfortable asking patients to submit to multiple scans post therapy administration. While this does impose an additional burden on the patient, the inconvenience is less than other common cancer treatment inconveniences such as weekly chemotherapy infusion visits or daily External Beam Radiation Therapy (EBRT) fraction delivery. These two successful treatment regimens are evidence that patient compliance is very high when the benefit-to-inconvenience ratio is high.

These are exciting times for nuclear oncology as personalized dosimetry becomes a reality and available to all clinics. These tools will empower nuclear oncologists to treat with intent. In early-stage patients, physicians can improve outcomes by increasing tumor dose and tumor control while improving quality of life by minimizing dose to normal tissues. In late-stage patients, physicians can improve quality of life through intentional disease management (not cure) or palliative intent via minimal normal tissue dose.



Advanced personalized dosimetry and treatment planning products will be important in realizing the vision of the “Right Dose” for every patient at the right time.

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3. Int J Radiat Oncol Biol Phys Vol 109 (4), 15 March 2021, Pages 891-901
4. PLoS ONE 13(4): e0196007

Voximetry is a Healthtech company specializing in commercialization of complex algorithms on high-speed Graphic Processing Units (GPUs). Currently focused on radiation transport science, Voximetry is advancing personalized treatment planning in advanced stage cancer patients. Torch™ Personalized Treatment Planning has not yet been submitted to FDA for review of its Indications for Use and is therefore NOT suitable for clinical use.