Software innovations for patient-specific theranostics and molecular radiotherapy

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Molecular radiotherapy (MRT) is a promising and quickly expanding set of therapeutic options for treating many cancer cases, including cases where conventional techniques are unsuccessful. Cancer cases have been treated with radiopharmaceuticals since the 1940s, but the number and range of radiotherapeutics on the market have recently expanded significantly.

To help optimizing radionuclides-based therapies in clinical routine, software and digital technologies are expected to play an innovative and primary role in the future. In parallel with their tremendous contribution over the past 20 years to the external beam radiation therapy (EBRT) domain, software technologies bear the same promise for MRT: image-based, 3D voxel-level precision, patient-specific adaptive treatment planning, in vivo dose control, etc. These well-known features and corresponding benefits in EBRT are fairly new to the MRT world and will become de facto standards of practice within the next few years.

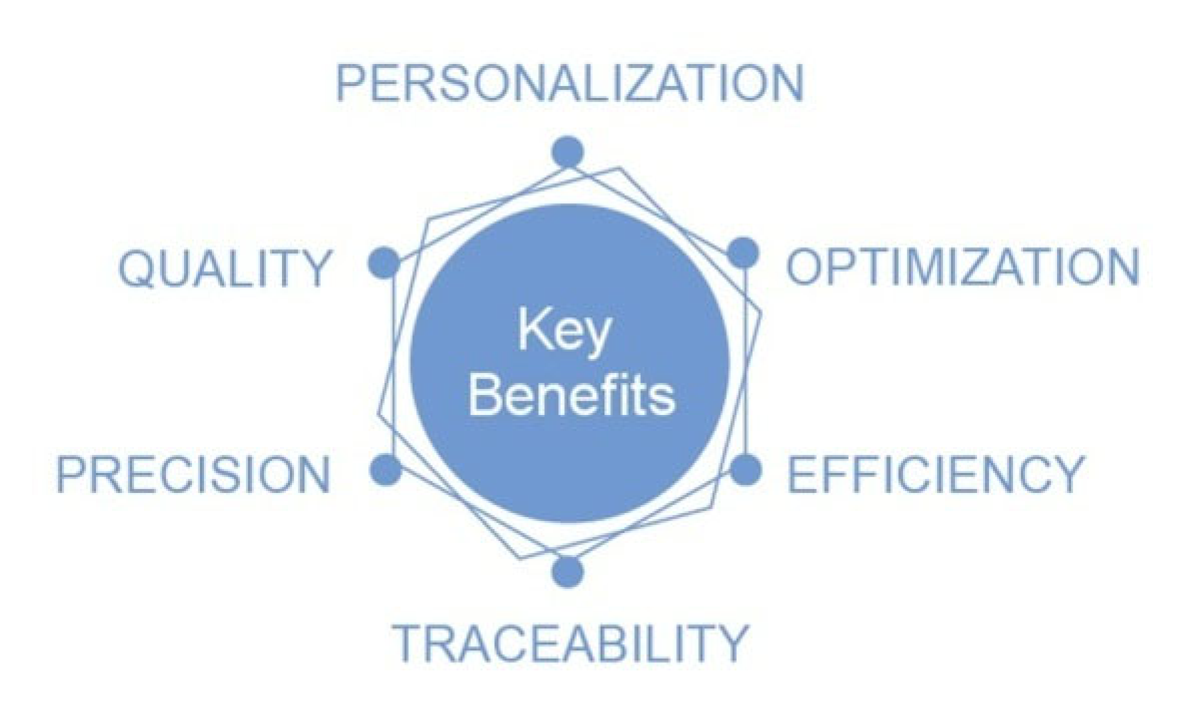
The even more recent software technologies, also called digital technologies, have an even bigger potential impact and benefit for the prognosis, improvement and personalization of cancer therapies. Indeed, the next challenge is to go from protocol-based treatments "one size fits all", to fully personalized diagnosis, prognosis, treatment planning and patient follow-up. A given patient being nowadays characterized by more than 10,000 descriptors, only software and data-driven machine processing can fully take into account such complexity.

Cancer diagnostics, treatment planning and patient follow-up in molecular radiotherapy
Nuclear medicine has the intrinsic potential of allowing pre- and post-therapeutic in vivo bio distribution studies. Molecular radiotherapy, which involves the metabolic vectorization of radioactive products within tumors and their selective destruction, is an alternative suggested in an increasing number of cancer treatment centers worldwide.

However, the increment of radionuclide therapy applications has brought the attention of both the scientific community and the institutional bodies to the need for personalized planning and verification of the absorbed dose delivered to individual patients, as is currently standard practice in external beam radiotherapy (EBRT).

It represents a challenge, especially, for radionuclide treatments given systemically, whose bio distribution and ultimate targeting is greatly heterogeneous among individuals and whose therapeutic effect is exerted over a long period of time (days or weeks in many cases, depending on both biological and physical properties of the radiopharmaceuticals).

Dosimetry-based individualization of treatment in MRT holds great promise to improve the therapy effectiveness and management for patients and healthcare professionals. Patient-specific treatment planning is also feasible in all cases, either from tracer studies with the therapeutic radionuclide, with surrogate imaging radionuclides as "companion diagnostics", or within an “adaptive planning” strategy in the case of multiple administrations.



The recent software dedicated to molecular radiotherapy providing fully integrated 3D and hybrid 3D/2D dosimetry workflows (for example for 90 Yttrium or 177 Lutetium based therapies) can allow medical teams to optimize patient therapy through personalized treatment planning and in vivo control dosimetry. This relies on different processing steps like Organ At Risk and tumor volumes definition, advanced quantification, automatic structure propagation between series, calculation of residence time and comparison between treatment planning and validation control dose maps. The well-known tools used in EBRT for dose planning and dose control, such as dose-volume histograms (DVH), are thus, now readily available for Molecular Radiotherapy as well.

These software solutions, relying on strong nuclear medicine imaging practice, are the foundation for a secured, tailored and efficient treatment practice for these promising cancer therapies. Also, from a regulatory point of view, enforcement of those ensuring safe and efficient practices, similarly to EBRT, will generalize. The recent European Union directive related to radiation protection clearly states that: “exposures of target volumes shall be individually planned and their delivery appropriately verified taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure”.

Radiomics and artificial intelligence perspectives

In nuclear medicine, the current classical therapies largely neglect the characterization of cellular and molecular mechanisms, which are associated with each patient's pathology and treatment follow-up.

The radiomics, an emerging and promising field powered by artificial intelligence (AI) technologies like “big data analysis” and “machine learning” have the potential to answer these questions. Advanced uses of such data are changing the landscape of therapy and show a new potential in the identification of prognosis and predictive parameters, which can help in the future to improve, avoid useless treatments, and better personalize cancer therapies.

For example, by taking into account the clinical diagnosis and follow-up information of patients, and based on the principle of Radiomics — development of statistical models characterizing tumors at the molecular level, extracted automatically from multimodal patient medical images — a real decision-making support system can be created, based on the predictive profile of disease control and the patient-specific toxicity risk.

By combing with additional information extracted from patient records (like genomics, specific biomarkers, etc.), the system can guide the physicians and help them to better choose or adapt treatment, or target the patient receiving a specific treatment.

Moreover, the "machine learning" technologies have the capacity to enhance existing products, either by automating various tasks or by improving, simplifying and accelerating complex algorithms. In the context of molecular radiotherapy, the latest generation of segmentation algorithms based on deep learning could help analyzing dosimetric effects for more organs with more precision, reproducibility, and with limited workloads.

The machine learning technologies all work with the assumption of a learning curve, incremental or not, based on the analysis of as large as possible data sets. The models extracted by these algorithms can then be applied to new patient cases. The consequence of this is that historical information contained in previous patient cases and patient databases is of significant value for such technologies and future systems. This has been quickly understood by all actors having "data". The value is in the data indeed. It is, however, of utmost importance that large data sets are being shared and put in common, instead of being kept in small silos.

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Conclusion

Software technologies are not curing cancer patients by themselves. But software technologies are bound to play an increasing and tremendous role, for the benefit of patients first, cancer centers, and the whole biotechnology industry. Impacts and benefits will be throughout the full cycle, from diagnosis to patient post-treatment follow-up. Without being exhaustive, software technologies will help: to better characterize patients responding to a given therapy, to improve safety and minimize side effects or impacts on healthy organs, to optimize and personalize therapies for a given patient, to control "in vivo" during treatments, and to quantify patient post-treatment response. Software technologies are the keys to move away from the one-size-fits-all standard protocols toward a truly personalized medicine of the future. Nuclear medicine and the expanding molecular radiotherapy domain will first inherit from the tremendous advances performed during the last 20 years in external beam radiation therapy, and then accelerate to include AI-powered theranostic features.

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