Theranostic Digital Twins: An indispensable prerequisite for personalized cancer care

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TO THE EDITOR: Recently, cancer patient digital twins have been astutely proposed as a conceptual framework with the vision of performing simulations for different treatment options before treatment is started (1). A digital twin is a virtual representation of the patient that uses mathematical and computational models to simulate personalized diagnosis and therapy. We strongly believe an optimal platform for more immediate actualization of the “cancer patient digital twin” framework is theranostic nuclear medicine. Here, the Theranostic Digital Twin (TDT) stands on the shoulders of two path-breaking visions: precision medicine and complexity modeling.

Nuclear medicine imaging techniques and the inherent advantage of utilizing theranostic pairs make treatment personalization based on physiologically-based pharmacokinetic (PBPK) models readily feasible (2,3). Patient-specific optimization and personalization of radiopharmaceutical therapies (RPTs) can be obtained within the TDT framework, even before the first therapy cycle; a paradigm shift from existing one-size-fits-all therapies.

New technological developments such as long axial field-of-view PET scanners provide a basis for extended-body PBPK modeling to strengthen TDTs (4). Artificial intelligence (AI) complements multiscale modeling (5,6), and offers the unique opportunity to improve every step of data acquisition, generation and analysis. Theranostic imaging combined with AI can be used to predict voxel-wise absorbed doses and the effectiveness of RPTs (7).

The five pillars of cancer management can be divided into loco-regional treatments (surgery, interventional-radiology, and radiation-therapy) and systemic treatments (oncology and RPT). Generally, the TDT serves not only as a prerequisite for personalized RPTs but will further support all five pillars. Residual disease after surgery or interventional-radiology results in an increased likelihood of local recurrence: theranostic imaging and TDTs can guide and verify the success. While radiation-therapy and brachytherapy are beneficial for localized diseases, systemic therapies present valuable treatment options for metastasized diseases: TDTs can help in the personalization of systemic therapies by highlighting
targets for medical oncology therapies using molecular imaging and PBPK within the TDT. For RPTs, we believe that improvements in outcomes are possible when optimizing treatment with a TDT in terms of radioactivity, tracer amount, number of therapy cycles, and their timing to individual patient’s needs and (pre-)conditions. There is evidence suggesting that with personalization, patient progression-free-survival and overall-survival can improve (8,9).

TDTs accept the challenge to combine existing multi-disciplinary knowledge of cancer management, patient-specific data and population-based models, and create a 3D digital model representing the individual patient physiology and disease. Macroscopic observations (organ, tissue-level) are merged with microscopic effects (cell damage, tumor microenvironment), and the TDT evolves based on (theranostic) imaging and physiological information (i.e. PBPK). Incorporation of radiomics, personal physiology, and genomics enables rich TDT models. In the future, TDTs could be essential in determining if a patient will benefit from one therapy, whether a different treatment is advisable, or even predict how a particular treatment may inevitably fail necessitating adjunctive and adjuvant therapies and interventions. TDTs will be updated continuously.

The TDT will facilitate and enhance therapeutic decisions to truly permit personalized cancer care. Being strongly committed to provide cancer patients with the best available treatment, we anticipate different solutions to enable TDTs to proliferate over the next decade. We encourage researchers to unlock the full potential of theranostics to support this important paradigm shift towards precision medicine.
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