Theranostic: A Step Toward Magic Bullet Concept

During the last 5 decades diagnostic and therapeutic nuclear medicine has been revolutionized due to robust development on frontiers of imaging technology like hybrid imaging and introduction of target specific diagnostic and therapeutic radiopharmaceuticals. In recent years hybrid imaging modalities like PET/CT, SPECT/CT and PET/MR have become an integral part in management paradigm of various disease. Rapid advancement in biosciences is heralded by the development of various peptides receptors, monoclonal antibodies and immune check point inhibitors. As a matter of fact, this rapid advancement has transformed healthcare from a conventional treatment to personalized treatment. In August 1998 John Funkhouser, CEO of Myocardial Solution Inc. in a press release has coined the term *Theranostic*.[1]The term *theranostic* is a combination of two words, *therapeutic* (thera) and *diagnostic* (nostic). In current practice, theranostic is used to describe the ability to image tumor cell by combining a radiopharmaceutical (gamma emitters) to a receptor found on a particular tumor cell membrane. This is followed by tagging same receptor to a therapeutic radionuclide (Beta emitter like177Lu or 90Y or alpha emitter like Actinium-225) to kill the tumor cell. The sophisticated approach of theranostic in current era is in fact the outcome of concept of Magic Bullet. This concept was proposed by Paul Ehrlich (German Noble laureate) in 1900 to develop special drugs to precisely locate and kill disease foci without damaging healthy tissues.[2] We feel that this century old hybrid approach is the sentinel stimulus behind the development of hybrid imaging modalities (like PET/CT, PET/MR) and hybrid treatment strategy (like Theranostic). Furthermore, new terminologies like personalized medicine, targeted medicine, and precision medicine have been derived from Ehrlich s concept.[2]

However, we must not ignore that success of theranostic is linked with humongous research and development in the field of nanotechnology. Nanoparticles gained significant attention in theranostics because of their optimal characteristics, ability to get localized to specific disease site and significantly lower risk of undesirable side effects. For this scenario, nanoparticles are promising in theranostic (nanotheranostic) because of their target specific nature due to help of biomarkers/targeting ligand and controlled drug delivery system.[3] Worth mention that theranostics despite a great breakthrough in personalized healthcare, has faced failures in in-vivo studies/clinical trials due to host immune response and less efficient penetration of drug into cancer tissue compromising therapeutic efficiency. Thanks to nanotechnology which has provided solutions for these problems by preparing biomimetic materials. Biomimetic are nanoparticles which are coated with a membrane mimicking properties of natural cell membranes which helps them to escape from host immune system and successfully reach the target sites and deliver the specific drugs. Similarly, drug penetration into cancer cell has been addressed by fusing a vascular disrupting agent with cytotoxic drug to overcome the problem with drug penetration. Interestingly vascular disrupting agent acts on cancerous cells at a distance from blood vessels and cytotoxic drug eradicate tumor cells close to the blood vessels.[3] Theranostics in current era has gelled molecular biology, immunology, immunotherapy, genomics, radiomics, artificial intelligence, and other highly refined fields in a coherent way to benefit personalized medicine.[4]

In principle, theranostics refers to any combination of diagnostic and therapeutic modalities for any disease. In breast cancer, immune-histochemical (IHC) staining for human epidermal growth factor receptor-2 (HER2) guides to select patients suitable for specific treatment with anti-HER2 receptor antibodies (e.g., trastuzumab) is an established theranostic approach.[5] However, in current literature, the term theranostics has been more frequently associated with in-vivo nuclear medicine oncologic applications. Most primitive example of theranostic approach in clinical practice dates back 1936. It was Dr. Saul Hertz who used iodine isotope to study iodine metabolism in thyroid and 1941 Drs Hertz and Arthur started using radioiodine-131 for treatment of hyperthyroidism at Massachusetts General Hospital.[6]

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Radioiodine-based diagnosis, evaluation, and therapy for differentiated thyroid cancer and toxic goiters has maintained its high clinical relevance in modern medicine even after 8 decades. In last two decades, extensive developments in molecular biology, radiochemistry (both beta and alpha emitters), and imaging technology (particularly hybrid imaging) has helped the theranostic to acquire most promising place in oncology. Indeed, nuclear theranostic approach has given an impetus to the growth in molecular imaging and personalized medicine and customized management for various diseases. It has helped the physicians in better patient selection, prediction of response, prognosis and toxicity, and avoiding futile and expensive diagnostic and treatment strategies.[7] Currently nuclear theranostic is being widely used in thyroid (well differentiated cancer and toxic goiter ablation ^{131}I), pheochromocytoma and paraganglioma (^{123}I-MIBG/^{1311}1-MIBG), neuroendocrine tumor (^{68}Ga-DOTATOC and ^{177}Lu/^{90}Yt DOTATOC), metastatic bone disease (^{99m}Tc-MDP and ^{153}Sm-EDTMP) and carcinoma of prostate (^{18}F-PSMA and ^{177}Lu/ ^{225}Ac-PSMA).

Theranostic being a hybrid terminology (same drug but with different radiolabels for therapy and diagnosis) with hybrid imaging (PET/CT and PET/MRI) has revolutionized personalized medicine by proper patient s selection, targeted nuclear therapies with proven efficacy and a favorable safety profile. With continuous development on frontiers of academia and technology, it is expected that theranostics is approaching Paul Erlich s concept of magic bullet withhope of having a profound effect on the lives of patients worldwide.

Conflict of Interest: None

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