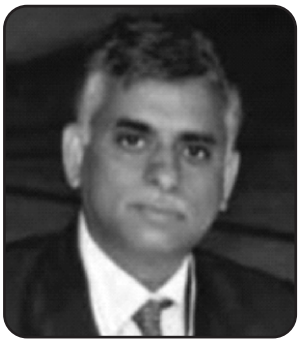
Dr. T. B. Patel Oration Award 2018



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Nuclear Medicine Cancer Theranostics: Exploring the New Horizons

The term 'Theranostics' encapsulates the integration of diagnostics and therapeutics in the individualized management of disease. Implicit in the Theranostic paradigm is the assumption that diagnostic test results can precisely determine whether an individual is likely to benefit from a specific treatment. This assumption underpins the recent focus on companion diagnostics as an integral part of drug development.

An excellent example of the concept of theranostics in oncology is the requirement that, to be selected for Trastuzumab therapy (Herceptin; Genentech), a candidate must have a tumor on which the presence of human epidermal growth factor receptor 2 (HER2) has been demonstrated. However, this requirement is limited by the potential sampling bias intrinsic in tissue biopsy. Molecular imaging of HER2 expression using ^{89}Zr-radiolabeled Trastuzumab provides an alternative vision of how the selection of candidates for expensive and sometimes toxic therapies might look in the future. Molecular imaging with ^{89}Zr-trastuzumab can be used to detect heterogeneity of HER2 expression. Because it can image the whole body, it has the potential to improve selection of patients for Trastuzumab and antibody–drug conjugate therapy. It also opens the way for therapeutic application of radionuclide therapy.

Nuclear medicine is ideally placed to play a central role in Theranostics by allowing visualization of molecular targets and thus enabling so-called in vivo Immune-Histochemistry, by which noninvasive biomarkers can be provided to select targeted drugs labeled with therapeutic Radionuclides and monitor the response to them. The staging and treatment of thyroid cancer with the diagnostic use of ^{123}I or ^{124}I complementing the therapeutic efficacy of ^{131}I has paved the way for theranostics in therapeutic nuclear medicine. Successful treatment of metastatic thyroid cancer was achieved even before the molecular basis of radioiodine uptake through the sodium-iodide symporter was characterized, speaking to the power of this paradigm. The use of radiolabeled meta-iodo-benzyl-guanidine in diagnosis and treatment of metastatic Neuroblastoma, Paraganglioma, and Pheochromocytoma or of radiolabeled somatostatin analogs in Neuroendocrine tumors (NETs) has extended the paradigm to other cancers. Despite the impressive results achieved using these agents, they have generally been developed in academic centers and used on a compassionate basis. This has led to limited resources for establishing the evidence base that usually accompanies registration and approval of cancer therapies. Beyond the expected clinical benefits of personalized medicine, theranostics could also have a significant positive economic effect.

Nuclear medicine is ideally placed to play a central role in Theranostics by allowing visualization of molecular targets and thus enabling so-called in vivo immunohistochemistry, by which noninvasive biomarkers can be provided to select targeted drugs labeled with therapeutic radionuclides and monitor the response to them. Limited resources for establishing the evidence that usually accompanies registration and approval of cancer therapies, in particular there has been a lack of randomized controlled trial data comparing radionuclide therapies with other forms of therapy and virtually none testing the integrated theranostic approach. In order to take benefit of the unique qualities of theranostics with radionuclides therapies and save costs in developing countries with huge patient load we need to develop theranostics tools locally and identify agents that can modulate target expression or increase radiation-induced cellular damage (radio sensitizing agents), and encourages the combination of Cytostatic treatments between radioactive sessions while identifying reliable and accurate biomarkers of therapeutic response.