ELSEVIER

Seminars in
NUCLEAR
MEDICINE

Volume 49, Number 5 September 2019

Letter from the Editors

The recent evolution and growth of nuclear medicine have truly been impressive, mostly due to an improved effort in translating innovative radiopharmaceuticals into clinical testing by a multidisciplinary approach. Basic research has enabled the clinicians to identify key steps of disease-related biologic processes that can be targeted with imaging tracers, as well as to define targets of treatment and assess responses.[1] This issue addresses some of the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of clinical trials and the major impact on the practice of health care.

A paper by Vermeulen et al offers a nice introduction to the current issue, giving the readers an overview of the current understanding on the design and challenges of radiopharmaceuticals.

This article reviews the literature involving the radiopharmaceutical for diagnosis and therapy in terms of the radionuclide vector concept including basic concepts, small molecules, peptides, proteins, and particles.[2] The paper further discusses the radionuclide with regards to the diagnosis for both SPECT and PET as well as alpha, beta, and auger electron emitters for therapy. Aspects regarding the design of new radiopharmaceuticals from basic requirements, the radiochemical space, validation path, and translation to clinical studies are well illustrated. The authors conclude by emphasizing the challenges of radiopharmaceuticals, starting from production, stability and quality control, and regulatory and economic challenges.[2]

The implementation of novel radiopharmaceuticals in clinical practice requires a careful research that relates the results of basic science to knowledge of targets, pharmacology, radiochemistry and, finally, medical needs. The review by Lee et al discusses how target selection requires a good understanding of the physiologic changes involved in the disease processes and renewed interest in targets for theranostics based approaches to therapy of diseases ranging from oncology to cardiology and neurology.[3] The authors illustrate how various factors can influence cellular metabolism associated with many disease states, and the significance of identification of these changes which permits the development of radiopharmaceuticals that can assist in the diagnosis of these diseases. Lee et al uses several clinical examples to show that the target for radiopharmaceuticals used in nuclear medicine imaging should have an abundance of expression in the cells or tissues involved in the disease processes.

The impact of preclinical studies is well illustrated with the elucidation of the multiple molecular mechanisms that may be responsible for the acquisition of drug resistance, as well as in identifying the best combination of drugs for a given mechanism of resistance.[4] Further, these preclinical studies can help to prove the concept that it is feasible to visualize the expression of immune checkpoints. Iommelli et al provides a glimpse on how preclinical imaging studies can provide noninvasive tools to evaluate drug target expression and identify the compounds that have a high probability of success in the subsequent experimental clinical phases.[4] This paper demonstrates the translational process moving newly developed targeted anticancer agents from discovery to clinical applications with more common tracers such as 18F-Fluorothymidine and 18F-Fluorodeoxyglucose by testing the inhibition of the target and downstream pathways through the evaluation of early changes of proliferation and glucose metabolism allowing the identification of sensitive and resistant tumors.

The success of preclinical studies on targeted radionuclide imaging and therapy has led to several new clinical radiopharmaceuticals and thus a need to better document and report adverse reactions. Schreuder et al to provide an overview of the most common adverse events and their characteristics such as frequency, severity, and proposed mechanism, for diagnostic radiopharmaceuticals.[5] They report that the majority of the adverse events are related to six system organ classes and that most adverse events are in the system organ classes skin and subcutaneous tissue disorders and general disorders and administration site conditions. Although they found the majority of the reported events were minor in severity and often resolved without sequelae, the authors caution the nuclear medicine community to be vigilant with the introduction of new radiopharmaceuticals and the increasing use of PET/CT.

The effect of Glucose control in imaging is of interest about the accuracy of data measurement. In addition, clear consensus on the real impact of glycemia on several nuclear medicine procedures is lacking. This review brings to our

https://doi.org/10.1053/j.semnuclmed.2019.06.014

attention the increasing complexity created by multiple new diabetes drugs for metabolically dependent nuclear medicine procedures. Sheikh et al provides useful summary proposals for studies utilizing FDG in oncologic, neurology, cardiology, and infection and inflammation.[6] They also raise awareness with guidelines for amino acid, choline, and other metabolite scans, and also provide a summary proposal for the pregastric emptying scintigraphy glucose assessment. Support for multicenter studies to understand the mechanisms of these new medications will help to develop recommendations for optimum glycemic control for preparation for nuclear medicine studies.

Theranostics in nuclear medicine and successful integration of basic and clinical research plays a significant role in the implementation of precision oncology. The Bench to Bedside experience of the Bad Berka group has demonstrated how collaborations can successfully navigate the complex bottlenecks that can prevent conversion of promising discoveries into medical advances and precision oncology.[7] Zang et al describes several of their first-in-human studies have contributed to the validation of new targets, optimization of pharmacokinetics, theranostic radionuclide pairs, and improvements in dosimetry, with the goal of improving clinical outcomes. This paper also discusses a number of radiometals potentially useful for radiotheranostics.

Radiomics in nuclear medicine imaging is leading in providing quantitative imaging data that adds information on tissue phenotype, disease biology, and surrounding microenvironment. Ibrahim et al reviews various tools for radiomic features that must be studied in clinical trials to establish how the agents may be used to affect clinical outcomes favorably.[8] The paper show how radiomics addresses unmet clinical needs with examples such as neuroendocrine tumors and prostate cancer. The workers present a way forward for standardization and implementation of radiomics in order to facilitate its transition to clinical use and contribute to the current AI research.

Dr Cutler concludes this issue by presenting how the radiopharmaceutical targeted treatments tend to be more cost effective than standard chemotherapy treatments which require multiple doses over a longer period of time, and the fact that they are not cheap and the earlier physician can determine that a patient is not responding, more costs can be saved by not treating a patient with drugs that are not effective for that patient and even toxic.[9] The author gives several successful examples of nuclear medicine and theranostics as being critical to improve the efficiency and efficacy of routine imaging and targeted therapies.

Summarizing, we hope, that the current issue brings new insights into basic studies of targets and ligands, pathways for the delivery of novel radiotracers to patients, and assessment of the socioeconomic impact. Lastly, we thank all our esteemed colleagues who have contributed to this issue capturing the diversity of applications of these complex topics.

M. Michael Sathekge, MD, PhD
Kirsten Bouchelouche, MD, DMSc

References

1. Bravo PE, Bengel FM: The role of cardiac PET in translating basic science into the clinical arena. J Cardiovasc Transl Res 4:425-436, 2011
2. Vermeulen K, Vandamme M, Bormans G, et al: Design and challenges of radiopharmaceuticals. Semin Nucl Med 49:339-356, 2019
3. Lee ST, Burvenich I, Scott AM: Novel target selection for nuclear medicine studies. Semin Nucl Med 49:357-368, 2019
4. Iommelli F, De Rosa V, Terlizzi C, et al: Preclinical imaging in targeted cancer therapies. Semin Nucl Med 49:369-381, 2019
5. Schreuder N, Koopman D, Jager P L, et al: Adverse events of diagnostic radiopharmaceuticals: a systematic review. Semin Nucl Med 49:382-410, 2019
6. Sheikh A, Anolik J, Maurer A: Update on serum glucose and metabolic management of clinical nuclear medicine studies: current status and proposed future directions. Semin Nucl Med 49:411-421, 2019
7. Zhang J, Singh A, Kulkarni H R, et al: From bench to bedside—the Bad Berka experience with first-in-human studies. Semin Nucl Med 49:422-437, 2019
8. Ibrahim A, Vallières M, Woodruff H, et al: Radiomics analysis for clinical decision support in nuclear medicine. Semin Nucl Med 49:438-449, 2019
9. Cutler C: Economics of new molecular targeted personalized radiopharmaceuticals. Semin Nucl Med 49:450-457, 2019