

The Evolving Role of Nuclear Medicine and Molecular Imaging: Theranostics and Personalized Therapeutic Applications

Nükleer Tıp ve Moleküler Görüntülemenin Gelişen Rolü: Teranostikler ve Kişiselleştirilmiş Tedavi Uygulamaları

M. Fani Bozkurt¹, D Zehra Özcan²

¹Hacettepe University Medical School, Department of Nuclear Medicine, Ankara, Turkey ²Ege University Medical School, Department of Nuclear Medicine, İzmir, Turkey

During the last decade, there have been excellent and very rapid advances in "Nuclear Medicine and Molecular Imaging" throughout the world. The developments in radiopharmaceuticals induced evolution of nuclear medicine from imaging certain biologic features to targeted drug delivery designed for the specific characteristics of an individual patient's disease. While the use of therapeutic radioisotopes was an important but minor component of the therapeutic oncology in the past, now with the development of "Theranostic" applications, intelligent options for targeted internal radionuclide treatments became possible in a variety of tumors and Theranostics started to give rise to a paradigm shift in oncology.

"Theranostic" concept in nuclear medicine represent both diagnostic and therapeutic function in one drug formulation and while bridging these two goals. The term "Theranostic" is generated from 'therapy' and 'diagnostics/ diagnosis' (1). Actually Iodine-131 is the oldest and the most common isotope in theranostic applications. In this case, the same radioisotope lodine-131 serves for both diagnostic and therapeutic purpose on the basis of using the same target, although Iodine-123 which is the pure gamma emitter isotope of lodine can take part as the diagnostic agent. Theranostic approach also includes the use of different radioistopes but again depending on the principle of using the same target for both diagnosis and therapy Recently, there have been new "theranostics" agents in clinical practice, which are good examples for theranostic approach with two different radioisotopes. For instance, somatostatin receptors on the surface of the neuroendocrine neoplasia have been used as targets for radionuclide imaging and treatment on the basis of "theranostic" approach. PET Imaging with positron emitter Ga-68 labelled peptides which show affinity to somatostatin receptors and treatment with beta emitter Y-90/Lu-177 labelled peptides targeting these receptors gained wide acceptance in the field (2,3).

There has been a growing interest also for the use theranostic approach in prostate cancer which affects a great number of males. The presence of prostate specific membrane antigen (PSMA) expression in prostate cancer served as a basis for the idea of targeting these receptors for PET imaging using Ga-68 labelled PSMA and consequently treating with Lu-177 labelled PSMA (4,5). The potential for drug delivery system using theranostic basis also enables us to administer therapy according to the individual requirements of the patient. As the tumor nature is heterogenous, a specific drug indicating a certain characteristic will be a therapeutic option only for a subset of tumors. So the treatment will be customized for only patients whose tumor contains very specific proteins or receptors, which will eventually result with a more "precise" therapy.

Recently, Radium 223 which is a calcium mimicking radioisotope has been introduced as an effective treatment in metastatic castration resistant prostate cancer patients with bone involvement only (6). While delivering alpha emission to the metastatic deposits detected by bone imaging tracers, Ra-223 provides improvement in patient survival and skeletal related events. Therefore, Ra-233 treatment became available in all over the world and

Address for Correspondence: Zehra Özcan MD, Ege University Medical School, Department of Nuclear Medicine, İzmir, Turkey E-mail: zehra.ozcan@yahoo.com ORCID ID: orcid.org/0000-0002-6942-4704 Received: 15.01.2018 Accepted: 15.01.2018

> [©]Copyright 2018 by Turkish Society of Nuclear Medicine Molecular Imaging and Radionuclide Therapy published by Galenos Yayınevi.

covered in most European countries (7). Being recently licensed in Turkey, it is believed that this new targeted radionuclide treatment will also be available in our patients and alpha emitting radionuclides will open a new era in therapeutic nuclear medicine.

It is clear that nuclear medicine and molecular imaging will enlarge its role in the early diagnosis and treatment of cancer and also will be a driving force in personalized medicine using theranostic concepts. Finally, while completing a successful year and starting a new year, we, the editors of MIRT, hope that scientific researches in our field will expand more and MIRT will be a leading publication for all these new ideas and researches promoting diagnostic and therapeutic Nuclear Medicine applications.

References

- 1. Durak H. Onkolojide Kişiselleştirilmiş Tedavi ve Teranostik Yaklaşımlar. Nucl Med Sem 2015;1:80-84.
- Bozkurt MF, Virgolini I, Balogova S, Beheshti M, Rubello D, Decristoforo C, Ambrosini V, Kjaer A, Delgado-Bolton R, Kunikowska J, Oyen WJG, Chiti A, Giammarile F, Fanti S. Guideline for PET/CT imaging of neuroendocrine neoplasms with 68Ga-DOTA-conjugated somatostatin receptor targeting peptides and 18F-DOPA. Eur J Nucl Med Mol Imaging 2017;44:1588-1601.
- Strosberg J, El-Haddad G, Wolin E, Hendifar A, Yao J, Chasen B, Mittra E, Kunz PL, Kulke MH, Jacene H, Bushnell D, O'Dorisio TM,

Baum RP, Kulkarni HR, Caplin M, Lebtahi R, Hobday T, Delpassand E, Van Cutsem E, Benson A, Srirajaskanthan R, Pavel M, Mora J, Berlin J, Grande E, Reed N, Seregni E, Öberg K, Lopera Sierra M, Santoro P, Thevenet T, Erion JL, Ruszniewski P, Kwekkeboom D, Krenning E; NETTER-1 Trial Investigators. Phase 3 Trial of 177Lu-Dotatate for Midgut Neuroendocrine Tumors. N Engl J Med 2017;376:125-135.

- Afshar-Oromieh A, Hetzheim H, Kratochwil C, Benesova M, Eder M, Neels OC, Eisenhut M, Kübler W, Holland-Letz T, Giesel FL, Mier W, Kopka K, Haberkorn U. The Theranostic PSMA Ligand PSMA-617 in the Diagnosis of Prostate Cancer by PET/CT: Biodistribution in Humans, Radiation Dosimetry, and First Evaluation of Tumor Lesions. J Nucl Med 2015;56:1697-1705.
- Kabasakal L, Toklu T, Yeyin N, Demirci E, Abuqbeitah M, Ocak M, Aygün A, Karayel E, Pehlivanoğlu H, Alan Selçuk N. Lu-177-PSMA-617 Prostate-Specific Membrane Antigen Inhibitor Therapy in Patients with Castration-Resistant Prostate Cancer: Stability, Bio-distribution and Dosimetry. Mol Imaging Radionucl Ther 2017;26:62-68.
- Hoskin P, Sartor O, O'Sullivan JM, Johannessen DC, Helle SI, Logue J, Bottomley D, Nilsson S, Vogelzang NJ, Fang F, Wahba M, Aksnes AK, Parker C. Efficacy and safety of radium-223 dichloride in patients with castration-resistant prostate cancer and symptomatic bone metastases, with or without previous docetaxel use: a prespecified subgroup analysis from the randomised, double-blind, phase 3 ALSYMPCA trial. Lancet Oncol 2014;15:1397-1406.
- Poeppel TD, Handkiewicz-Junak D, Andreeff M, Becherer A, Bockisch A, Fricke E, Geworski L, Heinzel A, Krause BJ, Krause T, Mitterhauser M, Sonnenschein W, Bodei L, Delgado-Bolton RC, Gabriel M. EANM guideline for radionuclide therapy with radium-223 of metastatic castration-resistant prostate cancer Eur J Nucl Med Mol Imaging 2017. doi: 10.1007/s00259-017-3900-4.