



Nuclear Theranostics in Turkey

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Received: 3 December 2018 / Revised: 10 December 2018 / Accepted: 10 December 2018 / Published online: 15 December 2018

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Abstract

Nuclear theranostics functions as a bridge which connects targeted diagnosis to targeted therapy, just like Turkey functions as a geographical bridge which connects Asia to Europe. This unique geographical site of the country plays an important role with regard to introduction of novel scientific and technologic improvements, which originate from one continent to another, in the era of accelerated information. The first nuclear medicine practice in Turkey started in the beginning of 1950s with the first radioiodine treatment, which actually was a debut for nuclear theranostics in Turkey, years before many other countries in the world. For the time being, along with radioiodine treatment, many other theranostic applications such as I-131 MIBG treatment, Lu-177/Y-90 DOTA peptide treatment, Lu-177 PSMA treatment, Y-90 microsphere treatment, and bone palliative treatment are being performed in many centers countrywide. As science and technology improves, novel theranostic applications are eagerly awaited to be introduced in near future. This paper summarizes the story of nuclear theranostics in Turkey and aims to give an overview on the current status of theranostic applications in Turkey.

Keywords Theranostics · Nuclear medicine · Turkey · I-131 · I-131 MIBG · Radionuclide therapy

Introduction

Theranostics is a term which refers to all procedures starting from diagnostic work-up that leads to therapeutic approaches by using the same targeting tools towards a certain disease state. Nuclear theranostics is a specific application of theranostics under supervision of nuclear medicine which specifically uses radionuclides for both diagnosis and therapy. Since nuclear medicine uses tracer methodology in order to diagnose and treat the disease states, almost all nuclear medicine techniques have in fact a naturally born targeted approach to some extent. Theranostics increases the targeting and provides a much more individualized nuclear medicine practice with this regard [1].

The Initial Experience of Nuclear Theranostics in Turkey

Turkey is a country which functions as a bridge between the continents Asia and Europe, just as theranostics functions as a

bridge between targeted diagnosis and therapy. This unique geographical site of the country plays an important role with regard to introduction of novel scientific and technologic improvements, which originate from one continent to another, in the era of accelerated information.

The first nuclear medicine practice in Turkey started in the beginning of 1950s, which actually was a debut for nuclear theranostics in Turkey, years before many other countries in the World. Professor Suphi Artunkal and his team-workers were the medical professionals who first used I-131 to treat the patients at Radioisotope Laboratory, of which they were the founders within Haseki Hospital Therapy Clinic in Istanbul (Fig. 1). This initial use of radioisotopes gave a successful start for nuclear medicine as a separate medical discipline in Turkey. In the year 1961, the first radioisotope production in Turkey started at Cekmece Nuclear Education and Research Center in Istanbul and therefore Turkey appeared as one of the first countries which was able to produce its own radioisotopes for medical use. In 1962 Professor Fevzi Renda and his colleagues founded Radiobiology Institute within Ankara University in Ankara with support from International Agency of Atomic Energy (IAEA), which was followed by foundation of other Nuclear Medicine institutes in the cities of Istanbul and Izmir. These gave rise to establishment of Nuclear Medicine as an individual discipline in Turkey and the first examples of theranostics in Turkey dated back to those

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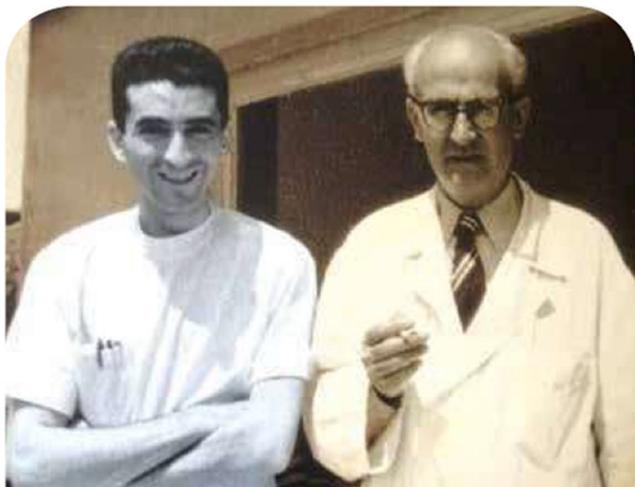


Fig. 1 Professor Suphi ARTUNKAL, M.D. (on the right) the founder of Nuclear Medicine in Turkey and Professor Coskun BEKDIK, M.D. (on the left) who was—at that time—one of his team members and later on founded Nuclear Medicine Department at Hacettepe University, in Ankara, Turkey

times, with the use of I-131. Professor Suphi Artunkal was therefore accepted as the founder of Nuclear Medicine in Turkey. Turkish Society of Nuclear Medicine grants the most prestigious award in the field of Nuclear Medicine each year during the Annual Meeting in the name of Suphi Artunkal [2, 3].

In Turkey, any use of nuclear energy and radiation is under supervision and authority of Turkish Atomic Energy Authority, which was established in the year 1982. Nuclear theranostic applications are also authorized by the Turkish Atomic Energy Authority, like all the other diagnostic and therapeutic procedures with the use of radiation. The following tasks of the Turkish Atomic Energy Authority are especially related with the applications in the field of Nuclear Medicine [4]:

- To establish and operate the radioisotope production, quality control, scaling, and distribution installations.
- To determine the guiding principles and provisions for protection against the damages of ionizing radiation in the activities performed using radiation equipment, radioactive materials, special fissionable materials, and such ionizing radiation sources and to determine the limits of legal liability.
- To give license as a basis for authorization to governmental or private bodies or persons who keep, use, import or export, transport, store, and trade in radioactive materials and radiation equipments and to control those regarding radiation protection; to enforce the responsibility of liability for implementing the above activities; to cancel the given license permanently or temporarily, in contradictory cases to radiation regulations; if necessary to decide for the termination of above organizations and to provide the

commencement of legal investigations within the general legal principles.

- To prepare the decrees and regulations governing the general principles for the use, export, import, transport, and insurance liability of radioisotopes.
- To grant approval, permission, and license related to the site selection, construction, operation, and environmental protection of nuclear power and research reactors and nuclear fuel cycle facilities; to do necessary inspections and controls, to limit (restrict) the operating authority in case of noncompliance with the permission or license; to cancel permanently or temporarily the permission or license given and to make recommendations to the Prime Minister for closing down those installations; to prepare the necessary technical guides, decrees, and regulations for those purposes.
- To take the necessary measures or have them taken for the safe process, transport, permanent or temporary storage of the radioactive waste from nuclear facilities and radioisotope laboratories.

Current Nuclear Theranostics in Turkey

Theranostic applications are increasingly performed in many nuclear medicine centers widespread in Turkey. Most of the diagnostic radiopharmaceuticals can be produced locally by the industrial companies which even can provide radiopharmaceuticals to many other countries along with Turkey. In addition to cyclotrons operated by industrial companies, there are a few number of cyclotrons which belong to state universities, mostly aimed to promote scientific research in the field. These improvements highly accelerate the introduction of new theranostic applications in Turkey.

The first theranostic application in the field of nuclear medicine in Turkey was I-131 treatment for both hyperthyroidism and differentiated thyroid cancer patients. Currently, there are 67 centers in which radioiodine treatment can be performed. Most of these centers are either university hospitals or state hospitals and few of them are private centers. Approximately, 3000 patients were treated in those centers per each year. As an example, at Hacettepe University which is located in Ankara, about 200 patients with differentiated thyroid cancer as well as 150 patients with hyperthyroidism are treated with I-131 each year.

I-131 metaiodobenzylguanidine (MIBG) treatment is another theranostic application that has been in use for about 25 years in Turkey. Most of the patients which were treated with I-131 MIBG had the diagnoses of neuroblastoma followed by pheochromocytoma and some other types of neuroendocrine/neuroectodermal originated tumors such as medullary thyroid cancer. This theranostic application is

mainly held at university hospitals, which have pediatric oncology units and which are experienced in pediatric nuclear medicine, such as Hacettepe University, Cerrahpaşa University, and Ankara University. Hacettepe University has a dedicated pediatric hospital as well as oncology hospital which includes a separate ward of pediatric oncology. That is why, there is high number of patient referral to this center with the diagnosis of childhood neuroectodermal tumors, mostly neuroblastomas. Approximately 50 patients are treated with I-131 MIBG per year.

Theranostic applications for neuroendocrine tumors with Lu-177 DOTA peptides along with Y-90 DOTA peptides are also among the most appreciated therapeutic procedures in the recent years in Turkey. Currently, around 25 centers are capable of performing such treatment options. Most of these centers are university and training hospitals and some of them are private centers. Approximately 2500 treatments are given per year countrywide and this number will be expected to increase extensively in the next few years.

Prostate cancer is also one new indication in which theranostic approach with Lu-177 PSMA is performed to treat metastatic castration resistant prostate cancer patients. In Turkey, there are currently 20 centers in which this theranostic modality is being performed. About 600 patients per year are treated with Lu-177 PSMA per year countrywide.

Yttrium-90 (Y-90) microsphere treatment for the primary and metastatic liver tumors is one of the theranostic applications in Turkey. Y-90 microsphere treatment has been licensed and registered by Ministry of Health of the Turkish Republic in the year 2008. Since that time, 35 centers in Turkey applied this treatment modality in about 1500 patients countrywide. Both resin and glass microspheres are available in Turkey. In the last year, first application of Holmium-166 microsphere treatment was also completed in Istanbul too.

Bone pain palliation is also among theranostic applications, in which beta-emitting bone seeking radiopharmaceuticals are used for palliative therapy of metastatic bone disease after confirmation of adequate radiopharmaceutical uptake of bony metastases with bone scintigraphy. In Turkey, Strontium-89 used to be preferred for this indication in the past but currently newer bone seeking beta-emitting radiopharmaceuticals such as Samarium-153 EDTMP is being used especially in multi-disciplinary centers.

For prostate cancer Radium-223, chloride treatment was also experienced in a limited number of centers in Turkey. However, it is not under coverage of the national reimbursement system, even if it has been licensed in Turkey.

There are some other novel theranostic applications that have been introduced in Turkey in the recent years. An alpha-emitting radiopharmaceutical Actinium-225 labeled

PSMA treatment for prostate cancer was first used in Ankara University in 2018. New radiopharmaceuticals are eagerly awaited to be experienced in the near future.

Conclusion

Nuclear theranostics functions like a bridge which connects targeted diagnosis to targeted therapy, just like Turkey functions as a geographical bridge which connects Asia to Europe. As scientific and technological improvements emerge in the field of medicine, much more number of theranostic applications are expected to be introduced in Turkey in order to provide more targeted and individualized radionuclide treatment in different disease states.

Acknowledgements This paper would have never been possible without the visionary support of Executive Board members of Turkish Society of Nuclear Medicine Prof Gamze CAPA KAYA M. D. (President), Prof Dogangun YUKSEL M.D. (Vice-President), Prof Tevfik Fikret CERMIK M.D. (Secretary), Prof Elvan SAYIT BILGIN, Prof Gulin UCMAK, M. D. (member), and Prof Hakan DEMIR (member) as well as the valuable data support from the industrial partners in the field, in particular “Monrol-Eczacibasi” and “BTG” companies.

Compliance with Ethical Standards

Conflict of Interest Murat Fani BOZKURT declares that he has no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by the author.

Informed Consent For this type of study, formal consent is not required.

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