Message from the Editor-in-Chief

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Here in the middle of 2017, I have witnessed the growth of the impact factors (IFs) of our benchmark journals, the *Journal of Nuclear Medicine* (IF: 6.6) and *European Journal of Nuclear Medicine* (IF: 7.2). The increase of citations of the *European Journal* was a pleasant surprise, and the IF of the *Journal of Nuclear Medicine* was the same. As Editor-in-Chief in charge of Nuclear Medicine Molecular Imaging, after contemplation, I now think that we need to ruminate on a plausible cause for this.

This year in Denver during the Society of Nuclear Medicine and Molecular Imaging (SNMMI) meeting, the attendees were impressed by the rise of the discipline of therapy and theranostics, which was emphasized in the plenary lecture as the highlight of the talks, while the main country of interest this year was Germany, and the opening plenary Wagner lecture was given by Dr. Richard Baum. Both the presentation by the President of the German Society and the lecture by Dr. Baum were about the concerted efforts and success of the last 20 years in the innovation of theranostics and therapy by German leaders and the pioneering and consequent success of radionuclide therapy by Dr. Baum.

This looked like a prelude to the change of emphasis in the American SNMMI from the ever-emphasized imaging to therapy and theranostics, while Europeans had already been seeking changes since a decade ago. A decade ago, the European Association of Nuclear Medicine introduced a new symposium in their annual congress, ISTARD, the International Symposium of TArgeted Radiotherapy and Dosimetry. I remember the fresh impact of its novelty in Milan in 2012,

which was my first time to attend the ISTARD Congress in the EANM Congress. After several years, this became the Do.MoRe session, which followed the spirit of ISTARD but included presentations on individual novel investigations. Another significant move emanated from Dr. Richard Baum, when he held, for the first time, the Theranostic World Congress (TWC) in Bad Berka in 2011. The first wave of leaders from all over the world, mostly from Germany and Europe, gathered together at that event.

This was a cornerstone of the close collaborations between experts of different sub-disciplines (ISTARD was organized by the radionuclide therapy, radiopharmacy and dosimetry committees of EANM) and the lone innovative move of an expert who had finally found a good platform for communication networks (TWC). Afterwards, the tides moved on to the 4th TWC in Melbourne last year, and after attending this conference consisting of mostly invited speakers in plenary formats, I can now summarize the recent success of RI therapy and theranostics as (1) an already achieved cure, at least in some, of neuroendocrine tumors (NET) by using Lu-177/Ga-68 DOTATOC, DOTATATE or DOTANOC, (2) a recent serious trial to improve patient outcomes in castration-resistant prostate cancer using Ga-68 PSMA 11/Lu-177 PSMA617 or imaging only so far and using F-18 DCFPyL (PSMA ligand) and F-18 Fluciclovine® (a leucine analog) and (3) successful palliation of metastatic bone diseases using Ra-223.

In Korea, we have joyfully witnessed the exponential growth of FDG-PET in clinical practice during the last decade. The number of institutions providing PET in Korea has grown to around 117, and the annual volume was over 400,000 in 2014, doubling compared to 2006. The year 2006 was a turning point for Koreans because insurance coverage started for PET and PET/CT. However, 2015 was another heartbreaking point that dashed the hopes of Korean physicians and patients with the prevention of its use because of an anachronistic

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government-implemented guideline for PET reimbursement. In 1 year the volume returned to 220,000, similar to the number in 2006. In round terms, the number of PET/CTs doubled over the course of a decade and then returned to the level of a decade before. Therefore, the number of patients taken care of by each PET/CT machine was halved.

Summarizing the current situation, we are equipped with a well-developed infrastructure of institutions/instruments as well as experts, and we have experienced the popularity of using PET for clinical purposes by the public and all of the clinics. The initial success was followed by a sudden decline mediated by an inappropriate government policy. Referring physicians have already experienced the merits of PET/CT for their cancer patients and the reassuring power of negative PET/CT results in their follow-up patients having been cured or in remission from their initially successful anticancer treatment. They are prohibited from undergoing PET not because of the unavailability in their area but because of the ‘positive indication’ policy defining which of the followed patients are allowed to have the procedure. As is well known, the ‘positive indication’ policy means that the guideline defines the allowed indications by sentences and phrases, and all the undocumented cases are prohibited. Explicit and implicit shackles are placed on the institutions and referring physicians, with the final disadvantage and suffering experienced by the patients. From the suppliers’ side, the hospitals and nuclear medicine physicians alike, who are carrying out medical practices in nuclear medicine, we are now trying to develop anything to help our patients.

I now interpret our global current situation in nuclear medicine as (1) many more cancers are awaiting our nuclear therapy, and (2) we are wasting our efforts to optimize imaging agents and therapeutic agents separately. To overcome this dilemma and bottleneck, I propose we put our emphasis on and thus invest our passion and energy to endeavor to develop theranostic and therapeutic radiopharmaceuticals and radionuclides. In this work, we need to invite the participation of our long-standing colleagues, the radiochemists, radiopharmacists and physicists. Personalized dosimetry using voxel-based Monte Carlo simulation-based studies is warranted on the physicists’ bucket lists and development of in vivo companion diagnostics or development of chemistry for alpha-emitting radionuclides on chemists’ lists.

Joint efforts by all the nuclear medicine physicians in any country, whether developing or developed, and most of the chemists and physicists that a country has produced currently are the brain and hands resources for now. This endeavor will open a new epoch in our field of nuclear medicine globally. Now I envision, in the near future, a world where nuclear medicine physicians are routinely helping the patients with our radionuclide theranostic probes with individualized choices of relevant radiopharmaceuticals and optimized administration/dosimetry plans. Circumstances are encouraging in that in a

hospital in Nanjing, China, 20 or more theranostic procedures are being carried out every day. The important point is that in the recent past, Dr. Feng Wang, who made this possible, could only envy the atmosphere in advanced European countries. I strongly urge that in Korea, too, we need to work toward this promising long-desired future. The Korean Societies Honorary President, the deceased Dr. Chang-Soon Koh, encouraged us to achieve this goal in nuclear medicine in Korea. Under his name, dozens of Asian fellows and recently an African fellow have been learning as invited international fellows in Korea and are expected to practice this endeavor in their own countries when they came or went back to their home countries.

For the starting-to-develop countries such as Bangladesh, Myanmar or Nigeria, this endeavor will be more easily adopted. Fewer people can make a remarkable difference in establishing the novel treatment strategy *de novo* from scratch in any country of his or hers, while a considerable amount of budgets should be invested in installing a nuclear medicine imaging facility. I hope that concerted global efforts will be exercised in this initial campaign, and modest help for these developing countries from Korean institutions would be fruitful. Heterochronous characteristics of the development of our discipline should be avoided for the development and the propagation of this new endeavor.

From 1–3 March 2019, the 5th TWC will be held on Jeju Island, and international participants are expected to convene there to discuss the future. While looking forward to this convention, I encourage our domestic colleagues to carry out many theranostic investigations, attend this meeting and give a talk. As this is an entirely plenary conference and Dr. Jae Min Jeong and I are the co-organizers, we would like to invite as many as of you as possible to speak and explain how you have overcome or are overcoming the technical and regulatory difficulties of clinical translations in Asia and Korea, where we have witnessed the rise and fall of PET/CT and the hype and resolution of thyroid cancer treatment.

In our journal, *Nuclear Medicine Molecular Imaging*, I recently invited eight Associate Editors to organize ten Editorial/Review series, among which planning of six has been completed. Fortunately, four of the six are about therapy or theranostics. The other four should be completed soon and also make recommendations about the novel therapy in one way or another. I would like to draw my colleagues’ attention to the field of therapy and theranostics. Reassuringly, we Koreans have globally competent chemists and physicists. I would encourage our chemist colleagues, having just finished the development of red-ocean amyloid/tau for brain imaging, to join the efforts to open a new era of nuclear theranostics/therapy. I would also encourage our physicist colleagues, having just finished the industry transfer of next-generation PET construction, to join the efforts to make nuclear theranostics/therapy an individualized medicine. Individualized dosimetry

is the starting point, and in vivo companion diagnostics is the next thing to do.

Regarding molecular imaging, after 15 years of joint global efforts, in which Korea has been earnestly participating, I propose that we have a criterion for good research in molecular imaging in nuclear medicine: ‘is this at least remotely applicable to clinics?’ We are fascinated by super-resolution microscopy for cellular molecular imaging, and now the architecture of the brain has almost been comprehended by molecular imaging at the micro/meso connections. What remains to be seen as a development is how to translate this knowledge into clinical application.

In vitro companion diagnostics are already in the regulation guidelines of the Korean FDA. Precision medicine and the consequent in vitro biomarker development might compete with PET/CT or PET/MR studies, and deep learning or artificial intelligence might make the requirements of simple image readers of radiology and nuclear medicine obsolete. In this

period of great challenges, I will save the following messages for the next issues: (1) the introduction of novel therapies for brain diseases that have been mainly intractable so far, (2) in vivo companion theranostics and (3) keeping our discipline alive and vivid with concerted efforts of scientists (radiochemists and nuclear medicine physicists). To achieve this goal, the quality of science in nuclear medicine should be improved to the globally competent level, and the efforts of pioneers from developing nations should be greeted with openness.

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Compliance with Ethical Standards

Conflict of Interest Dong Soo Lee declares no conflict of interest.