The Current Status and Future Perspectives of Nuclear Medicine in Korea

Myung Chul Lee · So Won Oh · June-Key Chung ·
Dong Soo Lee

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Abstract Since the introduction of nuclear medicine in 1959, Korea accomplished a brilliant development in terms of both clinical practice and research activities, which was mainly due to the dedication of nuclear medicine specialists, consisting of physicians, technicians, and scientists, and strong support from the Korean Government. Now, Korea has 150 medical institutes, performing approximately 561,000 nuclear imaging procedures and 11.6 million in vitro studies in 2008, and ranked fourth in the number of presentations at the Annual Meeting of the Society of Nuclear Medicine (SNM) in 2008. The successful progress in this field has allowed Korea to focus on the international promotion of nuclear medicine, especially in the developing and underdeveloped countries. In consequence, the Asian Regional Cooperative Council for Nuclear Medicine (ARCCNM) was established in 2001, and Seoul hosted the 9th Congress of the World Federation of Nuclear Medicine and Biology (WFNMB) in 2006. In the future, Korea will strive to sustain its rate of advancement in the field and make every effort to share its progress and promote the exchange of scientific information at the international level.

Keywords Current status · Future perspectives · Nuclear medicine · Korea

Introduction: History and Milestones

The history of nuclear medicine in Korea could be classified into five stages: the Beginning Stage (1959–1968), the

Settlement Stage (1969–1978), the Development Stage (1979–1988), the Upgrading Stage (1989–1998), and the Globalization Stage (1999–) [1].

In June 1959, nuclear medicine took its first step in Korea, when a patient suffering from hyperthyroidism was treated with radioactive iodine in Seoul National University Hospital. This was the first time a radioactive isotope had been used clinically, and represented the beginning of the practice of clinical nuclear medicine in the nation. The following year, a Radioisotope Clinic was established in Seoul National University Hospital, and with the assistance of the American Atomic Energy Council, nuclear medicine clinics were established at four other national universities. In 1961, increasing interest in nuclear medicine led to the foundation of the Korean Society of Nuclear Medicine (KSNM), and in 1963, the Radiation Medicine Research Institute was established at the Korean Atomic Energy Research Institute (KAERI). Further, epoch-making events followed. The TRIGA Mark II reactor began operating in 1962 at KAERI, and nuclear imaging was initiated by the introduction of the first photo-scanner 2 years later. These events ushered in a new era of patient care in Korea, and 1967, the first issue of the *Korean Journal of Nuclear Medicine* was published [2].

In 1969, nuclear imaging formally commenced with the introduction of the scintillation gamma camera and the development of computer systems capable of processing large amounts of data for dynamic studies during the Settlement Stage, which witnessed the introduction of radioimmunoassay (RIA) in 1970 that enabled in vitro studies to be conducted more easily in clinical practice [1].

During the Development Stage, our abilities to perform sophisticated analyses using multi-head SPECT supported by a high-powered computer increased enormously, and continue to support clinical research on nuclear medicine today. As a result of this progress in the field of nuclear

M. C. Lee (✉) · S. W. Oh · J.-K. Chung · D. S. Lee
Department of Nuclear Medicine,
Seoul National University Hospital,
28 Yongon-Dong, Jongno-Gu,
Seoul, Republic of Korea 110-744
e-mail: mclee@plaza.snu.ac.kr

medicine, Seoul was given the honor of hosting The 3rd Asian and Oceanic Congress of Nuclear Medicine in 1984. Another milestone of note was the installation of the first medical cyclotron at the Korea Cancer Center Hospital in 1984 [1].

Korea has now achieved an internationally recognized expertise in nuclear medicine, which is largely due to investment in multi-head single-photon emission computed tomography (SPECT) systems during the Upgrading Stage. Three years after the installation of the first two positron emission tomography (PET) systems (1994), at Seoul National University Hospital and the Samsung Medical Center, a third was installed at the Korea Cancer Center Hospital. In 1995, the construction of a multipurpose 30-MW nuclear reactor was completed, and the Korean Board of Nuclear Medicine, which was initially formed in March 1993, was officially approved by the Korean government. These two accomplishments mark 1995 as a significant point in the history of nuclear medicine in Korea. By the end of the Upgrading Stage in 1998, most general hospitals had an independent nuclear medicine department [1].

The clinical use of PET increased substantially during the Globalization Stage (1999–). At the beginning of the twenty-first century, PET systems were acquired by many medical institutions; the Korea Cancer Center Hospital and the Yonsei University Health System both established PET systems in 2000, and the National Cancer Center and the Asan Medical Center followed 1 year later. The most critical moment with respect to the use of PET occurred in 2006 when the National Health Insurance Program allowed reimbursement for PET scans. This single act markedly accelerated the development of nuclear medicine in Korea. In addition, the introduction of portable SPECT and a 30-MeV capacity cyclotron for the exclusive production of radioisotopes are expected to increase the use of radioisotopes in the future [1].

The successful progress of nuclear medicine practice throughout the latter half of the twentieth century has allowed Korea to focus on loftier goals, and during the Globalization period, attention has been focused on the international promotion of nuclear medicine. Accordingly, the Asian Regional Cooperative Council for Nuclear Medicine (ARCCNM), an organization dedicated to increasing the awareness and progress of nuclear medicine in developing and less developed Asian countries, was established in 2001 as a consequence of a Korean initiative. Furthermore, in recognition of the progress made in the nuclear medicine field, Seoul hosted the 9th Congress of the World Federation of Nuclear Medicine and Biology (WFNMB) in 2006. In the future, Korea will strive to sustain its rate of advancement in the field and make every effort to share its progress and promote the exchange of scientific information at the international level.

Medical Facilities Practicing Nuclear Medicine

Nuclear medicine began to expand nationwide in the latter half of the 1970s. In the 1980s, a rapid increase in medical facilities practicing nuclear medicine occurred due to the establishment of nuclear medicine departments and radioisotope laboratories in hospitals around the country (Fig. 1). Furthermore, this introduction of radioisotope technology to clinical practice was followed by an increase in capital investments. In 2008, 150 medical facilities throughout Korea utilized radioisotopes for treatment and research, at this time, 128 conducted in vivo imaging studies, and 109 operated in vitro laboratories [3]. Today, there are 85 dedicated beds for radionuclide therapy in Korea. This recent increase in clinical-class medical facilities is largely due to the great number of RIAs performed in nuclear medicine laboratories.

Manpower in the Nuclear Medicine Field

The rapid development of nuclear medicine has increased demands for specialists trained and licensed in the clinical use of radioisotopes, although the first training course was established as long ago as 1960. General and special radioisotope practice licenses have been awarded to those that have passed an examination after completing a training course managed by the Ministry of Education, Science, and Technology since 1962. A 4-year curriculum for nuclear medicine residency started in 1996, which includes training for 6 months in internal medicine, 6 months in radiology, and another six months in an elective course [1].

As of 2008, 843 specialists in this field had acquired special licenses, and since the Korean Board of Nuclear Medicine was formally established, the number of nuclear medicine physicians actively involved in clinical practice has increased to 146. Of the 817 nuclear medicine technologists involved in diagnostic imaging and RIAs, 67% have a

Fig. 1 Medical facilities practicing nuclear medicine in Korea by year. A rapid increase in medical facilities practicing nuclear medicine occurred around the country in the 1980s

background in radiology and 38% a background in clinical pathology. In addition, there are 113 nuclear scientists, which include 20 scientists, 87 nuclear researchers, and six radio-isotope pharmacists [3].

Nuclear Imaging Equipment

During the Beginning Stage, rectilinear scanners, and gamma and beta calculating machines were mainly used by the specialists. However, these instruments were replaced by RIAs and gamma cameras in 1969. In particular, the number of rotating gamma cameras notably increased after the introduction of SPECT machines in 1983, due to their ability to generate tomographic images of the body. A total of 256 gamma cameras (49 conventional gamma cameras and 207 SPECT cameras) and 127 PET machines are currently used throughout the nation. The year 1990 saw the introduction of the triple-head gamma camera, which has better resolving power than the standard single-head gamma camera and allows the user to observe even subtle biochemical changes in the early stages of various diseases. The number of these multi-head SPECT cameras has increased markedly, and in 2008, 181 double-head cameras and 13 triple-head cameras were operating in Korea. Approximately, 80% of these are SPECT units [3].

Due to the ability of PET machines to visualize directly changes at the cellular and molecular levels, PET system-based research and treatment systems have quickly progressed in the United States, Europe, and Japan. However, in Korea, the high costs of cyclotrons and other nuclear medicine equipment have hampered the introduction of PET systems. The first PET system in Korea was acquired jointly by Seoul National University Hospital and the Samsung Medical Center in 1994, and shortly afterwards, PET systems were installed at the Yonsei University Health System (1997), the National Cancer Center (2001), and at the Asan Medical Center (2001). In 2008, 127 PET machines (14 PET and 113 PET/CT) were installed in 78 PET centers, and this process of acquisition continues at smaller regional hospitals [3].

Radioisotope Utilization and Production

Radioisotope use in clinical practice has increased rapidly from 1970, when only 2.6 Ci was used in Korea. In parallel with the overall progress of nuclear medicine during the 1980s, the amount of radioisotope used in clinical practice significantly increased to 202 Ci in 1982 and 320 Ci in 1985. By 1990, 1,060 Ci was being used clinically, and in 2008, this rose to 8,672 Ci, 57.2% of which was accounted for by Tc-99m (4,961 Ci), 19.4% by I-131 (1,683 Ci), 21.9% by F-18 (1,900 Ci), 1.4% by

Tl-201 (121 Ci), and the remaining 0.1% by other radionuclides (Fig. 2) [4].

From 1960 to the first half of 1970, I-131, Au-198, and P-32 were primarily used to perform liver and thyroid scans. However, in the latter half of 1980, the number of liver scans performed rapidly reduced. On the other hand, numbers of thyroid, kidney, and bone scans sharply increased. In addition, static and dynamic studies of these organs and of other internal organs became possible due to the introduction of the gamma camera, which resulted in the replacement of I-131, Au-198, and P-32 by Tc-99m, the most frequently used radionuclide [1].

Full-scale radioisotope production began in Korea in 1962 with the completion of the TRIGA Mark II reactor at the KAERI. The TRIGA Mark II reactor has supplied approximately 66% of I-131 consumed in Korea, and is also able to produce Tc-99m, P-32, Dy-165, Ho-166, Au-198, and Ir-192. The nation's first medical cyclotron, which was installed at the Korea Cancer Center Hospital in 1985, produced Tl-201, Ga-67, In-111, and I-123. In 1995, the Korea Cancer Center Hospital was producing In-111, I-123, and Cr-51 daily, and was supplying 52.1% and 7.1% of the nation's requirements for Ga-67 and Tl-201, respectively [1]. Currently, the KAERI and the Korean Institute of Radiological and Medical Sciences (KIRAMS) are the only facilities with radioisotope production capabilities. Nevertheless, nearly 90% of all Mo-99/Tc-99m and RIA kits used in Korea are imported [4].

Nuclear Medicine Practice

Conventional Nuclear Imaging Studies

Due to its unique ability to provide function-specific information, nuclear imaging is an effective diagnostic tool, especially when utilized in conjunction with clinical data and radiological findings. The clinical applications of nuclear imaging have changed appreciably over the past two decades. From 1960 to the first half of 1970, liver and thyroid scans using I-131, and Au-198 were primarily used in clinical practice, but as was mentioned above, the use of liver scans rapidly decreased in the latter half of 1980, but this was more than counterbalanced by a sudden rise in the number of thyroid, kidney, and bone scans. Today, almost all organs can be examined using radioisotopes [1].

Approximately 561,000 nuclear imaging procedures were performed in 2008, which is twice that performed in 2000. Of the nuclear imaging studies conducted in 2008, 298,000 (110,000 in 2000) were for bone scans, 106,380 (68,000 in 2000) for thyroid scans, 78,800 (29,000 in 2000) for heart scans, and 6,000 (20,000 in 2000) were for liver scans. This marked increase in the number of heart and

Fig. 2 Growth in the clinical use of radioisotopes. Radioisotope use in clinical practice has increased rapidly since the 1980s, and the amount of radioisotope used in clinical practice significantly increased from 320 Ci in 1985 to 8,672 Ci in 2008

bone scans continues, and in particular, the increased usage of myocardial perfusion SPECT is prominent. Furthermore, nuclear cardiology studies only accounted for 2% of total nuclear imaging studies in 1985, but 10% in 2008. On the other hand, the number of renal and lung studies performed did not increase over the same period (18,893 and 10,523 in 2002, respectively), and the number of liver scans decreased after reaching a peak in the early 1990s (from 32,705 in 1994 to 6,000 in 2008) [3].

The resolving powers of nuclear medicine imaging systems are somewhat low, and it is important that these be increased. In this context, the introduction of SPECT in 1983 represented a step toward solving this issue by providing tomographic images with higher resolution. In 2008, SPECT accounted for about 13% (73,000) of all nuclear imaging studies [74% (53,700) and 21% (15,500) of these were myocardial and brain SPECT studies, respectively [3].

Nuclear imaging use in the neurology field has boomed since 1997. Brain perfusion SPECT and brain PET became the most commonly and widely performed types of nuclear neuroimaging study, whereas other studies, such as conventional brain scan, radionuclide cisternography, and shunt function test, remained stationary or declined. The number of brain SPECT studies performed has approximately doubled every 3 years since 1991, and in 2008, a total of 15,500 brain perfusion SPECT and 6,000 Diamox brain perfusion SPECT studies were performed. In particular, Diamox brain perfusion SPECT, which accounted for 25% of all brain SPECT studies, is now commonly used to evaluate cerebrovascular reserve in patients with cerebrovascular disease. Numbers of brain perfusion SPECT studies are expected to increase due to the aging of Korean society, and thus, the prevalences of cerebrovascular diseases will

inevitably increase. On the other hand, more than half of all brain SPECT studies are conducted to assess epilepsy and neurovascular disorders. In addition, recently introduced neuroreceptor imaging studies introduce a new dimension to SPECT and are expected increase demand in the near future.

The use of brain PET, although it is not used as frequently as brain perfusion SPECT, has also rapidly increased over the last several years. PET studies comprise 15% of all nuclear neuroimaging studies conducted in Korea, and 14% of these are brain PET studies. Brain PET is mainly used to assess epilepsy, brain tumors, dementia and other psychiatric disorders, and cochlear implants. Between 2000 and 2008, the number of brain PET studies increased more than tenfold from 812 to 9,135 [3].

Nuclear cardiology studies have increased in number and in terms of the proportion of nuclear imaging studies performed, and in 2008, almost 78,000 cases were conducted; a proportion of 14%. Conventional nuclear cardiology studies (multi-gated acquisition scans and single pass studies) have declined in number from the 1990s, but myocardial SPECT studies have increased dramatically to 49,000 cases per year (27,500 cases for Tl-201 and 21,500 for Tc-99m-MIBI scans in 2008). However, as compared to other developed countries, only a small number of myocardial SPECT studies are performed in Korea, which is notable given the incidence of heart disease. This difference demonstrates that the use of myocardial SPECT should be actively promoted in clinical practice [3].

PET Application

Korea has adopted PET technology wholeheartedly. The number of PET machines and PET studies performed

soared after the National Health Insurance Program agreed to reimburse PET study costs in 2006, as demonstrated by the number of studies performed, i.e., 41 PET machines (11 PET and 30 PET-CT) and 100,000 PET scans in 2004, to 127 PET machines (14 PET and 113 PET-CT) and 248,000 PET scans in 2008 (Fig. 3). In 1995, PET was most commonly used for neurological imaging (60%). However, this proportion has since declined because oncologic PET applications have increased dramatically, and in 2008 these accounted for almost 90% of studies performed. In contrast, the number of cardiologic studies performed was minimal (Fig. 4) [3].

Radionuclide Therapy

Regarding radioisotope treatments, only radioiodine therapy is actively used in daily clinical practice. Nevertheless, novel treatments based on Ho-166 and Re-188 have been devised and trialed. In 2008, 25,078 patients were treated with radionuclides, i.e., 24,485 underwent radioiodine therapy (99.2%), 34 Ho-166 treatment, 49 underwent Sr-89 therapy as a palliative bone metastasis treatment, and 34 I-131-MIBG therapy. For interest, the numbers of radioiodine treatments performed in 1982, 1988, and 1994 were 837, 3,387, and 4,710, respectively [3].

Current Status of In Vitro Studies

Despite the considerable challenges presented by competitive methods like ELISA, in vitro nuclear medicine studies have increased in line with in vivo studies. The number of RIA studies conducted per annum has continuously increased since 1993. In 2008, 11.6 million studies were performed, which represents a 78% increase from 2000 (6,490,000) and an approximately ninefold increase from 1991 (1,351,000), which also represented a remarkable increase compared with the 261,813 conducted in 1982. Hepatitis antigen/antibody

assays and thyroid function tests were the main types of in vitro studies conducted in the 1980s (37% and 34% respectively in 1985), but tumor marker assays significantly increased from 13% in 1985 to 25% in 2008. In 2008, hepatitis assays accounted for 14%, thyroid assays for 38%, and other hormone assays for 14% of all in vitro studies conducted [3].

In accordance with the increased popularity of in vitro studies, the numbers of associated instruments has also markedly increased. In 2008, 178 gamma counters and 38 autoanalyzers were being used in Korea, whereas in 1990 and 2000 gamma counter numbers were 31 and 100, respectively. In addition, RIA kits have been produced domestically for several years, and to a large extent, the number of in vitro studies conducted is due to the domestic production of some 22 types of RIA kits, which include the T3, T4, FT4, and HCG kits, and a series of hepatitis kits [3].

Primary Research Activities

Scientific activity in the nuclear medicine field has progressed remarkably during the past 7 years. Korea ranked fourth in terms of the number of papers presented at the Annual Meeting of the Society of Nuclear Medicine (SNM) in 2008 by submitting 128 papers, compared with 85 in 2001 and 96 in 2004 (Fig. 5) [3]. Currently, many nuclear medicine research projects are being conducted, the majority of which are oncologic and brain studies. In order to enhance the quality of research activities, data analysis methods utilizing new image processing technologies have been developed. For example, myocardial SPECT studies have evolved into quantitative gated SPECT studies. In addition, considerable advancements have been made in the use of rhenium- and holmium-based radionuclide therapies.

Fig. 3 Numbers of PET studies performed in Korea by year. The number of PET studies soared after the National Health Insurance Program agreed to reimbursing PET study costs in 2006, as demonstrated by the number of studies performed: from 100,000 PET scans in 2004 to 248,000 PET scans in 2008

Fig. 4 Annual changes in the proportion of PET study types. Neurological imaging has declined because oncologic PET applications have increased dramatically, while there was only a minimal change in the number of cardiologic studies

Furthermore, radioisotope-based molecular imaging and reporter-gene imaging have emerged as new exciting technologies with the potential to be used to support the developments of gene therapies and stem cell transplantation. Furthermore, with support from the Korean Government, the scientific community is making a concerted effort to expand clinical PET research and to promote PET and cyclotron applications.

Future Perspectives

The factors largely responsible for the successful development of nuclear medicine in Korea are as follows: the utilization of SPECT for neurological and cardiovascular disorders, the increased utilization of multi-head SPECT, the production of more domestic radionuclides and radiopharmaceuticals, the promotion of PET technology, the support of the Korean Government, a strong Korean Society of Nuclear Medicine, and above all, the establishment of the Korean Board of Nuclear Medicine. The roles played by pre-existing national institutions should also be recognized, these include the Korean Radioisotope Association, the Korean Atomic Energy

Research Institute, the Radiation Health Research Institute, the Korean Institute of Radiological and Medical Sciences, and others.

Considerations of the above-mentioned status of radio-nuclide uses in clinical practice suggest that the future of nuclear medicine in Korea is assured. The Ministry of Education, Science and Technology has established a comprehensive promotion plan to ensure the utilization, research, and development of radiation and radioisotopes by increasing the standing of Korea in the nuclear power field. This plan includes increasing the research and development grant budget and enhancing the domestic production of radioisotopes, radiopharmaceuticals, and new radionuclides. Furthermore, plans are being devised to establish multiple regional cyclotrons and PET centers throughout Korea. These centers are expected to promote molecular nuclear medicine technology and PET applications.

Korea has now stood firmly on the global nuclear medicine stage since the successful 9th Congress meeting of the WFNM and the formation of the ARCCNM. Furthermore, the KSNM intends to increase its international participation, and accordingly, has established links with the International Atomic Energy Agency (IAEA), World Health Organization

Fig. 5 The number of abstracts presented at annual Society of Nuclear Medicine meetings. Korea ranked fourth in terms of the number of papers presented at the Annual Meeting of the Society of Nuclear Medicine in 2008, by submitting 128 papers

(WHO), Society of Nuclear Medicine (SNM), Japanese Society of Nuclear Medicine (JSNM), and European Association of Nuclear Medicine (EANM).

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