The Current Status of SPECT or SPECT/CT in South Korea

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Abstract The first step to nuclear medicine in Korea started with introduction of the gamma camera in 1969. Although planar images with the gamma camera give important functional information, they have the limitations that result from 2-dimensional images. Single-photon emission computed tomography (SPECT) due to its 3-dimensional image acquisition is superior to earlier planar gamma imaging in image resolution and diagnostic accuracy. As demand for a hybrid functional and anatomical imaging device has increased, integrated SPECT/CT systems have been used. In Korea, SPECT/CT was for the first time installed in 2003. SPECT/CT can eliminate many possible pitfalls on SPECT-alone images, making better attenuation correction and thereby improving image quality. Therefore, SPECT/CT is clinically preferred in many hospitals in various aspects. More recently, additional SPECT/CT images taken from the region with equivocal uptake on planar images have been helpful in making precise interpretation as part of their clinical workup in postoperative thyroid cancer patients. SPECT and SPECT/CT have various advantages, but its clinical application has gradually decreased in recent few years. While some researchers investigated the myocardial blood flow with cardiac PET using F-18 FDG or N-13 ammonia, myocardial perfusion SPECT is, at present, the radionuclide imaging study of choice for the risk stratification and guiding therapy in the coronary artery disease patients in Korea. New diagnostic radiopharmaceuticals for AD have received increasing

attention; nevertheless, brain SPECT will remain the most reliable modality evaluating cerebral perfusion.

Keywords Gamma camera · SPECT · SPECT/CT

Introduction

The first step to nuclear medicine in Korea started with introduction of the gamma camera in 1969 [1]. Although planar images with the gamma camera give important functional information, they have the limitations that result from 2-dimensional images. Single-photon emission computed tomography (SPECT) due to its 3-dimensional image acquisition is superior to earlier planar gamma imaging in image resolution and diagnostic accuracy. Since the first installation of SPECT with a single head in 1983, there have been great advances in SPECT from generation to generation. SPECT with a dual- or a triple-detector SPECT (200 SPECT scanners and 33 SPECT/CT scanners in 2013) has recently been widely used in most hospitals in Korea [2]. Since SPECT has been widely used for evaluation of cerebral and cardiac perfusion, the number of SPECT imaging continuously increased to 2008. Thereafter, the number of SPECT cases decreased since 2008 because of the decline in myocardial SPECT cases that accounted for over 70 % of all SPECT cases. Since demand for a hybrid functional and anatomical imaging device has increased, integrated SPECT/CT systems have been used. In Korea, SPECT/CT was installed for the first time in 2003 [1].

SPECT/CT is capable of co-localization the region identified on functional and anatomical imaging, and elimination of many possible pitfalls on SPECT-alone images, and allows improvement of the accuracy in the interpretation. In addition, the CT component lends itself to a better attenuation correction and thereby improves image quality. Therefore, SPECT/

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CT is clinically preferred in many hospitals in the cardiac, neurologic, skeletal, oncologic and endocrine diseases. In 2013, a total of 33 SPECT/CT scanners were used in clinical practice throughout the nation, and SPECT/CT applications have increased over the last several years. The clinical usefulness of SPECT/CT has been demonstrated in skeletal imaging, especially in the hand and foot which have complex structures. More recently, additional SPECT/CT images taken from the region with equivocal uptake on planar images have been helpful in making precise interpretation as part of their clinical workup in postoperative thyroid cancer patients.

The aim of this review was to describe the current status of SPECT or SPECT/CT in the field of nuclear medicine in Korea.

Cardiac Imaging

Myocardial perfusion imaging with SPECT plays a vital role in risk stratification and the establishment of individual therapeutic strategies. Cardiac event rates in patients with normal or low-risk myocardial perfusion SPECT using Tl-201, Tc-99 m sestamibi, or Tc-99 m tetrofosmin have been shown to be <1 % per year of follow-up [3–5]. In addition, myocardial perfusion SPECT makes it possible to quantify regional perfusion and visualize the viability of myocardium [6, 7]. Before invasive coronary angiography, myocardial perfusion SPECT is more cost-effective than exercise electrocardiography or stress echocardiogram [8, 9]. In accordance with these substantial benefits of myocardial perfusion SPECT, the number of myocardial perfusion SPECT cases continued to increase in Korea. However, the number of myocardial perfusion SPECT cases decreased after reaching a peak of 55,000 in 2006 and to 31,000 in 2013. One cause appears to be increased coronary CT angiography cases, and reduced need for myocardial perfusion SPECT [2]. Concerns about increased radiation exposure seemed to be another cause for the decline of the number of myocardial perfusion SPECT cases, although nuclear medicine physicians and manufacturers of SPECT equipment put great effort into reducing radiation exposure.

The abnormalities of myocardial sympathetic innervation can be evaluated by using I-123 MIBG cardiac SPECT [10]. In the cardiac sympathetic nervous system, molecular imaging using I-123 MIBG, which is a norepinephrine analogue, has been used. Although most of the I-123 MIBG studies are based on heart to mediastinum ratio in the planar scintigraphy, several studies included measurement from I-123 MIBG cardiac SPECT. They demonstrated that a reduced myocardial uptake in I-123 MIBG cardiac SPECT is associated with heart failure and inducible arrhythmia [11, 12]. I-123 MIBG cardiac SPECT provides better visualization of decreased cardiac uptake with 3-dimensional regional information not available on planar scintigraphy. Therefore I-123 MIBG cardiac SPECT can be a noninvasive tool to evaluate local cardiac

autonomous innervation and systemic autonomic function in heart failure patients.

I-123 MIBG myocardial imaging has also been applied to differentiate Parkinson's disease (PD) from non Parkinson's tremor [13, 14]. In a previous study that evaluated 52 PD patients and 16 healthy controls, higher diagnostic value in PD was found on I-123 MIBG SPECT than on planar imaging [14]. The sensitivity, specificity, and accuracy for the diagnosis of PD were 84.6 %, 100 %, and 88.2 %, respectively, on planar imaging, and 96.2 %, 100 %, and 97.1 % on SPECT, respectively.

Neurology

Since the introduction of SPECT to Korea in 1983, the number of brain perfusion SPECT cases has been increasing gradually, and thus brain perfusion SPECT has been considered one of the major imaging modalities for the diagnosis of the various clinical conditions [1]. In 2013, a total of 14,000 brain perfusion SPECT cases using Tc-99 m HMPAO or Tc-99 m ECD (10,000 brain perfusion SPECT cases and 4000 Diamox brain perfusion SPECT cases) were performed [2]. In Korea, most of the brain perfusion SPECT cases have been conducted to measure cerebral blood flow and to evaluate functional network with surrounding tissue or contralateral unaffected tissue. Brain perfusion SPECT is capable of localizing blood supply defects and the extent of infarction as well as representing the infarct core and the peri-infarct zone [15]. Diamox, a vasodilator, has been widely used for the evaluation of cerebrovascular reserve in cerebrovascular disease patients [16]. In Korea, brain perfusion SPECT using Diamox accounted for 25 % of all brain perfusion SPECT cases in 2008 and 29 % in 2013, with an increased trend. In addition, brain perfusion SPECT provides important information about cerebral perfusion and its alteration due to electrophysiological changes in epilepsy patients. An epileptogenic area reveals hyperperfusion on ictal brain perfusion SPECT and hypoperfusion or normal perfusion on interictal brain perfusion SPECT [17].

A large meta-analysis showed that pooled sensitivity and specificity of brain perfusion SPECT for the diagnosis of Alzheimer's disease (AD) are 79 % and 84 %, respectively [18]. Although brain PET has a potential value in the diagnosis of AD with advances in developing radiopharmaceuticals, brain perfusion SPECT is still the most frequently used neuroimaging modality in the field of nuclear medicine in Korea.

In 1997, I-123 FP-CIT SPECT, a dopamine transporter imaging modality, was first performed, and 200 I-123 FP-CIT SPECT in 2000 [2]. Dopamine transporter SPECT has been used to evaluate the functional impairment of presynaptic dopaminergic integrity in PD [19]. Until recently, the

number of both I-123 FP-CIT SPECT and F-18 FP-CIT PET cases has been insensibly increasing in the diagnosis of PD.

Bone

Bone scintigraphy is a widely used nuclear imaging modality that is utilized for the evaluation of traumatic patients or for the follow-up of bone metastasis in oncology patients. Bone scintigraphy is relatively difficult to localize a lesion in complex structures, such as the hand and foot, compared to other musculoskeletal imaging modalities. Bone SPECT can overcome this drawback of bone scintigraphy because it provides depth information that cannot be obtained from planar bone scintigraphy. Early-stage bone SPECT is only used to assess the disorders of the head and neck, spine, pelvic bone, hip, and knee joint. Integrated SPECT/CT has recently been used to evaluate the disorders of the hand and foot. The application of SPECT/CT is becoming increasingly common as a result of wide dissemination of integrated SPECT/CT equipment [20]. Even-Sapir et al. [21] reported that SPECT/CT gave the final diagnosis in 59 %, and provided the basis to decide the best modality for further imaging leading to diagnosis in 30 % of bone scans of non-oncologic patients. Additionally, Linke et al. [22] documented that SPECT/CT has additional diagnostic accuracy in patients with orthopedic disorders confined to the peripheral extremities compared to SPECT. The number of bone scintigraphy cases grows in geometrical progression from 58 in 1976 to 272,893 in 2013. The number of bone SPECT cases gradually increased from 54 in 1988 to 5785 in 2004; however, it decreased to 3000 in 2009. Since 2010, the number of bone SPECT cases increased, and SPECT was performed on 7723 patients in 2013 [2]. The second rise in the number of SPECT cases since 2010 probably resulted from the expansion of SPECT indication due to the SPECT/CT installation.

Bone SPECT/CT cannot be approved by New Health Technology Assessment in Korea, and bone SPECT/CT adopted as bone SPECT in Korean national health insurance payment. In this regard, wide spread of bone SPECT/CT has obstacles. If we extensively perform SPECT/CT in various musculoskeletal disorders with appropriate indication criteria, we will expect a substantial increase in bone SPECT cases.

Oncology

Ga-67 and Tl-201 planar scintigraphy as well as SPECT has been used to detect various types of tumors in the oncology field. Use of these gamma imaging modalities has decreased over time due to the explosive use of PET/CT, and thus they are currently only seldom used in some clinical conditions, such as endocrine tumors and sentinel node lymphoscintigraphy. The number of Ga-67 scintigraphy cases in Korea was 2922 in 2006

and remarkably reduced to 103 (SPECT 99 cases) in 2013 [2], which may have resulted from the increased use of PET/CT.

Thyroid Cancer

Radioiodine scintigraphy plays a decisive role in treatment planning, including I-131 ablation, surgical resection, chemotherapy, and external beam radiotherapy, in thyroid cancer patients. When planar radioiodine scintigraphy shows unusual radioiodine distribution, SPECT/CT can be additionally performed to differentiate physiologic uptake from metastatic foci [23, 24].

I-131 whole body planar scintigraphy was performed on 16 patients in 1979 in Korea, whereas it was performed on 29,041 patients including 1459 patients who underwent scintigraphy combined with SPECT/CT in 2013, with a remarkable increase in number [2]. Radioiodine SPECT/CT is performed in many hospitals since its approval by the Korean Center for New Health Technology Assessment in 2012, and clinical use of SPECT/CT is in a growing trend. The number of thyroid cancer patients who underwent PET/CT markedly decreased due to the strict policy of the Korean National Health Insurance Service; however, the increase of appropriate indications for SPECT/CT can overcome the decreased cases.

Neuroendocrine Tumor

MIBG scintigraphy and somatostatin receptor scintigraphy, such as octreotide scintigraphy, are representative neuroendocrine imaging modalities in nuclear medicine. Rozovsky et al. [25] showed that SPECT/CT defines anatomical locations in patients with equivocal CT findings or MIBG foci, and distinguishes malignant from benign lesions that have uncertain CT findings. In addition, Krausz et al. [26] suggested that SPECT/CT improves the diagnostic value of somatostatin receptor scintigraphy in 32 % of patients with neuroendocrine tumors and alters the treatment plan in 14 %.

The number of neuroendocrine gamma imaging cases have decreased according to the development of PET/CT. Neuroendocrine tumor scan was performed in a small number of cases of neuroendocrine tumors in 2013 in Korea: 314 MIBG SPECT cases (154 cases in combination with SPECT/CT) and 33 octreotide SPECT cases (13 cases in combination with SPECT/CT) [2]. Recent studies reported that PET/CT using Ga-DOTA peptide has better diagnostic accuracy than octreotide scintigraphy in patients with neuroendocrine tumors [27, 28]. However, since Ga-DOTA peptide is not extensively used in Korea, SPECT and SPECT/CT using somatostatin receptors are still valuable imaging methods for the diagnosis and treatment of neuroendocrine tumors.

Sentinel Node Lymphoscintigraphy

Lymphoscintigraphy for the localization of sentinel nodes has been developed in clinically node-negative patients with breast cancer or melanoma over the past two decades. Application of SPECT/CT can allow for more accurate nodal staging, decrease unnecessary lymph node dissection, and consequently improve patients' quality of life. A recent prospective IAEA sentinel node trial recommends SPECT/CT in patients with no lymphatic drainage, those with unexpected drainage, and those with deep intra-abdominal or retroperitoneal drainage on planar scintigraphy [29]. A recent study showed that hybrid SPECT/CT enhances anatomical localization of sentinel nodes in patients with breast cancer and predicts metastatic involvement of sentinel nodes in T1 primary tumors [30]. Currently, SPECT and SPECT/CT are not widely used because planar images of sentinel scintigraphy are mostly used in clinical practice. Sentinel node scintigraphy was performed in 10,770 cases in 2013 and SPECT (SPECT/CT) 208 (186) cases [2]. Among the sentinel node scintigraphy, only 1.9 % cases obtained additional SPECT (SPECT/CT). If we appropriately utilize the SPECT or SPECT/CT when sentinel lymph node cannot be visualized on planar scintigraphy, sentinel node SPECT or SPECT/CT can provide additional benefit for patients' surgical outcome.

Conclusion

SPECT and SPECT/CT have various advantages, but its clinical application has gradually decreased in recent few years. While some researchers investigated the myocardial blood flow with cardiac PET using F-18 FDG or N-13 ammonia, myocardial perfusion SPECT is, at present, the radionuclide imaging study of choice for the risk stratification and guiding therapy in the coronary artery disease patients in Korea. New diagnostic radiopharmaceuticals for AD have received increasing attention; nevertheless, brain SPECT will remain the most reliable modality evaluating cerebral perfusion.

Spread of integrated SPECT/CT can improve the utility of bone scintigraphy in pathologic lesions of complex body structures, such as the hand and foot. Recently, the clinical practice of oncologic nuclear medicine has decreased by the strict regulation of PET/CT by the Korean National Health Insurance Service. However, if SPECT or SPECT/CT is widely used in clinical practice, it can help increase the number of patients receiving imaging studies in the field of oncologic nuclear medicine. If SPECT or SPECT/CT provides accurate diagnostic information through extending its indications to all areas of nuclear medicine imaging, then nuclear medicine will represent great advances that compensate for the decreased number of PET/CT cases.

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Compliance With Ethical Standards

Conflict of Interest Ikdong Yoo, Eun Kyoung Choi and Yong-An Chung declare that they have no conflict of interest.

Ethical Statement The study was approved by an institutional review board or equivalent and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The institutional review board waived the need to obtain informed consent.

The manuscript has not been published before or is not under consideration for publication anywhere else and has been approved by all co-authors.

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