Comparative Study of Imaging Characteristics of I-125 Imaging Using the Siemens Inveon Scanner and Siemens Symbia TruePoint

Young Jun Kim¹, Ilhan Lim¹,²*, A Ram Yu¹, Byung Il Kim¹,², Chang Woon Choi¹,², Sang Moo Lim¹,², Jin Su Kim¹,³,⁴*

¹Molecular Imaging Research Center, Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences (KIRAMS), Seoul, Korea
²Department of Nuclear Medicine, Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Sciences (KIRAMS), Seoul, Korea
³Korea Drug Development Platform Using Radio-Isotope (KDePRI), Seoul, Korea
⁴Radiological and Medico-Oncological Sciences, University of Science and Technology (UST), Seoul, Korea

Email: *ilhan@kirams.re.kr, kjs@kirams.re.kr

Received 21 August 2015; accepted 10 October 2015; published 13 October 2015

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Abstract

Objective: Although Iodine-125 (¹²⁵I) has been widely used for in vitro studies because of its relatively long half-life (60.1 days), ¹²⁵I imaging is limited because of its low energy (27 - 35 keV), even in an animal-dedicated system. In this study, imaging characteristics of ¹²⁵I were assessed using a small animal-dedicated imaging system and clinical scanner. Methods: Using the Siemens Inveon and Siemens Symbia TruePoint systems, imaging characteristics such as resolution, sensitivity, and image quality were compared. Mouse high resolution (MHR-0.5), mouse general purpose (MGP-1.0), and mouse high sensitivity (MHS-2.0) collimators were used for the Inveon scanner, and low energy high-resolution (LEHR) and low energy all-purpose (LEAP) collimators were used for the Symbia TruePoint. For animal imaging, 16.8 MBq of ¹²⁵I was administered to BALB/c mice intravenously, and the planar image and single-photon emission computed tomography (SPECT) were obtained using both scanners. Results: The resolution of ¹²⁵I for the Inveon scanner was 3.98 mm full width at half maximum (FWHM) at a 30-mm distance with the MHR-0.5 collimator, and the value of Symbia scanner was 8.72 mm FWHM at a 30-mm distance with the LEHR collimator. The sensitivity of ¹²⁵I for the Inveon scanner was 21.87 cps/MBq, and the value for the clinical scanner was 30.55 cps/MBq. The planar images of mice were successfully obtained at the level of evalu-
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1. Introduction

Iodine-125 (125I) has been widely used for in vitro research because of its relatively long half-life (60.1 days). Various 125I-labeled nucleic acids, antibodies, and ligands are commercially available or easily made in the laboratory using commercially available reagents and kits [1] [2]. Recently, in vivo 125I imaging methods were developed, and both in vivo and in vitro experiments were performed using the same 125I-labeled tracers [3]-[7]. However, in vivo imaging in animals using 125I is limited because of its low energy (27 - 35 keV) compared to Technetium-99m (99mTc) or Iodine-123 (123I) [8].

Although the clinical scanner was designed for imaging human patients, the clinical scanner has been used for animal imaging. Small animal imaging using a clinical scanner with a pinhole collimator and 99mTc or 123I has been reported [6] [9]-[12]. Although a small animal-dedicated scanner provides high resolution (submillimeter range), the clinical scanner is ready to use in clinics. Another advantage of the clinical scanner is the large field of view.

In this study, we investigated the feasibility for 125I imaging using a clinical scanner without a pinhole collimator and compared its performance characteristics to a small animal scanner.

2. Materials and Methods

2.1. System Description

The Symbia TruePoint (Siemens Medical Solutions USA, Inc., Knoxville, TN, USA) clinical single-photon emission computed tomography (SPECT)/computed tomography (CT) imaging system designed for human patients was used to assess 125I characteristics. Low energy high-resolution (LEHR) and low energy all-purpose (LEAP) collimators were used. Each collimator consisted of 148 holes with a 1.11-mm diameter and 90 holes with a 1.45-mm diameter across the flats. Each of the two detector heads of the Symbia TruePoint SPECT system consisted of a 15.8-mm crystal thickness and a SPECT field of view of 40 cm (axial) by 50 cm (diameter).

The Siemens Inveon small animal positron emission tomography (PET)/SPECT/CT imaging system (Siemens Medical Solutions USA, Inc.) was used to assess the performance of 125I. Mouse high resolution (MHR), mouse general purpose (MGP), and mouse high sensitivity (MHS) collimators with pinhole diameters of 0.5 mm, 1.0 mm, and 2.0 mm across the flats, respectively, were used. The Inveon SPECT/CT system consisted of two detector heads, an active area of 15 cm × 15 cm, [NaI(Tl)] scintillator crystal material, and 4624 crystal elements.

2.2. Spatial Resolution and Sensitivity

For the measurement of spatial resolution and sensitivity, a 1-mm point source was made using capillary tubes. The activities of 125I and 99mTc were 2.2 MBq and 3.3 MBq, respectively. The data acquisition time was 600 s. To determine the spatial resolution, profiles through peaks in count distributions were drawn in two orthogonal directions in middle slices. For each profile, full width at half maximum (FWHM) was measured by linearly interpolating the adjacent pixels at half or tenth of their maxima in the profile.

2.3. Image Quality

For the assessment of image quality, the National Electrical Manufacturers Association (NEMA) NU 4 Image Quality (IQ) Phantom was used [13]-[15]. The NU 4 IQ phantom is a cylindrical chamber that consists of three parts: five fillable rods with diameters of 1, 2, 3, 4, and 5 mm arranged in the top part; a uniform region in the
middle part; and two cold components with a 10-mm diameter attached to the bottom part. The top and bottom regions are filled with nonradioactive water and air, respectively. The nonuniformity, recovery coefficient, and spillover ratio (SOR) were assessed using the NU 4 IQ phantom [14]. The initial activities for $^{99m}$Tc and $^{125}$I were 11.87 MBq and 11.36 MBq, respectively.

2.4. Data Acquisition
The step-and-shoot mode was used for data acquisition. The acquisition time for each view was 100 s, total imaging time was 3200 s, rotation degree was 180°, degree of configuration was 180°, and magnification factor was 3.2.

2.5. Reconstruction
The ordered subset expectation maximization three-dimensional (OSEM-3D) algorithm was used in the small animal scanner, and the Flash 3D algorithm was used in the clinical scanner. The number of iterations was 8, and the number of sets was 4. The windows for $^{125}$I and $^{99m}$Tc were 35 ± 11 keV and 140 ± 14 keV, respectively.

2.6. Animal Studies
Animal study was carried out in accordance with guideline provided by the Institutional Animal Care and Use Committee (IACUC) and Institutional review board (IRB) in Korea Institute of Radiological and Medical Sciences. In addition, all experimental protocols were approved by IACUC and IRB in Korea Institute of Radiological and Medical Sciences.

$^{125}$I was injected into BALB/c mice (weight: 20 g, female, SLC JAPAN) and the mice were scanned for 1 hour after injection. Planar mode imaging and SPECT mode imaging were performed. The 1.0-MGP collimator was used in the small animal scanner, and the LEAP collimator was used in the clinical scanner. The activity concentrations for the animal scanner and clinical scanner were 18.9 MBq and 14.4 MBq, respectively.

In vivo radiolabeled antibody imaging was assessed using a human breast cancer mouse model. KPL-4 and MDA-MB-231 xenografts were established in female nude mice (6 weeks) began by subcutaneously implanting approximately $5 \times 10^6$ KPL-4 cells in the right hind leg and $5 \times 10^6$ MDA-MB-231 cells in the left hind leg. The size of the HER2-positive KPL-4 tumors and the HER2-negative MDA-MB-231 tumors were approximately 300 mm$^3$. $^{125}$I-labeled HER2-targeting antibody was injected, and its activity concentration was 8.81 MBq.

3. Results
3.1. Spatial Resolution
Figure 1(a) shows the mean resolution as a function of source-to-collimator distance. The resolution measurements using $^{125}$I point sources are summarized in Figure 1(a). At source-to-collimator distances of 25, 30, and 35 mm, the spatial resolutions of $^{125}$I measured using the Inveon scanner were 3.32, 3.98, and 4.20 mm full width at half maximum (FWHM), respectively, using the MHR 0.5-mm pinhole (MHR-0.5) collimator; 3.98, 4.42, and 4.86 mm FWHM, respectively, using the MGP 1.0-mm pinhole (MGP-1) collimator; and 4.35, 4.88, and 5.43 mm FWHM, respectively, using the MHS 2.0-mm pinhole (MHS-2.0) collimator.

At source to collimator distances of 25, 30, and 35 mm, the resolutions of $^{125}$I measured using the Symbia TruePoint system were 8.28, 8.72, 8.89 mm FWHM, respectively, using the LEHR collimator and 9.06, 9.19, and 9.25 mm FWHM, respectively, using the LEAP collimator.

Figure 1(b) shows the spatial resolution of $^{99m}$Tc point sources. The results were similar to a previous study and specification sheets provided by the manufacturer [15]-[17].

3.2. Sensitivity
Figure 2 shows the sensitivity of $^{125}$I point sources as a function of source-to-collimator distance. At source-to-collimator distances of 25, 30, and 35 mm, the sensitivities for the Inveon scanner using the MHR-0.5 collimator were 29.49, 21.87, and 17.12 cps/MBq, respectively; the MGP-1.0 collimator were 64.41, 44.37, and 32.69 cps/MBq, respectively; and the MHS-2.0 collimator were 163.42, 116.88, and 87.18 cps/MBq, respectively.
Figure 1. The resolution of the clinical scanner compared to the small animal scanner presented as a function of the source-to-collimator distance with each collimator. (a) Iodine-125 ($^{125}$I) point source and (b) Technetium-99m ($^{99m}$Tc) point source.
At source-to-collimator distances of 25, 30, and 35 mm, the sensitivities for the Symbia TruePoint were 30.83, 30.55, and 30.35 cps/MBq, respectively, using the LEHR collimator and 68.89, 68.13, and 67.68 cps/MBq, respectively, using the LEAP collimator.

Figure 2(b) shows the sensitivity using $^{99m}$Tc point sources. These results were similar to a previous study [15]-[17].

3.3. Nonuniformity

Figure 3(a) shows the nonuniformity (%STD unif) of $^{125}$I measured by the NU 4 IQ phantom. The nonuniformities measured using the Inveon scanner were 87.97%, 29.74%, and 14.72% with the MHR-0.5, MGP-1.0, and MHS-2.0 collimators, respectively. The nonuniformities measured using the Symbia TruePoint scanner were 46.32% and 17.86% with the LEHR and LEAP collimators, respectively. These results indicated that uniformity enhanced by acquired counts.

The nonuniformity of $^{99m}$Tc measured by the NU 4 IQ phantom was similar to $^{125}$I (Figure 3(b)).

3.4. Recovery Coefficient

Figure 4 shows the recovery coefficient of each hot rod in a cold background as a function of rod diameter. However, there are two problems, image noise and resolution of the clinical scanner, for evaluating recovery coefficients. Generally, the theoretical maximum value of $RC_{rod}$ is 1.0, but it can be more than 1.0 because of image noise. The resolution of the clinical scanner was 8.89 mm FWHM in the LEHR collimator and 9.25 mm FWHM in the LEAP collimator for $^{125}$I point sources. Therefore, detecting hot rods (1.0 - 5.0 mm) was impossible. For these reasons, calculation of this parameter on the clinical scanner was incomplete and was predicted by the position of the hot rod in the object based on the physical dimensions of the phantom.

3.5. Spillover Ratio

Figure 5(a) shows the results of SOR using the $^{125}$I-filled NU 4 IQ phantom. The SOR$_{wat}$ was 20.41%, 19.79%, 16.95% in the Inveon scanner with the MHR-0.5, MGP-1.0, and MHS-2.0 collimators, respectively. The SOR$_{air}$ in the Inveon scanner was 14.71%, 12.65%, 8.96%, with the MHR-0.5, MGP-1.0, and MHS-2.0 collimators, respectively. The SOR$_{wat}$ in the Symbia TruePoint scanner was 36.30% and 32.30% with the LEHR and LEAP collimators, respectively. The SOR$_{air}$ in the Symbia TruePoint scanner was 28.14% and 23% with the LEHR and LEAP collimators, respectively.

Figure 5(b) shows the SOR results measured by $^{99m}$Tc-filled NU 4 IQ phantom.
Figure 3. Nonuniformity (%STD_{unif}) of the clinical scanner compared to the small animal scanner. (a) NU 4 Image Quality (IQ) Phantom filled with Iodine-125 (^{125}\text{I}) and (b) Technetium-99m (^{99m}\text{Tc}).

Figure 4. Recovery coefficient for Iodine-125 (^{125}\text{I})-filled rods of 1, 2, 3, 4, and 5 mm diameter.
3.6. Animal Studies

Small Animal Imaging

Figure 6(a) and Figure 6(b) show the $^{125}$I images of a BALB/c mouse acquired by the Inveon scanner using the planar and SPECT modes, respectively. Figure 6(c) and Figure 6(d) show the $^{125}$I images of a BALB/c mouse acquired by the Symbia TruePoint scanner using the planar and SPECT modes, respectively.

Figure 6(e) shows the $^{125}$I-affibody image of human breast cancer KPL-4 and MDA-MB-231 xenograft mice using the Symbia TruePoint scanner. Two mice were scanned simultaneously using the clinical scanner at 1 hour after $^{125}$I-affibody injection. The tumors were faintly visualized as accumulation regions on the hind leg.
4. Discussion

This comparative result of $^{125}$I showed that the sensitivity was comparable between the Inveon scanner and Symbia TruePoint scanner. An important limitation of the evaluation of the clinical scanner stemmed mostly from the source-to-collimator distance and small phantom object size. The recovery coefficient was indefinite, and the spillover ratio was overestimated in the clinical scanner. Nevertheless, the uniformity of the clinical scanner was acceptable because of the parallel collimator.

For the reasons mentioned above, attempting small animal imaging by a clinical scanner is more important than statistically analysis. Not surprisingly, the performance of the small animal scanner was undoubtedly better than that of the clinical scanner. Even small components could be distinguished with less blurring than clinical scanner. However, Figure 6(e) implies an unexpected possibility for small animal imaging beyond numeric data. Accumulation of $^{125}$I-labeled target agents in the hind legs of a xenograft mouse model of human cancer was confirmed sufficiently for the purpose in spite of planar mode imaging. These results are acquired by the daily routine methods for patient imaging in hospitals without special modifications, such as attaching pinhole collimators.
The small animal imaging system is an important tool with great potential for development of pharmaceutical agents aimed at diagnosis and therapy. Therefore, the research demand for small animal imaging has also increased over the last decade [4]-[7]. The resolution of small animal scanners is generally in the submillimeter range. This range is a considerable improvement compared to the 8 mm or higher range resolution of existing clinical scanners [18] [19]. Because a high-resolution imaging system is not always available in clinical environment, clinical scanner for small animal imaging would be feasible imaging modality for animal imaging and research.

5. Conclusion
This study collectively showed that $^{125}$I animal imaging using the Symbia TruePoint scanner was feasible for animal imaging. The advantages of using the clinical scanner include its large field of view, which would allow imaging of 2 - 3 mice, and availability, since it could be used where a dedicated small animal scanner system is not available. Small animal imaging using a clinical scanner is more accessible and readily available. This study shows that using clinical scanner can expand small animal imaging research opportunities. Our results also showed the possibility of $^{125}$I for clinical use although $^{125}$I imaging was not feasible due to low energy of $^{125}$I for clinical imaging.

Conflict of Interest
The authors declare that they have no conflict of interest.

Supported
This work was supported by Priority Research Centers Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (50458-2011 (PI: Ilhan Lim)). This work was supported by the Korea Science and Engineering Foundation (KOSEF) (No. 2015001667 (PI: Joo Hyun Kang) and No. 1711026888 (PI: Kook-Hyun Yu)).

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