Performance improvement of Compton imaging of astatine-211 by optimising coincidence time windows

Y. Nagao, M. Yamaguchi, S. Watanabe, N.S. Ishioka, N. Kawachi and H. Watabe

Takasaki Advanced Radiation Research Institute, National Institutes for Quantum Science and Technology, 1233 Watanuki-machi, Takasaki, Gunma 370-1292, Japan
Cyclotron and Radioisotope Center, Tohoku University, 6-3 Aoba, Aramaki, Aoba-ku, Sendai, Miyagi 980-8578, Japan

E-mail: nagao.yuto@qst.go.jp

ABSTRACT: Astatine-211 is one of the promising radioisotopes for targeted alpha therapy. Optimising treatment strategies as well as determining the suitability of a given agent for a particular patient requires to image the time-dependent distribution of the targeted radiotherapeutic agent both in tumours and in normal tissues. Since the biodistribution of astatine is different from that of iodine, imaging astatine-211 directly is essential. In the previous study of astatine-211 Compton imaging, random coincidence events due to polonium K-shell X-rays were dominant and seemed to cause saturation of counts. Thus optimisation of the coincidence time windows is important to reduce random coincidence events. In this study, we have optimised the coincidence time windows of a Compton camera and improved the sensitivity, noise and spatial resolution of astatine-211 imaging.

KEYWORDS: Compton imaging; Instrument optimisation

*Corresponding author.
1 Introduction

Astatine-211 is one of the promising radioisotopes for targeted alpha therapy [1, 2]. Optimising treatment strategies as well as determining the suitability of a given agent for a particular patient requires to image the time-dependent distribution of the targeted radiotherapeutic agent both in tumours and in normal tissues [3–5]. Since the biodistribution of astatine is different from that of iodine [6, 7], imaging astatine-211 directly is essential [3, 8].

Astatine-211 and its daughter radioisotope polonium-211 emit gamma rays with energies of 570 keV, 687 keV and 898 keV at the total intensity of 0.9% per astatine-211 decay. Recently, Nagao et al. [9] have proposed to image astatine-211 with the gamma rays using a Compton camera and demonstrated its imaging capability by the experiments of a point-like astatine-211 source with relatively wide coincidence time windows of 160ns. Since random coincidence events due to polonium K-shell X-rays were dominant and seemed to cause saturation of counts in the experiments, optimisation of the coincidence time windows is important to reduce random coincidence events. In this study, we have optimised the coincidence time windows and evaluated the performance of the camera.

2 Materials and methods

2.1 Imaging system

The Compton camera has two detectors: a scatterer and an absorber. The scintillator material of both the detectors is gadolinium aluminum gallium garnet (GAGG). The scatterer is a 20.8-mm
× 20.8-mm × 5-mm GAGG array block optically coupled to a silicon photomultiplier S11064-050P (Hamamatsu Photonics K. K.). The size of a single GAGG element of the scatterer is 0.85 mm × 0.85 mm × 5 mm. The absorber is a 41.7-mm × 41.7-mm × 10-mm GAGG array block optically coupled to a flat-panel-type multianode photomultiplier tube H12700MOD (Hamamatsu Photonics K. K.). The size of a single GAGG element of the absorber is 0.85 mm × 0.85 mm × 10 mm. The distance between the front ends of the two GAGG array blocks is 15 mm. The data acquisition system consists of weighted-summing amplifiers, 100-MHz free-running analog-to-digital converters, and a field-programmable gate array (FPGA). The FPGA detects a coincidence of the two detector signals in variable time windows from 10 ns to 160 ns. Detailed specifications for the camera can be found in ref. [10].

2.2 Optimisation of coincidence time windows

A 0.6-MBq point source of barium-133 was placed at 6 cm in front of the camera. We used barium-133 instead of astatine-211 to measure under the condition that there were few random coincidence events. The coincidence time windows were optimised as narrow as the coincidence count rate didn’t decrease apparently by the following two steps.

First, the source was measured for 10 s each with changing the coincidence time windows for both the scatterer and absorber simultaneously. The left of figure 1 shows the dependence of the coincidence count rate on the coincidence time windows with a curve fit using error functions. The minimum coincidence time windows where the coincidence count rate exceeds the plateau of the fitting curve (117 cps) are 80 ns.

Second, the source was measured for 100 s each with changing the coincidence time window for either the scatterer or absorber with fixing the other to 80 ns. The coincidence count rate decreased with decreasing the coincidence time window for the absorber more rapidly than with decreasing the coincidence time window for the scatterer. The right of figure 1 shows the dependence of the coincidence count rate on the coincidence time window for the scatterer. The minimum...
coincidence time window where the coincidence count rate exceeds 95% (108 cps) of the plateau of the fitting curve is 40 ns. Finally, the optimised coincidence time windows are 40 ns for the scatterer and 80 ns for the absorber.

2.3 Performance evaluation

2.3.1 Production of astatine-211

Astatine-211 was produced using the cyclotron at the Takasaki Ion Accelerators for Advanced Radiation Application, National Institutes for Quantum Science and Technology. A 0.25-mm-thick bismuth foil target was irradiated by 28.1-MeV alpha beams with beam current of 3 μA for 3 h. The irradiated target was dissolved in 0.5-mL concentrated nitric acid. A 0.125-mL portion of the nitric acid containing 20-MBq astatine-211 in a 0.5-mL conical vial was used as a point-like source. Detailed descriptions of astatine-211 production can be found in refs. [9, 11].

2.3.2 Experimental setup

The point-like source of astatine-211 was placed at 3 cm in front of the camera. The source center was around \((x, y) = (0, -1) \text{ cm}\). A similar setup can be found in ref. [9]. First, the 17.9-MBq source was measured for 10 min with the coincidence time windows of 160 ns. Second, 133 min after the first measurement start, the 14.5-MBq source was measured for 10 min with the optimised coincidence time windows.

2.3.3 Image reconstruction

The measured coincidence events were filtered by any of the three energy windows at 570 keV ± 53 keV, 687 keV ± 64 keV or 898 keV ± 84 keV. Two sets of the filtered events were imaged by list-mode maximum-likelihood expectation maximization algorithm [12]. Each image size is 128 mm × 128 mm with 4-mm × 4-mm pixels. A detailed description of the image reconstruction can be found in ref. [10].

3 Results

The numbers of the filtered events were 9,273 for the first measurement and 11,128 for the second measurement. The filtered coincidence count rates normalized by the activities and measurement time are calculated as 51.7 MBq⁻¹ min⁻¹ for the first measurement and 76.8 MBq⁻¹ min⁻¹ for the second measurement.

Figure 2 shows the reconstructed image in the twentieth iteration in each measurement. Figure 3 shows the x profiles of the reconstructed images in figure 2 with fitting curves using Lorentzian functions. The full widths at half maximum of the Lorentzian functions are 11.3 mm for the first measurement and 9.5 mm for the second measurement.
Figure 2. (Left) Reconstructed image in the twentieth iteration before the optimisation of the coincidence time windows. (Right) Reconstructed image after the optimisation.

Figure 3. (Left) The $x$ profile of the reconstructed image in the twentieth iteration before the optimisation of the coincidence time windows. (Right) The $x$ profile of the reconstructed image after the optimisation. Solid curves represent fitting curves using Lorentzian functions.

4 Discussion

Simple comparison of the filtered coincidence count rates before and after the optimisation indicates that the sensitivity was improved by a factor of 1.5. This might be due to reduction of the random coincidence events by the optimisation of the coincidence time windows.

The result of figure 2 indicates that the noise artefact on the periphery of the image center was reduced by the optimisation of the coincidence time windows. This noise reduction, which also appears in each right side of figure 3, seems to contribute to the improvement of spatial...
resolution by approximately 16%. This noise reduction might also be due to reduction of the random coincidence events.

This study has demonstrated the reduction of the random coincidence events caused by dominant X-rays by the optimisation of the coincidence time windows. However, attenuation of X-rays by a body is large and can affect the amount of the random coincidence events. Therefore, the effect of attenuation on the amount of the random coincidence events and images should be investigated with imaging experiments using a water-filled phantom. This will be a future study.

This study has imaged only a single point-like source of astatine-211. The studies on Compton imaging of astatine-211 were published in two papers [9, 13] in our knowledge, both of which were successful only for single point-like sources. Although one of them tried small-animal imaging, Compton imaging was unsuccessful [13]. Therefore, Compton imaging of astatine-211 with multi-point sources, extended sources or small animals is necessary to advance to the next stage and will be a future study.

5 Conclusions

We have optimised the coincidence time windows of the Compton camera and improved the sensitivity, noise and spatial resolution of astatine-211 imaging. Future research plans include attenuation studies using a water-filled phantom and imaging experiments with multi-point sources, extended sources or small animals.

Acknowledgments

This work was supported by JSPS KAKENHI Grant Numbers JP16K15351 and JP21K15855.

References

[1] F. Guérard, J.-F. Gestin and M.W. Brechbiel, Production of $[^{211}\text{At}]$-astatinated radiopharmaceuticals and applications in targeted α-particle therapy, Cancer Biother. Radiopharm. 28 (2013) 1.

[2] G. Vaidyanathan and M.R. Zalutsky, Astatine radiopharmaceuticals: prospects and problems, Curr. Radiopharm. 1 (2008) 177.

[3] G. Vaidyanathan and M.R. Zalutsky, Targeted therapy using alpha emitters, Phys. Med. Biol. 41 (1996) 1915.

[4] R.J. Ott, Imaging technologies for radionuclide dosimetry, Phys. Med. Biol. 41 (1996) 1885.

[5] Y. Seo, Quantitative imaging of alpha-emitting therapeutic radiopharmaceuticals, Nucl. Med. Mol. Imaging 53 (2019) 182.

[6] P.K. Garg, C.L. Harrison and M.R. Zalutsky, Comparative tissue distribution in mice of the α-emitter $^{211}\text{At}$ and $^{131}\text{I}$ as labels of a monoclonal antibody and F(ab')2 fragment, Cancer Res. 50 (1990) 3514, https://cancerres.aacrjournals.org/content/50/12/3514.

[7] J. Spetz, N. Rudqvist and E. Forssell-Aronsson, Biodistribution and dosimetry of free $^{211}\text{At}, ^{125}\Gamma$ and $^{131}\Gamma$ in rats, Cancer Biother. Radiopharm. 28 (2013) 657.
[8] T.G. Turkington, M.R. Zalutsky, R.J. Jaszczak, P.K. Garg, G. Vaidyanathan and R.E. Coleman, Measuring astatine-211 distributions with SPECT, Phys. Med. Biol. 38 (1993) 1121.

[9] Y. Nagao, M. Yamaguchi, S. Watanabe, N.S. Ishioka, N. Kawachi and H. Watabe, Astatine-211 imaging by a Compton camera for targeted radiotherapy, Appl. Radiat. Isot. 139 (2018) 238.

[10] Y. Nagao, M. Yamaguchi, N. Kawachi and H. Watabe, Development of a cost-effective Compton camera using a positron emission tomography data acquisition system, Nucl. Instrum. Meth. A 912 (2018) 20.

[11] Y. Ohshima et al., Antitumor effects of radionuclide treatment using α-emitting meta-211At-astato-benzylguanidine in a PC12 pheochromocytoma model, Eur. J. Nucl. Med. Mol. Imaging 45 (2018) 999.

[12] L. Parra and H.H. Barrett, List-mode likelihood: EM algorithm and image quality estimation demonstrated on 2-D PET, IEEE Trans. Med. Imaging 17 (1998) 228.

[13] A. Omata et al., Performance demonstration of a hybrid Compton camera with an active pinhole for wide-band X-ray and gamma-ray imaging, Sci. Rep. 10 (2020) 14064.