Investigation of radiopharmaceutical labeling of ^{141}Ce with DOTA

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For stable supply of therapeutic radionuclides in Japan, it is important to develop radionuclides that can be produced domestically using accelerators. A candidate radionuclide for theranostics (therapeutics + diagnosis) that can be produced using accelerators is cerium-141 (^{141}Ce, $T_{1/2}$ = 32.5 d). The cyclotron production route for ^{141}Ce is the ^{138}Ba$(\alpha, n)^{141}$Ce reaction. This nuclide emits β-particles (maximum β energy: 580.7 keV) and γ-rays with energy 145.4 keV. Therefore, ^{141}Ce can be used for tumor therapy and imaging by single photon emission computed tomography (SPECT).

We have previously reported the accelerator production and chemical separation of ^{141}Ce.[1,2] In this study, the radiopharmaceutical labeling of ^{141}Ce using DOTA (1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic Acid), which is widely used for chelate labeling of therapeutic radionuclides, was investigated. Cerium is a rare earth element, and the stable oxidation state of Ce in aqueous solution is +3. The ionic radius of trivalent Ce (101 pm)[2] is relatively close to that of trivalent actinium (Ac, 112 pm),[2] whose isotope ^{225}Ac has been widely studied as an α-emitting therapeutic radionuclide. Therefore, the radiopharmaceutical labeling of ^{141}Ce with DOTA was performed based on the labeling condition for ^{225}Ac.[4]

A ^{nat}BaO pellet target was irradiated with a 29-MeV alpha beam delivered from the RIKEN K70 AVF Cyclotron to produce a ^{141}Ce tracer in the ^{nat}Ba$(\alpha, xn)^{141}$Ce reaction. The produced ^{141}Ce was separated from the ^{nat}Ba target material by column chromatography using a Ln resin and HCl solutions. After separation of ^{141}Ce, the ^{141}Ce fraction was evaporated to dryness and redissolved in 0.2-M ammonium acetate solution. 10-μL of this ^{141}Ce solution, 80-μL of 0.2-M ammonium acetate solution, 30-μL of 7% sodium ascorbate solution, and 90-μL of 1 mM DOTA aqueous solution were mixed in a 1.5-mL sample tube. The mixture was heated to 80°C. To check the labeling yield, approximately 1 μL of the mixture solution was extracted every 20 minutes during 80°C heating and spotted on a silica gel TLC (thin-layer chromatography) plate. The TLC plate was developed using 20% v/v methanol/50 mM EDTA-2Na aqueous solution based on the literature.[5,6] The TLC result was visualized using an imaging plate and scanner.

Figure 1 shows the result of TLC for ^{141}Ce solution (0.2-M ammonium acetate) and ^{141}Ce-DOTA sample after 120-min heating at 80°C. $^{141}Ce^{3+}$ ions were observed at a R_f value of 0.6, whereas a signal of R_f value of 0.35 was observed for the ^{141}Ce-DOTA sample. In the present TLC analysis, unlabeled Ce^{3+} reacts with EDTA and migrates toward the solvent front. Therefore, the signal with R_f value of 0.35 would be derived from the DOTA-labeled ^{141}Ce.

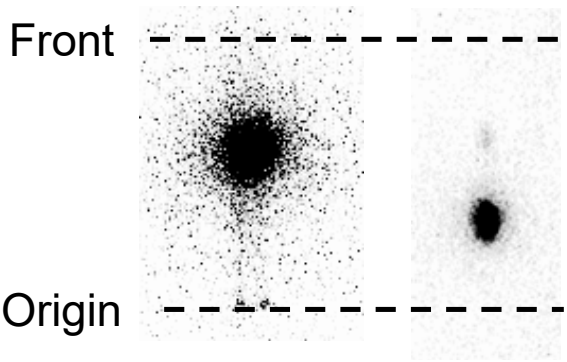

Fig. 1. TLC images for ^{141}Ce solution (0.2 M ammonium acetate, left) and ^{141}Ce-DOTA sample after 120 min heating at 80°C (right).

Figure 2 shows the dependence of labeling yield (radiochemical purity) on reaction time at 80°C for ^{141}Ce-DOTA sample checked by TLC analysis. A labeling yield of approximately 93% was observed at a reaction time of 40–60 min. The labeling time of ^{225}Ac to DOTA chelator was reported as 2 hours.[4] There-

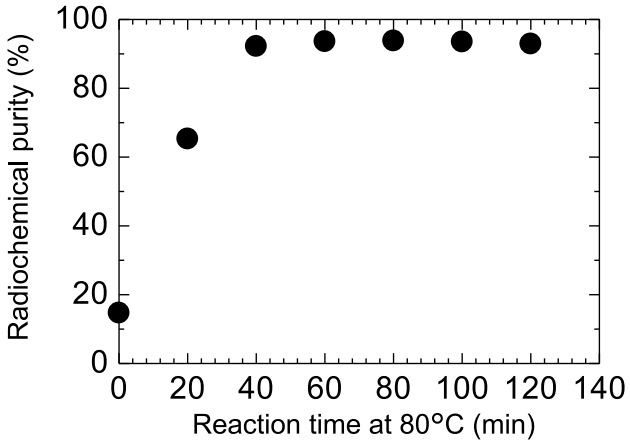

Fig. 2. Dependence of labeling yield (radiochemical purity) on reaction time at 80°C for ^{141}Ce-DOTA sample.

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DOI:10.34448/RIKEN.APR.57-085

fore, ^{141}Ce can be labeled to DOTA chelator with the labeling condition for ^{225}Ac (the reaction of Ce with DOTA may be faster than that of Ac). This result indicates that ^{141}Ce could be used to study the labeling conditions for ^{225}Ac, which is in low supply.

References

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