Investigation of the usability of RIKEN ^{44m}Sc for radiolabeling on chelate-compounds

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Scandium-44m (^{44m}Sc) with a half-life of 58.61 h decays to scandium-44 (^{44}Sc) with a half-life of 3.97 h by emitting gamma rays. ^{44}Sc has been reported to be a promising radioisotope (RI) in positron emission tomography imaging, while ^{47}Sc, which emits a beta particle, is proposed as a promising therapeutic nuclide.[1] Furthermore, ^{44m}Sc appears to be useful as an imaging RI[2] and a surrogate nuclide for other Sc isotopes in basic science research because of a relatively long half-life. A study on the optimization of ^{44m}Sc radiolabeling of macrocyclics-functionalized biomolecules has been published.[3]

We have been developing a production method of ^{44m}Sc via the nuclear reaction ^{44}Ca$(d, 2n)^{44m}$Sc at the RIKEN AVF cyclotron and distributing purified ^{44m}Sc (RIKEN ^{44m}Sc) to users.[4] To confirm the quality of the RIKEN ^{44m}Sc for research on radiolabeling, we performed ^{44m}Sc radiolabeling on chelate-compounds in this study. To investigate the structural effect of chemical-compounds on ^{44m}Sc radiolabeling, four commercially available compounds were selected: DOTA-Substance P (DOTA-SP), DOTA-RGD$_2$, NOTA-RGD$_2$ and NODAGA-RGD$_2$. The operations for ^{44m}Sc radiolabeling are as described below.

Step 1: RIKEN ^{44m}Sc (9.1 MBq) was dissolved in 0.05 M hydrochloric acid to prepare a ^{44m}Sc solution (79 MBq/mL). The radioactivity of ^{44m}Sc was determined using a germanium semiconductor detector.

Step 2: Each chelate-compound was dissolved in 0.75 M sodium acetate buffer at pH3.0, 4.0, 5.0, and 6.0 to prepare 1.4×10^{-4} M sample solutions.

Step 3: 1.5 μL of the ^{44m}Sc solution was added to 3 μL of each sample solution: the specific radioactivity of each sample solution was 0.29 MBq/nmol.

Step 4: The mixtures in Step 3 were heated at 97°C for 10 min and kept at 20°C for 5 min.

Step 5: Radiolabeling yields of ^{44m}Sc-labeled compounds were determined using thin-layer chromatography (TLC) with a C18 reverse phase TLC plate (NAGEL RP-18W/UV254), which was eluted with a mixture of acetonitrile, 0.5 M ammonium acetate, methanol, and tetrahydrofuran in a volume ratio of 4 : 3 : 2 : 1 using an image analyzer.

Consequently, the radiolabeling yields of each compound were over 90% at pH 5.0–6.0, although they were different from each other at lower pH values. In case of compounds with the same affinity moiety, DOTA-RGD$_2$ was radiolabeled over 70% at pH 3.0 which was higher than that of NODAGA-RGD$_2$ and NOTA-RGD$_2$.

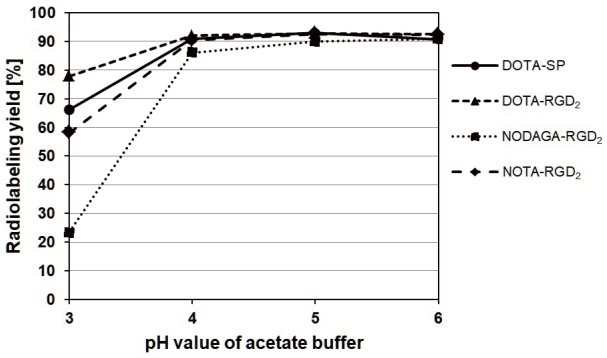

Fig. 1. Relation between pH value of acetate buffer and radiolabeling yield (%) of ^{44m}Sc-labeled compounds at 0.29 MBq/nmol ($n = 1$).

It has been reported that the suitable pH range for ^{44m}Sc labeling with DOTA-based ligands is from 4 to 5.5.[3] The result obtained in our study was consistent with the result of the previous study. Moreover, regarding the difference in reactivity among chelators, one report shows that DOTA is a better chelator than NODAGA because NODAGA is more susceptible to contamination metals than DOTA.[5] Another report shows that the thermodynamic stability of Sc-DOTA is high compared to that of Sc-NOTA.[6] These reports are consistent with our radiolabeled result at pH 3.0. Hence, these results support the possibility of further radiolabeling studies using RIKEN ^{44m}Sc.

We investigated the possibility of RIKEN ^{44m}Sc for radiolabeling studies and compared our results with those of previous reports of Sc radioisotopes. In addition, the pH responsiveness of the ^{44m}Sc radiolabeling yield to compounds having different chelating sites was confirmed. In future, we plan to optimize the radiolabeling condition of Sc isotopes, such as ^{44}Sc, which is eluted from the ^{44}Ti/^{44}Sc generator, and conduct a feasibility study for imaging tracer with ^{44m}Sc.

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