Synthesis of ^{44m}Sc-DOTA-TATE for multiple-isotope PET imaging

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Positron emission tomography (PET) is a useful tool for radio-tracer imaging in a living organism. However, conventional PET can only be adapted for a single tracer because of the energy constancy of annihilation photons, which are utilized for PET imaging. To overcome this disadvantage, we have developed a new PET system that can be used for multiple-tracer simultaneous imaging. Our PET system, named multiple-isotope PET (MI-PET), detects not only annihilation photons but also prompt γ-rays, which are emitted successively after positrons. We have succeeded in proving the basic principle of MI-PET using a prototype system.[1)]

The MI-PET system uses a positron-γ emitter, which emits a de-excitation γ-ray after the positron emission in β^+-decay, as a tracer, and identifies the tracer by detecting the prompt γ-ray. For the MI-PET tracer, a proper half-life, prompt γ-ray energy, and emission ratio are required by the positron-γ emitter to ensure future clinical use. One promising candidates for this type of positron-γ emitter is ^{44}Sc (^{44m}Sc), which emits 1157 keV prompt γ-rays (99.9%) with a half-life of 3.97 h (^{44m}Sc: 58.6 h). The imaging ability of MI-PET for ^{44}Sc (^{44m}Sc) has been already evaluated by several experiments using phantoms and animals.[2,3)] Therefore, as a next step, we have begun to develop a useful drug, such as a cancer diagnosing reagent labeled by ^{44}Sc (^{44m}Sc). In our first attempt, we synthesized a ^{44m}Sc labelled DOTA-TATE, which is a compound containing tyrosine3-octreotate and a somatostatin receptor for numerous malignancies.

^{44m}Sc was produced *via* the reaction of ^{44}Ca(d, $2n$)^{44m}Sc with a 24 MeV deuterium beam and was purified by chemical processes at the RIKEN AVF cyclotron. The produced ^{44m}Sc was transported to the RIKEN Kobe campus for the drug synthesis.

The labelling protocol was based on a method developed by Huclier-Markai *et al.*[4)] The protocol scheme is shown in Fig. 1. DOTA-TATE (DOTA-[Tyr3]-octreotide) was purchased from BACHEM (Switzerland). A total of 2.1 nmol of DOTA-TATE and 7.7 MBq of ^{44m}Sc were resolved into 55 μL of NaOH (0.1 M) and 200 μL of ammonium acetate (pH 4.0, 0.25 M) and incubated at 95°C for 30 min with shaking. After incubation, 5.7 MBq of ^{44m}Sc labeled DOTA-TATE was washed out using an ion-exchange column (Sep-Pak C18 1cc Vac cartridge) by 500 μL of ethanol.

To evaluate the radio-labeling yield, TLC analyses

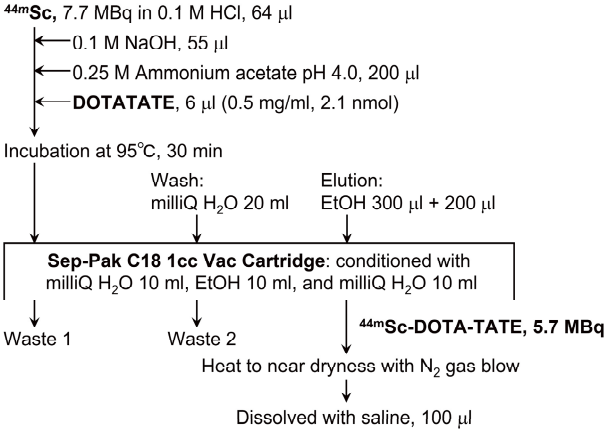

Fig. 1. Scheme for synthesis of ^{44m}Sc labeled DOTA-TATE.

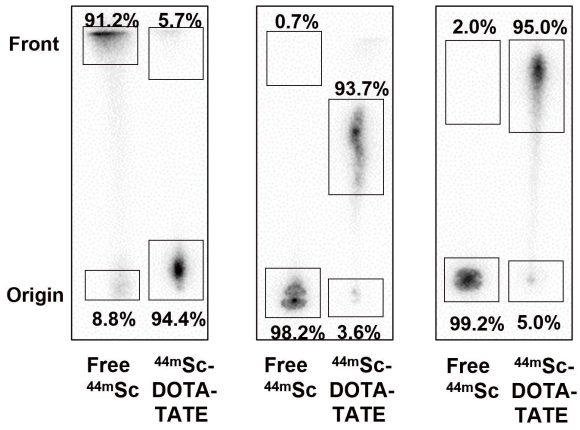

Fig. 2. TLC profiles of the free ^{44m}Sc and ^{44m}Sc-DOTA-TATE with developing solutions of citric acid (left), NaCl/MeOH (center), and NaCl/MeOH/NH_3 (right). An imaging plate was used for analysis.

were performed by spotting onto TLC plates (silica gel 60 F_{254}) with developing solutions of citric acid (pH 4.0), NaCl/MeOH (3 : 1), and NaCl/MeOH/NH_3 (3 : 1 : 1). The TLC results obtained through an analysis of an imaging plate are shown in Fig. 2. These results indicate that the labeling ratio for ^{44m}Sc-DOTA-TATE was above 90%.

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References
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