# Separation of $^{44}$Ti and $^{nat}$Sc

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**Introduction**: $^{44}$Ti / $^{44}$Sc radionuclide generators are of interest for molecular imaging. The 3.92 hours half-life of $^{44}$Sc and the high positron branching of 94% may stimulate the application of $^{44}$Sc labelled PET radiopharmaceuticals [1,2]. However, both $^{44}$Ti production and $^{44}$Ti / $^{44}$Sc generator design represent challenges for basic radiochemistry. Recently, the production of 5 mCi of $^{44}$Ti was described following $^{nat}$Sc(p,2n) nuclear reactions [3]. This paper covers the radiochemical purification of $^{44}$Ti prior to the development of $^{44}$Ti / $^{44}$Sc radionuclide generators. Basically, high separation factors for gramm-amounts of scandium target material and for chemical and radionuclidic impurities are required.

**Experimental:** 1.5 g irradiated scandium were dissolved in 18 ml of 2 M HCl. For the initial separation two aliquots A – $^{44}$Ti in 9 ml 2 M HCl (742.5 MBq) and B – $^{44}$Ti in 9 ml 2 M HCl (740.5 MBq) were prepared. These solutions contained about 10 MBq of $^{46}$Sc (T½ = 82.8 d) as produced via neutron capture on $^{45}$Sc induced by the neutrons created within the $^{nat}$Sc(p,2n)$^{44}$Ti process. For cation exchange chromatography, a large column (H=350 mm, S=2 cm$^2$, $V_0$=35 ml) of AG-50Wx8, 200-400 mesh ($H^+$-form) was washed with 1.5 l 4 M HCl and 50 ml $H_2O$. Probe A was brought in the column, followed by 7.5 ml $H_2O$ and 8 ml 1 M HCl consecutive. After that, probe B was brought in the column, then 9 ml $H_2O$ and 17.5 ml 1 M HCl. The column was washed with 45 ml 1 M HCl, 30 ml 2 M HCl, 160 ml 3 M HCl, 200 ml 0.5 M $H_2C_2O_4$ consecutively. Table 1 shows the activities of $^{44}$Ti and $^{44}$Sc measured in the different fractions using different detectors: Curie-meter (activity 1) and γ-ray spectroscopy MOPS 41 (activity 2).
The second separation, i.e. purification was performed using a similar column (H=360 mm, S=2 cm$^2$, $V_0$=36 ml) with AG-50Wx8, 200-400 mesh ($H^+$-form). The column was washed with 1 l 4 M HCl and 50 ml $H_2O$. The probe N 5 from the first separation was brought in the column, then 170 ml $H_2O$, 45 ml 1 M HCl, 180 ml 2 M HCl and 190 ml 4 M HCl consecutive. Measurements have been performed similar to the protocol used for the first separation.

**Results and Discussion:** The chromatographic profiles of the two separations are summarized in Tables 1 and 2.

Table 1: initial $^{44}$Ti / $^{nat}$Sc separation, AG-50Wx8, 200-400 mesh ($H^+$-form)

| N | Solution | V [ml] | Activity [MBq] | | | |
|---|---|---|---|---|---|---|
| | | | Curie-meter | | γ-spectroscopy | |
| | | | 1st day | 2nd day | $^{44}$Ti | $^{46}$Sc |
| 1 | 1 M HCl | 40 | 0.281 | 0.219 | 0 | 0 |
| 2 | 1 M HCl | 45 | 1.268 | 1.182 | 0 | 0 |
| 3 | 1 M HCl | 45 | 0.552 | 0.448 | 0 | 0 |
| 4 | 2 M HCl | 47 | 1.556 | 1.816 | 0.18 | 0 |
| **5** | **3 M HCl** | **48** | **1321** | **1485** | **204.35** | **2.56** |
| 6 | 3 M HCl | 49 | 81.37 | 21.30 | 0.100 | 2.36 |
| 7 | 3 M HCl | 41 | 34.05 | 10.33 | 0.410 | 1.14 |
| 8 | 3 M HCl | 18 | 11. 80 | 3.931 | 0.007 | 0.280 |
| 9 | $H_2C_2O_4$ | 32 | 19.04 | 9.385 | ~0.020 | ~0.150 |
| 10 | $H_2C_2O_4$ | 47 | 3.382 | 0.953 | 0.025 | 0.109 |
| 11 | $H_2C_2O_4$ | 37 | 2.373 | 0.568 | 0.008 | 0.077 |
| 12 | $H_2C_2O_4$ | 39 | - | 0.600 | 0.008 | 0.850 |

Table 2. second $^{44}$Ti / $^{nat}$Sc purification, AG-50Wx8, 200-400 mesh ($H^+$-form)

| N | Solution | V [ml] | Activity [MBq] | | | |
|---|---|---|---|---|---|---|
| | | | Curie-meter | | γ-spectroscopy | |
| | | | 1st day | 2nd day | $^{44}$Ti | $^{46}$Sc |
| 13 | 1 M HCl | 30 | 0.051 | 0.003 | | |
| 14 | 1 M HCl | 30 | 0.078 | 0.012 | | |
| 15 | 1 M HCl | 30 | 0.088 | 0.020 | | |
| 16 | 1 M HCl | 30 | 0.117 | 0.026 | | |
| 17 | 1 M HCl | 30 | 0.117 | 0.029 | | |
| 18 | 1 M HCl | 30 | 0.125 | 0.029 | | |
| 19 | 1 M HCl | 30 | 0.125 | 0.027 | | |
| 20 | 1 M HCl | 30 | 0.117 | 0.020 | | |
| 21 | 2 M HCl | 30 | 0.110 | 0.016 | | |
| 22 | 2 M HCl | 30 | 2.417 | 3.152 | 0.54 | |
| 23 | 2 M HCl | 30 | 802.0 | 1102 | 188.42 | |
| 24 | 2 M HCl | 30 | 221.2 | 298.5 | 51.04 | |
| 25 | 2 M HCl | 30 | 19.72 | 18.56 | 0.06 | |
| 26 | 2 M HCl | 30 | 1.205 | 0.422 | 0.004 | |
| 27 | 4 M HCl | 30 | 2.208 | 0.092 | 0.003 | 0.0004 |
| 28 | 4 M HCl | 30 | 137.0 | 7.342 | | 1.017 |
| 29 | 4 M HCl | 30 | 66.46 | 4.436 | | 0.614 |
| 30 | 4 M HCl | 30 | 34.51 | 2.330 | | 0.323 |
| 31 | 4 M HCl | 30 | 18.36 | 1.006 | | 0.140 |
| 32 | 4 M HCl | 30 | 12.82 | 0.512 | | 0.071 |
| 33 | 4 M HCl | 30 | 7.771 | 0.258 | | 0.036 |

**Conclusions:** About 99.9% of the $^{44}$Ti have been isolated in a 48 ml fraction of 2 M HCl. As expected, the scandium separation was not complete with about 400 mg scandium still present in the $^{44}$Ti fraction. About 99.6% of the $^{44}$Ti activity have been recovered following cation exchange purification of the no-carrier-added radionuclide from about 1.5 g of a macroscopic scandium target. The second chromatography provided a more complete separation with a separation factor of about $10^5$, i.e. less than $10^{-3}$ % of the initial scandium still remaining in the $^{44}$Ti fraction. The final content of scandium is about 15 µg.

However, further purification occurred to be useful. The fractions # 23 and 24 thus were further purified using anion exchange chromatography, as described later, cf. [4].

**References:**

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