

Thermochromatographic isolation of ^{45}Ti from irradiated Sc

Kai Giesen^{1*}, Ingo Spahn¹, Bernd Neumaier¹

¹Institute of Neuroscience and Medicine, INM-5: Nuclear Chemistry, Forschungszentrum Jülich, Jülich, Germany

*E-mail: k.giesen@fz-juelich.de

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Titanium-45 (^{45}Ti , $t_{1/2} = 3.08$ h) is an important non-standard radio nuclide exhibiting favorable decay properties for PET imaging due to its relatively low maximum positron energy ($E_{\text{max}} = 1040$ keV, $E_{\text{avg}} = 439$ keV) and high β^+ intensity ($I_{\beta^+} = 84.8\%$). Furthermore, ^{45}Ti might be of high interest since titanium(IV) complexes with high therapeutic anti-cancer potential have been reported^[1,2]. Therefore, labelled Ti-complexes have the potential to gain information about the biodistribution and therapeutic efficiency of Ti-complexes.

However, application of ^{45}Ti is hampered by the lack of separation methods which enable to obtain ^{45}Ti in a chemical form suitable for radiometal complex syntheses. The aim of this work was to isolate ^{45}Ti from scandium by the formation of volatile [^{45}Ti]titanium(IV)chloride, which can be used for further conversions and the synthesis of tetravalent titanium complexes.

For ^{45}Ti production a scandium metal disc was irradiated with 16 MeV protons. The irradiated scandium was heated in a stream of chlorine-argon gas to 900°C yielding scandium(III)chloride and [^{45}Ti]titanium(IV)chloride. Both compounds can be separated by exploitation of their different sublimation points. Hereby, [^{45}Ti]titanium(IV)chloride was trapped at -29°C either directly in a dry vessel or in dry acetonitrile while the scandium(III)chloride was deposited before. First experiments showed a ^{45}Ti -recovery of 25%. The trapped [^{45}Ti]titanium(IV)chloride was directly used for further conversions.

To demonstrate the reactivity of trapped [^{45}Ti]titanium(IV)chloride, the complex ligand FL⁴ was added to afford the hydrolytically stable [^{45}Ti]Ti(IV)salan complex [^{45}Ti]TiFL⁴. The reaction was carried out in the trapping vessel using dry acetonitrile as a solvent at -29°C in 30 min reaction time. N-ethyl-N-(propan-2-yl)propan-2-amine (DIPEA) was used to activate the salan ligand and to neutralize formed HCl. The radiolabelled complex was obtained in a RCY of 40% (HPLC) and its identity and purity was determined by HPLC analysis using a non-radioactive standard as a reference.

The thermochromatographic work up of the scandium target enabled the isolation and recovery of ^{45}Ti as the corresponding ^{45}Ti -tetrachloro compound which in the future can be converted to clinically relevant complexes.

References

1. Lümmen, G., Sperling, H., Luboldt, H., Otto, T. & Rübber, H. Phase II trial of titanocene dichloride in advanced renal-cell carcinoma. *Cancer Chemother. Pharmacol.* **42**, 415–417 (1998).
2. Meker, S., Braitbard, O., Hall, M. D., Hochman, J. & Tshuva, E. Y. Specific Design of Titanium(IV) Phenolato Chelates Yields Stable and Accessible, Effective and Selective Anticancer Agents. *Chem. - A Eur. J.* **22**, 9849 (2016).