Rapid strategy for separation of no carrier added ^{90}Nb from zirconium target for application in *immuno*-PET.

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Introduction: ^{90}Nb is a potential PET nuclide ($T_{½}$ = 14.6 h and a high positron branching of 53%). Promising results in labeling and *in vitro* evaluations of ^{90}Nb-labeled monoclonal antibodies confirmed the potential of ^{90}Nb as an appropriate isotope for *immuno*-PET [1]. However, the current separation method [2] of ^{90}Nb from irradiated Zr-targets is complicated and time consuming. For this reason an alternative separation strategy should be developed in this study.

Methods: As analogue of ^{90}Nb, reactor produced ^{95}Nb ($T_{½}$ = 35 days) was chosen and Zr metal targets were irradiated at the TRIGA reactor Mainz and BER II, Berlin. Distribution coefficients for Zr(IV) and Nb(V) in various media for different ion exchange resins were investigated. Based on these distribution coefficients, a new separation strategy was developed.
Anion exchange chromatography in hydrofluoric acid for crude Zr isolation was applied and und these conditions ^{95}Nb absorbed on the column. For elution of Nb(V) 6 M HCl/1% H_2O_2 was used. In a second step, UTEVA resin (Eichrom) was employed for further purification by washing Zr(IV) traces with 6 M HCl and eluting Nb(V) with 1 M oxalic acid. To reduce the dose burden during separation and to simplify the separation procedure, a semi-automated separation module was developed (Figure 1). Decontamination factor of $^{90/95}$Nb was measured by ICP-MS and gamma spectroscopy.
Test labeling with a monoclonal antibody (rituximab) functionalized with desferrioxamine [3] was performed at room temperature for 1 hour at pH 7.2.

Results: The developed manual separation strategy resulted in high separation yields after the anion exchange column with more than 99% of ^{95}Nb. The final volume of 400 µl 1 M oxalic acid contained more than 95% of ^{95}Nb. The whole separation procedure takes around 1.5 hours and is almost 4-times faster than previous methods. The decontamination factor after the initial anion exchange column was $0.97 \cdot 10^5$ and after an additional UTEVA purification $3.36 \cdot 10^8$.
A semi-automated separation module showed slightly lower separation yields of ^{95}Nb of 90% in the final fraction. The reduced yields can be explained by losses on valves and tubes during the automated procedure. On the other hand, the module-based separation safes on third of the time (only 1 h) and allows remote working with less direct handling of irradiated target material. A reduced dose is a very important factor in case of up-scaling to higher activities.

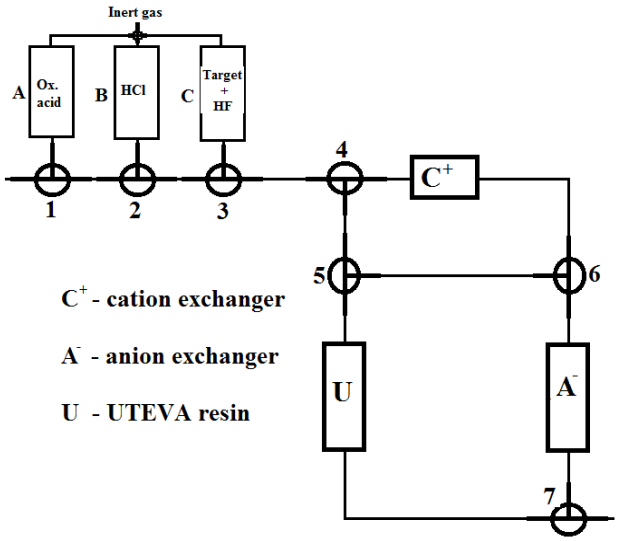

Figure 1: Scheme of the semi-automated separation module.

The HPLC analysis showed that a TFP-N-suc-Df modification yielded about 1.5 molecules of Df per molecule of rituximab. The labeling yield of ^{95}Nb-DF-mAb was ≥80% (84% by ITLC, 81% by size exclusion chromatography) after 1 hour at room temperature. Labeling kinetics indicated that the labeling reached 60% already at 15 min and increased to more than 80% after 50 min. After SEC separation using a PD-10 column, the ^{95}Nb-Df-mAb derivatives were 99.0% pure.

Conclusions: Based on the results, the effectiveness and suitability of the newly developed separation strategy was confirmed by the successful labeling of ^{95}Nb-rituximab. Consequently, *in vivo* evaluations of ^{90}Nb-labeled biomolecules will follow.

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References

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