^{55}Co/^{58m}Co-labeled anti-HER2 nanobody as a theranostic pair for 3-gamma PET and Auger electron therapy

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Introduction

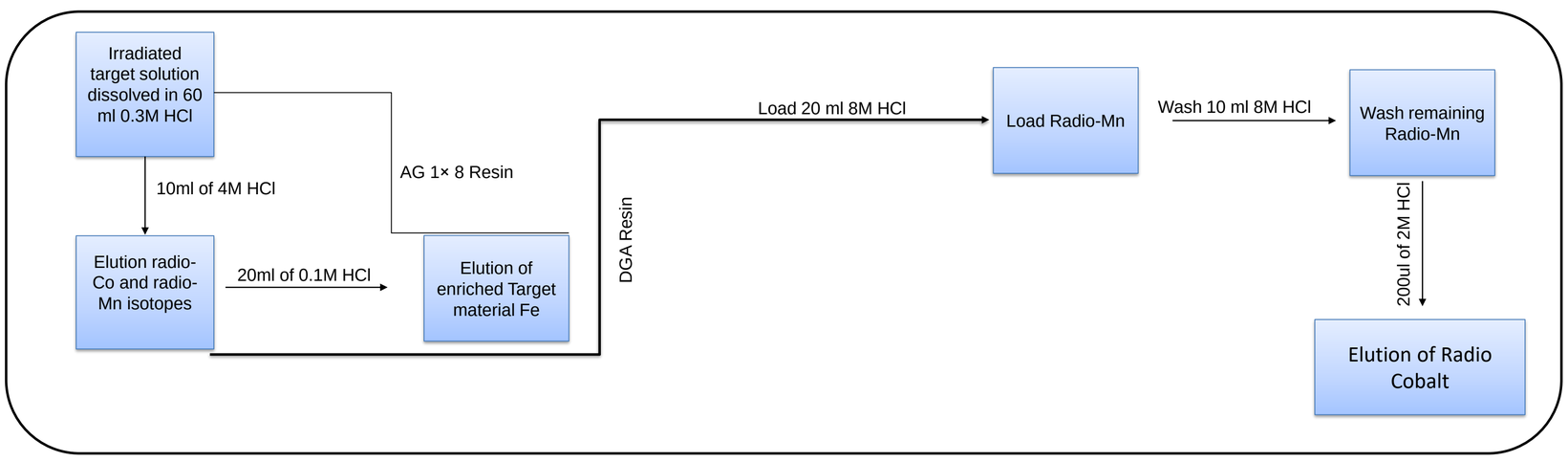
- 3 γ PET is a new technique that allows for more accurate imaging. Additionally it also allows for the determination of the positronium lifetime, which allows, for example, the determination of hypoxia state.
- Cobalt-55 ($t_{1/2}$ = 17.53h) is a β^+ emitter (β^+ = 77% $E_{\beta max}$ = 1498 keV) which emits additional promt γ quanta 931 keV which is suitable for immaging using 3 γ technique on Jagielonian J-PET scanner.
- Co-58m ($t_{1/2}$ = 9.10h, 100% IC) an Auger electron emitter forms promising theranostic pair with Co-55 due to similar half-lives, identical chemical properties, and easy labeling of DOTA bioconjugates, like PSMA-617 and DOTA-nanobodies
- Both of these radionuclides can be produced on low energy medical cyclotrons on metallic iron enriched targets by reactions:

^{54}Fe(d, n)^{55}Co and ^{58}Fe(p, n)^{58m}Co

Radiochemical isolation and preparation

All radiochemical separation steps will be done by following the protocol Barrett et al. (Barrett et al. 2021, Cobalt-55 and cobalt-58m. *Diagnostics*, *11*(7), 1235.).

- In the first stage of the project, the isolation of cobalt radionuclides from iron targets in two step procedure is carried out.
- After dissolution of irradiated target in 0.3M HCl, target material solution is load on AG1x8 anion exchange resin
- Cobalt is eluted from the resin with 10 ml of 4M HCl and iron with 20 ml of 0.1 M HCl.
- After separation from iron cobalt solution is loaded on N, N, N', N'- tetrakis-2-ethylhexyldiglycolamide (DGA branched extraction resin) for the removal of coproduced radio manganese.



Flow diagram of the two-column method for the separation of cobalt-55/58m from iron target. Reproduced from Barrett et al. *Diagnostics* 2021, 11, 1235.

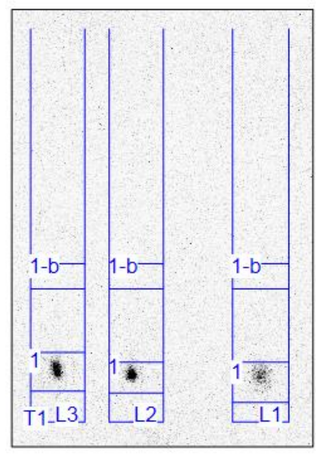
As part of the project, we investigated using ^{58}Co as a surrogate:

We successfully labelled synthesized DOTA antiHer2nanobody (NB-DOTA) conjugate with ^{58}Co

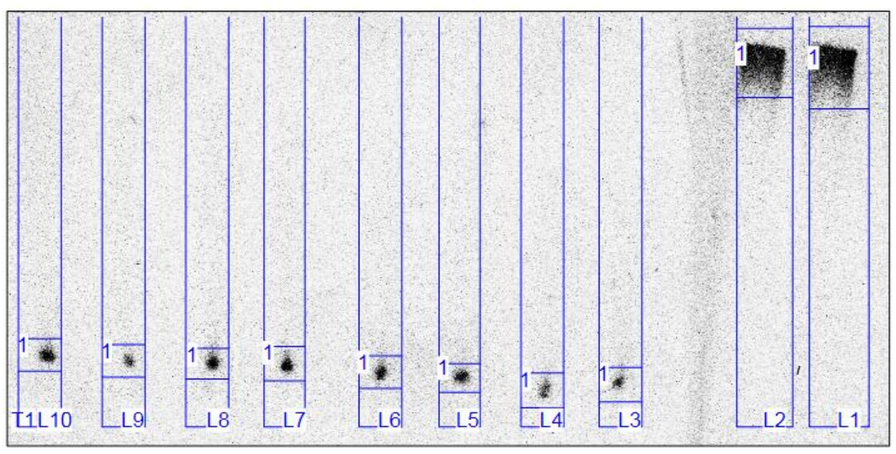
Reaction kinetics of the complex was 15 mints

The complex is purified with the help of PD-10 column

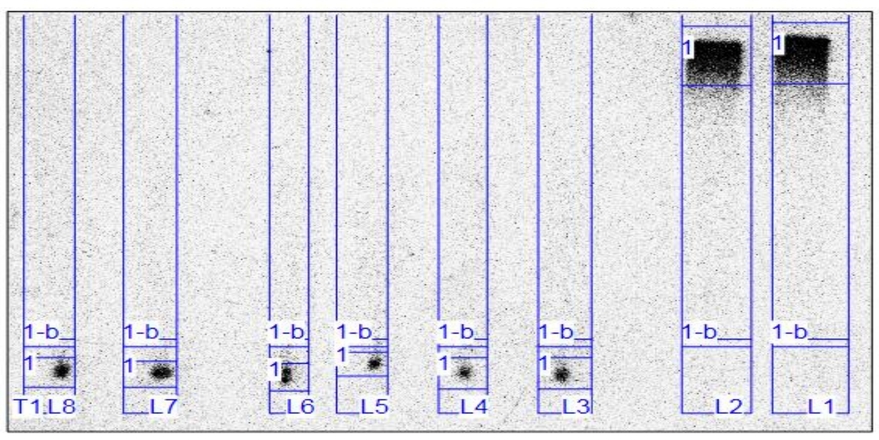
The complex is also stable in human serum up to 72h



Labeling of ^{58}Co-*DOTA-nanobody*



Stability of ^{58}Co-DOTA-nanobody in human serum, after 15(L10,L9), 30(L8,L7), 60(L6,L5), 120(L4,L3) min, free Co-58 (L1, L2)



Stability of 58Co-DOTA-nanobody in human serum after 24h (L8,L7) 48h (L6,L5), 72h (L4,L3), free Co-58 (L2,L1)

Summary

^{55}Co and ^{58m}Co form a theranostic pair that is one of the most promising pair in nuclear medicine. As part of the project, we investigated using ^{58}Co as a substitute. In the first stage of the project, using Co-58 as a surrogate, we study the labeling efficiency, stability of the radiobioconjugate, receptor affinity and internalization. We successfully labelled of synthesized nanobody with ^{58}Co and the affinity of this conjugate to Her2 receptor on the SKOV cell is left as the project is still in progress

Acknowledgements

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References

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- Sitarz, M., Cussonneau, J. P., Matulewicz, T., & Haddad, F. (2020). Radionuclide candidates for β+ γ coincidence PET: an overview. *Applied Radiation and Isotopes*, *155*, 108898.