Development of cyclotron-produced cobalt-55/58m for theranostic radiopharmaceutical applications

Wilson Lin

Under the supervision of Dr. Jonathan W. Engle

At the University of Wisconsin-Madison

Abstract

Recent FDA approvals for treating metastatic disease with radiopharmaceutical therapy (RPT) have spurred considerable interest to evaluate the therapeutic potential of novel radionuclides. Radionuclides emitting low-energy electrons (LEE) are promising for treating micro-metastatic disease due to their potential to reduce off-target toxicity at the cellular level. In this paradigm, ^{58m}Co is one of the most favorable candidates because of its low photon-to-electron ratio, optimal emission spectra, accessibility and theranostic matching with the positron-emitting ^{55}Co.

This dissertation aims to improve iron target separation for cyclotron produced $^{55/58m}$Co, elucidate cobalt radiochemistry with clinically relevant chelators and explore theranostic ^{55}Co/^{58m}Co RPT applications. Results demonstrate that cation exchange/extraction chromatography can achieve better radiochemical purity and reduce processing time compared to previously published methods using anion exchange-extraction chromatography. The separated no carrier added (n.c.a.) ^{55}Co could be radiolabeled to Sar derivatives and resulting complexes were suitable for *in vivo* applications with retained tumor-targeting properties, though complex formation was slower than with other clinically relevant chelators. Also, upon complexation with NO2A, NOTA and DO3A, Co and n.c.a. ^{55}Co exhibited redox activity which contrasts with previously published work using ^{55}Co. Cobalt-55 served as a convenient diagnostic congener for ^{58m}Co, and ^{58m}Co was able to demonstrate the desired characteristics of LEE RPT *in vitro* but likely requires probes with higher tumor uptake and less tendency for receptor saturation to induce therapeutically meaningful responses *in vivo*. Nevertheless, the outlook for theranostic ^{55}Co/^{58m}Co RPT remains exciting and further research is warranted.