Production and novel radiochemical separation of ^{194}Au from Pt for use in multi-modality nanoparticles

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Introduction

Gold nanoparticles (AuNPs) have demonstrated their incredible versatility in applications such as *in vitro* and *in vivo* imaging, cancer therapy, and drug delivery.[1-3] These AuNPs come in many shapes including nanospheres, nanorods, nanoshells, and nanocages. Their versatility stems from the ability to construct or label a single AuNP with many functions. Many types of AuNPs are inherently flourescent, allowing for *ex vivo* utilization as well as small animal fluorescence imaging.[4] High atomic number and physical density allow for the possibility of using AuNPs as computed tomography (CT) contrast agents, especially in dual energy applications.[5]

Some attempts have been made to bring AuNPs into the realm of nuclear medicine, mostly involving the extrinsic labeling of chelated radiometals. Although these strategies have brought some success, an intrinsic labeling strategy could reduce concerns of *in vivo* instability, and changes in pharmacokinetic behavior.[6] Intrinsic radiolabeling strategies involve synthesizing the nanoparticles in the presence of a gold radioisotope, which is thereby structurally incorporated. The isotope of choice for this technique has typically been ^{198}Au ($t_{½}$ = 2.7 d, E_{γ} = 411.8 keV) as it is reactor produced and commercially available. However with such a high energy gamma ray, SPECT aquisition is far from optimal.

Motivated by the shortcomings of previous intrinsic labeling techniques, we have sought to develop ^{194}Au ($t_{½}$ = 1.48 d, β^{+} = 1.73 %) as a potential PET isotope for labeling AuNPs. Although this nuclide has a weak positron branching ratio, it also has prominent gamma ray energies of 328 and 294 keV which are closer to the optimal SPECT energy window, allowing for the ability to image with both PET and SPECT.

Material and Methods

^{194}Au was produced by ^{nat}Pt(p,x) using 16 MeV protons. Target construction consisted of a water jet cooled platinum disc.

Following irradiation, targets were etched by fresh concentrated aqua regia at 80 °C for four hours. The resulting solution was diluted by a factor of four and loaded onto a 50 mg UTEVA (Eichrom extraction resin) column equilibrated by 1 M HNO_3. The column was rinsed with 10 mL 1 M HNO_3, and the product was eluted using concentrated HNO_3 in less than 1 mL.

Results and Conclusion

End of bombardment (EOB) yield for ^{194}Au was measured to be 0.134 mCi/µAh by high purity germanium analysis. The half life was measured to be 38.5 ± 2.8 hours, which agrees well with the true half life of 37.92 hours. In addition to the production of ^{194}Au, the production of $^{190–193}$Au and ^{196}Au was observed. Most notably, the EOB yield for ^{193}Au ($t_{½}$ = 17.7 h) was 0.189 mCi/µAh.

Target dissolution was slow and incomplete after four hours of etching. Alternative dissolution strategies i.e. electrolytic dissolution may be needed moving forward. The separation of ^{194}Au from bulk Pt via the UTEVA extraction resin was robust and efficient, with an average separation efficiency of 96 %. An extensive literature review revealed no other Au/Pt separation from solutions containing aqua regia. Future goals include synthesis of ultrasmall ^{194}Au incorporated AuNPs using a facile thermal reduction method.PET, CT and fluorescence imaging will also be carried out in vivo to establish the multimodal capabilities of the intrinsically radiolabeled nanoplatforms.

To conclude, a novel separation technique has been developed to separate ^{194}Au from Pt for use in intrinsically radiolabeled multi-modal AuNPs.

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