Radiolabeling with astatine-211

Ning Zhou,[1] Xinkai Sun,[1] L.A. McIntosh[2] G.C. Tabacaru[2] and S.J. Yennello[2]
[1]*UT Southwestern Medical Center, Dallas, Texas 75390*
[2]*Cyclotron Institute, Texas A&M University, College Station, Texas 77843*

Astatine-211 (^{211}At) is a highly promising alpha-emitting radionuclide for targeted alpha therapy (TAT) in cancer treatment. It exhibits 100% alpha emission, with only one alpha particle released per decay. This characteristic minimizes the risk of unpredictable dose localization caused by the detachment of radioactive daughter products from the carrier vector. Additionally, its half-life of 7.2 hours is ideal: less than 1% of radioactivity remains after two days, which may reduce exposure to normal tissues while still allowing sufficient time for radiochemistry and clinical application.

We have proposed an ^{211}At -labeled, PSMA-targeted small molecule for the treatment of prostate cancer. The compound was successfully labeled with ^{211}At at the Cyclotron Facility at Duke University. Given the half-life of ^{211}At as shown in Fig.1, the Texas A&M University Cyclotron Institute (TAMU-CI) serves as an ideal source of ^{211}At for us to plan clinical trials with the radiopharmaceutical in the Dallas-Fort Worth area.

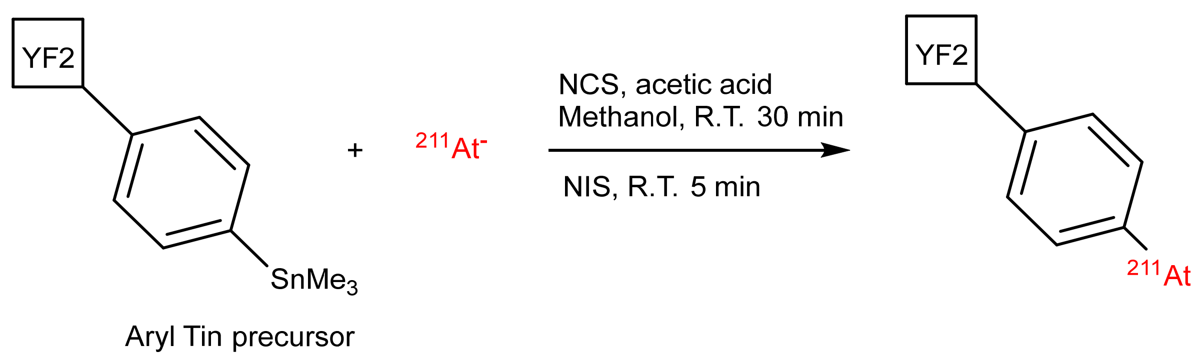

Fig. 1. NCS: N-chlorosuccinimide; NIS: N-iodosuccinimide.

TAMU-CI has provided us with three batches of ^{211}At, including two on-site tests and via shipment to Dallas, for labeling experiments with the corresponding aryl tin precursor. In Dallas, we received 10 mCi of ^{211}At retained on the column after approximately seven hours of shipping and processing.

Initially, we followed the published protocol [1] to elute ^{211}At from the 3-octanone extraction column and add it to the precursor solution. However, no product was formed. HPLC and radioTLC analyses suggested that the eluted ^{211}At was not present in astatide (At^-) form.

To address this, we explored three different strategies:

1. Neutralization of residual HNO_3: We modified the elution protocol to neutralize residual nitric acid in the eluted solution. Despite this adjustment, no labeled product was observed.
2. Addition of hydroxylamine hydrochloride ($NH_2OH{\cdot}HCl$): Introducing this reducing agent to the eluted ^{211}At solution led to the formation of unidentified radioactive peaks. But no desired product was found.

3. Hydrogen gas treatment of the loaded column: Passing hydrogen gas through the 3-octanone column prior to elution. The labeling was not successful.

Our current efforts are focused on identifying the chemical forms of ^{211}At species present in the eluted solution. Based on this characterization, we aim to develop a reliable method to generate the ^{211}At(I) species required for efficient labeling. To support this optimization, we plan to use TMSnBG as a model compound for screening various labeling conditions.

[1] Lauren A. McIntosh *et al*., Nuclear Medicine and Biology **126**, 108387 (2023).