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- The NanoTek Microfluidic Synthesis System is a modular microfluidic chemistry system with the ability to combine both microscale and macroscale process steps. Modular components give the user maximum flexibility for both discovery and clinical applications.

Application Note

Sequential Back-to-Back Preparation of Two Radiotracers from One Delivery of ^{18}F

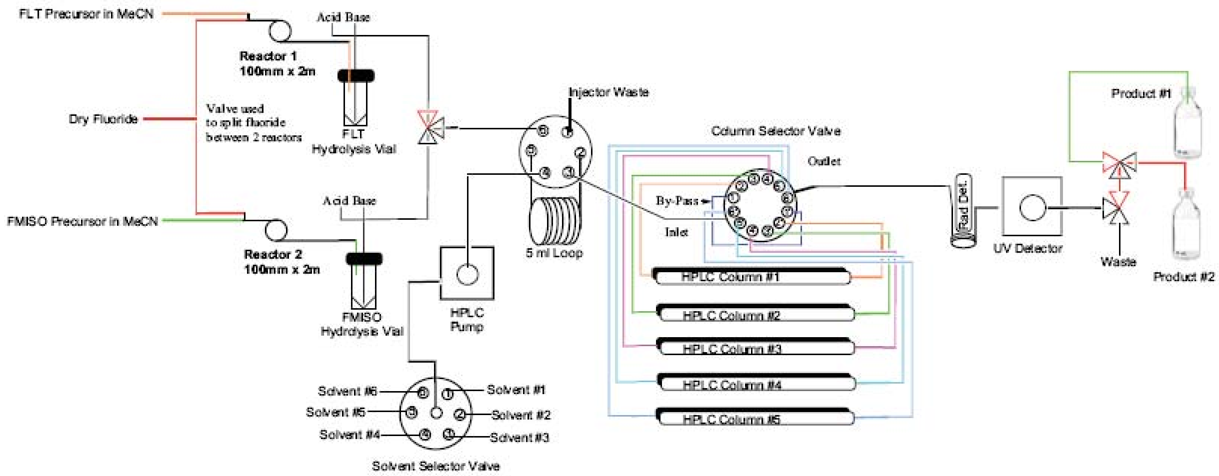
Introduction

The NanoTek Microfluidic Synthesis System provides a flexible platform for offering dual benefits of high efficiency and fast synthesis. This application note describes how the NanoTek system can be configured for the sequential back-to-back preparation of two different radiotracers from one delivery of [^{18}F]fluoride. The University of Tennessee has demonstrated how a NanoTek can be used for routine production of medium scale batches (200 mCi, 7.5 GBq) of FLT and FMISO (Akula, M.R., et al.; & Collier, T.L., et al.; JNM Meeting abstracts, May 2010). The experiments described in this application note were performed as a single synthesis run for the preparation of [^{18}F]FLT, followed by cleaning of the HPLC injector and a synthesis for the preparation of [^{18}F]FMISO, followed by the standard cleaning of the unit. To measure the carryover, a further cold synthesis was performed, but only the solvents used in the synthesis were used.

This ability to produce two different tracers from one system and one delivery of ^{18}F is a major benefit at any center where there is a requirement to produce multiple compounds on the same day but has a constraint on hot cell space. A full technical document is available from info@advion.com for a detailed description of the process.

Setup

A standard NanoTek system was used, comprised of a base module, a reactor module and two Concentrator/Evaporator (CE) Modules. The Reactor Module contained 4 microreactor positions, each with its own independent temperature controller. In this configuration, the top reactor slot was used to heat an external vial used for hydrolysis of the FMISO intermediate. For purification, the integrated digital outputs from the NanoTek were used to control external valves and HPLC equipment including stopping and starting the HPLC pump. A column-selector valve allowed the user to select the appropriate HPLC column, so a dedicated column could be used for each compound.



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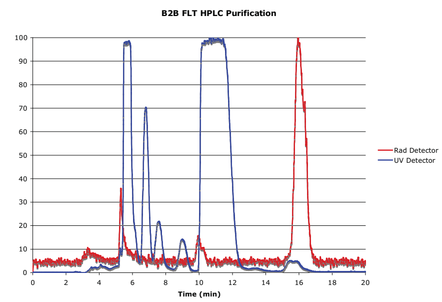
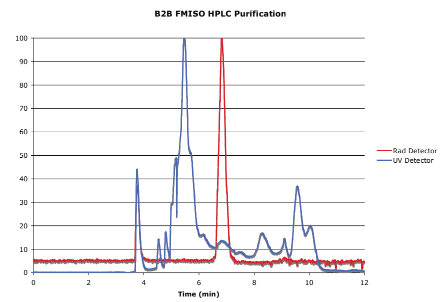
Method

FLT and FMISO were produced in accordance with previously published methods. FLT, which has the lower radiochemical yield, was produced first. Approximately half of the dry fluoride was dispensed through reactor 1 with the NOSYL precursor for FLT. Hydrolysis and neutralization was then performed in the vial of the second CE module before loading onto the HPLC loop and purification. The HPLC loop was then cleaned and the FMISO column selected in preparation for FMISO production. The remaining half of the dry fluoride was then dispensed through reactor 2 with the NITTP FMISO precursor, followed by hydrolysis in the additional vial, mounted in the spare reactor slot.





Results

Batches of 59.4 mCi (2.2Gbq) and 57.4 mCi (2.1Gbq) of purified FLT and FMISO were produced from a starting delivery of 678 mCi (25 GBq) of ^{18}F. Corrected for the amount of fluoride present at the start of each synthesis, the decay corrected yields were 18.9% and 28% respectively. A kryptofix spot test was used to determine the amount of kryptofix in the product. This showed that kryptofix was below the acceptable limit of 50 µg/ml.

Item	Activity (mCi)	Time Activity Measurement	% Radiochemical Yield at EOS‡	Specific Activity
Starting Fluoride	678	10:25		
FLT	59.4	11:42	17.5 %	>2.0 Ci/µmol
FMISO	57.4	12:35	28 %	>2.0 Ci/µmol

EOS = End of Synthesis, ‡ % Radiochemical yield at EOS was determined by taking the amount of activity obtained in the final product vial (which could be used in studies) and dividing by the activity used at the start of the radiosynthesis (1/2 of the starting fluoride activity) * 100.

Cleaning

A standard cleaning macro was run to clean the entire system, including syringes pumps, reactors and distribution valves. Following this routine cleaning a second cold synthesis was performed without precursors or carbonate/kryptofix. The effluents were then analyzed using analytical HPLC to detect any residual amounts of precursor or activity from the earlier synthesis runs. Carryover was found to be <0.1%

Summary

The results demonstrate that it is possible to produce medium scale batches of two different compounds from one delivery of ^{18}F. The analysis of the cleaning process shows there are no unacceptable contaminants and no significant carryover from one compound to the next.