Electrochemical Concentration of Aqueous [18F]Fluoride into an Aprotic Solvent in a Disposable Microfluidic Cell

VII. 1.   Electrochemical Concentration of Aqueous [18F]Fluoride into an Aprotic Solvent in a Disposable Microfluidic Cell

Saiki H.[1], Iwata R.[2], Wong R.[2], Furumoto S.[3], Ishikawa Y.[2], Nakanishi H.[1], and Ozeki E.[1]

[1]Technology Research Laboratory, Shimadzu Corporation,
[2]Cyclotron and Radioisotope Center, Tohoku University
[3]Graduate School of Medicine, Tohoku University

Microfluidic technology is an attractive strategy found viable in PET radiochemistry.   As PET probes demand high specific activities, this technology is predicted to find wide applications in PET radiosynthesis due to the rapid and efficient nature of its reactions.   Although several microreactor systems have been developed to date, these were merely proof-of-concept studies limited from the lack of interfacing techniques in introducing target products into a microreactor[1,2].   We present a novel and practical approach of transferring [18F]fluoride from the target water into an aprotic solvent by means of electrochemical separation in a micro-flow cell.

The present method was developed based on the principle of electrochemical separation of nca [18F]fluoride from [18O]water[3,4].   A conceptual design of a disposable flow-cell with the aftermentioned method for electrochemical concentration of aqueous [18F]fluoride is as illustrated in Fig. 1.   The volume capacity of the utilized flow-cell is 16 μL (40 x 4.0 x 0.1 mm). Water (*ca.* 1.5 mL) containing no-carrier-added [18F]fluoride was first flowed through the cell (0.1~1.0 mL/min) under a constant electric potential of 1 ~ 10 V applied between the Pt cathode and glassy carbon anode.   The cell was then flushed with anhydrous CH_3CN (1.0 mL/min for 2 min) under the same electric potential.   Voltage was then disconnected and an aprotic solvent (CH_3CN, DMSO or DMF) containing the K.222-$KHCO_3$ complex (ca. 40 mM) was introduced into the cell and left stagnant.   This was followed by heating up of the cell to a preset temperature.   Accordingly, a reversed electric potential (1 ~ 10 V) was applied and cell flow was allowed to resume.   A radiation sensor was used to detect the released [18F]fluoride, which was then either collected in a vial or sent to a subsequent chip to be used as a labeling agent.   The above procedure was

fully automated using syringe pump modules (Hamilton PSD/3) as shown in Fig. 2.

The deposition of [^{18}F]fluoride within the cell clearly depended on the flow rate and the voltage. It was rapidly increased up to 80% between 1 and 4 V followed by a gradual increase to over 90% at 10 V (Fig. 3a), while linear decrease was observed with increasing the flow rate (Fig. 3b). The optimized parameters of 10 V and 0.7 mL/min gave 90% deposition within 3 min. Efficient release of [^{18}F]fluoride from the GC surface required heating at >80°C (Fig. 4a). With a reversed voltage of 2 V and a flow rate of 0.7 mL/min, more than 70% in the trapped [^{18}F]fluoride was recovered in ca. 60 within 2 min (Fig. 4b, Fig. 5). The variation of the overall recovery efficiency in successive use of the same chip was evaluated and it was decided to be usable up to several times without notable decrease in recovery efficiency (Fig. 6). The reactivity of [^{18}F]fluoride thus obtained was exemplified by radiosynthesis of [^{18}F]FDG. High [^{18}F]Fluorination yields of over 80% with mannose triflate were observed in short-time reactions of over 3 sec at 80°C.

In conclusion, the present microfluidic method demonstrated that aqueous [^{18}F]fluoride was electrochemically concentrated in 60 μL within 6 min. The recovered [^{18}F]fluoride showed high reactivity in the synthesis of [^{18}F]FDG in a microreactor.

References

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   L. Liu, CA. Huh, Earth and Planetary Sci. Lett. **180** (2000) 163.
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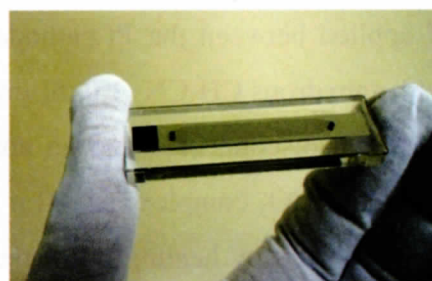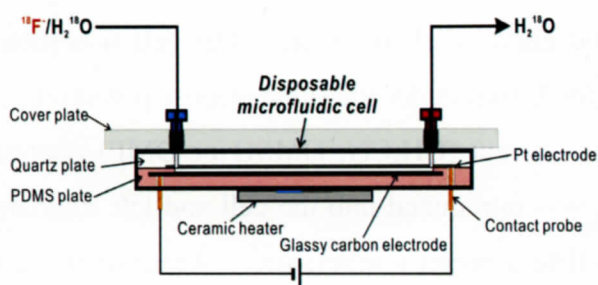4) Hamacher K., Hirschfelder T., Coenen H.H., Appl. Radiat. Isot. **56** (2002) 519.
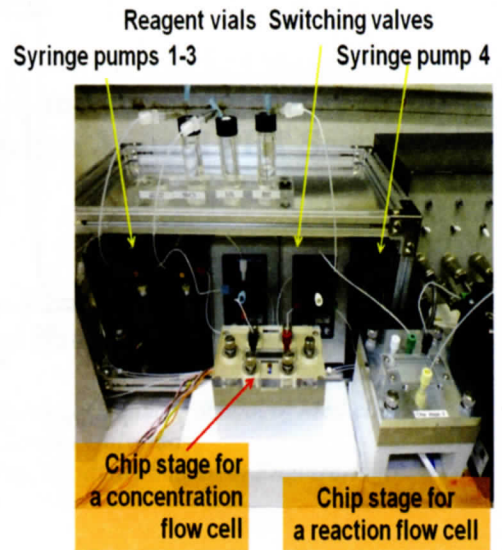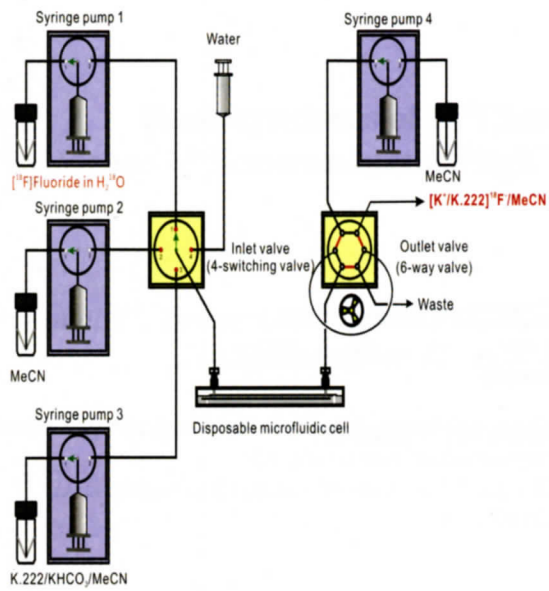
Figure 1. Disposable flow cell.

Figure 2.   Automated module.
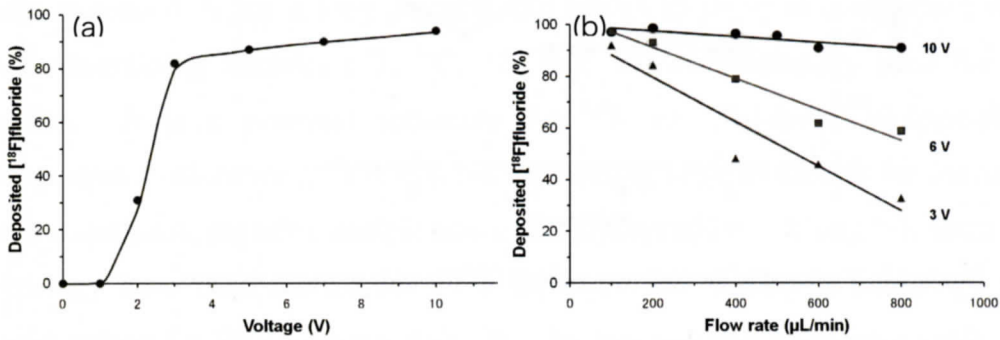

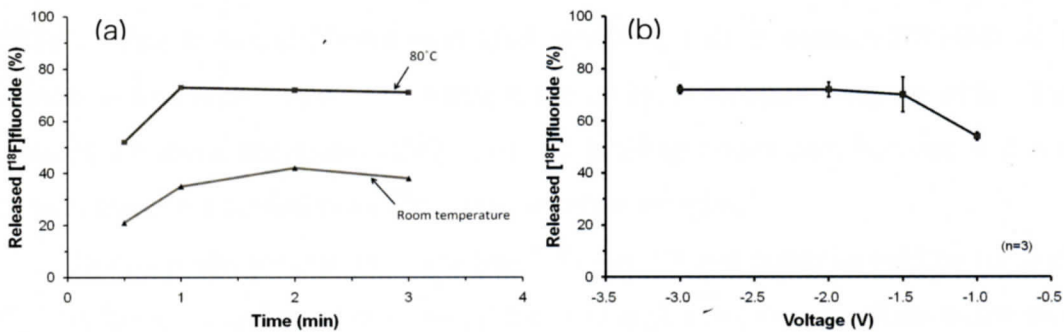Figure 3.   Dependences of the deposition of [^{18}F]fluoride on voltage (a) and flow rate (b).

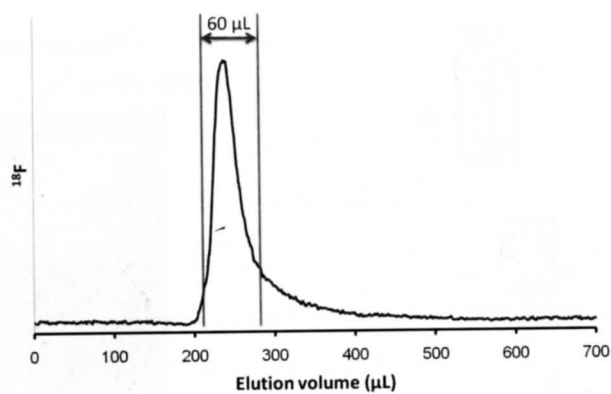Figure 4.   Dependences of the release of [^{18}F]fluoride on time (a) and voltage (b).

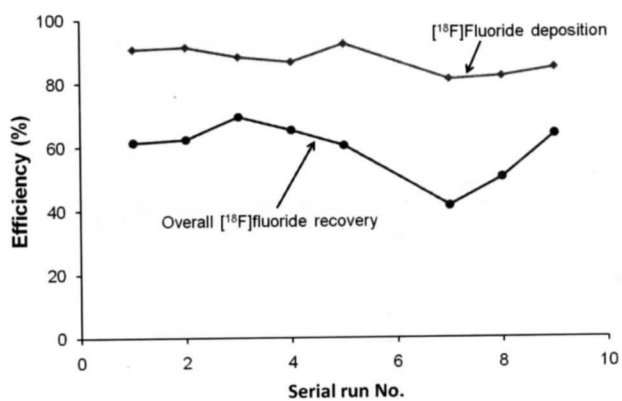Figure 5.   Elution profile of [^{18}F]fluoride.

Figure 6.   Variation in the recovery yield of [^{18}F]fluoride in successive use.