Electronic Supplementary Material (ESI) for Lab on a Chip

Batch-reactor microfluidic device: First human use of a microfluidically produced PET radiotracer.

Supporting information.

Artem Lebedev*[a], Reza Miraghaie[a], Kishore Kotta[b], Carroll E. Ball[a], Jianzhong Zhang[a], Monte S. Buchsbaum,[b,c] Hartmuth C. Kolb, Arkadij Elizarov[a]

[a] *Molecular Imaging Biomarker Research, Siemens Healthcare, 6100 Bristol Pkw, Culver City, California, USA. Fax: +1-310-568-9491; Tel: +1-310-864-1684; E-mail: artem.lebedev@siemens.com*
[b] *Department of Radiology, University of California, San Diego, 11388 Sorrento Valley Road, Suit #100, San Diego, California, USA; E-mail: mbuchsbaum@ucsd.edu*
c Department of Psychiatry, University of California, San Diego

Algorithm for determination of liquid-gas transition using optical interface sensors.

The detector is polled every second, and once it detects liquid, a software flag is raised and the timer starts. The polling continues until the detector reports gas. At this point another timer starts, and the polling continues. If the detector does not report liquid within 10 seconds of the second timer onset, the process is considered finished. If more than a predefined time (normally 10 min.) expires from the onset of the first timer, a detector failure is assumed and the process is considered finished anyway. This algorithm allows eliminating most of false gas detections while avoiding indefinite waiting in case of a malfunctioning detector.

Reactor pressure test procedure.

If we are to use this system to perform syntheses, the microreactor must withstand the vapor pressures that arise when heating organic solvents in sealed environments. To determine the pressure that could be withstood within the gasket-free reactor, we performed the following experiment. A transparent piece of tubing connected to the chip was filled with a tiny volume of colored water. After applying pressure to the tubing and waiting for it to stabilize, we measured how far the colored liquid moved within 1 min; this distance allowed us to calculate the volume of gas that escaped from the reactor during this period of time. Assuming that any leaks greater than 1 μL/min would be detrimental to the syntheses performed in a 60-μL reaction chamber, we ramped up the pressure until we reached this rate of loss. We consider the pressure recorded at this point to be the "cutoff pressure." Pressurizing a channel with open valves (cf. Figure 2b) provided a cutoff pressure of 30 psi. When we repeated this process with the valve closed (instead of passing into the reactor, the liquid was diverted into the bypass channel), the cutoff pressure remained at 30 psi (because the seal around the plunger was rather weak). In contrast, with all the valves closed and the pressure applied to the reaction chamber through a non-valved port, the cutoff pressure exceeded 300 psi because strong seals were formed by the ends of each plunger pushing against a flat end of the barrel. Therefore, this microreactor is capable of withstanding high pressures required to accelerate synthetic reactions by superheating beyond the boiling points of the solvents used.

Fallypride production instrument settings

1. Trapping of $^{18}F^-$: 2 ml of target water, 20 psi, automatic procedure, approx 3 min.
2. Release of ^{18}F to the reactor: 800 μL gas dispense at 50 μL /s; 600 μL gas dispense at 5 μL /s
3. Drying of fluoride: 240 s at 120^{o}C, 4 psi pressure in the blow line.
4. Adding precursor: 1 mg of Fallypride-Tos in 45 μL of dry MeCN, 600 μL gas dispense at 50 μL /s; 30 μL gas dispense at 5 μL /s
5. Fluorination: Sealed reactor, 300s, 181^{o}C
6. Transfer to HPLC loop: 1000 μL of 40% EtOH in phosphate buffer pH 6.27; 50 μL /s
7. HPLC purification: Macherey-Nagel Nucleodur column, 4.6x250 ml, 20% EtOH in phosphate buffer pH 6.27; 4 ml/min. Product retention time 1535-1600 s.

Detailed report on the reaction conditions optimization and the chemistry of the fallypride synthesis is currently in preparation.

Electronic Supplementary Material (ESI) for Lab on a Chip

Additional pictures

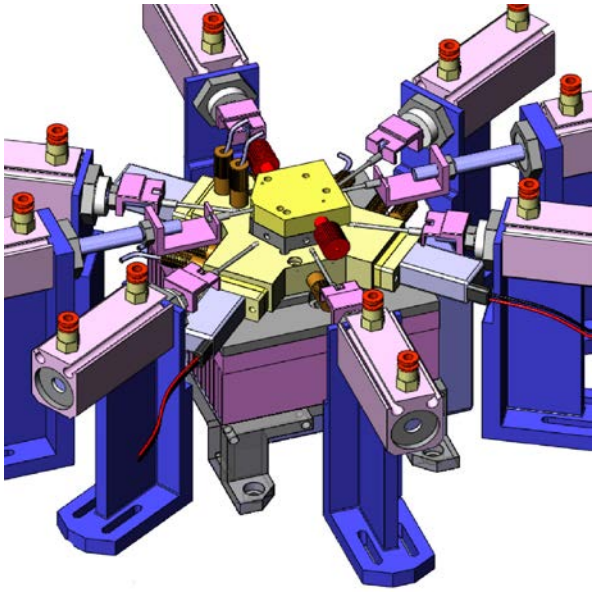

Fig S1. Reactor assembly with valve actuators and heater assembly.

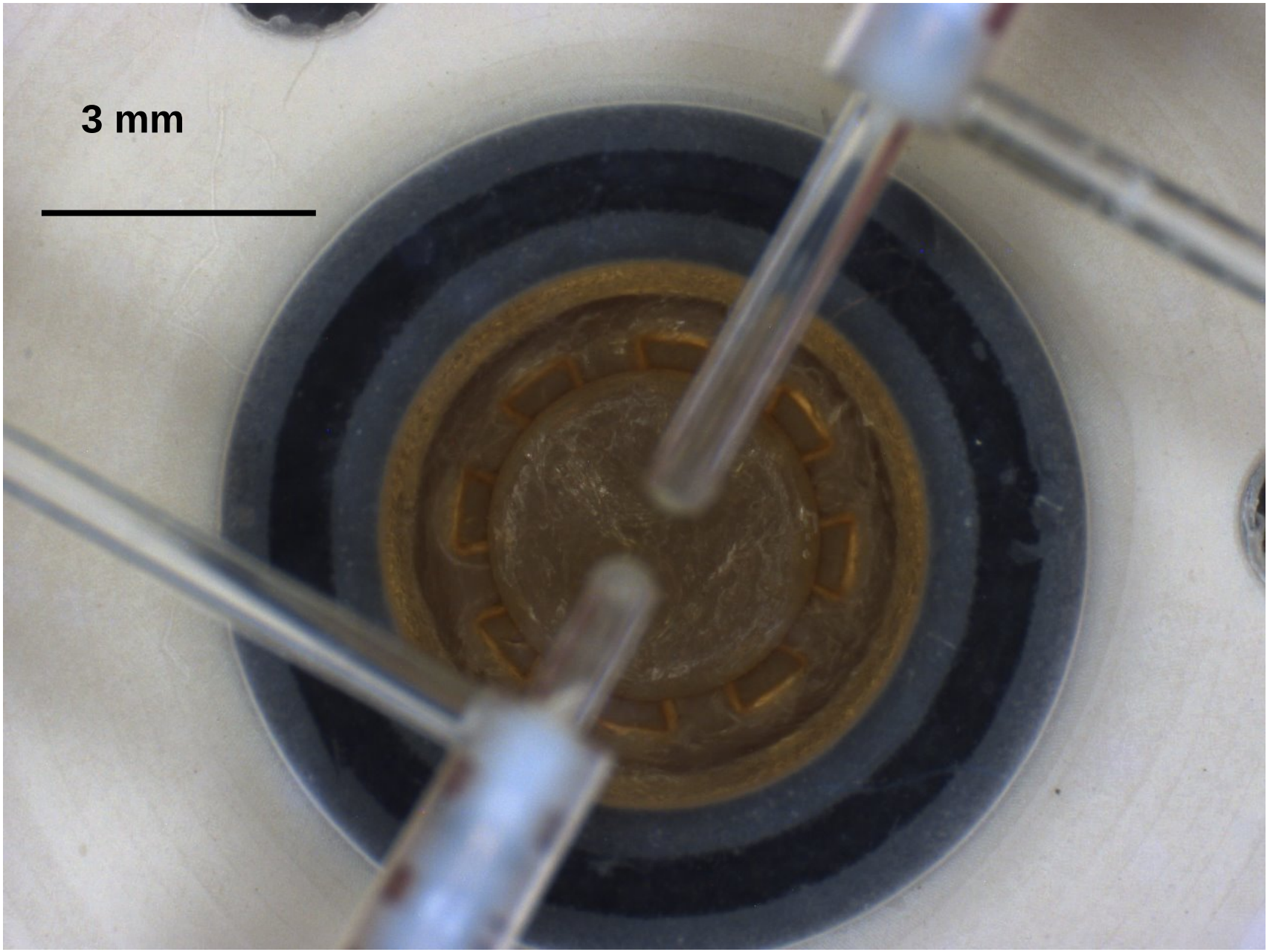

Fig S2. Camera view of reactor after the F-/K_{222} complex has been dried

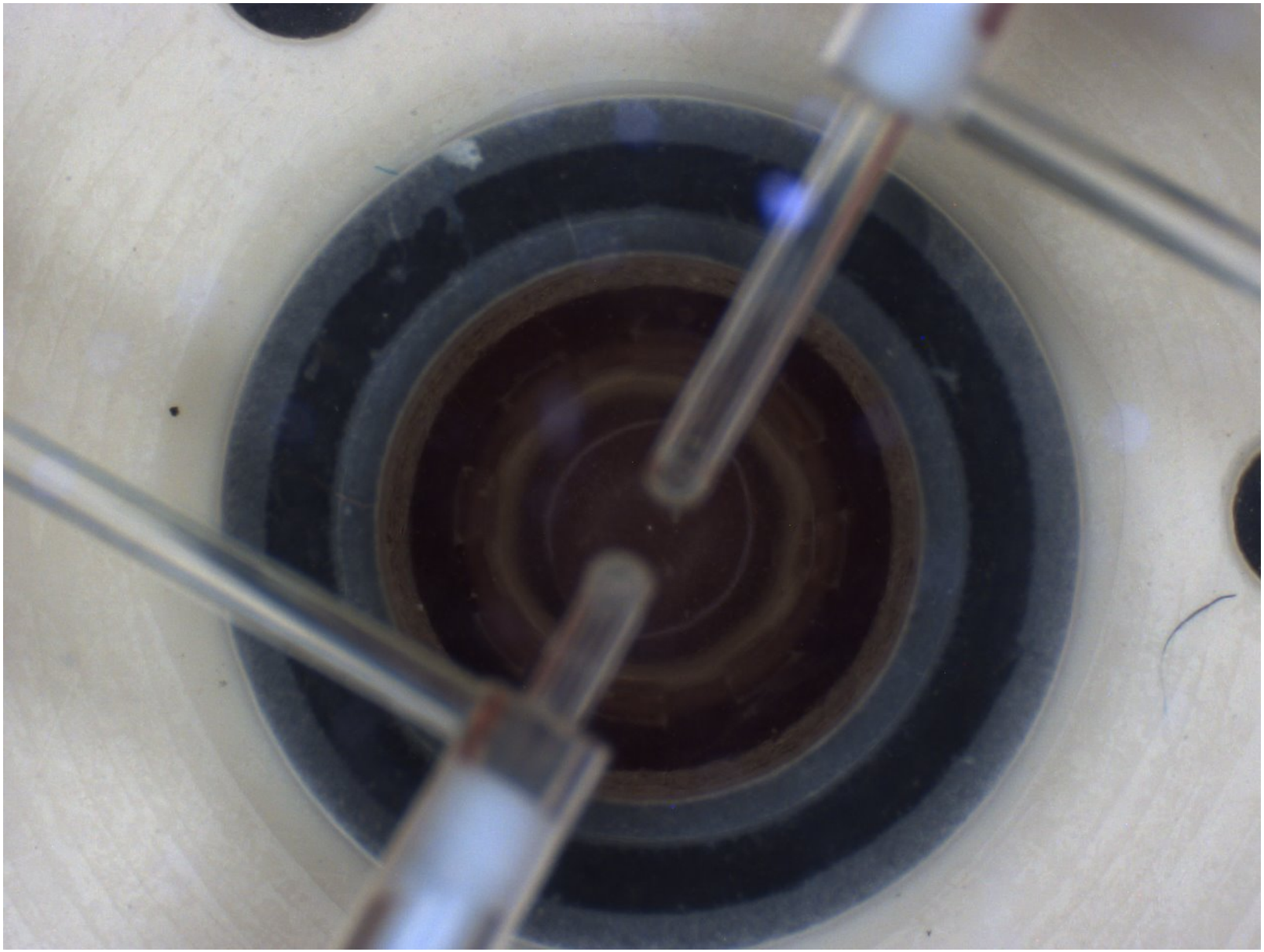

Fig S3. Camera view of reactor after the MeCN/water solution of F-/K_{222} complex has been added to the reactor

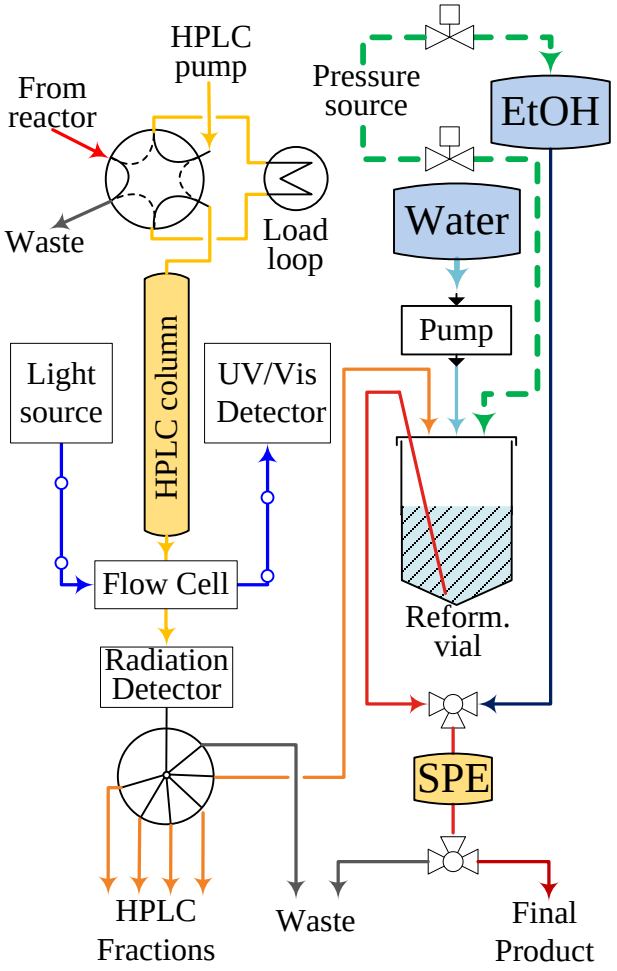

Fig S4. General scheme of purification and reformulation system

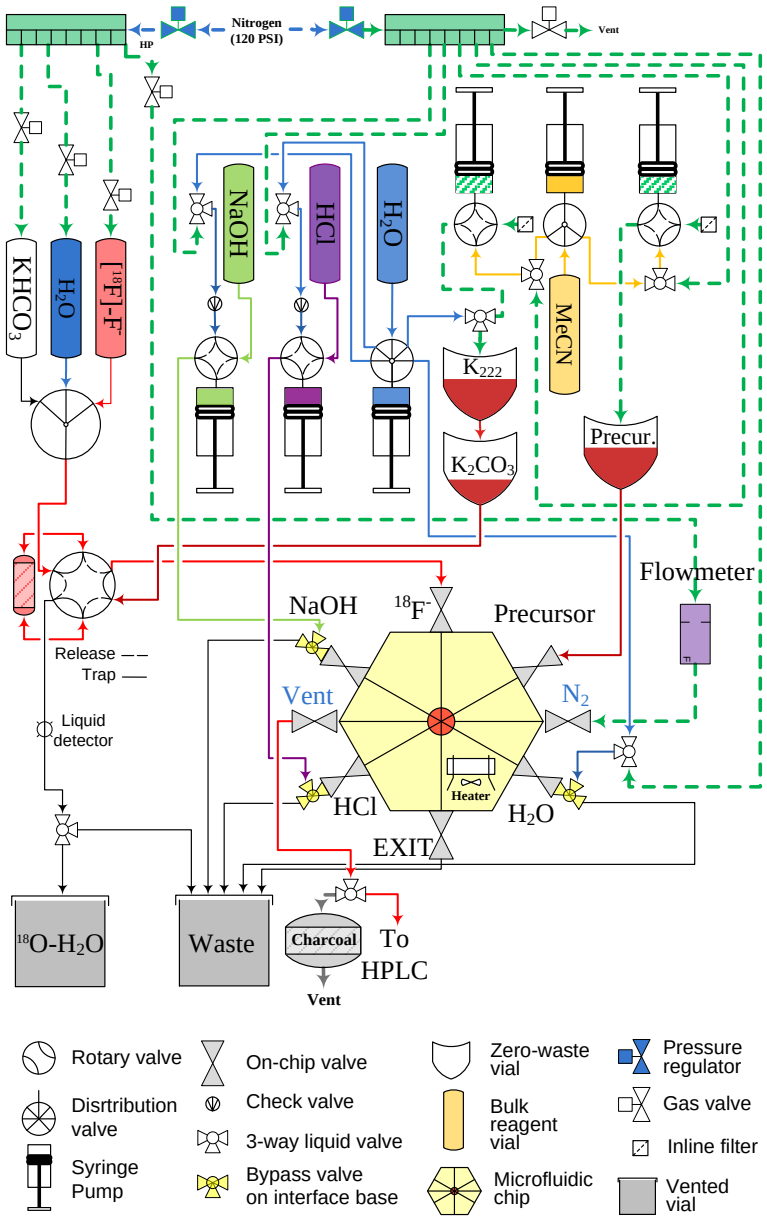

Figure S5. Detailed schematic of the liquid routing in the synthetic unit

Electronic Supplementary Material (ESI) for Lab on a Chip