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Application of microfluidics in PET

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Microreactor technology (microfluidics) has shown enormous potential for optimising synthetic efficiency, particularly in the preparation of sensitive compounds. The high surface-to-volume ratios in microfluidics offer many possibilities to more efficient syntheses (1). Advantages of the use of very small quantities include simplification of purification steps and increased specific activity. Furthermore, microfluidic reactors offer possibilities to increase reaction speed dramatically, improve reproducibility, and reduce costs. Recently, the synthesis of 2-deoxy-2-[^{18}F]fluoro-D-glucose ([^{18}F]FDG), in an integrated microfluidic device was described in Science (2). In addition, preliminary reports have appeared on [^{11}C] methylation of carboxylic acids in microchips (3).

The use of microfluidics in PET-radiosynthesis has several advantages.

1. Effect on specific activity: In order to have sufficient radioactive signal for the PET-scanner, PET-radiopharmaceuticals have to be of sufficiently high specific activity (to provide a high-count rate while not violating the tracer principle. Normally applied specific activities result in the administration of tens of picomoles of radiopharmaceutical in a typical µPET-study. In addition to the need for high specific activity there is a need for high specific activity concentration in µPET-studies. This requirement stems from the fact that the volume to be injected can be maximally 0.5 ml. miniaturisation provides the opportunity to use small amounts of starting materials, therefore the contribution of mass to the specific activity will be decreased.
2. The role of PET in drug development: To increase the role of PET in the drug development process, radiochemistry development will play a key role.
   By broadening the scope of radiolabelling possibilities the role of PET will become increasingly important. Several labelling strategies are already available and many are under development. The radionuclides ^{11}C and ^{18}F are most practical to use in radiolabelling of drugs. Microfluidics has the potential to facilitate PET-radiolabelling procedures that are challenging under conventional conditions. Microfluidics can play a crucial role in the role of PET in drug development, because new ^{11}C and ^{18}F radiopharmaceuticals will become more readily available. Microfluidics is a fast technology and therefore many reaction conditions can be tested in a very short time span, so sufficient amounts of radiopharmaceutical will become available at an earlier stage of drug development.

Microfluidic technology to prepare PET-radiopharmaceuticals will be implemented in new generation synthesis modules. The production of conventional synthesis modules is an expanding well-established market. In recent years new companies have come in the field.

Recently several companies have shown preliminary work on the preparation of PET-radiopharmaceuticals using microfluidic technology eventually in combination with table-top cyclotrons for patient-tailored PET-radiotracer synthesis.

References

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2. Lee CC et al. Science. 2005, 310:1793-6.
3. Gillies JM et al. Appl Radiat Isot. 2006 64:333-6.