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Automation strategies in PET-radiopharmaceutical production

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Apart from general aspects, such as to reduce the radiation burden to the personnel and compliance with pharmaceutical regulations, automation in radiopharmaceutical production is recommended to ensure high reproducibility, high reliability and constant product quality.

Several different approaches and strategies for large scale tracer production (remote controlled, semi-automated, fully automated) have been developed and commercialized. Some modules have been designed in a tracer specific manner; others have been developed to allow a broader use for a series of similar reactions, e.g. nucleophilic F-18-fluorinations or C-11-methylations. Due to the costs of these modules, most of the radiopharmaceutical labs worldwide have developed their own, self-made tracer-specific apparatuses and thus have gained significant experiences on how to automate a radiopharmaceutical synthesis. Thus, newer approaches try to establish modular systems which would allow these groups to create their specialized solution using commercially available components.

To simplify the commonly used modules, radiochemistry can significantly contribute by investigating straight forward labelling approaches with reduced synthesis steps, developing fast on-line and loop techniques, implementing efficient and specific solid phase extraction techniques, and testing reactions under milder conditions to reduce side product formation. In the same context and with the aim to reduce the production costs and infrastructure necessary for GMP production of radiopharmaceuticals, newer approaches suggest the use of microfluidic structures for fast and efficient tracer production. Although the first successful productions of radiopharmaceuticals using microfluidic devices have been demonstrated by some groups, it remains unclear, whether a scale-up to routine syntheses with clinically relevant quantities of isotopes will be successfully.

References

1. Alexoff DL (2003) Automation for the synthesis and application of PET radiopharmaceuticals. In: Welch MJ, Redvanly CS (eds) Handbook of Radiopharmaceuticals. Radiochemistry and Application. Wiley, pp 283-305
2. Satyamurthy N, Phelps ME, Barrio JR (1999) Electronic generators for the production of positron-emitter labelled radiopharmaceuticals: Where would PET be without them? Clin Posit Imag 2:233-253
3. Lee CC, Sui G, Elizarov A, Shu CJ, Shin YS, Dooley AN, Huang J, Daridon A, Wyatt P, Stout D, Kolb HC, Witte ON, Satyamurthy N, Heath JR, Phelps ME, Quake SR, Tseng HR. (2005) Multistep synthesis of a radiolabeled imaging probe using integrated microfluidics. Science. 310(5755):1793-6.
4. Lu SY, Watts P, Chin FT, Hong J, Musachio JL, Briard E, Pike VW. Syntheses of 11C- and 18F-labeled carboxylic esters within a hydrodynamically-driven micro-reactor. (2004) Lab Chip. 4:523-5.
5. Gillies JM, Prenant C, Chimon GN, Smethurst GJ, Dekker BA, Zweit J. Microfluidic technology for PET radiochemistry. (2006) Appl Radiat Isot.64:333-6.