Radiotracers for positron emission tomography (PET) are a powerful imaging tool with ever increasing clinical relevance for diagnosis in versatile applications comprising tumor staging, cardiac perfusion and neuropsychiatric disorders among others. Most relevant PET-nuclides for radiolabeling of those imaging vectors are carbon-11, fluorine-18 and gallium-68. Since radiochemical procedures are constrained by radioactive decay, this small niche of chemistry requires special prerequisites like a short reaction time as well as an optimized radiopharmaceutical quality control and precaution regarding radiation protection during all operative steps. In this light, many chemical synthesis procedures and respective quality control assays of radiopharmaceuticals emerge as rather sophisticated, cumbersome or even unsuitable. Thus, an improvement of those processes is beneficial. Consequently, research is requested to put emphasis on the optimization of radiochemical syntheses and quality control procedures for a suitable application within a standardized clinical setting.

The presented study comprises the improvement of radiosynthesis and quality control using a couple of model systems and radiotracers out of clinical trials and routine. In particular, 68Ga-labeling of [68Ga]Ga-DOTA-NOC, [68Ga]Ga-PSMA-11 and [68Ga]Ga-NODAGA-RGDyk using a HEPES buffered system was performed by means of continuous flow microfluidic- and microwave assisted synthesis. Microfluidic 68Ga-labeling was performed successfully in high radiochemical yields. Likewise, microwave assisted synthesis showed excellent radiochemical conversion rates, especially for the radiotracers, [68Ga]Ga-PSMA-11 and [68Ga]Ga-NODAGA-RGDyk. Hence, this study revealed high efficiency of unconventional microfluidic and microwave assisted 68Ga-labeling.

Furthermore, the problematic quality control procedure for HEPES quantification via TLC according to the European Pharmacopoeia (Ph. Eur.) and a reported HPLC assay were evaluated and a novel, improved TLC assay was developed. The quantification of HEPES by TLC according to the Ph. Eur. was neither conclusive nor reproducible. An HPLC assay according to Antunes et al. achieved a good linearity of the created calibration curve. Furthermore, a novel TLC method was developed which is outperforming the TLC assay currently published in the Ph. Eur. in terms of limit of linearity, reliability and conclusiveness. The influence of HEPES on cell viability in three different PC3 cell lines was assessed by an MTT assay. Synergistic effects of HEPES and [68Ga]Ga-PSMA-11 were investigated by incubation of the radiotracer in presence of different HEPES concentrations in PSMA expressing PC3-B9 cells.

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behavior up to a concentration that exceeds the currently prescribed limit by more than a factor of 103. Preliminary results showed similar [68Ga]Ga-PSMA-11 uptake in PC 3 B9 cells in the presence of different HEPES concentrations and no influence on the uptake at higher HEPES amounts present.

Another challenging experimental setting is radiolabeling using carbon-11 due to its short half-life of 20 min. In this context, sophisticated 11C-labeling of (+)-HNO was significantly improved by omitting heating and cooling procedures during radiosynthesis and therefore, accelerating the whole process.

Skipping heating and cooling during (+)-[11C]PHNO synthesis resulted in a remarkable reduction of synthesis duration of about 5 min counteracting radioactive decay of about 13%. Moreover, byproducts and intermediates of (+)-[11C]PHNO synthesis were synthesized on purpose and chromatograms thereof were compared for facilitated failure analysis after unsuccessful syntheses. The investigation of the influence of reagents on byproduct formation enabled the creation of a decision tree facilitating troubleshooting in a generalized way.

Ultimately, this successful work optimized particular procedures within PET-tracer synthesis and quality control. It evoked several questions that need further attention, especially about the reasonability of the currently prescribed HEPES limit and HEPES quantification.