DEVELOPMENT OF AN IN-HOUSE METHOD FOR THE SYNTHESIS OF SODIUM [^{18}F]FLUORIDE PREPARATION

Abstract ID #268

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Background and goal of the present work

Sodium [^{18}F]fluoride is PET radiopharmaceutical containing fluorine-18 in the form of sodium fluoride, for visualization of the skeletal system and microcalcification.

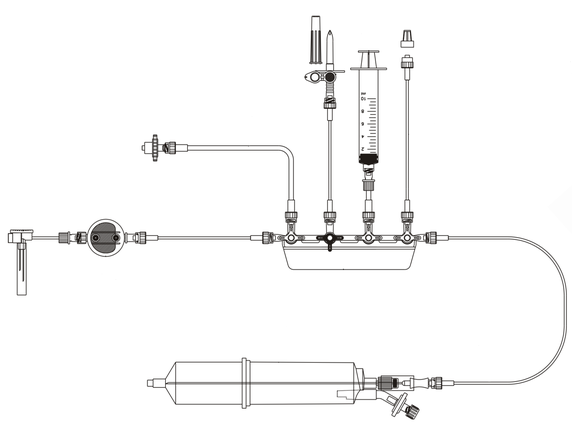
Aim: Development of an in-house method for [^{18}F]NaF production using only a dispensing module for both, radiopharmaceutical synthesis and dose dispensing.

Materials and methods

For the production of [^{18}F]NaF, the modification of the kit was done. On the dispensing kit, the Y connector and anion-exchange cartridge and sterile vial with 0.9% sodium chloride solution were installed. The preconditioned QMA cartridge was connected to the distal part of the Y connector and attached to the first valve of the kit. One proximal ending of the Y connector was connected to the [^{18}F]F$^-$ cyclotron transfer line and the other proximal ending to the vial with 5 mL 0.9% NaCl solution for elution.

Clio
(Comecer S.p.A.)

Semi-automatic dispenser

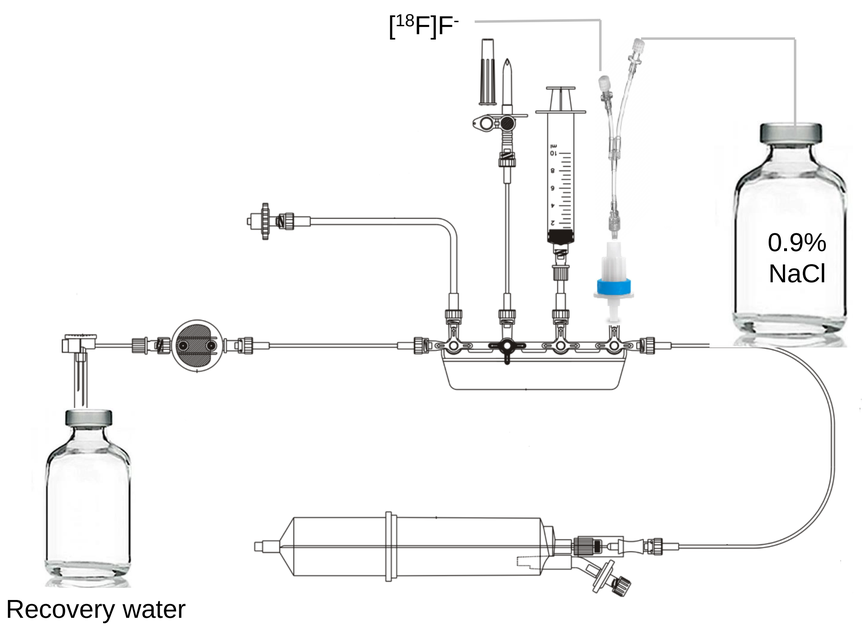


Single-use sterile disposable kit
(BTC Medical Europe)

The kit includes four three-way valves, lines for different purposes, and a 0.22 µm sterilization filter

Y connector
(B Barun)

QMA cartridge
(Waters)

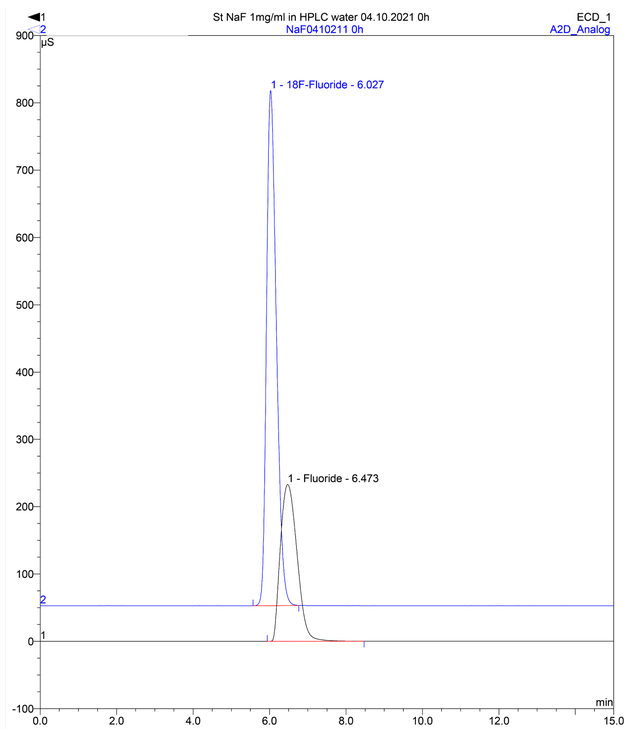


Modified kit for production of [^{18}F]NaF

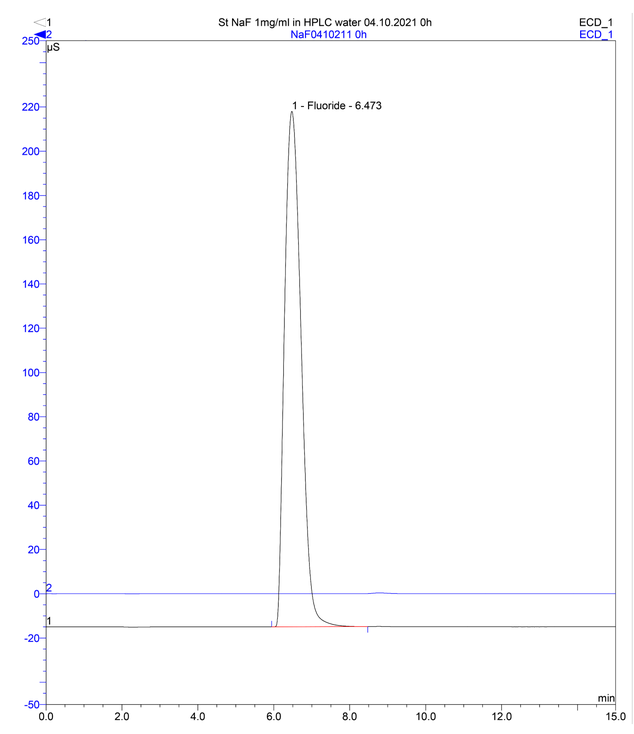
Results

After development of our in-house method for synthesis, the process optimization was carried out, 10 production batches were performed, with yield higher than 98%, decay-corrected. All obtained QC results confirmed that the quality of [^{18}F]NaF meets the acceptance criteria defined in the specification.

Test		Method	Acceptance criteria	Results
Pre-release tests				
Appearance		Visual inspection	Clear, colorless solution	Clear colorless solution
Identification	**Half-life determination**	Radioactivity measurements	1.75-1.92 hours	1,832 ± 0,014
	Difference in retention time	HPLC	≤ 40 s	26,899 ± 4,763
Approximate pH value		pH strips	5.5 - 8.0	6.5-7.0
Chemical purity: fluoride (F$^-$)		HPLC	≤ 0.452 mg/mL	≤ 0.452
Radiochemical purity: [^{18}F]fluoride		HPLC/gamma detector	min 98.5 % of the total radioactivity	100%
Post-release tests				
Bacterial endotoxins		Chromogenic LAL method	≤ 17.5 IU/mL	< 5.00
Sterility		Test for sterility (Ph. Eur)	Sterile	Sterile
Radionuclidic purity Fluorine-18		Gamma-ray spectrometry	min 99.9 % of the total radioactivity	1,34 x 10^{-05} ± 7,63 x 10^{-06}



Radiochemical purity



Chemical purity

Conclusion

The in-house method for [^{18}F]NaF synthesis was successfully designed and developed. The produced [^{18}F]NaF radiopharmaceutical meets the acceptance criteria defined in the specification, based on Ph. Eur. monograph.

International Symposium on Trends in Radiopharmaceuticals (ISTR-2023), CN-310
Vienna, Austria; 17-21 April 2023