Purification of ^{68}Ga combining cation and anion exchange processes

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Introduction: The ^{68}Ge/^{68}Ga radionuclide generator provides an excellent source of positron emitting ^{68}Ga for the routine synthesis and application of ^{68}Ga-labeled compounds using PET. However, newly available "ionic" ^{68}Ge/^{68}Ga radionuclide generators are not necessarily optimized for the routine synthesis of ^{68}Ga-labelled radiopharmaceuticals in a clinical environment. The eluates have rather large volumes (up to 10 ml for complete elution), a high concentration of H^+ (pH of 1), a breakthrough of ^{68}Ge of 10^{-2} %, increasing with time or usage frequency, and impurities such as stable Zn(II) generated by the decay of ^{68}Ga, Ti(IV) a constituent of the ^{68}Ge adsorption column material and Fe(III) as a general impurity.
Recently, we have introduced a post-processing approach to absorb ^{68}Ga on line from generator eluates on a small cation exchange resin (a) to purify it using HCl / acetone mixture N1 (b) and to desorb ^{68}Ga from the resin quantitatively using 0.4 ml of an 0.005 M HCl / 98.5 % acetone solution N2 (c). The overall content of acetone in the purified ^{68}Ga fraction is small and non-toxic [1]. However, for some reasons it may be reasonable to reduce this amount of acetone further.
Alternatively, the use of acetone may be avoided completely. In this work, we kept the strategy of ^{68}Ga purification on cation exchange resins by using HCl / acetone mixtures from metallic impurities and ^{68}Ge breakthrough, but investigated the possibility to further remove the acetone by adding a second anion exchange purification step. Pre-concentration of ^{68}Ge/Ga eluates using anion exchange resins have been introduced earlier, e.g. [2,3]. The key question is, whether the ^{68}Ga can be eluted from the cation exchange resin quantitatively with solutions not containing acetone, but applicable to subsequent anion exchange processing.

Experimental: The first step of concentration and purification of the initial ^{68}Ge/Ga generator eluate was performed utilizing a miniaturized column with organic cation (AG 50 W-X8, -400 mesh) exchanger resin and HCl / acetone media. The ^{68}Ga eluted with 7 ml of 0.1 N HCl was transferred within 1-2 min on the chromatographic column. This represents the basic step to recover radio gallium from the generator eluate and to remove the main parts of the chemical and radiochemical impurities. In the next step, the column was eluted with 1 ml solutions of 80% acetone / 0.15 N HCl (N1). The cation exchange column was washed with various volumes of HCl solutions of different concentration and with water. The results are summarized in Table 1 in terms of ^{68}Ga activity eluted with the HCl fraction, with the water fraction and the one remaining on the cation exchange resin. The ^{68}Ga fraction is than on line transferred to a small (50 mg) column with organic anion (AG 1-X8, 200-400 mesh) exchanger resin.

Results and Discussion: Yield of ^{68}Ga eluted with 0.5, 1.0, 2.0 ml of various concentrations of HCl are shown in table 1.

Table 1: relative ^{68}Ga distribution for various desorption processes of ^{68}Ga from the cation exchange resin after N1 purification

	Concentration of HCl					
	1 N	2 N	4 N	5 N	6 N	8 N
0.5 ml HCl	17.5	83.6	93.6	-	27.3	10.7
2 ml H_2O	3.6	5.0	3.6	-	4.5	7.2
Cat.	78.9	11.4	2.8	-	68.2	82.1
1.0 ml HCl	43.7	95.2	97.1	-	33.3	17.3
2 ml H_2O	4.2	1.2	0.2	-	3.9	3.3
Cat.	52.1	3.6	2.7	-	62.8	79.4
2.0 ml HCl	80.1	98.6	98.6	90.3	44.7	14.5
2 ml H_2O	1.1	0.3	0.1	1.2	2.0	4.6
Cat.	18.8	1.1	1.3	8.5	53.3	80.9

All ^{68}Ga elutes from the cation exchange cartridge and quantitatively stays on the anion exchange resin. Afterwards, 75-85 % ^{68}Ga was eluted from the anion-exchanger with 1 ml of H_2O as described in [2,3].

Conclusions: If the cation exchange resin is eluted very slowly with 2 ml of 2 – 4 N HCl, about 98.5(5) % of the ^{68}Ga activity can be desorbed from the cation exchange resin. However, quantitative adsorption on anion exchange resin is achieved with HCl concentrations of 5 – 8 N only. Thus, 2 ml of 5 N HCl are relevant, with a ^{68}Ga recovery of 91(1) %. ^{68}Ga is adsorbed completely on the anion exchange resin, and can be eluted using small volumes of water as described in [2,3].
In this case of combined processing of generator eluates, acetone is not present in the final solutions. The process takes about 5-10 min longer (compared to post-precessing using cation exchange and HCl / acetone solutions, [1]). The overall ^{68}Ga yields are about 80% referred to a non-processed ^{68}Ga eluate, i.e. about 15% less compared to [1]. However, the high purification factor concerning ^{68}Ge and other metallic impurities is still preserved due to the initial cation exchange resin.

References:

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