Quantitative determination of ^{68}Ge breakthrough of ^{68}Ge/^{68}Ga generators via TLC

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^{68}Ge/^{68}Ga generators contain initial activities of 20, 30 or more mCi of ^{68}Ge, respectively ^{68}Ga. In the first period of generator usage the breakthrough levels of ^{68}Ge are between 10^{-4}% and 10^{-2}%. This is a critical parameter in the context of clinical use of ^{68}Ga-radiopharmaceuticals. Due to the lack of sufficiently distinctive radiation, ^{68}Ge is "invisible" within the excess of ^{68}Ga activity. Therefore, ^{68}Ga solutions (e.g. eluate, product) usually have to be kept in storage for several hours or even days before a detection of ^{68}Ge is possible. This work aims for an easy and instant analysis of ^{68}Ge, i.e. prior to the release of ^{68}Ga-radiopharmaceuticals. The concept was used to discriminate between ^{68}Ge and ^{68}Ga and even ^{68}Ga-labeled peptides (e.g. ^{68}Ga-DOTATOC) on a TLC plate in order to determine the ^{68}Ge content in ^{68}Ga-pharmaceutical preparations within one hour post elution.

A ^{68}Ge/^{68}Ga Obninsk generator was used with a ^{68}Ga yield of 100 MBq and a ^{68}Ge breakthrough of 85 kBq. It was eluted with 5 mL of 0.1M HCl through a cation exchange resin (Biorad: AG 50W-X8, -400 mesh) to adsorb ^{68}Ga from the eluate. DOTATOC was labeled according to standard protocol. For the separation of ^{68}Ge from ^{68}Ga and ^{68}Ga-DOTATOC on TLC plates, various solvent mixtures and different stationary phases were investigated. The distribution of ^{68}Ge, ^{68}Ga and ^{68}Ga-DOTATOC was detected at instant imagers. The radioactivity detection on the TLC plate was performed at various time-points after the development of the TLC.

Using 220 mg of AG 50 W-X8 or a combination with additionally 120 mg of SCX provided a quantitative separation of ^{68}Ge from ^{68}Ga. Accordingly, radioactivity in the processed eluate started to increase immediately, indicating the radioactivity represented by ^{68}Ge. The count rate increased according to the secular characteristics of the ^{68}Ge/^{68}Ga radionuclide equilibrium. ^{68}Ge radioactivity was easily quantified within one hour, just letting ^{68}Ga grow for one (or a half) half-life of 67.7 min in the purified ^{68}Ge-fraction. Four mobile phases in accordance to Mirzadeh and Lambrecht [1] and the generally used 0.1M citric buffer were analyzed with regard to R_f-values of ^{68}Ge, ^{68}Ga and ^{68}Ga-DOTATOC. Four potential TLC-systems were identified, in which ^{68}Ge, ^{68}Ga and ^{68}Ga-DOTATOC show sufficiently different R_f values (Table.1).

While the radioactivity of ^{68}Ga and ^{68}Ga-DOTATOC spots decreased according to the ^{68}Ga decay, the ^{68}Ge spot showed an increasing count rate. Using the count rates and the absolute radioactivity for calibration of the imager, the breakthrough of ^{68}Ge can be quantified momentarily, i.e. already in the first hour after generator elution

Table 1: Investigated mobile phases for TLC separation of ^{68}Ga, ^{68}Ga, ^{68}Ga-DOTA-TOC and resulting R_f-values.

Mobile phase	R_f (Ga)	R_f (Ge)	R_f Ga-DOTATOC
0.1 M citric buffer	1	1	0.1 – 0.2
5% NaCl : MeOH : 25% NH_3 (3:1:1)	0	0.4 - 0.6	0.1 – 0.2
2 M HCl : acetone (1:1)	1	0	0.4
0.01 M $NaC_4H_5O_6$: MeOH (3:1)	0	0.4	0.1 – 0.2
Cyclohexanone : 2 M HCl (20:1)	0.4 - 0.5	0.1 – 0.2	0

^{68}Ge was quantitatively separated from ^{68}Ga using cation exchange columns AG 50 W-X8 and SCX, either separately or in combination. ^{68}Ge can be quantified directly within one hour after initial elution of the generator.

We successfully developed an instant method of measuring ^{68}Ge activity levels in a ^{68}Ge/^{68}Ga generator eluate and even in ^{68}Ga-radiopharmaceuticals without the need of γ-spectroscopy. All investigated TLC-systems are applicable for sufficient separation of ^{68}Ge from ^{68}Ga or ^{68}Ga-DOTA-TOC to quantify the amount of ^{68}Ge in an eluate within the first hour post elution.^{68}Ge levels of up to 10^{-4} are detectable. Thus, a new and fast method of measuring ^{68}Ge radioactivity levels in ^{68}Ge/^{68}Ga generator eluates without using γ-spectroscopy has been developed. With minor modifications, the same approach can be used to quantify the content of ^{68}Ge in ^{68}Ga-radiopharmaceutical preparations.

References

[1] Mirzadeh, S.; Lambrecht, R. M.; *J. Radioanal Nucl. Chem.* **1996**, *202*, 7-102