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Reduction of ^{68}Ge activity containing liquid waste from ^{68}Ga PET chemistry in nuclear medicine and radiopharmacy by solidification

Erik de Blois · Ho Sze Chan · Kamalika Roy · Eric P. Krenning · Wouter A. P. Breeman

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Abstract PET with ^{68}Ga from the TiO_2- or SnO_2- based ^{68}Ge/^{68}Ga generators is of increasing interest for PET imaging in nuclear medicine. In general, radionuclidic purity (^{68}Ge vs. ^{68}Ga activity) of the eluate of these generators varies between 0.01 and 0.001%. Liquid waste containing low amounts of ^{68}Ge activity is produced by eluting the ^{68}Ge/^{68}Ga generators and residues from PET chemistry. Since clearance level of ^{68}Ge activity in waste may not exceed 10 Bq/g, as stated by European Directive 96/29/EURATOM, our purpose was to reduce ^{68}Ge activity in solution from >10 kBq/g to <10 Bq/g; which implies the solution can be discarded as regular waste. Most efficient method to reduce the ^{68}Ge activity is by sorption of TiO_2 or Fe_2O_3 and subsequent centrifugation. The required 10 Bq per mL level of ^{68}Ge activity in waste was reached by Fe_2O_3 logarithmically, whereas with TiO_2 asymptotically. The procedure with Fe_2O_3 eliminates ≥90% of the ^{68}Ge activity per treatment. Eventually, to simplify the processing a recirculation system was used to investigate ^{68}Ge activity sorption on TiO_2, Fe_2O_3 or Zeolite. Zeolite was introduced for its high sorption at low pH, therefore ^{68}Ge activity containing waste could directly be used without further interventions. ^{68}Ge activity containing liquid waste at different HCl concentrations (0.05–1.0 M HCl), was recirculated at 1 mL/min. With Zeolite in the recirculation system, ^{68}Ge activity showed highest sorption.

E. de Blois · H. S. Chan · E. P. Krenning · W. A. P. Breeman (✉)
Department of Nuclear Medicine, Erasmus MC, 's Gravendijkwal 230, 3015 Rotterdam, The Netherlands
e-mail: w.a.p.breeman@erasmusmc.nl

K. Roy
Department of Chemistry, University of Calcutta, Kolkata, India

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Introduction

PET scintigraphy with ^{68}Ga-labelled peptides is of increasing interest in PET imaging in nuclear medicine [1–8] and performed at >40 centres in Europe (current situation, 2010). In general, radionuclidic purity (RNP) of the eluate of these generators varies between 0.01 and 0.001% (^{68}Ge vs. ^{68}Ga activity). Liquid waste containing low amounts of ^{68}Ge activity (further referred as ^{68}Ge waste) is produced by eluting the ^{68}Ge/^{68}Ga generators and residues from PET chemistry. For several reasons in our facility, solid ^{68}Ge containing waste ($t½ = 9$ months) is preferred over liquid waste. Since clearance level of ^{68}Ge activity in waste may not exceed 10 Bq/g, as stated by European Directive 96/29/EURATOM, our aim was to reduce ^{68}Ge activity in solution from >10 kBq/g to <10 Bq/g; which implies the solution can be discarded as regular waste. As an example: when a 1,110 MBq ^{68}Ge/^{68}Ga generator with a RNP of 0.005%, is eluted with 6 mL 1 M HCl, the eluate contains 55.5 kBq ^{68}Ge activity. Eluting a 1,110 MBq ^{68}Ge/^{68}Ga generator three times a day, 200 days per year, and for 1 year will result in 33.3 MBq in 3.6 L (9.25 kBq/g). Although national legislation within the EU may vary per country, the rules may only be more strict. For example in our country, The Netherlands, legislation does not allow to store radioactive waste with half-lives of more than 100 days at local institutes for more than 2 years. After 2 years it is obligatory to store the here described waste in a special external waste facility, and at additional costs. In this facility waste is preferably compressed, therefore, liquid content is limited to <1% (v/w). The purpose of this study was to quantify ^{68}Ge activity in our ^{68}Ge

liquid waste, and to concentrate and to transform ^{68}Ge liquid waste to solid waste. In short: $^{68}Ge_{liquid} \Rightarrow {}^{68}Ge_{solid}$, initially on a small scale. Liquid ^{68}Ge waste was transformed to ^{68}Ge solid waste by sorption of TiO_2, Fe_2O_3 (325 and 500 mesh, respectively, Sigma-Aldrich, Zwijndrecht, The Netherlands) and Zeolite ($Na_2Al_2Si_3O_{10}{\cdot}2H_2O$, Zeolyst international, Conshohocken, PA, USA). Elution of ^{68}Ge/Ga generator is performed with HCl, therefore ^{68}Ge waste is acidic. Zeolite was investigated because high sorption at low pH could be achieved (manuscript Kamalika Roy submitted).

Experimental

^{68}Ge-containing liquid waste

Fractionated elution of the generator revealed at the activity of ^{68}Ge (eg. Bq per mL) was constant during elution, whereas the main ^{68}Ga activity could be collected in a small volume (1 mL) [1]. Eluate from generators and left-over after ion-exchange prior radiolabelling is acidic and contain a certain amount of ^{68}Ge activity [4, 8]. Quantification of ^{68}Ge activity was performed in a well-type gamma counter as described earlier [1]. During 5 years of daily practice with $4TiO_2$- and $4SnO_2$-based ^{68}Ge/^{68}Ga generators (0.4–2 GBq per generator) the total amount of ^{68}Ge activity was 160 MBq in 48 L.

TiO_2 and Fe_2O_3 as sorbent

Sorption of ^{68}Ge activity on variable amounts of TiO_2 and Fe_2O_3 was investigated with 1 mL samples of ^{68}Ge waste as *f*[pH] (pH range 1–10) and time (range 1–24 h). These results were used for further up scaling. Typical example: 150 mL of ^{68}Ge waste was mixed with ±1.5 g of TiO_2 or Fe_2O_3 and centrifuged at 200×*g*. One mL of supernatant was taken as a sample and ^{68}Ge activity was quantified 24 h after sampling as described earlier [1].

Recirculation system

Eventually, to simplify the processing of $^{68}Ge_{liquid} \Rightarrow {}^{68}Ge_{solid}$ a recirculation system was used to investigate ^{68}Ge activity sorption (see Fig. 1) on TiO_2, Fe_2O_3 and Zeolite. Eluate of ^{68}Ge/Ga generator is acidic, therefore Zeolite was also investigated because high sorption at low pH could be achieved (Kamalika Roy manuscript submitted). ^{68}Ge waste at different HCl concentrations (0.05–1 M HCl), was recirculated at 1 mL/min and sorption of ^{68}Ge activity on TiO_2, Fe_2O_3 or Zeolite was monitored time-dependently. Recirculation system contained ±1 g of sorption material enclosed with cotton, glass fiber and filters of 35 and 0.45 µm.

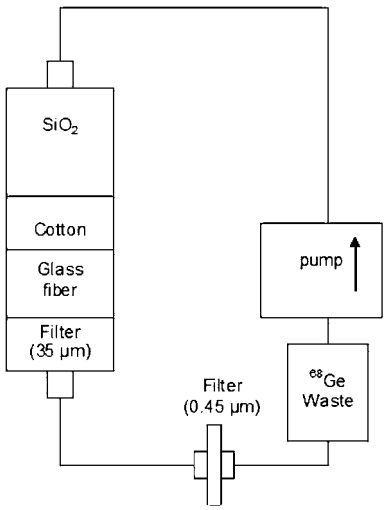

Fig. 1 Recirculation system containing ±1 g of TiO_2, Fe_2O_3 or Zeolite as sorption material enclosed with cotton, glass fiber and filters of 35 and 0.45 µm. ^{68}Ge activity containing waste was recirculated at a flow rate of ±1 mL/min. Samples of the circulating liquid were taken at indicated time points (see also Figs. 5, 6)

Results and discussion

Firstly, sorption on TiO_2, Fe_2O_3 was investigated time-dependently. Sorption of ^{68}Ge activity on TiO_2 (0.5 g/50 mL ^{68}Ge waste) was low (<20%) at pH <2 and high (>99%) at pH >6 (Fig. 2). Sorption of ^{68}Ge activity on Fe_2O_3 (0.5 g/50 mL ^{68}Ge waste), showed better result at pH 1–3 (>75% Fe_2O_3 and <25% TiO_2) and increased also as *f*[pH] up to >99% at pH 8. Optimal sorption was obtained at pH ≥5 (Fig. 2). Secondly sorption on TiO_2, Fe_2O_3 was investigated as *f*[mass] and additions of sorption

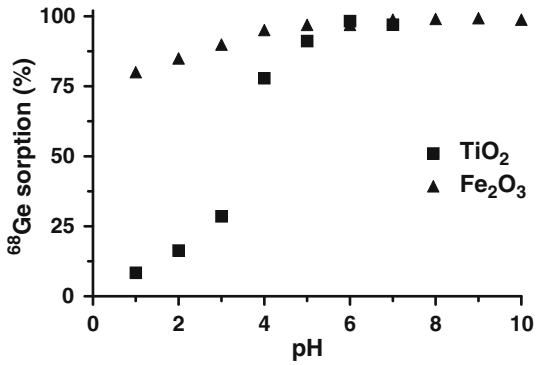

Fig. 2 Sorption of ^{68}Ge activity (10 kBq/g) on Fe_2O_3 or TiO_2 was investigated as *f*[pH]. After 24 h the samples were centrifuged. Supernatant was decanted and ^{68}Ge activity was quantified. Sorption of ^{68}Ge activity using TiO_2 or Fe_2O_3 was optimal at pH >8

material. Sorption of ^{68}Ge activity increased after each addition of sorption material. Moreover, Fe_2O_3 surprisingly continues to lower the ^{68}Ge activity logarithmically after each addition of Fe_2O_3, whereas with TiO_2 the value of 10 Bq ^{68}Ge per mL level was reached asymptotically. The procedure with Fe_2O_3 as sorption material reduces the ^{68}Ge activity by approximately 90% after each addition of sorption material (Fig. 3), eg. from >10 kBq/g to <10 Bq/g in six procedures. Low amounts (10 mg/mL) of sorbent showed similar ^{68}Ge activity sorption at later time points in comparison with an amount of 100 mg/mL (Fig. 4a, b).

Zeolite was introduced since this has high sorption at low pH, therefore it was tested as *f*(pH) (Fig. 5). With Zeolite in the recirculation system (Fig. 1), ^{68}Ge waste (0.05–1.0 M HCl) showed highest sorption (Figs. 6, 7). In our facility, eluate purification and concentration with anion chromatography with 5 M HCl is also applied [4]. The waste stream is thus very acidic, but Zeolite as sorption material showed similar results as with 1 M HCl (Fig. 7). Summarized, recirculation system, using Zeolite as sorbent, is more efficient, less time consuming and reduces ^{68}Ge waste mass in comparison with TiO_2 and Fe_2O_3 procedure. The overall ^{68}Ge containing liquid waste was 160 MBq in 48 L and could be concentrated to 160 MBq in <1 kg solid waste.

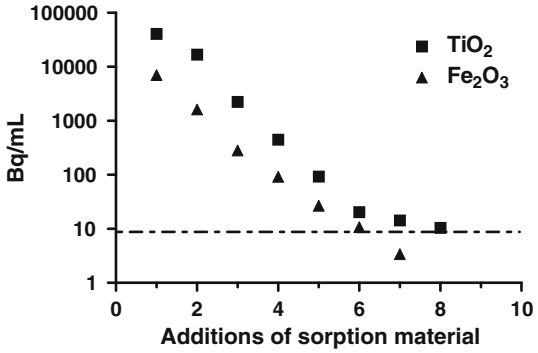

Fig. 3 Samples of ^{68}Ge/^{68}Ga generator eluate (50 mL) were used to investigate ^{68}Ge activity sorption on 0.5 g TiO_2 or 0.5 g Fe_2O_3. pH of the eluate was controlled by addition of phosphate buffer, final pH was ~8, and gently vortexed. Twenty-four hours after each addition, the 50 mL was centrifuged and a sample of the supernatant was collected to quantify ^{68}Ge activity

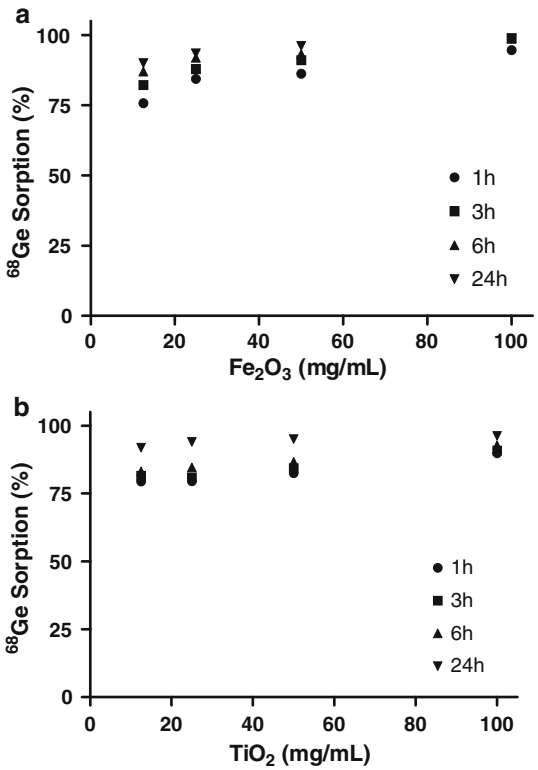

Fig. 4 Complexation of ^{68}Ge activity of ^{68}Ge containing liquid waste (pH 8) with Fe_2O_3 **(a)** or TiO_2 **(b)** as sorbent as function of time (1–24 h) and mass of sorbent (10–100 mg/mL)

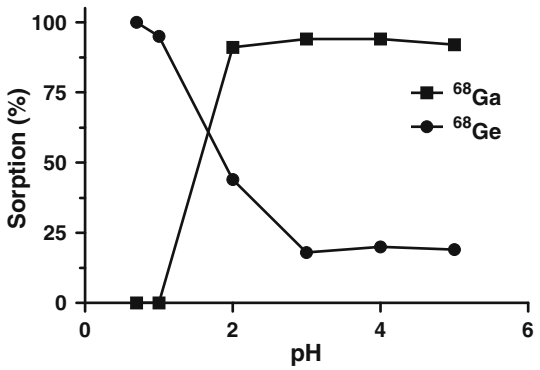

Fig. 5 Sorption of ^{68}Ge activity on Zeolite was investigated as *f*[pH]. After 24 h the samples were centrifuged. Supernatant was decanted and ^{68}Ge activity was quantified. Sorption of ^{68}Ge activity using Zeolite was optimal at pH <1

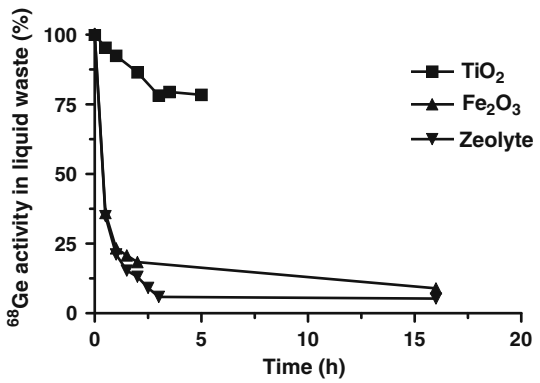

Fig. 6 Recirculation system with ^{68}Ge waste in 1 M HCl. One gram of sorption material was enclosed, see Fig. 1. ^{68}Ge activity was quantified at indicated time points. Zeolite showed optimal sorption of ^{68}Ge activity within 4 h (>95%)

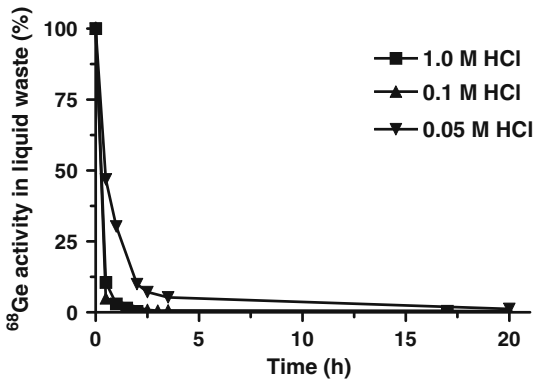

Fig. 7 Since Zeolite showed an optimal sorption of ^{68}Ge activity (Fig. 5), a column containing Zeolite (±1 g, Fig. 1) was tested with ^{68}Ge waste in 0.05, 0.1 or 1.0 M HCl. ^{68}Ge activity was quantified at indicated time points. Recirculation system using higher concentration of HCl showed high sorption of ^{68}Ge activity at earlier time points

Conclusion

TiO_2, Fe_2O_3 and Zeolite as sorbent, lower ^{68}Ge-containing liquid waste down to 10 Bq/g. Recirculation procedure using Zeolite as sorbent is preferred since less intervention with ^{68}Ge containing liquid waste has to be performed and solid waste mass is reduced.

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