

ENRICHED WATER-H₂¹⁸O PURIFICATION TO BE USED IN ROUTINE ¹⁸F⁻FDG PRODUCTION

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Abstract

Oxygen-18 enriched water has been recovered from IBA (Ion Beam Applications) recovery system followed by purification and then used in the production of ¹⁸F⁻. The purification process has been carried out by irradiation with UV followed by a distillation under vacuum. After purification, 95% of water is recovered and organic compounds, radioisotopes, trace metals and gases are eliminated efficiently. Results show that there are no significant differences in (2-deoxy-2-[¹⁸F]fluoro-D-glucose ([¹⁸F]FDG) production yield using purified water by the proposed method and new enriched water. Tritium was detected in the irradiated enriched water. Contamination precautions during purification should be considered. Tritium was not present in ¹⁸F⁻FDG or Na-¹⁸F final products.

1. INTRODUCTION

[¹⁸F]fluoride has become one of the most important isotopes and large quantities are being produced for the sake of diagnostics in nuclear medicine especially for ¹⁸F⁻FDG radiopharmaceutical production. Due to the high consumption of water-H₂¹⁸O in PET centers, the necessity to purify the enriched water from impurities in order to be used again in ¹⁸F⁻FDG production became a high priority. GMP guidelines require the use of well established and validated methods to purify and recycle the enriched water.

The organic impurities in irradiated enriched water make it impossible to irradiate the water twice by proton beam since if it is irradiated twice, high pressures are often encountered in the target. The presence of these impurities results in a very low ¹⁸F⁻FDG synthesis yield. Also this water will be contaminated by ions sputtered from the Havar target foil and target body [1-4]. Tritium is another radioactive by-product produced by the nuclear reaction ¹⁸O(p,t)¹⁶O [5].

Different methods have been used for the purification of recovered enriched water from FDG synthesis units. Ozonolysis has been used to remove organic contaminants from used enriched water [6]. UV, Ozone and solid-phase extraction methods were used also used as purification methods [7].

This work was undertaken for the evaluation of a combined UV and distillation under vacuum method for the purification of used water-H₂¹⁸O in ¹⁸F⁻ production in order to be reused in ¹⁸F⁻FDG production.

2. EXPERIMENTAL

The production of ¹⁸F⁻ was performed through ¹⁸O(p,n)¹⁸F reaction using 17.5 MeV proton beam energy and 97% enriched water H₂¹⁸O from ISOFLEX. The titanium target body has the volume of 2 ml and uses a 25 μm Havar window (from Goodfellow). The target is water cooled and the window is helium cooled there is no filter mounted between the target and the water recovery system. The bombardment beam current is fixed at 30 micro-amperes giving target pressure of 34 bars. The bombardment time is 90 minutes. The average activity of ¹⁸F⁻ under these conditions is

2565 ± 140 mCi at the End of Bombardment. Activities are measured using a calibrated Capintec CRC 15 dose calibrator.

^{18}F with enriched water H_2^{18}O is transferred to a separated recovery module. ^{18}F is trapped in the QMA cartridge (Waters) the enriched water is recovered to a separate vial and ^{18}F is eluted by 100 μl K_2CO_3 (Merck) then by 300 μl water to the first reactor of the ^{18}F FDG synthesizer. Figure 1 shows a schematic of the recovery process. ^{18}F FDG (2-deoxy-2- ^{18}F fluoro-D-glucose) is prepared based on nucleophilic substitution reaction, described in Ref. [8] using the automated module from IBA which is also shown in Figure 1.

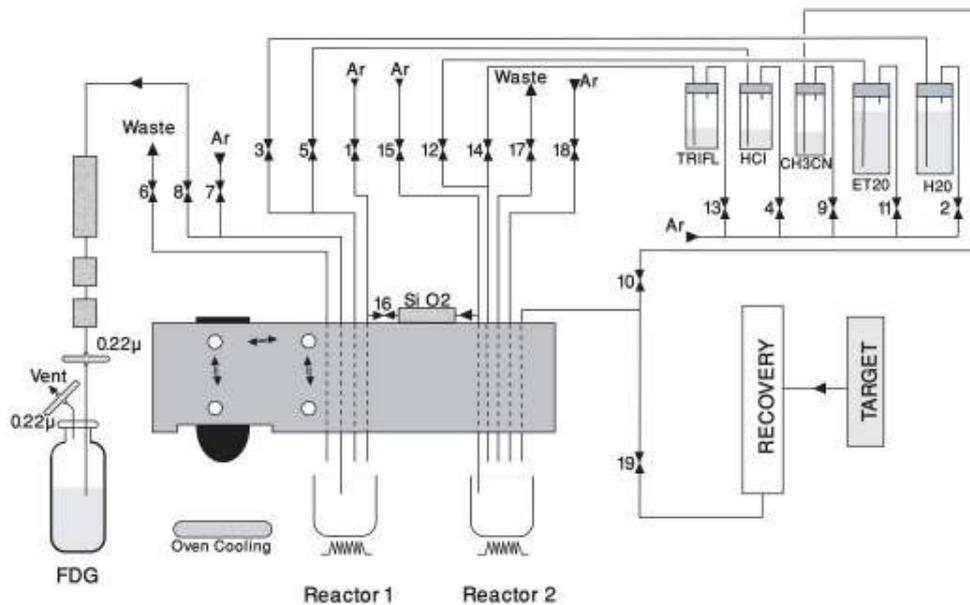


FIG. 1. Schematic representation of the experimental process used for ^{18}F FDG synthesis.

The purification of ^{18}O -water recovered from IBA- ^{18}F FDG synthesis system is performed in three steps:

- 1) Irradiation with UV.
- 2) Centrifuging if necessary.
- 3) Distillation in pre-evacuated atmosphere.

UV irradiation of recovered enriched water was performed by 705 UV digester system from Metrohm. This system is comprised of a wet part and a control unit. The wet part contains the UV high pressure mercury lamp, the cooling system and the sample holder for 12 quartz glass tubes each can contains 12ml. The PTFE stoppers act as cooling fingers and prevent atmospheric contamination. After UV treatment the enriched water was distilled in a pre-vacuum and closed system equipped with membrane vacuum pump.

Several types of analysis were performed in order to qualify the purified enriched water. The by-product radioisotopes were analyzed by gamma spectrometry using HPGe detector with 100 cm^3 and 25% efficiency where the amplifier output of the detector was processed 4096 channels MCA system. The detection of organic materials in the purified water was carried out using gas

chromatography from Shimadzu equipped with FID detector and capillary column, CBP20-M25-025 (25mx0.22mm), filled with polyethylene glycol. A programmed temperature from 50°C to 165°C and nitrogen gas carrier was used.

A developed Anodic Stripping voltammetry system from Metrohm (VA processor 693 with VA stand 694) is used for trace metals analysis. The determination of Tritium was performed using Liquid Scintillation Counter (LSC – Wallac Gardian, from Perkin Elmer). Samples of 500 micro liters of enriched water were mixed with 10 ml of Scintillation cocktail (Hi Safe 3) and beta ray measured and compared with standard water.

3. RESULTS AND DISCUSSION

Twenty six irradiations of the new enriched O-18 enriched water were performed.

Concentration of radioisotopes in the enriched water after irradiation:

Due to proton irradiation of the target body and target window, radioisotopes are formed. Ten radioisotopes have been detected in the recovered enriched water from the ¹⁸F¹⁸FDG synthesis system. The activities of these radioisotopes are shown in the Table 1. Table 1 also shows the activities of different radioisotopes measured in the QMA cartridge. From this table we can conclude that QMA retained from 25 to 90% of metallic radioisotopes depending on radioisotopes identity.

TABLE 1. ACTIVITIES OF THE RADIONUCLIDES DETECTED BEFORE AND AFTER PURIFICATION.

Isotope	T(1/2) hr	E(KeV)	Gamma(%)	Activity in the 2 ml enriched water before purification (Bq) ± Uncertainty	Activity measured in QMA (Bq) ± Uncertainty	Activity in the 2 ml enriched water after purification (Bq) ± Uncertainty
⁵⁷ Co	6522.48	122.06	85.6	52.0 ± 2	665.6 ± 7.9	0.2
⁵¹ Cr	664.87	320.08	9.8	-	1925 ± 111.7	0.1
⁹⁵ Tc	20	765.64	94.3	2.5 ± 1.5	39.7 ± 13.9	-
⁹⁶ Tc	104.4	778.1	100	-	18.8 ± 6.2	-
⁵⁸ Co	1698.72	810.67	99.4	53.2 ± 3.6	2773.6 ± 22.2	0.3
⁵⁴ Mn	7488	835	99.9	0.4 ± 0.8	20.2 ± 4.8	0.12
⁵⁶ Co	1850.88	846.7	99.92	14.0 ± 2	661.9 ± 11.9	0.16
⁵⁵ Co	17.54	931.2	75	11.5 ± 2.7	8914.4 ± 115.9	-
⁴⁸ V	383.4	983.4	100	0.4 ± 0.8	16.3 ± 5.7	-
⁵² Mn	136.8	1433.9	100	46.7 ± 2.4	1018.3 ± 31.5	-

The gamma ray spectrum of this water is shown in the Fig. 2.

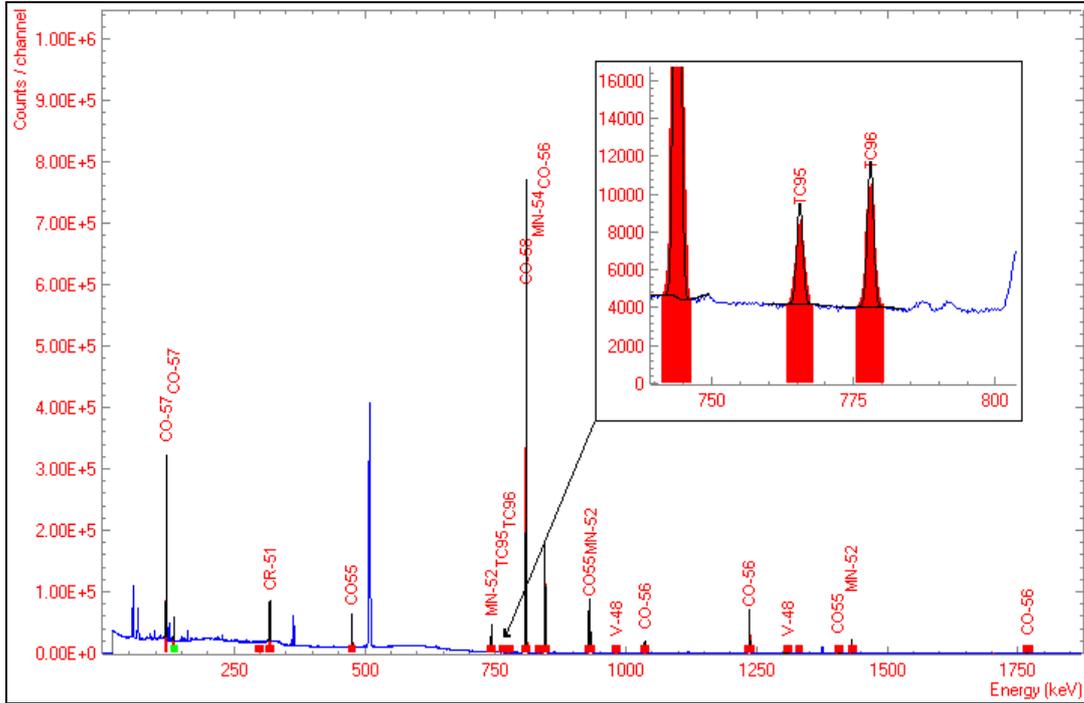


FIG. 2. γ -spectrum of recovered water from the recovery system, picks of ^{95}Tc and ^{96}Tc are shown in the separate spectrum.

The gamma ray spectrum of the QMA cartridge is shown in the Fig. 3.

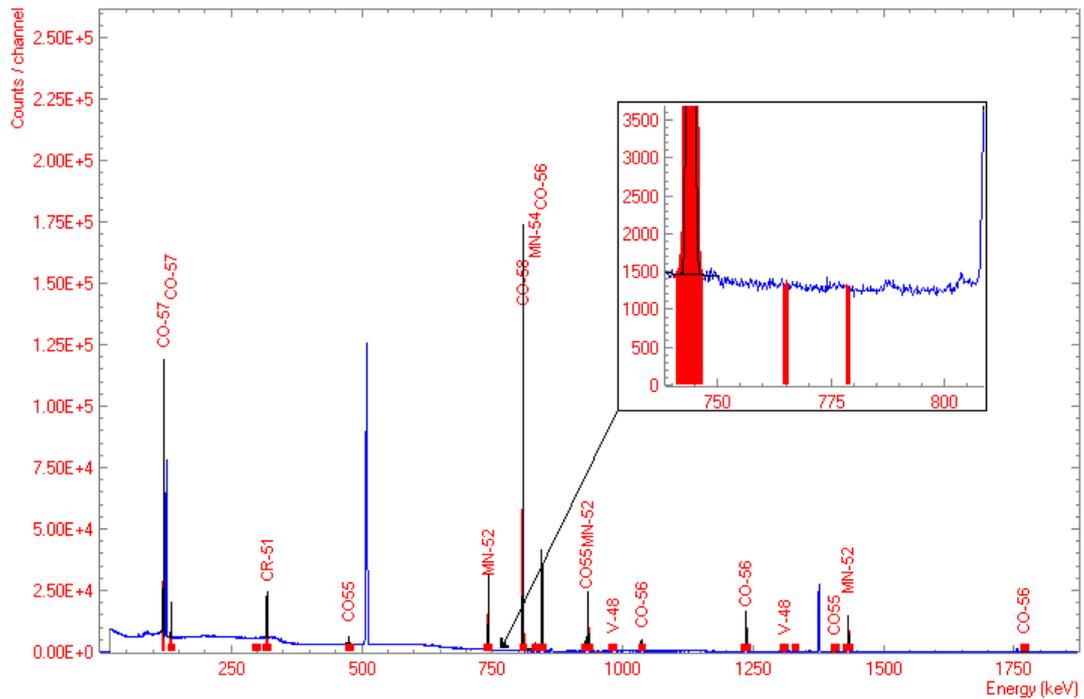


FIG. 3. γ -spectrum of the QMA cartridge.

Organic impurities in the enriched water before its purification:

Due to the fact that there is no contact between the organic solvent used in the FDG production module and the separate recovery system we do not detect any trace of MeOH, EtOH, Acetone and CH₃CN in the enriched water obtained from the recovery system as analyzed by gas chromatography. After every FDG production run the recovery module is washed with sterilized water and dried by pure Argon gas.

The only organic substances can be present in the used enriched water are from QMA cartridge.

Radioisotopes concentration in the enriched water after its purification:

Eight hours of UV irradiation have been found to be the optimum time to eliminate all organic compounds coming from QMA cartridge and wash-out process of the enriched water recovery module. An aliquot of 2 ml of the purified water has been counted by gamma spectrometry. The results from this analysis are contained in Table 1 reflecting the activities of different radioisotopes present in this water.

It can be concluded from these results that a very low traces of different radioisotopes are present in the purified enriched water giving the indication of an efficient method of purification.

In addition, produced ¹⁸FDG samples are analyzed by gamma spectrometry and found that no radionuclides coming from target body or target window were detected.

Trace metals can be present in the enriched water.

Analysis of stable trace metals, coming from the target and target window, in the recovered and purified enriched water had been carried out by Anodic Stripping Voltammetry using Metrohm 746 VA trace analyzer. The concentration of Ti in the enriched water was 2.7 mg/l ± 0.04 mg/l in the recovered water, whereas Co, and Cr concentration were below of detection limit. The concentrations of all these trace elements were below the detection limits in the purified enriched water. The detection limits of Ti, Cr and Co were 4, 0.3 and 0.4 µg/l respectively.

The presence of tritium in irradiated enriched water, with protons, has been detected. The different samples have been extracted from the process of ¹⁸FDG and ¹⁸FNa production. Table 2 shows results the Tritium activities of in different extracted samples.

TABLE 2. TRITIUM ACTIVITIES IN DIFFERENT SAMPLES

Sample	Activity of Tritium
purified irradiated enriched water	113 ± 2 (KBq/ml)
enriched water after irradiation and passing QMA	115 ± 2 (KBq/ml)
prepared FDG 5 days old	0.02 ± 0.01 (Bq/ml)
Prepared NaF 5 days old	0.04 ± 0.01 (Bq/ml)
Standard water	0.10 ± 0.03 (Bq/ml)

Due to the fact that radioactive properties of Tritium (beta emitter, T_{1/2}= 12.3 years) our method of distillation in a closed atmosphere offer the necessary precaution for the possible contamination during the open distillation used in many centers.

¹⁸FDG production yield using purified and fresh enriched water:

Eleven successive ¹⁸FDG production runs have been carried out using the recycled purified water and compared with 26 ¹⁸FDG production runs using the new enriched water. The mean radiochemical yield of ¹⁸FDG using purified enriched water was 59.72±4.17 while this yield was 58.84±8.38 using fresh new enriched water. This means that no significant differences in ¹⁸FDG production yield between using purified enriched water by the proposed method and using new enriched water. Figures 3 and 4 show the ¹⁸FDG production yields using purified enriched water and fresh enriched water.

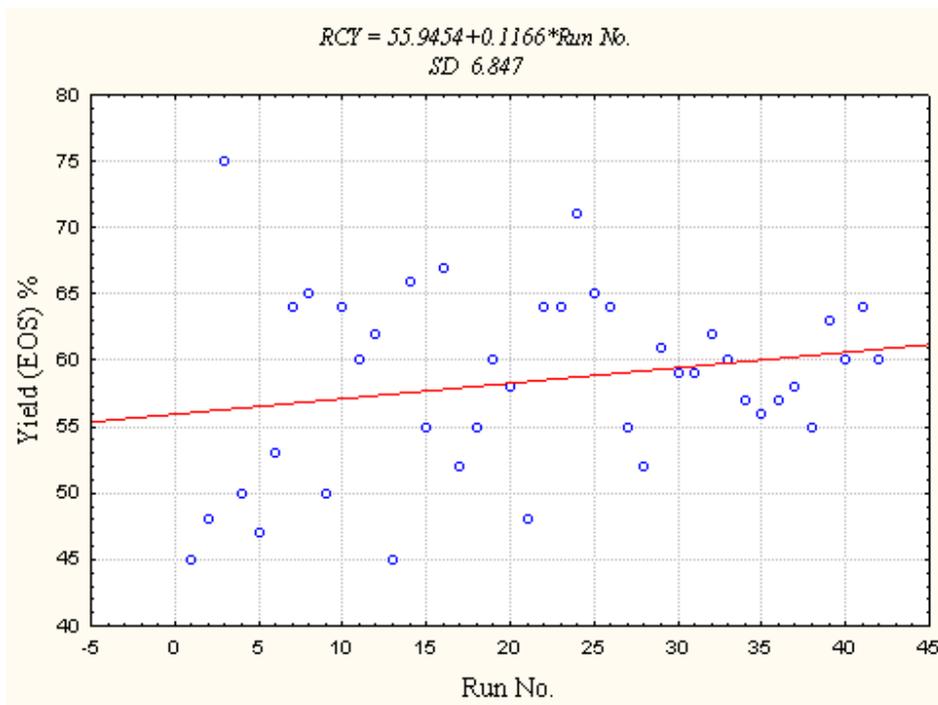


FIG. 4. ¹⁸FDG production yield using fresh new enriched water.

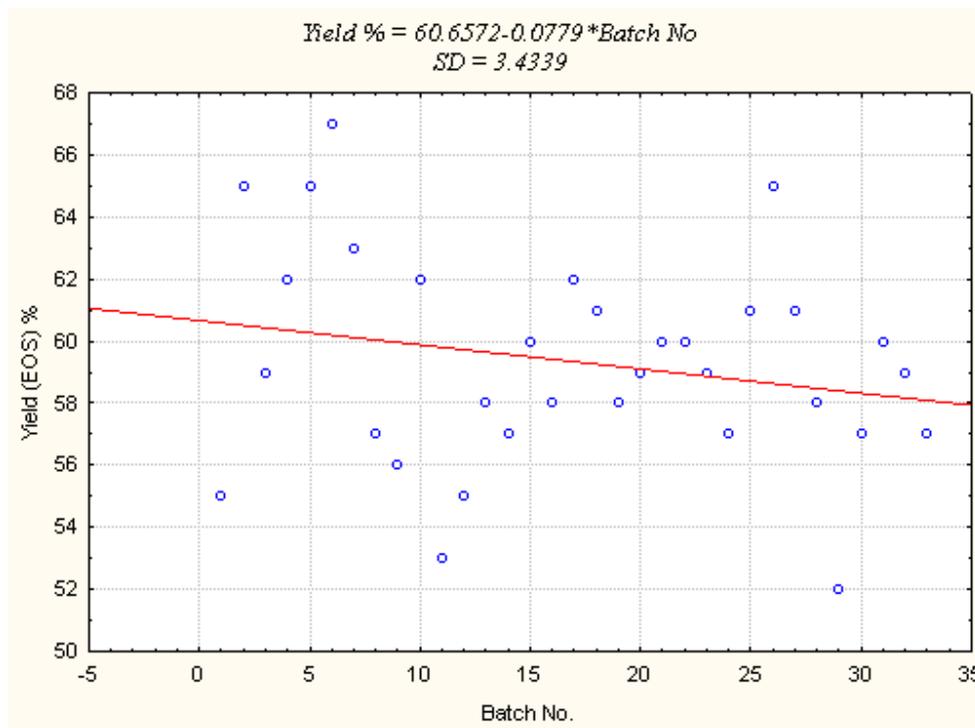


FIG. 5. ¹⁸F-FDG production yield using purified enriched water.

4. CONCLUSION

The proposed method of purification of the recovered enriched water from an FDG synthesis system show that at least 95% of water is recovered after the purification, organic compounds, radioisotopes, trace metals are eliminated efficiently. The results show that no significant differences in ¹⁸F-FDG production yield between using purified water by the proposed method and using new enriched water. The presence of tritium in the irradiated enriched water is detected. Our method of purification of the enriched recovered water by the sequence mentioned above offer the necessary precaution to avoid the contamination by Tritium. Tritium is not present in the produced ¹⁸F-FDG or Na-¹⁸F.

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