NUKLEONIKA 2002;47(1):13–18

ORIGINAL PAPER

Rapid production of ^{18}F fluoride from 2-fluoroaniline via the ^{19}F(n,2n)^{18}F reaction using 14 MeV neutrons

Renata Mikołajczak, Joanna Staniszewska, Stefan Mikołajewski, Edward Rurarz

Abstract No carrier-added ^{18}F fluoride was produced via the ^{19}F(n,2n)^{18}F reaction by 14 MeV neutron irradiation of 2-fluoroaniline and subsequent extraction of the produced ^{18}F fluoride ion with water. The fluoride was then purified by liquid chromatography on a Chromabond-NO_2 column. The time required for all chemical procedures was about 1 h. The average chemical separation yield was about 70%. The ^{18}F activity obtained after 3 hours of irradiation at a flux rate of 10^8 n cm^{-2}s^{-1} after a necessary 20-min delay was equal to several kBq per gram of fluorine in a 2-fluoroaniline sample, in accordance with the theoretically expected value. Improvement of the ^{18}F production yield can be achieved by increasing neutron fluxes. Neutron generators with 14 MeV neutron fluxes of the order of 10^{10} n cm^{-2}s^{-1} can produce tens MBq of ^{18}F, sufficient for whole-day work in biomedical applications. Our results show that 14 MeV neutron irradiation of 2-fluoroaniline is a low cost alternative for the production of this nuclide in the countries which do not posses either cyclotrons or electron linear accelerator facilities.

Key words chemical and production yields • fluorine-18 • 14 MeV neutrons • radiochemical separation • (n,2n) reaction cross section

R. Mikołajczak, J. Staniszewska
Radioisotope Centre POLATOM,
05-400 Otwock-Świerk, Poland

S. Mikołajewski, E. Rurarz✉
The Andrzej Soltan Institute for Nuclear Studies,
05-400 Otwock-Świerk, Poland,
Tel.: +48 22/ 718 0459, Fax: +48 22/ 779 3481,
e-mail: rurarz@india.ipj.gov.pl

Received: 4 June 2001, Accepted: 15 November 2001

Introduction

Radiopharmaceuticals labelled with positron emitter(s) (^{11}C, ^{13}N, ^{15}O and ^{18}F) have been recognised to play a major role in the development of Positron Emission Tomography (PET) as an *in vivo* modality in bio-medical research. The use of ^{11}C, ^{13}N and ^{15}O is particularly advantageous since these isotopes are naturally occurring elements in living systems. Thus labelling with these radioisotopes does not alter the metabolic course of naturally occurring organic matter. Various biomolecules (including simple alcohols, sugars, amino acids, steroids, alcaloids and host drugs) can be labelled with positron emitters without altering their bio-chemical and physiological activity. Since these radionuclides are short-lived, radiopharmaceuticals labelled with them cannot be manufactured commercially and have to be prepared on site for every individual patient separately.

Although ^{18}F is not a significant element in living organisms, its nuclear properties make its use in labelling of considerable value. Fluorine-18 decays almost exclusively (96.9%) by positron transition to the ground state of the stable daughter ^{18}O and in 3.1% by electron capture. It is an ideal tracer for PET due to its convenient half-life (it provides an ideal time frame for PET investigation) and low β^+ energy. Fluorine-18 is the longest-lived radionuclide of fluorine.

In addition to the PET application, ^{18}F is used in gamma-cameras for bone scanning scintigraphy for tracer studies

and diagnostic examinations. Fluorine-18 is an excellent bone imaging agent. It may be administered orally or intravenously, with about 50% of the administered dose localising in bone, and the remainder cleared rapidly by the kidneys. However the annihilation photons are far from ideal for a conventional gamma-camera which needs changes of its collimator for higher energies.

Fluorine-18 can be and has been produced by a variety of nuclear reactions using either nuclear reactors or charged particle accelerators (including electron accelerators). The nuclear reactions most commonly employed are: (1) $^{18}O(p,n)^{18}F$, (2) $^{20}Ne(d,\alpha)^{18}F$, and (3) $^{16}O(\alpha,xnyp)\ ^{18}F$, in view of their requirements for only a moderate projectile energy (reaction (1) and (2)) and a moderate beam currents to give a useful yield. Only reaction (3) demands higher energy machines ($E_\alpha \geq 40$ MeV). Fluorine-18 can also be produced by a two-stage nuclear reaction $^{6}Li(n,\alpha)t$ and $^{16}O(t,n)^{18}F$ by thermal neutron irradiation of Li-O targets (natural lithium or highly enriched in ^{6}Li) in a nuclear reactor. However cyclotron (reactor) is expensive to operate, and it will always be restricted to large scale production of positron emitters.

We focused our attention on low cost, rapid, simple and reliable production methods aided by improved targetry and processing procedures to produce no-carrier-added (NCA) fluorine-18 in amounts sufficient for experiments with small animals (rats, guinea pigs, monkeys, and dogs) or for investigations with humans. The lack of cyclotron facility and ^{18}O enriched water have encouraged us to search for an alternative method of ^{18}F production. An acceptable proposal is to produce ^{18}F from stable (monoisotopic) fluorine-19 via the $^{19}F(\gamma,n)^{18}F$ reaction by irradiation of fluoroorganic compounds. As a result of Szilard-Chalmers effect ^{18}F in an ionic form is obtained using a bremsstrahlung photon beam from a linear electron accelerator [5, 10, 11, 14]. As shown clearly in Refs. [10, 11], the most suitable compound for this purpose is 2-fluoroaniline ($C_6H_4NH_2F$). Fluorine-18 can also be generated by irradiation of 2-fluoroaniline with fast neutrons in the $^{19}F(n,2n)^{18}F$ reaction. Accelerators that can induce these reactions, such as electron accelerators or neutron generators, are common and thus easily accessible. We intend to obtain ^{18}F in the $^{19}F(n,2n)^{18}F$ reaction suggested by authors of Refs. [10, 11]. In the present work the separation method described in detail [11] was applied to separate ^{18}F from a 2-fluoroaniline target. Before its implementation the method was checked in a "cold" experiment in a similar way as already described [11].

Experimental

Preliminary information about the activities encountered in the activation of $C_6H_4NH_2F$ molecule by 14.4 MeV neutrons can be obtained from Table 1. The three predominant reactions in the neutron energy range of interest are (n,2n), (n,p) and (n,α), although for light elements such as C, N, F in the 2-fluoroaniline target other reactions with the emission of tritons (t) and helium-3 (τ) are also possible.

The radioactive nuclides produced in the (n,2n) reaction from F, C, N can be ^{18}F, $^{11,12}C$ and $^{13,14}N$. Among them ^{12}C and ^{14}N are stable nuclides, ^{11}C is not formed because the energy of bombarding neutrons is lower than the threshold energy of the $^{12}C(n,2n)^{11}C$ reaction, 18 MeV. Only ^{18}F and ^{13}N have favourable nuclear properties. The production of ^{13}N (for nearly equal abundance for ^{14}N and ^{19}F in a 2-fluoroaniline molecule) is 6 times lower than that of ^{18}F due to lower cross section (about 7 mb *vs.* 45 mb, respectively). In order to obtain the spectrum of pure ^{18}F, the β^+ activity of ^{13}N must fall to a negligible level.

A large number of B, C, and O radionuclides are induced by (n,p), (n,np), (n,pn) and (n,d) reactions. A few of them: $^{12,13}B$, ^{12}C, ^{19}O have very short half-lives and they decay during transportation of the target. Boron-11, carbon-13 and oxygen-18 are stable. Boron-12 is not formed in these reactions (see Table 1) because the energy of bombarding neutrons is lower than the threshold energies of the ^{13}C (n,pn) and ^{13}C(n,d) reactions i.e. 17.5 MeV and 15.3 MeV, respectively. Carbon-14 decays by soft β rays and due to its long half-life is formed with negligible activities.

The same applies to Be, B and N radioisotopes formed in (n,α) reactions, ^{9}Be and ^{11}B are stable, ^{12}B and ^{16}N have short half-lives, and the long lived ^{10}Be is practically absent. Therefore ^{18}F and ^{13}N are the only β^+ emitters present in the irradiated sample.

The 14.4 MeV neutrons [12] for our irradiations were produced in the $^{3}H(d,n)^{4}He$ reaction by bombarding thick tritium-titanium targets with a deuteron beam from a small Cockroft-Walton type accelerator of 100 kV, installed at Soltan Institute for Nuclear Studies at Świerk, Poland.

Two different types of neutron detectors were used in our experiment. The first one was a multisphere Bonner type neutron detector [2]. We also used a second detector (frequently used in neutron laboratories) in the form of copper

Table 1. Nuclear reaction energies Q (in MeV) and products (with their half-lives) of the 14 MeV neutron induced reactions of ^{19}F, $^{12,13}C$ and $^{14,15}N$ isotopes.

		$_{6}C$		$_{7}N$	
Reaction	$^{19}_{9}F$ 100%	$^{12}_{6}C$ 98.89%	$^{13}_{6}C$ 1.11%	$^{14}_{7}N$ 99.64%	$^{15}_{7}N$ 0.36%
(n,2n)	$^{18}_{9}F$ -10.4 109.7 min β^+ 96.9% EC 3.1%	$^{11}_{6}C$ -18.7 20.4 min β^+ 99.76% EC 0.24%	$^{12}_{6}C$ -4.45 stable	$^{13}_{7}N$ -10.6 9.96 min β^+ 100%	$^{14}_{7}N$ -10.8 stable
(n,p)	$^{19}_{8}O$ -4.0 26.9 s β^-	$^{12}_{5}B$ -12.6 0.02 s β^-	$^{13}_{5}B$ -12.7 0.017 s β^-	$^{14}_{6}C$ 0.6 5730 y β^-	$^{15}_{6}C$ -9.0 2.45 s β^-
(n,α)	$^{16}_{7}N$ -1.5 7.1 s β^-, γ	$^{9}_{4}Be$ -5.7 stable	$^{10}_{4}Be$ -3.8 16×106 y β^-	$^{11}_{5}B$ -0.2 stable	$^{12}_{5}B$ -7.5 0.02 s β^-, γ
(n,pn)	$^{18}_{8}O$ -8.0	$^{11}_{5}B$ -16.0	$^{12}_{5}B$ -17.5	$^{13}_{6}C$ -7.6	$^{14}_{6}C$ -10.2
(n,d)*	-5.0 stable	-13.8 stable	-15.3 0.02 s β^-, γ	-5.3 stable	-8.0 5730 y β^-

*Q(n,d) = Q(n,np) + 2.22 MeV

disc(s). The activity of ^{64}Cu ($T_{1/2}$ = 12.8 h) induced in the copper disc in the reaction $^{65}Cu(n,2n)^{64}Cu$ with a well known reaction cross section was used as a measure of the neutron flux. Because of its high threshold energy (9.9 MeV) this reaction is insensitive to low energy neutrons. The ^{64}Cu activity was identified and measured by detecting γ-rays of 1346 keV of known intensity (I_γ = 0.471% per decay) [4].

2-Fluoroaniline (2F-A) with chemical purity >98% as well as n-hexane (99%), K_2CO_3 (99%), KOH (>85%) were obtained from Merck (Germany), and the solid extraction phase Chromabond-NO_2 column from Macherey and Nagel (Germany).

We used a liquid target in the form of 2-fluoroaniline. Fluorine is a corrosive element, therefore a material inert to corrosion was used. Acetal (polyoxymethylene copolymer) was chosen because of its easiness in modelling and resistance to acids, fluorine and most organic solvents. Two irradiation chambers were made from this material and used in our experiments. One of them is shown in Fig. 1. The target chamber consisted of an acetal plate containing a cylindrical recess 5 mm deep and 40 mm in diameter. About 6 cm^3 of 2-fluoroaniline was retained in the target chamber by a 1 mm thick window. Copper monitor foils 44 mm in diameter and 1 mm thick (13.3 g) were attached to a 26.5 mm thick back surface of the target cell. Chemical purity of cooper was over 99.9%. A hole in the base of the target chamber led to a solution withdrawal port and a hole in the top led to a small funnel for filling the target cell.

The complete target chamber was attached to the end of a neutron generator beam tube by a transparent glued tape so it could easily be removed from the irradiation position and transferred to a shielding container for transportation to the radiochemical laboratory. Prior to irradiation, the target cell was thoroughly cleaned and flushed with twice distilled H_2O, ethyl alcohol and then stoppered. The target chamber is then filled with ~5 cm^3 2F-A.

Both samples (2F-A and Cu) were placed behind each other in a stack-like arrangement along the deuteron beam axis (Fig. 1), and were irradiated by the same incident flux. The loss of neutrons and their energy change in the samples were negligible.

After passing through a 3.4 cm diameter aperture formed by a system of collimators, a continuous, stable and homogeneous 100 keV deuteron beam bombarded a water-cooled ^3H-Ti target on a copper backing mounted in a thin-wall target chamber made of copper.

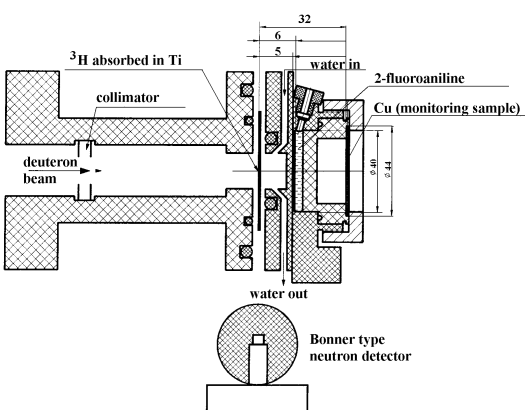

Fig. 1. Schematic diagram of the experimental arrangement. The 14.4 MeV neutrons beam passes through the 2-fluoroaniline sample and then through the monitoring cooper sample.

The 2-fluoroaniline chamber was placed at the back face of the tritium target chamber (the shortest possible distance). The distance from the surface of the ^3H-Ti target to 2F-A sample was 6 mm; and that to the Cu sample was 32 mm. The solid angles subtended by the circular samples (40 mm in diameter for 2F-A and 44 mm for copper) viewing a thin circular neutron source were calculated using the tables in Ref. [7].

The overall weighted average of neutron energy was 14.4±0.2 MeV, given by the dimensions of the samples and by the fact that the layer of tritium targets in our experiments was thick enough to stop completely the deuterons from the accelerator.

In the calculations of neutron fluxes from the ^{64}Cu activ-ities, the cross section value for the $^{65}Cu(n,2n)^{64}Cu$ reaction at 14.4 MeV neutron energy was taken as 968 mb (the same as that at 14.5 MeV within experimental error) from Refs. [3] and [6]. Prolonged irradiation of the ^3H-Ti target by the deuteron beam can produce a ^2H target through implantation of deuterium into titanium. Parasitic neutrons ($E_n \approx 3$ MeV) produced in the subsequent $^2H(d,n)^3He$ reaction, however, cannot induce ^{64}Cu activity because the threshold of the $^{65}Cu(n,2n)$ reaction is 9.9 MeV. The process of radioactive capture at 14 MeV neutron energy on the 69.17% abundant ^{63}Cu leads to ^{64}Cu activity with a cross section of 2.6 mb [9]. The error in neutron flux calculations involved by this process lies in the error range of a standard cross section for the $^{65}Cu(n,2n)^{64}Cu$ reaction, and may be ignored. To induce the ^{18}F activity ($T_{1/2}$ = 1.83 h) the duration of bombardment of 2F-A samples was kept for 1, 1.83 and 3 h.

The activities of the radionuclides produced in the individual targets as well as ^{18}F fractions chemically separated from 2F-A were measured by gamma-ray spectroscopy. The 511 keV annihilation gamma quanta from the liquid 2-fluoroaniline samples were measured at the Metrological Laboratory of Radioactive Materials (MLRM) of the Radioisotope Centre POLATOM at Świerk. The gamma-ray spectra were registered with a high purity germanium (HPGe) detector (Canberra GC 1520, 72 cm^3 volume, 1.8 keV energy resolution for 1332 keV), connected to a ND-76 (Nuclear Data) computerised spectrometric system. The data were processed using the ASAP program on a personal computer.

All separated and non-separated liquid samples of 2F-A were measured in glass vials. The thickness of these vials was carefully selected (taking into account the maximum energy of positrons emitted from ^{18}F). It was sufficient to stop more than 99% of the emitted positrons in the samples. Positrons thermalize very quickly in solids, within a few picoseconds. Thus, the 511 keV peak in the gamma-ray spectra was used for determination of positron intensity.

For measurement of 2F-A radioactive samples it was desirable to calibrate the germanium detector with calibrated liquid samples in glass vials (penicilline vials). All radionuclide solutions used, 5 cm^3 in volume were supplied, in glass vials.

The gamma-ray spectra from the monitoring copper foil were obtained with a 177 cm^3 HPGe detector (Ortec, model GMX with berylium window), connected via a linear amplifier (Tennelec TC245) to a 4096 channel analyzer. The calibration for the absolute energy and efficiency (in the low-energy region below 2 MeV) of both spectrometric systems were carried out by using standard calibration sources and a mixed radionuclide gamma-ray reference source (Du Pont Company).

Chemical separation of fluorine-18 from 2-fluoroaniline

As reported previously [10, 11] and verified in our laboratory, the chemical technique for $^{18}F^-$ separation from bulk liquid 2-fluoroaniline targets was completely satisfactory. In the present work the solvent extraction separation procedure was applied. The irradiated target was shaken with water (4 cm^3) to extract fluorine ions into the water phase. Separation of phases was made in a centrifuge (1 min at 500 g) and the aqueous extract containing $^{18}F^-$ was washed with of n-hexane (1 cm^3). The water phase was then purified by liquid chromatography on a chromabond-NO_2 column. The column was previously conditioned using 0.5 M HCl (1 cm^3), followed by water, until the pH of the eluate reached a value between 5 and 6. After putting the fluorine extract on the top of the column, the following eluents were used subsequently 20 cm^3 water, 20 cm^3 50 mM K_2CO_3 solution and 20 cm^3 50 mM KOH at a flow rate of about 2 cm^3 min^{-1}. The eluent fractions of 10 cm^3 each were collected and their radioactivity measured using a germanium detector. The main peak of fluorine-18 ion was found in the fraction 4 to 6 (most of the activity collected in the fraction 5 with the separation yield of 69±3%. Our experimental separation yields were by a few percent lower than those reported by Psarros and Weber [11]. It should be noted that the chemical procedure is simple, rapid and may be readily adapted to the remote operation.

Results

Calculation of the $^{19}F(n,2n)^{18}F$ reaction cross section at 14.4 MeV neutron energy

The cross section for the $^{19}F(n,2n)^{18}F$ reaction induced by 14.4 MeV neutrons was calculated using a re-arranged activation formula, and served as a proof of our experimental method. After moving the irradiation chamber with radioactive 2-fluoroaniline from the neutron generator and pouring the solution into a glass vial for an initial non-destructive γ-ray spectrometric measurement of 10 min duration, a chemical separation was made. A typical γ-spectrum of the radioactive 2-fluoroaniline with a strong 511 keV peak is shown in Fig. 2. The γ-ray spectrum shows that the irradiated sample does not contain any other radionuclides than positron emitters, which are detected via the annihilation radiation. As mentioned earlier, ^{13}N ($T_{1/2}$=10 min) was the only contaminant activity that had to be taken into account.

If a mixture of two independently decaying species, e.g. ^{13}N and ^{18}F, is viewed by a suitable radiation detector, the resulting decay data obtained within a short time will be the sum of the effects of the two separate activities A = A(^{13}N)+A(^{18}F). Thus, if the 511 keV annihilation γ-ray was used for activity determination, ^{13}N contaminant activity had to be quantitatively determined. That was done by measuring the decay of the 511 keV peak activity in the spectra for more than 7 hours.

Figure 3 shows the decay curve of an irradiated 2-fluoroaniline sample. The two lines shown in Fig. 3 correspond to the two components in the sample. The analysis yields the half-life values of 10 min and 110 min for ^{13}N and ^{18}F, respectively, in accordance with our expectations.

The analysis shown in Fig. 3 yields the values of activities at the end of bombarding (EOB) and as a function of time. From two independent measurements we estimated the ratio of ^{13}N to ^{18}F activities to be 18% at EOB. Due to the short half-life of 10 min, the ^{13}N contamination quickly decreases with time. Since our measurements of 511 keV gamma quanta started at 17, 19 and 22 min after EOB the percentage value of ^{13}N contamination were equal to 6, 5.4 and 4.5% respectively. After subtracting this contaminant activity, the cross section value of the $^{19}F(n,2n)^{18}F$ reaction was estimated to be 42 mb, the mean value from three measurements equal to 43, 43 and 41 mb. Uncertainties in the cross section values result from various sources. The dominant sources are gamma-ray detector efficiency, photopeak counting statistics, the neutron flux and the self-absorption of gamma-rays in the sample. Other uncertain-

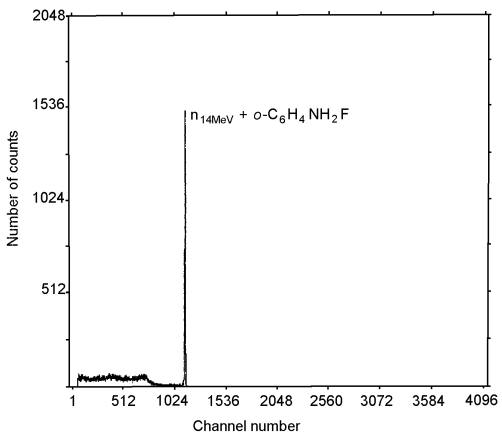

Fig. 2. The gamma-ray spectrum (taken with HPGe detector Canberra GC 1520) produced by the 2-fluoroaniline sample of 8.55 g irradiated with 14.4 MeV neutrons for 1 h. Total neutron output 5.9×10^{11} (n/4π/1h), transport time 17 min, measuring time 10 min.

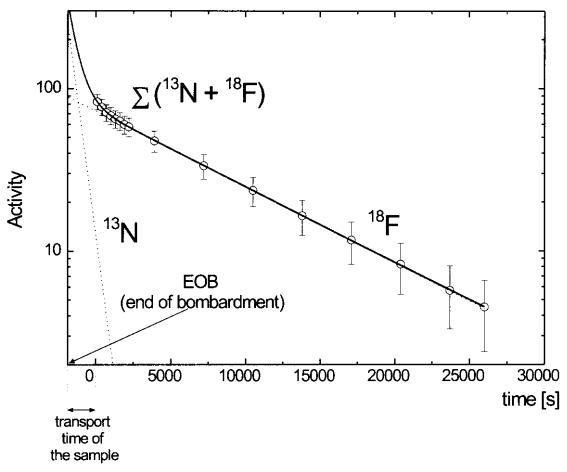

Fig. 3. A two-component 511 keV peak measured from a 14.4 MeV neutron irradiated 2-fluoroaniline sample.

Table 2. ^{18}F activities produced with a low intensity neutron generator in the present work.

	Irradiation chamber		
	First	Second	
Mass of fluorine in the 2F-A sample (g)	1.46	1.11	0.73
Irradiation time t_i (hours)	1	1.83	3
Delay time t_d (min)	17	19	22
Time of measurements (min)	10	10	10
Total neutron flux ($\Phi_{4\pi}$)	5.9×10^{11} n/1 h	2×10^{12} n/1.83 h	4×10^{12} n/3 h
Neutrons per seconds (ns^{-1})	1.6×10^{8}	3×10^{8}	3.9×10^{8}
Neutrons per second per cm^{-2} of the sample (n $cm^{-2}s^{-1}$)	2.5×10^{7}	1.75×10^{8}	3.7×10^{8}
^{18}F activity from 2F-A sample (kBq)	0.48	2.5	4.4
^{18}F activity normalized to 1 g of the fluorine sample (kBq)	0.28	2.3	6
Reaction cross section (mb)	43	43	41
Calculated ^{18}F activity under our conditions using the above cross section and delay time t_d = 20 min (kBq)	0.4	2.9	6.1
Ratio of the experimentally measured ^{18}F activity to the calculated one (%)	70	77	98

ties such as the sample weight and irradiation-, cooling- and measuring-times are very low. The resulting total uncertainty in the cross sections reported here is between 8 and 10%. We have accepted the value of ±10%.

The ^{19}F(n,2n)^{18}F reaction has already been investigated. Many years ago attempts were made [1] to describe the compiled experimental values by evaluated excitation functions from the threshold of up to 28 MeV. Recently, similar evaluation has been made [1]. Our experimental value of the ^{19}F(n,2n)^{18}F reaction cross section measured at 14.4 MeV is shown in Fig. 4, together with the evaluated excitation functions. The cross section is in agreement with both excitation functions. As mentioned earlier, an extended circular cylindrical cell with 2-fluoroaniline was irradiated with neutrons from an extended neutron source (effective area of tritium target) in the angles range of 0–73°, so that neutrons were incident at the sample with energies of 14.2–14.6 MeV. We accepted the mean value of the neutrons energy as 14.4 MeV, with the error ±0.2 MeV. The good agreement of our (n,2n) cross section values with the literature data [1, 13] is a good proof that our experimental method and data evaluation are correct.

Production rates of ^{18}F

The 100 keV deuteron beam from the small cascade accelerator at Świerk with the energy below that of resonance in the (d,t) reaction (109 keV) with additional deuteron energy loss in the oxidised surface of the tritium-titanium target cannot warrant high 14 MeV neutron fluxes and therefore high production yield of ^{18}F. The advantage of this procedure is the fact that the time required for all chemical procedures is about one hour, and due to low activities we did not need the hot cells. For such purposes, two irradiation chambers for liquid 2F-A samples were used. In the first one (the prototype) the distance between the tritium target and the 2F-A sample (placed on the axis of the deuteron beam) was 18 mm to assure good irradiation geometry for the cross section determination of the ^{19}F(n,2n)^{18}F reaction. Consequently, the neutron fluxes at the sample were low ($10^7 n^{-2}s^{-1}$) and the yields were disappointing.

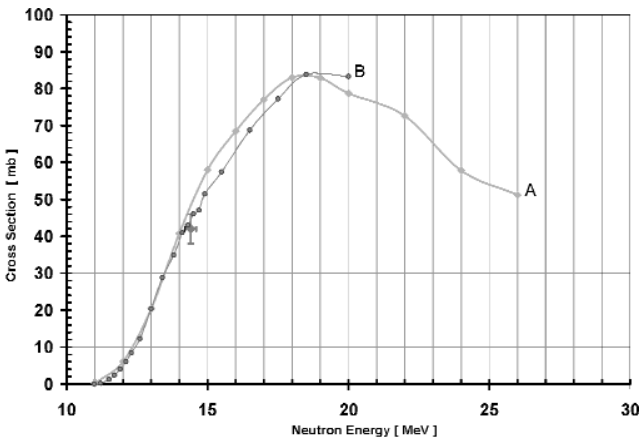

Fig. 4. The experimental cross section for the ^{19}F(n,2n)^{18}F reaction induced by 14.4±0.2 MeV neutrons (the point), compared with two evaluations [1, 13]. Curve A: Ref. [1], curve B: Ref. [13]. The solid lines are eye guided.

The most convenient way for increasing the yield would be to increase the time of irradiation and put the 2F-A sample closer to the neutron source (tritium target). After initial tests, which verified the chemical separation procedure and irradiation conditions, a new irradiation chamber (also placed on the axis of the deuteron beam, Fig. 1) was installed and the irradiation times were increased (1.83 h and 3 h). The conditions of operation and the ^{18}F yield from these two-irradiation chambers are summarised in Table 2. It may clearly be seen from this Table that our small cascade accelerator delivers up to 10^7–10^8 n $cm^{-2}s^{-1}$. By utilising low neutron fluxes and a small 2-fluoroaniline sample, small amounts of ^{18}F can be obtained. We have made a direct comparison of the experimental yields of ^{18}F with the theoretically calculated values (Table 2). In practice, the experimental yields are invariably lower than those calculated.

Our yield (corrected for the cooling time necessary for the ^{13}N activity to decay) represents 70% of the theoretical value in the first measurement. A similar percentage was estimated for the results obtained in the second experiment for nearly two hours of irradiation with an improved irradiation chamber. In the third experiment, the experimentally measured yield agrees quite well with the calculated value.

The low cross section of 42 mb for the ^{19}F(n,2n)^{18}F reaction is in fact disadvantageous for the production of radioactivity needed in routine applications of ^{18}F but this problem can be overcome by irradiating larger amounts of 2F-A, by placing the probes closer to the tritium target of the neutron generator, by increasing the irradiation time,

Table 3. Calculated ^{18}F activities which could be produced with commercial (pumped) or sealed tube and intense neutron generators [8] from 1 g of fluorine in a 2-fluoroaniline sample (with the delay time of 20 minutes, necessary to allow any short-lived contaminating species to decay).

Duration of irradiation (hours)	Type of neutron generator and expected activities	
	Commercial or sealed tube neutron generator 10^9 n cm^{-2}s^1	Intense neutron generator 10^{10} n cm^{-2}s^{-1}
1	2.1×10^6 Bq 58 μCi 4×10^5 Bq/cm^3	21.5×10^6 Bq 580 μCi 4×10^5 Bq/cm^3
1.83	3.4×10^6 Bq 92.3 μCi 6.8×10^5 Bq/cm^3*	3.4×10^6 Bq 923 μCi 6.8×10^6 Bq/cm^3
3	4.6×10^6 Bq 125 μCi 9.2×10^5 Bq/cm^3	4.6×10^7 Bq 1.25 mCi 9.2×10^6 Bq/cm
5.5	6×10^6 Bq 162 μCi 1.2×10^6 Bq/cm^3	6×10^7 Bq 1.62 mCi 1.2×10^7 Bq/cm^3

*A similar experimental value was published [10] for 14 MeV neutron fluxes of 10^9 n cm^{-2}s^{-1}.

and by increasing the neutron flux. Because of the interest in the production of larger quantities of ^{18}F, the data obtained in the present work have been used to predict the amount of activity that can be expected from high intensity neutron generators under various conditions. These data are presented in Table 3.

Conclusion

We have determined the production yields of ^{18}F using a low intensity 14 MeV neutron generator. Our results, however, proved to be disappointing. In order to obtain higher quantities of ^{18}F some improvement can be made: (1) by increasing the mass of 2-fluoroaniline; (2) by decreasing the distance between the irradiated sample and neutron source; (3) by increasing the time of irradiation; and (4) by increasing the neutron flux rate to its maximum possible value. The results show that 14 MeV neutron irradiation of 2F-A and subsequent extraction with water and chromatographic purification of the [^{18}F] fluoride produced is a convenient alternative for the production of this nuclide, sufficient for whole day work in different biomedical applications. That can be of particular interest for groups which have no access either to cyclotron or electron linear accelerator facilities.

Acknowledgments The authors wish to thank Professor Marian Jaskóła, the former director of the Soltan Institute for Nuclear Studies at Świerk for his friendship, continuous interest, financial support and help when it was needed. The authors also wish to thank Dr Kazimierz Nowak, the former Director of the Radioisotope Centre at Świerk, for his kindness and consent to collaboration with their chemists. We express our thanks to Mr Eng. Jerzy Olszewski for making drawings of both irradiation chambers and the mechanical workshop of the Radioisotope Centre POLATOM for their execution. The authors wish to thank Mrs Ewa Kołakowska for her help in the measurements with the Ge(Li) detector of the activities during chemical procedures. We are much indebted to Dr Tomasz Ludziejewski for his invaluable help in the resolution of radioactive decay curves of 2-fluoroaniline samples with a computer program. Finally we wish to address our special words of thanks to Mr Jan Piętka for operation of the cascade accelerator and his tireless efforts and assistance during the irradiation.

References

1. Baosheng Yu, Hlavac S, Csikai J (1999) 1-st Draft international references data library of Neutron Activation Cross Sections. IAEA, Vienna
2. Bramblett RI, Ewing RI, Bonner TW (1960) A new type of neutron spectrometer. Nucl Instrum Meth 9:1–12
3. Bychkov YM, Manokhin VN, Pashchenko AB, Plashkin YI (1982) Handbook of cross sections for neutron induced threshold reactions. Energoizdat, Moscow (in Russian)
4. Christmas P, Judge SM, Ryves TB, Smith D, Winkler G (1983) The decay scheme of ^{64}Cu. Nucl Instrum Meth 215:397–408
5. Donnerhak A, Sattler EL (1980) The preparation of fluorine-18 with an electron linear accelerator for applications in medical and biological investigations. Appl Radiat Isot 31:279–285
6. Handbook on nuclear activation data (1987) Technical Report Series vol. 273. IAEA, Vienna
7. Konijn J, Tolander B (1963) Solid angle computations for a circular radiator and a circular detector AE-101. Aktiebolaget Atomenergi, Studsvik
8. Manual for troubleshooting and upgrading of neutron generators (1996) IAEA-TECDOC-913. IAEA, Vienna
9. Marion JB, Fowler JL (Eds.) (1963) Fast neutron physics. Pt. II. Interscience Publishers, New York
10. Psarros N, Duschner H (1988) Production and use of carrier free ^{18}F in studies of the effect of trace amounts of fluoride on the metabolism of the oral cariogenic bacterium *Streptococcus mutans*. J Radioanal Nucl Chem 122:327–331
11. Psarros N, Weber R (1995) Rapid production of no-carrier-added $^{18}F^-$ from 2-fluoroaniline via the $^{19}F(\gamma,n)^{18}F$ reaction using a hospital electron linear accelerator. Appl Radiat Isot 46:123–124
12. Seagrave JD, Graves EP, Higwood JS, McDole CJ (1958) $D(d,n)^3He$ and $T(d,n)^4He$ Neutron source handbook LAMS-2162. Los Alamos National Laboratory
13. Wagner M (1991) Update of the evaluation of the cross sections for the neutron dosimetry reactions $^{19}F(n,2n)^{18}F$ and $^{93}Nb(n,2n)^{92m}Nb$. Report INDC (Aus)-014. IAEA, Vienna
14. Yagi M, Amano R (1980) Production of ^{18}F by means of photonuclear reactions and preparation of anhydrous $H^{18}F$. Appl Radiat Isot 31:559–561