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# Evaluation of excitation functions of proton, $^{3}$He- and α-particle induced reactions for production of the medically interesting positron-emitter bromine-76

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ABSTRACT

Cross section data for production of the medically interesting radionuclide $^{76}$Br ($T_{1/2}$=16.2 h) via the proton induced reactions on $^{76}$Se, $^{77}$Se, $^{78}$Se and $^{79}$Br, and $^{3}$He- and α-particle induced reactions on $^{75}$As were evaluated. The nuclear model codes STAPRE, EMPIRE and TALYS were used to check the consistency in the experimental data and a statistical procedure was applied to derive the recommended excitation functions. A comparison of various production routes of $^{76}$Br (and of $^{75}$Br) is presented.



## 1. Introduction

Positron emission tomography (PET) is one of the most modern and progressive non-invasive diagnostic techniques used in nuclear medicine. Standard PET studies utilize the so-called organic positron emitters, i.e. $^{11}$C ($T_{1/2}$=20.3 min), $^{13}$N ($T_{1/2}$=10 min), $^{15}$O ($T_{1/2}$=2 min) and $^{18}$F ($T_{1/2}$=110 min). The first three radionuclides are short-lived and have to be produced in the close vicinity of the medical center (cf. Stöcklin et al., 1995). The radionuclide $^{18}$F is somewhat longer lived and can be transported to PET centers a few hundred kilometers away from the production site. The ongoing development in the field of diagnostic imaging requires longer lived positron emitters for study of slow metabolic processes. These radionuclides could also be of advantage in quantification of single photon emission computed tomography (SPECT) radiopharmaceuticals and pre-therapy dose assessments using positron emitting homologs of pure β$^-$-emitting therapeutic radionuclides (cf. Qaim, 2008; Nayak and Brechbiel, 2009). Some of the prominent non-standard positron emitters are $^{55}$Co ($T_{1/2}$=17.5 h), $^{64}$Cu ($T_{1/2}$=12.7 h), $^{73}$Se ($T_{1/2}$=7.1 h), $^{76}$Br ($T_{1/2}$=16.2 h), $^{86}$Y ($T_{1/2}$=14.7 h) and $^{124}$I ($T_{1/2}$=4.18 d). Some aspects related to the production and application of those radionuclides were discussed in a recent workshop [see special issue of the Quarterly Journal of Nuclear Medicine and Molecular Imaging 52 (No. 2), 101–206 (2008)].

The radiohalogens have been extensively used in nuclear medicine for both therapeutic and diagnostic applications (cf. Stöcklin, 1977; Adam and Wilbur, 2005). Due to the strong C–Br chemical bonding, higher lipophilicity of bromine as compared to iodine and non-accumulation of bromine in the thyroid, radiobromines have been finding considerable interest in medical application (cf. Coenen et al., 1983; Mazière and Loćh, 1986; Mazière et al., 1992). The radionuclides $^{75}$Br ($T_{1/2}$=1.6 h) and $^{77}$Br ($T_{1/2}$=57.04 h) were used till mid 1980s in PET and SPECT studies, respectively. However, due to the relatively high doses, the interest in both the radionuclides decreased. In more recent years, $^{77}$Br has become a potentially important radionuclide for Auger electron therapy. The radionuclide $^{76}$Br ($T_{1/2}$=16.2 h) is another potentially important radionuclide for medical purposes. Its therapeutic application was pioneered in the 1980s and 1990s by the Orsay group (cf. Mazière et al., 1986, 1995). Its importance has been increasing further in recent years (cf. Rowland et al., 2003). It mainly decays via positron emission ($I_{\beta^+}$=58.2±1.9%; $E_{\beta^+}$=3.98 MeV) accompanying the dominant γ-rays of 559 keV (74%), 657 keV (15.9%) and 1854 keV (14.7%). The β$^+$ emission intensity has been recently

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accurately determined (Qaim et al., 2007). It is considered a suitable candidate for labeling of antibodies for radioimmunoimaging and radiotracer studies via PET (Lövqvist et al., 1997; Sundin et al., 1999; Höglund et al., 2000; Nayak and Brechbiel, 2009). Furthermore, it can be used for tumor cell proliferation studies in therapeutic applications (Bergström et al., 1998; Borbath et al., 2002; Rossin et al., 2007). The associated disadvantage with $^{76}$Br is the high end point energy of the positron and prompt γ-rays, which results in the degradation of the spatial resolution and increased noise of the PET image (Lubberink et al., 1999; Ribeiro et al., 1999). However, with the development of new reconstruction algorithms for imaging the PET quality can be improved (cf. Laforest and Liu, 2008). The high positron energy can be potentially effective in therapeutic applications. The availability of $^{76}$Br of very high purity and specific activity, however, is a pre-requisite of those studies.

The production of useful radiobromines has been occasionally reviewed (cf. Qaim and Stöcklin, 1983; Qaim, 1986; Qaim, 2000). The radionuclide $^{76}$Br can be produced either through several direct routes or via the indirect method, i.e. from the decay of $^{76}$Kr ($T_{1/2}$= 14.8 h). In this work the cross section data for five charged particle induced direct production reactions, viz. $^{76}$Se($p$,$n$)$^{76}$Br, $^{77}$Se($p$,2$n$)$^{76}$Br, $^{78}$Se($p$,3$n$)$^{76}$Br, $^{75}$As($^3$He,2$n$)$^{76}$Br and $^{75}$As($\alpha$,3$n$)$^{76}$Br, were evaluated. The formation of $^{76}$Br via the indirect $^{79}$Br($p$,4$n$)$^{76}$Kr→$^{76}$Br reaction is also discussed. It is interesting to mention that most of the considered experiments were performed in connection with the development of production route for $^{77}$Br or $^{75}$Br, i.e. not specifically for $^{76}$Br production. Apart from the above reactions several other processes have also been studied for the production of $^{76}$Br, e.g. $^{76}$Se($^3$He,$t$)$^{76}$Br and $^{77}$Se($^3$He,$tn$)$^{76}$Br (He et al., 1982) and $^{78}$Kr($d$,$\alpha$)$^{76}$Br (Scholten et al., 2002; Scholten et al., 2004), which all require highly enriched target isotopes and yet the cross section for the reactions is very small leading to insufficient amount of $^{76}$Br for practical applications. We therefore did not analyze those data. Furthermore, deuteron induced reactions in the intermediate energy range have also been investigated: the $^{76}$Se($d$,2$n$)$^{76}$Br reaction for direct production (Paans et al., 1980) and the $^{nat}$Br($d$,$xn$)$^{76}$Kr→$^{76}$Br process for indirect production (Qaim et al., 1977). The cross sections for those two processes are not small. However, since in each case only a single measurement has been reported, and since the available codes cannot describe the deuteron induced reactions in the intermediate energy region satisfactorily, we did not undertake any analysis of those reaction data. It is important to point out that $^{77}$Br and $^{76}$Br have isomeric states of short half-lives 4.28 min and 1.31 s, respectively. Those isomers are, however, irrelevant due to their rapid decay.

In this work a critical evaluation of the excitation function for each of the above mentioned reactions was done and the consistency of the measurements was checked against the calculations of nuclear model codes, namely STAPRE, EMPIRE and TALYS. A statistical procedure discussed in the next section was then applied to deduce the recommended excitation function for the production of $^{76}$Br. The cross sections for the formation of $^{77}$Br and $^{75}$Br impurities were also evaluated to optimize the production conditions for the desired $^{76}$Br through a specific reaction. Furthermore, as a supplementary result, evaluated data for production of $^{75}$Br, also an interesting non-standard positron emitter, were obtained.

## 2. Selection of experimental data and evaluation procedure

The processes investigated for production of $^{76}$Br, along with their Q-values and references to experiments are given in Table 1. Similarly, the details relevant to the formation of the $^{77}$Br and $^{75}$Br impurities are given in Table 2. The available experimental details were analyzed with respect to the standard cross section data of the used monitor reactions (Gul et al., 2001) and the precise decay data of the reaction products from NuDat, except for the $\beta^+$-emission intensity of $^{76}$Br, which was taken from Qaim et al. (2007). Generally the stacked-foil irradiation technique was used for the experimental determination of the cross section. Overall no significant discrepancies were observed as multiple monitor reactions were used for beam current measurements. On the other hand the reported excitation functions of the proton induced reactions by Levkovskij (1991) were decreased by 20% in accordance with the new measurements for the $^{nat}$Mo($p$,$x$)$^{96m,g}$Tc monitor reaction (Takács et al., 2002).

The evaluation methodology was based on the statistical treatment of the data as discussed in a few previous articles (Sudár et al., 2002; Aslam et al., 2009, 2010; Hussain et al., 2010). The procedure started by taking the ratio of experimental cross

**Table 1**
Investigated nuclear reactions for the production of $^{76}$Br, Q-values and references.

| Nuclear reaction | Q-value (MeV) | References |
|---|---|---|
| $^{76}$Se($p$,$n$)$^{76}$Br | −5.74 | Paans et al. (1980), Kovács et al. (1985), Levkovskij (1991), Hassan et al. (2004) |
| $^{77}$Se($p$,2$n$)$^{76}$Br | −13.16 | Janssen et al. (1980), Levkovskij (1991), Hassan et al. (2004), Spahn et al. (2009) |
| $^{78}$Se($p$,3$n$)$^{76}$Br | −23.66 | Levkovskij (1991), Spahn et al. (2009) |
| $^{75}$As($^3$He,2$n$)$^{76}$Br | −3.95 | Paans et al. (1980), Alfassi and Weinreich (1982), Misaelides et al. (1987) |
| $^{75}$As($\alpha$,3$n$)$^{76}$Br | −24.5 | Nozaki et al. (1979), Paans et al. (1980), Alfassi and Weinreich (1982), Hermanne et al. (1994) |
| $^{79}$Br($p$,4$n$)$^{76}$Kr→$^{76}$Br | −32.05 | Dikšić et al. (1979) |

**Table 2**
Nuclear reactions leading to the formation of different bromine impurities during the production of $^{76}$Br.

| Nuclear reaction | Q-value (MeV) | References |
|---|---|---|
| $^{76}$Se($p$,2$n$)$^{75}$Br | −14.97 | Paans et al. (1980), Kovács et al. (1985), Levkovskij (1991), Hassan et al. (2004) |
| $^{77}$Se($p$,$n$)$^{77}$Br | −2.15 | Johnson et al. (1958), Fedorec et al. (1977), Janssen et al. (1980), Levkovskij (1991), Hassan et al. (2004), Spahn et al. (2010) |
| $^{77}$Se($p$,3$n$)$^{75}$Br | −22.38 | Levkovskij (1991), Spahn et al. (2009) |
| $^{78}$Se($p$,2$n$)$^{77}$Br | −12.64 | Janssen et al. (1980), Levkovskij (1991), Spahn et al. (2010) |
| $^{78}$Se($p$,4$n$)$^{75}$Br | −32.88 | Spahn et al. (2009) |
| $^{75}$As($^3$He,3$n$)$^{75}$Br | −13.18 | Paans et al. (1980), Alfassi and Weinreich (1982) |
| $^{75}$As($\alpha$,2$n$)$^{77}$Br | −13.5 | Waters et al. (1973), Nozaki et al. (1979), Alfassi and Weinreich (1982), Qaim et al. (1986), Hermanne et al. (1994) |
| $^{75}$As($\alpha$,4$n$)$^{75}$Br | −33.7 | Paans et al. (1980), Alfassi and Weinreich (1982), Hermanne et al. (1994) |
| $^{79}$Br($p$,3$n$)$^{77}$Kr→$^{77}$Br | −22.82 | Dikšić et al. (1979), Levkovskij (1991) |