Applied Radiation and Isotopes 140 (2018) 24–28

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

Improved small scale production of iodine-124 for radiolabeling and clinical applications

Denis Lamparter[a], Bernd Hallmann[a], Heribert Hänscheid[a], Francesca Boschi[b], Mario Malinconico[b], Samuel Samnick[a,*]

[a] Department of Nuclear Medicine, University Hospital Würzburg, 97080 Würzburg, Germany
[b] Comecer S.p.a., Via Maestri del Lavoro, 48014 Castel Bolognese, Italy

HIGHLIGHTS

- A small scale production of Iodine-124 for radiolabeling and clinical applications.
- Production via a ^{124}Te(p, n)^{124}I reaction using a16.5 MeV cyclotron.
- Up to 150 MBq pure sodium [^{124}I]iodide after a 2 h irradiation time.
- Generated [^{124}I]NaI in PBS is sterile, non-pyrogenic and ready for clinical uses.

ARTICLE INFO

Keywords:
Iodine-124
ALCEO Halogen EVP 2.0
Radiolabeling
PET imaging

ABSTRACT

Aim: This work describes a small-scale production of iodine-124 using a 16.5 MeV cyclotron, and a subsequent validation of the formulated sodium [124I]iodide solution for routinely clinical applications.
Methods: Iodine-124 (^{124}I) was produced via the ^{124}Te(p, n)^{124}I reaction using a 16.5 MeV GE PETtrace® cyclotron. Irradiation was performed with a pre-prepared solid target consisting of [^{124}Te]TeO_2 (99.93%) and Al_2O_3. Different layer thicknesses, irradiation and extraction parameters were tested. After irradiation at the cyclotron, the shuttle with irradiated material was transferred fully automatically via a tube system to the Comecer ALCEO® Halogen 2.0 extraction unit. Iodine-124 was subsequently extracted in form of sodium [^{124}I] iodide ([^{124}I]NaI) in 0.05 N aqueous NaOH solution, followed by reconstitution and validation for preclinical and clinical uses.
Results: Good result was achieved using a beam degradation foil of 500 µm thickness in combination with beam currents between 10 and 15 µA. Under these conditions, up to 150 MBq no-carrier-added [^{124}I]NaI was obtained after a 2 h irradiation time in less than 500 µl 0.05 N NaOH. Isolation of [^{124}I]NaI, including evaporation and extraction at the ALCEO® Halogen EVP unit was accomplished in 90 min 24 h after production (irradiation), the amount of iodine-123 as assessed by gamma-ray spectroscopy was less than 1.5%. The undesirable iodine-125 was not detectable by gamma spectroscopy. The extracted [^{124}I]NaI could be used directly for radiolabeling purposes, and after buffering with phosphate buffered saline (PBS) and sterile filtration for clinical applications.
Conclusions: Through the optimized conditions for irradiation and extraction, iodine-124 was produced in good radiochemical yields and high radionuclide purity. The generated injectable [^{124}I]NaI solution was sterile, non-pyrogenic and ready for preclinical and clinical applications after a sterile filtration through a 0.22 µm membrane filter.

1. Introduction

Iodine-124 (^{124}I) is an attractive long-lived positron emitting radionuclide for PET chemistry and molecular imaging by using PET. Its convenient half-life of 4.2d allows extended radiosyntheses and longitudinal PET imaging studies. Applications of ^{124}I range from simple imaging of the thyroid and parathyroid to functional studies of neurotransmitter receptors, through monoclonal antibodies for the study of cancer. Furthermore, ^{124}I has been in use for labeling single molecules such as meta-iodobenzylguanidine (MIBG), amino acids, and fatty acids, to name only some, allowing investigation of diseases of different organs such as brain and heart (Seo et al., 2012; Israel et al., 2008;

* Correspondence to: Department of Nuclear Medicine, University of Würzburg, Oberdürrbacher Straße 6, D-97080 Würzburg, Germany .
E-mail address: Samnick_S@ukw.de (S. Samnick).

https://doi.org/10.1016/j.apradiso.2018.06.014
Received 19 March 2018; Received in revised form 20 May 2018; Accepted 15 June 2018
Available online 18 June 2018
0969-8043/ © 2018 Elsevier Ltd. All rights reserved.

Farmakis et al., 2018; Samnick et al., 2018; Kulkarni and Corbett, 1990). Therefore, there has been a high demand for an efficient, reliable small-scale production of ^{124}I for PET chemistry and for routinely clinical applications by using commercially available low energy cyclotrons.

Iodine-124 has mainly been produced by using enriched tellurium-124 via the ^{124}Te(d, 2n)^{124}I nuclear reaction (Lambrecht et al., 1988; Nagatsu et al., 2011; Firouzbakht et al., 1993; Knust and Weinreich, 1997; Bastian et al., 2001). In recent years, with the worldwide increase in the number of low-energy proton cyclotrons for the production of common PET isotopes such as fluorine-18 or carbon-11, the alternative ^{124}Te(p, n)^{124}I reaction has been increasingly used (Knust and Weinreich, 1997; Scholten et al., 1995; Qaim et al., 2003; Sajjad et al., 2006). Despite the slight decrease in yields noted with the ^{124}Te(p, n)^{124}I reaction, this reaction might offer the possibility of obtaining the highest levels of ^{124}I purity at the time of administration (Braghirolli et al., 2014; Aslam et al., 2010). In addition, previous studies on the production of ^{124}I showed that the ^{124}Te(p, n)^{124}I pathway might be the method of choice for small cyclotrons with energies below 16 MeV as available in our department (Hohn et al., 2001; Aslam et al., 2010; Braghirolli et al., 2014).

Recently, Comecer offered commercially a new unit (ALCEO Halogen 2.0) for small-scale productions of iodine-124 and copper-64. Herein, we described the optimization of the production of iodine-124 in terms of radiation parameters, radiochemical yield, purity, extraction temperature and volume, and a validation of the generated sodium [^{124}I]iodide solutions for preclinical and clinical applications, using the 16.5 MeV GE PETtrace® cyclotron and the new ALCEO Halogen 2.0 unit.

2. Materials and methods

All chemicals and solvents were from Sigma-Aldrich (Deisenhofen, Germany) and were used without further purification. Sterile phosphate buffered saline (Braun) and 0.1 N HCl were obtained via the hospital pharmacy. Injection material was taken from the clinical inventory. Te-124 oxide ([^{124}Te]TeO_2) in powder form (99.93%) was purchased commercially from STB Isotope Germany GmbH (Hamburg, Germany).

Test for sterility was performed commercially by L&S (Bad Bocklet-Grossenbrach; Germany), according to the European Pharmacopoeia (Pharm Eur.) guidelines. Test for pyrogens was carried out on a Charles River Endosafe® PTS Endotoxin Testing System (Charles River Endotoxin, Ecully, France) using the limulus amebocyte lysate (LAL) test.

2.1. Production of iodine-124 and preparation of the injectable [^{124}I]NaI solution

Iodine-124 (^{124}I) was produced via a ^{124}Te(p, n)^{124}I reaction using a 16.5 MeV GE PETtrace® cyclotron (GE Medical Systems, Uppsala, Sweden). Irradiation was performed with a pre-prepared solid target consisting of enriched [^{124}Te]TeO_2 (99.93%) and neutral alumina powder (Al_2O_3). [^{124}Te]TeO_2 (300 mg) was mixed with 5% w/w Al_2O_3 (15 mg) in a small beaker with 2 mL of MeOH. To ensure the homogeneity, the suspension was stirred manually and evaporated to dryness at 55 °C on a heat plate. This approach was used instead of mixing in a mortar, because using a mortar resulted in large (20–30 mg) losses of target material. The size of the metal plate with the molten $^{124}TeO_2$/Al_2O_3 was a circle with a diameter of 10 mm and the estimated size of the melt was ca. 4 mm^3. The target material was distributed into the target shuttle using a spatula for radiation.

In order to optimize the thick target yield for iodine-124, using the 16.5 MeV proton beam of the GE PETtrace cyclotron, we tested aluminum foils with different thicknesses (320 μm, 500 μm and 640 μm) Based on the recommendation of the supplier, 10–15 μA proton beam was applied for 1–5 h irradiation time. Optimal results were achieved by using a beam degradation foil of 500 μm thickness in combination with beam currents between 10 and 12 μA (2 h irradiation time).

After irradiation at the cyclotron, the shuttle was transferred fully automatically via a tube system to the ALCEO Halogen 2.0 extraction module (Comecer S.p.a., Castel Bolognese, Italy). Extraction was performed by heating the shuttle up to 740 °C for 10 min and trapping of the vaporized iodine-124 into a glass tube, which was previously precoated with 50 μl of 0.05 N NaOH. After the system was cooled by air to less than 50 °C, the trapped iodine-124 was eluted in form of sodium [^{124}I]iodide ([^{124}I]NaI) with 500 μl aqueous 0.05 N NaOH.

The extracted [^{124}I]NaI solution could be directly used for radioiodination purposes without further purification. In view of preclinical or clinical applications, the extracted [^{124}I]NaI solution was neutralized with 25 μl HCl (0.1 N), buffered with phosphate buffered saline (pH = 7.0; Braun) and sterile-filtered through a 0.22 μm filter (Millipore, Cork, Ireland) into a sterile vial for preclinical and clinical applications.

2.2. Quality insurance of sodium [^{124}I]iodide ([^{124}I]NaI)

The [^{124}I]NaI solution underwent immediately a thin layer chromatography (TLC) to assess the radiochemical purity. For this aim, an aliquot of 1.0–1.5 μl of the formulated solution was analyzed by TLC, using a ITLC-SG stripe (Varian, Lake Forest, USA) as stationary phase, and MeOH/H_2O (80:20; v/v) as mobile phase. A TLC-scanner (mini-GITA®, Raytest, Straubenhardt, Germany) was used for quantification of the radiochemical purity. In view of potential clinical applications, [^{124}I]NaI buffered with phosphate buffered saline (PBS, pH 7.0) was tested for pyrogens using LAL and for sterility after radiation decay. The tests were conducted according to the European Pharmacopoeia (Pharm Eur.) guidelines. In addition, a gas chromatographic (GC) analysis was performed retrospectively after radiation decay of the sterile solution to exclude any possibly residual solvents in the formulated injection solutions. Furthermore, the pH value of the injection solution was determined and the radionuclide identity and purity were determined using gamma-ray spectrometry.

3. Results and discussion

This work describes an easy small-scale production of iodine-124 for routinely in-house uses using Alceo® solid target processing system (Fig. 1).

3.1. Excitation energy

The rationale behind this work is that iodine-124 can be produced under mild conditions via the ^{124}Te(p, n)^{124}I reaction with extremely low impurities using a low energy cyclotron (Braghirolli et al., 2014). Previous studies showed that the proton-induced reaction on enriched ^{124}Te targets is the method of choice for small cyclotrons with energies below 16 MeV. The reaction is superior to the ^{124}Te(d, 2 n)^{124}I scheme owing to lower impurity levels (Hohn et al., 2001; Aslam et al., 2010). In particular, the co-produced iodine-125 is expected to be extremely low.

The production of radionuclides by irradiation can be explained by the nuclear excitation functions for the energetically allowed decay channels. Compilations of theoretical and experimental data on the excitation functions of reactions for ^{124}Te irradiated with protons have been widely described previously (e.g. Aslam et al., 2010; Artun and Aytekin, 2015). For 16.5 MeV proton energy or less, 2 reactions are energetically possible, the ^{124}Te(p, n)^{124}I reaction with a threshold energy of 4 MeV and the ^{124}Te(p, 2 n)^{123}I reaction with 12 MeV threshold energy. While highest cross sections for the (p, n)reaction are observed for energies between 9 and 13 MeV, the production of ^{123}I becomes dominant for energies of 14 MeV or higher (Scholten et al., 1995). In order to optimize the thick target yield for ^{124}I along with reasonable low contamination with ^{123}I, the 16.5 MeV proton beam of

Download English Version:

https://daneshyari.com/en/article/8208368

Download Persian Version:

https://daneshyari.com/article/8208368

Daneshyari.com