Fully Automated Radiosynthesis and Formulation of [11C]MeAIB Applied for In Vivo Imaging of Glioblastoma

Dam, Johan Hygum; Halle, Bo; Thisgaard, Helge; Hvidsten, Svend; Kristensen, Bjarne Winther; Någren, Kjell

Published in:
Journal of Labelled Compounds and Radiopharmaceuticals

DOI:
10.1002/jlcr.3058

Publication date:
2013

Document version
Publisher's PDF, also known as Version of record

P-025 Fully automated radiosynthesis and formulation of [^{11}C]MeAIB applied for *in vivo* imaging of glioblastoma

Dam, Johan Hygum[1*]; Halle, Bo[2]; Thisgaard, Helge[1]; Hvidsten, Svend[1]; Kristensen, Bjarne Winther[2]; Någren, Kjell[1]

1 PET- & Cyclotron Unit, Department of Nuclear Medicine, Odense University Hospital, Odense, Denmark; 2 Department of Neurosurgery, Odense University Hospital, Odense, Denmark; 3 Department of Pathology, Odense University Hospital, Odense, Denmark

Objectives: Amino acids and analogues thereof play an important role in the growth of many tumor cells. The clinical value of radiolabelled amino acids such as methionine, fluoroethyltyrosine and fluorodopa has been confirmed in a plethora of studies [1]. We sought to prepare, formulate and apply a metabolically stable analogue of the amino acid alanine for system A transport, namely [*N-methyl*-^{11}C]α-methylamino-isobutyric acid, [^{11}C]MeAIB [2].

Methods: The labelling precursor, [^{11}C]MeOTf, was prepared on a Tracerlab FXc Pro by standard in-line gas-phase conversions from [^{11}C]CO_2. The [^{11}C]MeOTf was bubbled through a cooled solution of precursor in CH_3OH, CH_3CN and pentamethylpiperidine at 5 °C. The solution was warmed to 60 °C for 1 min, where 2 M NaOH was added. The heating was continued for 3 min. Shortly after, the mixture was automatically injected onto a semipreparative HPLC column via a 2 mL loop.

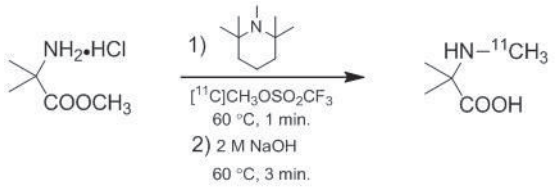

Figure 1: Synthesis of [^{11}C]MeAIB

The HPLC purification was performed in aqueous, buffered CH_3CN. Hence, the fraction containing the product was separated and diluted with 0.2 M H_3PO_4. This solution was loaded onto a Strata-X-C column, which was washed with sterile 0.1 M HCl and isotonic, sterile saline. The product was eluted with sterile 10 mL 2% Na_2HPO_4 through a sterile filter and into a sterile vial. Male athymic nude rats (HsdHan™:RNU-*Foxn1^{rnu}*) were intracranially implanted in the right hemisphere with 300.000 low passage human glioblastoma single cells suspended in HBSS (Invitrogen) with 0.9% glucose (SAD 500 mg/mL). Four weeks post-implantation, rats with infiltrating glioblastomas were anesthetized and PET/CT scanned using a Siemens Inveon system after tail vein injection of [^{11}C]MeAIB, [^{11}C]methionine or [^{18}F]FDG. Immediately after injection a dynamic acquisition was commenced.

Results: The full synthesis of [^{11}C]MeAIB including purification by prep. HPLC, solvent exchange by solid phase extraction and formulation takes about 35 min. delivering 2-5 GBq in 10 mL sterile phosphate-buffer. In all cases pH was maintained between 6.3-6.8 and the content of CH_3CN was below 350 ppm. We have produced and more than 40 productions in the described manner. After administration to orthotopically implanted nude rats the glioblastoma were visualized with a tumor to background (normal brain) ratio for [^{18}F]FDG, [^{11}C]methionine and [^{11}C]MeAIB of 1.5, 2.3 or 8.2, respectively.

Conclusions: We have demonstrated the fast and reliable production of GMP-grade [^{11}C]MeAIB. Also, [^{11}C]MeAIB was successfully used in the imaging of human infiltrating glioblastoma in nude rats. [^{11}C]MeAIB was found to have a significantly higher tumor to background ratio than [^{11}C]methionine and [^{18}F]FDG.

References: [1] McConathy J, et al. (2008) Cancer Metastasis Rev, 27, 555-73. [2] Någren K, et al. (2000) J Label Compd Radiopharm, 43, 1013-21.