STABLE AND CONSISTENT PRODUCTION OF ^{13}N-AMMONIA IN A NIOBIUM TARGET

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Introduction

Medisch Centrum Alkmaar (MCA) is a hospital located in the city center of Alkmaar, in the Netherlands, around 30 min from Amsterdam. We recently installed a radiopharmaceutical production facility, equipped with an IBA Cyclone® 18 TWIN, an 18 MeV proton accelerator with 2 proton ion sources for higher reliability.

The facility produces every day the PET tracers required for patient examinations performed on the 2 PET cameras within the Nuclear Medecine department: ^{18}F- labelled molecules such as FDG, NaF and F-Choline, ^{13}N-NH_3, and in the future ^{11}C- and ^{15}O- labelled molecules.

In this poster, we focus on ^{13}N-NH_3 production and the improvement of the production by changing the target material from Aluminum to Niobium. This change was done with the support of IBA through a collaboration contract, where we tested the Ammonia production capacity of IBA's new Conical 8 target.

IBA Cyclone ® 18 TWIN in our vault in Alkmaar, NL

^{13}N is a positron emitter with a very short half life of 9.97 minutes, therefore requiring an on-site cyclotron for its production, through the nuclear reaction: $^{16}O(p,\alpha)^{13}N$. The ion beam passes through a thick carbon foil (300 µm) in order to lower its energy to 16 MeV, avoiding the production of ^{15}O (nuclear reaction $^{16}O(p,pn)^{15}O$). Synthesis of NH_3 occurs directly inside the target. After irradiation, the solution is sent through a QMA cartridge for $^{18}F^-$ removal to the pre-loaded mother vial in the dispensing cell followed by syringe filling via 0.22 µm sterilizing filter.

Background

A protocol has been developed to assess coronary blood flow reserve (CFR) in patients with Coronary Artery Disease (CAD) with two ^{13}N-ammonia PET scans made at a 15 minutes interval. The first scan is made at rest after administration of 300 MBq, the second under pharmacologic stress, after a dose of 400 MBq.

A day's scanning program comprises 8 to 12 patients; 2 patients are scanned simultaneously on 2 adjacent scanners. The doses required on one day are produced in 4 to 6 cyclotron runs, each run producing an amount of ^{13}N-ammonia sufficient to fill 4 syringes.

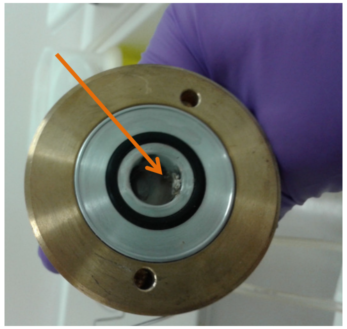
The theoretical amount of activity required is 6 – 7 GBq at start of filling, based on mean times between dispensing and administration of 7 – 11 min (rest scan) and 15 – 21 min (stress scan), but in practice a minimum of 11 GBq is aimed for to allow for filling or administration delays. Requirements for both amount of activity and timely dispensing make high demands on cyclotron target reliability and yield consistency.

From Aluminum to Niobium target

^{13}N-ammonia was initially produced in an aluminum target. With a fill volume of 1800 µL (Water for Injection (WFI), 5µMol ethanol), beam current of 20 µA and average beam time of 20 – 25 min, mean activity at end of beam (EOB) was 17.3 GBq (calculated by the cyclotron software) and mean amount of activity harvested in the filling hotcell around 12.5 GBq.

However, after around 80 runs, variation in yield increased sharply, with occasional run yields below 20%. Runs with very low yield coincided with significant amounts of gaseous 13N in the hotcell, probably either N_2 or various nitrous oxides.

The target was exchanged for a new aluminum one. On inspection, the removed target interior showed white deposits of aluminum oxide. Because of intense use, identical problems occurred with the replacement target already after only 60 runs. We suspected that the aluminum oxide was the cause of the formation of other chemical forms of ^{13}N and decided to install a target made from an inert material. In cooperation with IBA we replaced the aluminum target with a Nirta® Conical 8 target with niobium body.



White deposits inside aluminum target body

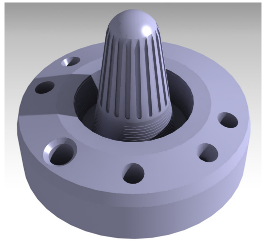
New conical design #: Niobium insert, target body, water diffuser

Nirta® Niobium Conical target

The new Niobium target insert has a complex shape with drilled channels on the outside of the chamber and a deep channel next to the beam strike area to ensure efficient cooling.

The water inlet lines are directly inserted in the Niobium body to avoid potential contamination of the water because of contact with small o-rings.

In operation, besides the carbon degrador and the titanum vacuum foil, a 35µm Havar® target foil is used, reducing helium cooling requirements.

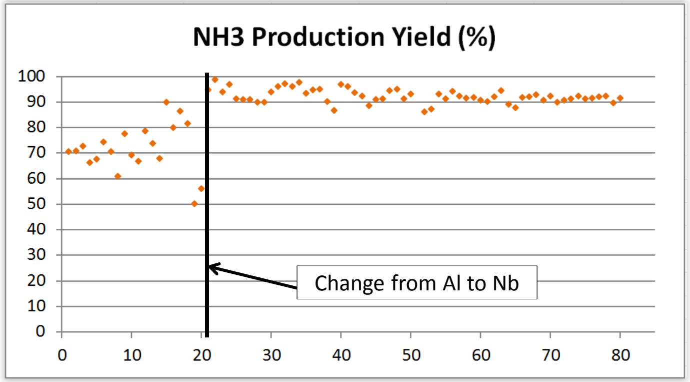


new conical shaped Niobium insert #

Results

The following parameters were used in routine production: single beam currents of 20 – 22 µA and beam times of 12 – 15 min.

Between June 2014 and end of December 2014 a total of 273 cyclotron runs were performed over 51 production days. Mean beam time over these runs was 13.7 minutes (sd 0.64 minutes) resulting in a mean activity at EOB of 14.7 GBq (sd 0.75 GBq) and mean collected activity for dispensing of 11.4 GBq (sd 0.7 GBq). Mean radiochemical purity (rcp) was 99.93% and, after implementation of a QMA column in the transfer line, rcp increased to 100%. It should be noted that, to date, not a single run has failed due to technical problems of cyclotron or target.



The production yield is calculated as the percentage ratio of the actual activity value measured in the dose calibrator of the dispensing hotcell (before starting the syringe filling) to the theoretical activity production EOB. The difference, corrected for decay, comes from other chemical reactions occurring inside the target and leading to ^{13}N-NO_x gas compounds.

High capacity production

Conical 8 target has a cavity volume of 3.7 ml, whereas typical NH_3 production targets have a cavity volume of around 2.4 ml for the production of around 15 GBq EOB.

Part of the collaboration with IBA was to evaluate the maximum NH3 production capacity of this target and an IBA engineer came to optimize cyclotron run parameters in order to extract the maximum activity from the target.

We were able to produce over 40 GBq EOB (> 1 Ci) by irradiating 3000 µl (WFI, 5µMol ethanol) during 20 minutes with a proton beam current of 50 µA.

Conclusion

We were able to demonstrate that the use of a Niobium target for high activity, frequent 13N-ammonia productions is a very reliable improvement over production in an Aluminum target.

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