

## **Direct production of Ga-68 from proton bombardment of concentrated aqueous solutions of [Zn-68] Zinc Chloride.**

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Expecting a drastic increase in use of Ga-68 in the coming years, we have reconsidered the possibilities for direct production by small cyclotrons. Although the Ge-68 generator is widely available and easily used, it often does suffer problems from limited lifetime (shorter than the physical  $T_{1/2}$  of Ge-68), high price and limited activity output. It is also our concern that a global creep from Tc-99m examinations towards Ga-68 PET-CT counterparts could rapidly exhaust the present global supply of Ge-68.

The direct production by electroplated, solid, highly enriched Zn-68(p,n)Ga-68 is well known and closely mimics the production of the blockbuster isotope Ga-67. Same target, same chemistry, just a little more energy to give the (p,2n) reaction. However the prospect of doing an enriched electroplated solid target, bombardment, etching, ion exchange separation and target material recovery chemistry for a single patient dose of Ga-68 does not seem feasible for routine use.

For this reason we have tested a “solution target”, where we bombard ZnCl<sub>2</sub> in high concentration in water. Of course, the water does “eat up” some useful cross section and gives more stopping, but for a high yield “easy” (p,n) reaction and with a short lifetime product, this is certainly possible.

From the outset, we only had four concerns:

1. Can highly concentrated zinc chloride solutions be contained in a metal target and behind a target foil during bombardment? It is, after all, strongly acidic, and popularly used as strong soldering flux, dissolving many metal oxides.
2. Can the yield be predicted and is it high enough for routine application?
3. Will zinc remain as zinc chloride during the rather unusual conditions during proton bombardment? And will Ga-68 come out in solution from the target?
4. Can the Ga-68 be extracted rapidly from the target solution and will it be possible to reuse the enriched zinc chloride solutions directly?

We have addressed all four problems experimentally, and will report the very satisfying outcome.

As target we used a slightly modified Niobium target body (designed for F-18 production), kindly provided with very few questions by Tomas Eriksson of GE Medical Systems in Uppsala. As target foil we chose 100 micrometer thick Niobium foil, partly to degrade 16.5 MeV proton beam of our PETtrace down to more optimal (p,n) energies, partly because we wanted to lower the risk of getting foil breaks and loss of the brine solution into a routinely used cyclotron.

We have kept a piece of this Nb foil in a concentrated ZnCl<sub>2</sub> solution for 6 months without any signs of attack, loss of luster or change of weight. The target has survived many bombardments at 5, 10 uA and a single 20 uA run. We have not yet pressurised the target beyond atmospheric, and we thus did get boiling through the target filling line at 20 uA. But pressurisation should allow higher currents. After bombardments, the target body chamber and the foil look completely untouched.

Clear ZnCl<sub>2</sub> solutions at room temperature can be prepared with more than 3 grams of ZnCl<sub>2</sub> to 1 gram of water. We did the early target testing with 2 grams of ZnCl<sub>2</sub> to 1 gram of water. When testing with enriched Zn-68, we used 1 gram ZnCl<sub>2</sub> to 1 gram water.

The cross section for Zn-68(p,n)Ga-68 is well known (F.Szelecsneyi *et al.* JARI, **49**,1005 (1998). Using this and a straight forward stopping power calculation made by SRIM (version 2008.04, J.F.Ziegler *et al* 2008 [WWW.SRIM.ORG](http://WWW.SRIM.ORG)) we predicted a saturation yield for 1μA of 1500 MBq for a one-to-one ZnCl<sub>2</sub> solution. This again corresponds to 1500 MBq at EOB after 20 minutes bombardment at 5 μA.

Experimentally we found values a little higher than this (1800 MBq Ga-68 @ EOS), measured by both dose calibrator after 1 hour and by gamma spectroscopy and thus corrected for influence of other positron emitters. With pressurisation of target, higher current on target and a higher Zn concentration, yields above 10 Gbq EOS should be obtainable.

We have used a batch of Zn-68 from Campro with 99% enrichment for our target solution. The only observed radionuclidic impurity (after chemical separation of the Gallium, see below) was Ga-67 (probably from the (p,2n) process), and this accounted for less than 0.1% of total activity EOB.

To extract the Ga-68 from the target solution (still having a pH around 2 after bombardment) we passed it through a preconditioned Waters C-18 sep-pak. From old literature, it is known that Gallium chloride complexes behave “lipophilic”, - but the success of this was still a pleasant surprise to us. Zinc chloride passes through while more than 90% of Ga-68 sticks on the seppak. The seppak was washed by 2 fractions of 10 ml water to remove effectively the remaining Zinc. The primary eluate and the water washings were collected and concentrated by simple boiling up the original ZnCl<sub>2</sub> concentration. Another successful production with same yield was done on this solution. The Ga-68 could be eluted from the seppak in a small volume of 0.1 Molar HCl. Thus, both activity extraction and target material recovery can be done rapidly and simple.

Ga-68 activity will be of limited use, if it cannot be reclaimed in more or less metal free form. The large initial load of Zinc on the column is however effectively washed out by the water fractions. Using Zn-63 and Zn-65 as indicators, the Zinc “decontamination” factor of this process is better than 5000. Other metals, like for example Iron impurities in target solution, can be more difficult to separate out by this method and should thus be avoided.

We believe that this method with some more development can be of value for local production of large activities of Ga-68 for subsequent radiopharmaceutical production. It also looks like the “solution target” with Niobium body and Niobium foil is a viable approach to a broader class of metal radioisotopes, bypassing the need for electroplating and solid targets.