



## Optimized $^{52}\text{Mn}$ Production for Longlived PET Applications

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**TITLE:** Optimized  $^{52}\text{Mn}$  Production for Long-lived PET Applications

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**ABSTRACT BODY:**

**Abstract Body: Introduction**

$^{52}\text{Mn}$  ( $t_{1/2} = 5.59$  d,  $\beta^+ = 29.6\%$ ,  $E\beta_{\text{max}} = 0.58$  MeV) presents itself as an excellent candidate for a variety of PET applications. Chelation of  $^{52}\text{Mn}$  would allow for radiolabelled antibody imaging 2-4 weeks post-injection, and free  $^{52}\text{Mn}^{2+}$  has shown promise as a reporter gene probe in stem cell tracking applications [1]. The goals of this work were to develop an efficient  $^{52}\text{Mn}$  production target, to optimize separation chemistry, and to demonstrate effective chelation.

**Methods**

$^{52}\text{Mn}$  was produced by 16 MeV proton irradiation of natural chromium metal (approximately 750 mg, 99.999%, GFS chemicals) hydraulically pressed into 0.5 mm thick silver disk. With direct jet water cooling on the rear face, these targets were shown to withstand 60  $\mu\text{A}$  of beam current for one hour without failure. Targets were etched by 2 mL 12.1M HCl and then diluted with 48 mL ethanol and 0.5 mL of 12.1M HCl.  $^{52}\text{Mn}$  was radiochemically isolated from the target solution (96% Ethanol, 0.12M HCl) by loading the activity onto approximately 150 mg of AG-1x8 strong anion exchange resin, followed by rinsing.  $^{52}\text{Mn}$  was eluted in 1 mL of 6M HCl, before repeating the purification with two additional separation cycles. The final product was eluted in approximately 500  $\mu\text{L}$  of 0.1M HCl. DOTA labeling was performed at pH 4 using 0.25M pH 4.5 NaOAc to buffer the activity.

**Results**

Average end of bombardment  $^{52}\text{Mn}$  yield was  $0.14 \pm 0.05$  mCi/ $\mu\text{Ah}$  ( $n=4$ ). Radionuclidic purity was measured to be greater than 99% by high-purity germanium analysis. Target etching resulted in approximately 450 mg of chromium metal dissolution. An average radiochemical separation yield of  $72 \pm 17\%$  ( $n=2$ ) has been observed. Total chromium mass in the separated product was measured to be  $1.1 \pm 0.1$   $\mu\text{g}$  ( $n=1$ ) by microwave plasma atomic emission spectrometry, corresponding to an overall separation factor of approximately  $1.6 \times 10^5$ . DOTA chelation of  $^{52}\text{Mn}$  was found to be complete after one hour at room temperature, resulting in a measured effective specific activity of 0.05 Ci/ $\mu\text{mol}$  ( $n=1$ ).

**Conclusions**

Production, separation, and chelation of  $^{52}\text{Mn}$  have been demonstrated with very simple targetry and chemistry. These methods significantly improve over previous techniques [2-3] by improving Cr target purity from 99.95% to 99.999% and by allowing for a trap-and-release chromatographic separation. With such an approach, specific activities have been increased and the  $^{52}\text{Mn}$  production process can be automated to reduce radiation dose to personnel. These developments will allow for rapid translation into imaging applications.

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## References

- [1] CM Lewis, SA Graves, *et al.*, *Theranostics*, 5(3): 227-239, 2015.  
[2] S Lahiri, *et al.*, *Anal Chem*, 78: 7517–21, 2006.  
[3] GJ Topping, *et al.*, *Med Phys*, 40: 042502, 2013.

## TABLE TITLE: Trace Metal Analysis of Mn52 Product

<b>Trace Metal Analysis of Mn52 Product</b>

Element	Mass ( $\mu\text{g}$ , $\pm 10\%$ )
Cr	1.07
Mn	0.11
Fe	0.19
Co	0.00
Ni	0.00
Cu	0.14
Zn	3.30

<b>Table 1:</b> Trace metal analysis by microwave plasma atomic emission spectrometry of the radiochemically separated Mn52 product.

(No Image Selected)