Novel Preparation Methods of $^{52}$Mn for ImmunoPET Imaging

$^{52}$Mn ($t_{1/2} = 5.59$ d, $\beta^+ = 29.6\%$, $E_{\beta\text{ave}} = 0.24$ MeV) shows promise in positron emission tomography (PET) and in dual-modality manganese-enhanced magnetic resonance imaging (MEMRI) applications including neural tractography, stem cell tracking, and biological toxicity studies. The extension to bioconjugate application requires high specific activity $^{52}$Mn in a state suitable for macromolecule labeling. To that end a $^{52}$Mn production, purification, and labeling system is presented, and its applicability in preclinical, macromolecule PET is shown using the conjugate $^{52}$Mn-DOTA-TRC105. $^{52}$Mn is produced by $60$ µA, $16$ MeV proton irradiation of natural chromium metal pressed into a silver disc support. Radiochemical separation proceeds by strong anion exchange chromatography of the dissolved Cr target, employing a semi-organic mobile phase, $97.3$ (v:v) ethanol: HCl (11M, aqueous). The method is $62 \pm 14\%$ efficient ($n=7$) in $^{52}$Mn recovery, leading to a separation factor from Cr of $(1.6 \pm 1.0) \times 10^6$ ($n = 4$), and an average effective specific activity of $0.8$ GBq/µmol ($n = 4$) in titration against DOTA. $^{52}$Mn-DOTA-TRC105 conjugation and labeling demonstrate the potential for chelation applications. In vivo images acquired using PET/CT in mice bearing 4T1 xenograft tumors are presented. Peak tumor uptake is $18.7 \pm 2.7$ %ID/g at 24 hours post injection and ex vivo $^{52}$Mn biodistribution validates the in vivo PET data. Free $^{52}$Mn$^2+$ (as chloride or acetate) is used as a control in additional mice to evaluate the non-targeted biodistribution in the tumor model.

General information
State: Published
Organisations: Center for Nuclear Technologies, The Hevesy Laboratory, Department of Electrical Engineering, University of Wisconsin-Madison, TRACON Pharmaceuticals, Inc.
Pages: 2118–2124
Publication date: 2015
Peer-reviewed: Yes

Publication information
Journal: Bioconjugate Chemistry
Volume: 26
Issue number: 10
ISSN (Print): 1043-1802
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 4.4 SJR 1.801 SNIP 0.984 Web of Science (2017): Impact factor 4.845
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 5.12 SJR 2.02 SNIP 1.201 Web of Science (2013): Impact factor 4.821
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 4.8 SJR 2.064 SNIP 1.263 Web of Science (2012): Impact factor 4.58
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes