ABSTRACT

This dissertation investigates positron-emitting radioisotopes of manganese: ^{51}Mn ($t_{1/2}$=46 min, $E_{\beta+,Avg}$= 963 keV) and ^{52g}Mn($t_{1/2}$=5.6 d, $E_{\beta+,Avg}$= 242 keV) and establishes their potential as a surrogate for Ca^{2+} to image peripheral pain generators. Voltage-gated calcium channels (VGCC) regulate the influx of Ca^{2+} in response to an action potential initiated by noxious stimuli. VGCC then act as biological transducers, converting electrical signal of action potentials to intracellular signaling along the pain processing pathway. Understanding the regulation of Ca^{2+} *in vivo* may be crucial for diagnosing and treating pain. Previously used imaging techniques for Ca^{2+} are effective in depicting the behavior of the ion *in vitro* but are not translatable to clinical diagnostics. Manganese, in the form of $MnCl_2$, has been utilized as a contrast agent in magnetic resonance imaging (MRI), serving as a surrogate for Ca^{2+}. The use of Mn^{2+} as a magnetic resonance (MR) contrast agent is limited due to safety concerns, where excessive exposure can lead to neurotoxicity resulting in a condition known as "manganism". To avoid the apparent toxicity problem associated with Mn^{2+} as an MR contrast agent, researchers have looked to positron-emitting Mn. This dissertation explores production and purification of ^{51,52g}Mn from proton bombardment of ^{54}Fe and ^{nat,52}Cr targets on a low energy cyclotron. This work also investigates ^{51,52g}Mn's potential for imaging pain resulting from both nociceptive and neuropathic models. Imaging studies were conducted using small animal μPET/CT, μMRI, and clinical PET/MR scanners to visualize the uptake of Mn-based tracers in the neuroanatomy of animals experiencing pain. The uptake and distribution of [^{5x}Mn]$MnCl_2$ were compared between pain model and control animals using *in vivo* and *ex vivo* analysis. The findings of this dissertation demonstrate positron-emitting manganese's ability to serve as a novel imaging biomarker for non-invasive identification of peripheral pain generators, paving the way for improved clinical diagnostics and pain management strategies.