# AbstractID: 9460 Title: Modulating Mn<sup>2+</sup> Efflux with SEA0400, Using Cardiac Manganese-Enhanced MRI (MEMRI) T<sub>1</sub>-Mapping in a Murine Model

**Purpose:** $Ca^{2+}$ is an important regulator of contractile function in the heart. Efflux mechanisms of the intracellular $Ca^{2+}$ concentration are regulated by the $Na^{+}/Ca^{2+}$ exchanger (NCX) and plasma membrane $Ca^{2+}$-ATPase (PMCA). During myocardial ischemic-reperfusion intracellular $Ca^{2+}$ overloads via the reverse mode of the NCX, exacerbating myocardial injuries. Protocols that selectively inhibit this exchanger have shown potential therapeutic effects. Cardiac manganese-enhanced MRI (MEMRI) can be implemented to quantify $Mn^{2+}$ concentration *in vivo*, where $Mn^{2+}$ has be sugested as a surrogate marker for $Ca^{2+}$. This study introduces a potential technique to study cardiac $Mn^{2+}$ efflux by inhibiting the NCX using SEA0400. **Method and Materials:** Male C57Bl/6 mice (6-13 weeks) were separated into two groups to study the rate of $Mn^{2+}$ efflux; a control group and a group treated with SEA0400. Both groups were infused with a single dose of 190±2 nmoles/g BW $Mn^{2+}$. The SEA0400 group were injected with 50 mg/kg SEA0400 one hour post-$Mn^{2+}$ infusion. Images were acquired on a horizontal 7.0 T Bruker BioSpec MRI spectrometer equipped with a micro imaging gradient. $T_1$-maps were acquired pre-$Mn^{2+}$ infusion and at various time points post-$Mn^{2+}$ infusion using an ECG-gated, flow-compensated Look-Locker MRI pulse sequence. The change in relaxivity, $\Delta R_1$, in the left ventricular free wall (LV Wall), was calculated at different time points post-infusion. **Results:** In the LV Wall 50% of the signal enhancement is attenuated within ~3-4 hours post-$Mn^{2+}$ infusion. SEA0400 demonstrates the effectiveness of reducing the rate of $Mn^{2+}$ efflux. At a SEA0400 dose of 50 mg/kg the $Mn^{2+}$ efflux half-life was approximately two times longer than the control group. **Conclusion:** This $T_1$-mapping technique can be used to quantify $Mn^{2+}$ efflux rates from the myocardium. By using a NCX inhibiting agent this technique can potentially be employed to interrogate individual $Mn^{2+}$ efflux mechanisms and rates *in vivo*.