AbstractID: 10523 Title: Modeling Myocardial Mn²⁺ Efflux Rates Using Manganese-Enhanced MRI T₁ Mapping in a Murine Myocardial Infarction Model.

Purpose: Alterations in myocyte Ca^{2+} handling appear to be centrally involved in the dysfunctional characteristics of the failing heart. This study uses quantitative manganese-enhanced MRI techniques to detect changes in the Mn^{2+} efflux relative to Ca^{2+} fluctuations in mice following inhibition of the sodium calcium exchanger (NCX) with SEA0400. Furthermore, the technique was applied to a mouse myocardial infarction (MI) model. Segmentation and modeling analyses were used to examine regional changes in Mn^{2+} efflux rates, allowing for a study of the dynamics in the peri-infarction zone. **Methods and Materials**: $MnCl_2$ was infused via the tail vein into C57Bl/6 mice (n=88). T_1-maps were obtained both pre- and post-infusion at multiple time points. Time dependent changes in the relaxation rate (ΔR_1) were calculated in the myocardium. For the MI mice various affected zones within the myocardium were identified and analyzed using segmentation software. The results from control and SEA0400 treated mice were applied to a pharmacokinetic model in order to estimate the Mn^{2+} transfer rates. **Results**: The ΔR_1 efflux half-life was doubled following treatment with 50 mg/kg SEA0400, with the two compartment model predicting a reduction in the myocardial efflux rate by more than a factor of two. In the MI group constant ΔR_1 values for viable and infarcted tissue were fit with radial analysis. A significant difference was observed between the efflux rates of the infarcted region to that of the viable region, with a continuous range of efflux rates in the peri-infarcted region. **Conclusions**: Quantitative MEMRI with T_1-mapping has demonstrated the sensitivity to observe changes in Mn^{2+} efflux with the ability to model the relative efflux rates. The technique also provides enough sensitivity for identifying the potentially salvageable adjacent zone as well as examining regional alterations in Mn^{2+} fluxes leading to relative Ca^{2+} information, potentially applicable to monitoring disease progression.