# Tracking hMSCs Under Ischemic Neuronal Injury Utilizing $^{1}$H and $^{23}$Na MRI at 21.1T

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## Introduction

Human mesenchymal stem cells (hMSCs) are known to secrete factors for regulating inflammatory processes in association with neural damage [1]. In addition, hMSCs exposed to low oxygen tension (hypoxia), which is their native physiological condition, may enhance therapeutic effects. In this *in vivo* study, hMSCs exposed to normoxic and hypoxic conditions were transfected with superparamagnetic iron oxide (SPIO) nanoparticles and injected intra-arterially to treat stroke resulting from a middle cerebral artery occlusion (MCAO). Serial MRI at 21.1 T was performed to acquire $^{1}$H and $^{23}$Na images of lesion progression and cell migration.

## Experimental

hMSCs were cultured following Grayson *et al* [2] and transfected with 0.86-µm SPIOs (Bangs Laboratory) for 12 h. Immediately following a 1-h transient MCAO [3], $1\times10^{6}$ cells were injected intra-arterially through the exposed common carotid artery (CCA) of Sprague-Dawley rats. *In vivo* MRI was performed using the 21.1 T (900 MHz) ultra-wide bore magnet at NHMFL. Images were acquired 24 h and 7 days after surgery utilizing high resolution, $T_2$-weighted ($T_2$W) spin echo, gradient recalled echo (GRE) and 3D $^{23}$Na GRE sequences. After scanning, animals were sacrificed by transcardinal perfusion using 4% paraformaldehyde. All heads were imaged at 11.75 T using a 100-µm 3D GRE sequence. Correlative histology was performed on 20-µm brain sections treated with Hoechst nuclear stain.

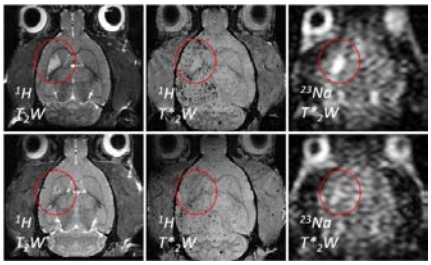


**Figure 1**: $T_2$W and $T_2$*W sequences using $^{1}$H and $^{23}$Na nuclei showing the ischemic lesion and labeled cells.

Stroke lesion was determined by visually delineate the hyperintense lesion on $T_2$W and $^{23}$Na images using AMIRA 5.3.4 (Visage Imaging). Cell labeling efficiency and subsequent clearance was determined by segmentation of signal voids created by the SPIOs by defining voids less than $S_{Contralateral} - 3*\sigma_{Contralateral}$ as a SPIO labeled cell.

## Results

*In vivo* images of the ischemic stroke lesion (red circles in **Figure 1**) show increased signal as evidence of the influx of extracellular water and sodium. Increases in tissue sodium concentration (TSC) are seen by $^{23}$Na MRI. SPIO-labeled cells are localized only within the stroked hemisphere, and after one week of the initial MRI, decreases in SPIO contrast are evident on $T_2$*W images. Sodium images show significant reductions in lesion volume for hypoxic cells compared to normoxic treated cells (**Figure 2b**).

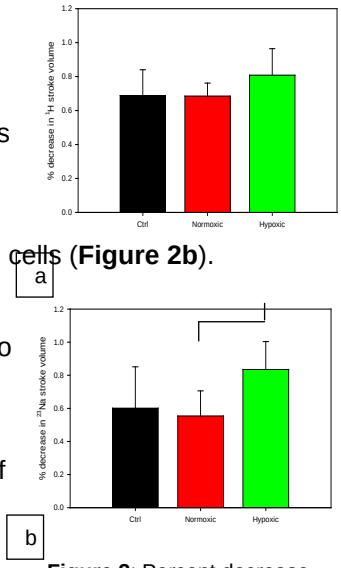


**Figure 2**: Percent decrease in a) $^{1}$H and b) $^{23}$Na stroke lesion volume. Significance determined with one-way ANOVA and LSD posthoc test ($p<0.05$)

## Conclusions

This study shows that hypoxic cells provide improved lesion recovery compared to normoxic cells as measured with $^{1}$H and $^{23}$Na sequences. Cells are visible with GRE images, and significant clearance within one week is seen. $T_2$W and $^{23}$Na images show volumetric lesion reduction but the $^{23}$Na is the only one showing significant recovery. The 21.1-T magnet provides increased $^{23}$Na sensitivity for measurements of TSC, with potential for identifying penumbral regions [4].

## Acknowledgements

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## References

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