Advancing Tools for Magnetic Resonance Image Analysis of Neurovascular Inflammation

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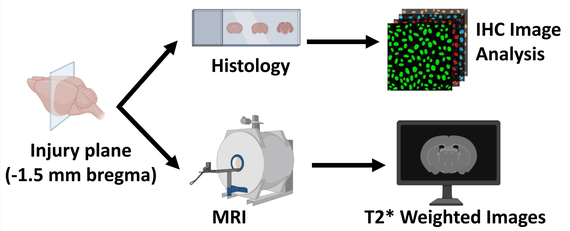
Introduction

Traumatic brain injury (TBI) is caused by a mechanical impact to the head, resulting in immediate damage to neuronal tissue. This primary injury then triggers secondary injuries involving neurovascular inflammation, leading to leukocyte infiltration and sustained inflammatory responses. During this time, inflammation can disseminate to other regions of the brain [1]. Current imaging methods, like computed tomography and conventional magnetic resonance imaging (MRI), lack the ability to accurately track and assess the inflammatory phenotype in the cerebrovasculature following TBI [2]. To address this challenge, the Wang lab has developed monocyte membrane-coated nanoparticles encapsulating superparamagnetic iron oxide nanoparticles (MoNP-SPION) as a contrast agent, which can selectively target and enhance the delivery of imaging agents to the inflamed vasculature. **The overarching goal of this project is to assess the potential of MoNP-SPION to enhance the MRI detection of neurovascular inflammation following TBI.**

Methods

Immunohistochemistry (IHC) and MRI Analysis



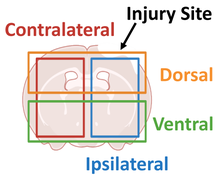


Figure 1. Two complementary analyses were performed across the injury plane: IHC with image analysis of naïve and injured brains (QuPath). MR analysis of T2* was conducted on naïve and injured mice administered MoNP-SPION. ROIs were manually selected in the injury and the cortex corresponding to distance relative to the injury. Anatomical regions were defined using the Allen Brain Atlas.

MRI Analysis Workflow

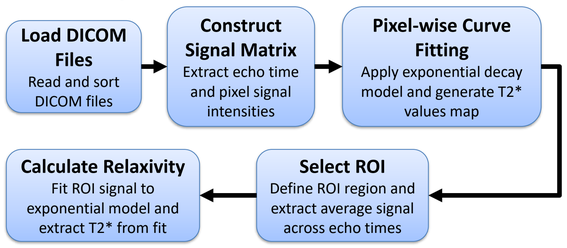


Figure 2. MRI analysis workflow implemented in Google Colab.

Results

IHC Stained Images

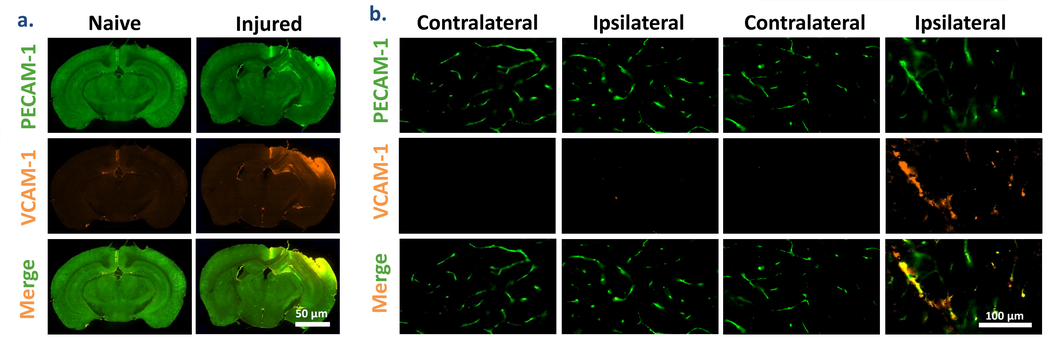


Figure 3. IHC stained brain slice showing **(a)** the full coronal section and **(b)** magnified view of selected region. VCAM-1 was labeled with TRITC (orange) and PECAM-1 with FITC (green). VCAM-1: marker for endothelial activation; PECAM-1: endothelial marker. **The IHC revealed a spatially heterogenous inflammatory response in the neurovasculature.**

Ex Vivo MRI Images

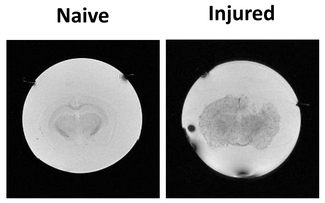


Figure 4. Representative *ex vivo* MR image of mouse brain embedded in agarose gel. Images were acquired using a multi-echo gradient. **Changes in T2* are not localized to the injury region.**

VCAM-1 Expression and MRI T2* Correlation

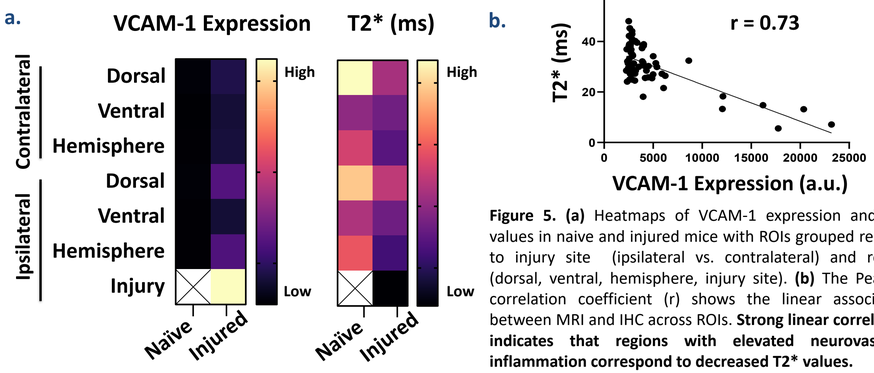


Figure 5. (a) Heatmaps of VCAM-1 expression and T2* values in naive and injured mice with ROIs grouped relative to injury site (ipsilateral vs. contralateral) and region (dorsal, ventral, hemisphere, injury site). **(b)** The Pearson correlation coefficient (r) shows the linear association between MRI and IHC across ROIs. **Strong linear correlation indicates that regions with elevated neurovascular inflammation correspond to decreased T2* values.**

Conclusion

- The strong correlation between MoNP-SPION induced T2* decay and VCAM-1 expression supports the specificity of this imaging approach for detecting neurovascular inflammation.
- **Future Work:** Expand spatial analysis to incorporate adjacent slices around injury plane and refine MRI analysis application UI.

Acknowledgments

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References

[1] Shi, K., Zhang, J., Dong, J. F., & Shi, F. D. (2019). Dissemination of brain inflammation in traumatic brain injury. *Cellular & molecular immunology*, *16*(6), 523–530. https://doi.org/10.1038/s41423-019-0213-5

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