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Lesion Extension and Neuronal Loss after Spinal Cord Injury Using X-Ray Phase-Contrast Tomography in Mice

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Abstract

Following spinal cord injury (SCI) the degree of functional (motor, autonomous, or sensory) loss correlates with the severity of nervous tissue damage. An imaging technique able to capture non-invasively and simultaneously the complex mechanisms of neuronal loss, vascular damage, and peri-lesional tissue reorganization is currently lacking in experimental SCI studies. Synchrotron X-ray phase-contrast tomography (SXPCT) has emerged as a non-destructive three-dimensional (3D) neuroimaging technique with high contrast and spatial resolution. In this framework, we developed a multi-modal approach combining SXPCT, histology and correlative methods to study neurovascular architecture in normal and spinal level C4-contused mouse spinal cords (C57BL/6J mice, age 2–3 months). The evolution of SCI lesion was imaged at the cell resolution level during the acute (30 min) and subacute (7 day) phases. Spared motor neurons (MNs) were segmented and quantified in different volumes localized at and away from the epicenter. SXPCT was able to capture neuronal loss and blood–brain barrier breakdown following SCI. Three-dimensional quantification based on SXPCT acquisitions showed no additional MN loss between 30 min and 7 days post-SCI. In addition, the analysis of hemorrhagic (at 30 min) and lesion (at 7 days) volumes revealed a high similarity in size, suggesting no extension of tissue degeneration between early and later time-points. Moreover, glial scar borders were unevenly distributed, with rostral edges being the most extended. In conclusion, SXPCT capability to image at high resolution cellular changes in 3D enables the understanding of the relationship between hemorrhagic events and nervous structure damage in SCI.