Advanced neuroimaging I: Brain & Spinal Cord/Imaging correlates of spinal cord atrophy

Govind Nair **email: bhagavatheeshg@mail.nih.gov**

Highlights

 Atrophy is typically recognized as an abnormal narrowing of the spinal cord on routine clinical scans.

. Recent advances in acquisition and analysis techniques have enabled quantification of cord atrophy with increasing sensitivity and specificity.

 While several challenges remain to be addressed, in-vivo quantitative measurements of atrophy in the CNS are increasingly being thought of as direct measures of disability in many neurodegenerative disorders and trauma, and may even serve as surrogate endpoints in clinical trials of disease modifying agents.

Title: Imaging correlates of spinal cord atrophy

Target audience: Researchers with an interest in applying MRI to quantify spinal cord atrophy.

Atrophy in the central nervous system arises from loss of myelin and/or neurons and their connections. CNS atrophy is well described in neurodegenerative disorders such as multiple sclerosis (MS), Alzheimer's and Parkinson's diseases, as well as in stroke and trauma. MRI derived brain atrophy measurements have been used as indicators of clinical disability as well as predictor of future disease burden. However, several challenges exist in translation of such measures into the spinal cord.

The small size of structures within the cord, coupled with movement of the cord from CSF pulsation and of the nearby structures during respiratory and cardiac cycles, makes it relatively more difficult to image than brain. Furthermore, while there are several tools easily available for accurate calculation of brain volume through cross-modality registration, tissue segmentation, and classification, these need to be adapted for use in the spinal cord – which is technically challenging. Recent advances to MR imaging technologies such as improved pulse sequences and phased array receive coils enable routine high-resolution scans (axial in-plane resolution of <1 mm^2) from the cervical- and thoracic-spine in a clinically feasible time.

While moderate to severe atrophy in the spinal cord is appreciable as thinning in routine clinical MRI images, its quantitative assessment, particularly in subtle cases, can improve our understanding of the disease in question, as well as contribute to therapeutic monitoring. Atrophy of the cord may be focal or generalized. It is more accurately measured on MRI images as a decrease in cross-sectional area on high-resolution scans than as a change in thickness in the anteroposterior direction. Changes to cross-sectional area measured at even a single vertebral level have been shown to correlate with clinical measures of disability in MS.[1] Early studies using tissue segmentation methods showed that cross-sectional area corresponds with clinical disability scores (such as the Expanded Disability Status Score or EDSS), but it has also proved to correlate with changes in EDSS in longitudinal studies. These changes were initially described in average size measures over a large segment of the spinal cord.[2] Based on these observations, algorithms for semiautomatic segmentation and measurement of cord structures through modeling have been proposed.[2,3] However, changes to cross-sectional area may reflect changes to WM, GM or both, and is relatively nonspecific in this respect.

A change in MRI signal as a result of functional activation (fMRI) is thought to be more specific for characterization of grey matter, and fMRI studies of the spinal cord is discussed in more de-

tail in an earlier lesson in this session. Arterial spin labeling technique, which measures the rate of perfusion (blood flow) has been developed for spinal cord.[4] However, unlike the brain, perfusion imaging in the cord needs to account for slower and multi-directional blood flow resulting in much larger watershed regions, and also requires to be done at a relatively high-resolution. Feasibility of imaging spinal cord perfusion with a single measurement technique such as modified QUIPSS-II sequence has also been demonstrated.

Diffusion tensor imaging (DTI) is sensitive to microstructural changes in the white matter. Decreased fractional anisotropy and increased perpendicular diffusivity are thought to be indicative of loss of axonal integrity and to a lesser extent demyelination in the white matter. DTI has been applied to the spinal cord in several neurodegenerative diseases, and these topics have been extensively covered in earlier talks. Other techniques such as MR spectroscopy and magnetization transfer imaging in the spinal cord have also revealed good correlations with disability. However, these techniques are debatably less specific to spinal cord atrophy.

MRI derived quantitative indices of cord atrophy are powerful indicators of neurological disability and should be studied in conjunction with brain atrophy for a more complete understanding of the disease process.

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