Towards Understanding the Whiplash Condition at 3 Tesla

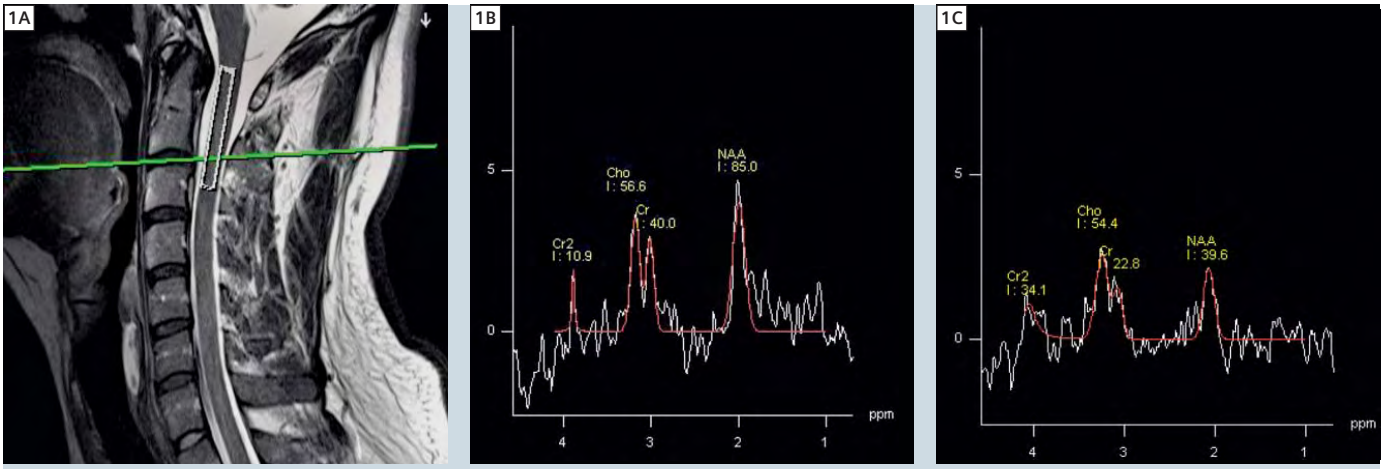
Elliott JM, PT, Ph.D.[1,2]; McMahon K, Ph.D.[3]; Cowin G Ph.D.[3]; Parrish TB, Ph.D.[4]

[1]Department of Physical Therapy and Human Movement Sciences, Feinberg School of Medicine, Chicago, IL, USA
[2]School of Health and Rehabilitation Sciences, Division of Physiotherapy, Centre for Clinical Research Excellence in Spinal Pain, Injury and Health. The University of Queensland, Brisbane, Australia
[3]Centre for Advanced Imaging, The University of Queensland, Brisbane, Australia
[4]Department of Biomedical Engineering and Radiology, Feinberg School of Medicine, Chicago, IL, USA

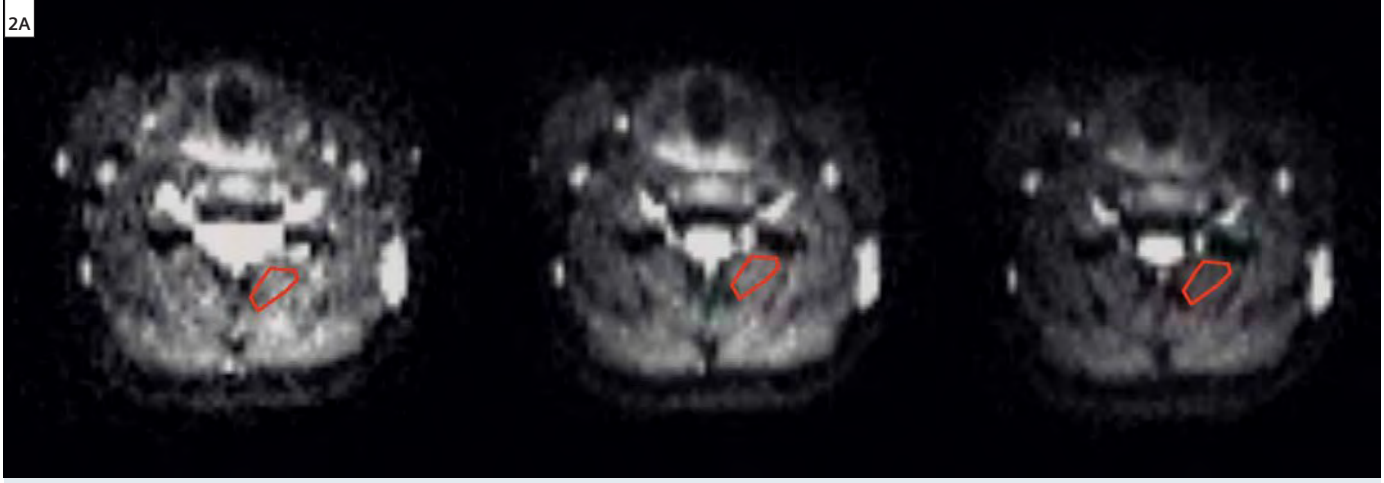
The accurate and consistent radiological observation of head and neck soft-tissue damage in patients with whiplash injuries has been largely inconsistent and highly variable [6, 33, 34, 39, 40, 44]. As a result there exists the proposition that tissue damage does not, or cannot occur, as a result of a low-speed motor vehicle collision [9]. Engineering applications [26–28, 37, 38, 49] and controlled animal studies [48, 51-53] have informed us of what can happen to a number of vulnerable tissues in the cervical region following whiplash, including the facet capsule, dorsal root ganglion and nerve roots [36, 46, 48, 51–53] At the forefront of clinical enquiry however, is how to best determine what has happened to these tissues in patients with whiplash injury. Due to the persistent nature of symptoms in some subjects with whiplash injury, it is clinically important that objective and quantifiable measures to characterize the whiplash condition be made available. This is especially important for the exploration and development of more informed treatment strategies aimed at retarding if not preventing the expression of persistent pain for some patients.

For many of the laboratory-created lesions shown to occur in animal and bioengineering models, there are currently very few, if any, clinical means for their diagnosis available to practicing clinicians. Plain films lack sensitivity for ruling out bony lesions and the images lack the detail to quantify strained facet joint capsules and/or tears in discs. Computed tomography (CT) can identify some cervical spine fractures but rigorous longitudinal studies have not been undertaken to determine fracture prevalence in this population. More importantly, CT is unable to assess soft tissue damage in the cervical spine and surrounding muscles.

Conventional magnetic resonance imaging (MRI) has largely failed to consistently reveal soft-tissue damage in patients with whiplash, but this may relate to the use of generic clinical protocols (typically 1.5T and lower) and limitations in the resolution. The advent of higher-field systems (3T and greater) has provided a foundation for measuring physiologic processes that could be associated with tissue damage. Preliminary MRI evidence identifying the unique expression of neck muscle degeneration (fatty infiltrates) at 4-weeks post injury in those who transit from acute to chronic pain suggests that this may be so [12]. Muscle changes



1 **(1A)** Localization of SVS for the cervical cord at the C2/3 segmental level with **(1B)** corresponding metabolic peaks for NAA, Cr, and Cho in healthy control and **(1C)** subject with chronic whiplash *(adapted from Elliott et al., Spinal Cord [16])*.



2A DWI scans of a ROI over the left cervical multifidus muscle (b-values of 0–250 s/mm²).

did not occur in patients with lower levels of initial pain or in patients with chronic non-traumatic neck pain [13] suggesting traumatic factors play a role in altering the make-up of the neck muscles.

We have developed a comprehensive advanced MR imaging protocol that assesses the cervical spine at the metabolic, microscopic and macroscopic level. Furthermore, by applying this protocol, in tandem with clinical signs and symptoms, over several weeks, it may be possible to classify which patients are at risk for transiting to a persistent pain state. This non-invasive methodology to quantify several physiologic processes may afford clinicians the ability to triage their patients with confidence. Furthermore, it may be possible to determine if a person has suffered a traumatic event, which may be contributing to their pain and disability.

Table 1: SVS_SE Sequence

TR 2000 ms
TE 135 ms
160 averages with HEP
coil elements neck 1,2
coil elements spine 1

Table 1: Parameters for the SVS_SE Sequence.

MR Spectroscopy – metabolite scale

Alterations in MR visible metabolites, such as Lactate (Lac), N-Acetylaspartate (NAA), Creatine (Cr) and Choline (Cho) have been demonstrated in neurological disorders [5, 31] traumatic brain injury [7], and cervical myelopathy [24] and may have predictive capacity [7]. Our previous work has reported the presence of altered cord biochemistry in a small sample of patients with chronic whiplash related pain and disability [16]. However, this study did not resolve the temporal development of these changes or if they are unique to those with poor functional recovery. Such work is well underway.

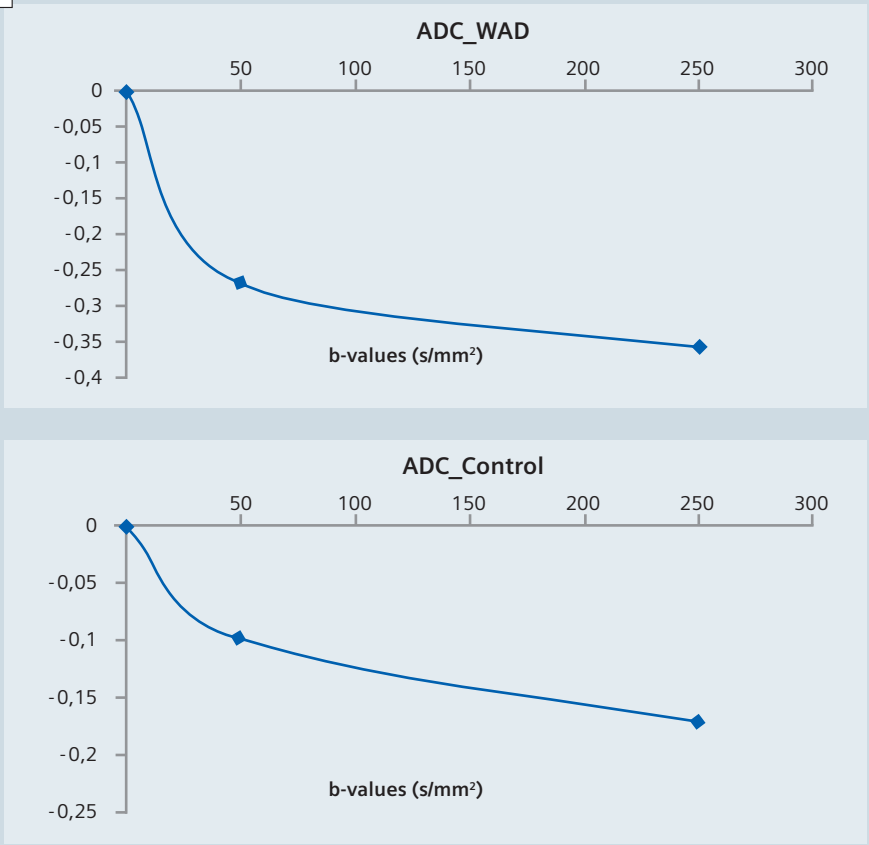
The current protocol uses a single voxel spectroscopic (SVS) technique to investigate the spinal cord at the C2-C3 level. Using a high resolution T2 TSE sagittal scan along with the axial and coronal localizer scans, a long rectangular voxel (5 mm x 7 mm x 40 mm) is placed in the middle of the cord (Fig. 1). The parameters are listed in Table 1. The acquisition is not cardiac triggered but this is possible to reduce movement artifacts induced by CSF flow. We currently are using a long TE (135 ms) SVS PRESS acquisition to reduce the contamination of short T2 metabolite species as well as have lactate out of phase with the nearby lipid signal. This acquisition is 5:28 minutes after the voxel has been shimmed properly. We are using the ADVANCED shim* WIP that provides a robust and rapid shim map. The typical shim result is a FWHM of ~15 Hz at 3T, which translates into a metabolite line width of 6 Hz. The optimized shim is achieved by manually setting the shim volume to be slightly larger (5 mm in each direction) than the actual acquisition voxel. Following this acquisition, a quick (8 average) acquisition is obtained without water suppression to use as a standard over time, which is helpful with repeated measures. These 30-second spectra assess the total amount of water present and can be used for control over placement of the voxel over time and calculate actual concentration of metabolites.

*Work in progress. This information about this product is preliminary. The product is under development and not commercially available in the U.S., and its future availability cannot be ensured.

Diffusion-weighted imaging of muscle – microscopic scale

Diffusion-weighted imaging (DWI) of the muscle system has the potential advantage over conventional sequences to help uncover the early physiological mechanisms underlying the manifestation of intra- or inter-muscular fatty infiltrates. Diffusion properties of water have been quantified with DWI in many different organ systems (e.g. brain and spinal cord, kidneys, heart, lumbar intervertebral disc and the prostate) [1, 2, 29, 22, 25, 30, 35, 43, 17, 18, 47, 3, 4, 50]. Normal water diffusion is affected by the presence and orientation of physical tissue barriers (e.g. cell membranes,

2B



2B ADC maps (at 1.5T) for the left cervical multifidus muscle in patients with chronic whiplash associated disorders (WAD) and healthy controls [16].

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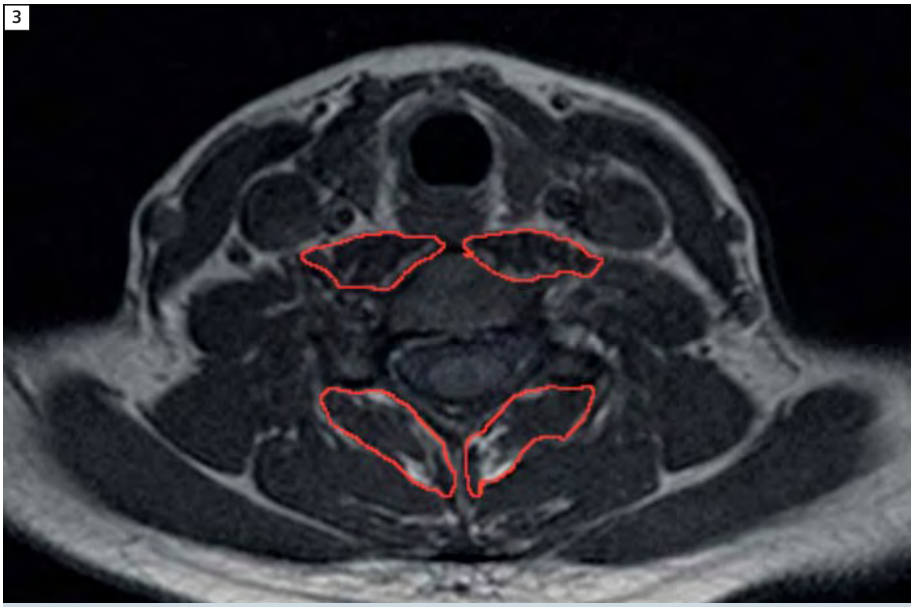


3 T1-weighted axial MR image at the C6 vertebral level demonstrating outlined ROIs for the right and left longus colli and the right and left posterior cervical multifidus. Increased signal, indicative of fatty infiltration, is noted in both sets of muscles in a subject with chronic whiplash associated disorders.

proteins, myelin sheaths and/or lipids) [45]. The measure quantifies the microscopic movements of water diffusion via the mean apparent diffusion coefficient (ADC) [20, 45, 39]. Passive enlargement of the muscle cell following tissue damage may be associated with an increase in ADC [23]. We have shown altered ADC maps for the cervical multifidus in a small sample of subjects with chronic whiplash when compared to healthy controls [16], suggesting a passive enlargement of the muscle cell (e.g. atrophy) (Figs. 2A, B). However, the temporal development of such changes and whether they are unique to those at risk for chronicity is unknown at this stage. Such evidence could provide for a sensitive indicator of early tissue injury at a stage when muscle degeneration remains potentially salvageable [23, 32]. Thus, the potential diagnostic and prognostic value of in-vivo DWI sequences for quantifying the temporal degeneration of muscle tissue, at a cellular level, in whiplash is clear.

Diffusion-weighted imaging parameters:
The DWI scan uses a spin-echo, echo-planar acquisition with an in-plane resolution of 1.6 mm, a thickness of 5 mm, TR 4000 ms and TE 65 ms to reduce artifacts. The acquisition is taken in the axial plane using an inversion pulse to reduce the signal from fat with a TI of 160 ms. The diffusion scan is the simple 3-scan trace acquisition but the number of diffusion-weightings is increased to 5. The b-values used at 3T are 0, 50, 100, 200, and 300 s/mm^2. This is quite different from brain DWI where a typical b-value is 1000 s/mm^2. Due to signal-to-noise constraints and distortions of the signal, the b-values are small. From all of the b-value data, trace and ADC images are generated for each of the 14 slices in 7:08 minutes.

Fat/water imaging – macroscopic scale

The demonstration of neck muscle fatty infiltrates on T1-weighted imaging in chronic whiplash (Fig. 3) [11, 14, 15] is interesting as such findings were not

featured in those with chronic non-traumatic neck pain [13] and their expression (between 4 weeks and 3 months post-injury event) on standard T1-weighted images appears unique to only those who transit [12]. It is postulated that these muscle changes represent one neurophysiologic basis for the transition to chronic pain in this population. While the mechanisms underlying their temporal development and contribution towards the transition remain unclear, it is possible that newer MRI techniques (MRS and DWI) could help quantify earlier physiologic changes at the spinal cord and muscle cell that may precede observable muscle changes on T1-weighted sequences. An earlier detection of such mechanisms could prove crucial for identifying the early presence of select biochemical changes in spinal cord metabolism with the attendant later changes in muscle physiology and the development of chronic pain and disability.

Fat/water separation

Several approaches are possible to measure the water and fat composition of a voxel. These include a dual acquisition method, where one image is fat suppressed [19] (water image) and a standard image is collected (fat and water image). The difficulty of this type of acquisition is that it relies on the uniform frequency difference between water and fat across the whole volume of excitation, which is often difficult to obtain especially at high magnetic fields. A fat suppressed acquisition using a short-tau inversion recovery (STIR) sequence is possible, but the T1 of fat has to be assumed, which may vary depending on the subject or the evolution of the infiltration of the muscle [8]. An alternative is the Dixon method [10], where one collects data at an echo time when water and fat are in-phase and at an echo time when water and fat are out of phase. The data can be combined in such a way that they generate a fat and water image. This method works well when there are no field inhomogeneities, which is often not the case. Current methods collect multiple echo time data to improve the estimation of the fat and water images. This method has been applied successfully in the liver and musculoskeletal application using an iterative least squares solution called IDEAL [41, 42]. The method we have used in the study of whiplash subjects collects 8 different echo times sufficiently spaced on the unit circle to provide adequate phase information for the variable projection (VARPRO) algorithm*, generating a globally optimal solution for the water/fat decomposition [21].

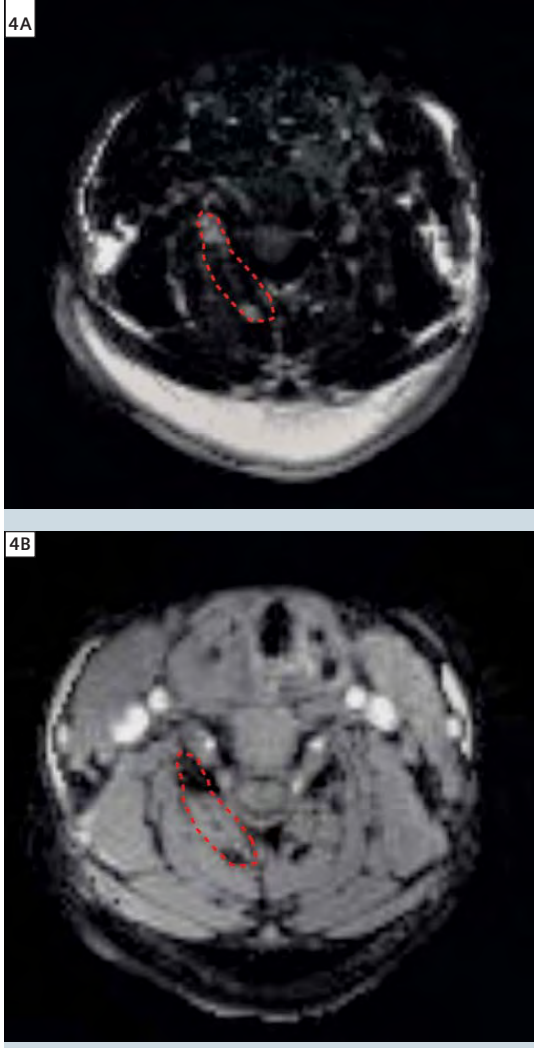
Saurabh Shah implemented the VARPRO algorithm and acquisition sequence in the Cardiovascular R&D team located at Northwestern University, Chicago, IL, USA. Currently this feature is a WIP at *syngo* MR B17 software (Fig. 4A, B).

A three-dimension 230 mm field-of-view (FOV) axial gradient echo acquisition was used to collect the data required for the VARPRO algorithm. The sequence parameters are TR 23.81 ms, 8 echo times with a spacing of 1.78 ms starting at 1.36 ms. A single slab is placed over the cervical spine with 36 partitions and a partition thickness of 3 mm and slab oversampling of 22% to prevent aliasing in the 3D direction. The in-plane resolution is 1.4 mm using a rectangular FOV of 75% resulting in an acquisition time of 2:06 minutes.

*Work in progress. This information about this product is preliminary. The product is under development and not commercially available in the U.S., and its future availability cannot be ensured.

Conclusions

The observed alterations in spinal cord biochemistry, muscle water diffusion, and fatty infiltration in chronic whiplash [16] provides preliminary evidence for the early detection and classification of the patient with a whiplash injury. Current studies indicate that the physiologic measures assessed with the multi-dimensional imaging protocol outlined above show promise for detecting which patients may be at risk for transitioning from acute to persistent pain following a low-velocity traumatic event involving the head and neck.



4 ROIs in **(4A)** fat (VARPRO* based) and **(4B)** water for the right cervical multifidus muscle. The ROIs are automatically copied to the same location for both images and relative differences (signal loss) between the fat and water images can be calculated.

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Contact
James M. Elliott PT, Ph.D.
Department of Physical Therapy
and Human Movement Sciences
Feinberg School of Medicine
Northwestern University
645 N. Michigan Ave
Suite 1100
Chicago, IL, 60611
USA
j-elliott@northwestern.edu