

# Acute Whiplash: Clinical and Finite Element Analysis

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**Abstract:** *Study Design:* A prospective 1-year study of whiplash patients presenting with either isolated neck pain (WADI/II), or neck pain with neurological signs/or symptoms (WADIII).

*Objective:* We hypothesize that WADI/II and WADIII are distinct entities with significant differences in clinical presentation, pathoanatomy, and prognosis.

*Summary of Background Data:* Whiplash associated disorders (WAD) are disparate and can range from mild neck pain (WADI/II), to insults associated with neurologic sequellae (WADIII), and even fracture/dislocations (WADIV). To date, literature considers post whiplash syndrome a single clinical and pathologic entity along a spectrum with escalating grades of severity (WADI-IV). However, a diverse pathogenesis may underlie the different grades of WAD, and these distinctive pathoanatomies may better portray the prognosis of these entities.

*Methods:* Thirty one subjects were divided into a WADI/II control group and a WADIII study group. All subjects underwent H&P, radiographic evaluations, and clinical outcome measures (collected at 3, 6, and 12 months). A finite element analysis (FEA) technology (SCOSIA©) was used to predict stresses within the neuraxis. Statistical analysis was performed (Student T-test, Wilcoxon Signed-Rank test) with significance set at p=0.05.

*Results:* At presentation, WADI/II group demonstrated better neurologic assessments, functional performances, and higher quality-of-life measurements in comparison to WADIII cohort. Yet VAS scores were comparable between the two groups. At final follow-up, both groups reported improvements in neurologic status and disability symptoms. However, functional recovery and quality-of-life measures significantly improved in WADIII, and conversely deteriorated in WADI/II. Additionally, WADI/II also portrayed notable worsening of pain symptoms. Litigation claims were comparable between the two groups. FEA predicted higher stress within the neuraxis of WADIII, most notably in subjects with preexisting stenosis and odontoid retroflexion.

*Conclusion:* WADI/II and WADIII are distinct entities with different pathoanatomy and outcomes. Musculoskeletal injury precipitates WADI/II pain symptoms while neuronal stretching leads to WADIII neurologic injuries. Notably, most of the neurologic injuries in WADIII are recoverable.

**Keywords:** Whiplash, whiplash associated disorder (WAD), neck pain, cervical cord stress injury, finite element analysis.

## BACKGROUND

There are 1.5 million cases of whiplash each year in the United States. Whiplash is most commonly the result of acceleration deceleration injuries during motor vehicle accidents, but can also occur from a fall or a sports injury. Traditionally, neck pain resulting from whiplash injury is considered to be caused by injuries to muscles and/or ligaments. Imaging studies (i.e. radiographs, MRI, and CT) most often show no evidence of fracture, instability, or disruption of soft tissue [1, 105-107]. Symptoms associated with whiplash injury range from mild neck pain with no physical findings to debilitating injuries with long-

term neurological sequellae. Patients may complain of headache, paresthesia, dysesthesia, weakness, vision disturbance, auditory changes, imbalance, vertigo, altered memory, personality change, dysarthria, dysphagia, and sleep apnea.

To improve communication among practitioners and assist with prognosis, a classification system for whiplash associated disorders (WAD) was described as follows: [2] WAD I are those injuries with neck pain but no physical findings; WADII are those injuries with neck pain and physical exam findings such as tenderness to palpation of the posterior neck; WAD III include injuries with associated neurological signs or symptoms, and WAD IV have an associated fracture or dislocation. Numerous studies have evaluated outcomes following acute whiplash injury, but most studies are retrospective including a wide range of injury. According to previous literature, the more severe

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**Table 1. Brainstem Disability Index**

The following 20 symptoms may be referable to pathology at the level of the brainstem. Please indicate yes or no whether you have any of the following symptoms on a recurring or chronic basis.
Double vision
Memory loss
Dizziness
Vertigo
ringing in the ears
Speech difficulties
Difficulty swallowing
Sleep apnea
Snoring or frequent awakening
Choking on food
Hands turn blue in cold weather
Numbness in your arms and shoulders
Numbness in your back and legs
Get tired very easily
Unsteady walking
More clumsy than you used to be
Urinate more often (every 1-2 hours)
Irritable bowel disease or gastro esophageal reflux disease
Weaker than you would expect in your arms or hand
Weaker in your legs
5% each positive response, 0-100%

injuries of whiplash are associated with the worse long term outcomes, and persistent, often disabling symptoms [3, 4].

In this study, the authors hypothesize that whiplash patients with neurological findings (WAD III) are distinct from whiplash patients with neck pain but there are no neurological findings (WAD I/ II) with regard to not only clinical presentation, but also in terms of pathoanatomy and prognosis. In the following prospective comparison of subjects presenting with acute whiplash injury, illustrative finite element analyses of the neuraxis under conditions of deformative stress are presented in the two comparison groups of WAD. The authors theorize that a preexisting, underlying condition or deformity may predispose some individuals to pathological deformative stress of the neural elements at the time of the injury, in contrast to others who manifest only muscular/ligamentous injury. Therefore, these two groups of WAD subjects should be considered as distinct entities in terms of etiology, treatment, prognosis, and range of associated conditions.

## MATERIALS AND METHODS

Institutional Review Board (IRB) approval was obtained prior to conducting the study. Subjects between the ages of 18 and 80 years old who were involved in a MVA or fall, presenting to a Level I trauma center, with complaints of neck pain were reviewed for eligibility. Exclusion criteria

included: fracture, dislocation, or instability (WAD IV patients); patients with a potentially atraumatic etiology of neck pain, including infection, tumor, congenital or metabolic disease; patients requiring spine surgery following their presentation (i.e. for degenerative, traumatic, infectious, or neoplastic pathology); and patients with late presentation following their whiplash injury.

Whiplash patients with no neurological signs or symptoms (WAD I/II) were enrolled into the comparison or control group. Whiplash patients with associated neurological signs and/or symptoms (WAD III) were enrolled into the study group. Upon presentation, patients underwent routine cervical spine x-rays, including anteroposterior (AP), lateral, and odontoid views. When the x-ray series was inadequate (C7-T1 not visualized), a cervical CT scan with coronal and sagittal reconstructions was performed. All patients (i.e. study and comparison groups) underwent a cervical MRI.

A history and physical examination was performed on each subject, including history of the traumatic event (i.e. mechanism, speed of vehicle, direction of impact, loss of consciousness, presence of seatbelt, associated injuries) as well as the nature, severity, and location of the pain and any associated neurological symptoms. Pain was assessed objectively using the Visual Analog Scale (VAS) ranging 0 (no pain) to 10 (extremely severe pain). The patient's neurological status was assessed with the American Spinal Injury Association (ASIA) Impairment Scale. Brainstem disability was assessed using the Brainstem Disability Index [5], a collation of 20 symptoms of brainstem dysfunction, see Table 1. Function was assessed with the Karnofsky Performance Scale and Neck Disability Index. Quality of life was assessed with the SF-36 physical component and mental component questionnaires. Clinical outcome measures were repeated at 3, 6, and 12 months following the injury for the study group and at 12 months for the comparison group. At 12 months all subjects were questioned on litigation status. All data collected was entered into a computerized database and password protected.

The data were collected by a research assistant, and therefore not subject to the influence of the investigator during the patient interview. The SF-36 is valid when tested against other outcome instruments and is an approved instrument for measurement of aspects of physical and mental functions [6-8]. The ASIA scale is useful in measuring slight changes in sensory and motor function. The Karnofsky Index is another instrument that is useful in measuring function [9]. Although not validated, The Brainstem Disability Index [5] is an instrument used to measure improvement in symptoms ascribed to neurological dysfunction of the brainstem [10-21]. A score of 100 represents the presence of all 20 symptoms and significant disability (Table 1).

All data were entered into a computerized database managed by a third-party (Elder Research Inc., Charlottesville, VA). Data were de-identified, time-stamped, and redundantly backed up. Cryptographic signatures derived from content of the data and times of entry were used to ensure against accidental loss or modification of data.

**Table 2. Gender, Age, and Mechanisms of Injury Distribution**

	Gender	Age (mean)	MVC	Fall	Sports	Miscellaneous (Hyper-extension)
Cases <i>n=21</i>	62%M vs. 38%F	45y+7months	57.14%	28.57%	14.29%	0%
Controls <i>n=10</i>	60%M vs. 40%F	47y +4months	40%	50%	0%	10%
<i>P-value</i>	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

**Table 3. Objective Neurologic Assessment - ASIA Score**

ASIA	0 months	12 months	<i>P-values</i>
Cases	284	318	0.0002
Controls	324	324	0.5
<i>P-values</i>	0.01	0.0139	

Groups were compared both with Student T-tests and with non-parametric Wilcoxon Signed-Rank tests, in order to lessen reliance upon the normality assumption. Our null hypothesis was that there was no significant difference in prognosis between the two groups. Statistical significance was set at  $p = 0.05$ .

The PRIMEGen program of finite element analysis (FEA) was used for modeling the loading and strain of the brainstem and spinal cord. The magnitude and location of the stress experience within the brainstem and spinal cord are computed with Spinal Cord Stress Injury Analysis (SCOSIA ©) technology [5]. Accordingly, the SCOSIA system uses the Young's modulus of elasticity for grey and white matter from bovine as provided by Ichihara *et al.* to model the properties of stress in the grey and white matter as well as the pons and mid thorax [22]. As Ichihara *et al.* note, the elastic properties has little difference between live vs. dead spinal cord tissue [23], and the histopathological changes are the same from the compression of the bovine cervical spinal cord or compression of the human cervical spinal cord [24]. Thus, it was reasonable to extrapolate the material properties derived by Ichihara *et al.* for bovine spinal cords in a human spinal cord model.

## RESULTS

Between March 2006 and December 2007, Thirty-one subjects met study criteria. Of these subjects, there were 19 males and 12 females. The study group (WAD III), consisted of 21 subjects (13 male and 8 female). The comparison group (WAD I/II) consisted of 10 subjects (6 male and 4 female). The average age of all subjects was 46 years (range 21 years to 71 years). There was no significant difference in the age (Mean age in study group = 46 years, mean age in comparison group = 47 year) or sex distributions between WAD I/II and WAD III (Table 2).

### Mechanisms of Injury

Within the study group (WAD III), twelve subjects suffered MVA (57%), 6 subjects a fall (29%), and 3 subjects a sports related injury (14%). In the comparison group

(WAD I/II), four subjects suffered MVA (40%), 5 subjects a fall (50%), and 1 subject a sports related injury (10%).

### Neurological Assessment

At presentation (day 0), the WAD III group scored significantly lower (i.e. more pathological) than the comparison group on the ASIA scale (284 vs. 324 points) ( $p < 0.01$ ). At final follow-up (12 months), the WAD III group improved their neurological scoring by 34 points (total 318 points), and this improvement was statistically significant ( $p = 0.05$ ). The comparison group (WAD I/II) maintained their original ASIA score (324 points). (Table 3) The difference in prognosis between the two groups was statistically significant ( $p = 0.013$ ).

At presentation (day 0), the WAD III group showed numerous bulbar symptoms with an average score of 84.55% (16.9 bulbar symptoms out of the 20 listed) on the brainstem disability scale. On the other hand, the control group (WAD I/II) presented with an average score of 15% (3 out of 20 symptoms). The difference in bulbar symptoms, based on the brainstem disability scale, between these groups was significant at  $p < 0.001$ . At final follow-up (12 months) the WAD III group noted improvement of symptoms reflected by a significant improvement in brain-stem score to an average of 35.60% (7.14 out of 20 possible bulbar symptoms), ( $p = 0.05$ ). (Table 4)

Amongst subjects with whiplash, the most common presenting bulbar symptoms were dizziness, vertigo, and numbness or weakness in the arms and hands. Resolution was most commonly seen in vertigo, clumsiness, gait changes, and weakness in the arms and hands. At 12 months, persistent bulbar symptoms included sleep disturbances (including apnea and frequent awakening), sexual difficulties, and fatigue.

### Pain Assessment

At presentation (day 0), the WAD III group had a mean pain score of 5.6/10 which was similar to the mean score of the comparison group, 6/10. At final follow-up (12 months), the WAD III group had improved to an average VAS score

**Table 4. Brainstem Disability Index scores**

HMBSS (0-20 points)	0 months	12 months	P-values
Cases	84.55% (16.9/20)	35.60% (7.14/20)	0.05
Controls	15% (3/20)	8.45% (1.66/20)	
P-values	<0.001		

**Table 5. Pain Assessment – Visual Analogue Scale (VAS)**

VAS (0-10 points)	0 months	12 months	P-values
Cases	5.55	1.65	<0.001
Controls	6.00	3.87	
P-values	0.15	<0.001	

**Table 6. Neck Disability Index Score**

NDI	0 months	12 months	P-values
Case	42.24	19.60	< 0.001
Control	52.75	27.00	
P-values	0.02	0.01	

**Table 7. Disability Assessment – Karnofsky Performance Scale (KPS)**

KPS	0 months	12 months	P-values
Case	70.16%	88.13%	<0.001
Control	86%	84.24%	
P-values	< 0.001	0.01	

of 1.6/10, which was lower than the mean score for the comparison (WAD I/II) group of 3.8/10. The difference in these results at 12 months was significant ( $p<0.05$ ). Improvement within each group was statistically significant. (Table 5).

At day 0 mean NDI score in the WAD III group was 42.24 and mean score in the comparison group was 52.75 ( $p=0.02$ ). At 12 months, NDI score improved to 19.6 in the WAD III group and 27.0 in the comparison group ( $p=0.01$ ). Improvement within each group was statistically significant ( $p<0.05$ ). (Table 6)

#### Functional Assessment

At presentation (day 0), mean KPS score was 70.16% in the WAD III group and 86% in the WAD I/II group and this difference was statistically significant with  $p < 0.001$ . At final follow-up (12 months), subjects in the WAD III group scored significantly higher with mean of 88.13% ( $p<0.001$ ). In contradistinction, the comparison group had a non-significant decrease in mean score to 84.24%. (Table 7) The difference between the two groups at 12 months was significant at  $p=0.01$ .

#### Quality of Life Surveys

At presentation (day 0), the WAD III group had a mean SF-36 physical score of 32.61 while the WAD I/II had a

mean physical score of 54.59 and this score difference was statistically significant with  $p<0.001$ . At final follow-up (12 months), the WAD III group showed significant improvement in SF-36 score (mean of 49.17), while the comparison group showed a significant decline in SF-36 score (mean of 44.74), ( $p<0.05$ ). Absolute comparisons between WAD III and WAD I/II at 12 month follow up were not statistically significant, but comparisons between mean improvement (or decline) in each group were ( $p<0.001$ ). (Table 8)

At presentation (day 0) the WAD III group had a mean SF-36 mental score of 40.16, while WAD I/II had a mean mental score of 54.75. This difference in mental score between the two groups was statistically significant at  $p < 0.001$ . At final follow-up (12 months), the mean mental score of WAD III had improved to 49.05, a statistically significant improvement ( $p<0.05$ ). Mean mental score in the comparison group declined to 54.22 at final follow-up. This decline was not statistically significant. The difference in SF-36 mental score remained significant at 12 months ( $p<0.05$ ). (Table 9)

#### Litigation

At 12 month follow-up, the two groups were similar in regards to pending litigation claims. 19% of subjects within

**Table 8. Physical Health Survey – (SF36 Physical)**

SF36-Physical (0-90 Points)	0 months	12 months	P-values
Case	32.61 points	49.17 points	< 0.001
Control	54.59 points	44.74 points	
P-values	< 0.001	0.05	

**Table 9. Mental Health Survey – (SF36 Mental)**

SF36-Mental (0-90 Points)	0 months	12 months	P-values
Case	40.16 points	49.05 points	< 0.001
Control	54.75 points	54.22 points	
P-values	< 0.001	< 0.001	



**Fig. (1).** Flexion X-Ray of WAD III subject J10.

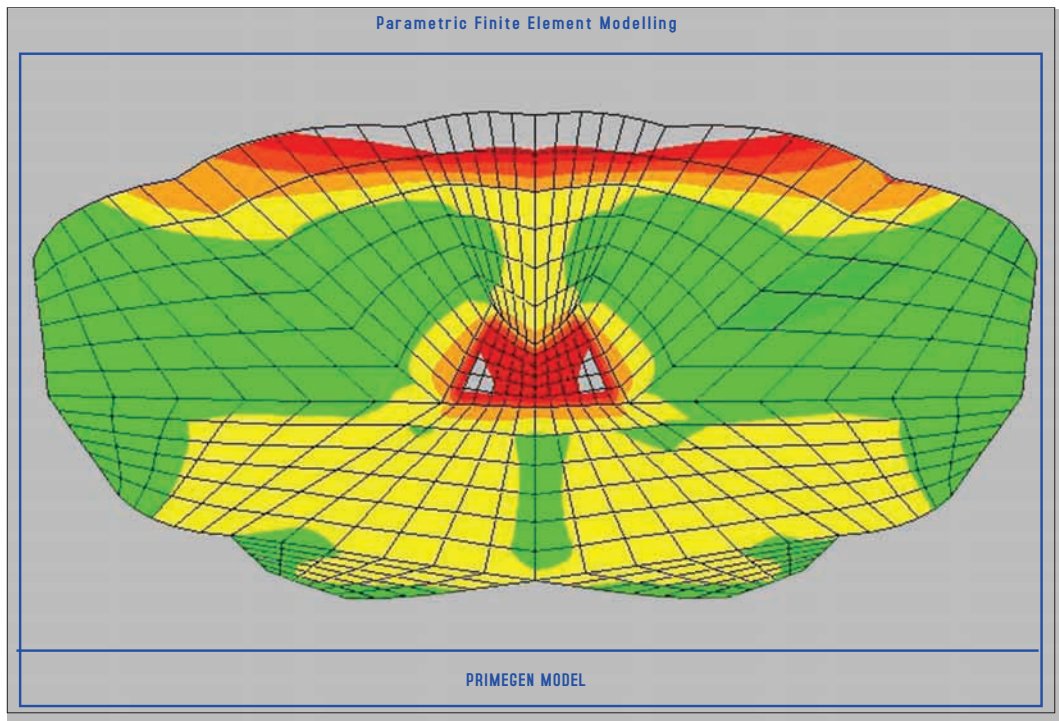
the WAD III group (4 patients) and 20% of the WAD I/II group (2 patients) were involved in litigation.

**Finite Element Analysis (FEA)**

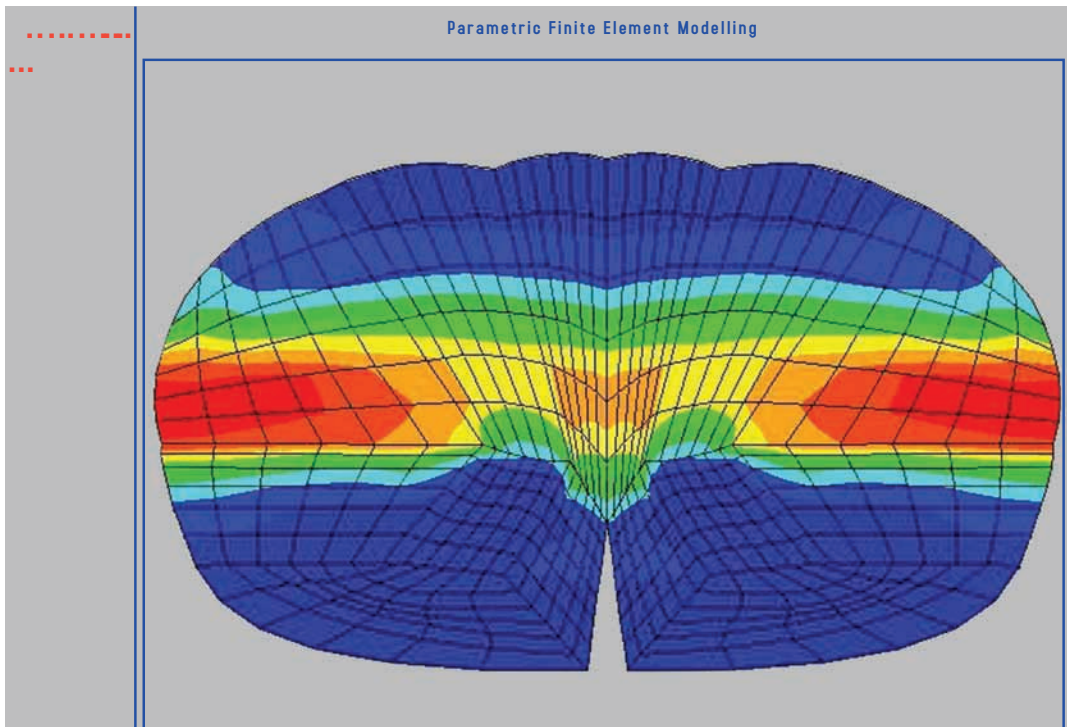
FEA was performed on two representative patients. FEA of the neuraxis (brainstem and spinal cord) of a WAD III subject with pre-existing spinal stenosis and retroflexion of the odontoid process upon flexion of the neck is compared to a subject from the WAD I/II group. A comparison of these axial representations of predicted stress that is developed during flexion provides insight into the pathophysiology underlying the neurological findings of subjects with whiplash injuries.

**Whiplash Subject with Spinal Stenosis and Retroflexion of Odontoid**

Prior to the incident, WAD III subject 10 was neurologically intact. Following the motor vehicle accident (rear-end collision), the subject reported the following symptoms of moderate pain (3/10), headache, sleeping disturbances, weakness in the arms and hands, and numbness in the arms, shoulders, hands, and legs. His gait was unsteady. His KPS score of 70 reflected moderately severe disability. The flexion X-Ray revealed retroflexion of the odontoid which violated Wackenheim’s line, thereby constituting mild basilar invagination on full flexion Fig. (1). The

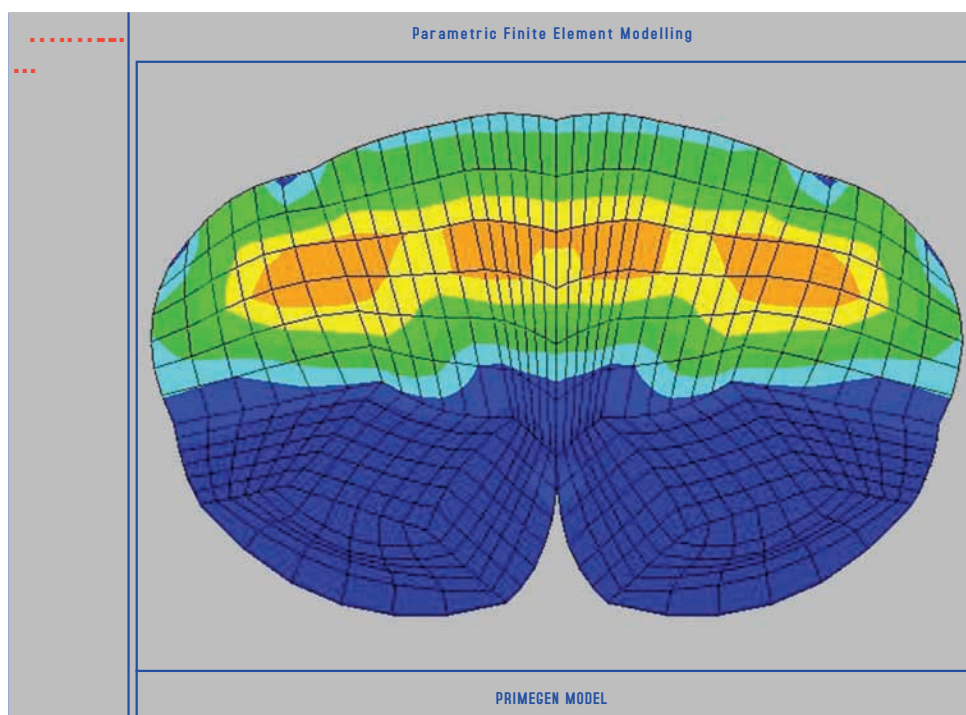


**Fig. (2A).** Predicted stresses in the lower brainstem on normal neck flexion in WAD III subject J10. Mild basilar invagination sets up deformative stress in the brainstem on full craniocervical flexion.



**Fig. (2B).** Predicted stresses at the C3 level on normal flexion in WAD III subject J10. Spinal stenosis leads to deformative stress in the cervical spinal cord on flexion.





**Fig. (2C).** Predicted stresses at the C4 level on normal flexion in WAD III subject J10. Spinal stenosis leads to deformative stress in the cervical spinal cord on flexion.

MRI demonstrated stenosis, presumably preexisting, at C3-4, C4-5, C5-6, C6-7.

The axial views of the upper spinal cord (Figs. 2A-C) show very high predicted von Mises stresses (the aggregate of strain and compression). Predicted stresses in the lower medulla were evident, most prominently in the dorsal areas. The FEA predicted high stresses of  $58\text{N/cm}^2$  in the mid-region of the cord, in the region of the corticospinal tracts. Lower in the spine, the stresses were predominately dorsal, reflecting injury to the dorsal columns. At 12 months the patient reported no pain, weakness, or sensory loss as well as no headache or sleep disturbances. He reported the ability to carry on normal activities with minimal discomfort, and a quality of life that was approaching his pre-injury quality of life.

### Comparison Subject

On presentation, the comparison WAD I/II subject 18, reported substantial musculo-ligamentous pain, but no neurological symptoms. On exam there were no neurological findings and no radiological abnormalities. Axial views through the medulla and the spinal cord show predicted von Mises stress is very low (less than  $5\text{N/cm}^2$ ) during flexion (Figs. 3A and 3B).

### DISCUSSION

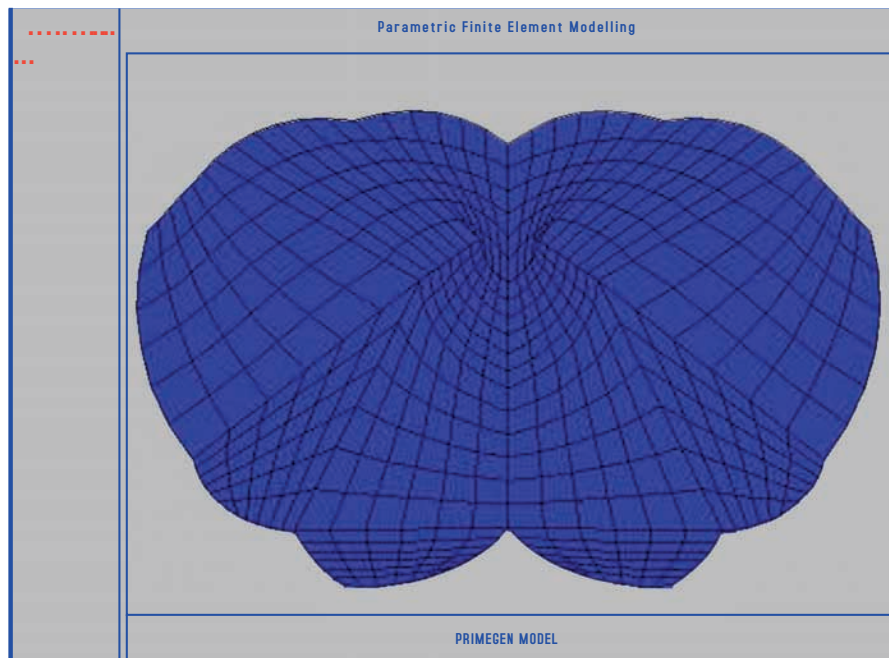
At follow up of one year, the present study demonstrates significant improvement in neck pain and neurological findings in both the study (WAD III) group and the comparison (WAD I/II) groups. Somewhat surprisingly, however, the magnitude of improvement was statistically greater in the WAD III group. Indeed, at one year, neck pain symptoms in the study WAD III group were significantly less than the comparison (WAD I/II) group.

Neurologic symptoms improved in the study WAD III group. At one year following injury, the WAD III group, sensori-motor deficits, showed significant improvement as measured by the ASIA score (Table 3). Furthermore, the Brainstem Disability Index demonstrated a significant improvement in the WAD III group; that is, the brainstem ("bulbar") symptoms had to a large extent resolved at 12 months.

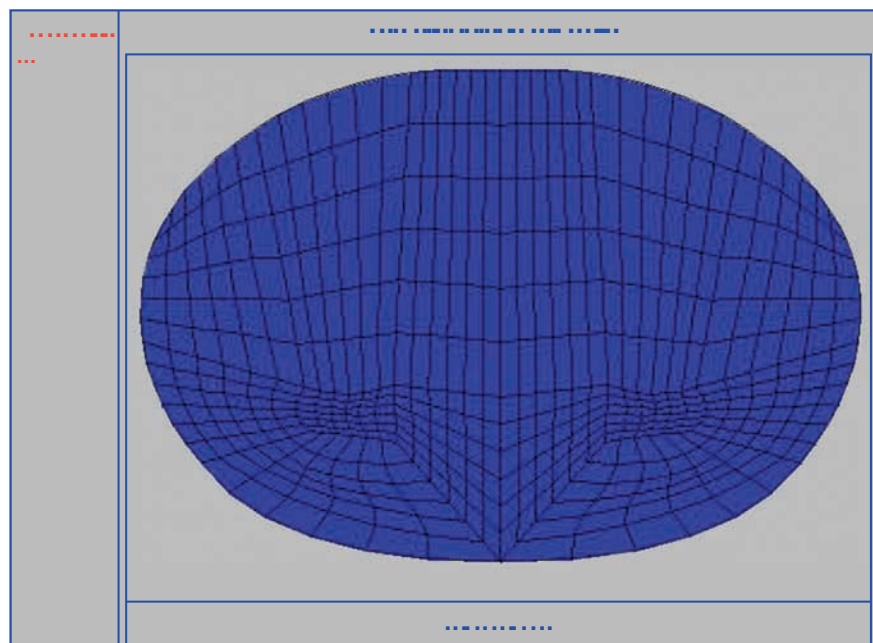
Neurological improvement was also mirrored in both function and quality of life. In the WAD III group, function measured by Karnofsky scale was significantly impaired following the acute whiplash injury (average 70 in the Karnofsky scale), but improved to near normal (average Karnofsky scale of 90) at 12 months. In Contrast, the comparison (WAD I/II) group demonstrated no improvement; the Karnofsky scale decreased slightly from 88 to 84 over the 12 month period.

The physical and mental health status of each subject, as assessed by the SF-36 health survey, demonstrated quality of life approximately paralleled function in both groups. In the WAD III group, quality of life, though significantly impaired after the traumatic event, improved to normal at 12 months. On the other hand, in the WAD I/II group, the SF-36 scores showed a significant deterioration over the same 12 month period. This observational disparity between the two groups was evident in both the physical component and the mental component of the SF-36. The difference in quality of life, as assessed by the SF-36 health survey, between the WAD III and comparison groups was highly significant.

The results of this study are consistent with the previous findings of Kamper *et al.* who reported in their meta-analysis review that the majority of pain recovery following whiplash occurs during the initial 3 months post injury [25]. Yet, our results are at variance with others, who report that severe



**Fig. (3A).** Predicted stresses in the lower brainstem on normal neck flexion in the comparison subject. Stresses are low throughout.



**Fig. (3B).** Predicted stresses at the C1 level on normal neck flexion in the comparison subject. Stresses are low throughout.

whiplash associated with neurological sequelae (WAD III) is persistent and debilitating [108]. Nevertheless, there has been no consistent characterization of clinical outcome for whiplash patients. Recently, Carroll et al performed a meta-analysis of the literature pertaining to whiplash injury. In consideration of all whiplash patients, 44% to 66% of patients had symptoms at one year, but only 12% reported daily neck pain and only 9% reported significant health impairment as a result of the whiplash injury [26-28]. Another study has shown that 90% of patients presenting with neck pain and neurological signs (WAD III) have continued symptoms at one-year following the injury [29]. The severity of symptoms at initial presentation is thought to

be prognostic of a poor outcome at 12 months follow-up [26, 108-110].

#### **Neurological Outcomes after Whiplash Injury**

The clinical outcomes in this study are consistent with observations in experimental models that demonstrate rapid recovery of axons enduring strain [30-32]. Furthermore, in neurosurgical series, where anatomical alignment has been restored, profound clinical deficits have been shown to be recoverable [5, 12, 14, 17, 33-40]. Taken together, improvement in pain, bulbar symptoms, ASIA index, Karnofsky index and quality of life assessment support the concept that restoration of the neutral position of the cervical



spine and craniocervical junction with a neck brace decreases the deleterious effects of flexion in the setting of both abnormal movement and abnormal anatomy.

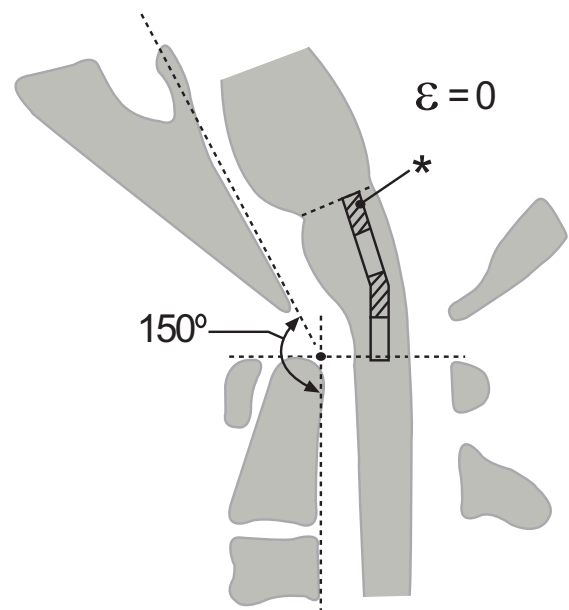
Acute whiplash injury without neurological deficit (WAD I/II) appears to be the result of osteo-musculo-ligamentous trauma. It is unclear whether symptoms from the latter may persist in the absence of clinical intervention, and the extent to which psycho-social features influence outcome. Schmitt *et al.* found that depression and anxiety impose a negative impact on patient's recovery [41]. Carstensen reported that pre-collision psychological distress and pre-injury neck pain are predictive of poor outcome in patients with WAD [42]. Similarly, in a study by Wenzel *et al.* they note that pre-injury health related factors, namely poor baseline health and mental impairment, was strongly associated with the reporting of whiplash trauma [111]. Persistent five year disability after whiplash injury was found to coincide with higher reporting of poor psychological health; that is to say depression, post-traumatic stress and decreased life satisfaction was found in subjects with the highest disability after whiplash injury [112]. Positive expectations, along with other psychosocial factors at the time of the initial injury are prognostic of good outcome [26, 43]. Carroll *et al.* showed that the recovery from WAD symptoms is comparable to the natural history of neck pain in the general population and workers [26]. Secondary gain is another concern that can also affect the reported recovery of the patient with neck pain post motor vehicle crash and/or a work related injury. The literature regarding the prognostic value of compensation and litigation is scarce [44, 45]. Sterling *et al.*, reported that compensation claim submission had a detrimental effect on the recovery of symptoms of pain/disability and posttraumatic stress disorder following whiplash [113]. In our study 20% of subjects within each group were involved in a litigation claim. The low number of subjects precludes a meaningful statistical comparison.

#### Pathophysiology of Whiplash Injury Associated with Neurological Deficit

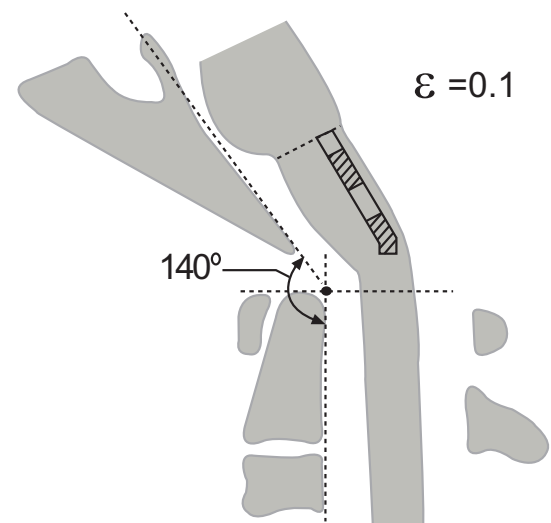
During whiplash injury, flexion and extension of the cervical spine results in abnormal strains that may exceed the physiological limit and consequently generate neurological dysfunction. Experimentally, large strains have been shown to arise even from normal flexion of the spinal cord and brainstem [46-50]. The effect of strain on axons is faithfully recapitulated in experimental models of stretch-induced axonopathy where electron micrographs show accumulations of axoplasmic material identified as "retraction balls" [47, 51-63]. In human histopathological studies, the histological substrate of stretch injury is the axon retraction bulbs in the cortico-spinal tracts of the brainstem in infants with "Shaken Baby Syndrome" [64] and in the cases of chronic brainstem deformity such as basilar invagination [52, 59, 60, 65]. The rate of strain increase directly relates to the magnitude of axonal injury [66]. Rapid occurrence of these strains on axons can exceed the material properties of the tissue, thus leading to tissue disruption. However, Progressive neurofilament alteration and delayed axotomy can occur even with only mild stretch [67]. The loading rate and the peak strain determine the degree of injury to the nerve. As the fibers bear tensile load, the cord becomes progressively

stiff [53, 68]. Different levels of injury can occur with stretching of the axolemma: myelin damage resulting in conduction block, irreversible changes with membrane changes, or decreased amplitude coupled with increased latency [66]. Deformative stress acting upon the Na<sup>+</sup> channel mechanoreceptors increases Na<sup>+</sup> influx that in return leads to voltage-gated Ca<sup>++</sup> channel depolarization, and which all together subsequently trigger pathological influx of Ca<sup>++</sup> [67, 69].

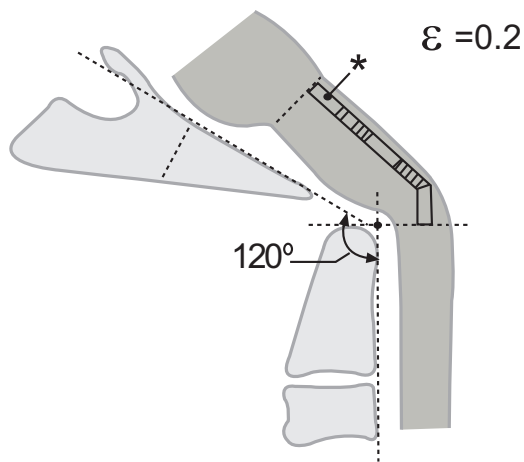
The deformative stress imposed upon the neuraxis by flexion of the neck and craniocervical junction, such as occurs in whiplash injury, is manifested radiologically by the measurement of increased length of the medulla and spinal cord [5, 12, 14, 17, 18, 22, 46, 49, 51, 52, 61, 64, 68, 70-79]. (Figs. 4A-C).



**Fig. (4A).** Normal craniocervical junction in the neutral position. The clivo-axial angle varies from 150-165 degrees. There is minimal or zero deformative strain in the neutral state.



**Fig. (4B).** Normal craniocervical junction in flexion. The neuraxis stretches by approximately 10% of its total length with flexion of the craniocervical junction creating a strain  $\epsilon = 0.1$ .



**Fig. (4C).** Pathological craniocervical junction with an abnormal clivo-axial angle in flexion. Upon full flexion at the craniocervical junction, the increase in the tangent arc creates a deformative strain approaching  $\epsilon = 0.2$ . In vivo and in vitro models demonstrate decreased or loss of neurological function with strains of 0.2

The mechanically induced stretching of the axon is an important epigenetic factor of gene expression. Accordingly, deformative stress results in up-regulation in neurons of N-Methyl D-Aspartate receptors and concomitant DNA fragmentation with mitochondrial dysfunction [80]. Calpain activation, after stretch injury, leads to progressive intra-axonal structural damage [62], or neuron apoptosis [52, 80-83].

#### **Cranio-cervical Anatomical Abnormalities that may give rise to increased Neurological Deficit with Acute Whiplash Injury**

The authors believe that whiplash injury may be exacerbated by underlying stenosis, compression, or cervical/craniocervical deformity. Deformative stress, due to chronic flexion/extension injuries, were noted in patients with angulation of the brainstem [76, 78, 79, 84]. Furthermore, this stress coupled with angulation of the brainstem, draped over the odontoid, contribute to the fulcrum effect of the medullo-spinal junction [17]. Deformative stress is evident in multiple diseases and disorders such as achondroplasia [85-89], platybasia [84, 90, 91], acquired bone-softening conditions (e.g. rickets), hyperparathyroidism, spondyloepiphyseal dysplasia, acroosteolysis, achondroplasia, osteomalacia, Hurler's Syndrome, degenerative conditions, renal osteodystrophy, Paget's disease [35, 51, 72, 92-99] and osteogenesis imperfecta [100, 101]. The horizontally tipped odontoid may deform the brainstem, especially in flexion [18, 102]. Our illustrative case J10 was emblematic of the ventral brainstem compression that results from a retroflexed odontoid in pathological flexion, as occurs in a whiplash injury. Platybasia results in anterior concavity of the brainstem with consequent medullary kink [10, 34]. The significance of the Clivo- vertebral angle in causing neurological deficit has been noted by many [5, 10, 20, 34, 71, 76, 79, 103].

#### **Stress Modeling with Finite Element Analysis**

Notwithstanding its potential utility, FEA modeling in the neuraxis is simplistic. The analysis used in this report assumes stereotypic response under various degrees of

compression and strain, but assigns different moduli of elasticity to white and gray matter. Presently FEA does not take into account strain rate, or alteration of compliance due to circulatory factors (e.g. ischemia) previous injury, age, and metabolic. Use of FEA should be considered only an approximation of relative stress. The stresses do not integrate measurements of stress over time or stress over the full length of the neurologic tract. Clearly, the shortcomings of FEA need to be addressed. Nevertheless, the FEA generated stress calculations may aid in recognizing the underlying pathophysiology of acute and chronic deformative stress injuries of the spinal cord and brainstem [46, 48, 75, 104].

#### **CONCLUSION**

Whiplash associated disorder consists of two distinct etiologies: deformative neuraxial stress injury resulting in the neurological findings in subjects with WAD III, and musculoskeletal injury resulting in chronic pain and tenderness in subjects with WAD I/II. Both etiologies result in significant pain, loss of function, and poor quality of life. In this study, the improvement in pain, function and quality of life in WAD III subjects suggests that neuronal injury due to deformative stress are in many instances recoverable. This notion is supported by evidence in neurobiological and clinical studies which demonstrate recovery of function after removal of neuraxial deformative stress.

#### **DISCLOSURE**

Authors William A. Wilson, IV., Fraser C. Henderson, Sr., and Alexander R. Vaccaro hold an equity ownership interest in Computational Biodynamics, LLC., and are entitled to royalty payments from the Spinal Cord Stress Injury Analysis (SCOSIA ©) upon commercialization. Research related to potential Computational Biodynamics, LLC. products, including early-stage research essential to the development of these products, has been conducted by individuals who hold a financial stake in the successful outcome of that research.

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#### **CONFLICT OF INTEREST**

The authors confirm that this article content has no conflicts of interest.

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