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CORRELATION OF BLUNT CERVICAL SPINAL CORD INJURY MRI TRACTOGRAPHY WITH THE AMERICAN SPINAL INJURY ASSOCIATION (ASIA) IMPAIRMENT SCALE MOTOR SCORES

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SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS IN RESPECT OF THE MASTER'S DEGREE (MMED) IN THE DEPARTMENT OF CLINICAL IMAGING SCIENCE IN THE FACULTY OF HEALTH SCIENCES AT THE UNIVERSITY OF THE FREE STATE

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DECLARATION OF AUTHORSHIP

I, Dr O. Seboco, declare that the coursework Master's Degree mini-dissertation and interrelated publishable article that I herewith submit for the degree in MMed (Clinical Imaging Science) at the University of the Free State are my own independent work and that I have not previously submitted it for a qualification at another institution of higher education. Where help was sought, it has been acknowledged.

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LIST OF ABBREVIATIONS

ASIA	THE AMERICAL SPINAL INJURY ASSOSCIATION
SAJR	THE SOUTH AFRICAN JOURNAL OF RADIOLOGY
SLICS	SUB-AXIAL CERVICAL SPINE INJURY CLASSIFICATION SYSTEM
DTI	DIFFUSION TENSOR IMAGING
FA	FRACTIONAL ANISITROPY
MRI	MAGNETIC RESONANCE IMAGING
CT	COMPUTED TOMOGRAPHY
DTT	DIFFUSION TENSOR TRACTOGRAPHY
HSREC	HEALTH SCIENCES RESEARCH ETHICS COMMITTEE
MR	MAGNETCI RESONANCE
TE/TR	TE = TIME TO ECHOE / TR = REPETITION TIME
PD	PROTEIN DENSITY
ROI	REGION OF INTEREST
DLC	DISCOLIGAMENTOUS SOFT TISSUE COMPLEX

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CHAPTER 1

BACKGROUND

1.1 INTRODUCTION

Traumatic spinal cord injury can impact everyone regardless of age, sex, socioeconomic background, or race. The global annual incidence of traumatic spinal cord injury ranges from 15 to 40 cases per million[1], with causes including vehicular accidents, community violence, outdoor sports activity, and occupational. Cervical spine trauma contributes 3% to 4% of all patients presenting to the emergency unit due to blunt trauma[2].

The Spinal Trauma Study Group introduced the Subaxial Cervical Spine injury classification System (SLIC score) in 2007 in other to improve the management of cervical spine injury patients[3]. The classification is based on the assessment of three injury components that include:

a) injury morphology, determined by the pattern of spinal column disruption on computed tomography or x-rays;
b) discoligamentous soft tissue complex (the intervertebral disc material, anterior and posterior ligamentous structures) integrity best accessed on Magnetic Resonance Imaging; and
c) the patient's neurologic status[4] which is assessed clinically by using the American Spinal Injury Association classification system.

Current imaging strategies don't reflect the current classification system as they are still centered on anatomical data and neglect the neurological (functional) component. The introduction of functional imaging techniques like Diffusion Tensor imaging has increased the possibility of having one-stop-shop holistic imaging that will complement the Subaxial Cervical Injury Classification System by adding neurological information to the already preexisting anatomical information. This literature review is intended to outline the

current state of Diffusion Tensor Imaging (DTI) as a prospective imaging tool for assessing patients with acute blunt cervical spine traumatic injury. We sought to produce synopses that will highlight the most up to date technological advances in DTI and its current clinical utility.

1.2 METHODS

1.2.1 Electronic literature research criteria

The PubMed database was searched for articles published during the last decade (2010 & 2019) with the following search terms: "diffusion tensor imaging" AND "acute cervical spine trauma". Due to a low number of articles (only two articles out of the seven were concerned with DTI in acute cervical spine injury) no filter was used. Following the title and abstract review, a total of seven articles were obtained from PubMed for the final review. Due to the small article review, sample citations from the preselected articles were screened for additional relevant articles (Figure 1) resulting in an additional 21 studies inclusion.

1.2.2 Inclusion criteria

Articles that contained information relevant to the use of DTI in acute traumatic spinal cord injury, principles of Magnetic Resonance Imaging DTI, and the pathophysiology of acute traumatic spinal cord injury were included.

1.2.3 Data evaluation

Pertinent facts from preselected articles were grouped and organized into the following categories:

a) Principles of DTI;
b) Current clinical use for DTI;
c) Pathophysiology of acute spinal trauma injury;
d) DTI clinical limitations; and
e) Epidemiology of acute spinal cord.

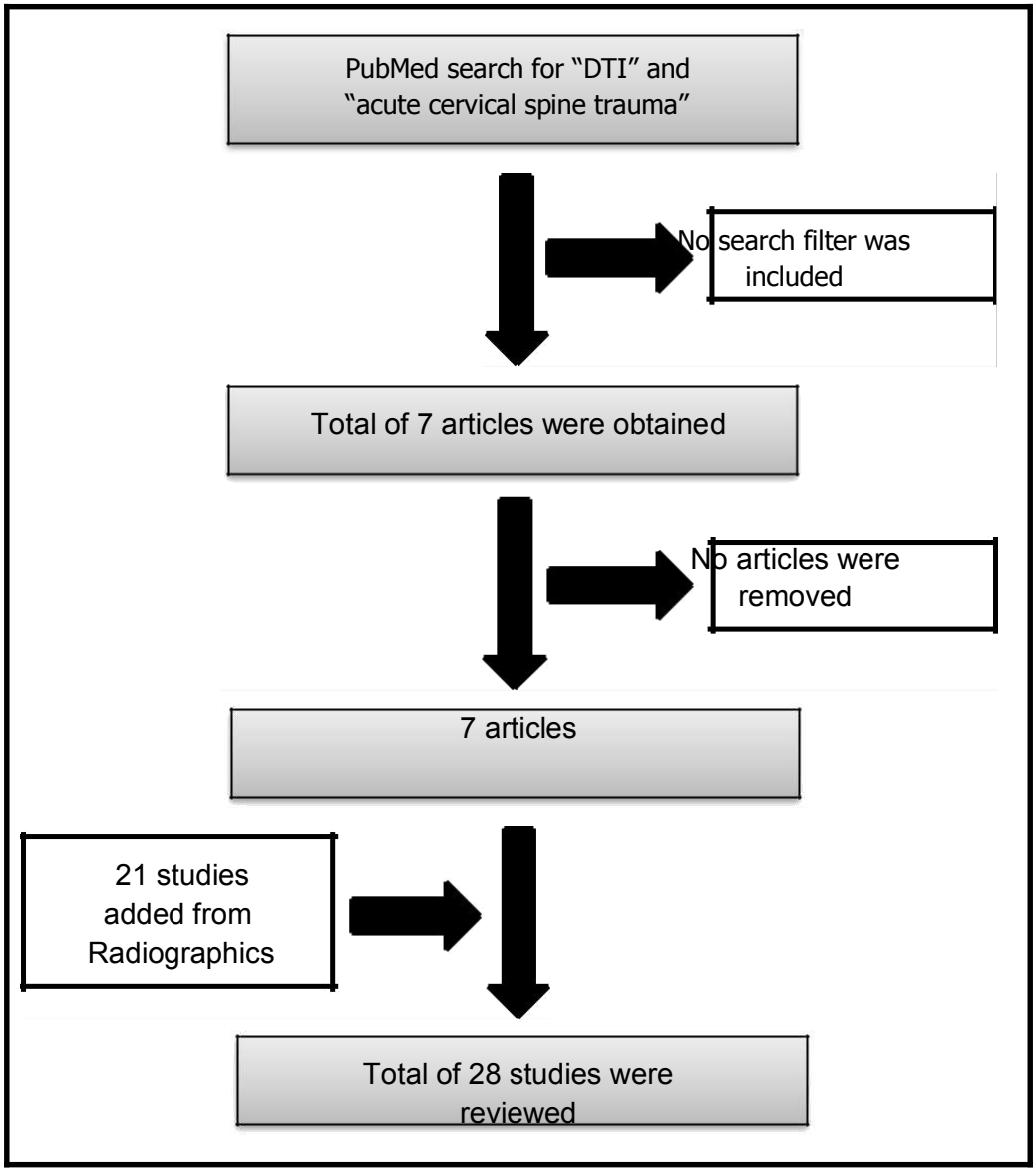

Figure 1: The PubMed search strategies and results

1.3 The epidemiology of spinal cord injury

A South African study by Philips *et al.*[5] noted an annual spinal cord incidence rate of 75.6 people per million in a study conducted in Cape Town, which is among the highest in the world when compared to a global incidence of 50 per million population[6]. Most spinal cord injuries (54%) involved males between the ages of 18 and 30 years of age. An accurate incidence rate requires enumeration of all injured individuals as well as a valid count of the population at risk. The percentage of admission mortality for acute spinal cord injury ranges from 48.3% to 79% despite their relatively low incidence[7].

The most important premorbid prognostic factors for survival after acute spinal cord injury are age, level of injury, and neurologic grade, with C1–C3 (quadriplegia) patients having 6.6 times higher mortality rate when compared to those of paraplegic patients[7]. Despite advances in the diagnosis and treatment, traumatic spinal cord injury remains a huge problem with 40% of traumatic injuries classified as ASIA A (complete neurological fallout) and remaining 60% having mixed neurological fall out (ASIA B, C, D)[5] as noted in Table 1.

Table 1: Acute traumatic spinal cord injury neurological severity

The severity of neurological fallout	Incidence
a) ASIA - A	40%
b) ASIA - B	15%
c) ASIA - C	15%
d) ASIA - D	30%

American Spinal Cord Association impairment scale (ASIA) is a neurologic deficit grading system.

A decade and a half ago, the cost of management for all traumatic spinal cord injuries management in the United States was estimated at $4 billion annually[8] with personal assistance costs and costs of institutional care averaged $6269 per year[9]. Lack of infrastructure development in developing countries also lends itself to the poor reintegration of disabled individuals into society.

The cause of spinal cord injuries varies between countries, as they do between regions within a country. Table 2 summarizes the causes of SCI globally. Due to the lack of acute spinal cord registry in most developing countries most available epidemiologic figures and management policies are derived from developed countries.

Table 2: Traumatic spinal cord injury causes

Cause of injury (a mechanism)	Incidence (%)
vehicular incidence	40-50
Occupation	10-25
Outdoors activity	10-25
Falls	25
Violence	10-25

1.3.1.1 The Pathophysiology of acute traumatic spinal cord injury

Acute spinal cord injury is a complex and dynamic process that is subdivided into a primary and secondary process based on the mechanism of cord injury. The primary process entails physical disruption or distortion of the spinal column which is easily depicted on conventional imaging like Computed Tomography or x-ray (the key evaluation is for stability). The secondary process encompasses microscopic cellular function disruptions which exacerbate the neuronal tissue damage

and even cell death.

The Primary mechanism: traumatic spinal cord injury frequently results from a direct impact to the spine column (the bony column and discoligamentous structures). The initial mechanical forces applied to the spinal cord at the time of injury are known as primary forces[10]. The applied forces led to displaced bone fragments tear into the spinal cord while the discoligamentous injury results in the vertebral column instability cord. The mechanism of injury includes acute compression, distraction, and laceration.

The Secondary mechanism: A plethora of theories for secondary cord injury have been proposed with few of them gaining traction in the medical community in recent years. Allen *et al.* postulated a secondary mechanism to acute spinal cord injury after noticing an improvement in neurology after removal of post-traumatic hematomyelia in dogs who underwent experimental acute spinal cord injury. In the 1970s, the free radical hypothesis movement was introduced by Dr. Demopoulos and thought to be crucial to the injury process. A decade later the focus shifted onto the role of calcium, opiate receptors, and lipid peroxidation[9]. The current movement is implicating apoptosis, intracellular protein synthesis inhibition, and glutaminergic mechanisms, among a myriad of pathophysiologic pathways that mediate secondary injury mechanisms. There is considerable evidence that the primary mechanical injury initiates a cascade of secondary injury mechanisms, including the following:

a) Vascular changes, including ischemia, impaired autoregulation, neurogenic shock, hemorrhage, microcirculatory derangements, vasospasm, and thrombosis;
b) Ionic derangements, including increased intracellular calcium, increased extracellular potassium, and increased sodium permeability;
c) Neurotransmitter accumulation, including serotonin or catecholamine and extracellular glutamate the latter causing excitotoxic cell injury;
d) Arachidonic acid release and free radical production, eicosanoid production, lipid peroxidation, and endogenous opioids;
e) Inflammation with increased vascular permeability and edema; and
f) Loss of adenosine triphosphate-dependent (ATP) cellular processes with eventual programmed cell death or apoptosis.

1.3.1.2 Physics of Diffusion Tensor Imaging

MRI diffusion provides a measure and direction of hydrogen molecules Brownian movement in tissues. The MRI diffusion scan measures the signal intensity attenuation, produced by water molecule positional change. By using this technique, we can characterize the way water diffuses inside imaging objects. An example of free diffusion or isotropic diffusion is a movement of water molecules inside a pool; due to lack of

impediments water can move freely all in all directions. Conversely, In vivo hydrogen molecules frequently encounter numerous flow impediments, such as cytoplasmic organelles, cell membranes, and protein fibers. When these structures restrict water molecule diffusion it is called "restricted diffusion". If water molecules are in an environment with highly ordered (or aligned) structure, they tend to diffuse along with the structure, resulting in so-called "anisotropic diffusion". In other words, the water diffusion has directionality. As in all MRI techniques, DTI images emanate from the signal acquired from hydrogen molecules after the application of an excitation pulse, but distinct from conventional MRI imaging, it looks not at the orientation of the molecule but the degree of freedom of movement of hydrogen molecules within a set volume (voxel) [11]. The highly Directional architecture of the spinal cord has allowed DTI to accurately map out its neuronal pathways, and thus assess spinal cord structural integrity, by modeling the direction and magnitude of water diffusion[12]. The directionality of diffusion is depicted by Eigenvectors, and the actual magnitude of diffusion in each direction is depicted by scalar eigenvalues (represented as λ1, λ2, and λ3), as noted in Figure 2. The primary eigenvector of a voxel is the one with the largest eigenvalue and represents the preferential direction of diffusivity in that voxel. These eigenvectors provide the basis of generating 3D tractography by using post-processing software.

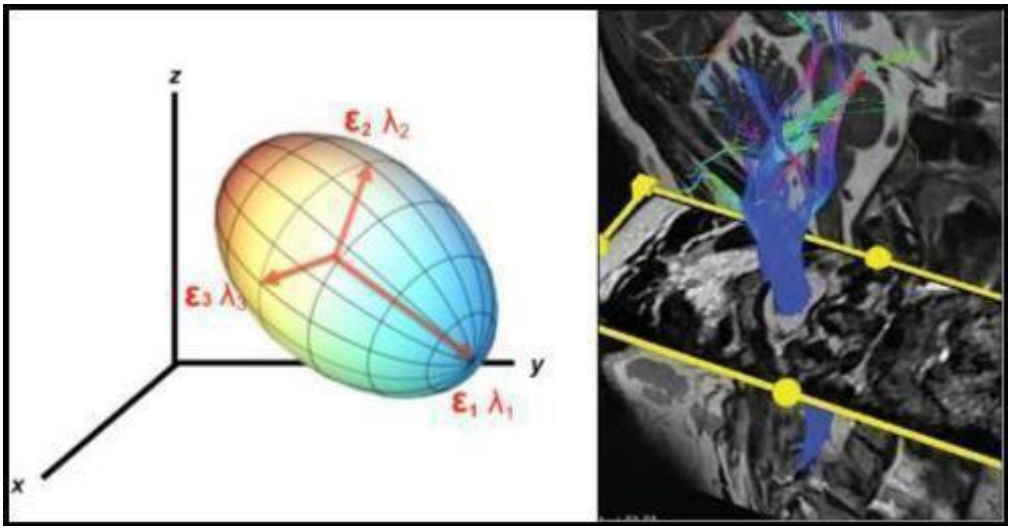

Figure 2: Graphic representation of diffusion tensor, Eigenvectors in three primary axes, and their relative scalar dimensions are shown on the left and sagittal cervical spine diffusion tractography on the right

MRI Tractography axonal integrity can be objectively defined by using the following quantitative variables:

a. Fractional anisotropy (FA): is a scalar value between zero and one that describes the degree of anisotropy (uniformness) of a diffusion process. A value of zero means that diffusion is isotropic, i.e. it is unrestricted (or equally restricted) in all directions and a value of one means that diffusion occurs only along one axis and is fully restricted

along with all other directions.

b. Apparent diffusion coefficient (ADC): is a measure of the magnitude of diffusion (The higher the value the higher the diffusion rate and the less the membrane integrity[13].

1.3.1.3 DTI animal studies

Most DTI studies have been experimental studies conducted on animals within in vivo spinal cord coil implantation and high MRI magnetic field strength (5 and 7 Tesla) [14,15,16,17]. The results of these DTI studies indicate that an excellent contrast is noted between grey matter and white matter regions, with the highly anisotropic white matter having much higher FA values than the central grey matter due to diffusion occurring preferentially along with the axonal bundle. Diffusion properties were also noted not to be the same throughout the length of the spinal cord and varied according to the level being studied. FA, ADC, and SCI severity have been correlated with several clinical assessment metrics including the American Spinal Injury Association motor score. The severity of injury in these studies was confirmed histologically in the hyper-acute injury setting as early as 6 hours after the initial injury. This result has been corroborated in multiple mouse models where comparison of DTI indices to spinal cord histopathology and to locomotor recovery demonstrates ADC to be an accurate predictor of the degree of intact white matter and recovery of locomotion. The study by Xiao-Hui Li *et al.*[18] noted that ADC does not show

any significant changes with time in both the mild and moderate injury groups, suggesting that ADC is not effective in assessing these injuries. FA decreased significantly after six hours post-injury even though no changes in ADC were observed, suggesting that FA value is a sensitive marker of acute spinal cord injury and FA is more strongly related to the severity of the injury.

1.3.1.4 Normal DTI values

Due to infrequent diffusion tensor imaging studies in healthy subjects a normative database is yet to be established, thus hindering clinical integration of MRI Diffusion tensor imaging. Studies conducted on the healthy subject found varying FA values with Mamata *et al.*[19] noting FA value of 0.66, while Xiangshui *et al.*[20] and Takashima *et al.*[21] noting FA value of 0.72 and 0.64 respectively as summarized in Table 3. The previously mentioned discrepancies can be attributed to age, the measurement site, the imaging device, and the imaging method[19] used.

Table 3: Normative DTI parameters

Study	Number of cases	ADC (um2/msec)	FA
Mamata *et al.*	11	0.75	0.66
Xiangshui *et al.*	21	0.78	0.72
Takashima *et al.*	10	1.0	0.64

Mamata *et al.*[19] noted that in a healthy subject, ADC increased with age, whereas FA tended to decrease as demonstrated in Figure 3. In this study, as in previous reports, ADC was significantly higher in subjects >40 years of age; however, there was no significant difference in FA, and no difference between ADC and FA was found between men and women. The upper cervical spine (C2-C3) has a higher mean value for ADC and FA than the lower levels (C4-C7). These findings further highlight the importance of compare DTI measurements in patients with age-matched controls.

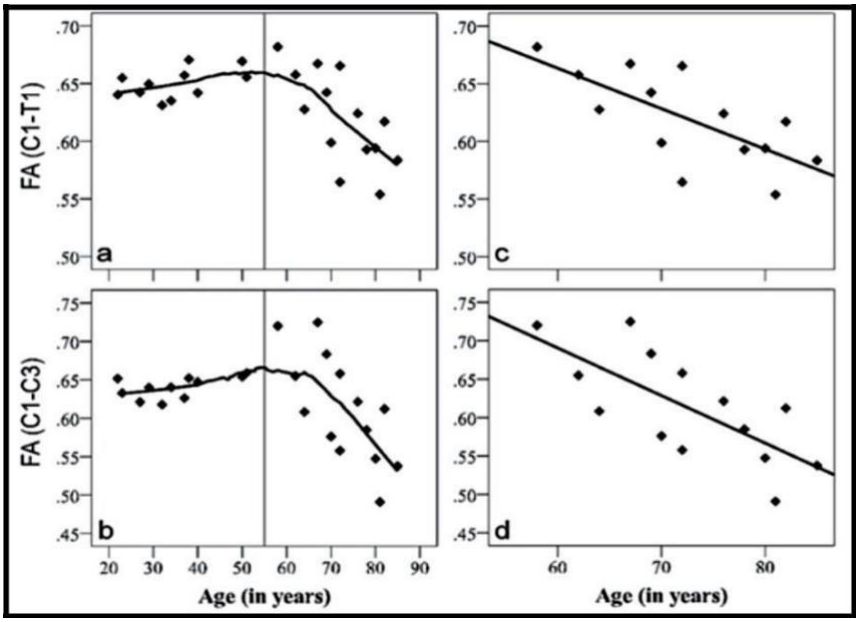

Figure 3: Scattered plots showing the relationship between FA values and age

1.3.1.5 DTI in non-traumatic spinal cord injury

Demir et al.20 demonstrated that DTI was more sensitive at detecting neurological damage in patient with chronic stenotic myelopathy with a sensitivity of 80% when compared to T2 with a sensitivity of 61%. The finding that diffusion tensor imaging is more sensitive at detecting chronic stenotic myelopathy changes than the regular T2 weighted imaging has been validated by other authors14, 20. DTI indices (FA/ ADC) in chronic stenotic myelopathy patients appear to depend on the degree of cord damage as noted by Budzik et al.21 in a study done in 2019 when he observed a positive correlation between FA values and clinical assessment using the America Spinal Cord Injury Association (ASIA) impairment scale. It is therefore, apparent that diffusion tensor imaging has a part to play in the pre-surgical planning for chronic stenotic myelopathy patients, but the use of diffusion tensor imaging in surgical intervention or monitor recovery is yet to be evaluated in details. The use of diffusion tensor managing in animal models with chronic stenotic myelopathy has been described only in a few studies, showing a decreased FA and increased ADC values at the stenotic level22.

1.3.1.6 DTI in acute traumatic spinal cord injury

Imaging is a critical aspect of traumatic spinal cord injury evaluation and management, with magnetic resonance imaging (MRI) universally acknowledged as an ideal non- invasive technique for examining spinal cord injury examination. Although conventional MRI plays a critical role in the diagnosis and management of spinal cord injury, it is neither sensitive nor specific in accurately assessing the functional integrity of the spinal cord in the hyperacute phase post after spinal cord injury due to the temporary flaccid paralysis that accompanies spinal shock. Mamata et al.20 reported that in nerve fiber impairment, the medullary sheath is destroyed and water molecules exhibit increased diffusion in the direction in which they are normally restricted (i.e., diffusion anisotropy is lost thus, ADC increases and FA decreases). Limited studies have been published concerning DTI and acute spinal trauma. A study by D'souza et al.21 noted that the mean FA values in a traumatic cervical spine injury were notable lower at the level of injury when compared to the same level in healthy controls, but not at levels above or below the injury. The left and right hemi cord corticospinal tracts FA values were found to correlate moderately with the laterality of neurological symptoms and the American Spinal Injury Association (ASIA) scores. Shanmuganathan et al.22 also found a significant reduction in FA between the injured (Hemorrhagic and Non-Hemorrhagic Contusion) and control groups, with non -hemorrhagic spinal contusion injury site FA values correlating strongly with The American Spinal Injury Association (ASIA) impairment scale motor scores. However, no correlation was observed when comparing the hemorrhagic contusion FA values to The American Spinal Injury Association (ASIA) impairment scale motor scores.

1.3.1.7 DTI limitations

Human spinal cord imaging using DTI Magnetic Resonance Imaging sequences still has several limitations due to reduced spatial resolution induced by the following technical issues:

A Low signal-to-noise ratio caused by the small volume of spinal cord tissue;
The cerebrospinal fluid (CSF), cardiac and respiratory motion pulsation
artifacts; and The magnetic susceptibility artifacts caused by the adjacent bone.

The Signal to Noise ratio can be ameliorated by the utilization of a 3 Tesla MRI machine but is not universally available. To date, no South African spinal trauma register or database is available that records individuals with traumatic spinal cord injury making large sample-based spinal cord injury studies quite difficult.

1.4 THE CONCLUSION

Given a better understanding of the pathophysiology of acute traumatic spinal cord injury and the current introduction of a new cervical spine injury system (SLIC), it is only prudent to reevaluate the current imaging protocol to include a functional image that will enable us to comment about the neurological status. The ability of DTI to complement conventional spinal cord injury imaging protocols by diagnosing subtle cord injuries, predicting the need for early therapeutic intervention, and monitor interventional outcomes has yet to be demonstrated.

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CHAPTER 2

ARTICLE 1:

CORRELATION OF BLUNT CERVICAL SPINAL CORD INJURY MRI TRACTOGRAPHY WITH THE AMERICAN SPINAL INJURY ASSOCIATION (ASIA) IMPAIRMENT SCALE MOTOR SCORES

The article was prepared according to the journal submission guidelines for the *South African Journal of Radiology (SAJR)* (cf. Appendix A).

CORRELATION OF BLUNT CERVICAL SPINAL CORD INJURY MRI TRACTOGRAPHY WITH THE AMERICAN SPINAL INJURY ASSOCIATION (ASIA) IMPAIRMENT SCALE MOTOR SCORES

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Abstract

Background: The introduction of the Sub-axial Cervical Spine Injury Classification System (SLICS) in the management of cervical spine trauma has created the need for a holistic imaging approach that encompasses both functional (neurological) and morphological (anatomical) factors .This study aimed to determine if there was a correlation between the diffusion tensor imaging (DTI) Fractional Anisotropy (FA) values of blunt cervical spinal cord injury and the America Spine Injury Association (ASIA) impairment scale motor score.

Material and methods: DTI was performed on 26 patients with blunt cervical spine injury (all males, median age 46 years) admitted to the spinal unit of Pelonomi tertiary Hospital, South Africa. The cervical spine was imaged using 1.5T Siemens Magnetom Aera machine with a built-in spine DTI protocol. Sagittal FA values were acquired at four different cervical spine regions (medulla oblongata, above the injury site, at the injury site, and below the injury site).

Result: Eight out of 26 participants had complete neurological fall out. 30% of the participants had injuries at the C4/C5 level, while injuries involving segments below and above C4/C5 affected 15% and 55% participants respectively. Injury site FA values (median 0.30) were significantly lower ($p<0.001$) than the above injury site FA (median 0.46, $p=0.26$) and below injury site FA (median 0.42 and $p =0.019$). A significant correlation was noted between the injury site FA values and the ASIA impairment scale motor scores ($p=0.001$, $r=0.87$).

Conclusion: DTI is sensitive at detecting cervical spinal cord injury with FA value showing excellent correlation with the ASIA impairment scale motor scores

INTRODUCTION

Traumatic spinal cord injury can affect anyone irrespective of age, gender, or socioeconomic background with catastrophic social and economic implications. A South African study by Philips et al.[1] noted an incidence rate of 75.6 people per million spinal cord injuries in the public sector and 20 per million in private sector in a study conducted in Cape Town in 2018 which is among the highest in the world, with the injuries mostly involving males (54%) between the ages of 18 and 30 years of age. The same study also noted that the cervical spine (C1 – C8) was the most common site of spinal injury (53.1%) followed by the thoracic spine (38.6%) and lumbar spine (8.3%). Despite advances in diagnosis and treatment, traumatic spinal cord injury remains a huge problem with 40% of traumatic injuries classified as ASIA A (complete neurological fallout) and the remaining 60% having mixed neurological fall out (ASIA B, C, D). The lack of proper infrastructure in developing countries hinders proper social reintegration of the disabled

The introduction of the ASIA in the mid-1970s helped facilitate the exchange of data and management ideas among health care providers involved in the management of traumatic spinal cord jury patients. The ASIA impairment scale is a standardized examination consisting of a motor examination, sensory examination, and an anal sphincter tone examination. The motor examination consists of grading five specific muscle groups in the upper extremities and five in the lower extremities, each muscle is grade from zero (no power) to five (normal power). The sensory examination evaluates 28 specific dermatomes bilaterally for light touch (generally a piece of cotton) and pinprick (generally a clean safety pin) sensation[2] for a total score 56.

Magnetic Resonance Imaging (MRI) has long been an excellent complementary imaging tool to Computed Tomography (CT) in acute traumatic spine injury imaging due to its better soft-tissue resolution. The limitation of conventional MRI is the depiction of white matter as uniform tissue despite being composed of a complex array of directionally oriented nerve fibers thus limiting its ability to detect finite axon pathology[3]. In vivo methods to map the neurological pathways of the white matter have long been sought to increase the degree of pathology detection with diffusion tensor tractography (DTT) imaging demonstrating excellent ability at depicting axon structural integrity. The highly directional architecture of the spinal cord has allowed DTI to accurately allow assessment of the spinal cord structural integrity by modeling the direction and magnitude of water diffusion[3]. The ability of DTI to complement conventional spinal imaging by diagnosing subtle cord injuries, predict the need for early therapeutic intervention and monitor

interventional outcome has yet to be demonstrated[4]. To our knowledge, only two human studies reported DTI changes following acute cervical spine injuries [4.5] with the majority of the studies conducted on animals[6.7.8.9]. This study attempted to correlate fractional anisotropy (FA) of patients with acute blunt cervical spine injury with the ASIA impairment scale motor scores by using sagittal DTI instead of the more commonly used axial views.

RESEARCH METHOD AND DESIGN

Design

A retrospective study was conducted on a cohort of 26 patients who were admitted to the Pelonomi tertiary Hospital spinal unit in Bloemfontein, South Africa, following blunt cervical spine injury between 01/ 01/ 2018 and 01/ 12/ 2019. Patients with penetrating neck injury, younger than 18 years, and patients whose neurological exams could not be assessed due to the low Glasgow coma scale were excluded from the study. Ethics approval from the University of the Free State Health Sciences Research Ethics Committee (HSREC) and permission to conduct the study at a state hospital was granted by the Free State health department.

Consent not needed in the study.

Images protocol

All MR imaging was acquired with a 1.5T Siemens Magnetom Aera. Conventional MR imaging sequences included sagittal T2 (TE/TR, 33/5250 ms), sagittal T1 (TE/TR, 9.5/1470ms), sagittal PD (TE/TR, 9.9/3240ms) and fluid-attenuated inversion recovery (TE/TR, 102/8000 ms). DTI images were obtained by using sagittal ep2d_diff_mddw (TE/TR, 82/2800ms). A 12 channel head-neck array coil was used with a field of view from the base of the skull to cervicothoracic junction.

Data collection

Conventional sagittal MRI (T1/T2/PD with fat suppression) images were viewed for evidence of abnormal intramedullary spinal cord signal-intensity to indicate the presence of a cord injury. Color corded Diffusion tensor imaging (Figure 2) was also evaluated for injury as depicted by alteration in spinal cord color intensity. FA values were obtained in the sagittal plane from four regions (the Medulla oblongata, the region above injury, the injury site, and below the injury site) using an ellipsoid ROI (Region of interest) with an area of 54mm^2 with Figure 1 showing conventional T2 weighted images.

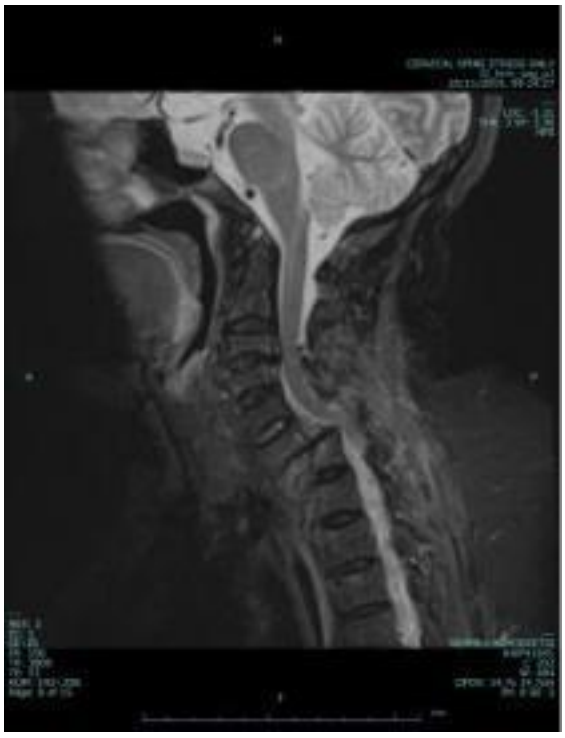

FIGURE 1: Cervical T2 weighted sagittal views

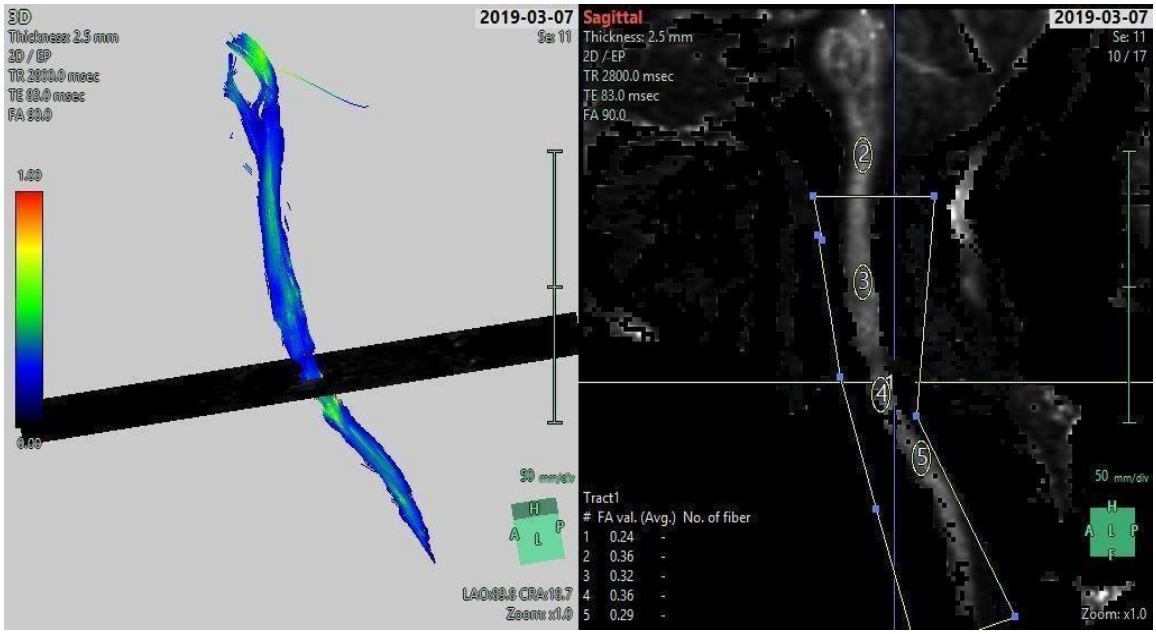

FIGURE 2: Sagittal cervical neck tractography with four levels of interest

Neurological assessment was performed by the spinal unit orthopedics registrar using the ASIA impairment scale form and patients were classified as having complete or incomplete spinal cord injury.

Statistical analysis

Numerical variables were summarized by means, standard deviations and categorical variables by frequencies and percentages. Correlations were assessed using Spearman rank correlations. Independent numerical variables were compared using Mann-Whitney tests and paired data using signed-rank tests. Analyses were performed using SAS Version 9.4.

Results

DTI tractography was performed on a total of 26 patients (all males with a median age of 46 years) with 30% of the patients having an injury at the C4/C5 level while injuries involving segments below and above C4/C5 affected 15% and 55% of patients respectively. Following assessment with ASIA impairment scale eight of the participant were clinically classified as having completed neurological fallout with the remaining 18 classified as having an incomplete spinal cord injury.

Out of 26, one patient's above injury site and medulla oblongata values were not obtained due to metal artifact from upper cervical spine fixation and 3 had a cervicothoracic junction injuries (DTI has a poor resolution in the thoracic spinal cord) hindering evaluation of below injury site FA readings (Table 1). Injury site FA values (median 0.30) were significantly lower ($p<0.001$) than above injury site FA (median 0.46) and below injury site FA (median 0.42).

TABLE 1: Cervical regions DTI FA values

Variables	Patient size	Mean (10^{-3} mm^2/s)	Standard deviation	Median ($10^{-3}mm^2/s$)	Minimum (10^{-3} mm^2/s)	Maximum (10^{-3} mm^2/s)
Medulla FA values	25	0.33	0.03	0.34	0.22	0.38
Above injury site FA	25	0.45	0.05	0.46	0.33	0.55
Injury site FA values	25	0.31	0.10	0.30	0.12	0.49
Below injury site FA values	23	0.40	0.6	0.42	0.23	0.49
Motor scores	26	68	36.4	85	10	100

As shown in Table 2 statistically significant correlations ($P<0.05$) were noted when injury site FA was compared to medulla oblongata FA ($r=0.48$, $P=0.016$), below injury site FA ($r=0.58$, $P=0.001$) and above injury site FA ($r=0.47$, $P=0.017$). The injury site FA values also had a significant correlation with the ASIA impairment scale motor score ($r=0.87$, $P=0.001$).

TABLE 2: Compares the findings using Spearman correlation coefficient (rs)

	Medulla FA	FA above the injury site	FA injury site	FA below the injury site	Motor score
Medulla FA	1.000	0.25 (0.213)	0.48 (0.016)	0.18 (0.434)	0.28 (0.159)
FA above injury site		1.000	0.47 (0.017)	0.48 (0.026)	0.47 (0.016)
FA injury site			1.0000	0.58 (0.001)	0.87 (0.001)
FA below injury site				1.000	0.49 (0.019)

* P valve inserted in brackets

Patients with neurological fall out were divided into complete and incomplete neurological fallout based on their sacral motor and sensory findings (Table 3). Patient with complete spinal

cord injury had an injury site median FA value of 0.18 ($p<0.001$) and those with incomplete spinal cord injury showed a median value of 0.30 ($P<0.001$).

TABLE 3: Breakdown of findings in patients with complete and incomplete neurological fallout

Type of injury	Total Number of patients	Variables	Number of observations	Median	Lower quartile	Upper quartile
Complete	8	Medulla FA	7	0.34	0.31	0.35
		Above injury FA	7	0.41	0.41	0.46
		Injury site FA	8	0.18	0.15	0.25
		Below injury FA	5	0.33	0.28	0.39
		Time (in days)		7.50	2.50	11.0
Incomplete	18	Medulla oblongata FA	18	0.34	0.32	0.37
		Above injury FA	18	0.46	0.44	0.48
		Injury site FA	17	0.34	0.30	0.44
		Below injury site FA	17	0.42	0.41	0.44
		Time (in days)		5.00	4.00	10.0

DISCUSSION

The Spine Trauma Study Group developed the SLICS after noticing a need for a more practical and comprehensive lower cervical spine classification system directly linked to clinical decision-making algorithms [10]. The system is based on the evaluation of three major injury characteristics: (1) injury morphology, determined by the pattern of spinal column disruption on available imaging studies, (2) Integrity of the discoligamentous soft tissue complex (DLC) represented by both anterior and posterior ligamentous structures as well as the intervertebral disc and (3) patient's neurologic status determined by clinical assessment[10]. Given the recent introduction of SLIC score in managing patients with cervical spine trauma, the need for a holistic imaging protocol that can encompass both functional (neurology) and structural (anatomical) integrity has become crucial.

Imaging plays a critical role in traumatic spinal cord injury evaluation and management, with MRI universally acknowledged as an ideal noninvasive technique for examining acute spinal cord injury. Although conventional MRI plays a critical role in the diagnosis and management of spinal cord injury, it is neither sensitive nor specific in assessing spinal cord functional integrity. Chronic stenotic myelopathy (CMS) often appear normal on conventional MRI images even in patient with neurological fallout, Demir et.al .[11] noted that DTI (80%) had a high sensitive when compared to T2 weighted images (60%) at detecting CMS. DTI indices (FA/ ADC) in chronic stenotic myelopathy patients appear to depend on the degree of cord damage.[11] It is apparent that DTI has a part to play in the pre-surgical planning for chronic stenotic myelopathy patients, but the use of diffusion tensor imaging in surgical intervention or recovery monitoring is yet to be evaluated in details.

Few studies have been conducted on healthy subjects to adequately establish a comprehensive database for cervical spine DTI parameters thus hindering the clinical integration of DTI imaging. The studies that have been conducted on healthy subjects showed varying results with Mamata et al.[12] noting an average cervical spine FA value of 0.66 while Xiangshui et al.[13] and Takashima et al.[14] noted values of 0.74 and 0.64 respectively. Facon et al.[15] noted that precise measurement of FA values are difficult to obtain because they are affected by age, the measurement site, the imaging device, and the imaging method used even in healthy spines. We attempted to overcome this inconsistency by comparing the injury site FA to normal adjacent cervical spine regions (region without DTI signal loss). Injury site FA values were demonstrated to be significantly lower than those obtained at the medulla oblongata, the level above and the level below injury site FA. These indicated that changes in DTI FA values were a good marker of cervical cord injury.

FA and ADC values SCI have been correlated with several clinical assessment metrics including the American Spinal Injury Association motor score. A study by Cheran et al.[5]noted a good correlation between DTI fractional and ASIA impairment scale motor scores in patients with a non-hemorrhage contusion on FA values measured on axial views. The objective of our study was to determine if it was possible to correlate DTI FA values with the ASIA impairment scale motor scores in patients with blunt cervical spine trauma using sagittal views. Like the Cheran at el[5]our study also noted a good correlation between injury site FA values and the ASIA impairment scale motor scores (P=0.001), with a marked difference in FA values between the patients with incomplete (0.30) and complete (0.18) neurological fallout. Neural injury is characterized by demyelination, axonal and cell membrane disruption, this process lead to reduction in FA and elevation of ADC values. FA and ADC values in spinal cord injury have been correlated with several clinical assessment metrics including the American Spinal Injury Association motor score.

The study presented the following limitation that will need to be addressed with future studies and new policy implementations. First, a large sample study is still needed to determine normal cervical spine DTI FA values. Secondly, the effects of time on the FA value still need to be addressed to determine the best imaging period. Thirdly to facilitate large sample volume studies a South African spinal trauma registry will need to be established. Li XHJ et al.[17] found good DTI image to histology correlation at 72hrs post-acute traumatic spinal cord injury, our injury to scan time for the incomplete and complete spinal cord was 5.00 days

and 7.50 days post-trauma respectively due to patient instability and logistical issues (difficult in getting after-hours MRI).

CONCLUSION

DTI is sensitive at detecting acute blunt cervical spinal cord injury with FA value showing excellent correlation with the ASIA impairment scale motor scores. Given the importance of neurological severity in the management and prognosis of the cervical spine the study highlights the need to including DTI in conventional cervical spine trauma MRI protocol.

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APPENDIX A

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Example 3	A.B. developed the theoretical formalism, performed the analytic calculations and performed the numerical simulations. Both A.B and B.C. authors contributed to the final version of the manuscript. B.C. supervised the project.

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Example 7	A.B. devised the project, the main conceptual ideas and proof outline. B.C. worked out almost all of the technical details, and performed the numerical calculations for the suggested experiment. C.D. worked out the bound for quantum mechanics, with help from D.E.. E.F. verified the numerical results of the xyz by an independent implementation. F.G. and G.H. proposed the xyz experiment in discussions with A.B.. B.C., C.D., G.H. and A.B. wrote the manuscript.
Example 8	A.B., B.C. and C.D. designed the study. A.B., D.E. and E.F. performed the xyz experiments. F.G. and G.H. performed XYZ simulations. I.H. and M.C. expressed and purified all proteins. A.B., H.J.., B.C. and C.D. analysed the data. A.B., B.C. and C.D. wrote the paper with input from all authors.
Example 9	A.B. and B.C. designed and directed the project; C.D., D.E., A.B. and B.C. performed the experiments; C.D. and B.C. analysed spectra; A.B. and E.F. made the simulations; B.C. developed the theoretical framework; C.D., A.B. and B.C. wrote the article.
Example 10	A.B., B.C. and C.D. performed the measurements, D.E. and E.F. were involved in planning and supervised the work, A.B. and B.C. processed the experimental data, performed the analysis, drafted the manuscript and designed the figures. F.G., and G.H. performed the xyz calculations. H.I., and I.J. manufactured the samples and characterized them with xyz spectroscopy, J.K. performed the xyz characterization. K.L. aided in interpreting the results and worked on the manuscript. All authors discussed the results and commented on the manuscript.
Example 11	A.B., B.C., C.D. and D.E. contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

Funding information
All research articles should have a funding acknowledgement statement included in the manuscript in the form of a sentence under a separate heading entitled 'Funding information'. The funding agency should be written out in full, followed by the grant number in square brackets.

The following are examples of a funding statement. If you use one of the examples, you should modify it to fit your specific relationship.

Scenario	**Suggested funding statements**
Example 1	The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Medical Research Council [grant number xxx].
Example 2	This work was supported by the Trust [grant numbers xxxx, yyyy]; the Natural Environment Research Council [grant number zzzz]; and the Economic and Social Research Council [grant number aaaa].

Example 3	The author(s) received no financial support for the research, authorship, and/or publication of this article.

Data availability statement
All research articles should have a data availability statement included in the manuscript in the form of a sentence under a separate heading entitled 'Data availability statement'.

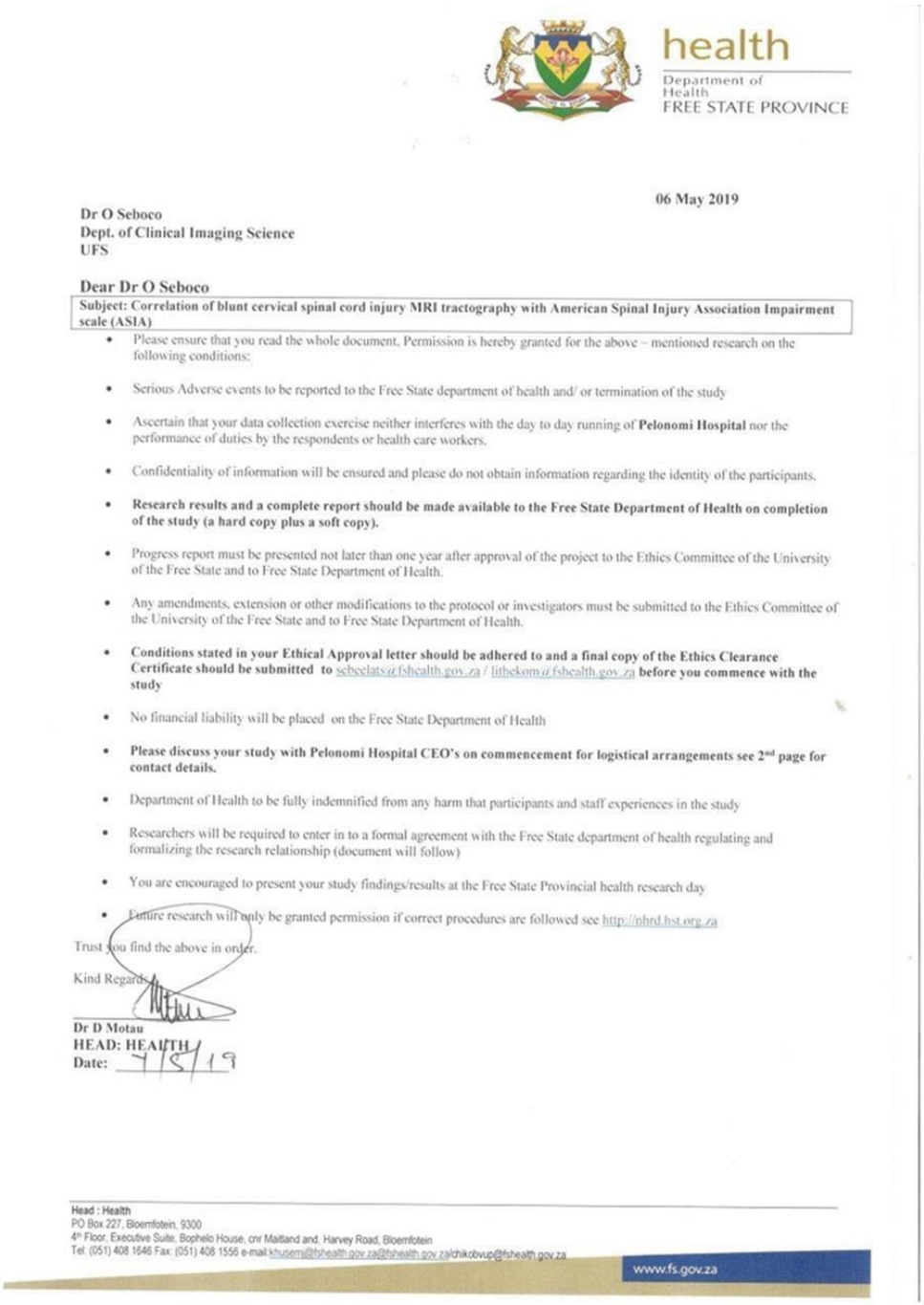
The following are examples of a data availability statement. If you use one of the examples, you should modify it to fit your specific relationship.

Availability of data	**Suggested data availability statements**
Data openly available in a public repository that issues datasets with DOIs	The data that support the findings of this study are openly available in [repository name e.g 'figshare'] at http://doi.org/[doi], reference number [reference number].
Data openly available in a public repository thatdoes not issue DOIs	The data that support the findings of this study are openly available in [repository name] at [URL], reference number [reference number].
Data derived from public domain resources	The data that support the findings of this study are available in [repository name] at [URL/DOI], reference number [reference number]. These data were derived from the following resources available in the public domain: [list resources and URLs]
Data available within the article or its supplementary materials	The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.
Data generated at a central, large-scale facility, available upon request	Raw data were generated at [facility name]. Derived data supporting the findings of this study are available from the corresponding author [initials] on request.
Embargo on data due to commercial restrictions	The data that support the findings will be available in [repository name] at [URL / DOI link] following a [6 month] embargo from the date of publication to allow for the commercialisation of research findings.
Data available on request due to privacy/ethical restrictions	The data that support the findings of this study are available on request from the corresponding author, [initials]. The data are not publicly available due to [restrictions, e.g. their containing information that could compromise the privacy of research participants].
Data subject to third party restrictions	The data that support the findings of this study are available [from] [third party]. Restrictions apply to the availability of these data, which were used under licence for this study. Data are available [from the authors / at URL] with the permission of [third party].
Data available on request from the authors	The data that support the findings of this study are available from the corresponding author, [author initials], upon reasonable request.
Data sharing not	Data sharing is not applicable to this article, as no new data were created or analysed in

applicable – no new data generated	this study.

Disclaimer
A statement that the views expressed in the submitted article are his or her own and not an official position of the institution

Appendix B: DOH letter of approval



health
Department of Health
FREE STATE PROVINCE

06 May 2019

Dr O Seboco
Dept. of Clinical Imaging Science
UFS

Dear Dr O Seboco

Subject: Correlation of blunt cervical spinal cord injury MRI tractography with American Spinal Injury Association Impairment scale (ASIA)

- Please ensure that you read the whole document. Permission is hereby granted for the above – mentioned research on the following conditions:
- Serious Adverse events to be reported to the Free State department of health and/ or termination of the study
- Ascertain that your data collection exercise neither interferes with the day to day running of **Pelonomi Hospital** nor the performance of duties by the respondents or health care workers.
- Confidentiality of information will be ensured and please do not obtain information regarding the identity of the participants.
- **Research results and a complete report should be made available to the Free State Department of Health on completion of the study (a hard copy plus a soft copy).**
- Progress report must be presented not later than one year after approval of the project to the Ethics Committee of the University of the Free State and to Free State Department of Health.
- Any amendments, extension or other modifications to the protocol or investigators must be submitted to the Ethics Committee of the University of the Free State and to Free State Department of Health.
- **Conditions stated in your Ethical Approval letter should be adhered to and a final copy of the Ethics Clearance Certificate should be submitted to** sebeclats@fshealth.gov.za / lithekom@fshealth.gov.za **before you commence with the study**
- No financial liability will be placed on the Free State Department of Health
- **Please discuss your study with Pelonomi Hospital CEO's on commencement for logistical arrangements see 2nd page for contact details.**
- Department of Health to be fully indemnified from any harm that participants and staff experiences in the study
- Researchers will be required to enter in to a formal agreement with the Free State department of health regulating and formalizing the research relationship (document will follow)
- You are encouraged to present your study findings/results at the Free State Provincial health research day
- Future research will only be granted permission if correct procedures are followed see http://nhrd.hst.org.za

Trust you find the above in order.

Kind Regards

Dr D Motau
HEAD: HEALTH
Date: 7/5/19

Head : Health
PO Box 227, Bloemfotein, 9300
4th Floor, Executive Suite, Bophelo House, cnr Maitland and, Harvey Road, Bloemfotein
Tel: (051) 408 1646 Fax: (051) 408 1556 e-mail:khusemj@fshealth.gov.za/@fshealth.gov.za/chikobvup@fshealth.gov.za

www.fs.gov.za

Health Science Research Ethics Committee

UNIVERSITEIT VAN DIE

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YUNIVESITHI YA FREISTATA

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HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

17-May-2019

Dear **Dr Orapeleng Seboco**

Ethics Clearance: **Correlation of blunt cervical spinal cord injury MRI tractography with American Spinal Injury Association Impairment scale (ASIA)**
Principal Investigator: **Dr Orapeleng Seboco**
Department: **Clinical Imaging Sciences Department (Bloemfontein Campus)**
APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is:**UFS-HSD2017/1299/2506**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite), Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

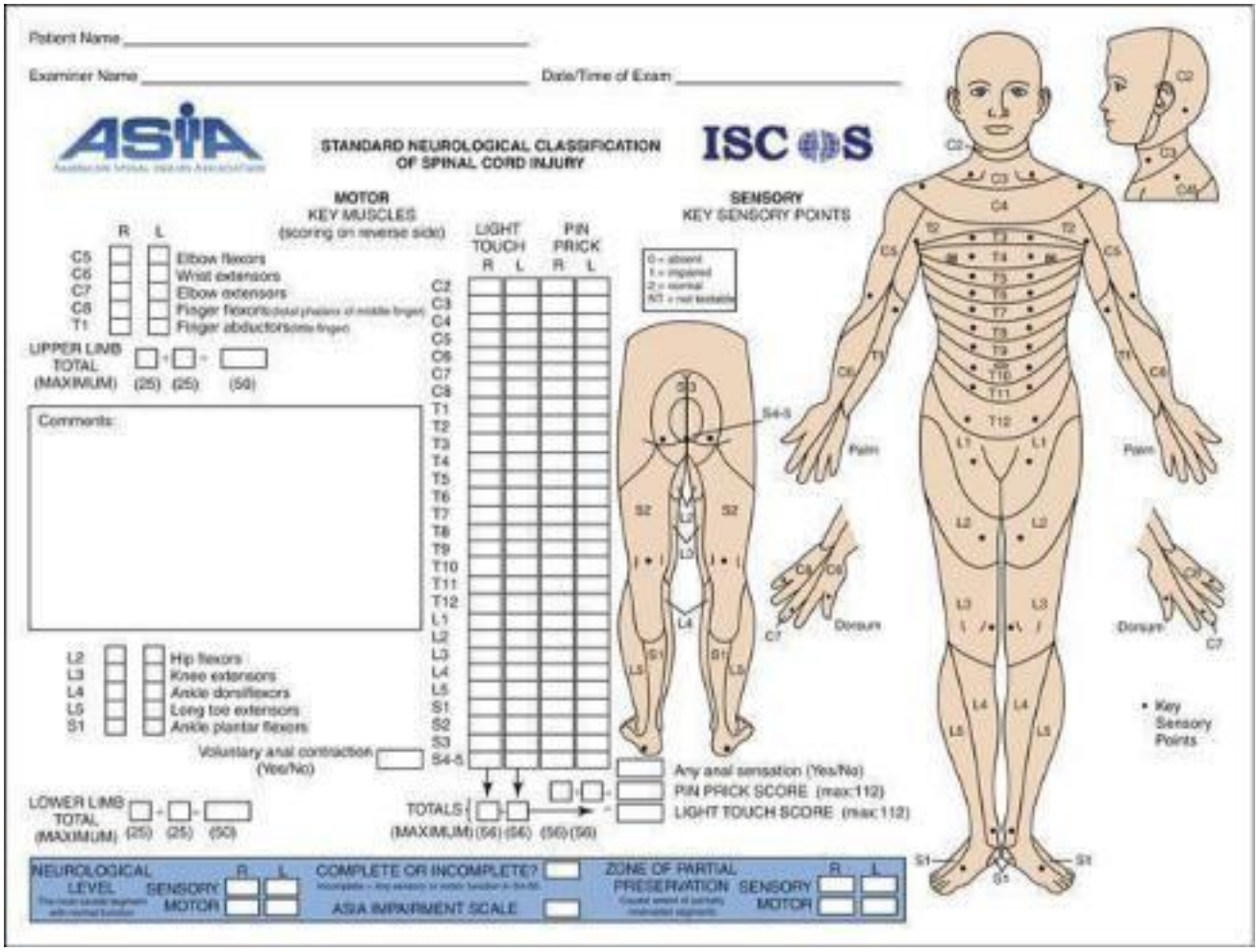
Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

Dr. SM Le Grange
Chair : Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee
Office of the Dean: Health Sciences
T. +27 (0)51 401 7795/7794 | E. ethicsfhs@ufs.ac.za
IRB 00006240; REC 230408-011; IORG0005187; FWA00012784
Block D, Dean's Division, Room D104 | P.O. Box/Posbus 339 (Internal Post Box G40) | Bloemfontein 9300 | South Africa

Appendix D1: Neurological



Radiological Findings:

Quantitative Values:

	FA	ADC
1		
2		
3		
4		

1 FA = standard measurement at the medulla oblongata

2 FA = level above the injury

3 FA = level at the injury

4 FA = level below the injury

FA ratio = FA/ 1 FA

Results:
Total motor score
Total sensory score
FA ratio

Appendix E1: Turnitin for the literature review

TITLE: Correlation of blunt cervical spinal cord injury MRI tractography with The American Spinal Injury Association (ASIA) impairment scale motor scores.

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Page count:	12
Word count:	3,465
Character count:	19,315
Submission date:	13-Jul-2020 06:00PM (UTC+0200)
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TITLE: Correlation of blunt cervical spinal cord injury MRI tractography with The American Spinal Injury Association (ASIA) impairment scale motor scores.

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Submission date:	13-Jul-2020 06:00PM (UTC+0200)
Submission ID:	1357030185

Med research protocol

TITLE: Correlation of blunt cervical spinal cord injury MRI tractography with American Spinal Injury Association Impairment scale (ASIA) impairment scale

Dr O. Seboco

Department of Clinical
Imaging Science University
of the Free State

1. **TITLE**:

Correlation of blunt cervical spinal cord injury MRI (Magnetic Resonance Imaging) Tractrography with ASIA (American Spinal Injury Association) impairment scale

2. RESEARCHERS:

Primary researcher
Dr. O Seboco
Registrar in the department of clinical imaging University of the Free State (UFS)

Supervisor
Dr. Fekade Gebremariam
Radiologist consultant at Pelonomi Hospital clinical imaging department

3. INTRODUCTION:

❖ Epidemiology

Spinal cord injury has become epidemic in modern society. Despite advances been made in the understanding of the pathogenesis, early recognition and treatment it still remains a devastating event often producing severe and devastating disability, with a peak incidence in young adult .traumatic spinal cord injury remains a costly problem for society with direct medical expenses accrued over a the patient's lifetime ranging from $500,00 to $2 million.[1]

The past decade has seen a resurgence in acute traumatic spinal cord injury research with resultant improvements in the understanding of traumatic spinal cord injury pathophysiology

The pathophysiology of acute spinal cord injury is divided into two phases

A) Primary trauma

- Mechanical injury to the spinal cord due to a combination of compression, laceration, distraction or shearing forces.

B) Secondary trauma:

There is disruption of the blood-spinal cord barrier, influx of inflammatory cells, vasoactive peptides, and release of coagulation factors. These events promote thrombosis and spasm of the microvessels leading hypoxia and oligodendrocytes cell aptosis with end results been demyelination.[2]

This current understanding of the pathophysiology of acute blunt spinal cord injury has inevitably led to improvements in management of acute spinal cord and stemmed novel therapies like stem cell regeneration (still in experimental phase)to be considered in regenerating oligodendrocytes with the end goal been remylination.[3]

Parallel (unrelated) technological advancement in MRI has led to actual visualization of spinal cord axons (nerve tracts)

- Previous imaging (X-rays and Computer Tomography) relied on evaluation of spinal column stability (primary injury) with little evaluation of the actual spinal cord. (Miyanji F. 2007)[4]

- The introduction of MRI led to the actual evaluation of the spinal cord with little information on the actual extend of nerve tracts damage.(S Cheran)[5]

- The latest MRI technique appropriately termed MRI tractography is a 3D modeling technique used to visually represent neural tracts using data collected by Diffusion Weighted images (DWI)

➢ Diffusion-weighted magnetic resonance imaging (DWI or DW-MRI) is an imaging method that uses the diffusion of water molecules to generate contrast in MR images. It allows the mapping of the diffusion process of molecules, mainly water, in biological tissues, in vivo and non-invasively. Molecular diffusion in tissues is not free, but reflects interactions with many obstacles, such as macromolecules, fibers, and membranes. Water molecule diffusion patterns can therefore reveal microscopic details about tissue architecture, either normal or in a diseased state.[6]

➢

In white matter, diffusion follows the pathway of least resistance along the white matter tract; this direction of maximum diffusivity along the white-matter fibers is projected into the final image

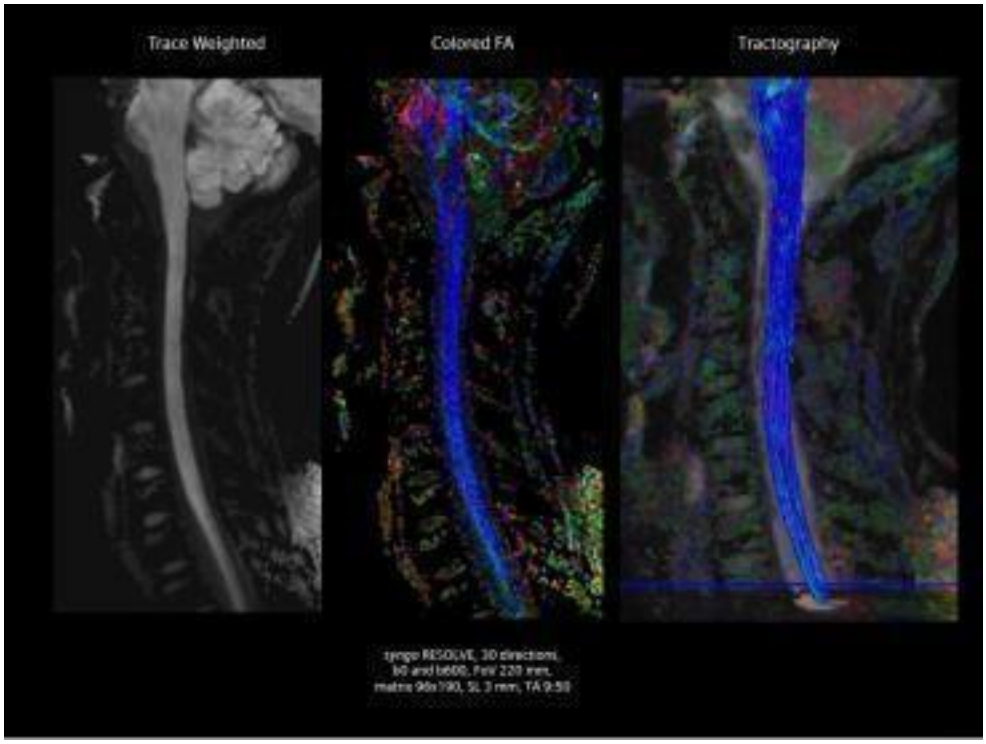

Fig1. MRI Tractography Sagittal view of cervical spine[7]

The following quantitative parameters can be derived from DTI (Diffusion Tensor Images) fig 1 above to provide insight into the status of the axon:

a) Fractional anisotropy (FA): is a scalar value between zero and one that describes the degree of anisotropy (uniformness) of a diffusionprocess

- A value of zero means that diffusion is isotropic, i.e. it is unrestricted (or equally restricted) in all directions

- A value of one means that diffusion occurs only along one axis and is fully restricted along all other directions.[8]

b) Apparent diffusion coefficient (ADC): is a measure of the magnitude diffusion.[9] (the higher the value the higher the diffusion rate and the less the membrane integrity)

❖ Evaluation of spinal trauma patient in Pelenomi Regional Hospital:

Evaluation of patient is divided into to 2 phases radiological and clinical

➢ Clinical evaluation

Neurological evaluation is divided into motor and sensory evaluation[10]

Motor

I. Only the limbs are evaluated, with each limb's power being evaluated separately out of a total score of 25
II. Major joint movement is scored from 0 to 5 III.
Total score of the joints evaluated add up to 50

Grade	Ability to move
5	The muscle can move the joint it crosses through a full range of motion, against gravity, and against full resistance applied by the examiner.
4	The muscle can move the joint it crosses through a full range of motion against moderate resistance.
3	The muscle can move the joint it crosses through a full range of motion against gravity but without any resistance.
2	The muscle can move the joint it crosses through a full range of motion only if the part is properly positioned so that the force of gravity is eliminated.
1	Muscle contraction is seen or identified with palpation, but it is insufficient to produce joint motion even with elimination of gravity.
0	No muscle contraction is seen or identified with palpation; paralysis.

Sensory

I. There are 28 (dermatomes) paired sensory spinal roots to be evaluated (from C2 to S4) each will be scored from 0 to 2 (0 = absent, 1 = is impaired, 2 = normal)
II. In total there will be 56 dermatomes to be evaluate each with a total score of 2 resulting in a maximum score of 112

➢ Radiological evaluation:

- Basic cervical spine x-ray /CT
- MRI is indicated when neurological fall out is diagnosed on clinical evaluation (as of 01/01/2018 it has become mandatory for every acute spinal trauma patient to have a ASIA impairment scale for MRI request)
- MRI imaging with diffusion weighted images is basic imaging tool for all patient with neurological fall out (Pelenomi hospital spinal care imaging protocol)

4. LITERATURE REVIEW:

Most study done on diffusion tensor imaging in a setting of acute spinal trauma have been experimental studies done on animals with few studies focusing on clinical significance of DTI as a corner stone of spinal trauma imaging

Li XHJ (2015)[11]conducted an experimental study to determine the characteristics of magnetic resonance diffusion tensor imaging (**DTI**) in acute spinal cord on rats where he found good correlation between the amount of axon injury on histology and DTI, he also noted that a good time to image is around 72hrs post initial assault.

Similar previous experimental study conducted on animals yielded the same results, (Kim JH 2007)[12], (Ellington 2008)[13], (Feng 2009)[14]

The reason for the limited clinical introduction of DTI was due to the

A) Low signal-to-noise ratio of the small volume of cord tissue,

B) Pulsation artifacts arising from the cerebrospinal fluid (CSF), cardiac and respiratory motion and

C) Magnetic susceptibility artifacts caused by adjacent bone.[15]

Current improvement in MRI imaging has let to improvement in evaluating cervical spine with DTI.

- Two major clinical studies have been conducted:

Sendhil Cheran et al (2011) found a good correlation between ASIA motor scores and DTI (FA values) performed at the injury site after conducting a study on with blunt spinal cord injury and 11 volunteers. The spinal cord

was divided into three regions to account for spatial and pathological variation in DTI parameters.

Vedantam et.al (2015) also conducted a similar a study on 12 patients to evaluate the FA changes rostral to the injury site and found poor correlation between sensory score and FA values, with a better correlation found between motor and FA.[16]

5) Research question and aim

a) Question

- Can FA values (DTI) be used to determine extent of blunt cervical spinal cord injury as classified by ASIA impairment scale

b) Future implication

- Evaluate the effectiveness of current therapy in reducing secondary
- injury Evaluation of stem therapy
- Evaluation of spinal cord injury without radiological abnormalities (SCIWORA)

6) Methodology

6.1) Study design:

Study will be a retrospectively cohort study

6.2 Participants:

•Acute blunt cervical spinal injury patient admitted / seen at Pelenomi regional hospital

•Patient seen from 01/01/2018 to 30/12/2019

•Sample size will be patient seen at Pelenomi for the above mentioned period (estimated size =48)

6.3 Exclusion criteria

Patient with known previous neurological fall out

Penetrating spinal injury

Patient with low GSC < 8 (neurological exam cannot be done) MRI

contraindication

6.4 Measurement

Material used

- 1.5T Siemens MRI machine
- Built in DTI spinal cord protocol which is used as part of a standard care at Pelonomi

Data collection:

a) Imaging information

1) DTI reconstruction protocol will be used to display the image in color display
2) Region of Interest Selection (ROI):
   - 4 FA values will be obtained using same sample volume size (ROI)
     - at the level of the medulla (will be regarded as the reference value)
     - at the level of the injury
     - one vertebral body above the injury site
     - one vertebral body below injury site
   - the ratio of the 3 spinal FA will be obtained (no standard FA value for normal spinal cord exist)

b) ASIA impairment scale (clinical information)

Enclosed (back)

Physical examination will be done by referring physician (spinal unit doctor) using a standardized ASIA impairment scale form.

ASIA impairment scale serve as part of a standard MRI (spinal trauma) request form at Pelenomi regional Hospital

6.5 Methodological and measurement bias

- Clinical data will be collected by different doctors
- Change in neurological status between clinical evaluation and imaging
- Different in ROI area / volume can give different values

6.5 Corrective measures

- Standardized ASIA impairment scale form
- The period between clinical exam and radiological exam will be noted
- Same ROI volume

6.6 Data analysis

Data analysis will be done with the help of a statistician from UFS biostatistics department. The researcher will enter the data into and Excel spreadsheet for analysis purposes. Results will be summarized by frequencies and percentages (categorical variables) and means, standard deviations or percentiles for numerical variables. Correlations will be assessed using Pearson or Spearman rank correlations depending on data distributions.

6.6 Pilot study

Pilot study will be done after the ethics approval of the study for a period of a month

7. Implementation

FA values will be used to grade severity of spinal cord injury

FA values will be used to evaluate therapy

8. Time schedule:

• Protocol will be submitted to the Health Science Research Ethics Committee (HSREC) in November

• Free State department of health after approval from HSREC inJanuary

• Data collection from patient seen between 01/01/2018 to 30/12/2019

9. Budget

• Data will be collected Monday to Friday after hours (NO transport cost)

• R300 for Radiological findings and ASIA impairment scale forms

• DTI imaging part of Pelonomi scanning protocol

10. Permission from relevant parties

• Free State department of Health

• Head of Pelonomi Regional Hospital radiology department

• HSREC

Reference

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10) https://meded.ucsd.edu/clinicalmed/pe_neuroexam.pdf

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nonhemorrhagic acute spinal cord injury. JOURNAL OF NEUROTRAUMA. Vol 28:1881–1892

16) Vedantam Aditya, Eckardt Gerald.(2015).Clinical Correlates of High Cervical Fractional Anisotropy in Acute Cervical Spinal Cord Injury. World Neurosurgery. Vol. 83

Appendix G: SAJR PUBLICATION NOTIFICATION

aosis@sajr.org.za
To: Orapeleng Seboco

****

Ref. No.: 2038
Manuscript title: Correlation of blunt cervical spinal cord injury MRI tractography with the American Spinal Injury Association (ASIA) impairment scale motor scores
Journal: South African Journal of Radiology
ISSN: 1027-202X, E-ISSN: 2078-6778

****

Dear Orapeleng Seboco

The journal has a double-blinded peer review process and your manuscript was assessed by two expert independent reviewers. Read our peer review process https://aosis.co.za/policies#peer_review.

Thank you for your revised manuscript. We have reached a decision regarding your submission. I am pleased to inform you that your manuscript has now been accepted for publication.

The Editorial Office will contact you by 25 January 2021 to finalise your manuscript for the Finalisation and Publication Office. If you need any assistance, kindly contact the Editorial Office at submissions@sajr.org.za with any questions or concerns.

Dr FA Gebremariam