PROTOCOL

I. PURPOSE OF STUDY

Patients frequently inquire about when they can safely resume driving after undergoing orthopaedic and spine surgery procedure. Compromise of any of the cognitive, neurological and musculoskeletal systems involved in operating a vehicle can significantly hinder one's ability to safely drive. There has been increasing interest in the literature regarding ability to safely drive following orthopaedic and spine surgery, with numerous studies analyzing the impact of a variety of orthopaedic interventions on driving performance. However, there have been no well-designed studies elucidating an appropriate timeframe to resume driving after cervical spine surgery. As a result, no evidence-based recommendations exist to determine a patient's "fitness to drive" in the perioperative or postoperative state. Using a validated driving simulator, the goal of this study is to delineate the effect cervical spine procedures have on driving performance in the perioperative time period.

Subjects who are indicated for cervical spine surgery will be screened for inclusion in the study. If the subject meets all of the eligibility criteria and agrees to participate in the study after informed consent, they will be enrolled to complete multiple phases of testing with the driving simulator set-up. Subjects will be divided into the following groups: single-level anterior cervical discectomy fusion (s-ACDF), multi-level anterior cervical discectomy and fusion (m-ACDF), cervical disc replacement (CDR), posterior laminectomy and fusion (PCLF), posterior cervical decompression procedure (PCD). Each group will contain a total of 30 subjects. The study will evaluate and compare peri-operative changes in driving performance following these procedures. We will evaluate driving performance at the pre-operative time period as well as 2-weeks, 6-weeks and 3-months post-operatively. A group of 40 healthy volunteers will also be tested with the driving simulator to serve as controls.

The primary hypothesis of this study is that there is a temporal effect on patient's driving ability after cervical spine surgery. We believe that pre-operative and post-operative clinical and functional measures will have an impact on driving performance. Pre-operative measures include pre-operative driving performance measures, neck disability index (NDI), PROMIS, numeric pain rating scale (NRS), pre-operative diagnosis, comorbidities, clinical and physical exam measures, maximum axial rotation of neck and torso, narcotic usage, questionnaire responses and demographic information. Post-operative measures include post-operative driving performance, type of surgery, complications, radiological outcomes, neck disability index (NDI), PROMIS, numeric pain rating scale (NRS), clinical and physical exam measures, maximum axial rotation of neck and torso, narcotic usage and questionnaire responses.

II. BACKGROUND

Degenerative changes in the cervical spine represent an important source of pain and disability in the middle-aged and elderly population (1-3). An estimated 50% of patients with symptomatic cervical disc disease report moderate to severe disability while driving (4). From 1990 to 2000, the total number of cervical spine procedures performed annually more than doubled (2), with recent data showing cervical spine fusions for degenerative cervical disease increased 206% among Medicare beneficiaries from 1992 to 2005 (5). Given the increasing amount of cervical spine procedures being performed annually, it is common for patients to inquire about their ability to drive after surgery.

Driving is a multi-system task that requires cognitive coordination of a variety of complex and coordinated muscular actions. The safe operation of a motor vehicle requires the driver to have adequate range of motion of the extremities to perform steering, braking, reversing and maneuvering of the vehicle. Automobile accidents are a significant cause of death and injury in the

United States with over ten million accidents every year and human error being a contributing factor in over 90% of all cases (6-9). In the United States, both the Council on Ethical and Judicial Affairs (CEJA) of the American Medical Association and National Highway Traffic Safety Administration (NHTSA) describe the central responsibility of physicians to assess physical and mental impairments that might adversely affect driving (9). The importance of establishing evidence-based guidelines is critical because the term 'fitness to drive' represents a multi-faceted issue with medical, legal and financial implications.

While guidelines for driving following numerous orthopaedic procedures related to the upper and lower extremities have been substantiated by numerous studies (10-17) there is a paucity of quality research in the context of surgical procedures of the spine. A majority of studies related to driving performance after spinal procedures utilize a simple analysis of break reaction time (BRT)or driving reaction time (DRT) (used interchangeably in the literature) to extrapolate driving performance.

Al-khayer demonstrated delayed DRT following selective nerve root block (SNRB) in patients with lower extremity radicular symptoms, which returned to pre-operative values at 6-week follow-up. The authors concluded that given these changes, radiculopathic patients should be cautious when driving immediately post-SNRB and that changes in DRT may persist a few-weeks post-SNRB (18).Two studies have evaluated driving reaction time in patients with lumbar radiculopathy undergoing micro-lumbar discectomy (MLD) (19, 20). In both studies, mean patient DRT was significantly slower than in controls at all time points; however, MLD was shown to improve DRT and severity of back pain was found to have a negative affect on DRT (19). A follow-up study by the authors found the effect of MLD on improving DRT was more pronounced in patients with pre-operative paresis (20). Given the immediate post-operative improvement in DRT and lack of a generally accepted threshold for DRT, the authors concluded that it is safe to continue driving after hospital discharge following MLD. Similarly, Liebensteiner et al measured driving performance after lumbar fusion surgery using DRT as the primary study end-point (21). The authors reported no significant difference in DRT in the immediate post-operative period; however, they did note that at 3-month follow-up there was a significant improvement in DRT, with back pain having a negative affect on DRT. Based on these findings and the lack of an accepted guideline for optimal DRT, the authors concluded that patients could be permitted to continue driving in the immediate postoperative period.

Only two studies have evaluated driving performance following cervical spine surgery using an experimental model. Lechner et al. evaluated brake reaction time and neck/arm pain pre-operatively, a day prior to discharge and 4 to 6 weeks post-operatively (22). The authors stated that it appears to be safe to resume driving after discharge from hospital. However, patients scheduled to undergo anterior cervical discectomy and fusion (ACDF) should be informed about increased DRT as compared to healthy individuals. Similarly, Wang and colleagues compared DRT in 37 patients at 2, 6 and 12-weeks following lumbar and cervical spine surgery to healthy controls (23). Patients undergoing multi-level lumbar fusion and posterior cervical surgery were found to have delayed DRT at baseline, with no significant improvement post-operatively. However, patients undergoing single-level lumbar fusion surgery were found to have significant improvements in DRT in the early post-operative period. Based on their findings, the authors concluded that it may be acceptable to allow patients having a single-level lumbar fusion who are not taking opioids to return to driving as early as 2 weeks following the spinal surgery. Aside from prospective controlled studies, one study has evaluated patient self-reported driving ability following cervical spine surgery. Kelly et al performed a post hoc analysis of patients' self-reported driving disability from neck pain via NDI measures on patients involved in an investigational device exemption study of ACDF and cervical arthroplasty.

The authors found that 80% of ACDF patients and 92% cervical disc arthroplasty patients reported none or little disability when driving at 6-weeks post-operatively, which was the first postoperative time point recorded in their study (4).

Truly evaluating a patient's ability to drive can only be evaluated in actual real-world driving scenarios, however, given the public safety risk and legal implications, a real-world experimental driving trial is not feasible. The use of the STISIM driving simulator, complete with computerized driving scenarios and driving hardware, has been validated in numerous studies (24-28) and allows for a more comprehensive investigation of driving performance. The simulated course recreates standard turns, traffic intersections, pedestrian crosswalks, lane changes and several hazardous conditions routinely encountered during driving situations. The robust data collection feature of this simulator allows for the creation of customized circuits, which can measure vehicle road position, average speed, driving reaction time and collisions encountered.

It is our hypothesis that in evaluating a patient's safety to return to driving after cervical spine surgery, there are numerous outcomes that would require investigation. The patient's pain and disability measures will likely play a role in the patient's ability to adequately operate a steering wheel and depressing the break pedal. This can be due to residual motor weakness and pain encountered when utilizing the upper extremities secondary to myelopathy or nerve root compression. This can be investigated by evaluating vehicle control in normal driving scenarios as well as hazardous scenarios that require evasive maneuvering.

Another critical factor is the patient's cervical and thoracic range of motion both pre-operatively and post-operatively. Adequate neck and torso range of motion is critical for performing driving tasks such as evaluating intersections, changing lanes and reversing. Studies suggest that reduced range of motion (ROM) and maximum angular velocity (MV) of head rotation have a negative impact on driving (29).Numerous studies have shown that cervical range of motion is decreased after both anterior and posterior cervical procedures, when compared to that of healthy controls (30, 31). Increasing the number of cervical levels that are fused progressively decreased the active cervical range of motion of the patient. A recent clinical study revealed that there are significant step-wise decreases in cervical range of motion when comparing 1, 2, 3, and 4 level ACDFs to controls. Cervical axial rotation decreased from 7 to 31 degrees with increasing levels of fusions. This study also revealed that in the early postoperative period defined as about 110 days postoperatively there was still approximately a 12% decrease in both cervical flexion and extension and a 12% decrease in axial rotation (29).Via the use multiple monitors to create an 180 degree field of view and the use of multiple simulated blind-spots, we will be able to provide a more robust analysis of driving performance following cervical spine surgery

This study aims to provide objective data regarding the driving ability of patients undergoing cervical spine surgery at both preoperative and postoperative time points. The goal of this project is to help provide evidence-based recommendations regarding the effects of cervical spine surgery on driving safety.

III. STUDY OBJECTIVE

This study is a single-center, prospective controlled simulation study designed to compare and evaluate driving performance of subjects who have underwent cervical spine surgery via the use of a validated driving simulator. The objective of this study is to delineate the effect cervical spine procedures have on driving performance in the perioperative time period.

IV. MATERIALS AND METHODS

A. TRIAL ORGANIZATION

The study will be conducted at a single institution: New York University Langone Medical Center – Hospital for Joint Diseases. Surgeries will be conducted at NYU-HJD and New York University Langone Medical Center, while patient follow up and visits will occur at the NYU Center for Musculoskeletal Care.

B. INVESTIGATORS

All patients are recruited through the NYU Department of Spine Surgery faculty group practice and their affiliated private offices. Patients who meet inclusion criteria and are seen for clinical visits and post-operative follow-up at the Center for Musculoskeletal Care and Madison Orthopedic Surgery Center will be consented and taken to the Center for Musculoskeletal Care Rehabilitation Center which houses the driving simulator apparatus. Patients will be consented by the investigator, persons completing research fellowships in orthopaedic surgery and/or persons working exclusively on clinical orthopaedic research projects. These researchers all have experience seeing and consenting patients. These patients will be consented if they meet inclusion criteria. Surgeries will occur at New York University - Hospital for Joint Diseases and Tisch Hospitals.

C. PATIENT SELECTION

STUDY SUBJECTS

This will be a prospective experimental model study. All non-control study participants will be patients seen by the NYU Department of Spine Surgery faculty group practice and their affiliated private offices. The same care will be provided independent of the patient's willingness to be a part of the study. Patients will be 18 years old or older. There will be no vulnerable subjects in study except for patients older than 65 and patients who are employees or students of NYULMC or NYUSOM. 210 subjects total will be recruited to comprise 7 groups of patients, which was calculated based on power analysis performed using a similar driving simulator study by the authors. Only patients who are able to understand the English language will be allowed to participate in the study due to the nature of the validated questionnaires that will be given to them. The patients will be made known that participation in the study will not affect the standard of care delivered by the investigators. No ethnicities will be prohibited from participating in the study. Males and females will participate in the study as close to a 1:1 ratio as possible. Operative patients who are required to complete research activity for four visits will be compensated. Patients from the CMC office and Madison Orthopedics office will be compensated $50 for all four visits. Patients who regularly see their physician at farther office sites including but not limited to Seaport Orthopedics and Long Island Branches will be compensated $100 for all four visits. Optional visits in this study will not be compensated. If all four visits are not completed, patients will be compensated at the end of their participation in accordance with the percent of visits they completed. IRB approved study advertisement will be used to better reach patients.

Payment for Participation

Subjects will be reimbursed using Greenphire ClinCard which will allow reimbursement and notification to patients instantly as mentioned in the Study Subjects section above.

Using Greenphire ClinCard instead of cash or money orders will reduce subjects' drop out. It will provide direct reimbursement to eliminate the financial hurdles that may keep participants from completing study visits. It will provide subjects with instant access to cash via a reloadable debit card. Subjects will be asked to provide their social security number or Alien Registration number, date of birth, and address. This is a requirement for participating in the Greenphire program as this information is needed for federal tax purposes and without this information, subjects cannot sign up the study. We do not anticipate that this will deter patients from enrolling. Optional visits in the study will not be reimbursed.

CONTROL SUBJECTS

40 healthy volunteers will be recruited to undergo one phase of testing using the driving simulator model to serve as a control group. 20 will undergo testing without a collar. 20 will undergo testing using a hard cervical collar vs. soft cervical collar vs. no collar to test limitations of cervical collars on subjects in the driving simulator.

The study will require utilization of the color control group to further elucidate any impact a hard and soft cervical collar will have on ability to drive. Given there will be restricted cervical range of motion when utilizing a cervical collar, the cervical control group will serve two purposes:

1) To elucidate whether the cervical range of motion restrictions result in decreased range of motion versus a healthy control population when surveying traffic for blind spots.

2) To elucidate whether cervical range of motion restrictions results in decreased driving performance in terms of driving simulator output as compared to a healthy control population.

Volunteers will not receive financial compensation for their participation as only one sitting is required. Compensation will be given to subjects who need to return for follow up visits based on the extent of their travel requirements.

SUBJECT WITHDRAWAL CRITERIA

Patients/subjects are free to withdraw at any time from the study. New subjects will be recruited to replace them.

D. STANDARD OF CARE VS. RESEARCH PROCEDURES

- Unique to Research Procedures
    - Questionnaires (Neck Disability Index, Numeric Pain Rating Scale, PROMIS , narcotic use survey, driving history survey, post-simulated driving survey, EQ5D, and mJOA)

- Measurement of cervical and thoracic axial range of motion using video motion capture technology
- Field of view testing
- 10s grip and release test, 10s step test, Tandem Gait (heel-to-toe) walk*
- Testing of driving performance using a customized driving simulator set-up

- All other procedures are standard of care for all investigators involved

E. *These tests tend to be done as part of standard of care identifying myelopathy patients, but in the case it is not performed as standard of care we will perform the tests as a research procedure. Only clinical research staff or non- clinical staff trained to perform the tests will perform the tests. For non-clinical staff who received training, we will still ensure a clinician is in close proximity if help is needed while doing the tests.

INCLUSION CRITERIA

- *Study Subjects:*
  - Age between 18 and 80 years
  - Indicated for elective cervical spine surgery (including ACDF [single or multi-level], posterior cervical laminectomy and fusion, posterior cervical laminoplasty, posterior cervical foraminotomy, cervical disc replacement) after failing at least 6 weeks of non-operative treatment modalities
  - Valid driving license
  - Regular use of a vehicle
  - Signed consent form

- *Control Subjects:*
  - Age between 18 and 80 years
  - No pre-existing or recent injuries to neck, torso, back
  - No neurologic or systemic debilitating conditions
  - Valid driving license
  - Regular use of a vehicle
  - Signed consent form

F. EXCLUSION CRITERIA

- Significant visual impairment
- Significant debilitating neurological condition with loss of function of one or more extremities
- Recent extremity surgery
- Recent eye surgery
- Previous history of motion sickness, vertigo in simulated settings
- Recent history of chemical or narcotic dependency

G. VULNERABLE POPULATION

Students and faculty of NYU School of Medicine and NYU Langone Medical Center will be recruited as potential control subjects and will be eligible to participate in the study. Students and faculty can voluntarily participate in this study without coercion. The Principal Investigator, Sub-Investigators, and research staff will ensure there are additional safeguards for these subjects. They will

emphasize that neither the subjects' academic status, grades, and/or employment will be affected by their decision to participate or not. The principal investigator, sub-investigators, and research staff will ensure that the subjects' record of participation cannot be linked to any type of academic or employee record. The Principal Investigator will ensure that the research design addresses such institutional pressures and preserves the right for subject to refuse participation

Subjects 65 years of age or older will also be recruited as potential subjects and will be eligible to participate in the study if their treating surgeon deems them eligible.

H. Potential Benefits

There are no absolute benefits for the patient or volunteer to complete this study. Patients may potentially become more aware of their post surgical condition and it may affect their ability to drive. Furthermore, from subject participation in the study, there will be a better understanding of the impact cervical spine surgery has on driving performance. This can then allow practitioners to make evidence-based recommendations regarding changes in driving performance in the post-operative period.

I. Adverse Events/Risks

There are no significant risks associated with this study. The driving simulator set-up has been used in three previous studies by the investigators and no adverse events have been reported. The simulated driving scenario can potentially result in motion sickness during the trial. Additionally, there is the possibility that axial rotation of the neck and/or torso may cause the patient discomfort when driving.

J. Protection against Risks

The study subjects will be instructed to inform the research coordinator if they experience motion sickness or discomfort. The simulated trials will be stopped immediately and the study subject will be asked if they would like to complete the trial. If the study subject does not wish to complete the trial, they will have the option to complete the trial at a later date or be removed from the study. The investigators are familiar with the protocol and have utilized this driving simulator in previous studies. For data collection, the research coordinator is knowledgeable in the field of orthopaedic care and clinical research. All personnel have completed CITI training and the investigators have a dedicated staff and nurse to attend to the patient's medical and psychological needs if needed. If patients require medical monitoring, ancillary care, or equipment, patients will be able to seek care in case of an emergency at the NYU-HJD Immediate Care Center, which is open 24/7. The research coordinator, will also be available to patients during regular office hours.

K. Investigation schedule and follow-up

Data will be collected regarding individual patient demographics,pre-operative diagnosis, procedure and driving history at the pre-operative and first post-operative time period. Patient-reported outcome instruments (NDI, PROMIS , NRS), physical exam measures, narcotic usage, driving performance measures, a post-simulated driving questionnaire and maximal axial rotation of the neck and torso will be collected at all time points. The EQ5D and mJOA survey will be collected only

from myelopathy patients at baseline, 3 month, and 6 month. This data will be recorded onto a de-identified data collection sheet by the researchers. The patient data sheets will then be entered into a protected electronic database, while the data sheets will be stored as a back-up until the study is complete. Once the completed database is analyzed and summarized, the results will be presented to the involved participants without any identifiable patient information. Follow-up will be the investigators' routine follow-up at 2 weeks, 6 weeks,3-months, and 6 month post-operatively. The 6 month routine follow up is unique to myelopathy patients only.

L. CASE REPORT FORMS

1. **PRE-OPERATIVE VISIT**
    a. Informed consent
        i. If informed consent is not obtained at pre-operative visit, the visit will not continue.
    b. Investigator Form (Complete Sections 1-9)
    c. NDI, PROMIS, NRS Forms
    d. Post-Simulation Subject Questionnaire
    e. EQ5D and mJOA survey*
2. **2-WEEK FOLLOW-UP**
    a. Investigator Form (Complete Sections 6-9)
    b. NDI, PROMIS, NRS Forms
    c. Post-Simulation Subject Questionnaire
3. **6-WEEK FOLLOW-UP**
    a. Investigator Form (Complete Sections 6-9)
    b. NDI, PROMIS, NRS Forms
    c. Post-Simulation Subject Questionnaire
4. **3-MONTH FOLLOW-UP**
    a. Investigator Form (Complete Sections 6-9)
    b. NDI, PROMIS, NRS Forms
    c. Post-Simulation Subject Questionnaire
    d. EQ5D and mJOA survey*
    e.
5. **6-MONTH FOLLOW-UP (OPTIONAL)**
    a. Investigator Form (Complete Sections 6-9)
    b. NDI, PROMIS, NRS Forms
    c. Post-Simulation Subject Questionnaire
    d. EQ5D and mJOA survey*

*patients will only be given these surveys if they have been diagnosed with myelopathy

M. Informed Consent Process

A patient of the investigators' will be asked to participate in the study if they both meet the inclusion criteria and not the exclusion criteria. The patients will be given an informed consent form, which will also be explained orally by the investigator/research coordinator. Documentation of informed consent will occur by keeping a hard copy of each informed consent form that is signed and initialed by the subject. In addition, the research coordinator will fill out an informed consent documentation process form similar to the one as follows:

"Subject _____ has been enrolled in the study _____ on _____. The study was explained to the subject by research assistant _____. The subject was given a copy of the consent whereby the informed consent was read by the subject and his/her family member. The subject and the family were given an opportunity to ask questions of his surgeon. A signed copy of the consent was given to the subject/family. Consent was obtained prior to the performance of any study procedures."

These will also be kept in a binder that is locked in a secure office that will only be access by study personnel.

N. Study Design

This is prospective, controlled study utilizing a validated driving simulator to assess driving performance following cervical spine surgery. There will be a total of 6 groups*:

1. Single-level anterior cervical discectomy fusion (s-ACDF); n=30
2. Multi-level anterior cervical discectomy and fusion (m-ACDF); n=30
3. Cervical disc replacement (CDR); n=30
4. Posterior laminectomy and fusion (PCLF); n=30
5. Posterior cervical decompression procedure (PCD); n=30
6. Myelopathy patients who do not undergo surgery (N=20)
7. Control group (C); n=40

*Patients who have myelopathy undergoing surgery fall under groups 1 -5 and have not been grouped differently given they belong first to the above groups before being sub-identified as the myelopathy group

The first aim of this study is to elucidate the time interval in the post-operative period in which there is the largest decline in driving performance. The second aim of this study is to evaluate the post-operative time interval at which patients' return to baseline driving performance. We will address all clinical questions by comparing the outcomes measures of driving performance pre-operatively and at three subsequent post-operative time points: 2 weeks (PO_2), at 6 weeks (PO_6) and at 12 weeks (PO_{12}). We will also use the NDI, PROMIS and NRS scores collected at each interval to elucidate whether these clinical questionnaires serve a predictive role in evaluating driving performance. This information will also be compared to control data obtained from healthy

volunteers. The driving-simulator experimental set-up will consist of the subject sitting in front of the driving simulator with three screens allowing for an 180° field-of-view with a camera positioned overhead; the subject will have markers placed over shoulders and head to allow for motion-capture analysis with objects placed at various locations to simulate blind spots. Figure 1 summarizes the experimental set-up.Table 1 summarizes all outcome measures and data collection timeline.

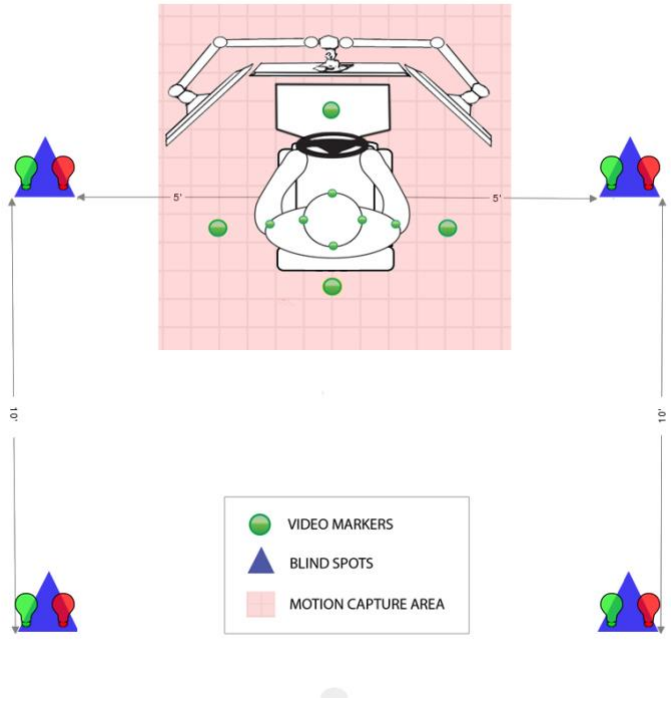

Figure 1: Experimental Set-Up

Driving Simulator

A driving simulator will be utilized to reproduce "typical" driving conditions in an automatic transmission vehicle. To assess the change in driving performance, a previously established testing model with software and hardware set-up will be employed (32-34). Specifically, automobile components of the driving simulator included brake and accelerator pedals connected to a brake cylinder and force transducer, an adjustable steering column, and an adjustable car seat. The pedal assembly is connected to an analog to digital converter that transmits positional information to the computer. Three monitors (Dell, Round Rock, TX) will be utilized to create a 180° field-of-view with the center of the screen located at eye-level through the midline of the subject. Surround speakers (Dell, Round Rock, TX) will be utilized to produce road sounds and to issue instructions to the subject. Labview software (National Instruments, Austin, TX) will be used to collect and display data via an analog or digital board (AT-EIO-64, National Instruments, Austin, TX) with a sampling rate of 1,000 Hz from the accelerator and brake pedals. Windows STISIM Drive V3.0 software (Systems Technology, Hawthorne, CA) will be used for acclimatizing subjects to the software as well as testing

subjects in simulated real-world driving conditions. Car and steering responses will be recorded with STISIM software. Data will be collected for specific events during the programmed driving scenario. Each subject will be allowed a single training circuit to familiarize to the simulator prior to any data collection. Patients will undergo testing using a simulated driving circuit (SDC) lasting approximately fifteen minutes. The SDC is designed to represent a combination of suburban, highway and residential driving environments. The course will recreate standard turns, traffic intersections, pedestrian crosswalks, lane changes and several hazardous conditions routinely encountered during driving situations. Patients will be instructed to stay below the indicated speed limit. In the event that subjects exceeded this limit, a computer-generated auditory warning will be issued. There will be pre-programmed prompts during the circuit to indicate to the driver to perform specific maneuvers (change lanes, turn at intersection, come to full stop). Subjects will be informed that the simulator could make them feel uncomfortable and they will be instructed to inform the experimenter if this happens, at which point, the scenario will be stopped immediately.

Measurement of Cervical Rotation

Cervical axial rotation will be recorded using an overhead camera(Canon, Melville, NY) positioned over the simulator set-up as graphically depicted in Figure 2. Four video markers will be placed on the subjects head, 2 markers will be placed on the acromio-clavicular joint and 4 markers will be placed on the ground to serve as reference points as depicted in Figure 1. Video motion analysis software (Dartfish, Atlanta, GA) will be used to measure cervical and thoracic rotation using the static ground video markers as a reference. Prior to beginning each trial, painless maximal axial rotation of the neck and torso will collected by having the patient sit in the simulator and follow these prompts:

1. *While keeping your torso still, please rotate your head as far right as you can, stopping at the point of discomfort. Now repeat, by rotating your head as far left as you can, stopping at the point of discomfort.* ***(maximal axial rotation of neck)***
2. *While keeping your neck still, please rotate your body as far right as you can, stopping at the point of discomfort. Now repeat, by rotating your body as far left as you can, stopping at the point of discomfort.* ***(maximal axial rotation of torso)***
3. *You can now rotate both your body and neck as far right as you can, stopping at the point of discomfort. Now repeat, by rotating your body and neck as far left as you can, stopping at the point of discomfort.* ***(maximal axial rotation)***

The amount of rotation during each specified lane change or turning event during each testing interval will be collected and recorded. Additionally, the time required to achieve maximal rotation and time required prior to initiating and completing a lane change will be collected. Finally, the average and maximal amount of axial range of motion will be collected over each testing interval and compared.

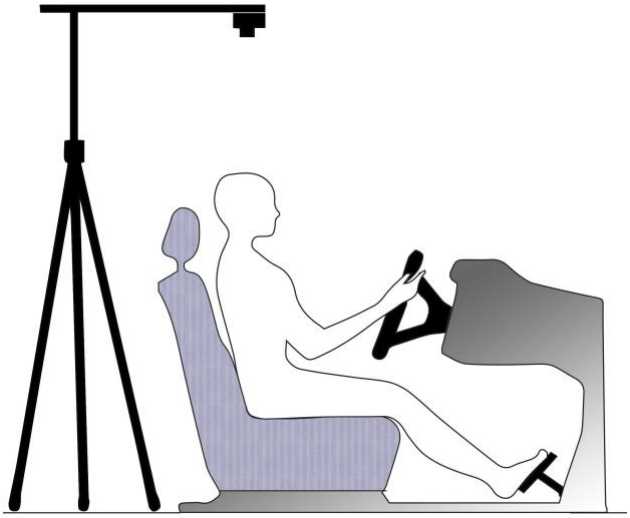

Figure 2: Lateral via of experimental set-up

Lane Changes and Blind Spot Detection

Visual inspection of the rearview and side mirrors and the blind spot using appropriate eye–head movements is generally needed before taking the decision to change lanes (35). The driving scenario will include 20 events for which the driver would require evaluation of blind spots prior to lane changes. Based on data published by the U.S. Department of Transportation, National Highway Traffic Safety Administration (Figure 3) from experimental analysis of blind spot position for 75 vehicles, four multi-colored LED lights (AOMEtech, Guangzhou, China) will be placed in constant locations relative to the subject to simulate the blind spot (36). The lights have a control feature, which allows the operator to change the color remotely. Prior to testing, subjects will be instructed that a "green" light will signify that there are no vehicles in the blind spot and a "red" light will signify that there is a vehicle in the blind spot (See Figure 1 for depiction). Prior to beginning the trials, patients will be instructed to check appropriate blind spots prior to all lane-changing events. If a subject changes lanes without checking the appropriate blind spot or changes lanes when a vehicle appears in a particular blind spot, an unsafe driving event (UDE) will be recorded. The total amount of UDE occurrences will be recorded for each patient in each trial. The appearance of vehicles in each blind spot will be remain constant for all patients in each particular phase of testing (i.e. pre-operative) however, locations will be randomized across each subsequent trial (i.e. 2, 6 and 12-weeks post-operatively) to prevent learning bias.

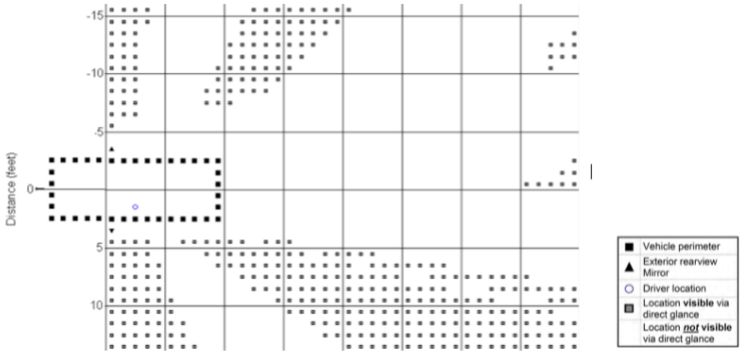

Figure 3: Actual vehicle representation of decreased visibility (Mazzae, NHTSA 2009)

Location 1 is located on the left, 5 feet lateral from the subject. (L1)
Location 2 is located on the left, 5 feet lateral and 10 feet posterior from the subject. (L2)
Location 3 is located on the right, 5 feet lateral from the subject. (R1)
Location 4 is located on the right, 5 feet lateral and 10 feet posterior from the subject. (R2)

Measurement of Driving Performance

In addition to the number of unsafe driving events (UDE), driving performance will be evaluated by examining the overall number of collisions, the number of centerline crossings, and the number of off road excursions. Total collisions encompass both "off-road" collisions, when patients veer too far laterally from the computerized boundaries of the driving circuit, and "on-road" collisions, which occur if a patient's vehicle collides with other cars, pedestrians, hazard work cones, or cyclists designed to be in the program. The number of centerline crossings will be measured by the number of times the patient's vehicle traverses the centerline crossing over into oncoming traffic. Lastly, "off-road excursions" will be determined by the number of times the patient's vehicle traversed the lateral road edge and travelled off onto the grass.

Clinical Evaluation

Neck Disability Index (NDI),NRS, PROMIS and clinical data (motor, sensory, pain) will be collected prior to each trial and will server as measure of functional clinical outcomes. Baseline active painless neck and torso range of motion (axial rotation) will be collected for each patient prior to each trial as described previously. The Dartfish Software has the option of selecting various points in space that will allow computer generated range of motion to be calculated and exported to excel format. The data will then be transferred to a secure data collection file. In addition, field of view evaluation, narcotic use and level of fatigue will be collected prior to each trial.

Demographic Information and Questionnaires
Prior to beginning testing, each patient will complete sections 1-6 of the Investigator Form:

Investigator Form (Sections 1-5)

1. **Demographic Information:** age, gender, ethnicity, height, weight, medical comorbidities, surgical history, history of ocular, neurologic and musculoskeletal conditions, history of

motion sickness, smoking history, worker's compensation status, current involvement in litigation

2. **Driving Information**: driving experience (years), self-judged frequency of driving, self-reported number of accidents over the last five years, participants' self-judged driving ability with three response categories [poor (1), average (4), and above average (7)]

The research coordinator will complete Sections 6-9 at all testing intervals:

Investigator Form (Sections 6-9)

1. **Surgical Information:** (diagnosis, procedure, complications)
2. **Clinical Information:** (symptom duration, myelopathic evaluation, motor/sensory evaluation, pain and fatigue level, field of view testing
3. **Narcotic usage:** recent intake, last intake, current medications, frequency of medication usage

After each trial, patients will receive a post-simulation questionnaire:

Post-trial Questionnaire

1. Participants' self-judged level of safety while driving with three response categories; unsafe (1), moderately safety (4), very safe (7)
2. Participants' self-judged level of comfort while driving with three response categories; uncomfortable (1); moderately comfortable (4); comfortable (7)
3. Participants' self-judged effect of surgery on driving ability with three response categories; made worse (1); no effect (4); improved (7)
4. Participant's belief that the simulator can reproduce real-world driving on a numerical scale of 0 – 10 (0=not realistic, 5=moderately realistic, 10=very realistic)

FDA Status of Driving Simulator

FDA Medical Device Definition

If a product is labeled, promoted or used in a manner that meets the following definition in section 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act it will be regulated by the Food and Drug Administration (FDA)as a medical device and is subject to premarketing and postmarketing regulatory controls. A device is:

- "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
  - recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
    - NOT APPLICABLE TO DEVICE.
  - intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
    - DEVICE CANNOT BE USED TO DIAGNOSE ANY CONDITIONS.
    - DEVICE SERVES TO DETECT CHANGES IN DRIVING PERFORMANCE IN A SIMULATED SETTING.
    - DEVICE NOT USED FOR CURE, MITIGATION, TREATMENT OR PREVENTION OF ANY CONDITION.
  - intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action

within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

- DEVICE CANNOT AFFECT STRUCTURE OR FUNCTION OF SUBJECTS.

Given that this device does not meet the criteria for a medical device, the device is exempt from FDA regulations. Furthermore, the STISIM simulator has been validated and used in numerous studies including FDA evaluation of drug performance on driving ability (1).

The U.S. Department of Transportation and National Highway Traffic Safety Administration have similarly conducted many studies using the STISIM simulated environment (2,3). Numerous clinical trials have been conducted using the STISIM simulator(4-8). The number of patients enrolled in these studies ranged from 20-30 subjects per group.

O. Data Analysis, Monitoring and Storage

1. Types of Data
    a. Data Accuracy
    b. Protocol Compliance
    c. Recruitment of Subjects
    d. Screen Failures
    e. Safety Monitoring/Management

2. Responsibilities and Roles for Gathering, Evaluating and Monitoring the Data
    a. Principal Investigator and Sub-Investigators:
        1. The principal investigators will be the monitoring entity due to the nature of this study – small number of subjects and the study is conducted only at one site
        2. Responsible for insuring protocol compliance
        3. Responsible for collecting and recording all clinical data pre- and post-operatively
        4. Responsible for monitoring data collected and evaluating the progress of the study, assessments of data quality, retention, and adverse events
        5. Responsible for monitoring safety of research participants from visits with patients
        6. Responsible for stopping or modifying protocol if needed
        7. Responsible for intraoperative data collection
    b. Research coordinator:
        1. Responsible for monitoring informed consents
        2. Responsible for reporting all IRB related matters, storing informed consents, and reporting all adverse events to the IRB
        3. Responsible for recruiting and consenting patients for study
        4. Evaluates protocol compliance with the above investigators to ensure data protection and patient confidentiality
        5. Responsible for maintaining regulatory documents
    c. Research Assistant:
        1. Responsible for recruiting and consenting patients for study
        2. Responsible for ensuring data collection from patients
        3. Responsible for escorting patients to the simulator, collecting data andoperating the simulator

4. Monitors and reports to PI and research coordinator the recruitment and retention status as well as adverse events
5. Facilitates intraoperative data collection and protocol compliance
6. Responsible for organizing and storing all patient data in a secure location where only authorized personnel have access
7. Responsible for completing informed consent procedural log

3. Reporting Adverse Events and Unanticipated Problems
    a. Adverse event (AE) grading and attributes
        1. No adverse event or within normal limits
        2. Mild AE, not requiring treatment
        3. Moderate AE, resolved with treatment
        4. Severe AE, resulting in inability to carry on normal activities and required professional medical attention
        5. Life threatening or disabling AE
        6. Fatal AE
    b. Safety Plan
        1. Adverse events related to study will be detected from follow up visits by the patient and during the post-operative period by the principal investigators, , through physical exam assessment and reviewing x-rays and CT scans of the subject. The investigator will try to determine if the adverse event is related to the research itself or an isolated event using the above criteria.
        2. The research coordinator, will perform safety reviews (collecting adverse events, reviewing them, and reporting them).
        3. The research assistant will score and review questionnaires to determine if a subject's condition has worsened (adverse event), and if determined by the PI to be related to the surgery, the event will be reported by the research coordinator.
        4. All adverse events identified are reported to the PI and the research coordinator
    c. Plan for periodic or annual reporting of AEs
        1. The IRB will be notified of a serious adverse event and unanticipated adverse event within 24 hours. All other adverse events will be reported annually to the IRB at the time of continuation renewal.
        2. All unanticipated adverse events related to the study will be reported to the IRB in an expedited manner if they are Grade 2 and above in severity. Unanticipated patient deaths are reportable within 7 days. The expedited report sent to other organizations can be copied to the GCRC. The investigator will continue to follow or obtain documentation of the resolution course of such an event.

4. Privacy and Confidentiality
    a. Case report forms and all other documentation collected by the investigators and research coordinator/assistant will not contain subject names. Each subject will be assigned a subject code. The subject code will consist of 8 characters in an alphanumeric combination. The site will maintain the link between the subject code and the names. Primary data collection will be based on source-documented hospital chart reviews, notes on the source worksheets and subject interviews will be performed by study coordinators/researchers or investigators at each clinical site. Data will be stored in individual subject binders and locked in a secure office. Only approved research coordinators/investigators will have access to the data.
5. Assessments

a. Safety reviews will be performed monthly by the monitoring entity (the principal investigator). The monitoring entity will be responsible for determining the relationship of an adverse event and the treatment received. Since the PI sees the subjects regularly for follow up visits, he will be familiar with the subjects' outcomes and patient histories, thereby making it easier to detect AEs if they do arise. This plan allows for prompt detection of unanticipated problems involving risks to subjects.
b. Monitor the incidents of pseudoarthrosis for both graft groups

6. Criteria for Action
    a. Subject stopping will occur if any adverse events occur that are level 4 or above, or if the subject is unlikely to comply with the follow-up evaluation schedule
    b. Study stopping will occur if there patients experience persistent pain following the simulator trials
    c. Study stopping will occur if patient cannot tolerate the simulator due to motion sickness

7. Data Storage and Confidentiality
    a. Case report forms and all other documentation collected by the investigators and research coordinator will not contain subject names. Each subject will be assigned a subject code. The subject code will consist of 8 characters in an alphanumeric combination. The site will maintain the link between the subject code and the names. Primary data collection will be based on source-documented hospital chart reviews, notes on the source worksheets and subject interviews will be performed by study researchers or investigators at each clinical site. Data will be stored in individual subject binders and locked in a secure office. Only approved research coordinators/investigators will have access to the data.

P. OUTCOME MEASURES

Table 1 summarizes all outcome measures and timeline of data collection

Time Line of Data Collection	Pre-operative	2 weeks FU	6 weeks FU	12 weeks FU	24 week FU (optional)
Patient Demographics **Driving History**	X				
NRS, PROMIS , NDI Questionnaires	X	X	X	X	X
EQ5D, MJOA, Tandem walk test, 10s grip test, 10s step test (myelopathy patients only)	X			X	X
Clinical/Physical Exam **Narcotics Usage**	X	X	X	X	X
Driving Performance Data: ***Simulator Output Data*** - Total Collisions (TC) - Centerline Crossings (CC) - Off-road Excursions (ORE) - Driving Reaction Time (DRT) ***Cervical Motion Data:*** 1. Blind Spot Data *a.* Unsafe Driving Event (UDE) *b.* Angular Velocity of Neck Rotation *c.* Time to initiate lane change *d.* Maximal axial rotation 2. Cervical range of motion (CROM) 3. Thoracic range of motion (TROM)	X	X	X	X	X
Post-Simulation Questionnaire	X	X	X	X	X
Surgical Data		X			

Table 1: Summary of Outcome Measures

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