AN EXAMINATION OF THREE NOVEL NEUROSURGICAL TREATMENTS FOR COMPLICATED SPINAL INSTABILITY

Timothy A. Gates

A dissertation submitted in partial fulfillment of
the requirements for the degree of
Doctoral of Philosophy

Department of Neuroscience

Central Michigan University
Mount Pleasant, Michigan
February 2014

ACKNOWLEDGEMENTS

I would like to thank the members of my dissertation committee: Dr. Gary Dunbar, Dr. Richard Backs, and Dr. Julien Rossignol. These faculty members provided valuable insight during the design of the project, drafting of the document, and creation of the final product. I would especially like to thank Dr. Gary Dunbar for his ongoing support and guidance throughout my graduate school and medical training. Finally, I would also like my family for their continuous support.

ABSTRACT

AN EXAMINATION OF THREE NOVEL NEUROSURGICAL TREATMENTS FOR COMPLICATED SPINAL INSTABILITY

by Timothy A. Gates

Spinal instability is a common condition encountered in the practice of neurosurgery. However despite its prevalence, the treatments are not always straightforward. This project examined three instances of complicated spinal instability and a novel treatment for each.

The first study of this project examined the case of an older female patient with a displaced odontoid fracture treated with a cervical-thoracic brace. This form of external fixation is more rigid than a cervical-alone collar and has been documented for lower cervical fractures, however little has been documented concerning its effectiveness for high cervical injuries. Monthly imaging was used to assess the success of the treatment.

The second study detailed a medically unstable patient with decompensating basilar invagination. For this patient, an attempt to treat his odontoid with focused radiation was attempted. The patient outcomes were measured via clinical assessment and periodic imaging. Measurements of odontoid size were made pre and post treatment to evaluate for changes. Comparisons of post treatment MR enhancement was also made to evaluate the extent of radiation

Finally, the third study of this project examined the problem of instability complicated by osteoporotic bone. The question of how to stabilize spinal anatomy with preexisting weak bone, is a difficult one. Study 3 of this dissertation analyzed the biomechanics of a new bone screw anchor designed for osteoporotic bone.

Ten cadaveric vertebral bodies with proven low bone density were examined. Each vertebral body had both a regular pedicle screw and an anchored pedicle screw placed, each side

was independently tested biomechanically for axial displacement and pullout strength. Measurements of displacement of the screw over time and the force required to cause pullout were compared and analyzed.

The results of the three studies were: (study 1) successful fracture healing was noted with the cervical-thoracic brace; (study 2) following radiation, clinical improvement, decreases in odontoid size, and no adjacent brainstem radiation changes were noted; and (study 3) increased bone pullout strength and decreased toggling was seen for the bone screw anchor group. Overall, each of these novel approaches successfully addressed aspects of instability for which few treatment options exist.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

FIGURE PAGE

CHAPTER I

INTRODUCTION

With advancements in modern medicine we are now seeing individuals staying active and living longer with diseases once thought to be fatal. This is especially true for diseases of the spinal neural axis. Medical and surgical options for conditions such as basilar invagination (Figure 1), cervical spine fractures (Figure 2), and neural compression from degeneration (Figure 3), now have a variety of treatment options. With many more patients being seen with these conditions than ever before, spinal instability has become an increasingly common condition encountered in the practice of neurosurgery (Pakzaban et al, 2012). However despite its prevalence, the treatments for spinal instability are not always straightforward.

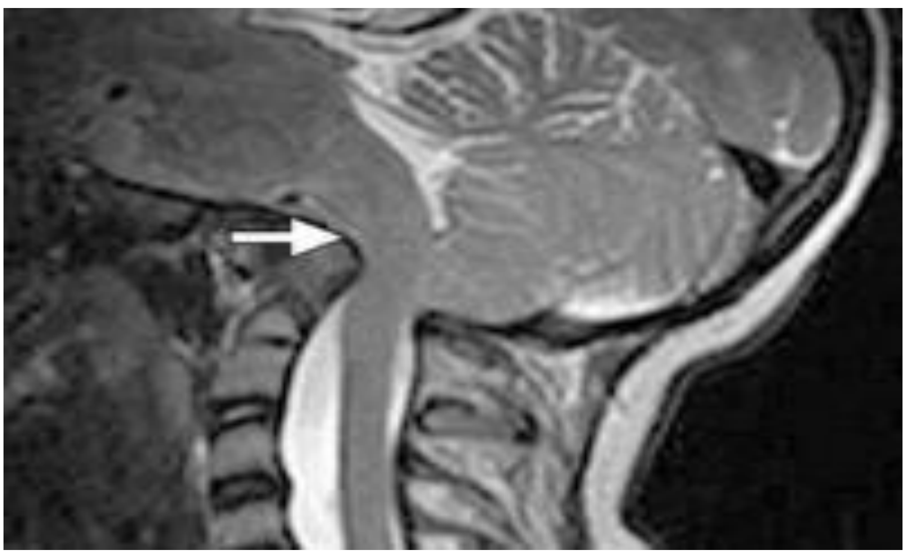


Figure 1. **Basilar Invagination (Khandanpour et al, 2012)**

Figure 2. **Type 2 Odontoid Fracture (wwwradiologytutorial)**

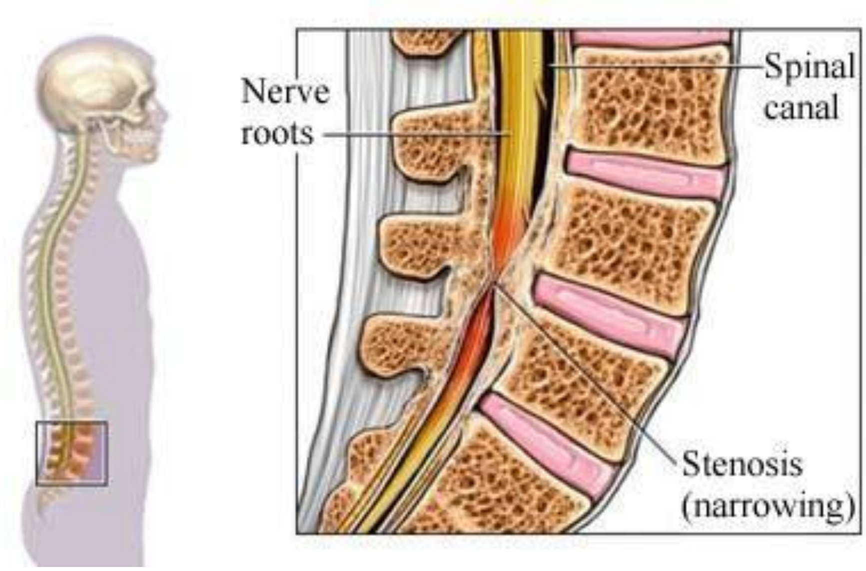


Figure 3. **Spinal Stenosis (wwwthirdagecom)**

It has been estimated that by the age of 65, 95% of the population will have some degree of spinal degeneration (Malcolm et al, 2002). These normal changes of aging are often asymptomatic or result in conservative treatment with medication (Arcangeli et al, 1996; Chen et al, 2012; Reginste et al, 2005; Stanos, 2013). However, these changes can be exacerbated by the addition of other disease processes, such as osteoporosis, rheumatoid arthritis, or advanced osteoarthritis (Ding et al, 2011; Gullick et al, 2012). The resulting instability that develops as these conditions worsen can lead to bony fractures, ligamentous instability, and advanced degenerative changes requiring neurosurgical intervention. Additionally, iatrogenic causes of instability, such as decompression surgery can also lead to neural compromise and require additional treatment if adequate spinal stability is not present following surgery (Papadakis et al, 2013).

The major goals of any neurosurgical intervention of the spine include one of three things: decompress compromised neural structures, stabilize unstable elements that may go on to compromise adjacent neural anatomy, and minimize future disease progression if possible. Given the complicated medical history with which some patients present, it is important that those involved in neurosurgical management of spinal pathologies continue to explore new and unique treatment modalities.

In this project, three instances of spinal instability, one traumatic, one degenerative, and one surgical were examined. In each case, the normal treatment had been complicated by the patient's history and pre-existent comorbidities. For each situation, a novel approach to treating the complicated spinal instability was examined.

The first part of this project examined the case of an older female patient with a displaced type II odontoid fracture who did not desire surgery, due to her age. While surgery is not always the treatment of choice for these types of fractures, the proximity to the spinal cord and instability of this type of odontoid fracture, required immediate stabilization by some means.

The second part detailed a medically unstable patient with decompensating basilar invagination, whose odontoid process had herniated through his foramen magnum and was causing severe midbrain compression. This patient had been determined to be unsuitable for surgery, due to his worsening ventilator-dependent status, yet his symptoms of brain stem compression were worsening. For this patient, an attempt to treat his condition with focused radiation to the bone was considered a viable treatment option.

Finally, the last section of this paper examined the problem of post surgical spinal instability complicated by osteoporotic bone. This is a problem that is increasingly common. The question of how to stabilize spinal anatomy following decompression surgery for spinal stenosis, with preexisting weakened bony architecture, is a difficult one. Part 3 of this dissertation details a cadaveric study examining the biomechanics of a new fixation device designed to limit axial movement and increase the pullout resistance of vertebral pedicle screws within osteoporotic bone.

The practice of neurosurgery involves diagnosing conditions of the neural axis and, with the patient, arriving at a treatment plan that will, hopefully, offer the best possible outcome. Given that no two patients present with the same medical histories or circumstances, the ability to select the right management is important. This may include surgical management, non-surgical management, or treatment via a different modality such as radiation therapy. This dissertation project examines three complicated spinal instability scenarios seen in the practice of neurosurgery and will explore a unique treatment option for each.

Study 1: Cervical-Thoracic Bracing Used As Initial Treatment for an Unstable Type II Odontoid Fracture in an Older Osteoporotic Patient Not Desiring Surgery

Cervical spine fractures in the elderly are an increasingly common problem encountered by today's neurosurgeons. Given that many seniors are now remaining active into their eighth and ninth decades, there exists a need to be able to adequately treat these fractures. Of cervical spine fractures seen in the aging population, type II odontoid fractures remain the most common (Elgafy et al, 2009) and are considered highly unstable (Greenberg, 2006). Yet, given the relatively common nature of the odontoid fracture in this age group, no clear consensus regarding management of these fractures exists (Chaudhary et al, 2010; Harrop et al, 2010; Schoenfeld et al, 2011; Smith et al, 2010).

Several methods of treating odontoid fractures in this age group are presently used including: surgical fixation of the atlantoaxial joint (Figure 4), surgical fixation of the odontoid (Figure 5), halo fixation (Figure 6), and cervical collar bracing (Figure 7). Each of these comes with its own benefits and disadvantages (Elgafy, 2009).

Figure 4. **Posterior C1-C2 Fixation Technique (pennyandbrainorg)**

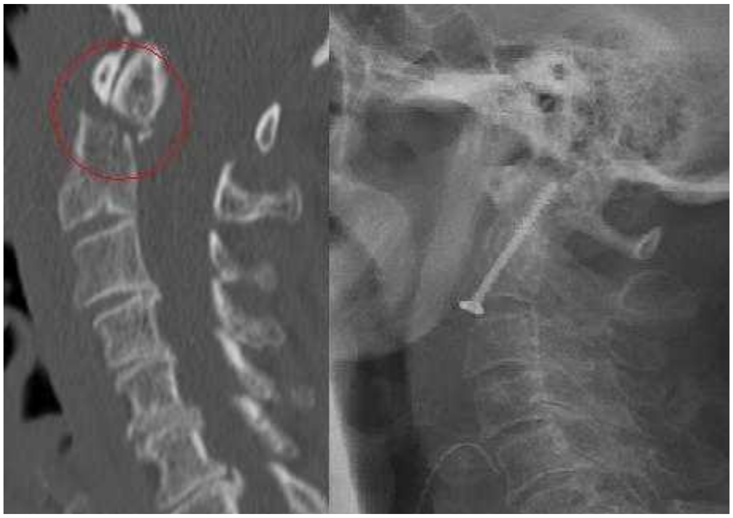


Figure 5. **Odontoid Screw Fixation of a Type 2 Odontoid Fracture (wwwlondonspineco)**

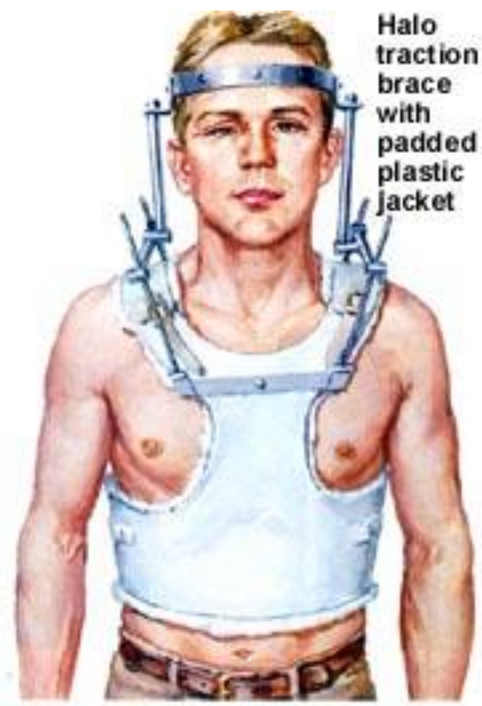


Figure 6. **Halo Fixation (wwwspineuniversecom)**

Figure 7. **Cervical Collar (wwwossurcoPages9842)**

Posterior atlantoaxial fixation, general consists of a creating a posterior cervical construct of cervical screws and rods or wires which adjoin C1 and C2. This usually provides the most rigid means of stabilization. However, this method does require a surgically fit patient (White et al, 2010), with adequate bone for hardware placement or fusion. Posterior cervical fixation also results in significant decrease in cervical spine motion (Melcher et al, 2002).

Odontoid screw fixation is a means of surgical fixation, developed in the last decade, in which single or dual screws are placed from an anterior approach, adjoining the base of the odontoid with the fractured fragment. While odontoid screw fixation does offer an alternative to rigid posterior fixation while also preserving cervical motion, it also requires a surgically fit patient and adequate bone quality for screw placement. In addition, the odontoid fixation is ideally designed for patients in whom the odontoid has fractured perpendicularly to the angle of the screw rather than in parallel, which is not always present (Rao et al, 2005).

Halo fixation has been a means of cervical fixation for many years (Nickel et al, 1968). In this method, fixation pins are seated anteriorly and posteriorly in the skull and attached to a metallic or carbide halo that encircles the patients head at the level of the forehead (Figure 6). The halo is then affixed to four stabilizing rods that are connected to a shoulder harness worn by the patient. While popular for many years as a non surgical means of cervical fixation, it is now used less commonly, as it has been found to be less rigid than was once thought, and often results in poor patient satisfaction (Ivancic et al, 2010; Shin et al, 2010).

Finally, several studies in recent years have also suggested that rigid cervical collars may also provided adequate stabilization of the cervical spine in older patients and allow for union of odontoid fractures, an outcome once believed to necessitate surgical intervention (Koech et al, 2008). Yet, understandably, this means of stabilization is the least permanent of the means mentioned, and is the most dependent on patient compliance (Chaudhary, 2010; Fagin et al, 2010; Polin et al, 1996).

Thus far, no study has looked at the use of cervical-thoracic bracing as a non-surgical means of treating type 2 odontoid fractures in older patients, for whom surgery and halo fixation are not desirable means of treatment. The cervical-thoracic brace consists of a rigid thoracic brace that extends superiorly, supporting the cervical spine and head under the patient's chin (Figure 8). Traditionally used for fractures of the cervical/thoracic junction, this type of a brace, while not permanent, is far more rigid than the traditional cervical collar, and also provides for support at the cranial/cervical junction.

Figure 8. **Cervical-Thoracic Brace (wwwossurcoukPages9862)**

This present study examined the use of this type of brace to treat a displaced odontoid fracture in an older patient who did not desire surgery. Monthly cervical imaging, in the form of CT scans, was used to assess the success of the treatment. Given that the patient had a good support system and was perceived to be compliant, fixation with a cervical-thoracic brace seemed a viable option.

Study 2**:** CyberKnife treatment of the Odontoid in a Patient with Inoperable Unstable Basilar Invagination

Basilar invagination is a rare condition of occipital/cervical instability, generally associated with trauma, congenital defects, or degenerative conditions of the atlantoaxial junction (Ames et al, 2005; Klimo et al, 2007; Smith et al, 2010). It is characterized by rostral herniation of the odontoid through the foramen magnum into the cranial cavity. In its earlier stages, it is characterized by worsening symptoms of pain, confusion, and dizziness, while its later stages exhibit symptoms of brain stem compression, and at times sudden death (McAllion et al, 1996; Menezes et al, 1985).

Early treatment is primarily symptomatic, and may include anti-inflammatory medication (Derkay et al, 1990), bracing (Sawin et al, 1997), or traction (Simsek et al, 2006). As the condition progresses, surgical resection of the odontoid process and cervical fixation are often necessary to arrest the brainstem compression (Goel et al, 1998). In a patient who has developed abnormal progression of brain stem systems and for which surgery is not possible, few treatment options exist, other than palliative treatment of symptoms or treatment of secondary effects, such as hydrocephalus.

The effects of radiation on bone are well documented (Marx, 1983). Exposure during treatment of malignancies in various parts of the body has shown that radiation can lead to thinning (Kwon et al, 2008), devascularization, and even increased resorption of bone (Støre et al, 1999). While these results are generally regarded as undesirable side effects, the fact that bone can be altered inadvertently by radiation treatment suggests that inoperable bony abnormalities may experience similar changes from direct exposure.

Therefore the second study describes the use of CyberKnife fractionated radiation treatment to the odontoid of an inoperable patient, with progressing brain stem symptoms from basilar invagination. The condition of this patient is believed to be secondary to degeneration related to his known history of osteogenesis imperfecta. In addition, he had previously undergone treatment for hydrocephalus, via ventriculo-peritoneal catheter placement.

Study 3: Cadaveric Biomechanical Analysis of a Novel Pedicle Screw Anchor Designed for Unstable Osteoporotic Spinal Vertebra following Spinal Nerve Decompression

Osteoporosis, or loss of bone density, is a common problem. Occurring postmenopausally in women, and with aging in both men and women, it can lead to weakening of the bones and the development of fractures (Bliuc et al, 2013; Lee et al, 2012; Riggs et al, 1982). Similar weakening of the bony matrix is also seen as a complication of pathologies including osteogenesis imperfecta, rheumatoid arthritis, and HIV infections (Brown, 2013, Dimitroulas et al, 2013; Rohrbach et al, 2012). Weakening of the normal bony architecture also poses challenges to surgical intervention, as weakened bone is difficult to stabilize and prone to failure (Ponnusamy et al, 2011). With both osteoporosis and spinal degeneration becoming increasingly more common in the older, active people, the overlap of these two pathologies can make treatment for conditions such as spinal stenosis surgically difficult.

Spinal stenosis, or narrowing of the spinal central canal, can have profound effects on neural functioning. It can lead to pain, weakness, paresthesias, difficulty ambulating, and in severe cases paralysis or death (Sigmundsson, Jönsson et al, 2013; Sigmundsson, Kang et al, 2011; Soultanis et al, 2013). The causes of spinal stenosis are many and can include spondylolisthesis, scoliosis, degenerative arthritis, fractures, infection, hematomas, and, at times, tumors. While mild cases of spinal stenosis can range from asymptomatic, to being treatable with medications or therapy, severe symptomatic stenosis often times requires surgical decompression (Amato et al, 2012) (Balakatounis et al, 2011). While not every decompression of the spine requires stabilization afterwards (Son et al, 2013), causes that require more bone removal to decompress the spinal cord, brain stem, or spinal nerves may cause iatrogenic instability of the spinal axis. When this occurs, replacement of removed bone with bone material from other locations or donated cadaver bone is necessary to rebuild the lost structure.

While the replaced bone hardens and heals, the addition of sterile metal hardware is often used to provide stability and support to the normal anatomy (Knaub et al, 2005). This medical grade metal, usually titanium, is attached to the skeleton above and below the bony defect and used to span the bony gap until the replacement bone grows in to place. This metal construct must, however, be seated firmly within the remaining bony anatomy to provide the necessary stability (Figure 9). The presence of weak bony architecture such as is seen in osteopenia and osteoporosis can cause failure of the metallic construct and ultimately lead to further neural compromise (Hart et al, 2007).

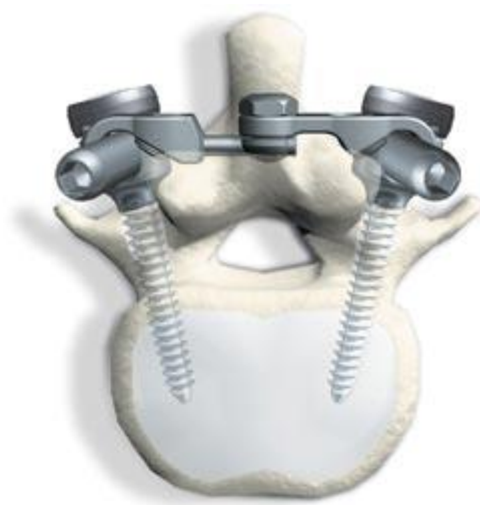


Figure 9. **Pedicle Screw Fixation (wwweuropestrykercom)**

Given that many of the common causes of spinal stenosis are more likely to occur or worsen with age, the potential for overlap of these conditions with the problem of decreased bone density is high (Lee et al, 2012). Past studies have attempted to reduce this risk of hardware failure by augmenting the hardware with bone cement (Aydogan et al, 2009; Becker et al, 2008; Xie et al, 2011) or through expandable screws (Wan et al, 2011). However, these methods, while useful at times, create permanent changes to the bone and make revision at a cement-augmented level difficult. In study 3, an examination of a novel approach to prevent hardware failure and pullout in low bone density vertebra, through the use of a fully removable pedicle screw anchoring sleeve, was conducted.

CHAPTER II

METHODS

Methods for Study 1

Patient

The patient assessed in this study was an 88 y/o female seen at Garden City Hospital in Garden City Michigan. She was evaluated by the neurosurgical service and found to have displaced type II odontoid fracture. The treatment for this type of fracture is widely believed to require surgical intervention given its instability and potential for spinal cord injury (Greenberg, 2006). The patient and her family, however were adamantly opposed to surgical intervention given her age.

Treatment

Given the patient's wishes, a means of non-surgical fixation was considered. Although fixation with a cervical collar alone was a possible, the ability to easily remove the collar was worrisome. For this reason, more rigid, non-surgical fixation was considered. Halo fixation, was considered less than ideal, given her age and her potential for complications (Tashjian et al, 2006).

As an alternative treatment option, a cervical/thoracic brace was proposed, as a means of stabilization. The use of this type of brace has been proposed occasionally in the literature as a treatment of cervical fractures, although very little has been documented as to its effectiveness in treating odontoid fractures (Sime et al, 2013; Benzel et al, 1992; del Sel, 1975).

This type of brace is attached as a vest to the chest and has a cervical extension to support the head under the chin. This was proposed as an alternative to a cervical collar alone, primarily due to its rigid structure and design. These features provided constant support while also decreasing the likelihood of accidental removal. This brace does require assistance from support staff for cleaning and adjustments. In this patient's situation, it was noted that she had a great deal of family involvement to assist her with these tasks.

The involvement of the author was as one of the primary treating physicians for Garden City Hospital's neurosurgical service. This included patient evaluation and follow-up, both clinically and radiologically. The author had no financial gain or conflict of interest related to the treatment or outcomes of this study.

Outcome Measures

For evaluation of the treatment, the patient was followed using monthly CT scans of the cervical spine to evaluate the fracture. Hounsfield Unit (HU) density measurements were taken and averaged for a set of five points located proximally, distally, and along the fracture line on each of the cervical spine CT scans of the patient. The goal was to evaluate healing along the fracture and to assess bony union between the odontoid fragment and C2 vertebral body. 400 HU was used as the threshold for bone growth based on radiologic guidelines (Brant et al, 2012). Permission to retrospectively to review the patient's outcomes was via the Garden City Hospital IRB committee, Garden City, MI.

Methods for Study 2

Patient

The patient was a 46-year-old male with a known history of basilar invagination. Basilar invagination is a condition in which the ligaments of the skull base and cervical spine have become lax and incapable of maintaining the structure of the occipital/cervical junction (Goel, 2009). Overtime, this laxity allows for the odontoid to herniate cranially through the foramen magnum into the cranial cavity (Khandanpour et al, 2012). This often times lead to brainstem compression, and eventually death (McAllion et al, 1996). This patient had previously been evaluated for surgical decompression, however, and was found not to be a suitable surgical candidate based on his comorbidities. He had become more ventilator-dependent over the course of his disease progression and had progressed from the ability to swallow to now receiving most of his nutrition via a gastric feeding tube. He was seen by the St. Mary's Hospital neurosurgical team and Seton Cancer Center in Saginaw, Michigan.

Treatment

It was proposed, given the limited treatment options and symptom progression that use of focused radiation, via CyberKnife to radiate the odontoid would be the best available option. Given the ability of the CyberKnife to deliver focal radiation treatment with minimal radiation to neighboring structures, it was theorized that by delivering a focal dose of radiation to the odontoid, it might be possible to use the secondary effect of bone resorption to relieve some of the direct pressure on the brain stem.

A pretreatment CT and MRI of the brain were performed and fused for use in contouring of the treatment area. Once finalized, 2500 cGy, 500 cGy dose per fraction in five fractions, was administered utilizing 6 MV photon beams. The patient received 126 beams using a 12.5 cm collimator. The CyberKnife treatment took place the St. Mary's Hospital Seton Cancer Center in Saginaw, Michigan.

The involvement of the author included being a part of the treatment team, as well as helping to compile, analyze, and summarize data regarding the patient's treatment, follow-up, and outcomes. The author had no financial interest or secondary gain from outcomes in this study.

Treatment Safety

Prior to treatment, planning was performed on CyberKnife software, to maximize treatment of the odontoid, while minimizing radiation exposure to surrounding structures. The radiation received by various important structures was calculated and determined to be within safe limits prior to treatment beginning (Table 1).

Table 1. Pretreatment Estimated Radiation Dose by Structure

Structure	Max Dose (cGy)
Odontoid Process	3125.00 (absorbed dose 2500)
Left Eye	404.79
Right Eye	577.78
Optic Chiasm	334.98
Brain Stem	1602.33
Lt Optic Nerve	180.92
Rt Optic Nerve	345.15

Outcome Measures

The patient outcome was measured by clinical assessment at 1-, 3-, 6-, and 12-month follow-up office appointments, and via periodic imaging of the cranial/cervical junction via CT and MR scans. Measurements of odontoid dimensions were made on pre- and post-treatment imaging, which was used to evaluate for changes in odontoid size. Comparisons of post treatment MR enhancement was also be made to evaluate the extent of radiation treatment on the brainstem adjacent to the odontoid. Permission to perform a retrospective review of the patient's outcomes was via the St. Mary's Hospital IRB committee in Saginaw, MI.

Methods for Study 3

Specimen Preparation

Ten lumbar vertebral bodies (mean age 61±8.8; 1M, 3F) from four fresh human lumbar spines were used in the study for the study. The spines were radiographed in both the anteroposterior and lateral planes to ensure visual lack deformity. The specimens were stored in double plastic bags at -20° Celsius. All specimen were defrosted overnight at room temperature with a consistent defrost period. The lumbar spines were then separated into individual vertebral bodies by removing the musculature.

Each vertebral body had a dual energy x-ray absorptiometry (DEXA) scan bone density analysis performed to assure only bones with decreased bone density were used (Singer, 2006). The average bone density t-score, from the DEXA scans, for the 10 vertebral bodies was -2.19. This indicated the specimens used were extremely osteopenic. Osteopenia is classified as having a t-score between -1 to -2.5, while osteoporosis is defined as a t-score below -2.5 (Singer, 2006). The t-score value for a DEXA scan represents the number of standard deviations the specimen density is from the mean bone density of a 30 year old specimen.

Treatment Groups

Two treatments were examined: (1) a pedicle screw alone group, n=10 and (2) a pedicle screw, plus CREO anchoring sleeve group, n=10. Given that each vertebral body has two pedicles (a left and a right), each vertebral body had one pedicle assigned to each group, thus each vertebral body had a plain pedicle screw, and an anchor sleeve/pedicle screw. This was done to decrease variability between groups and assured that the groups had equal bone densities, as well. The groups were also cross-matched so that an equal number of left and right pedicles were assigned to each group.

Equipment Specifications

The CREO anchor (Globus Medical Inc.; Audubon, PA) is made out of polytheretherketone (PEEK), a medical grade organic polymer thermoplastic and works by being introduced down a predrilled hole in the pedicle until it fits snuggly against the bone. The center is designed to fit the desired screw diameter.

As the screw is advanced into the superficial portion of the device, the anchor begins to expand in a cranial/caudal fashion within the pedicle, while the far end of the sleeve located within the vertebral body flairs in a medial/lateral fashion (Figure 10). These two changes are meant to help secure the screw more snuggly within the pedicle and vertebral body.

The anchoring sleeve is also designed to be easily removed. If the pedicle screw is removed, the device collapses back to its original shape and can be simply pulled back out. A Standard REVERE (Globus Medical Inc.) pedicle screw can be inserted through the anchor.

Figure 10. **The anchor is designed to flair outward once the pedicle screw as been introduced**

Outcome Measures

Fatigue Pullout Strength Testing. Fatigue loading was performed using an MTS mechanical test machine (Figure 11A and 11B). Standard REVERE® polyaxial pedicle screws and were randomly inserted into the right and left pedicles of the same vertebral bodies with and without an anchor . It has been suggested that wider and longer screws have a less likelihood of pullout failure (Helgeson et al, 2013). For this reason, the shortest (25 mm) and thinnest (4.5 mm diameter) pedicle screws made by Globus Medical were used in this study to simulate a worst case scenario.

An axial load of ±200 N was applied to the screw tulip by the actuator at a rate of 0.5 Hz for 1,000 cycles. Displacement was measured by the MTS machine (Figure 11A). After fatigue loading is reached all screws underwent axial pullout testing at a rate of 0.1 mm/sec until failure (Figure 11B). A paired two sample for means t-test was performed to determine significant differences between the two groups ($p \leq 0.05$), with each anchored pedicle paired with its non-anchored mate. This allowed for the truest comparisons based on the bone density cross-matching. A regression analysis was also performed between biomechanical testing results and bone density measures to evaluate if any relationship was noted with motion findings. The groups were cross-matched so that each group had the same number of pedicles tested first and second to decrease differences between groups related to testing order.

The contribution of the author included involvement with study design, placement of the pedicle screw and anchor devices and data analysis. The author had no financial gain or conflict of interest related to the study or its outcomes. Globus Medical did acquire the cadaveric specimens used in the study and created the device tested. However, the final analysis, biomechanical testing, and placement of hardware was under the guidance of the author as primary researcher.

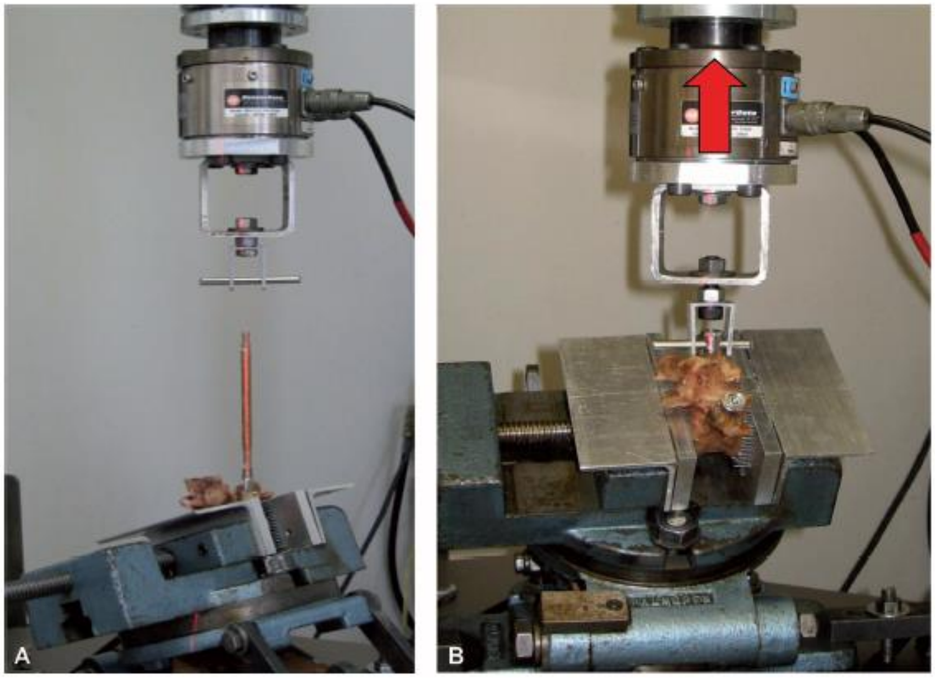


Figure 11**. Biomechanical testing was performed using the MTS machine for axial movement (A) and pullout strength (B)**

CHAPTER III

RESULTS

Study 1: Odontoid Fracture Treatment

The patient was followed with serial CT scans of the cervical spine as planned. Figure 12 shows the follow-up CT scans of the cervical spine taken at monthly intervals, respectively, following placement of the cervical thoracic-brace. After the fourth month in the cervical-thoracic brace, the patient was transitioned to a rigid cervical collar. The patient did not follow-up as scheduled for her next monthly visit while in the cervical collar, and, as a result, wore it for two months before having her final CT evaluation (Figure 12F).

As can be seen in the first of the serial CT scans, good alignment was maintained by the cervical-thoracic brace (Figure 12A and 12B). Bony callus formation is seen along the fracture margins and narrowing of the fracture line is noted to have begun, even after the second month (Figure 12C).

As the patient was braced for additional months, continued progression of bony healing between the base of the odontoid and the fragment was noted (Figure 12D). This union appears fibrous at 4 months (Figure 12E). By the sixth month post-injury, the fracture line was recorded as having an average Hounsfield density greater than 400, signifying bone growth (Table 2, Figure 12F, Figure 13). While healing of the fracture was noted to occur over a period of months, the patient reported decreased pain shortly after her initial brace was placed.

Table 2. Average CT Scan Density Measurements Adjacent to and Within the Odontoid Fracture

	Average Density (HU)		
Time of CT Scan	Proximal	Distal	Fracture Line
Point of Injury	496	502	118
Month 1	507	521	145
Month 2	508	501	208
Month 3	491	503	242
Month 4	489	510	347
Month 6	493	502	404

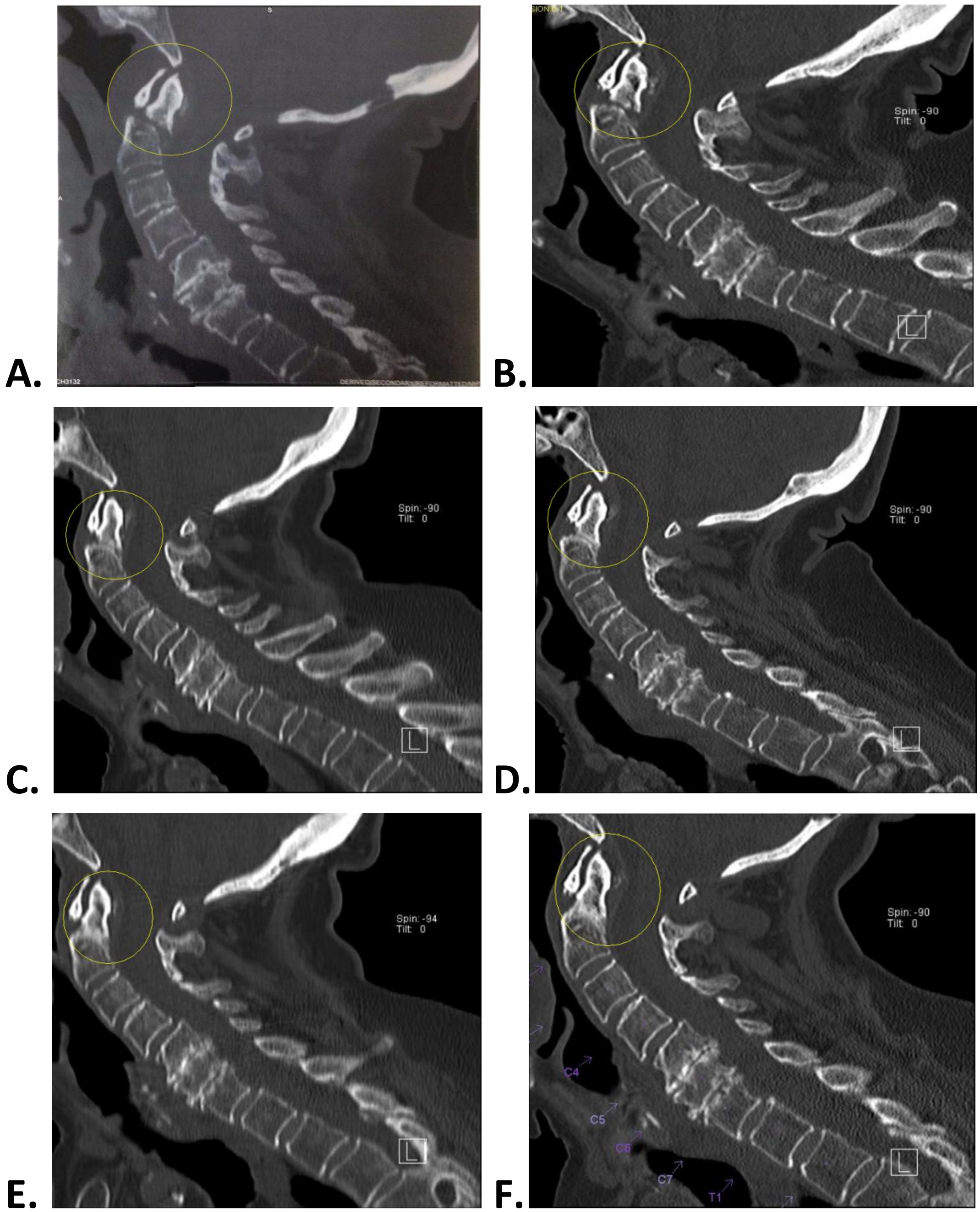


Figure 12. **Sagittal CT images of the cervical spine at the time of the initial injury (A), and subsequent follow-up visits at 1- (B), 2- (C), 3- (D), 4- (E), and 6 months (F) show reapproximation of the odontoid to the C2 vertebral body. Healing is noted to progress from bony callus to fibrous union and finally bone growth across the fracture line. The course of treatment included four months of cervical-thoracic bracing followed by 2 months of cervical collar alone.**

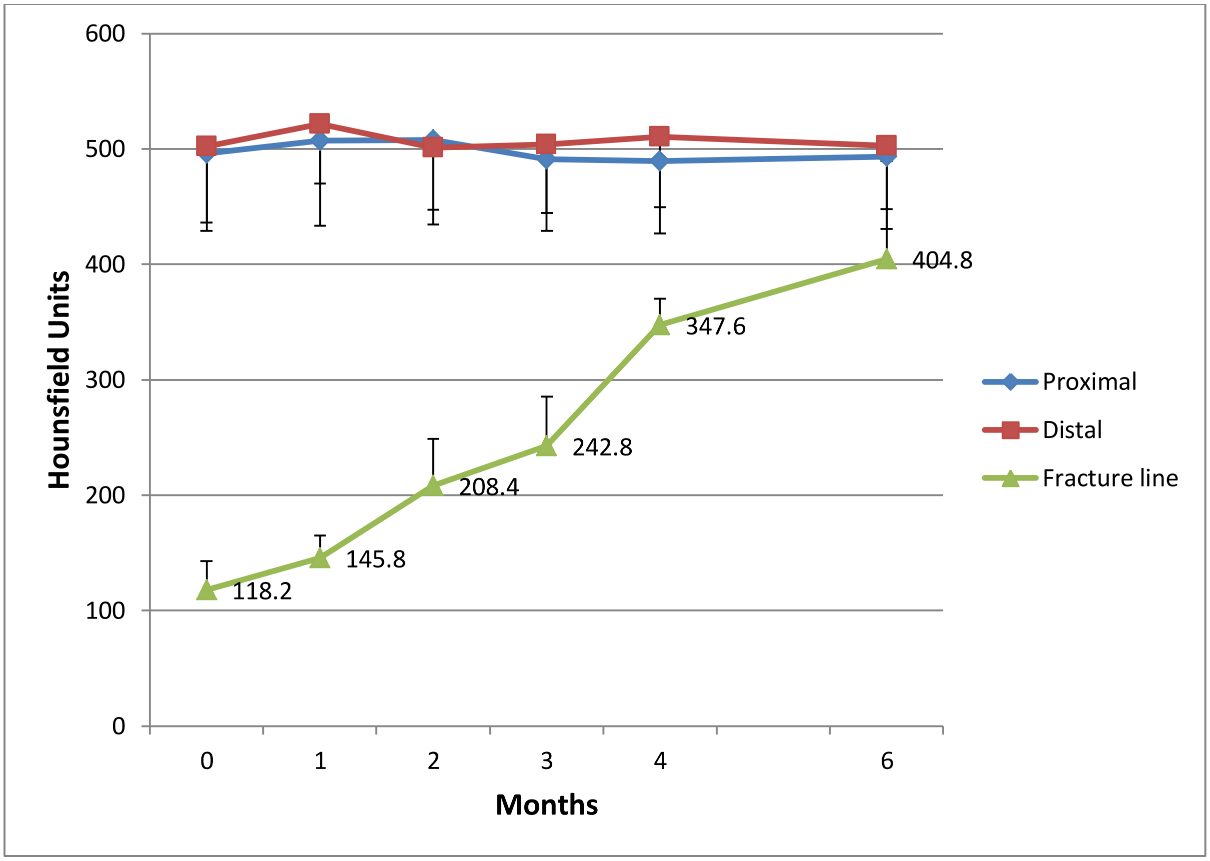


Figure 13. **By six months post-injury Hounsfield density measurements along the fracture line were found to be greater than 400 HU and indicated bony growth.**

Study 2: Basilar Invagination

Clinical Results

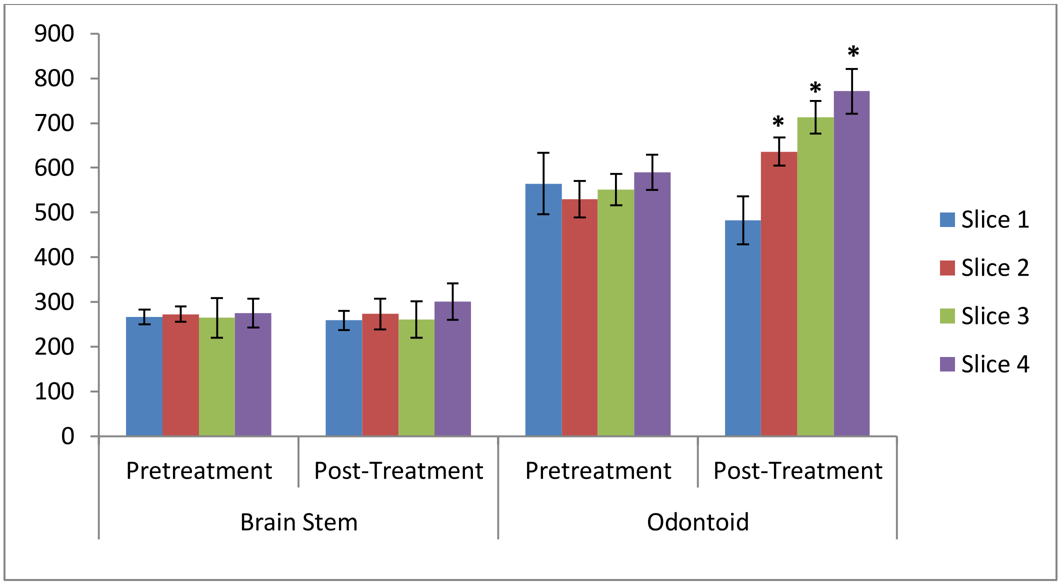
The patient tolerated treatment well. He was seen at three months post treatment by his radiation oncologist and at 12 months post treatment by his neurosurgeon. By three months post treatment the patient was noted to be feeling better, had some decrease in blurry vision and while he still had a gastric tube for feeding, he was able to swallow soft foods safely. The post treatment assessment by his neurosurgeon at 12 months indicated that the basilar invagination in the patient was stable, and the patient noted continued ability to safely swallow soft foods. However, the patient still reported difficulty with headaches following treatment.

Radiological Results

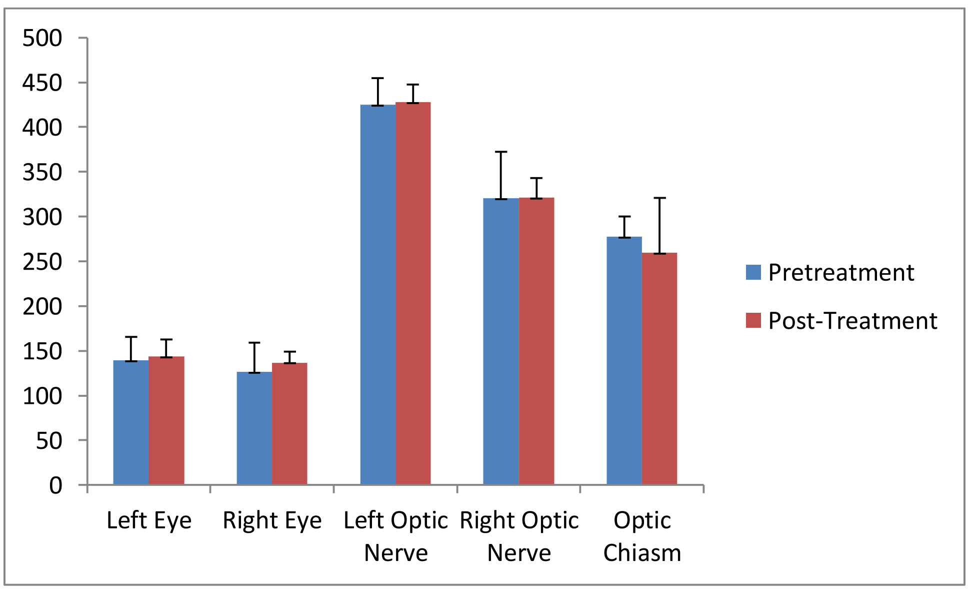
Several imaging studies were performed within the one-year post-treatment period, including a three month computer tomography (CT) scan. A review of this scan did not reveal any visually distinguishable differences in the size of odontoid, despite the noted clinical improvement. The ventriculo-peritoneal (VP) shunt was noted to have been correctly placed and appeared to be working well.

An analysis of magnetic resonance imaging (MRI) signal intensity was performed on the odontoid and the other structures outlined in treatment plan using Picture Archiving and Communication System (PACS) measuring tools. Sample areas from the structures outlined in the CyberKnife planning, as well as the odontoid, were compared on pretreatment and at three month post-treatment using MRI scans (Figures 14A and 14B).

These results show that at three months post-treatment, the patient had significantly increased signal, as noted on T1 post-contrast MRI sequences within the odontoid. However increased signal was not observed within the adjacent neuroanatomy. These signal changes were consistent with radiation induced enhancement and were found only within the odontoid and not the structures which the radiation treatment plan had been designed to avoid. While the observed size of the odontoid was reported by radiology as being roughly equivalent, exact measurements of the odontoid were taken on pre- and post-treatment CT scans. Anterior-Posterior (AP) and lateral measurements were compared on four slices through the odontoid at 5 mm intervals from the base to the apex (Figure 15A). While the lateral dimension of the slices remained fairly constant (Figure 15B), a decrease in AP dimensions of 1 mm and 2 mm was noted in the distal two slices, respectively.

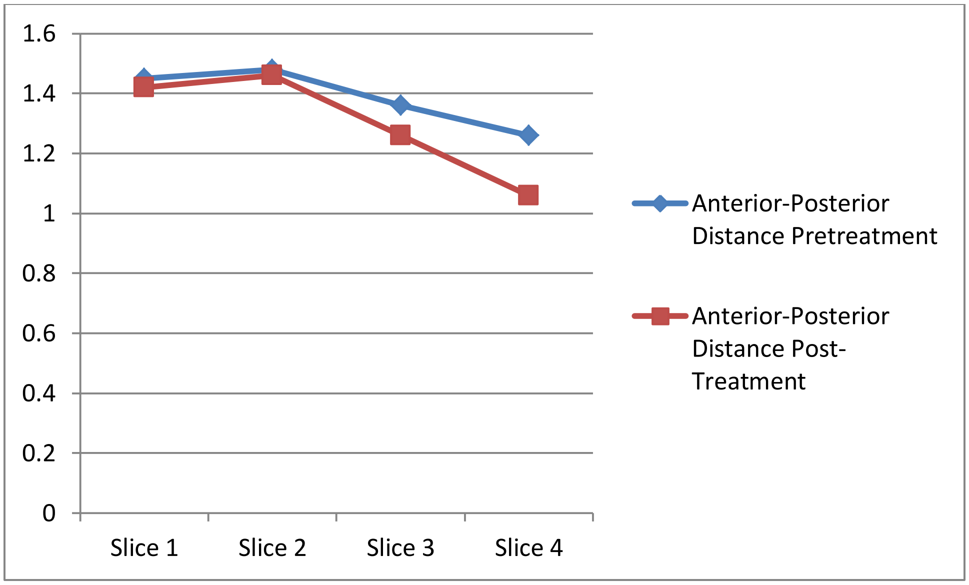


A.

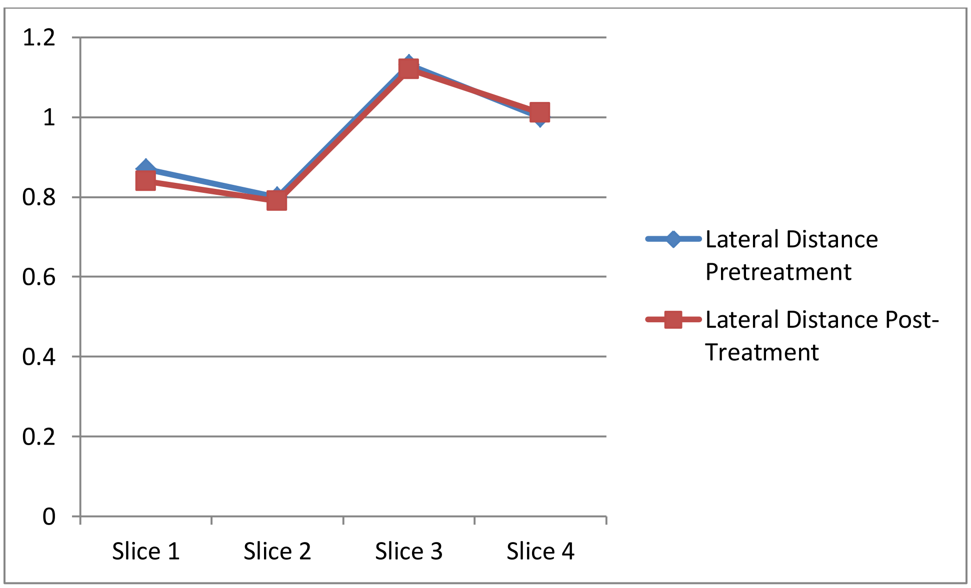


B.

Figure 14. **Examination of pre- and post-treatment MRI contrast enhancement (in Hounsfield units of signal intensity) showed enhancement post-treatment in the distal odontoid, but not in the adjacent brain stem (A) or neighboring visual system (B). These changes in enhancement are consistent with post-radiation changes limited to the area of focused treatment.**



A.



B.

Figure 15. **Measurements of the odontoid (in mm) showed a decrease in Anterior-Posterior length for the distal aspect of the odontoid post radiation treatment (A), but no changes in the lateral dimensions were observed (B).**

Study 3: Osteoporotic Bone Anchor

The results of the axial displacement at 1,000 cycles were reviewed. During testing the axial displacement at 1,000 cycles for the anchor and non-anchor groups were recorded as is 1.4 mm (SD=0.7 mm) and 2.9 mm (SD=1.2 mm), respectively. Statistical analysis revealed the anchor group had significantly less axial displacement compared to the no-anchor group ($p \leq 0.01$) (Figure 16).

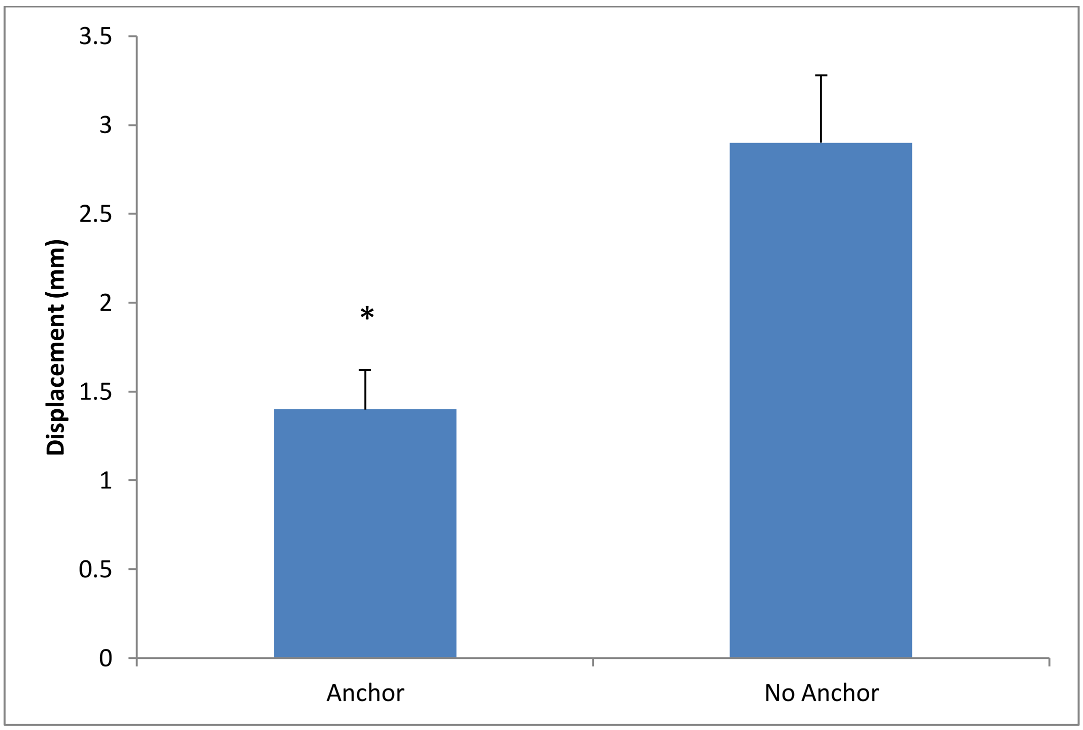


Figure 16. **The anchor group had significantly less axial displacement compared to the no anchor group ($p \leq 0.01$). Values are distance in mm +/- (SEM).**

The ultimate load during pullout was also tested. The anchor group reached an average maximum load of 702 N (SD=373 N) before pullout occurred. The average ultimate load achieved for the non-anchor group was 421 N (SD=293 N). The amount of pullout strength was found to be significantly greater for the anchor versus than the no-anchor group ($p \leq 0.01$) (Figure 17).

Regression analysis for pullout strength and bone density measurements showed no significant difference within groups for performance related to individual bone densities.

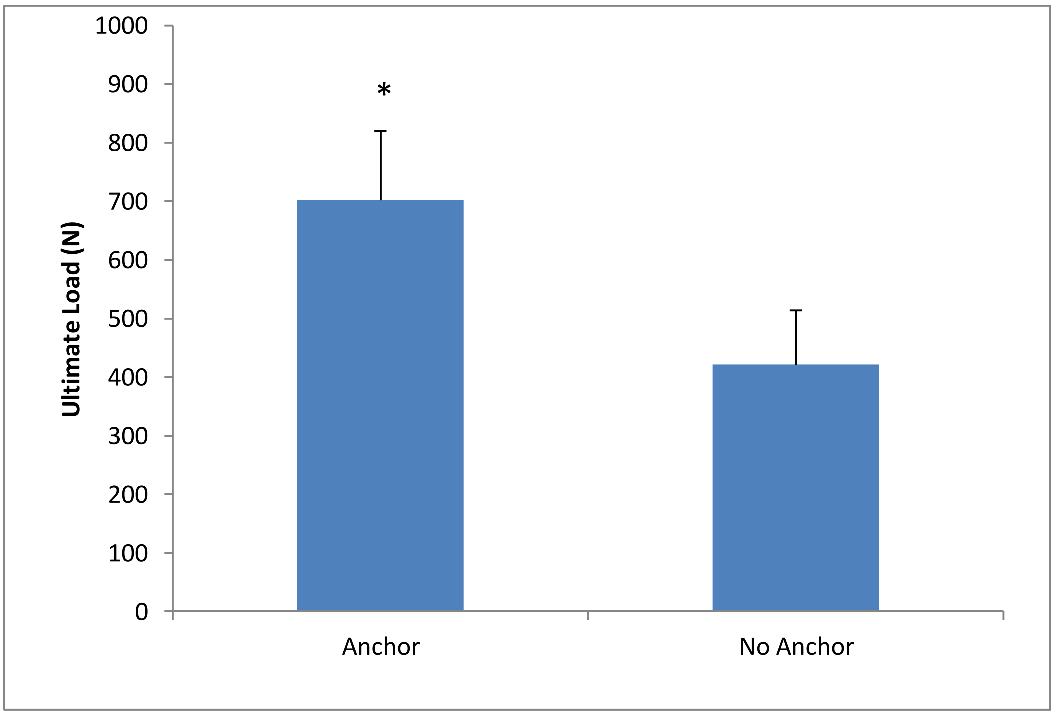


Figure 17. **The amount of pullout strength was found to be significantly greater for the anchor versus than the non anchor group ($p \leq 0.01$). Values are force in N +/-(SEM).**

CHAPTER IV

DISCUSSION

Study 1: Odontoid Fracture

With the prospects of a large portion of the population now approaching the seventh, eighth, ninth, and even greater, decades of life, cervical injuries within this age group are likely to become even more prevalent. Therefore, additional modalities to treat spinal fractures, specifically type II odontoid fractures, are needed. This is particularly true given the complicated nature of many patients within this age group. As it has been reported, the recommended treatments for younger patients do not always have the same results in older patients (Fagin et al, 2010; Malik et al, 2008). For this reason, additional efforts to expand the scope of treatments are important.

In the first study, the extended bracing with a cervical-thoracic brace offered an additional means of treating these types of complicated fractures. It was found that bony union was possible with a compliant patient, even with a displaced type II odontoid fracture. These results, while only in a single case, do offer promise for another possible means to treat patients in which surgical fixation may not be possible. Further studies are needed to determine when cervical-thoracic bracing may be most appropriate, versus simply using a rigid cervical collar alone.

Study 2: Basilar Invagination

The second study presented a case of inoperable degenerative cervical spine instability, resulting from osteogenesis imperfect, which caused basilar invagination with progressing brain stem symptoms. The symptom progression of the patient was noted to stabilize following

CyberKnife treatment, and he experienced clinical improvement. Based on the measurements of the odontoid, pre- and post-treatment, it appears as though the treatment of the odontoid with the CyberKnife may have contributed to a decrease in size of the distal portion of the odontoid (Figure 15A). These results are especially promising, given that the expectation that radiation exposure to the bone would induce increased bone resorption. While the change noted in the odontoid size was small, the improvement of the clinical status of the patient was encouraging.

Additionally, the findings of radiation-induce MRI enhancement was observed only within the odontoid and not in the neighboring brainstem, supports the idea that this means of focused radiation is indeed safe for treatment adjacent to critical structures. This is an important observation, especially given the known difficulties associated with the use of traditional radiation treatments to the head and neck (Astreinidou et al, 2005; Chen et al, 2011; Mavroidis et al, 2009).

Further investigation and follow-ups are needed to draw more definitive conclusions as to the long-term effectiveness of this as treatment modality on the bone. Additional follow-up studies will help to reveal if further changes in the odontoid are noted over time. As has been documented, the effects of radiation treatments on bone are, at times, not entirely realized until years after treatment (Chung et al, 2010).

Although the exact mechanism of the observed improvement in this patient is not fully known, the results of this case suggest this approach may represent an additional form of palliative treatment for worsening brainstem symptoms for inoperable basilar invagination.

Study 3: Osteoporotic Bone Anchor

The results of this study indicate the anchor was effective in acting as a bumper and not allowing the pedicle screw to translate during fatigue testing. This resulted in a significant reduction in axial motion compared to the screw alone. During pullout testing the anchor successfully provided a better bone to screw interface. The load at failure of the screw with the anchor is 702 N and significantly more than no anchor which failed at 421 N.

In the study, a worst case situation of 25 mm length and 4.5 mm diameter pedicle screws were used. In a clinical setting, pedicle screws of 45 mm length and 6.5 mm diameter would be more common. The increase in pedicle screw size combined with an anchor will only decrease the fatigue displacement and increase the ultimate load to failure numbers seen in our study. These results are promising given the success found with both a small screw and since the anchor device is means of securing low density bone that had previously not been investigated.

CHAPTER V

CONCLUSIONS

The overall goal of this project was to examine three complicated scenarios of spinal instability and assess novel treatments for each of them. From the findings of these studies, it was demonstrated that cervical thoracic bracing may offer an alternative, non-surgical means of rigid fixation for an aging patient with a displaced odontoid fracture. This is especially useful in the case of a potentially dangerous fracture when surgery is not desired or possible. By offering an alternative to traditional methods of internal and external fixation, cervical-thoracic bracing, in this instance, was shown to allow for bony reapproximation, until normal healing across the fracture site could occur.

Additionally, the second study in this project showed that radiation of the odontoid could be performed without radiation enhancement of the neighboring brain and visual system. In the case of this gentleman, who suffered from advancing terminal basilar invagination, clinical improvement was seen after radiation treatment of the odontoid. Additionally, post-radiation the region of the odontoid closest to the brain stem showed both radiation induced enhancement and a decrease in AP length without coinciding brainstem enhancement. These results, while not conclusive, are promising, given the very limited treatment options for this particular subset of the population. It is important to note that this treatment was hoping to provide some non-surgical palliation for the brain stem symptoms of the patient and did not specifically address the instability of the occipital-cervical junction. Further studies will be needed to examine the true applicability for the use of radiation as a means of secondary bony decompression of the odontoid possibly as a caveat to posterior cervical stabilization.

Finally, the third study of this project examined a means of addressing the problem of bone stabilization within patient populations who have low bone density. In the novel approach used in this study, a screw anchor was shown to significantly decrease axial toggling and pullout of bone screws within low density cadaver vertebral bodies. These results are quite exciting, as this type of device offers a chance to greatly improve surgical stability with only a sight modification of present surgical techniques.

Overall, while each of these novel treatments may be specific to a particular problem or patient population, they each address an area for which there exist few treatment options. Additional studies will be needed to examine the full potential for these approaches to be adopted as more standard treatment modalities. However the results of these studies, clearly lend additional information to understanding critical problems that need to be addressed to successfully treat these forms of complicated spinal instability.

BIBLIOGRAPHY

Amato V, Giannachi, L, Irace, C, Corona, C Thoracic spinal stenosis and myelopathy: report of two rare cases and review of the literature [Journal] // J Neurosurg Sci. - Dec 2012. - 4 : Vol. 56. - pp. 373-8.

Ames CP, Acosta, F, Nottmeier, E Novel treatment of basilar invagination resulting from an untreated C-1 fracture associated with transverse ligament avulsion. Case report and description of surgical technique [Journal] // J Neurosurg Spine. - Jan 2005. - 1 : Vol. 2. - pp. 83-7.

Arcangeli P, Andreotti, L, Palazzini, E Effective treatment of osteoarthritis with a 150 mg prolonged-release of diclofenac sodium [Journal] // Riv Eur Sci Med Farmaco. - Sep-Dec 1996. - 5-6 : Vol. 18. - pp. 217-23.

Astreinidou E Bel A, Raaijmakers CP, Terhaard CH, Lagendijk JJ Adequate margins for random setup uncertainties in head-and-neck IMRT [Journal] // Int J Radiat Oncol Biol Phys. - Mar 1, 2005. - 3 : Vol. 61. - pp. 938-44.

Aydogan M, Ozturk, C, Karatoprak, O, Tezer, M, Aksu, N, Hamzaoglu, AJ . The pedicle screw fixation with vertebroplasty augmentation in the surgical treatment of the severe osteoporotic spines [Journal] // Spinal Disord Tech. - Aug 2009. - 6 : Vol. 22. - pp. 444-7.

Balakatounis KC, Panagiotopoulou, KA, Mitsiokapa, EA, Mavrogenis, AF, Angoules, AG, Papathanasiou, J, Papagelopoulos, PJ Evidence-based evaluation and current practice of non-operative treatment strategies for lumbar stenosis [Journal] // Folia Med (Plovdiv). - Jul-Sep 2011. - 3 : Vol. 53. - pp. 5-14.

Becker S, Chavanne, A, Spitaler, R, Kropik, K, Aigner, N, Ogon, M, Redl, H Assessment of different screw augmentation techniques and screw designs in osteoporotic spines [Journal] // Eur Spine J. - Nov 2008. - 11 : Vol. 17. - pp. 1462-9. - Epub 2008 Sep 10.

Benzel EC, Larson, SJ, Kerk, JJ, Millington, PJ, Novak, SM, Falkner, RH, Wenninger, WJ The thermoplastic Minerva body jacket: a clinical comparison with other cervical spine splinting techniques [Journal] // J Spinal Disord. - Sep 1992. - 3 : Vol. 5. - pp. 311-9.

Bliuc D, Nguyen, ND, Nguyen, TV, Eisman, JA, Center, JR Compound risk of high mortality following osteoporotic fracture and re-fracture in elderly women and men [Journal] // J Bone Miner Res. - Apr 24, 2013 . - [Epub ahead of print].

Brant W.E., Helms, C.A. Fundamentals of Diagnostic Radiology [Book]. - Philadelphia : Lippincott Williams and Wilkins, 2012.

Brown TT HIV: An under-recognized secondary cause of osteoporosis? [Journal] // J Bone Miner Res. - Apr 29, 2013. - [Epub ahead of print].

Chaudhary A, Drew, B, Orr, RD, Farrokhyar, F Management of type II odontoid fractures in the geriatric population: outcome of treatment in a rigid cervical orthosis [Journal] // J Spinal Disord Tech. - Jul 2010. - 5 : Vol. 23. - pp. 317-20.

Chen C, Lee, C, Mah, V, Sharma, R, Landau, E, Garg, M, Wu, A Dose sparing of brainstem and spinal cord for re-irradiating recurrent head and neck cancer with intensity-modulated radiotherapy [Journal] // Med Dosim. - Spring 2011. - 1 : Vol. 36. - pp. 21-7.

Chen H, Onishi, K Effect of home exercise program performance in patients with osteoarthritis of the knee or the spine on the visual analog scale after discharge from physical therapy [Journal] // Int J Rehabil Res. - Sep 2012. - pp. 275-7.

Chung KY, Chiu, KH, Cheung, KW Osteoradionecrosis of the acetabulum in a total hip arthroplasty: a case report [Journal] // J Orthop Surg (Hong Kong). - Apr 2010. - 1 : Vol. 18. - pp. 110-2.

del Sel JM, Cibeira, JB, Espagnol, RO, del Sel, GM, del Sel, HJ. Stability following fracture-dislocations of the cervical spine [Journal] // Paraplegia. - Nov 1975. - 3 : Vol. 13. - pp. 203-7.

Derkay CS, Grundfast, KM, McCullough, DC Sudden onset of velopharyngeal insufficiency in Klippel-Feil syndrome [Journal] // Ear Nose Throat J. - Aug 1990. - 8 : Vol. 69. - pp. 548-52.

Dimitroulas T, Nikas, SN, Trontzas, P, Kitas, GD Biologic therapies and systemic bone loss in rheumatoid arthritis [Journal] // Autoimmun Rev. - Mar 29, 2013. - [Epub ahead of print].

Ding WY, Yang, DL, Cao, LZ, Sun, YP, Zhang, W, Xu, JX, Zhang, YZ, Shen, Y Intervertebral disc degeneration and bone density in degenerative lumbar scoliosis: a comparative study between patients with degenerative lumbar scoliosis and patients with lumbar stenosis [Journal] // Chin Med J (Engl). - Dec 2011. - 23 : Vol. 124. - pp. 3875-8.

Elgafy H, Dvorak, MF, Vaccaro, AR, Ebraheim, N Treatment of displaced type II odontoid fractures in elderly patients [Journal] // Am J Orthop. - Belle Mead, NJ : [s.n.], Aug 2009. - 8 : Vol. 38. - pp. 410-6. - Review.

Fagin AM, Cipolle, MD, Barraco, RD, Eid, S, Reed, JF 3rd, Li, PM, Pasquale, MD Odontoid fractures in the elderly: should we operate? [Journal] // J Trauma. - Mar 2010. - 3 : Vol. 68. - pp. 583-6.

Goel A Basilar invagination, Chiari malformation, syringomyelia: a review [Journal] // Neurol India. - May-Jun 2009. - pp. 235-46.

Goel A, Bhatjiwale, M, Desai, K Basilar invagination: a study based on 190 surgically treated patients [Journal] // J Neurosurg. - Jun 1998. - 6 : Vol. 88. - pp. 962-8.

Greenberg MS Handbook of Neurosurgery [Book]. - New York : Thieme Medical Publishers, 2006. - p. 1013. - (Paperback). - 9781588904577.

Gullick NJ, Scott, DL Drug therapy of inflammatory arthritis [Journal] // Clin Med. - Aug 2012. - 4 : Vol. 12. - pp. 357-63.

Hadley MN, Browner, C, Sonntag, VK. Axis fractures: a comprehensive review of management and treatment in 107 cases [Journal] // Neurosurgery. - Aug 1985. - 2 : Vol. 17. - pp. 281-90.

Harrop JS, Hart, R, Anderson, PA Optimal treatment for odontoid fractures in the elderly [Journal] // Spine. - Phila Pa : [s.n.], Oct 1, 2010. - 21 : Vol. 35. - pp. 219-27.

Hart RA, Prendergast, MA Spine surgery for lumbar degenerative disease in elderly and osteoporotic patients [Journal] // Instr Course Lect. - 2007. - Vol. 54. - pp. 257-72. - Review.

Helgeson MD, Kang, DG, Lehman, RA Jr, Dmitriev, AE, Luhmann, SJ Tapping insertional torque allows prediction for better pedicle screw fixation and optimal screw size selection [Journal] // Spine J. - Apr 17, 2013. - pii: S1529-9430(13)00295-7.

Ivancic PC, Telles, CJ Neck motion due to the halo-vest in prone and supine positions [Journal] // Spine. - May 1, 2010. - 10 : Vol. 35. - pp. 400-6.

Khandanpour N, Connolly, DJ, Raghavan, A, Griffiths, PD, Hoggard, N Craniospinal abnormalities and neurologic complications of osteogenesis imperfecta: imaging overview [Journal] // Radiographics. - Nov-Dec 2012. - 7 : Vol. 32. - pp. 2101-12.

Klimo Jr P, Rao, G, Brockmeyer, D Congenital anomalies of the cervical spine [Journal] // Neurosurg Clin N Am. - Jul 2007. - 3 : Vol. 18. - pp. 463-78.

Knaub MA, Won, DS, McGuire, R, Herkowitz, HN Lumbar spinal stenosis: indications for arthrodesis and spinal instrumentation [Journal] // Instr Course Lect. - 2005. - Vol. 54. - pp. 313-9.

Koech F, Ackland, HM, Varma, DK, Williamson, OD, Malham, GM Nonoperative management of type II odontoid fractures in the elderly [Journal] // Spine. - Dec 15, 2008. - 26 : Vol. 33. - pp. 2881-6.

Kwon JW, Huh, SJ, Yoon, YC, Choi, SJ, Jung, YJ, Oh, D, Choe, BK Pelvic bone complications after radiation therapy of uterine cervical cancer: evaluation with MRI [Journal] // AJR Am J Roentgenol. - Oct 2008. - 4 : Vol. 191. - pp. 987-94.

Lee BH, Moon, SH, Kim, HJ, Lee, HM, Kim, TH Osteoporotic profiles in elderly patients with symptomatic lumbar spinal canal stenosis [Journal] // Indian J Orthop. - May 2012. - 3 : Vol. 46. - pp. 279-84.

Malcolm GP Surgical disorders of the cervical spine: presentation and management of common disorders... [Journal] // J Neurol Neurosurg Psychiatry. - 2002. - pp. 134-41.

Malik SA, Murphy, M, Connolly, P, O'Byrne, J Evaluation of morbidity, mortality and outcome following cervical spine injuries in elderly patients [Journal] // Eur Spine J. - Apr 15, 2008. - 4 : Vol. 17. - pp. 585-91. - Epub 2008 Jan.

Marx RE Osteoradionecrosis: a new concept of its pathophysiology [Journal] // J Oral Maxillofac Surg. - May 1983. - 5 : Vol. 41. - pp. 283-8.

Mavroidis P, Stathakis, S, Gutierrez, A, Esquivel, C, Shi, C, Papanikolaou, N Expected clinical impact of the differences between planned and delivered dose distributions in helical tomotherapy for treating head and neck cancer using helical megavoltage CT images [Journal] // J Appl Clin Med Phys. - Jul 21, 2009. - 3 : Vol. 10. - p. 2969.

McAllion SJ, Paterson, CR Causes of death in osteogenesis imperfecta [Journal] // J Clin Pathol. - Aug 1996. - 8 : Vol. 49. - pp. 627-30.

Melcher RP, Puttlitz, CM, Kleinstueck, FS, Lotz, JC, Harms, J, Bradford, DS Biomechanical testing of posterior atlantoaxial fixation techniques [Journal] // Spine. - Nov 15, 2002. - 22 : Vol. 27. - pp. 2435-40.

Menezes AH, VanGilder, JC, Clark, CR, el-Khoury, G Odontoid upward migration in rheumatoid arthritis. An analysis of 45 patients with "cranial settling" [Journal] // J Neurosurg. - Oct 1985. - 4 : Vol. 63. - pp. 500-9.

Nickel VL, Perry, J, Garrett, A, Heppenstall, M The halo. A spinal skeletal traction fixation device [Journal] // J Bone Joint Surg Am. - Oct 1968. - 7 : Vol. 50. - pp. 1400-9.

Pakzaban P, Penar, PL, Talavera, F, Zamboni, P [Online] = Spinal Instability and Spinal Fusion Surgery // emedicine.medscape.com. - 2012. - http://emedicine.medscape.com/article/1343720overview.

Papadakis M, Aggeliki, L, Papadopoulos, EC, Girardi, FP Common surgical complications in degenerative spinal surgery [Journal] // World J Orthop. - Apr 18, 2013. - 2 : Vol. 4. - pp. 62-6.

Polin RS, Szabo, T, Bogaev, CA, Replogle, RE, Jane, JA Nonoperative management of Types II and III odontoid fractures: the Philadelphia collar versus the halo vest [Journal] // Neurosurgery. - Mar 1996. - 3 : Vol. 38. - pp. 450-7.

Ponnusamy KE, Iyer, S, Gupta, G, Khanna, AJ Instrumentation of the osteoporotic spine: biomechanical and clinical considerations [Journal] // Spine J. - Jan 2011. - 1 : Vol. 11. - pp. 54-63. - Review.

Rao G, Apfelbaum, RI Odontoid screw fixation for fresh and remote fractures [Journal] // Neurol India. - Dec 2005. - 4 : Vol. 53. - pp. 416-23.

Reginste JY, Bruyere, O, Fraikin, G, Henrotin, Y Current concepts in the therapeutic management of osteoarthritis with glucosamin [Journal] // Bull Hosp Jt Dis. - 2005. - 1-2 : Vol. 63. - pp. 31-6.

Riggs BL, Wahner, HW, Seeman, E, Offord, KP, Dunn, WL, Mazess, RB, Johnson, KA, Melton, LJ 3rd Changes in bone mineral density of the proximal femur and spine with aging. Differences between the postmenopausal and senile osteoporosis syndromes [Journal] // J Clin Invest. - Oct 1982. - 4 : Vol. 70. - pp. 716-23.

Rohrbach M, Giunta, C Recessive osteogenesis imperfecta: clinical, radiological, and molecular findings [Journal] // Am J Med Genet C Semin Med Genet. - Aug 15, 2012. - 3 : Vol. 160C. - pp. 175-89. - Epub 2012 Jul 12.

Sawin PD, Menezes, AH Basilar invagination in osteogenesis imperfecta and related osteochondrodysplasias: medical and surgical management [Journal] // J Neurosurg. - Jun 1997. - 6 : Vol. 86. - pp. 950-60.

Schoenfeld AJ, Bono, CM, Reichmann, WM, Warholic, N, Wood, KB, Losina, E, Katz, JN, Harris MB, Type II odontoid fractures of the cervical spine: do treatment type and medical comorbidities affect mortality in elderly patients? [Journal] // Spine. - May 15, 2011. - 11 : Vol. 36. - pp. 879-85.

Shin JJ, Kim, SJ, Kim, TH, Shin, HS, Hwang, YS, Park, SK Optimal use of the halo-vest orthosis for upper cervical spine injuries [Journal] // Yonsei Med J. - Sep 1, 2010. - 5 : Vol. 51. - pp. 648-52.

Sigmundsson FG, Jönsson, B, Strömqvist, B. (Phila Pa 1976). 2013 Apr 15. The Impact of Pain on Function and Health Related Quality of Life in Lumbar Spinal Stenosis: A Register Study of 14.821 patients [Journal] // Spine. - Apr 15, 2013. - [Epub ahead of print].

Sigmundsson FG, Kang, XP, Jönsson, B, Strömqvist, B Correlation between disability and MRI findings in lumbar spinal stenosis: a prospective study of 109 patients operated on by decompression [Journal] // Acta Orthop. - Apr 2011. - Vol. 82. - pp. 204-10.

Sime D, Pitt, V, Pattuwage, L, Tee, J, Liew, S, Gruen, R Non-surgical interventions for the management of type 2 dens fractures: a systematic review.Sime D, Pitt V, Pattuwage L, Tee J, Liew S, Gruen R. 2013 Oct 7. doi: 10.1111/ans.12401. [Epub ahead of print] [Journal] // ANZ J Surg. - Oct 7, 2013.

Simsek S, Yigitkanli, K, Belen, D, Bavbek, M Halo traction in basilar invagination: technical case report [Journal] // Surg Neurol. - Sep 2006. - 3 : Vol. 66. - pp. 311-4.

Singer A Osteoporosis diagnosis and screening [Journal] // Clin Cornerstone. - 2006. - 1 : Vol. 8. - pp. 9-18. - Review.

Smith HE, Kerr, SM, Fehlings, MG, Chapman, J, Maltenfort, M, Zavlasky, J, Harris, E, Albert, TJ, Harrop, J, Hilibrand, AS, Anderson, DG, Vaccaro, AR Trends in epidemiology and management of type II odontoid fractures: 20-year experience at a model system spine injury tertiary referral center [Journal] // J Spinal Disord Tech. - Dec 2010 . - 8 : Vol. 23. - pp. 501-5..

Smith JS, Shaffrey, CI, Abel, MF, Menezes, AH Basilar invagination [Journal] // Neurosurgery. - Mar 2010. - 3 : Vol. 66. - pp. 39-47.

Son S, Kim, WK, Lee, SG, Park, CW, Lee, K A comparison of the clinical outcomes of decompression alone and fusion in elderly patients with two-level or more lumbar spinal stenosis [Journal] // J Korean Neurosurg Soc. - Jan 2013. - 1 : Vol. 53. - pp. 19-25.

Soultanis KC, Sakellariou, VI, Starantzis, KA, Stavropoulos, NA, Papagelopoulos, PJ Insidious Onset of Tetraparesis due to Cervical Epidural Abscess from Enterococcus faecalis [Journal] // Case Rep Med. - 2013. - Epub 2013 Mar 20.

Stanos SP Osteoarthritis guidelines: a progressive role for topical nonsteroidal anti-inflammatory drugs [Journal] // J Multidiscip Healthc. - Apr 2013. - pp. 133-7.

Støre G, Granström, G Osteoradionecrosis of the mandible: a microradiographic study of cortical bone [Journal] // Scand J Plast Reconstr Surg Hand Surg. - Sep 1999. - 3 : Vol. 33. - pp. 307-14.

Tashjian RZ, Majercik, S, Biffl, WL, Palumbo, MA, Cioffi, WG Halo-vest immobilization increases early morbidity and mortality in elderly odontoid fractures [Journal] // J Trauma. - Jan 2006. - 1 : Vol. 60. - pp. 199-203.

Wan SY, Wu, ZX, Zhang, W, Liu, D, Gao, MX, Fu, SC, Shi, L, Lei, W Expandable pedicle screw trajectory in cadaveric lumbar vertebra: an evaluation using microcomputed tomography [Journal] // J Spinal Disord Tech. - Jul 2011. - 5 : Vol. 24. - pp. 313-7.

White AP, Hashimoto, R, Norvell, DC, Vaccaro, AR Morbidity and mortality related to odontoid fracture surgery in the elderly population [Journal] // Spine. - Apr 20, 2010. - 9 : Vol. 35. - pp. 146-57.

www.europe.stryker.com/index/st_pag_medic-home/st_pag_detailed-product-info/st_pag_spinal-implants/eu_pag_spine-thoracolumbar/eu_pag_diapason.htm). [Online]

www.londonspine.co.uk/index1ff1.html?page_id=1228). [Online]

www.ossur.co.uk/pages/9842. [Online]

www.ossur.co.uk/pages/9862. [Online]

www.pennyandbrain.org/odontoid-fracture.html. [Online]

www.radiologytutorials.com/main.cgi?tut=/
main.cgi&frame=main&tt=1&s=1&t=31&mod=all). [Online]

www.spineuniverse.com/conditions/spinal-cord-injury/halo-brace-use-cervical-fractures). [Online]

www.thirdage.com/hc/c/spinal-stenosis-photos). [Online]

Xie Y, Fu, Q, Chen, ZQ, Shi, ZC, Zhu, XD, Wang, CF, Li, M Comparison between two pedicle screw augmentation instrumentations in adult degenerative scoliosis with osteoporosis [Journal] // BMC Musculoskelet Disord. - Dec 21, 2011. - Vol. 12. - p. 286.