Ultrasound Imaging of Cervical Spine Motion for Extreme Acceleration Environments

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ABSTRACT

Neck and back pain is one of the most common musculoskeletal complaints in personnel in variable acceleration environments such as astronauts and military pilots. Ultrasound is known for dynamic imaging and diagnostic workup of the axial and appendicular skeleton, but is not currently used to image the cervical spine, the injury of which may change the biomechanics of the cervical vertebrae, which CT and MRI (the current gold standard in cervical spine imaging) are poor at capturing. To validate ultrasound as a modality for imaging dynamic motion of the cervical spine several experiments were performed in static and dynamic human and animal (ovine) models:

1. Static analysis of *ex-vivo* ovine cervical spines imaged by ultrasound, MRI, and CT demonstrated that the imaging modality affected the measured intervertebral disc height ($p<0.01$); similar evaluation was done *in-vivo* in Emergency Department patients who received a CT scan as part of their clinical course that showed that ultrasound could fit into existing clinical workflows.
2. Dynamic analysis of isolated *ex-vivo* ovine cervical spinal segments intervertebral disc displacement with a mounted ultrasound probe demonstrated a measurement uncertainty of ± 0.2 mm and no bias at low frequency sinusoidal spinal displacement. A similar evaluation *in-vivo* with humans with an ultrasound probe mounted on a cervical-collar found a 0.8-1.3 mm amount of cervical spine distraction from the C4-5 Functional Spinal Unit. In human cadavers subjected to passive flexion and extension of the cervical spine, ultrasound measurements of the relative flexion/extension angles between consecutive cervical vertebrae were similar to fluoroscopy.
3. Ultrasound was able to record dynamic motion of the cervical spine in-vivo in running on a treadmill, during parabolic flight, and traveling over a rough road in a military vehicle.

The ultrasound methods developed and tested in this thesis could provide an inexpensive, portable and safe technique that can identify and characterize cervical spine anatomy and pathology.

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Tell me the causes now, O Muse…
From the Aeneid by Virgil (I;10)

Over a 7 year (and counting) graduate career there are many people without whom I would not be where I am right now. Unfortunately, space constraints limit my listing of names, so please forgive me for those I do not mention by name, your help was much appreciated.

First thanks go to Brian Snyder, my primary thesis advisor. Brian is an excellent mentor who has already travelled the MD/PhD path I hope to follow and has provided invaluable resources and advice in choosing, developing, and accomplishing this work. Further thanks go to my MIT advisors throughout the years, Dava Newman, my thesis committee chair and academic advisor, Larry Young, my Bioastronautics mentor, and Chuck Oman, my master's thesis advisor and first mentor at MIT. Thanks to Rob Howe of Harvard for serving as the final member of my thesis committee, Jeff Hoffman and Jon Kaufman for serving as the necessary representatives to the committee for the proposal defense, and Corrie Yablon and Leia Stirling for serving as readers and providing valuable feedback and resources. Also, thanks to the many folks at the MIT Man-Vehicle lab, notably Liz Zotos; admin extraordinaire, Andy Liu, Alan Natapoff, and all the others who have made the lab my MIT home. I would also like to note the advice given to me by my undergraduate Aerospace Engineering advisor at Georgia Tech, Jerry Seitzman, who told me once that, "it all works out somehow." It certainly has, and that quote has provided a sustaining light when life in PhD world was darkest.

On the other side of the river, the staff and students of the BIDMC Center for Advanced Orthopedic Research provided my research home. Thanks to Paula Cohen, lab director Chris Evans, and everyone else. Also thanks must go to the many undergrad research assistants (Dora Aldama, Janet Lin, and Jim Moriarty) who have put in many hours of collecting data and preparing all manners of sheep and human specimens. Special thanks to Kevin Shiuan, BU Grad Student, for helping me with the final push at the end and continuing on with my work.

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Finally, my proudest and most unlikely accomplishment of my graduate career was convincing Dr. Sarah Miller to marry me. I don't know that I wouldn't have completed this work without her, but I certainly wouldn't be nearly as happy.

Dan Buckland
June 2011, Boston, MA

Biographical Note

Dan Buckland is (as of this writing) a MD/PhD candidate through Harvard Medical School Division of Health Science & Technology and the MIT Department of Aeronautics and Astronautics. Aside from this work on using ultrasound to look at the biomechanics of the cervical spine in differing flight environments he has done previous work on *A Training Methodology for Spatial Orientation in Spacecraft* under Dr. Charles M. Oman, Ph.D at the Massachusetts Institute of Technology. He was also a Research Study Coordinator at Brigham and Women's Hospital Emergency Department in 2007 where he planned a clinical research study on efficacy of novel antibiotic use on Methicillin-resistant Staphylococcus aureus (MRSA) caused cellulitis in emergency department patients and worked as a Research Engineer at NASA and Wyle Laboratories in 2007 where he quantified injury caused by current American spacesuit and applied results to recommendations for design of next generation suit for exploration of Moon and Mars. He received a BS in Aerospace Engineering from the Georgia Institute of Technology in 2004 and has been an instructor in the HST Anatomy course for multiple years. Other than academic and research positions he contributes to MedGadget (www.medgadget.com), an Online Journal of Medical Technologies, writing several stories a week on medical innovation in numerous fields and specialties. He also worked as a pool hall manager at Flat Top Johnny's in Cambridge, MA.

Dan has received a NSBRI Bioastronautics Fellowship (2007), a Children's Hospital Orthopedic Surgery Foundation Fellowship (2008), the Society of NASA Flight Surgeons Outstanding Student Award (2010), the Space Medicine Association Jeffery R. David Award (2011), and a Whitaker Foundation International Scholarship (2012).

He currently lives in Boston, MA with his wife, Dr. Sarah Miller, a Harvard College Fellow in the Harvard University Department of Molecular and Cellular Biology.

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List of Abbreviations

BIDMC	Beth Israel Deaconess Medical Center
C1, C2 etc	Cervical Spine Vertebrae 1, 2, etc..
CDDD	**C**ervical Degenerative Disc Disease
CT	Computed Tomography
DMSS	Defense Medical Surveillance System
EMG	Electromyography
FEM	Finite Element Model
FSU	Functional Spinal Unit
HMD	Helmet Mounted Display
HMS	Harvard Medical School
HRF	Human Research Facility
HSM	Head Supported Mass
ISO	International Standards Organization
IVD	Intervertebral Disc
MIT	Massachusetts Institute of Technology
MRI	Magnetic Resonance Imaging
NASA	National Aeronautics and Space Administration
NSW	Naval Special Warfare
RIB	Ribbed Inflatable Boat
US	Ultrasound

1 Introduction

Back and neck pain is a common occupational musculoskeletal complaint for workers in extreme environments such as NASA Astronauts and Army helicopter pilots[2]. It is also one of the most common work-related medical issues in the United States [3]. Countermeasures and treatments for this injury need to be developed, but an accurate understanding of the forces and biomechanics affecting the spine need to be understood first. These extreme environments make it difficult to get dynamic force and biomechanical information using traditional medical imaging methods, due to their size and power requirements. However, ultrasound can provide a robust, portable, small, and dynamic imaging technology that can be used in these environments to gather this information.

1.1 Motivation

As mentioned, back and neck pain is a problem (in cost, loss of productivity, and quality of life) in occupational health, both in aerospace and other fields. Extreme environment operators need imaging methods that can operate in the conditions to which they are subjected, which traditional methods for imaging the musculoskeletal anatomy cannot provide. An imaging solution is needed that can both capture the dynamic nature of the environment and survive the environment itself. Those limitations led to the exploration of ultrasound as an appropriate imaging technology.

The number of cervical spine injuries is expected to rise as a result of increased mission lengths and helmet technologies. Examples include longer spaceflight missions, Army requirements for extended mission durations, and the increased reliance on night vision devices and helmet mounted displays (HMD) by all Army and Navy Warriors. In the case of head-mounted hardware this increased weight significantly changes the center of gravity and the inertial forces and moments applied to the cervical spine, particularly during the dynamic loading conditions encountered during combat. Countermeasures such as redesign of helmets and seats or changing the weight distribution of the equipment are being considered, but to do so analytically requires a better understanding of the biomechanical parameters of the cervical spine injury. It is not feasible to get this information from traditional methods of musculoskeletal imaging as large size and power requirements of plain radiography, computed tomography (CT) and Magnetic Resonance Imaging (MRI) prevent their use in evaluating the anatomy and dynamic motion of the cervical spine during the extreme environments encountered during military operations. Ultrasound does not have these limitations, so the purpose of this project is to develop the capabilities of clinical ultrasound beyond its current indications. We will demonstrate that ultrasound provides a small, portable, robust, dynamic imaging method that can gather real-time information about the kinematics of the cervical spine and inter-vertebral disc mechanics in the extreme conditions of military operations. Furthermore, the technology developed here could have considerable applications in civilian settings. Neck pain is one of the most pervasive problems in occupational health and a common presenting complaint in physician offices, outpatient clinics and emergency rooms [4]. Developing an inexpensive, portable and safe technique that can identify and characterize cervical spine anatomy and pathology without exposing patients to ionizing radiation or requiring expensive MRI technology unavailable in resource poor environments could have important societal benefits beyond the patient populations initially intended as the focus of this work.

1.2 Thesis Objectives

With this work I intend to show that clinical ultrasound can provide a safe, inexpensive, portable, imaging modality to quantify intervertebral disc displacement and rigid body motion of functional spinal units comprising the cervical spine in response to static and dynamic loads *in-vivo* in extreme environments such as spaceflight and military training operations. This will be accomplished through three series of experiments that each aim to validate a different aspect of what would be needed in such a functional ultrasound system.

1.2.1 Static Ultrasound Imaging of the Cervical Spine Intervertebral Disc Space

This work will show that ultrasound can be used to measure the anatomy and height of cervical spine intervertebral discs and that intervertebral disc height as measured by ultrasound, is similar to disc height measured by MRI and CT both *ex-vivo* and *in-vivo*.

1.2.2 Ultrasound Imaging of the Rigid Body Motion of the Cervical Spine Vertebrae

This work will show that ultrasound can be used to measure the motion of cervical spine vertebral body motion under different loading conditions meant to simulate wearing a head supported mass in an operational environment and that clinical ultrasound can detect the contribution of individual cervical spine functional spinal units to the total motion of the cervical spine *in-vivo* and *ex-vivo.*

1.2.3 In-Vivo Ultrasound Imaging of the Motion of the Cervical Spine Vertebrae in Operational Environments

This work will show that clinical ultrasound can be used to image the cervical spine in astronauts and pilots to understand the effects of their respective gravitational environments by attempting to take the same types of dynamic images studied in the prior two experiments in several operational environments.

1.3 A Note on Format and Layout

This thesis is intended as the combined work of three separate papers drafted for submission to peer-reviewed journals. Chapters 4, 5, and 6 should be read as such and are formatted in this way. Much of the repeated background and introductory material has been omitted from these chapters and combined in Chapters 2 and 3. As an aid to the reader, the abstracts for the draft papers have been retained as a guide to each.

Chapter 4 is intended to be submitted to a radiology journal with the thesis author as first author. Other authors will be Jeannette Perez-Rosello, Erik Antonsen, Scott Sheehan, Anthony Samir, and Brian Snyder.

Chapter 5 is intended to be submitted to an orthopedics research or clinical practice journal with the thesis author as first author. Other authors will be Jeannette Perez-Rosello, and Brian Snyder

Chapter 6 is intended to be submitted to an occupational health or clinical practice journal with the thesis author as first author. Other authors will be Jeannette Perez-Rosello, and Brian Snyder.

Chapter 8 is intended to be the narrative section of a technology development grant application, such as an R21, again with the background content omitted.

2 Background

2.1 Incidence and Epidemiology of Cervical Spine Injury

Neck and back pain are an increasing problem among all military populations [5] and NASA Astronauts [6]. According to a survey of the Total Army Injury and Health Outcomes Database (TAIHOD) more than 1.2 million injuries to the spine were documented among Army personnel between 1980 and 2002. Cervical spine related injuries resulted in over 1,200 disability evaluations and almost 60,000 outpatient visits [7]. Most neck pain was related to intervertebral disc (IVD) degeneration, spondylosis with myelopathy and/or segmental/somatic dysfunction [7]. The incidence of cervical spine injury appears to be increasing: between 2003 and 2007 the Defense Medical Surveillance System (DMSS) database attributed 1,405 hospital admissions and 146,635 outpatient visits to cervical spine related injuries. These injuries result in high treatment costs, permanent disability, and excessive loss of experienced Warriors. It is also the second most common musculoskeletal complaint among NASA Space Shuttle Program participants [6, 8].

Warriors who work in extreme environments such as Army helicopter pilots, Navy RIB (Ribbed Inflatable Boat) operators, tactical operations officers, Special Forces members and high performance fixed wing aviators are at increased risk for injuries to the neck and back. Gollwitzer [9] described the effects of repeated shock impacts on crewmembers of Naval Special Warfare (NSW) boats during high speed operations. Occupants were exposed to severe, dynamic conditions characterized by discrete and repeated impacts as the craft repeatedly slammed into waves. Both acute and chronic injuries reduced the short- and long-term effectiveness of naval personnel who were repeatedly exposed to these shock impacts. A self-reported injury survey conducted by The Naval Health Research Center (NHRC) confirmed the disproportionate rate of spinal injuries sustained by occupants of high speed NSW crafts [10].

Military aviators were also found to have a significantly higher rate of neck and back pain than other military job specialties [7]. Aydog [11] reported that helicopter pilots had a higher incidence of arthritic changes in the cervical spine compared to pilots of other types of aircraft and non-aviators. Other investigators [12, 13] have also documented the increased rate of neck pain with or without radiculopathy among helicopter pilots. An increased incidence of degenerative changes of the cervical spine has been observed in fighter pilots as well [14, 15]. Using low-field MR imaging of the cervical spine, senior fighter pilots flying high-performance aircraft were compared to non-aviators matched for age and sex; among the male fighter pilots (35-37 years of age), there was a higher occurrence and greater degree of inter-vertebral disc degeneration.

Neck pain and cervical spine injury have been attributed to the added weight of protective gear and special equipment (e.g. communications, night vision) worn by Warriors in the harsh operational setting of combat; however, little is known about the effects of this gear on cervical spine function. Studies investigating spine injury in dynamic combat environments have focused on the effects of whole body vibration and/or repeated impacts to the lumbar spine [16-19] or the response of the neck supporting the mass of the head and head-mounted equipment and decreased performance associated with fatigue [20] and standards ISO 2631-1 and ISO 2631-5 are developed for it.. A few studies have evaluated the combined the effects of whole body vibration with the response of the cervical spine [21-23]. However all these studies have focused on global or external measurements of the head and neck using electromyography (EMG) to measure muscle activity, and accelerometers to measure the motion and acceleration of the head and spine. The kinetics and kinematics of the cervical vertebrae have not been measured directly, but surmised. Only a few retrospective studies [14]have attempted to use imaging methods to systematically investigate specific changes in cervical spine anatomy directly.

In astronauts these injuries are likely related to the prolonged unloading of the spine in microgravity, and the rapid reloading on landing [24, 25].

2.2 Anatomy of the Cervical Spine

The cervical spine consists of the first 7 vertebrae, C1-C7 (Figure 2-1). While included in the cervical spine C1 is not a true vertebra, as it has no vertebral body. This allows the additional rotational degrees of freedom for the head. C2-C7 are load bearing structures that support the head. The vertebrae are stacked upon one another with an intervening intervertebral disc (IVD) that provides cushioning between consecutive vertebral bodies and bending and rotational motion. The intervertebral discs are made up of two structures, the nucleus pulposus and annulus fibrosus. The nucleus pulposus is the center of the disc and consists of a gelatinous viscoelastic substance with a high glucosaminoglycan (GAG) concentration. It is surrounded by the annulus fibrosus, a tough, multilayered tissue that contains the nucleus and gives structural support to the disc. Cervical vertebrae have an articular interface formed by the facet joints posteriorly. Layers of multiply oriented muscles provide stability, support, and movement of the head and cervical spine.

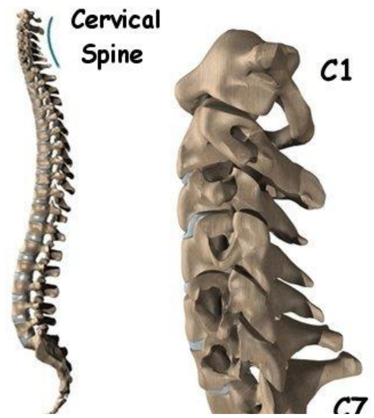

Figure 2-1. Cervical Spine anatomy (http://www.eorthopod.com/images/ContentImages/spine/spine_cervical/cervical_anatomy/spine_cervical_anatomy_intro01a.jpg)

2.3 Cervical Spine Pathology

Neck pain and back pain are strongly associated with degeneration of the IVD [26]. Degeneration of the disc is thought to be caused by both repetitive loading and natural aging [27]. Disc degeneration alters disc height and the extent of hydration of the nucleus pulposus, as well as the mechanics of the rest of the spinal column, including the surrounding ligaments and muscle. Over the long term, disc degeneration is thought to lead to disc herniation and/or spinal stenosis, both of which are major causes of acute pain [28]. Chronic neck pain, though less understood, is also believed to be associated with disc degeneration. The correlation between pain radiating from and in the neck and cervical degenerative disc disease (CDDD) has been reasonably established; however, the correlation between axial neck pain and CDDD has greater variability. Rarely is axial neck pain seen in the absence of CDDD, but an exception is often noted in whiplash (ligamentous) injury, which can fall in the category of highly dynamic cervical spine loading.

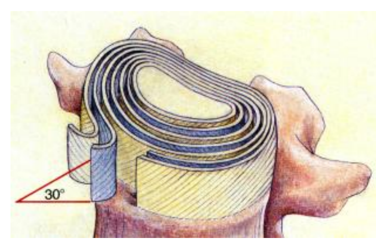

Figure 2-2. Anatomy of Intervertebral disc. Annulus Fibrosus surrounds the Nucleus Pulposus. From [1]

The relationship between loading and CDDD is also not well established. In the normal degenerative cascade, natural aging of the nucleus pulposus leads to loss of proteogylcans in the nucleus pulposus with resultant loss of hydration and nucleus pulposus pressurization. This is a multi-factorial response believed to be dependent on both genetic and environmental factors. Proteogylcan concentration in the intervertebral disc nucleus pulposus is well correlated to nucleus pulposus $T_{1\mathbf{rho}}$ signal [29]. It is hypothesized that the annulus fibrosis breaks down in response to altered annulus fibrosis loading brought on by the nucleus pulposus degenerative changes. Nucleus pulposus degenerative changes have been shown both experimentally and in finite element modeling to increase internal strains within the annulus fibrosis [30-35]. Moreover, it is hypothesized that the facet joints subsequently degenerate as alteration in disc loading increases facet loading. In the absence of macroscopic trauma, this theory of CDDD is supported by the clinical observations that the nucleus pulposus is observed to change hydration as observed on MRI before annulus fibrosis breakdown, which precedes facet degeneration. The Pfirrman classification for classifying CDDD based on MRI findings formalizes this degenerative cascade.

Acute disc rupture and ligament and facet capsule disruption are clearly in the spectrum of acute cervical injury, which would include vertebral fracture and cervical dislocation as well. In instances of acute disc rupture, the loss of nucleus pulposus hydration and pressurization often occurs rapidly and is assumed secondary to active enzymatic proteoglycan breakdown. Therefore, in these cases, alterations of the annulus fibrosis precede the nucleus pulposus degeneration. This nucleus pulposus degenerative process is much more acute than that of natural aging.

High amplitude, high frequency loading, common in extreme environments, is particularly challenging to the intervertebral disc. The energy absorbing function of the highly visco-elastic disc, which is due in large part to fluid flow, is lost at high frequencies where fluid path-lengths are short. Moreover, it is assumed that much of the damping occurring by the musculature at low frequency loading is lost at high frequency where voluntary actuation of muscle is unable to follow the load as a function of time.

2.4 Standard Methods of Imaging the Cervical Spine

MRI and CT are the current gold standards for imaging cervical spine anatomy and pathology [36]. MRI is particularly well suited for examining soft tissues and bone marrow. Clinical markers for evaluating the health of the IVD include the relative hydration of the nucleus pulposus observed on T2 weighted MRI images (degenerated discs lose water content and become dark on T2 weighted images), disc height, disc protrusion/herniation, presence of osteophytes and cross-sectional area of the dural sac. CT is better for visualizing 3D bony anatomy than MRI, particularly the presence of osteophytes, facet joint arthropathy (i.e. joint space narrowing, cyst formation) and measuring the cross-sectional area of the neural canal when evaluating stenosis of the cervical spine. Figure 2-3 shows how CT and MRI would image the same ovine specimen. Fluoroscopy (dynamic single plane X-ray) is sometimes used for dynamic motion analysis to evaluate the mechanical stability of the cervical spine during flexion and extension. None of these technologies can be used in extreme environments since the machines are large and require significant electrical power. Additionally MRI requires isolation from any ferro-magnetic surfaces and objects.

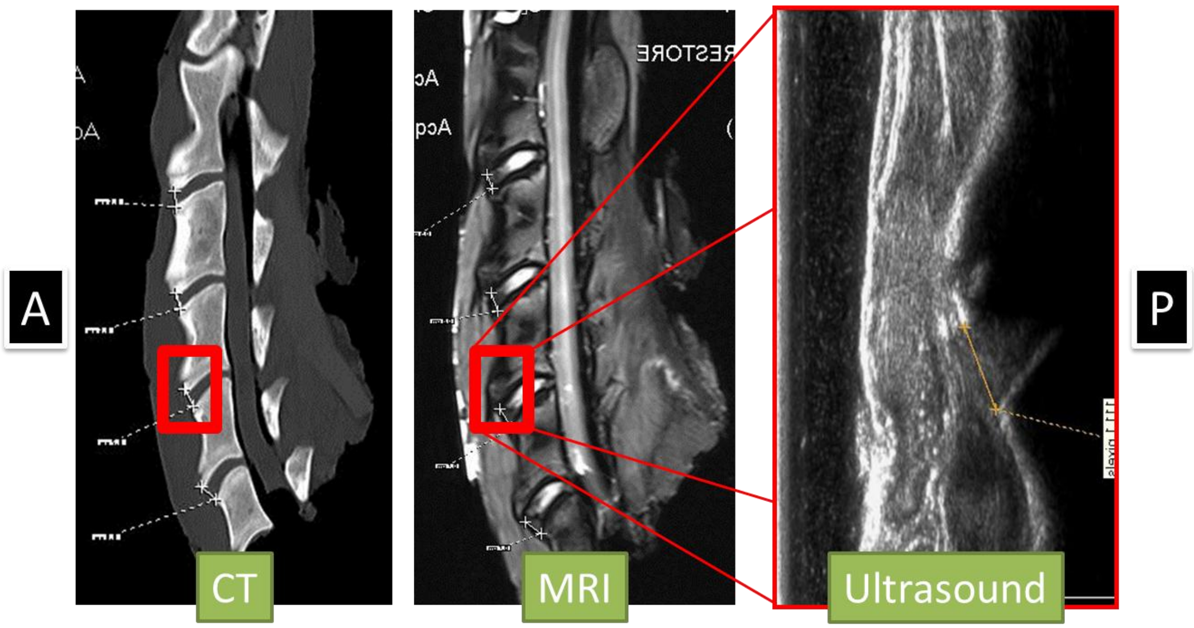

Figure 2-3. Three views of an ovine cervical spine. A = Anterior, P = Posterior

2.5 Ultrasound Imaging

Ultrasound provides a practical, cost-effective alternative to MRI and CT for imaging many anatomic sites and specifically for evaluating musculoskeletal pathoanatomy at the soft tissues and joints comprising the appendicular skeleton [37, 38]. It can be used to observe dynamic joint motion and mechanical stability in real time and has the potential to measure the material properties of tissues directly (since the velocity of the sound waves propagated through the material depends on its density and modulus of elasticity). Unlike CT, ultrasound does not risk exposure to ionizing radiation. Ultrasound devices have been certified to military specifications (MIL-STD 810F), allowing them to be used on Army Helicopters and Navy RIB boats with few additional certifications and modifications.

The HRF Ultrasound system aboard the International Space Station, though currently inoperative at least as of June 2011, has been used for both research and simple clinical evaluations [39, 40]. Non-physicians can and have been trained to take clinical and research quality images. These images can be analyzed by the crew in space to make initial diagnoses using simple checklists or reference images [41] and then be sent down to Earth to be analyzed by a physician.

Ultrasound produces images by measuring the time-of-flight of sound waves propagating through the tissue. The systems interpret differing echo times due to changes in acoustic impedance as tissue layers. Each piezoelectric crystal in an ultrasound probe can produce a 1 dimensional image (called A-Mode) that shows the tissue interfaces as a function of distance from the probe. When these A-Mode images are combined into a B-Mode image, the stereotypical 2 dimensional planar image is produced. Figure 2-3 shows a B-Mode image of a ovine cervical spine IVD and what the same anatomic area looks like in CT and MRI.

Previous studies have demonstrated that current clinical ultrasound systems can be used to image changes in IVD height [42]. Others have shown that the anatomy of the disc can be visualized using properly focused ultrasound imaging technology in animals [43] and in humans.

In-vivo surveys of human thoracic and lumbar spines detailed the extent that the IVD was visible from a posterior approach [44]. *Ex-vivo* comparisons between IVD anatomy imaged by ultrasound and direct histological evaluation [45] demonstrated that ultrasound could differentiate between the annulus fibrosus and nucleus pulposus. Others have shown that ultrasound can differentiate various anatomic structures in the cervical spine [46]. Ultrasound syatems can also be made portable (Figure 2-4). Therefore it is feasible to use both static and dynamic ultrasound imaging to measure the height of the IVD and dynamic motion of cervical vertebrae in military personnel and astronauts.

Figure 2-4. Laptop based portable ultrasound system. Coffee mug shown for scale.

2.6 Dynamic Behavior of the IVD

The biomechanics of the IVD has been studied under normal and abnormal loading conditions in a variety of ways. Although we have a reasonable understanding of disc degeneration and how it is affected by repetitive loads, the scientific community lacks knowledge of the IVD's response to dynamic, high-impact loads, and how these loads affect disc degeneration. Analysis of the mechanical behavior of the lumbar spine under static and quasistatic loading conditions has been studied extensively [47-53]. Panjabi's group was fundamental in establishing mechanical testing methods for the cervical spine [54]. They performed pivotal investigation of the mechanisms of whiplash injury and analyzed the effects of these injuries on the biomechanical behavior of the cervical spine using novel bench top models of cervical vertebrae subjected to whiplash trauma [55].

Most dynamic tests of human and animal cervical spines have been analyzed in the context of pure axial compression [56-59]. However, this loading condition does not approach those of the military personnel that we are attempting to model. The dynamic loading frequencies of Costi and Izambert fall short of the high-impact loads we seek to impose and the stiffness values reported by Yingling and Lee are not as high as the typical stiffness values observed in our preliminary experiments that simulated the representative loads encountered by fast boat operators during high velocity missions. Little work has focused on impact loading of the human cervical spine. Elias performed high impact loading experiments on baboon spines [60]. Zhu subjected human cadaver spines to dynamic loading, but their analysis only explored ranges of motion in the "neutral zone", and they did not investigate changes in the mechanical behavior of the spine for these dynamic loads [61]. Developing human, cadaveric, cervical spine models that simulate the dynamic, high-impact loads imposed during combat will allow a better understanding of the cervical spine injury patterns observed in our military personnel

In spaceflight there is extended unloading upon orbital entry which continues for the duration of the flight and leads to spinal elongation of 3-5 cm [62]. However, it is unknown which how the elongation is distributed along the spine. This is followed by rapid loading on landing, so rapid that all evidence of spinal elongation is gone by the time investigators could study flight crews [63]. There is also anecdotal evidence that flight crewmembers who spend time in spacesuits for Extra-Vehicular Activity (EVA) gain and lose up to 3 cm over several hours as they are strapped into the spacesuit and then released following EVA [64].

2.7 Standards Statement

Recognizing that there were no prior standards for measuring intervertebral disc height that could be applied for this work a Standards Meeting was held with several clinical and research specialties represented including Orthopedics, Emergency Medicine, Radiology, Pain Management, and Engineering and the following statement was produced:

> Clinically, there is no currently accepted quantitative measure of intervertebral disc height. There are qualitative indicators (relative disc heights in CT, MRI, or Fluoroscopy, and disc hydration and bulging in MRI), but they are not easily used for diagnosing quantitative differences from normal. Quantitative measurements of the height of the intervertebral disc height as measured from the anterior border of the disc using ultrasound would be a clinically useful metric to assess intervertebral disc heights and intervertebral disc height changes under loading conditions.

2.8 Modeling the Cervical Spine

The smallest unit of the spine to share the biomechanics of the entire spine is called the functional spinal unit (FSU) [54]; it consists of two adjacent vertebrae, the disc and all adjoining ligaments between them, excluding connecting tissues such as muscles, tendons, and skin. The motion of the FSU can be defined by the relative motion of the two vertebral bodies in relation to each other. One measure of the FSU that is useful clinically is the stiffness (k):

$$k = \frac{F}{\delta}$$

Equation 2-1

Where F = the axial force applied to the FSU and δ = relative displacement of the vertebral bodies. In practice the Compliance (C), or the inverse of stiffness is calculated since this represents the motion of the FSU as the result of an applied force:

$$C = \frac{\delta}{F} = \frac{1}{k}$$

Equation 2-2

Ultrasound has been used to measure the compliance of lumbar spine FSUs by submerging the patient in a water bath while applying longitudinal traction [65, 66]. These studies indicated that the lumbar spine was stiffer in older subjects than younger subjects. After age 35 there was a loss of compliance (or increase in stiffness) where the capacity of the spine to elongate when distracted decreased 0.01-0.04 mm/yr. There was no observed difference between male and female subjects.

Difficulty gathering *in-vivo* spine performance data in extreme work environments has led to an emphasis on modeling; the FSU is subjected to forces that simulate those applied to the spine in the work environment. However the complexity of the anatomy and the heterogeneity of the tissue properties can complicate modeling of cervical spine mechanical properties. If the focus is on performance of the IVD, or kinematics of the entire spine, the vertebra itself can be simply modeled as a homogenous bulk solid. Many models use recorded muscle potentials and muscle cross-sectional areas as inputs for determining muscle forces and then calculate the imposed spinal motion. These models have been tested using human or animal cadaveric spines subjected to static [67] and dynamic forces at low (~1Hz) frequencies. Analytic models using numerical methods have also been used to evaluate mechanical properties when simpler models were not appropriate such as the location of failure surfaces [68] and the effect of non-uniformly distributed loads [69]. Finite element models (FEM) have been developed that assess the mechanical performance of single and multiple contiguous cervical spine FSUs; however accurate specification of the heterogeneous material properties, boundary conditions and applied loads required to formulate the model and to evaluate the performance of the FSU in health and disease can be tricky. Few of these FEM have been carefully validated.

Estimating the contribution of muscles to the stability and structural support of the cervical spine is another focus of modeling. In the simplest representations, muscles are treated as powered springs attached to skeletal elements [70]. However, even these models can get complicated as there are many muscles in the neck that have varying levels of strength and directions of orientation. This complexity is handled by graphical programs that allow assignment of the origin, insertion and strength of each muscle. While these models are scalable and can account for the activity of each muscle, they lack the fidelity of individual muscle function. Most of these models assume that muscles are either on or off, where in actuality, each muscle is made up of individual fibers that are not necessarily all active or all inactive at the same time but instead depend on the skeletal motion being performed and the action of antagonistic muscle groups. Some models account for variability in muscle activation by measuring surface EMG *in-vivo* while subjects perform specific tasks [71]. However, surface EMGs record bulk muscle electrical activity and cannot differentiate individual muscle actions. Combinations of EMG and graphical modeling have been attempted with some success [72-74].

None of these spine models have be used to evaluate the performance of the cervical spine at high vibration states and few if any models have integrated direct measurement of vertebral motion during specific activities. Each of the extreme work environments in which our potential patient populations function has unique loading conditions that affect the biomechanical behavior of the cervical spine. Army Helicopter pilots are subjected to high amplitude vibrations on the order of 8-10 Hz. Since they are strapped into their seats, most of this energy is transmitted to the cervical spine.

3 Hypotheses

3.1 Global Hypothesis

Clinical ultrasound provides a safe, inexpensive, portable, imaging modality to quantify IVD displacement and rigid body motion of functional spinal units comprising the cervical spine in response to static and dynamic loads in-vivo.

3.2 Detailed Hypotheses

Static Ultrasound Imaging of the Cervical Spine Intervertebral Disc Space

1. Ultrasound can be used to measure the anatomy and height of cervical spine intervertebral discs
2. Disc height as measured by ultrasound, is similar to disc height measured by MRI and CT.

Ultrasound Imaging of the Rigid Body Motion of the Cervical Spine Vertebrae

1. Ultrasound can be used to measure the motion of cervical spine vertebral body motion under different loading conditions
2. Clinical ultrasound can detect the contribution of individual cervical spine functional spinal units to the total motion of the cervical spine *in-vivo* and *ex-vivo.*

In-Vivo Ultrasound Imaging of the Motion of the Cervical Spine Vertebrae in Operational Environments

1. Ultrasound can be used to image the cervical spine in astronauts and pilots to understand the effects of their respective gravitational environments

4 Static Ultrasound Imaging of the Cervical Spine Intervertebral Disc Space

4.1 Abstract

Purpose: Increased incidence of cervical spine disease in high performance pilots may be caused by variability in short-interval loading during high-G flight maneuvers. Currently, there is no method to assess cervical spine displacements during flight. We hypothesize that clinical ultrasound may provide a portable imaging modality capable of quantifying cervical spine intervertebral disc (IVD) displacement and compliance in response to applied forces.

Materials and Methods: 12 Adult cadaveric ovine cervical spines were imaged using Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Ultrasound (U/S). The U/S images were acquired using a standard ultrasound unit with a 15 MHz linear transducer. Images were analyzed to compare the ability of the three imaging modalities to assess IVD anatomy by measuring the anterior distance between vertebral bodies. Similar comparisons were done in-vivo in 8 humans during Emergency Department visits.

Results: Static analysis of ex-vivo sheep cervical spines imaged by ultrasound, MRI, and CT demonstrated that the imaging modality affected the measured intervertebral disc (IVD) displacement ($p<0.01$); post-hoc analysis indicated that IVD heights measured by CT were on average 1.1 mm greater than those measured by MRI ($p=0.09$), and 0.9 mm less than those measured by US ($p=0.04$); IVD heights measured by MRI were 2.0 mm less than those measured by US ($p<0.01$). Similar evaluation was done in-vivo in Emergency Department patients who received a CT scan as part of their clinical course.

Conclusion: This is the first study to demonstrate the ability of U/S to measure cervical spine anatomy and concludes that the accuracy of static measures may be adequate to develop the technique and equipment for clinical diagnostic use.

4.2 Introduction and Background

We propose that clinical ultrasound (US) can provide the appropriate technology to image the kinematics of the cervical spine and deformation of the intervertebral disc during exposure of personnel to extreme work environments.

Images of human and animal adult thoracic and lumbar spine *in-vivo* have been previously demonstrated [44, 75], but measurements of the intervertebral disc space by US have not been validated or compared to other imaging technologies such as CT and MRI. The purpose of this project is to expand the capabilities of clinical US beyond its current indications. We hypothesize that clinical US can provide a portable imaging modality capable of quantifying cervical spine intervertebral disc displacement and the mechanical compliance of a functional spinal unit in response to applied forces. Besides applications in work place environments to assess spine biomechanics under extreme conditions (that cannot be easily assessed by other means), the technology developed here will provide an inexpensive, portable and safe technique that can identify and characterize cervical spine anatomy and pathology without exposing patients to ionizing radiation or requiring expensive MRI technology unavailable in resource poor environments.

4.3 Methods

4.3.1 Ovine Methods

Twelve adult, fresh frozen, cadaveric ovine cervical spines (34 intervertebral disc spaces) were thawed and held in the neutral anatomic position. The spines were sequentially imaged using CT (Siemens Somatom Sensation 40, Forchheim, Germany), MRI, (Siemens 3T Trio, Erlangen, Germany) and US (Philips iu22, Bothel, WA) using a 15 MHz linear transducer. The paracervical muscles and adipose tissue were retained, but trachea, esophagus, skin, and wool were removed. The US transducer was placed in the interval between the sternocleidomastoid and the tracheal bed, with the US beam aimed at the midline of the anterior cervical spine similar anatomically to the anterior surgical approach to the cervical spine in humans. Static US images were obtained using a 1.5 cm stand-off pad. Due to physical limitations of the available US transducers only one intervertebral disc space could be imaged at a time; each disc space was imaged from the left and from the right. Additionally, one of the ovine cervical spine specimens was imaged using a standard GE E9 US unit with a 15 MHz linear transducer and Fusion software to compare the CT data with dynamic US images.

After a short training session, two board certified radiologists (with 10 years' experience respectively) measured the anterior distance between the vertebral bodies in the three imaging modalities. Images were randomized within imaging modality and viewed in a high resolution monitor (Dome C5i; Planar Systems, Waltham, MA) equipped with viewing software (Synapse, Fujifilm Medical, Tokyo, Japan). For CT and MRI the radiologist was allowed to scroll through the sagittal image stack before measuring the midline intervertebral body distance. The static US images were presented individually and the radiologist was not informed if they were seeing a repeated disc space from another side. The measured intervertebral disc space heights were analyzed by a Generalized Linear Model and post-hoc Tukey test to determine the effect of radiologist and imaging modality

4.3.2 Human Methods

8 subjects (48 total disc spaces) for the *in-vivo* study were recruited from the Brigham and Women's Hospital Emergency Department with approval from the Partners Heathcare Institutional Review Board. Inclusion criteria were that the subject (a) be over 18 years old and (b) have already received a CT C-spine study as a matter of their clinical course. After verbal consent an operator took ultrasound images in a manner similar to the ovine study, where the ultrasound transducer was placed in the interval between the sternocleidomastoid and the trachea, with the ultrasound beam aimed at the midline of the anterior cervical spine similar anatomically to the anterior surgical approach to the cervical spine (Figure 4-1). Static images of one or two intervertebral disc spaces were imaged at a time and each disc space was imaged from both the left and right. Additionally a 10 second long cine-loop was taken while the ultrasound probe traversed the length of the cervical spine. Subjects were continually asked their comfort level with the imaging technique and imaging was discontinued if the subject felt too discomforted by the pressure on their neck.

After a short training session, a resident radiologist measured the anterior distance between the vertebral bodies, and the height of the vertebral bodies themselves in the CT images. The same radiologist, an emergency medicine resident and an engineer independently measured the ultrasound images and agreed on a consensus value at a later meeting. Images were randomized and viewed in a high resolution monitor (Dome C5i; Planar Systems, Waltham, MA) equipped with viewing software (Synapse, Fujifilm Medical, Tokyo, Japan). For CT the radiologist was allowed to scroll through the sagittal image stack before measuring the midline intervertebral body distance. The static US images were presented individually and the measured intervertebral disc space heights were analyzed by a simple correlation test due to the low number of completed subjects.

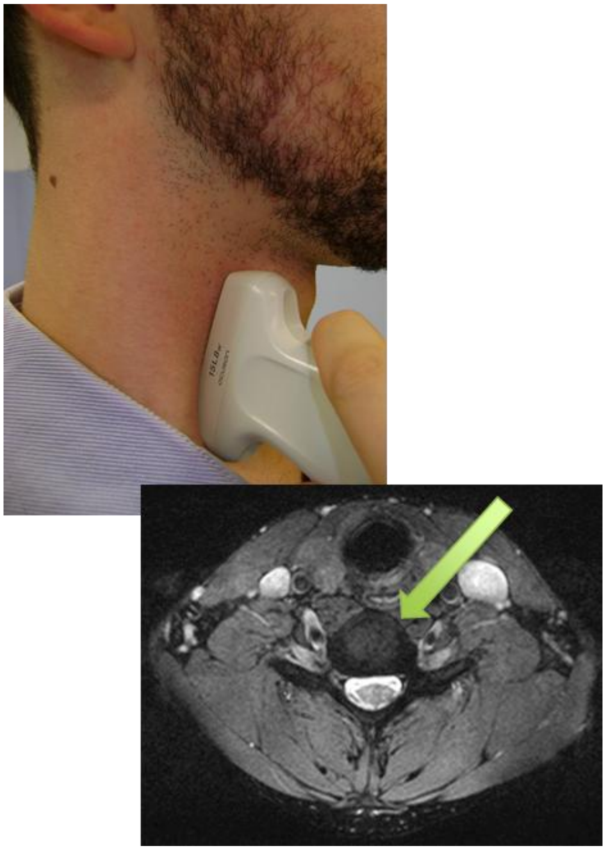

Figure 4-1. Placement of Ultrasound Probe and Path of Ultrasound Beam (Green Arrow) to C-Spine.

Additional human study was done *in-vivo* with 2 other subjects to determine the feasibility of using clinical ultrasound to image FSU compliance. The compliance of the C5-C6 FSU was calculated by measuring the change in height of the intervening disc in response to the application of known axial compressive and distractive loads applied to the head and neck using a customized traction device in human subjects.

4.4 Results

4.4.1 Ovine

The ovine cervical spine was imaged with CT, MRI and ultrasound, after which it was cut down the midline and imaged with a digital camera to give a saggital view Figure 4-2. This figure shows the various attributes of each modality. CT, where brightness of the image is proportional to density, is quite good at showing the border of bone but can’t differentiate between different soft tissues within the intervertebral disc. MRI, where brightness of the image is proportional to the presence of water (more specifically the relaxation time of hydrogen ions), can show the borders between soft tissues, but is not as precise at bone edges as CT. Ultrasound, where brightness of the image is proportional to acoustic impedance changes of tissue, can see soft tissue changes and precise bone edges, but cannot “see” into the bone or around corners of bone.

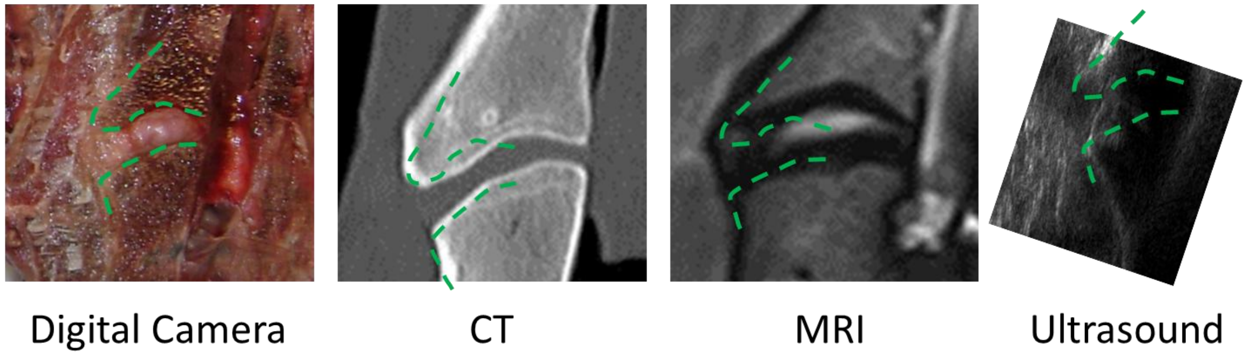

Figure 4-2. Sheep cervical spine intervertebral disc space under differing imaging modalities. The dotted green outline on the images shows the outline of the bone.

A Generalized Linear Model showed no significant effect of radiologist or a significant difference between left and right side US measurements and therefore was not included in subsequent analysis (Figure 4-3). That analysis showed an effect of Imaging Modality ($p<0.01$) and a post-hoc test of effect sizes showed heights measured from a CT to be not significant from MRI, CT 0.9 mm less than US ($p=0.04$), and MRI 2.0 mm less than US ($p<0.01$). There was no significant difference in variance between any two of the three modalities.

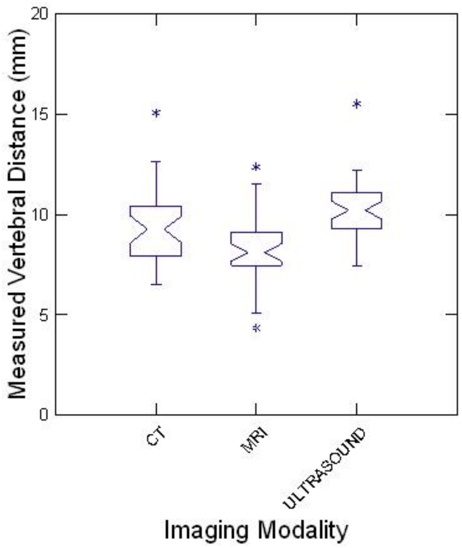

Figure 4-3. Box plot of measured ovine cervical spine intervertebral distances (n = 34 disc spaces in 12 animal specimens) by imaging modality, CT, MRI and US. Box defines values between 1st and 3rd quartiles, notches define 95 % confidence interval of the mean, whiskers define remaining values absent outliers defined by '*'.

The data in Figure 4-3 is also presented in table form as measures of uncertainty (standard deviation of means, Table 1) and bias (difference in means, Table 2) for each specimen and are pooled so the reader can get a sense of the range of values encountered. Finally, measurements done with the GE Fusion system in real time showed high anatomic correlation between the US and CT images as judged by a radiologist (Figure 4-4).

Table 1. Standard Deviation of Measures by Specimen (measures in mm)

Table 2. Measure of Means (Bias) by Specimen (measures in mm)

	Std Dev			Means		
Specimen	CT	MRI	US	CT	MRI	US
1	1.1	1.7	1.2	8.6	8.7	8.9
2	1.2	0.4	1.8	9.2	7.8	9.1
3	1.5	0.5	1.5	10.0	8.4	9.7
4	3.6	0.8	0.8	10.7	7.4	8.7
5	1.3	1.0	2.5	7.6	9.1	11.3
6	0.8	1.7	1.0	8.3	9.4	10.2
7	0.4	0.9	1.3	8.2	5.2	10.7
8	0.5	1.6	1.6	7.3	8.5	10.3
9	3.6	1.0	2.4	12.8	8.1	11.2
10	1.6	1.2	0.9	9.4	7.1	10.4
11	1.4	1.2	2.5	10.9	11.1	13.2
12	0.7	1.1	1.7	9.8	9.0	11.6
Total	2.1	1.8	1.9	9.3	8.3	10.5

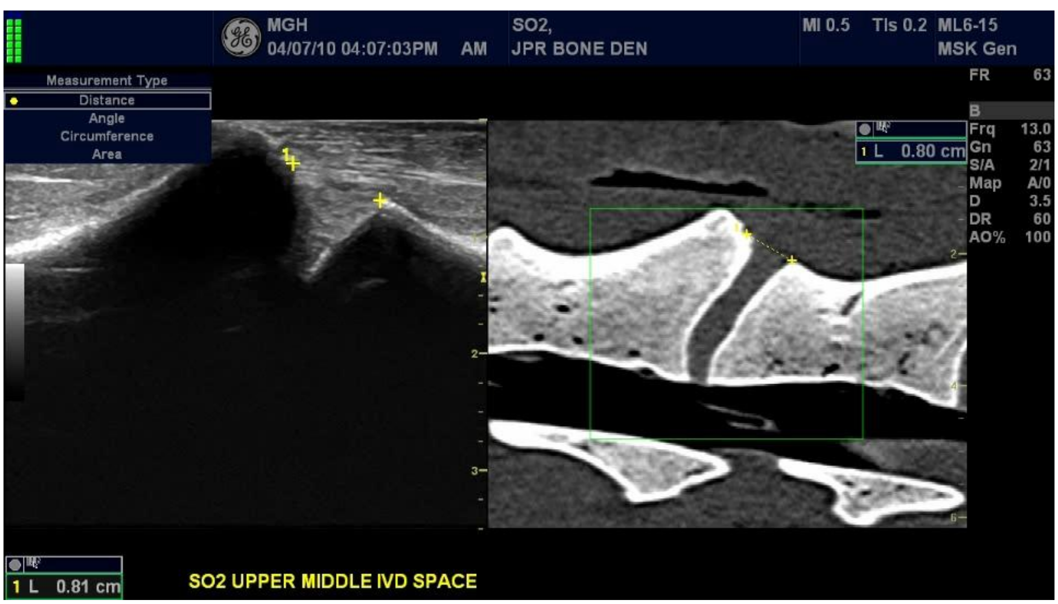

Figure 4-4. GE Fusion screenshot showing co-registered measurement of US (left, 0.81 cm) and CT (right, 0.80cm). Distances are measured between crosses in each respective image. Green box in CT corresponds to viewing area of US. Note: measurement technique for this image was different than for prior analysis.

4.4.2 Human Results

Of the 8 consented subjects (age 63.6±26.2), 7 were able to complete the imaging protocol. The incomplete subject was unable to tolerate the pressure of the probe on their neck. The remaining subjects were found to have 38 total disc spaces eligible for comparison due to pathologies such as fused vertebrae. CT measure of vertebral body height (not intervertebral disc height) was correlated with Ultrasound measure of vertebral body height (Pearson's correlation = 0.65 ($p<0.01$)). The intervertebral disc height has almost no correlation based on the 7 subjects currently analyzed given the inability to exactly position the neck the same as when the CT scan was taken. Bone edge and disc surface structure are well identified on patients with minimal pathology and smaller body habitus.

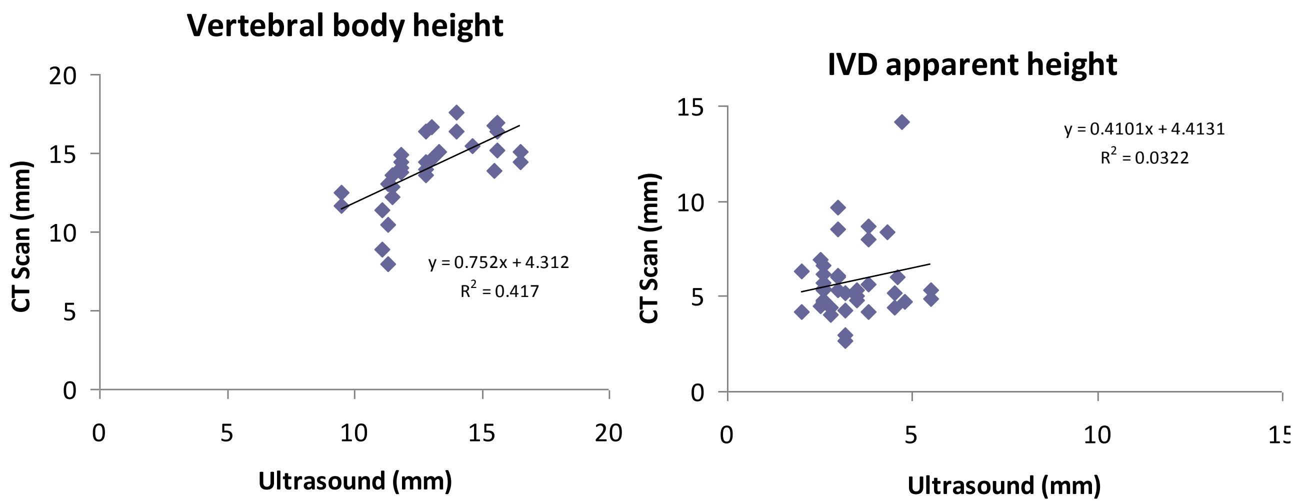

Figure 4-5. Correlation between CT and Ultrasound measurements for intervertebral disc space show an underestimation by ultrasound suggestive of positioning changes from removal of the c-collar. Determination of optimal patient positioning and ultrasound technique is still underway.

Other *in-vivo* results with the addition of MRI imaging reveal further correlations between anterior intervertebral disc bulges and narrowed disc spaces for cervical spines evaluated by both MRI and Ultrasound (Figure 4-7 and Figure 4-6). Further measurement of the mechanical compliance of a functional spinal unit determined from changes in intervertebral disc height measured in real time by US in response to applied uni-axial compressive and distractive loads demonstrated that the compliance of the C4-C5 functional spinal unit was decreased in older subjects compared to younger subjects (Figure 4-8). This is consistent with the observation that cervical spondylosis most commonly occurs at the C5-C6 level.

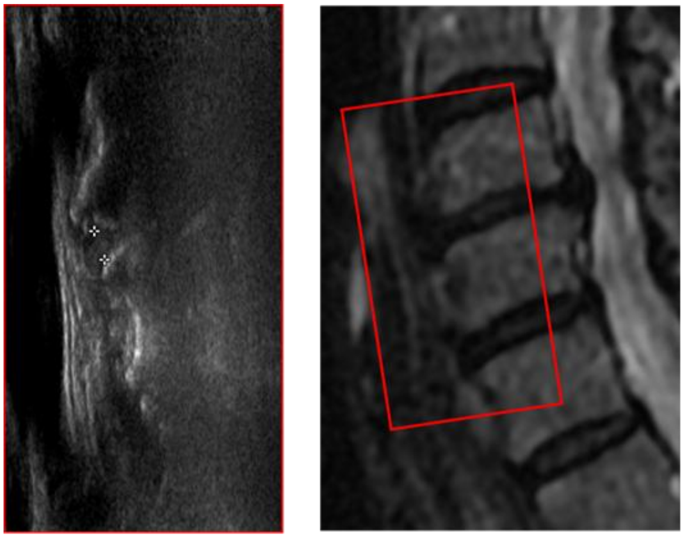

Figure 4-7. In-vivo US (left) and MRI (right) of human cervical spine. Red box in MRI corresponds to viewing area of US. Cross hatches in US show anterior disc protrusion also seen in MRI.

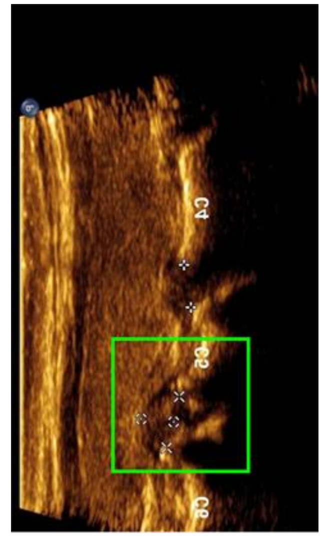

Figure 4-6. Anterior Cervical IVD Protrusion visible on ultrasound (Green Box).

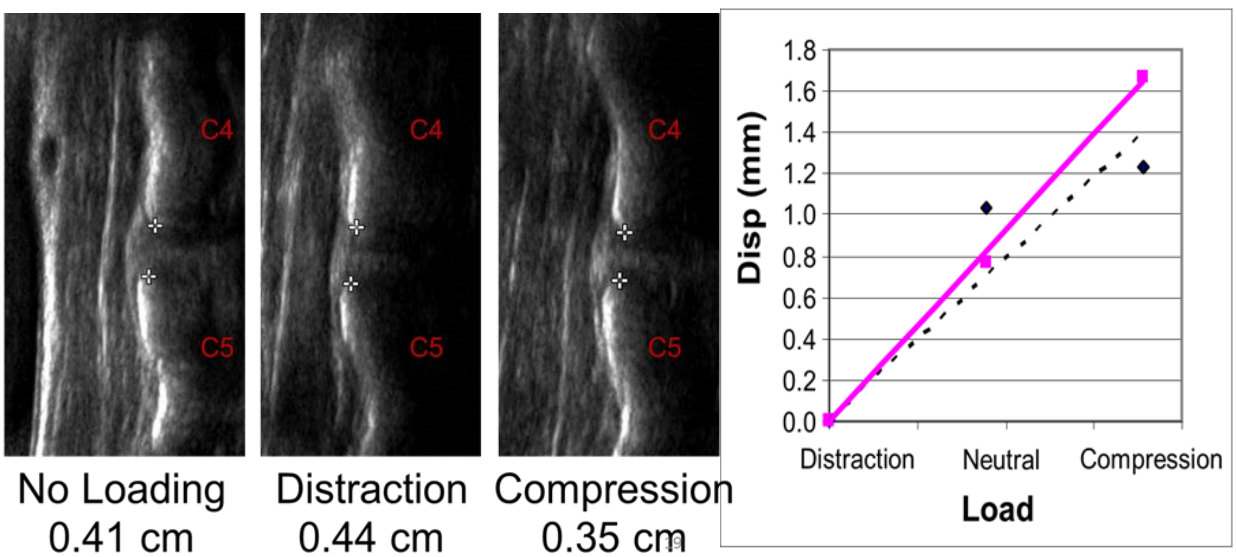

Figure 4-8. Change in *in-vivo* intervertebral disc height during axial loading of cervical spine in young human. From these images compliance of the intervertebral disc is calculated by Compliance = Δ height/ Δ force. Similar images and calculations were done on an older subject and the two results were plotted (right). Younger subject (solid line, slope =0 .009mm/N), older subject (dotted line, slope =0 .008mm/N). No loading = neutral, Distraction = 20 lb tension, Compression = 20 lb compression.

4.5 Discussion

This is the first study to demonstrate the ability of US to measure intervertebral disc anatomy in the cervical spine. The results suggests that clinical US systems may provide a low cost, portable, and convenient method to assess the cervical intervertebral disc space anatomy without the use of ionizing radiation. A perceived limitation of US is lack of repeatability but our model did not show a significant difference between measurements taken of the same disc space from the left or right side. Another limitation of US is the perceived operator dependence of both the individual taking the image and the radiologist interpreting it, but we did not see a significant difference between radiologists (n = 2), suggesting that sufficiently trained operators can obtain similar results. This study did not look at the dependence of the operator on the quality of the image acquisition. If CT is taken as the gold standard for intervertebrtal disc height, post-hoc analysis of the effect of imaging modality on measured disc height demonstrated a statistically significant difference of 0.9 mm greater intervertebral disc height when measured by US compared to CT. MRI measures of intervertebral disc height were not significantly different from CT. However, the statistical analysis of these results is only one metric in which to judge the utility of these measurements and the clinical significance of this small difference is unclear. The real-time co-registration analysis revealed that many anatomic features visible on CT and MRI, such as disc bulges and separated vertebral endplates were also visible on US.

In humans our preliminary data indicate that ultrasound is able to obtain high quality images of cervical spine anatomy including vertebral body edges and IVD geography. Image quality shows promise for measurements of bone edges and vertebral length in the cervical spine of healthy individuals but there are significant limitations to image quality and reproducibility that occur with spinal degeneration with age. Cervical spine ultrasound requires technique and positioning definitions to generate reproducible measurements, but image quality is sufficient to warrant further research in this area.

4.6 Conclusions

The *ex-vivo* ovine study demonstrated that US can measure intervertebral disc heights nearly equivalent to CT and MRI and helps establish that US may be useful tool to ascertain intervertebral disc height and the overall mechanical compliance of the functional spinal unit by measuring changes in disc height induced by compression and distraction of the cervical with known loads. Improvements in the temporal and spatial resolution of the US platform will be required before US can be used operationally to image the displacements of the cervical spine while subjected to extreme work environments.

The human results show that more work needs to be done to translate these findings into *in-vivo* practice, but that it is technically possible to fit in the workflow of pre-hospital care.

5 Ultrasound Imaging of the Rigid Body Motion of the Cervical Spine Vertebrae

5.1 Abstract

Dynamic analysis of isolated ex-vivo human lumbar and ovine cervical spinal segments intervertebral disc displacement with a mounted ultrasound probe demonstrated a measurement uncertainty of ± 0.2 mm and no bias at low frequency sinusoidal spinal displacement. A similar evaluation in-vivo with 4 human subjects that compared measures from an ultrasound probe mounted on a cervical-collar to the motion of the head relative to the top of the thoracic spine measured by motion tracking found a 17-38% contribution of cervical spine distraction (from the C4-5 Functional Spinal Unit) to the overall motion of the head with respect to the shoulders. This contribution was mostly a factor of subject differences rather than loading on the head or frequency of motion.

In human cadavers subjected to passive flexion and extension of the cervical spine, ultrasound measurements of the relative flexion/extension angles between consecutive cervical vertebrae were similar to fluoroscopy.

5.2 Introduction and Background

Previous work (Chapter 4) showed that ultrasound can measure intervertebral disc heights nearly equivalent to CT and MRI, the current "gold standards." In that work the tissue and subjects were not moving, but in this series of experiments we are interested in the ability of ultrasound to measure the dynamic motion of the cervical spine. Ultrasound is already used as a modality that can measure dynamic motion in cardiac and obstetric care, and we intend to apply methods used in those fields to the musculoskeletal system and also apply imaging processing methods and principles in order to get quantitative data from those images. We hope to show that ultrasound can be used to measure the motion of cervical spine vertebral body motion under different loading conditions and that clinical ultrasound can detect the contribution of individual cervical spine functional spinal units to the total motion of the cervical spine in-vivo and ex-vivo in order to be able to calculate the strain each functional spinal unit is subjected to during operational maneuvers.

5.3 Methods

5.3.1 Ex-vivo Methods

Four isolated adolescent ovine cadaveric cervical spines (C2-C6) were subjected to cyclic loads in combined axial compression and tension at different loading rates (1, 2, 4 and 8 Hz) and displacement amplitudes (2 and 4 mm total spine displacement). The spines were prepared, potted and mounted in an Instron, biaxial mechanical testing machine. The accuracy of ultrasound measures of vertebral motion was compared to those measured directly, using a mechanical tracking system. The paracervical muscles and adipose tissue were retained, but trachea, esophagus, skin, and wool were removed. The ultrasound transducer was placed in the interval between the sternocleidomastoid and the tracheal bed, with the ultrasound beam aimed at the midline of the anterior cervical spine similar anatomically to the anterior surgical approach to the cervical spine in humans (Figure 5-1). Dynamic ultrasound images were obtained using a 1.5

cm stand-off pad. Due to physical limitations of the available ultrasound transducers only one intervertebral disc space could be imaged at a time. The mechanical tracker was attached to the vertebral body on one side via fixed posts that were screwed into the bone on either side of the intervertebral disc space while the ultrasound probe was acoustically coupled to the spine and positioned using a clamp that secured the probe to the moving cross-head of the Instron and maintained the probes in fixed orientation relative to the disc space being imaged.

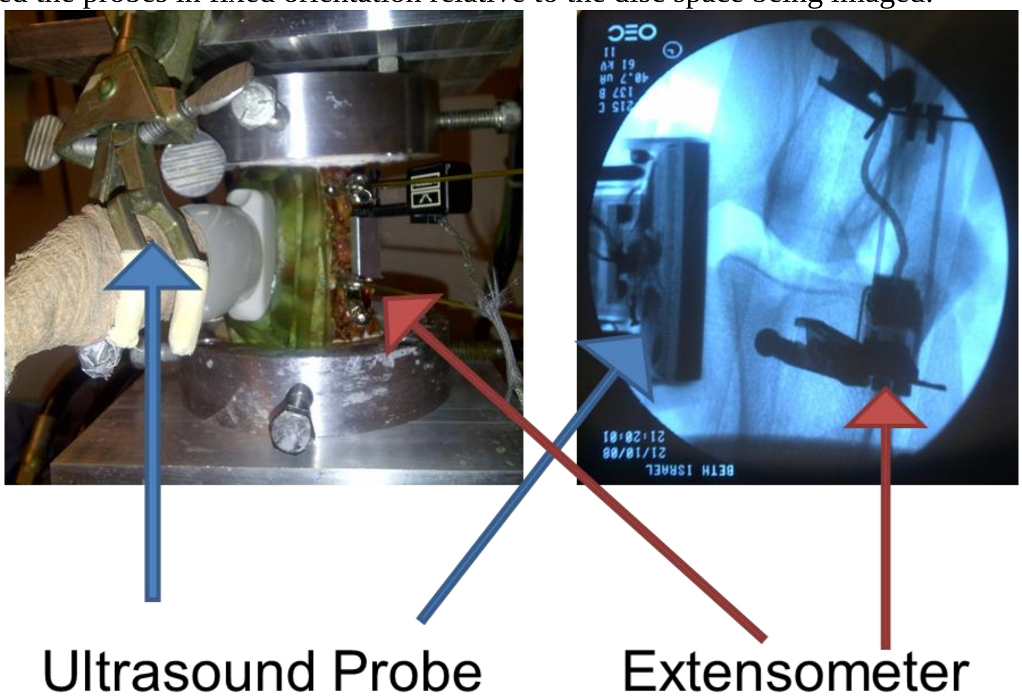

Figure 5-1. Placement of Ultrasound Transducer and Extensometer on Ovine Cervical Spine. Flueroscopic image (right) shows that both measurement methods viewed same intervertebral disc space.

Because the ultrasound data output is given a time signature by the internal software, rather than a hardware timer, there are inconsistences in the time code for the signal. This is especially prevalent when dealing with processor heavy images and compression for fast moving structures. This was corrected by finding an effective sampling rate of the ultrasound measures which varied by ± 0.1 sec per trial. As shown in Figure 5-2 analysis was completed by comparing measures from the ultrasound with mechanical tracking data. Ultrasound B-mode (video) images were exported in AVI format from the Terason system (Teratech, Burlington, MA). In the image analysis software (Mocha, Imagineer Systems, Guildford, UK) a region of interest was defined by two different users (to compare the reliability of the method) in the first frame and tracked through the image file while correcting every second using the methods of Loram[76]. Mechanically tracked extensometer data was collected by a LabView script and the displacement calculated. The ultrasound derived frame-by-frame location of the region of interest was exported to a MATLAB script where it was compared with the exported mechanical tracking data from the extensometer. The extensometer data was collected at 50 Hz, and the ultrasound images were collected at ~25.5 (+/-0.1) Hz. Because of the difference in time coding between the two data an interpolation function was used on the extensometer data to find what the measured displacement was at each data point for the ultrasound measures. From these two measures an uncertainty (defined as the error of the ultrasound measure with respect to the extensometer measured displacement) was calculated at each ultrasound measured time point.

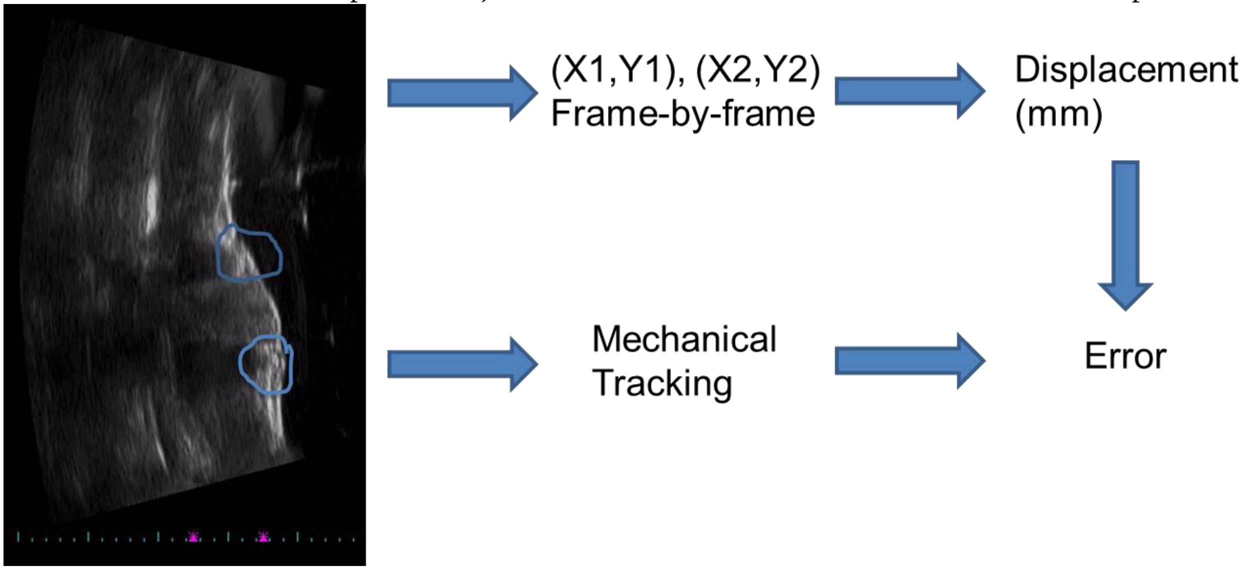

Figure 5-2. Ultrasound image (left) with regions of interest defined and workflow for measurements.

The effect of loading rate, displacement, user, and cross effects on uncertainty and goodness-of-fit (r^2) for each second of collected data were analyzed by General Linear Model.

Other ex-vivo work was done with two full human cadavers. Two intact cadavers with head, neck and torso were be subjected to flexion/extension motions. Ultrasound measures of vertebral body angles were taken using a single hand-held ultrasound transducer to measure cervical spine flexion/extension angles compared to those measured fluoroscopically. To approximate the “Cobb” angle [77] traditionally measured with a fluoroscope in flexion/extension imaging the ultrasound measurements assumed that the intervertebral disc width between the inferior and superior surfaces of the two adjacent vertebral endplates is

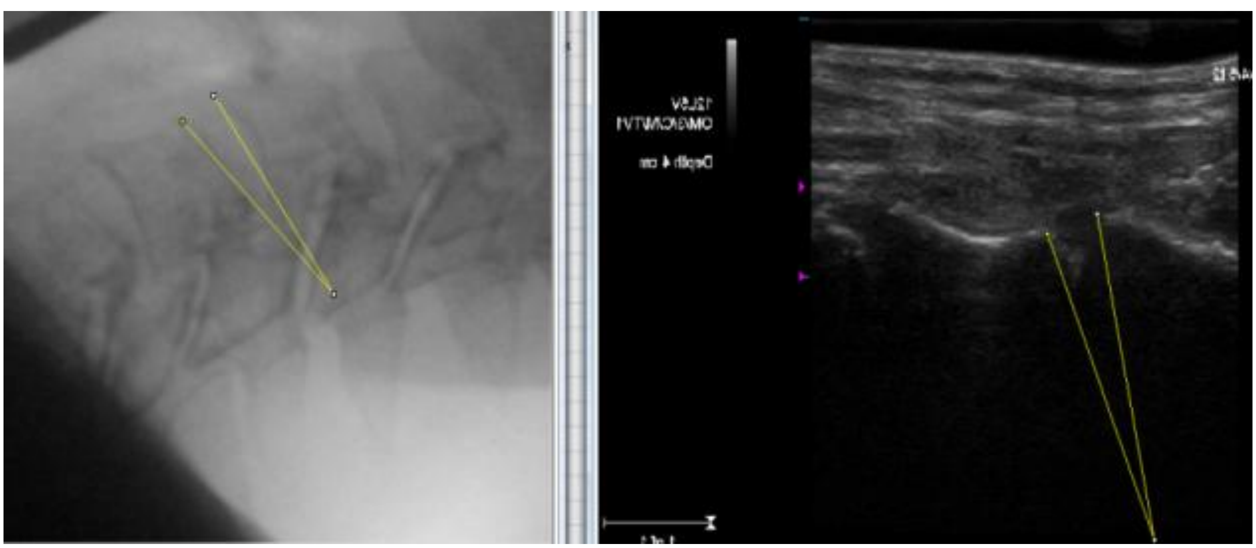

Figure 5-3. "Cobb" angle measured with fluoroscopy (left) and ultrasound (right).

approximately twenty percent greater than the length of the anterior surface on the body of a vertebra.

5.3.2 In-vivo Methods

Ultrasound images of cervical spine intervertebral disc spaces were taken on 4 subjects while jumping in place following MIT Instatutional Review Board approval. The placement of the ultrasound probe was similar to the *ex-vivo* experiments and similar to previous experiments (Chapter 4) and allowed the measurement of the dynamic motion of the anterior surface of the visualized cervical spine vertebral bodies (Figure 5-4). The ultrasound probe was placed externally against the front neck of subject and held in stable position by modified cervical collar (Figure 5-5, National Orthopedics and Prosthetics Corporation (NOPCO) at Children's Hospital Boston). Images were taken of subject's cervical spine intervertebral disc space during directed jumping motion at rates of 1 and 2 jumps per second. Subjects were instructed to jump at the rate of an audible metronome playing at the designeated frequency while trying to jump and land on the same spot on the ground. The analysis of the ultrasound images was done with the same method as the *ex-vivo* experiments. To simulate the effect of Head-Supported-Masses (HSM) such as Night Vision Goggles that an Army aviatior would be expected to wear, a football helmet was worn while jumping and the subject performed the motion with the helmet unweighted (No HSM) and weighted with an additonal 7.5 lbs (HSM) (Figure 5-5). Additionaly, motion was tracked by video interpretation of the three-dimensional position of reflective surfaces placed on the cervical collar and the helmet by a kinematic motion tracking system (Vicon, Oxford, UK). From the position of the markers the superior (C1) and inferior (C7) borders of the cervical spine could be derived and the total motion of C1 with respect to C7 could be calculated. Both the ultrasound derived measures of intervertebral disc height changes and the displacement of the were imported into a MATLAB script for further analysis.

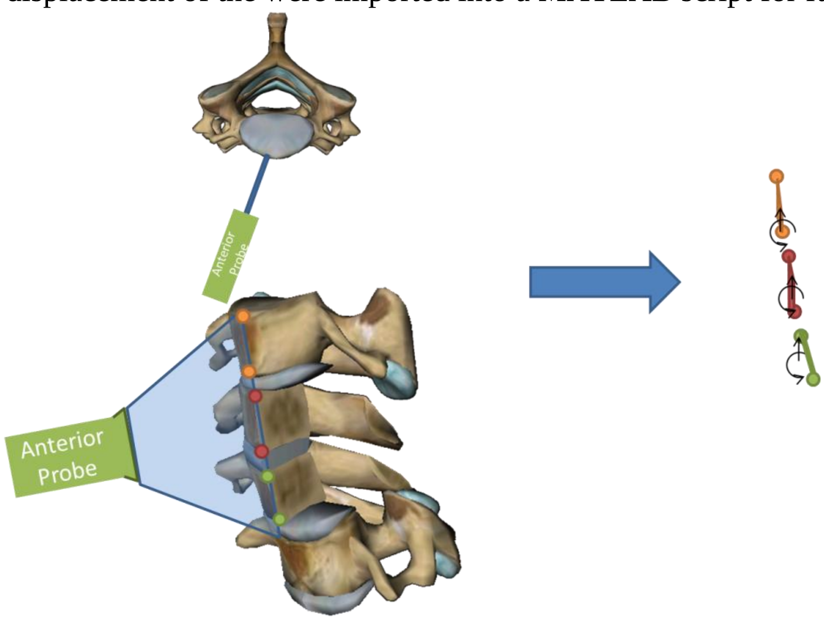

Figure 5-4. Schematic of ultrasound probe placement and cartoon of anatomic structures (C4-C6) visible. The ultrasound beam can visualize the anterior surface of the vertebral bodies, which can allow calculation of the displacement and rotation (right of image) of those surfaces in the place of the ultrasound beam.

Ultrasound motion was compared to measured head and neck displacement to determine the contribution (by fraction of total displacement) of functional spinal unit displacement to overall motion and the effect of the addional mass on cervical spine displacement. Ultrasound motion was calculated in the MATLAB script by finding the average maxium and minimum values of displacement in each experimental condition and then calculating the difference between them. Total displacement was calculated the same way from the motion tracking data. As the total displacement was sampled at a much higher rate (120 Hz) than the ultrasound data (~25.5 Hz) the total displacement data was run through a low-pass filter of 20 Hz to make the plots and data parsing simpler.

The effect of helmet loading and jumping frequency fraction on total displacement and fractional contribution of functional spinal unit displacement were analyzed by General Linear Model.

Figure 5-5. Placement of Motion Tracking Markers (silver spheres) and Ultrasound Probe on subject. Helmet is shown in weighted (7.5lbs) configuration.

5.4 Results

5.4.1 Ex-vivo Results

Dynamic intervertebral disc height measured by ultrasound was consistent with the data from the mechanical testing machine. Each 10 second ultrasound video was segmented into 8 non-overlapping one-second long samples. These second length samples were overlaid on each other in images similar to Figure 5-7 to visualize the accuracy and precision of the ultrasound measures in comparison to the mechanical tracking measures.

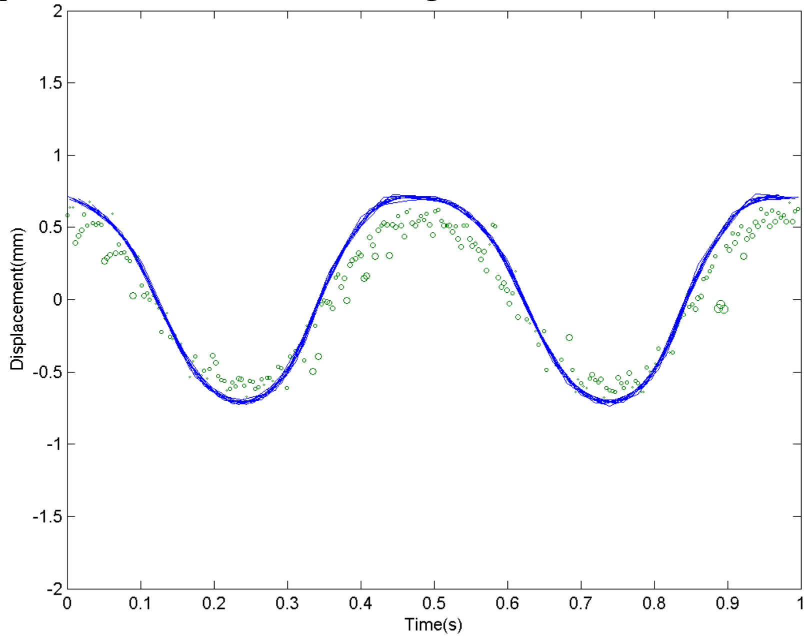

Figure 5-7. Sample data from a 2 Hz test. Green dots are individual ultrasound measures and the diameter of the dot is proportional to the error from the extensometer measured displacement at that point (blue line).

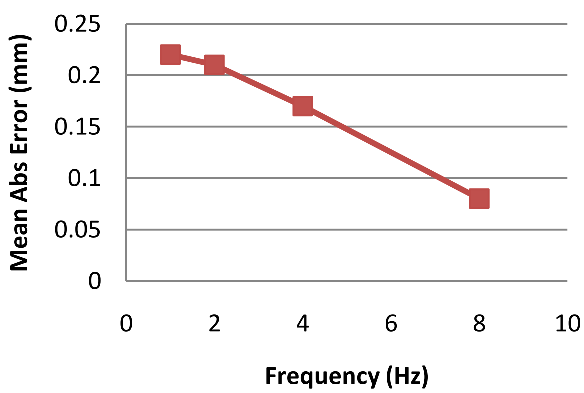

Figure 5-6. Mean Absolute Uncertainty of the ultrasound measures by frequency. Standard error of each point is less than the height of each square. Values (and standard errors) are Least Square Means calculated from General Linear Model.

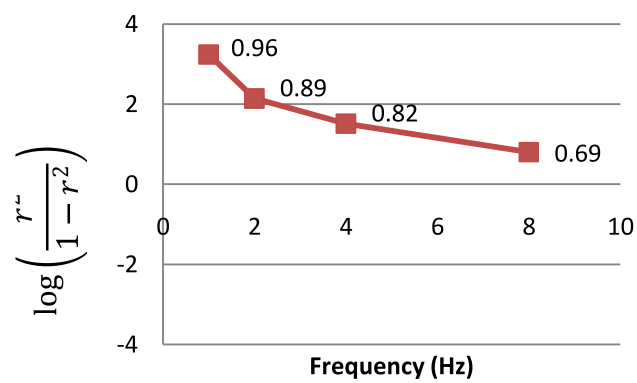

Figure 5-8. Goodness of Fit (or r^2) of each second of measured data by frequency. Standard error of each point is less than the height of each square. Values (and standard errors) are Least Square Means calculated from General Linear Model.

Prior to statistical analysis uncertainty and r^2 values were transformed to satisfy the normality assumption of the statistical tests. Both uncertainty and r^2 showed no significant effect of user or total input displacement. There was a significant effect ($p<0.01$) of the loading frequency (Figure 5-6, Figure 5-8) and the cross-effect of the total displacement and frequency. This cross effect can be thought of as the speed of the motion of the vertebral bodies, so it makes sense that it would have a significant effect on the error and fit. It may seem counter-intuitive that the uncertainty decrease as the frequency increases, however the effect of speed (not plotted) is to increase the uncertainty as the speed (which proportional to frequency) increases. The end result gives a relatively constant error of ± 0.2 mm for motion occurring at less than 8 Hz, which will be applied to the in-vivo results discussed in the next section. The r^2 value follows similar logic and decreases as the speed and frequency of the motion increases and approaches the Nyquist limit of the sampling rate of the ultrasound. However, as we are interested in motion occurring at frequencies below 8 Hz and we see that the r^2 value is above 0.7 in this range, we can conclude that ultrasound measures of phenomena in this range of frequencies are credible.

In the full cadaver experiments the flexion/extension Cobb angles measured by the ultrasound and fluoroscopy techniques were not significantly different (Figure 5-9). Owing to the stiffness of the cadaveric specimen we were unable to get full flexion of the neck, and so the "flexion" image was closer to the neutral position as delineated in the figure.

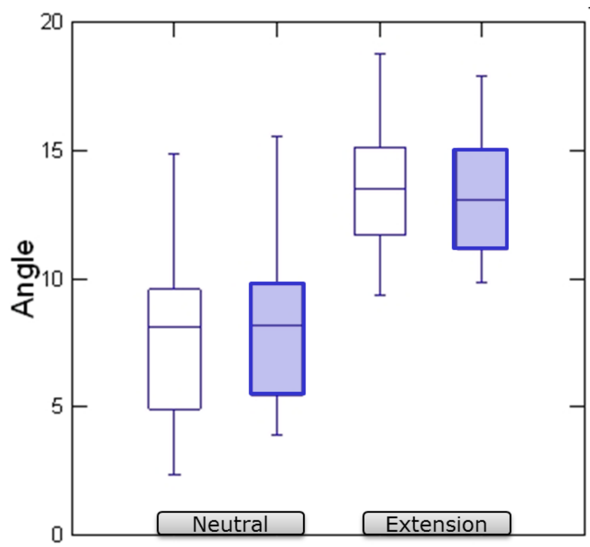

Figure 5-9. Box Plot Comparison of measured Cobb angle using ultrasound (blue filled boxes) vs. fluoroscopy (empty boxes). There was no significant difference between the modalities in the neutral or extended position.

5.4.2 In-Vivo results

The jumping study (n = 4) also showed that the ultrasound data was consistent with external measures. When the uncertainty of ±0.2mm calculated in the *ex-vivo* work was applied to the ultrasound measures taken in the *in-vivo* trials it was seen that the amount of motion seen by the ultrasound exceeded the uncertainty and usable data was collected (Figure 5-10).

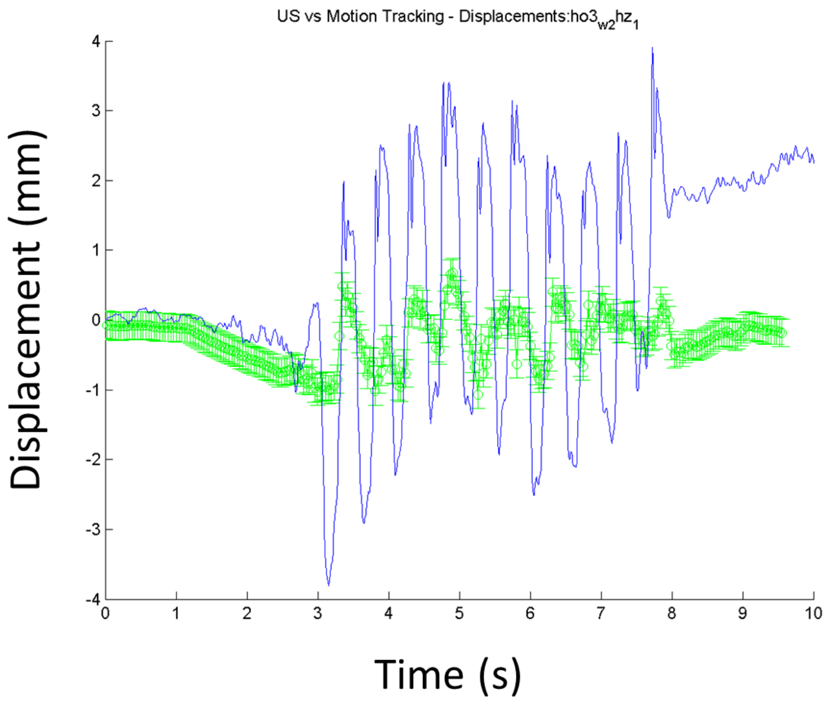

Figure 5-10. Collected data from a 2Hz in-vivo jumping trial with weighted helmet. Blue line is data from motion tracking. Green line is data from ultrasound, error bars on each data point of the ultrasound data reflect the ±0.2 mm uncertainty calculated in the previous work.

Calculation of the relative contribution of the visualized functional spinal unit (FSU) to the overall motion of the head with respect to the torso, by analysis of individual trials similar to Figure 5-11 and statistical comparison with a General Linear Model, found a much larger effect of subject (Figure 5-12, $p<0.01$) than of weighting (7.5 lbs of weight decreased %contribution by 2.5%, $p<0.05$) or frequency of jumping (NS). This implies that the method each individual subject chose to use to follow instructions varied more than the effect the experimental conditions had on the result. There was also a significant cross effect ($p<0.01$) of the Weighting with Subject, probably due to the differing methods the subjects used to compensate for the increased weighting.

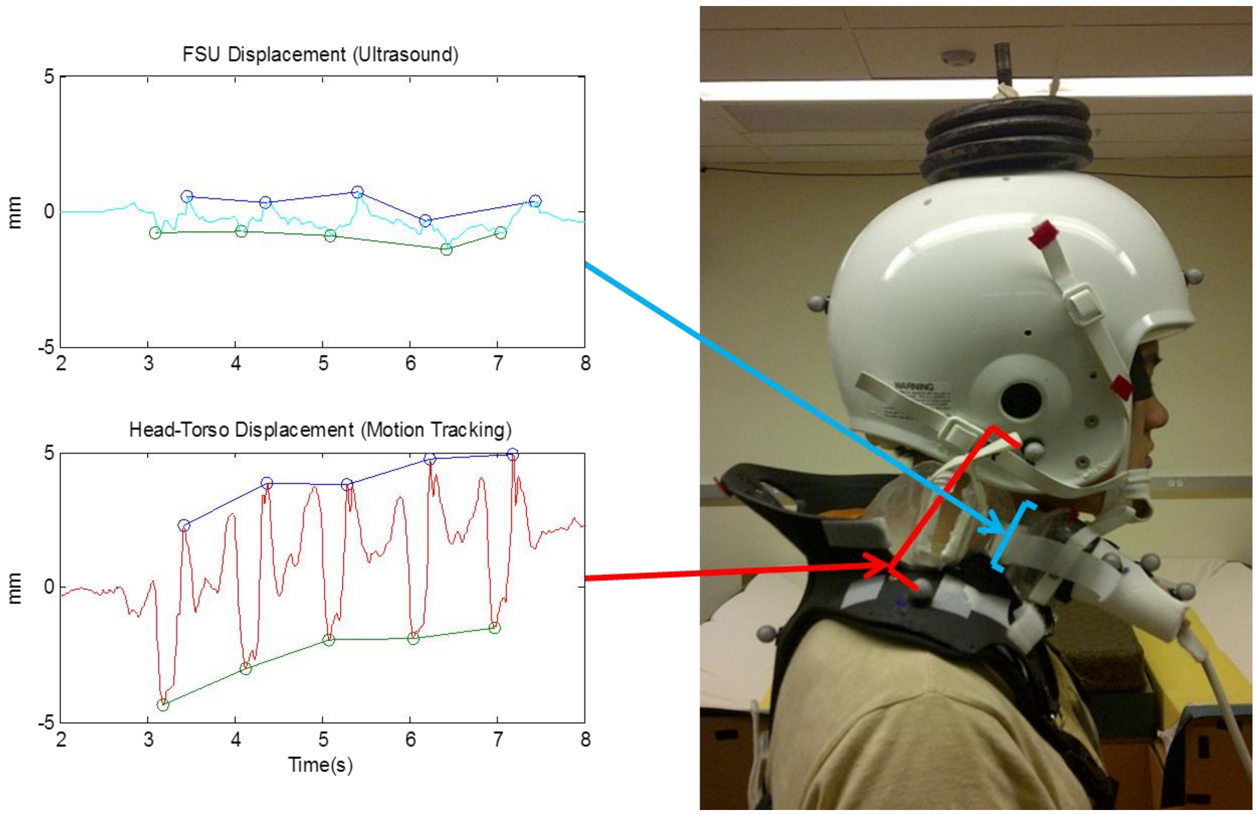

Figure 5-11. Calculated Ultrasound (top left) and Total Displacement (bottom left) during a 1 Hz weighted jumping trial. Blue lines in both plots show the maximum displacement values used for average calculation and Green lines show minimum values. Thick Blue and Red Arrows show approximate anatomic regions of where displacement occurred. All attempts were made to keep two displacement planes parallel.

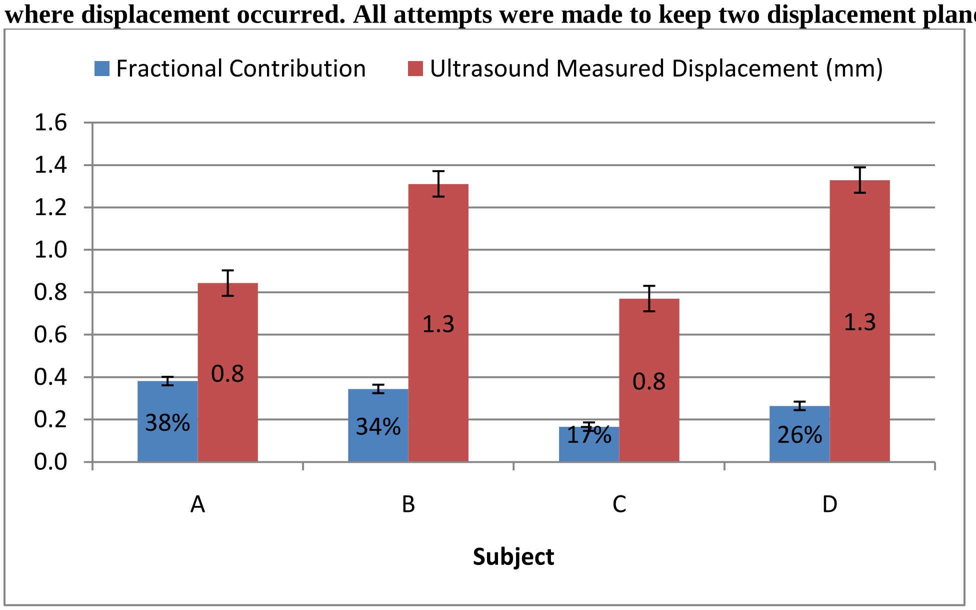

Figure 5-12. Fractional Contribution of the visualized FSU to overall motion of the cervical spine and ultrasound measured displacement of the FSU by subject. Values (and standard errors) are Least Square Means calculated from General Linear Model.

We also looked at just the displacement of the FSU rather than the relative displacement. A General Linear Model found a large effect of subject ($p<0.01$) but none of weighting (NS) or frequency of jumping (NS). However, there was a significant cross effect of both weighting and frequency with subject, again probably due to the differing methods the subjects used to compensate. This may imply that the subjects calibrated their comfort level with jumping by maintaining a consistent strain (derived from the change in length of the FSU divided by the initial length) in the FSU.

5.5 Discussion

In all of the *ex-vivo* experiments detailed fluroscopic (or x-ray) images produced a clearer image of the edges of bones than ultrasound. However, ultrasound provided a reliable dynamic imaging capability and did so without any ionizing radiation that would limit the types of *in-vivo* experiments that could be performed. With some specimens, in both the ovine and human cadaver trials, it was difficult to consistently recognize smooth lines that indicated the edge of a vertebrae and pathologic anatomic features, such as osteophytes and disc space fusions, on the body of the vertebrae in the cadavers made it more difficult.

As mentioned in the results, speed of bone motion has a larger effect on the uncertainty than just frequency or total displacement when the frequency of the motion under observation is less than the Nyquist limit, probably due to the way the B-Mode image is reconstructed in the ultrasound system. The refresh rate of the entire reconstructed image is different than the sampling rate and the components of the image are not all refreshed at the exact same moment, leading to blur that could contribute to the uncertainty. Functionally, this will limit the environments in which the ultrasound can provide reliable data. Anecdotally, Navy SEALS are thought to encounter 50 Hz impulses on some of their small boat maneuvers, so this method would not be appropriate for that environment unless the damping action of the human torso is found to bring the response of the neck to below 8 Hz. We chose 8 Hz as our limit because the literature referenced in the background section details that as the upper limit Army investigators are concerned with their population, so our method would be appropriate for the Army helicopter environment.

Further work on ultrasound hardware development should focus on increasing the sampling rate of the ultrasound systems in B-Mode, increasing the amount of video storage available (the system we used was unable to take more than 10 seconds of data), and having a hardware controller determine the rate of sampling. The variable sampling rate of the ultrasound system limited the types of analysis we could do with the data we collected. With a more reliable time signal on the ultrasound we would likely have been able to determine the transfer function between the motion of the visualized FSU and the total cervical spine motion, rather than the gross measures of comparing average displacement over a trial.

In this feasibility trial we only looked at the translation of the cervical spine vertebral bodies with the image analysis software. A limitation of this method is that when looking at only the anterior surface of the cervical spine during motion it becomes difficult to decouple rotation about the X axis (flexion/extention movement) from z-displacement (axial displacement). The software used is able to look at rotation of the regions of interest, but we found that the noisiness of our data made that analysis much more difficult for the software and required a great deal more manual correction which we worried would make the results much more dependent on the operator. Further work in this area could be focused on doing the image analysis entirely within MATLAB. However, even with the limitations encountered, the range of motion (17-38% of the total displacement of the cervical spine) we saw in the C4-5 disc space in the *in-vivo* trial is consistent with the values seen by Panjabi [78].

5.6 Conclusions

The *ex-vivo* ovine study demonstrated that ultrasound can measure dynamic intervertebral disc height changes with an uncertainty of ±0.2 mm and be reliable tracking motion occurring at less than 8 Hz. Improvements in the temporal reliability of the ultrasound platform will be required before ultrasound can be used operationally to image the displacements of the cervical spine while subjected to extreme work environments.

The human results show that ultrasound can be used to measure the motion of cervical spine vertebral body motion under different loading conditions and that clinical ultrasound can detect the contribution of individual cervical spine functional spinal units to the total motion of the cervical spine *in-vivo* in order to be able to calculate the strain each functional spinal unit is subjected to during operational maneuvers.

6 In-Vivo Ultrasound Imaging of the Motion of the Cervical Spine Vertebrae in Operational Environments

6.1 Abstract

We have demonstrated that it is feasible to characterize the mechanical properties of the cervical spine in-vivo during operational maneuvers. Previous work indicates that clinical ultrasound provides a safe, portable, imaging modality to quantify intervertebral disc displacement and rigid body motion of functional spinal units (i.e. adjacent vertebrae, the intervertebral disc and adjoining ligaments excluding muscles) comprising the cervical spine in response to static and dynamic loads. In-vivo field experiments have successfully collected useful data in treadmill running, parabolic flight, and rough terrain driving in an Army National Guard Humvee. Necessary improvements to the portable ultrasound system, probe collar, and analysis methods are detailed such as improvements in the temporal and spatial resolution of the Ultrasound platform will be required before ultrasound can be used operationally to image the cervical spine during the high G maneuvers encountered during flight.

6.2 Introduction and Background

Previous work (Chapter 4 and 5) showed that ultrasound can measure intervertebral disc heights nearly equivalent to CT and MRI and that ultrasound can be used to measure the motion of cervical spine vertebral body motion under different loading conditions. The intention of the previous work was to show that if ultrasound was able to be used in operational environments the data collected would be valid and comparable to data collected by CT or MRI in more traditional clinical settings. Having done so, we intended to determine if portable ultrasound systems currently available for purchase are able to collect this data in the operational environments that we are interested in evaluating. With this work we hope to show that ultrasound can be used to image the cervical spine in astronauts and pilots to understand the effects of their respective gravitational environments on possible mechanisms of back and neck injury.

6.3 Methods

Three environments were tested for operational feasibility: treadmill running, parabolic flight, and rough terrain driving in an Army National Guard Humvee. All environments utilized a modified cervical collar similar to Section 5.3.2 for consistent hands-free placement of the ultrasound probe, the development of which is detailed below. Most used a Terason Ultrasound system with S2-5 transducer or system with similar imaging and portable operating characteristics.

6.3.1 Transducer Holder Collar

A single ultrasound transducer was positioned just medial to the sternocleidomastoid muscles to provide unencumbered sonic wave trajectories to image the vertebral bodies of the lower cervical vertebrae (C3-C7). The alignment of the transducers relative to the cervical spine was stabilized by mounting them in a cervical collar that is fixed to the upper torso by a thoracic extension anchored at the prominence of the T1 spinous process (similar to shoulder pads). The measured motion of the lower cervical vertebrae will be relative to each other and to the torso and thorax. The device is designed to allow more natural neck movement and will withstand the operational environment. Several versions of the collar were made (Figure 5-10, Figure 6-2). The modified cervical collar was made by National Orthopedics and Prosthetics Corporation (NOPCO) at Children's Hospital Boston.

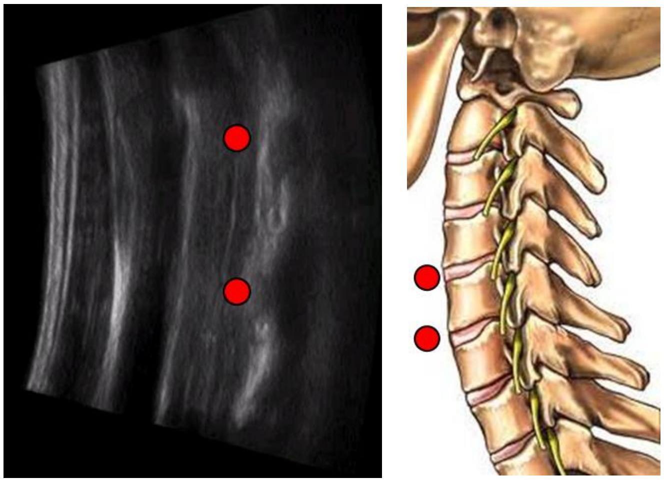

Figure 6-1. Image from video of ultrasound imaging of c-spine while running (left). Anatomic image on right shows area of imaging with red dots indicating cervical levels visualized.

6.3.2 Treadmill Running

In two subjects ultrasound images of cervical spine intervertebral discs were first taken with the subject in a stationary seated position to find the optimal transducer placement for the most robust image. This placement (Figure 6-1) was replicated with the collar so similar ultrasound images could be taken while jogging at two different speeds on a treadmill.

6.3.3 Parabolic Flight

In one subject (who had completed the Treadmill portion as well) ultrasound images of cervical spine intervertebral discs were first taken with the subject in a stationary seated position prior to flight to find the optimal transducer placement for the most robust image. This placement was replicated with the collar so similar ultrasound images could be taken while seated during an immediately following parabolic flight (operated by Zero-G Corporation). The flight profile entailed periods of microgravity, hypergravity (2 times body weight), and transitions between them. The subject was seated and strapped into an aircraft seat per Zero-G standard practice. To prevent injury and motion artifacts, the ultrasound system was fastened to the adjoining seat per Zero-G standard practice. In cases of motion sickness or discomfort from collar placement, which are common in parablolic flight experiments, the subject was instructed to remove the collar and attempt placement by hand if more comfortable. Since this environment was the first done chronologically an earlier version of the cervical placement collar was used (Figure 6-2).

Figure 6-2. Custom cervical collar used in parabolic flight

6.3.4 Humvee

In one subject ultrasound images of cervical spine intervertebral discs were first taken with the subject in a stationary seated position prior to the drive to find the optimal transducer placement for the most robust image. This placement was replicated with the collar so similar ultrasound images could be taken while seated during and immediately following drive over rough terrain in an Army National Guard Humvee with the subject seated in the front passenger

Figure 6-3. Humvee used in Trial at Ft. Rucker hitting Pothole

side seat. The rough terrain profile entailed having the vehicle drive forward at a constant 10 mph and hit an approximately 1 ft deep pothole with the passenger side tires (Figure 6-3). Several runs of the profile were also driven while not impacting the pothole to assess the ability of the ultrasound to detect magnitude of displacement differences between trials.

The subject was seated and strapped into front passenger seat per regulations and was wearing required US Army issued protective helmet (approx. 5 lbs). Acceleration and angular rate measurements were measured at the seat pan and at an accelerometer on the helmet.

6.3.5 Image Analysis

Same method as described in 5.3.1.

6.4 Results

In all field testing, the cervical collar provided a feasible platform for maintaining a constant imaging window of the cervical spine.

6.4.1 Treadmill Running

Qualitative analysis of the treadmill running in the two subjects showed minimal displacement of the visible intervertebral space during running trials on a treadmill. This was attributed to the fact that exercise treadmills are designed to be low impact exercise for cardiovascular health and footfall impacts are absorbed by the flexible treadmill surface as well as being transmitted up the legs to the spine of the runner. However, consistent images were achieved with both subjects at jogging and walking speeds.

6.4.2 Parabolic Flight

The subject remained seated in the second row of seats during parabolic maneuvers. The system was robust to parabolic maneuvers and being quickly stored and rebooted for take-off, landing, and transport. The battery lasted the entire flight. Images looked similar to Figure 6-1.

Use of the cervical collar in parabolic flight kept the ultrasound transducer in place. In parabolas that did not make use of the collar, an adequate way of holding the probe was utilized by supporting the arm holding the transducer with the other arm. Cleaner data were actually collected during these parabolas (Figure 6-4).

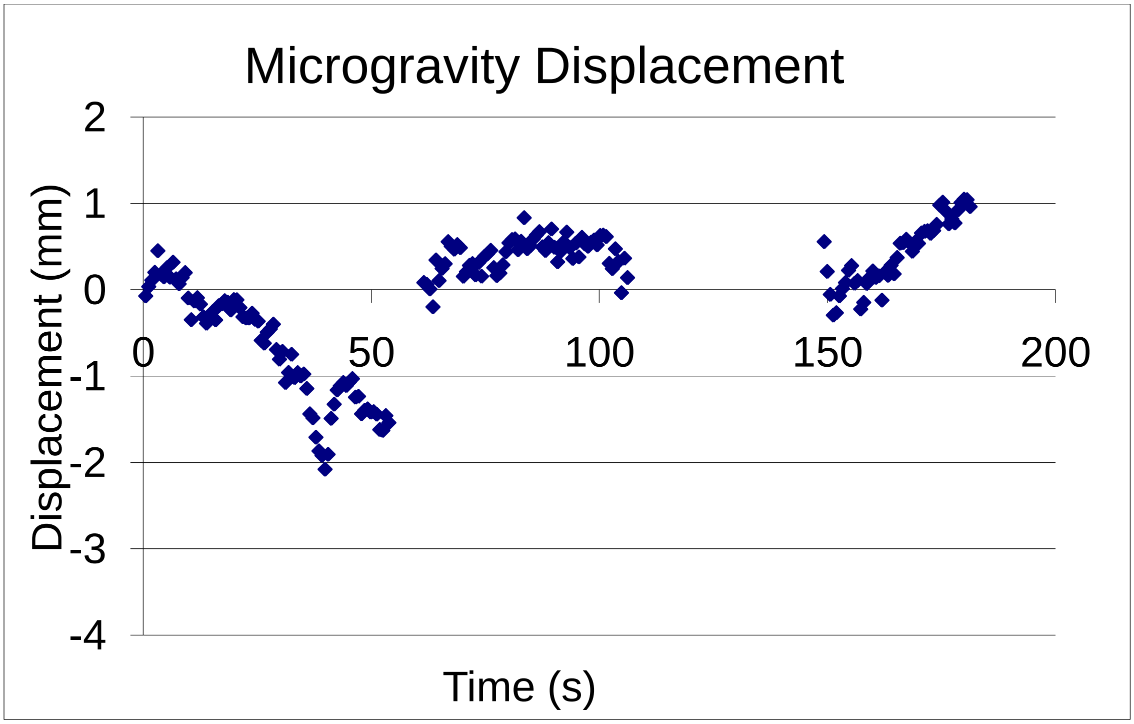

Figure 6-4. Parabolic flight data over two complete parabolas.

6.4.3 Humvee

As in the other conditions above, video of cervical spine motion was able to be analyzed in several of the test runs. Ultrasound images looked similar to Figure 6-1. When the video was not clear enough to be analyzed the most common reason for loss of image was acoustic decoupling between the transducer and the skin of the neck. Noise in the accelerometer signal and lack of coordination of measurement locations between the accelerometers and the ultrasound imaging area prevented direct comparison of displacements between measuring modalities. When comparing the pothole and no pothole profiles both the ultrasound and accelerometer were able to detect differences in their respective magnitudes; the ultrasound measured a larger displacement in the pothole profile and the accelerometers measured a greater acceleration of the head with respect to the seat in the pothole profile (Figure 6-5).

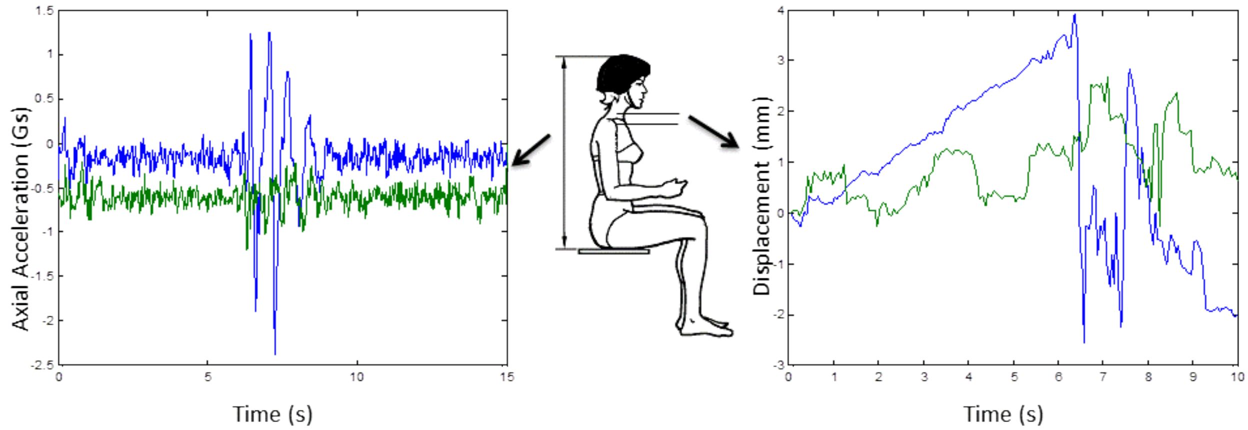

Figure 6-5. Data from feasibility trials in Humvee. Two experimental runs are displayed in two formats. The left graph shows acceleration data taken by subtracting data from an accelerometer on the seat pan from an accelerometer on the helmet. The right graph shows displacement data taken at the same time from ultrasound data. There is drift in the tracking data. The blue line displays data from a Humvee run where a pothole was encountered. The green line displays data from a run where the Humvee missed the pothole.

6.5 Discussion

The variable acceleration environment we were trying to simulate has several inherent common limitations to consistent medical imaging. When designing tools for use in aerospace and military environments efforts must be made to limit the mass, power, volume, time, and cost requirements. Mass and power requirements lead to lowered flight performance and increased fuel requirements. Volume is a scarce resource in flight vehicle design, so large equipment will often not be flight qualified, even if it is low power and mass. The time needed for data collection and analysis by crew-members during the mission is a scarce resource, as well as training time required for optimal performance. All of these prior issues also figure into the technology cost, beyond the cost of the equipment and development itself. The purposes of cost reduction should be self-evident in both medical imaging and government spending. Portable ultrasound has very desirable characteristics in all of these realms. It has low power, mass, and volume, requirements which are similar to a heavy laptop. In comparison, CT and MRI systems require entire rooms and considerable infrastructure. Portable X-ray is still much larger and comes with attendant radiation concerns. Portable ultrasound, at least in this application, does not require extensive training, nor large costs, when compared to other imaging modalities.

The cervical collar provided a feasible platform for maintaining a constant imaging window of the cervical spine. Each of the three testing scenarios led to further development of the system and informed future design choices.

Chronologically the parabolic flight was the first scenario tested; it used an early version of the cervical collar (Figure 6-2) and a different portable ultrasound system (Sonosite, Bethel, WA). The early collar was custom fit to the subjects' neck and shoulder anatomy and fit very closely to the neck in order to reduce motion artifact. However, this served to hold the head in an extended position, which is not desirable when trying to determine the amount of axial neck extension occurring due to the acceleration changes in the environment. Holding the head in position by the collar would also prevent this collar being used in pilots or other operators who need free motion of the head to properly asses the biomechanics of their operational activities.

This early collar also restricted blood flow to and from the head by pushing the ultrasound transducer against the neurovascular bundle in the neck (containing the carotid artery and jugular vein), negatively affecting the comfort of the subject and possibly increasing hypoxia induced motion sickness. Indeed the subject in the parabolic flight became ill during the flight and had to remove the collar in order to vomit, and then was too uncomfortable to replace it during parabolic maneuvers. Fortuitously this led us to find that it was possible for the subject to hold the transducer in the correct position free-handed and still obtain usable data which was much more dynamic than data acquired while the subject was wearing the collar, possibly due to the now free motion of the head unrestricted by the extension imposed by the collar.

The portable ultrasound system used in parabolic flight was a clinical system that was designed to be robust, and was in fact qualified to military grade specifications (MIL-STD 810F) for its designed use. It was able to maintain its battery charge throughout almost the whole flight and work in both the >90F heat of the pre-flight checkout and the ~60F cabin atmosphere at altitude during the flight. The battery did die in the final few parabolas but the system failed appropriately and no data was lost. However, since the system was designed for clinical use and not research, there were some limitations on controlling the ultrasound imaging parameters and the accuracy of the timing of the data acquisition points in the video. This prevented us from correlating the displacement measured via ultrasound with an external accelerometer the subject was wearing.

The lessons learned from the parabolic flights were then applied to the collar and ultrasound system used for the treadmill testing. Rather than a custom snug-fit collar, we modified a collar that was designed to protect motorcycle rider's necks in a fall to hold the ultrasound transducer up to the same position on the neck. This collar (Figure 5-10) allowed almost full range of motion of the neck and only interfaced with the neck at the transducer, it also allowed the subject full use of their upper extremities which allows us to see the motion of the neck in a more realistic environment. The transducer is secured in position by several Velcro straps that allow a large range of neck sizes to use the same collar. This increased size flexibility comes at the cost of image consistency, but can be minimized with adequate instructions to the subject about maintaining head position and our method of image analysis which uses relative motions of the vertebrae to each other within the field of view. Another ultrasound system (Terason, Burlington, MA) was selected for treadmill testing that allowed a higher degree of control of imaging parameters and more reliable timing feedback, but was not as robust to vibration and heat changes.

The collar and ultrasound system used in the treadmill testing was then used essentially unchanged in the Humvee. As noted in the results, we were able to detect differences in height changes of the cervical spine intervertebral disc height between testing runs that included a large axial acceleration due to terrain and testing runs that did not include large axial impulse. Future versions of this system should better integrate both the positioning and time signal of the ultrasound measures and accelerometers to allow more direct correlation and comparison.

6.6 Conclusions

These studies showed that clinical ultrasound can be used to image the cervical spine in astronauts and pilots to understand the effects of their respective gravitational environments on cervical spine biomechanics. Ultrasound imaging out performs other imaging modalities in the realm of mass, power, volume, time and cost. If further developed, this system could allow equipment designers and physicians to directly determine the effect of seating and helmet designs on the *in-vivo* biomechanics of the cervical spine in almost real-time. Future work should be focused on using a system similar to the one we have presented here, but with improved temporal resolution, reliability, and integration with other external measures such as accelerometers or motion tracking equipment, to assess the relationship of the biomechanics of the cervical spine with the mechanisms of injury of cervical spine degeneration.

7 Conclusions

The engineering challenges encountered in extreme acceleration environments such as space flight and military aviation present unique challenges to dynamic monitoring of biomechanics of the cervical spine. These challenges include vibrations at a broad range of frequencies and amplitudes as well as power, volume, and mass constraints. This thesis explored a way image the dynamic motion of the cervical spine using clinical ultrasound, an off-the-shelf technology that fits within the limitations of the flight environment.

Initially, this work expands on the work of others who showed that ultrasound can be used to image changes in IVD height [42] by adding the ability to image the cervical spine. While Naish and McNally have shown that the anatomy of the disc can be visualized using properly focused ultrasound imaging technology in animals [43] and in humans statically, this work expands their conclusions to apply to dynamic imaging of the cervical spine and shows that portable ultrasound systems can be used to image the height of the IVD and dynamic motion of cervical vertebrae in military personnel and astronauts.

This work also allows more realistic modeling of the loading conditions of military personnel by more accurately measuring the biomechanics of the cervical spine in conditions closer to flight. Further development of this concept will help refine the models of Costi and Izamvert, Yingling and Lee, and Elias [30, 56-60]. With this more mobile and robust method of measurement of cervical spine biomechanics, the FSU compliance measured in the cervical spine can be combined with the lumbar spine work of Kururtz [65, 66] to form a more complete model of the degenerative stiffness changes in the whole spine due to aging and injury. Alternatively, a modified version of this work could be used to validate the work of Kurutz.

Combining this methodology with EMG based models could also provide a more complete model of the biomechanics of the neck and musculoskeletal components of the spine, by more completely integrating the motion of the skeletal system with the electrical activity of various muscle groups.

Clinical ultrasound can provide a safe, inexpensive, portable, imaging modality to quantify intervertebral disc displacement and rigid body motion of functional spinal units comprising the cervical spine in response to static and dynamic loads *in-vivo* in extreme environments such as spaceflight and military training operations. **Static Ultrasound Imaging of the Cervical Spine Intervertebral Disc Space** showed that ultrasound can be used to measure the anatomy and height of cervical spine intervertebral discs and that intervertebral disc height as measured by ultrasound, is similar to disc height measured by MRI and CT both *ex-vivo* and *in-vivo*. **Ultrasound Imaging of the Rigid Body Motion of the Cervical Spine Vertebrae** showed that ultrasound can be used to measure the motion of cervical spine vertebral body motion under different loading conditions meant to simulate wearing a head supported mass in an operational environment and that clinical ultrasound can detect the contribution of individual cervical spine functional spinal units to the total motion of the cervical spine *in-vivo* and *ex-vivo.* **In-Vivo Ultrasound Imaging of the Motion of the Cervical Spine Vertebrae in Operational Environments** showed that clinical ultrasound can be used to image the cervical spine in astronauts and pilots to understand the effects of their respective gravitational environments.

Outside the subject populations previously mentioned the implications of this work could change the practice of diagnosing cervical spine instability. Current practice is to diagnose instability by inference based on radiologic signs in static images such as CT, X-Ray images, or

MRI. This method could allow direct visualization of instability by imaging of dynamic out of plane motion of the vertebral bodies during neck motion and the advantages of ultrasound with respect to mobility and cost could improve screening and diagnostic prevalence beyond the capabilities of current medical practice.

8 Future Work - Development of Dual Ultrasound System

To measure and calculate the three-dimensional motion of the cervical spine vertebrae ultrasound measurements will be obtained in a manner similar to previous studies where ultrasound images clearly indicate that the anterior surfaces of two or more adjacent vertebral bodies can be identified. In addition, the images also demonstrate that the inter-vertebral disk separation can also be estimated. In order to obtain the data necessary to achieve the objectives of this project, this preliminary approach will be extended by adding an additional ultrasound imaging array. This is necessary in order to obtain information on the three-dimensional (3D) motion of the vertebral bodies.

The optimal placement of the two transducers will be determined by the need to obtain complementary kinematic information (suggesting an orthogonal orientation of the two arrays); while at the same time being able to obtain sufficiently detailed information on the boundaries and surfaces of the vertebral bodies. Preliminary testing with a single transducer suggests that one transducer placed on the anterior surface of the neck with another placed on the lateral surface of the neck will allow both components (largely orthogonal orientations and high quality images) to be obtained. Note that the positioning of the transducers relative to one another will be fixed and known, through use of a collar/fixture, similar to that shown in Figure 6-2. This will allow the data from each set of ultrasound images (i.e., a set of images associated with one imaging array, and another set of images associated with the other imaging array) to be combined and processed in order to obtain the desired kinematic information in 3D (Figure 8-1).

We plan to use an ultrasound imaging system that will be able to be deployed on aviators and other military personnel. In order to do this, a portable, compact yet highly advanced ultrasound imaging system is required. Such a system has been identified and is produced by Terason, in Burlington, Massachusetts which has all the features of high quality clinical ultrasound imaging systems, but which is portable and relatively inexpensive. The Terason t3000 system is a sophisticated phased array imaging system that incorporates proprietary integrated circuit design and digital beam-forming technology. As noted, and of critical importance, is its capability to be deployed in the military environments being studied.

The Terason t3000 system runs as a Windows application on a standard laptop computer, which can be certified to MIL-STD 810. In our application, we will use two identical systems that are configured to save to an external hard drive the images acquired (at 25 frames per second for each system for about 5 minutes during each test run) from the two ultrasound array transducers. The two systems will be initiated simultaneously by hardware, and the images will be tagged so that images from the two arrays can be temporally matched. Various configurations of ultrasound imaging protocols will be used initially to determine optimal settings. These will include various ultrasound arrays to determine optimal operating frequency, as well as the investigating of harmonic imaging techniques.

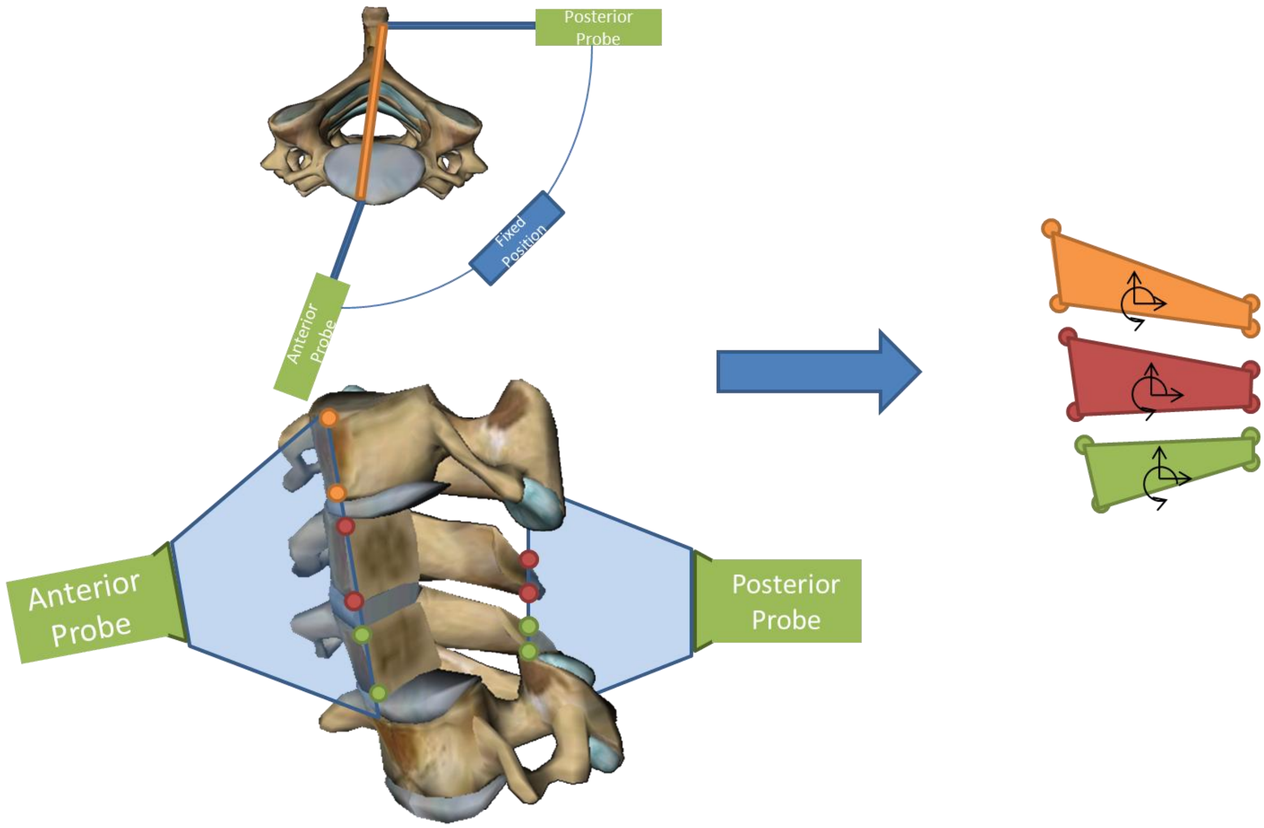

Figure 8-1.Ultrasound probe placement and calculated rigid body motion.

8.1 Image Processing

The images will be post-processed to obtain a set of kinematic data. Initially, for calibration and validation (using cadaveric and healthy volunteers), the data will be manually processed to obtain measures of inter-vertebral spacing from the two orientations. In addition, the relative motion of the two vertebral bodies being imaged will be analyzed from both arrays. This will entail manually detecting vertebral surfaces, and processing this data to obtain the desired relative motion of the vertebral bodies with respect to one another. This process will be carried out by two blinded (as to the type of motion under study) operators, and the kinematic data obtained will be assessed in terms of accuracy and precision. Once manual processing of the ultrasound images has been shown to be effective for assessing the relative kinematic motion, semi-automated image processing techniques will also be investigated. These will include edge detection and segmentation algorithms [79]. This portion of the work will also include techniques for automated detection of bone surfaces, as previously reported [80-82]

The detection and quantitative identification of the vertebral bone surfaces and inter-vertebral disc displacement is a complex problem, and therefore a combination of both manual and automated processing may be found to be the approach that provides the best results. Such an approach, although somewhat tedious owing to the high degree of manual overhead, should provide the kinematic information needed for successful completion of this project. Further studies aimed at fully automating the processing of the ultrasound images can be part of a subsequent research study.

Technology currently in clinical use (MedicalMetrix Inc) can automatically calculate the vertebral endplate angles; we believe this same technology can be applied to ultrasound. A cadaveric whole human study was done to compare fluoroscopy with ultrasound in the cervical spine. It shows both the placement of the transducer and the image taken at that moment. Intervertebral motion measurements will be made from the ultrasound imaging using computer-assisted patter recognition technology that has been previously validated to measure intervertebral motion in the lumbar and cervical spine with errors under 1 millimeter and 1 degree [83, 84] Applied to ultrasound, this same software facilitates pattern matching of anatomic features visualized in ultrasound images taken with the spine in different positions. After each vertebrae in the segment being analyzed has been tracked, the mathematics required to calculate intervertebral motion are identical to that used to measure intervertebral motion from X-rays, MRI, or other modalities. This step is accomplished by using the transformation matrices created during the tracking process to transform the coordinates of landmarks from one image to the other images in a sequence. This avoids the large errors that can occur when a human operator attempts to subjectively identify specific landmarks in a series of images. The landmarks are selected in only the first image of a series, and the coordinates are calculated for all subsequent images. This software has already been used to analyze multiple ultrasound studies of the spine.

8.2 Cadaveric Validation of Ultrasound System

We will determine axial compressive behavior of a full cervical human cadaveric spine loaded using a multi-axis servo-hydraulic test frame and compare disc displacements to displacement measurements made on the same spine during loading using the custom ultrasound. The objective is to validate the ultrasound measurements using an electromagnetic tracking system on human cervical cadaveric spine *in vitro*.

Full cervical spines with shoulders attached will be purchased from NDRI (Philadelphia). Samples will be prepared, potted and mounted on an Instron biaxial mechanical test machine. Ultrasound measurement equipment will be mounted to the cervical spine in the test frame. The cervical spine will also be instrumented with Polhemus electromagnetic tracking system sensor (with sampling rate capabilities up to 240 HZ) on each vertebra, which will be considered rigid bodies. Polhemus has worked with military entities since 1970. Their systems have flown on U.S. Air Force, Navy, and Army fixed and rotary wing aircraft as well as simulators of most airframe manufactures and in laboratories such as Wright Patterson AFB, NAWC, NAVAIR, Fort Rucker, NASA and DARPA. Spines (n=6) will be loaded in two strain rates simulating the accelerometer readings from the fast boat and flight readings during missions in addition to loading under quasi-static load conditions. Load-displacement measurements will be made using the Instron and the Polhemus displacement data. Displacement from ultrasound data will be compared to data from the Instron/Polhemus system. Differences between displacement measurements at different strain rates will be used to validate the ultrasound measurement system.

8.3 *In-vivo* Validation of Ultrasound System

Following the cadaveric validation of the ultrasound system, similar studies will be performed in Adult volunteers (n = 12) of the same demographics as the military population. The MRI compatible ultrasound collar will be used so that compression/distraction and flexion/extension images can be taken at the same time with both MRI and ultrasound and compared. A subset of the volunteers will be recruited based on known cervical intervertebral disc pathology, so that comparisons can also be made of pertinent clinical anatomy such as intervertebral disc anterior prolapse and compression.

8.4 Data and Power Analysis

For comparing ultrasound to other modalities, a sample size of 34 disc spaces (12-15 subjects) will provide 80% power (α=0.05, β=0.20) to detect a mean difference of 0.5 mm assuming a variability of 1mm using a paired t-test (version 7.0, nQuery Advisor, Statistical Solutions, Saugus, MA). This will be done by employing a paired t-test with the null hypothesis stated that there is a no difference in disc height between the two measurement techniques. In addition, 34 samples will allow provide a minimum power of 80% to detect a moderate Pearson correlation of r = 0.50 between measurement techniques assuming that the intervertebral disc heights follow a normal Gaussian-shaped distribution. If there are significant departures from normality, as tested by the Shapiro-Wilk test, the nonparametric Wilcoxon signed-rank test will be utilized to compare medians and boxplots will be constructed to summarize the results. The Bland-Altman method will be used to determine the mean difference in disc height between the imaging methods with 95% limits of agreement. The three primary statistical methods will include:

1. Paired t-test and nonparametric Wilcoxon signed-ranks test [85]
2. Pearson product-moment correlation coefficient [86]
3. Bland-Altman method for assessing agreement of Ultrasound to CT. Able to evaluate mean difference based on 34 disc spaces and 95% limitations of agreement which will provide context for how closely ultrasound agrees with other imaging techniques [87]

8.5 Operational Environment Testing

For the proposed study we will instrument the boat or helicopter to include acceleration and angular rate measurements on the deck, seat, lower lumbar spine, head and neck of each test participant. Typical high amplitude, high frequency loading exposures for both fast boat and rotary aircraft platforms will be quantified and the response data (global kinematics and accelerations) will be measured using the mounted accelerometers and ultrasound transducers. Inertial forces applied to the cervical spine will be derived from the multi-axial accelerometers mounted on the head and base of neck. The extent that the torso damps some of the impulses transmitted to the seat will be ascertained by comparing the accelerations of the seat relative to the head and neck.

8.6 Data Analysis

1) Collect kinetic and kinematic data from the cervical spine in helicopter pilots, fast-boat operators and matched controls *in-vivo* during operational conditions (if feasible) and/or during simulated operational conditions
    a. Relate kinematic data to the kinetic data – correlative analysis. Compare applied accelerations to head and neck to resultant displacements of C4 – C7 and changes in IVD heights measured by ultrasound.

    b. If enough subjects, relate kinetic and kinematic data to MRI based evaluation of intervertebral disc health

2) Perform multi-factorial analysis iteratively expressing Pfirrman disc grade other MRI based measures of IVD function @ C5-6, C4-5,C6-7 as function of: age, BMI, years of exposure to high impact loads, median load amplitude, median loading rate, high frequency (>30 Hz) power spectra, low frequency (<30 Hz) power spectra, maximum IVD displacement measured by ultrasound.

These studies will extend the research from this thesis to better visualize the three-dimensional rigid body motion of the cervical spine vertebrae.

9 References

This work contributed to the following abstracts and presentations:

1. D Buckland and B.D. Snyder (2011). "Dynamic Ultrasound Imaging of the Cervical Spine in an Extreme Environment." Aviation, Space, and Environmental Medicine, 82(3), p.233, (Presentation)
2. E Antonsen, D. Buckland, and D. Pallin (2011). "Comparison of Ultrasound Spinal Measurements with CT and MRI Imaging." Aviation, Space, and Environmental Medicine, 82(3), p.293, (Poster)
3. D Buckland, J. Perez-Rossello, JD Lin, J Moriarty and B.D. Snyder (2010). "Dynamic and Static Ultrasound Imaging of the Intervertebral Disc." Orthopedic Research Society 2011 Annual Meeting, (Poster)
4. D Buckland, J. Perez-Rossello, A.E. Samir, and B.D. Snyder (2010). "Ultrasound Imaging of the Cervical Spine Intervertebral Disc." Radiology Society of North America 2010 Meeting, (Presentation)
5. D Buckland, J. Perez-Rossello, and B.D. Snyder (2010). "Ultrasound Imaging of the Cervical Spine Intervertebral Disc." Aviation, Space, and Environmental Medicine, 81(3), p.236, (Poster)

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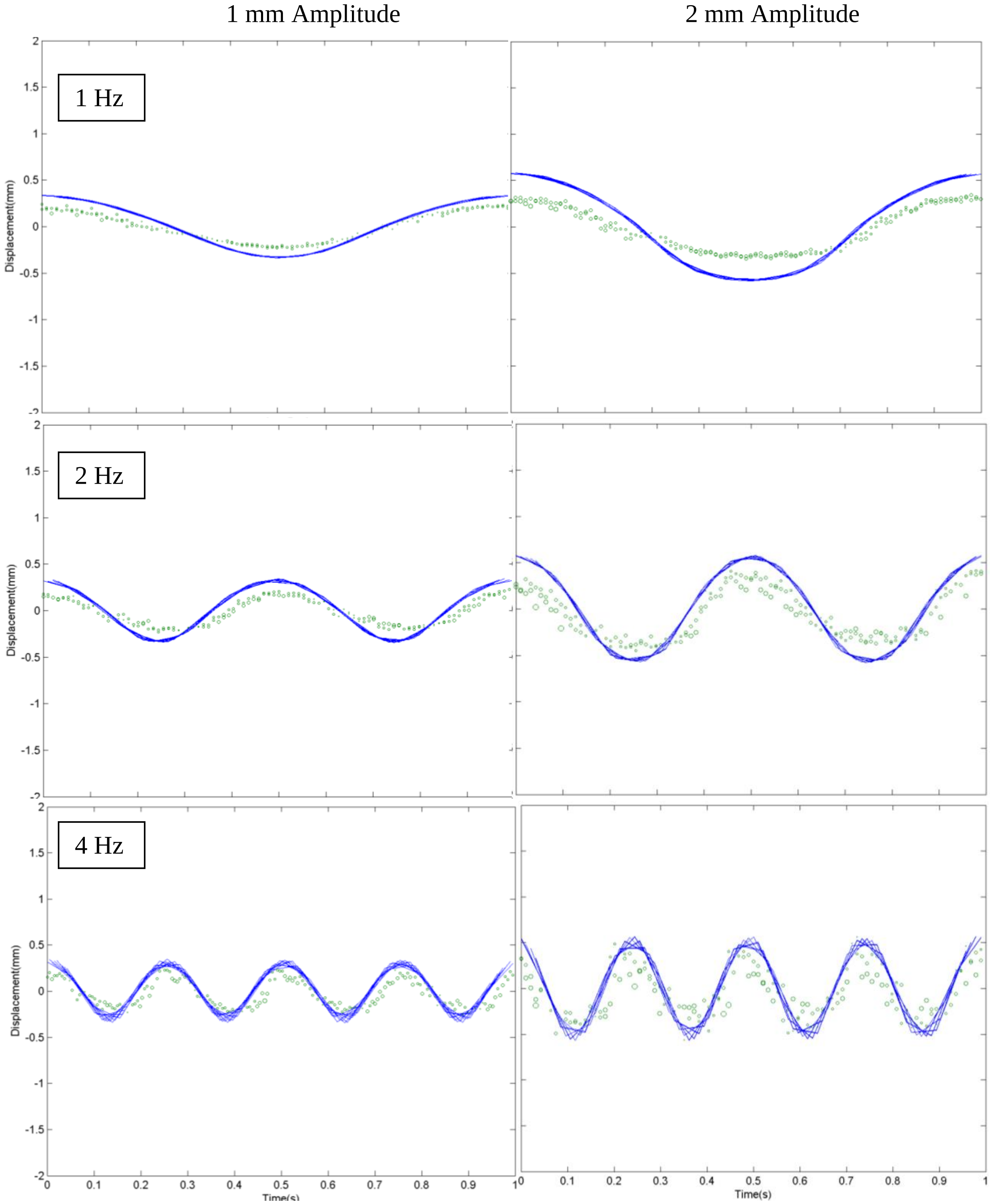
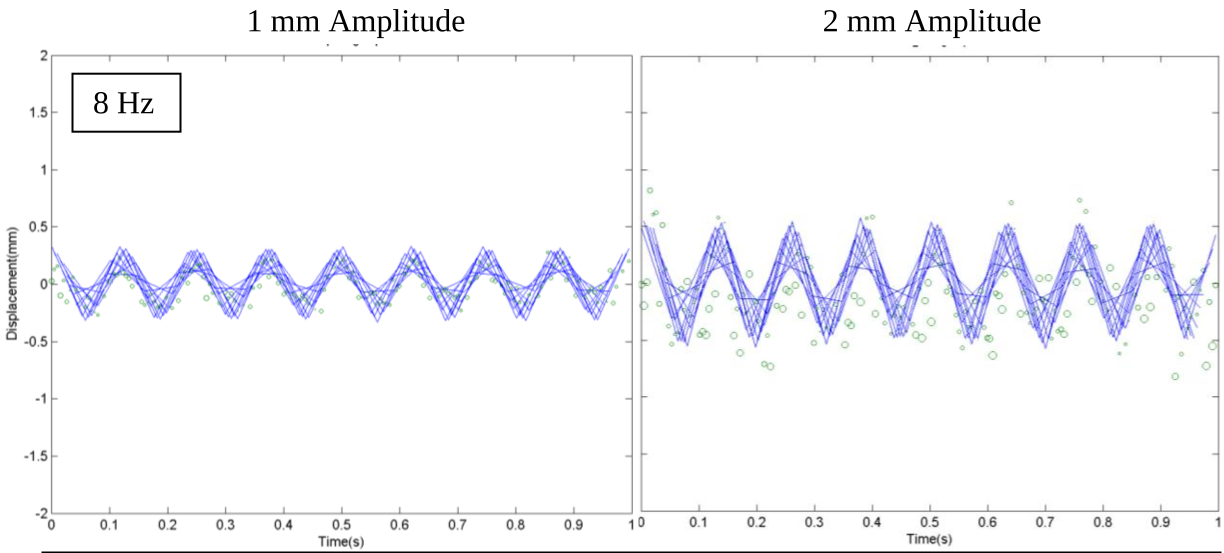
10 Appendices

Full Data set from Ovine Experiment in Chapter 4 (in mm)

Specimen	Disc	Rad 1CT	Rad 2 CT		Rad 1 MRI	Rad 2 MRI		Rad 1 LUS	Rad 1RUS	Rad 2 LUS	Rad 2RUS
1	L	9.82	10.21		9.25	11.81		8.99	10.9	12.33	11.64
1	M	8.22	7.73		7.45	7.46		8.38	7.96	10.06	8.73
1	U	8.42	7.41		7.54	8.57		10.42	7.87	11.7	9.74
2	L	10.75	9.7		8.23	7.58		8.8	8.31	9.54	8.98
2	M	10.18	8.79		7.03	7.71		9.75	10.47	11.48	12.54
2	U	7.71	8.02		8.16	7.85		6.96	9.33	10.54	10.83
3	L	11.81	10.91		8.63	8.58		12.55	7.73	13.91	8.7
3	M	11.13	9.7		7.94	9.09		7.75	7.79	9.14	8.62
3	U	8.9	7.74		8.32	7.9		7.54	7.66	8.17	9.12
4	L	10.81	8.86		8.39	7.65		10.45	9.55	11.05	9.39
4	U	15.72	7.48		6.42	7.15		6.21	8.62	8.36	11.19
5	L	8.7	8.75		8.77	10.62		9.85	10.53	11.41	12.7
5	U	6.91	6.09		8.65	8.36		10.17	10.82	11.75	11.64
6	L	8.41	8.13		11.03	11.97		12	11.82	12.54	12.37
6	M	8.79	9		8.39	8.14		9.15	9.82	13.51	10.01
6	U	8.85	6.84		8.24	8.74		8.44	7.01	9.46	4.92
7	L	8.05	7.76		3.85	4.84		8.45	8.77	8.49	9.47
7	LM	8.75	8.55		5.43	6.42		10.02	8.96	10.31	9.37
7	U	8.12	7.68		6.36	4.53		7.67	8.57	10.65	9.76
7	UM	8.01	8.35		4.85	5.38		7.88	8.88	9.2	11.33
8	L	8.26	7.72		8.9	9.96		10.02	8.87	10.45	10.28
8	LM	6.9	7.28		8.75	8.72		9.41	7.94	10.4	10.05
8	U	6.73	6.92		5.56	7.15		8.86	8.47	11.19	12.32
8	UM	7.03	7.2		7.83	10.74		9.47	8.95	10.51	11.15
9	L	18.33	11.8		9.44	8.81		15.07	13.86	17.39	15.78
9	M	15.91	9.3		8.08	7.58		11.67	9.46	14.42	9.94
9	U	11.69	9.5		8.21	6.43		10.13	9.76	13.9	9.9
10	L	10.72	11		7.58	8.21		11.04	8.96	11.35	9.84
10	M	9.76	9.99		7.62	7.83		10.51	10.77	11.67	11.21
10	U	7.13	7.55		5.97	5.27		8.97	7.84	7.54	9.91
11	L	10.91	10.62		10.71	9.72		10.13	11.31	14.32	12.23
11	M	13.11	9.79		11.86	12.87		10.67	10.24	13.95	11.96
11	U	9.41	11.8		11.4	9.91		9.11	10.5	11.55	11.1
12	L	9.81	10.9		9.18	11.23		11.48	10.19	11.7	10.53
12	LM	9.81	10.47		8.82	9.26		11.53	11.15	11.76	13.02
12	U	8.41	10.11		8.62	9.41		7.82	10.05	9.62	10.08
12	UM	9.38	9.55		7.59	8.28		11.54	11.36	12.62	12.27

Complete Data from One Ovine Specimen in Chapter 5



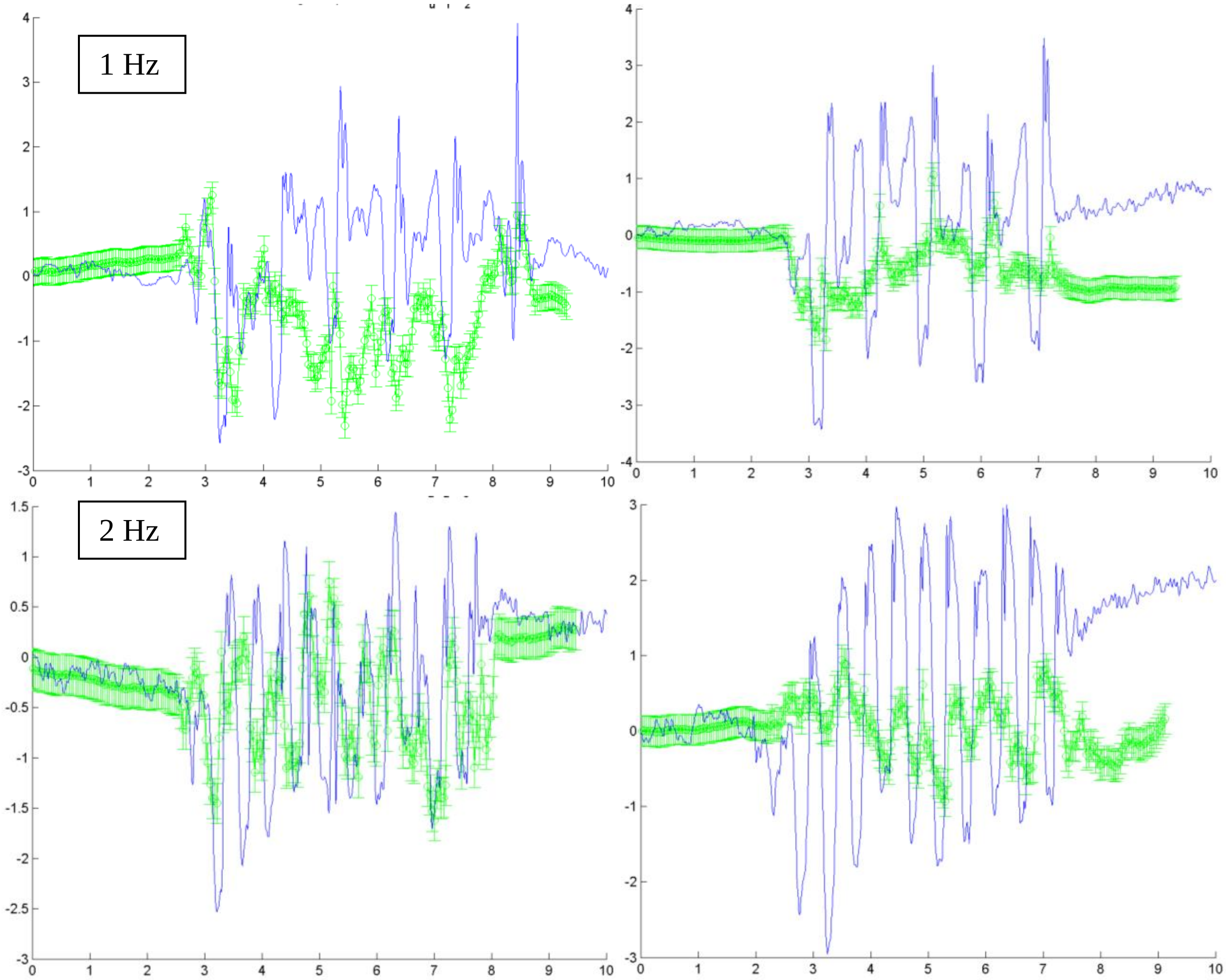


Green dots are individual ultrasound measures and the diameter of the dot is proportional to the error from the extensometer measured displacement at that point (blue line).

Complete Data from One Human Subject in Chapter 5

Without Helmet Weight

With Helmet Weighted



Collected data from a 2Hz in-vivo jumping trials with helmet. Blue line is data from motion tracking. Green line is data from ultrasound, error bars on each data point of the ultrasound data reflect the ±0.2 mm uncertainty calculated in the previous work.