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Fluoroscopic Investigation of Cervical Joint Motion in Healthy Subjects

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**FLUOROSCOPIC INVESTIGATION OF
CERVICAL JOINT MOTION IN
HEALTHY SUBJECTS**

**BY
XU WANG**

DISSERTATION SUBMITTED 2018



AALBORG UNIVERSITY
DENMARK

FLUOROSCOPIC INVESTIGATION OF CERVICAL JOINT MOTION IN HEALTHY SUBJECTS

PH.D. DISSERTATION

by

Xu Wang



AALBORG UNIVERSITY
DENMARK

Sensory and Motor Interaction, SMI®

Department of Health and Science Technology

Faculty of Medicine

Aalborg University

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Xu Wang, Aalborg, September 2016

PREFACE

The current Ph.D. thesis is based on three studies performed at the Center for Sensory-Motor Interaction (SMI), Aalborg University, Denmark, from 2013 to 2018:

Study I: Wang X, Lindstoem R, Carstens N, Graven-Nielsen T (2017). Cervical spine reposition errors after cervical flexion and extension. *BMC Musculoskeletal Disorders*. 2017 Mar; 18(1): 182.

Study II: Wang X, Lindstroem R, Plocharski M, Østergaard L, Graven-Nielsen T (2018). Repeatability of cervical joint flexion and extension within and between days. *J Manipulative Physiol Ther*. 2018 Jan;41(1):10-18.

Study III: Wang X, Lindstroem R, Plocharski M, Østergaard L, Graven-Nielsen T (2018). Cervical flexion and extension includes anti-directional cervical joint motion in healthy adults. *Spine J*. 2018 Jan;18(1):147-154.

LIST OF ABBREVIATIONS

ROM	Range of Motion
ICC	Intra-class Correlation Coefficient
SEM	Standard Error of Measurement
ANOVA	Analysis of Variance
SD	Standard Deviation
RM-ANOVA	Repeated Measure-Analysis of Variance
F1	Upright posture before the flexion motion
F2	Upright posture after the flexion motion
E1	Upright posture before the extension motion
E2	Upright posture after the extension motion

1 INTRODUCTION

Neck pain is a common health problem and will be experienced by most people at some point in their life (Daffner *et al.* 2003). The one-year prevalence rates range from 4.8% to 79.5% (Hoy *et al.* 2010). Neck pain is an increasingly financial burden for social health care systems. The costs of treating neck pain were estimated to be € 485 million in 1996 in the Netherlands (Driessen, Lin, and Tulder 2012). Neck pain is associated with the impairment of muscles, ligaments and bony structures (Gabriela F. Carvalho *et al.* 2014; Meisingset *et al.* 2016; Steilen *et al.* 2014; Waseem *et al.* 2014).

Restricted cervical range of motion (ROM) was observed in patients with neck pain (Hino *et al.* 1999; Houck, Yack, and Mulhausen 1997; Wibault *et al.* 2013). Cervical ROM is described as a principle parameter of global neck function (Takeshima *et al.* 2002). The cervical ROM is most frequently measured between head and a lower body parts, such as thoracic vertebrae or the sternal notch (Artz, Adams, and Dolan 2015; Wibault *et al.* 2013). However, the cervical ROM does not reveal intervertebral cervical joint motion.

Cervical joint motion has been proposed to be more important and clinically relevant for the understanding of cervical biomechanics and post-surgical assessments compared to cervical ROM (Auerbach *et al.* 2011; Puglisi *et al.* 2007; Wu *et al.* 2010). However, dynamic cervical joint motion has not been investigated in depth, and cervical joint motion patterns cannot be efficiently described from static images as large variations of joint motion were found between static images (Anderst, Donaldson *et al.* 2013a; Anderst, Donaldson *et al.* 2013b; Anderst *et al.* 2015).

Cervical ROM is highly correlated with neck problems and ROM is an important parameter for diagnosis and rehabilitation of the cervical spine (Hino *et al.* 1999; Houck *et al.* 1997). Patients with surgical fixation demonstrated smaller ROM in the fused joint(s) and larger ROM in the adjacent joints (Auerbach *et al.* 2011). Surgical fixations of cervical joints increased flexion and extension joint motion in the adjacent joints with approximately 15% in comparison with healthy controls (Anderst *et al.* 2013a). Studies of dynamic motion of cervical joint contribute to diagnosis and treatment of neck pain; however, the knowledge of dynamic cervical flexion and extension motion has not been investigated in depth.

Motor control is important for the assessment and treatment of patients with cervical disorders (Patroncini *et al.* 2014). Deficient motor control is defined as impaired controls of active movement compared to healthy subjects (Patroncini *et al.* 2014; Woodhouse and Vasseljen 2008). Impaired cervical motor control is believed to predispose patients to cervical lesions and/or pain (Patroncini *et al.* 2014). Unfortunately, the knowledge of cervical motor control is weak. The repeatability of

cervical motions is assumed in clinical examination; however, the repeatability of cervical joint motion has never been examined. A better understanding of repeatability of healthy cervical joint motion is important for comparisons of joint motions between and within day of healthy subjects and patients with neck pain (Anderst *et al.* 2013a). Because the repeatability of cervical motion is essential for diagnosis, rehabilitation and analysis of dynamic cervical spine motion.

Anti-directional, reversed or paradoxical joint motion (joint motion opposite the intended motion direction) was previously demonstrated during flexion/extension motion, and was observed in the two joints C0/C1 and C7/T1 (Anderst *et al.* 2015). The C0/C1 anti-directional motion was demonstrated at the beginning and end of cervical flexion, whereas the C7/T1 anti-directional motion occurs during the middle of cervical flexion (Anderst *et al.* 2015). However, anti-directional motion has never been quantified in cervical movements.

The cervical spine is commonly perceived with a motion strategy, where the deep muscles support and stabilize a spring-like spine, while the superficial muscles flexing or extending the neck (Bogduk 2016; Cramer 2014; Mathis 2006; Ombregt 2013). However, large variations in joint motions would indicate that the deep muscles play a more active role in the cervical motor control. Anatomically, the deep muscles provide precise motor control of movements of a single cervical joint, in contrast to the superficial muscles, which are activated across multiple cervical joints (Boyd-Clark, Briggs, and Galea 2002; O'Leary *et al.* 2009). The superficial muscles cannot flex or extend one single joint alone, as the muscles traverse several joints (Blouin *et al.* 2007; Siegmund *et al.* 2007). In contrast the deep muscles do traverse single joints and can flex or extend a single joint.

Reinartz *et al.* reported different rates of change in cervical joint motion, including changes in the motion direction (Reinartz *et al.* 2009). The motion patterns reported by Reinartz *et al.* do not suggest a linear and continuous motion strategy of the cervical joints. The motion pattern includes anti-directional motion of single joints and suggests a more active motor control function of the deep cervical muscles compared to the motion strategy without anti-directional motion (Ombregt 2013). Nonlinear motor control may suggest variance or reposition error between cervical joint motions. The upright head and neck posture is important for dynamic cervical motion as most cervical motions are initiated from this position. The single joint reposition errors between repeated upright positions after cervical motion have never been examined and it is unknown if every single cervical joint demonstrates reposition errors.

1.1 CERVICAL SPINE ANATOMY

The cervical spine consists of 7 vertebrae (C1- C7) and serves to orient the head and to attach the head to the rest of the body. The atlas (C1) is a ring without a vertebral

body whose superior facets articulate with the occipital condyles (C0) and whose inferior facets articulate with the axis (C2) (Bogduk, Amevo, and Pearcy 1995; Devereaux 2007; Mathis 2006). The axis acts as the rotational axis for the head and has an odontoid process and a prominent spire of bone thrust cranially from the axis vertebral body. Except for the first two vertebrae (atlas and axis), the other 5 cervical vertebrae share common morphologic features. Muscles and ligaments are involved in stabilizing and controlling the movement of the cervical spine. The multiple interconnections between two vertebrae will for simplicity be referred to as a joint in this thesis. The cervical joints contribute to cervical range of motion, and this thesis investigates cervical joint motion.

The sub-occipital anatomy and function are different when compared with the lower cervical spine (Ombregt 2013). The distinguished osseous structure of the occiput, atlas and axis underlie functional differences. Biomechanically, the cervical spine is subdivided into three regions, the upper (C0-C1-C2), the middle (C2-C5) and the lower (C5-T1) cervical spine (Panjabi and White 1980).

1.2 NECK PROPRIOCEPTION

Proprioception is essential for sensorimotor control of posture and movement (Brooks 1983; Jong *et al.* 1977; Taylor and McCloskey 1988). Afferent proprioceptive information is received from muscles, skin and joint receptors to control the position and movement in space (Gandevia *et al.* 1992). Joint receptors are believed to be activated near the end of motion, whereas muscle receptors are postulated to be activated throughout the physical range of motion (Brumagne *et al.* 1999). Clinically, altered proprioception is believed to be associated with diseases of joint and muscle, even though the clinical significance of this association remains unclear. The understanding of proprioceptive impairment on cervical joint reposition is important for diagnosis and rehabilitation of musculoskeletal problems (Allison and Fukushima 2003).

1.3 AIM OF THE PHD PROJECT

This PhD thesis aims to investigate cervical joint motion during flexion and extension in healthy subjects. The PhD thesis includes three studies of 1) the reposition error of individual cervical joint; 2) repeatability of cervical joint motion during flexion and extension; 3) anti-directional motion of cervical joint during flexion and extension (Fig 1). The included studies investigate the dynamic joint motion differences between two repeated cervical motions and characterize and quantify the abundant anti-directional motions found in dynamic cervical joint motion (Fig 1).

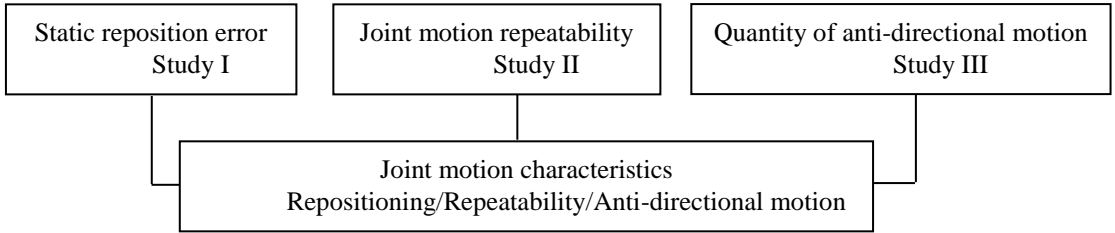


Figure 1. The *PhD thesis* consists of three studies of healthy subjects. The studies investigate the static reposition error of cervical joints, cervical joint motion repeatability and anti-directional cervical joint motion.

1.4 HYPOTHESES

Individual joint motion has provoked greater interest in order to detect potential clinical associations with diagnosis and rehabilitation (Anderst *et al.* 2013a; Branney and Breen 2014; Bogduk *et al.* 1995; Dvorak *et al.* 1988). Normative data for healthy cervical joint motion is a prerequisite for detection of such associations. The purpose of this PhD project was to investigate dynamic cervical joint motion for repeatability and reposition of the cervical spine. Three hypotheses were tested in three studies, with the main hypothesis that cervical joint motions are repeatable:

1. (Study I)

All cervical joints return to the upright posture after end-range cervical flexion and extension movements with uneven (unevenly distributed) reposition errors influenced by time delay.

2. (Study II)

Cervical flexion and extension joint motion initiated from the upright posture is repeatable throughout the motion with uneven (unevenly distributed) repeatability differences influenced by time delay.

3. (Study III)

Cervical joints demonstrate anti-directional motion during cervical flexion and extension motion.

2 METHODOLOGY DEVELOPMENT

2.1. FACILITIES AND EQUIPMENTS

Static end-range X-rays are often used to assess neck function. However, static X-rays fail to show the dynamic joint motion of individual joints. To address this problem, video fluoroscopy was developed for the analysis of dynamic cervical joint motion (Branney and Breen 2014; Reinartz *et al.* 2009; Wu *et al.* 2010).

Dynamic cervical movement was captured with video fluoroscopy and analyzed with the assistance of a Matlab-based program. The developed methods have high reliability and validity (Ahmadi *et al.* 2009; Croft *et al.* 1994; Muggleton and Allen 1997; Okawa *et al.* 1998; Wu *et al.* 2010).

Wu *et al.* assessed the cervical joint motion from C2 to C7 (Wu *et al.* 2010). Branney *et al.* assessed cervical joint motion from C1 to C6 (Branney and Breen 2014). Most of the previous studies have only investigated the middle and lower cervical joints (Anderst *et al.* 2013a; Anderst *et al.* 2013b; Wu *et al.* 2010). The unique anatomical shapes and complex imaging of the upper cervical joints are the explanation for the problems in analyzing these joints (Anderst *et al.* 2013a; Anderst *et al.* 2013b; Wu *et al.* 2010).

A pivot arm has been used to control cervical movements (Branney and Breen 2014). The pivot gives a better control of the movement range and speed, while sacrificing some of the freedom of the strategies of cervical motor controls. Most studies have investigated free and unrestricted cervical movements. Anderst *et al.* did this from end-range of flexion to end-range of extension in one continuous motion (Anderst *et al.* 2013a; Anderst *et al.* 2013b; Anderst *et al.* 2015). Wu *et al.* used a different method. They investigated free and unrestricted cervical movements from the upright position to end-range of flexion or extension (Wu *et al.* 2007; Wu *et al.* 2010).

Joint motion was previously assessed from selected video images of flexion and extension movements. Dynamic cervical flexion and extension motions have previously been divided into intervals or epochs for extraction of the joint motion (Anderst *et al.* 2013a; Anderst *et al.* 2013b; Anderst *et al.* 2015; Reinartz *et al.* 2009; Wu *et al.* 2007; Wu *et al.* 2010). Wu *et al.* investigated the cervical dynamic motion by dividing cervical motion into three intervals (Wu *et al.* 2010). Wu's method may have been flawed, as the motion was extracted in absolute values, and absolute values reflect the magnitude of the motion but neglect the direction of the motion. Wu *et al.* also divided flexion and extension motion into ten intervals (Wu *et al.* 2007). Dynamic joint motions have been assessed with automated analysis, which

allowed analysis of all images in a video (Anderst *et al.* 2013b; Branney and Breen 2014; Reinartz *et al.* 2009).

Most analysis methods are developed from the work of Frobin *et al.* (Frobin *et al.* 2002). Frobin *et al.* marked squared vertebral bodies in each of their corners, and the diverse anatomy of the upper cervical regions were marked with 2 points (Frobin *et al.* 2002) (Fig 2).

2.2. NOVEL METHODOLOGY FOR IMAGE ANALYSIS

Novel features improved the fluoroscopy and analysis method of dynamic joint motion. The most important improvement in the present work was the addition of external markers to identify C0. The external markers were four metal balls on pliable wires attached to a pair of glasses worn by the participants. These new markers were highly accurate compared to the previously applied skin markers, as the skin of ear and nose do move during cervical movements (Wu *et al.* 2007).

The new markers allow for calculation of cervical ROM for the entire neck with the head included, and this again allows for comparison of results with previous non-fluoroscopic ROM studies. The movement below C7 was controlled by straps as the movement below C7 may influence the cervical ROM (Auerbach *et al.* 2011).

Frobin's methods were further developed to identify upper cervical anatomy and several improvements were made to increase the accuracy of the manual marking system including the external markers for C0, improved corner marking procedures, improved marking of C1, protocols for enlargement of images during marking and change of the gray scale of the images (Fig 2). The Matlab-based program was written to calculate mid-planes from the marking points of each vertebrae.

The mid-plane of vertebrae with two marking points went through the anterior and posterior points. While the mid-plane of vertebrae with four marking points went through the midpoint of the two anterior points and midpoint of the two posterior points. Cervical joint angle was calculated as the angle between the mid-planes of two adjacent vertebrae (Fig 2).

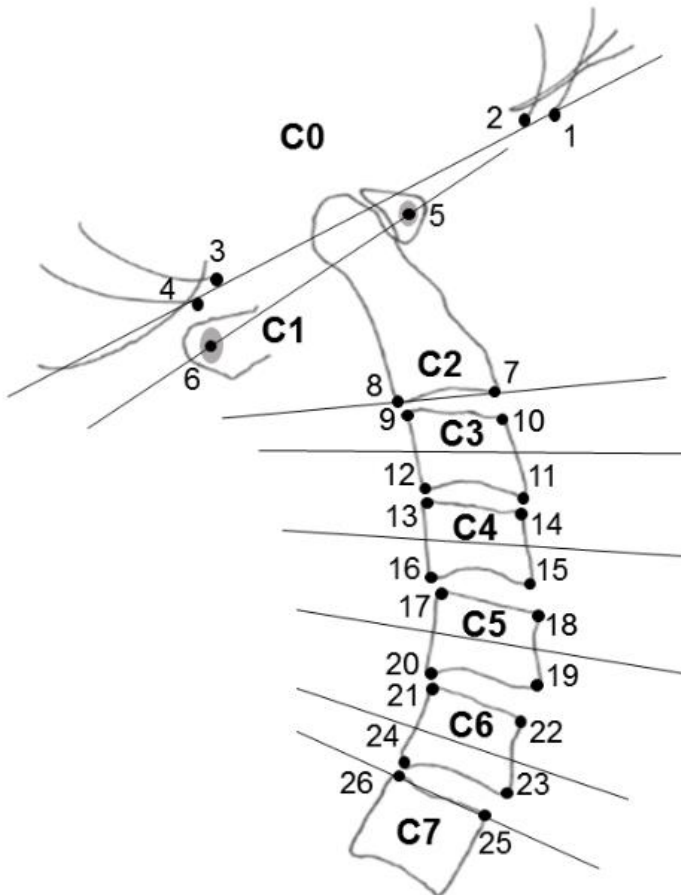


Figure 2. The analysis included 26 marking points. External markers for C0 were 4 metal balls attached on pliable wires on a pair of glasses. Two points for C1 were the central areas of the medullary cavities of the anterior and posterior arch. Two points for C2 were the inferior vertebral plate. Four points for C3- C6 were in proximity to the ends of the vertebral plates. Imaging of the lower part of C7 vertebrae was often obscured by the shoulder shadow and this vertebra was only marked with two points at the end of the superior vertebral plate.

The manual marking of images was time-consuming, and the marking error was the largest confounder; however, the marking error was indicated to be reliable as reflected by high ICCs (larger than 0.90) (Wang *et al.* 2017a). Nevertheless, it is possible that some of the variance found in the studies may originate from marking errors.

2.3. JOINT MOTION ANALYSIS

This thesis investigates cervical joint motions between C0 to C7. Fluoroscopic videos were applied to track the cervical movement from the neutral position to the end-range positions. The videos were evenly divided into 10 epochs with respect to the cervical C0/C7 ROM. When an image was not found at the exact 10% C0/C7 position, two images on either side of the 10% C0/C7 epoch were selected, marked and interpolated to obtain the exact 10% C0/C7 position. Therefore, nine interpolated position images, one neutral position image, and one end-range position image were selected and marked for analysis of cervical flexion or extension joint motion from C0/C1 to C6/C7 (Fig 3). Joint motion in each 10th epoch was computed as the difference between two adjacent 10% images. Thus, one flexion or extension video yielded seventy joint motion angles. Cervical C0/C7 ROM was the sum of the 70 joint motion angles.

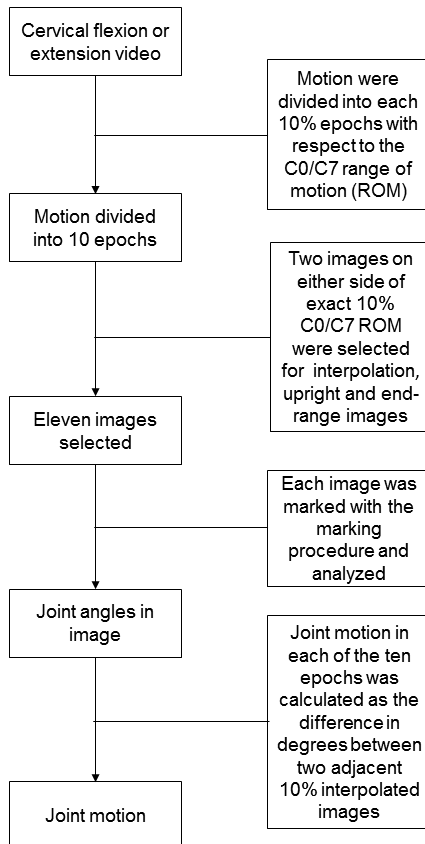


Figure 3. *The joint motion analysis process from fluoroscopic video to motion in degrees. Boxes on the left side show the joint motion analysis in more details.*

2.4. REPOSITION ERRORS OF CERVICAL JOINT (STUDY I)

Static reposition errors in the upright posture of all single cervical joints were assessed after flexion and extension movements in four tasks. The four tasks were explained in Figure 4 and named 'Flexion', 'Extension', 'Setup adaptation' and 'Complete sessions'. The four repeated tasks were completed in different time

deviations with 20 seconds for ‘Flexion’ and ‘Extension’, 300 s for ‘Setup adaptation’ and 340 s for ‘Complete sessions’. The reposition error was the difference in degrees between two upright joint positions. The reposition error was calculated between the start positions of the neck motions. The reposition error was calculated as real errors in real values and as absolute errors in absolute values.

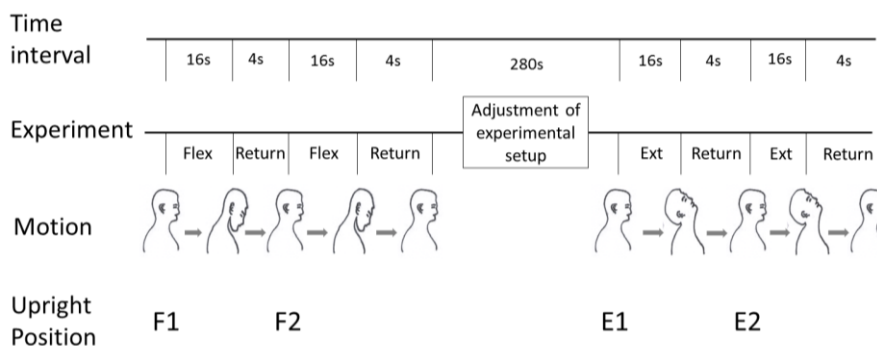


Figure 4. The experimental procedures of study I. The first row shows the time between each motion or of the setup adjustment. An adjustment of the setup was necessary between recordings of flexion and extension videos. The second row shows the motions of flexion (Flex), extension (Ext) and the return motions to upright after flexion or extension (Return), these motions are illustrated in the third row. The flexion and extension motions were recorded while the return motion was not recorded in order to reduce radiation exposure. The fourth row shows the four upright positions which were entered in the analysis of joint reposition errors. F1: the upright position before the first flexion F2: the upright position before the second or repeated flexion E1: the upright position before the first extension E2: the upright position before the second or repeated extension. The reposition errors for ‘Extension’ and ‘Flexion’ were calculated between two upright positions (F1, F2) and two upright positions (E1 and E2), respectively. The reposition error between F1 and F2 was called ‘Flexion’, and the reposition error between E1 and E2 was called ‘Extension’. ‘Setup adaptation’ was the reposition error between F2 and E1 (300s). ‘Complete sessions’ was the reposition error between F1 and E2 (340s).

2.5. REPEATABILITY OF CERVICAL JOINT MOTION (STUDY II)

Dynamic joint motion repeatability was investigated in repeated flexions or extensions. The experiments in Study II were conducted in two parts. The first part examined within-day repetitions of cervical flexion and extension motions with 20 s

between repetitions (Fig 5). The second part examined between-day repetitions with 1 week between repetitions (Fig 5).

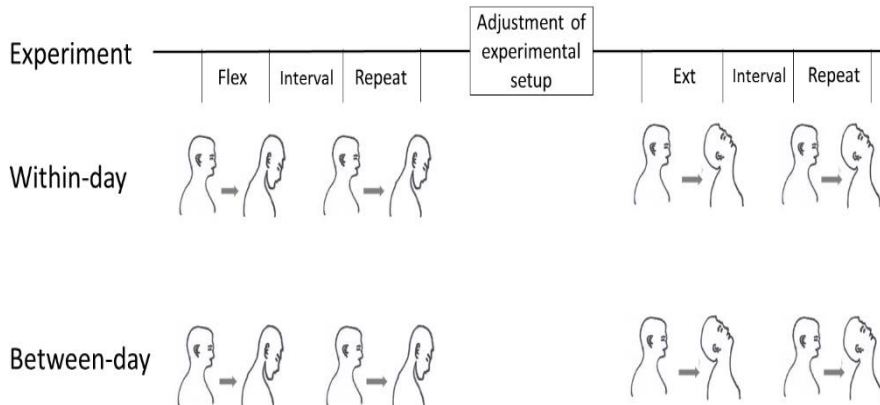


Figure 5. The experimental procedures of study II. The first row shows the flexion (Flex) or extension (Ext), Interval (time interval between first and second or repeated motion), Repeat (second or repeated flexion or extension motion). The second row illustrates the 20 second within day time intervals between two repeated flexions or extensions. The third row illustrates the 1 week between day time intervals.

The dynamic joint motion was calculated as joint motion angles for 7 joints and in 10 epochs for each joint. Repeatability differences were extracted by subtraction of joint motion angles in corresponding epochs between two repeated flexions or extensions. Each repeated within-day or between-day flexion or extension yielded 7 X 10 joint motion angle differences. Likewise, the absolute values of the joint motion angle differences were extracted.

2.6. CERVICAL JOINT ANTI-DIRECTIONAL MOTION (STUDY III)

Anti-directional joint motion was defined as the opposite motion to the intended motion direction (pro-directional). Joint motion was calculated as the difference in degrees between two adjacent interpolated images. Each flexion or extension yielded 70 joint motion angles (10 joint motion angles for each joint from C0/C1 to C6/C7). Two repeated flexion or two repeated extension movements were analyzed and averaged to 70 joint motion angles before computing the anti- and pro-directional joint motions (Fig 6).

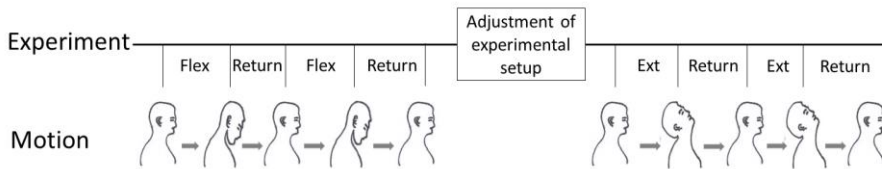


Figure 6. *The experimental procedures in study III. The first row shows the recorded flexion (Flex) and extension (Ext) and the not recorded return motions (Return). The first row also shows a box, which indicates time used to change the setup between flexion and extensions recordings. The second row shows the motion orders. This experiment includes two recorded repetitions of flexion and extension from neutral to end-range position. The return motion to the upright position was not recorded as precautionary measure to reduce radiation exposure.*

The pro-directional or anti-directional joint motion was extracted from each epoch as positive or negative number in degrees, respectively. The actual range of motion of C0/C7 was the sum of all the 70 joint motion angles. For extension the pro-directional C0/C7 motion was the sum of the positive numbers among the 70 joint motion angles, while the sum of the negative numbers was the anti-directional C0/C7 motion, and vice versa for flexion. Joint specific pro- or anti-directional motion across all epochs were extracted and summed for joints. The ratio between anti-directional and pro-directional motions was calculated in percent (0% = no anti-directional movement).

2.7. STATISTICAL ANALYSIS

Data distribution was tested with Shapiro-Will test and Q-Q plot. For each single joint real errors or absolute errors in the four tasks ('Flexion', 'Extension', 'Setup adaptation' and 'Complete session') were compared using the Friedman test followed by post hoc Wilcoxon test if significant. Kruskal-Wallis test was applied to detect the difference between joints in each task. Two-way repeated measure analysis of variance (RM-ANOVA) were performed to compare the joint motion angles for the first and second repetitions with within-subject factors as epoch (10) and repetition (1st, 2nd). Post hoc test Tukey was used for pair-wise comparisons when significant. The joint motion angle differences and the absolute joint motion angle differences over time for flexion or extension were compared with a mixed model ANOVA with epochs as within-subject factor and time (20s interval, 1-week interval) and joint (C0/C1 to C6/C7) as between-subject factors. The ratios between anti- and pro-directional motion were compared by a mixed model ANOVA with joint (7 cervical joints) as between-participant factor and movement (flexion and extension) as within-participant factor. Post hoc analysis Tukey's test was followed for pairwise comparisons. Significance level was set at $P < 0.05$. Statistical analysis was performed in SPSS (version 22, IBM, New York, US).

3 UPRIGHT REPOSITION ERROR

3.1 REPOSITION ERROR AFTER CERVICAL MOVEMENT

The human upright head and neck posture is abundant in our daily life, and the upright posture of the neck is probably the most common neck posture. Clinically, the upright head and neck posture is the baseline position for cervical spine examinations such as cervical ROM and radiographic examination of the cervical spine. Thus, the upright neck posture and the variation of the upright neck posture are integrated in the daily life of healthy subjects, as well as the evaluation of trauma and disease in patients with neck pain. In research, the upright head and neck posture served as the baseline for assessment of cervical spine motion or head and neck proprioception (Armstrong, McNair, and Williams 2005; Pinsault and Vuillerme 2010; Reid *et al.* 2014; Treleaven, Jull, and Sterling 2003; Wibault *et al.* 2013). Reposition error was an important outcome in proprioception studies, while individual cervical joint position sense and reposition error have received little attention, because it was assumed that the upright neck posture was stable and always reestablished with reposition errors of no consequences.

The repositioning error of the cervical spine has been measured by different methods, including the 3Space Fastrak device, Cervical Range of Motion (CROM), and the ultrasound-based motion analysis system (Armstrong *et al.* 2005; Treleaven *et al.* 2003; Wibault *et al.* 2013). All the methods were validated with good reliability (Lee *et al.* 2006; Percy and Hindle 1989; Wibault *et al.* 2013). Most of these studies measured head repositioning acuity with respect to a lower body part, for instance the sternal notch (Artz *et al.* 2015). This method assessed the neck as one unit and without stating that repositioning errors of the head and neck are composed of reposition errors from multiple individual cervical joints.

3.2 CERVICAL JOINT REPOSITION ERRORS

3.2.1 REAL ERROR

The real reposition error of the cervical joints indicated that the cervical spine can return to the upright posture after flexion and extension movements with average variations of 0.21 degrees for flexion and 0.01 degrees for extension in Table 1 (Study I).

Study I showed that the average upright head reposition error in healthy subjects approaches zero in Table 1. The study also showed that single joint could have large reposition errors. These large reposition errors were often counterbalanced by large reposition errors in other joints to maintain a suitable head posture.

Joints	Flexion	Extension	Setup adaptation	Complete Session
Task time	20 s	20 s	300 s	340 s
Average	0.21 ± 0.28	0.01 ± 0.30	0.12 ± 0.45	0.34 ± 0.44
C0/C1	1.74 ± 0.88	1.74 ± 0.68	-4.82 ± 1.98*	-1.35 ± 2.01
C1/C2	0.05 ± 0.79	-0.66 ± 1.20	1.66 ± 1.09	1.06 ± 1.33
C2/C3	-0.70 ± 0.71	-0.52 ± 0.60	1.96 ± 0.67	0.74 ± 0.71
C3/C4	-0.63 ± 0.58	-0.65 ± 0.69	0.25 ± 0.81	0.27 ± 0.54
C4/C5	1.49 ± 0.61	-0.37 ± 0.66	-0.32 ± 0.69	0.80 ± 0.80
C5/C6	-0.31 ± 0.67	0.27 ± 0.79	0.42 ± 0.76	0.38 ± 0.85
C6/C7	-0.29 ± 0.78	-1.14 ± 0.81	1.89 ± 0.98	0.46 ± 1.37

Table 1. Mean (\pm SEM) reposition errors in single joints and the average of all the single joints in degrees from tasks ('flexion', 'extension', 'setup adaptation' and 'complete session'). The 'task time' indicates the time cost of each task. Significantly different from C2/C3 compared to the other joints in the 'setup adaptation' task. (*, $P < 0.05$). Partly reused from Study I with permission (Wang et al. 2017).

3.2.2 ABSOLUTE ERROR

The absolute reposition errors showed that the cervical spine returns to the upright posture with an average error of 2.36 degrees for flexion and 2.50 degrees for extension in Table 2 (Study I). In addition, visual inspection of Table 2 showed that the upper cervical joints (C0/C1, C1/C2) showed larger errors compared with that of the other cervical joints, especially for 'Setup adaptations' and 'Complete sessions' (Wang et al. 2017).

Joints	Flexion	Extension	Setup adaptation	Complete Session
Task time	20 s	20 s	300 s	340 s
Average	2.36 ± 0.19*	2.50 ± 0.22*	3.31 ± 0.35	3.45 ± 0.33
C0/C1	2.36 ± 0.67	2.34 ± 0.59	5.98 ± 1.80	6.13 ± 1.47
C1/C2	2.50 ± 0.54	2.92 ± 1.00	3.67 ± 0.80	4.06 ± 0.98
C2/C3	2.14 ± 0.54	2.13 ± 0.37	2.60 ± 0.54	2.21 ± 0.52
C3/C4	1.98 ± 0.38	2.49 ± 0.42	2.56 ± 0.57	1.75 ± 0.37
C4/C5	2.19 ± 0.48	2.28 ± 0.41	2.57 ± 0.37	2.94 ± 0.47
C5/C6	2.32 ± 0.37	2.45 ± 0.53	2.37 ± 0.51	2.75 ± 0.53
C6/C7	2.32 ± 0.55	3.01 ± 0.45*	3.29 ± 0.73	4.35 ± 0.89

Table 2. Mean (\pm SEM) reposition errors of single joints and the average of the single joints in degrees across 'flexion', 'extension', 'setup adaptation' and 'complete session'. The 'Task time' shows the time cost of each task. The reposition errors in 'Flexion' and 'Extension' were different compared with 'complete session' by Friedman test (*, $P < 0.05$). Partly reused from Study I with permission (Wang *et al.* 2017).

3.3 TIME EFFECTS ON REPOSITION ERRORS

The real errors demonstrated no time effects.

Reposition errors from longer time intervals (340s) were larger compared to reposition errors from shorter time intervals (20s) (Study I). This time effect on cervical joint repositioning errors was found in absolute errors but not in real errors in Table 1 & 2. The study showed conflicting results which indicate that increased absolute errors in the 340 seconds task ('Complete sessions') compared to the 20 seconds tasks ('Flexion' and 'Extension'). However, a similar result was not shown for comparisons with the 300 seconds task ('Setup adaptation') in Table 2 (Study I).

3.4 DISCUSSION

The results supported the hypothesis that all single cervical joints showed uneven reposition errors after cervical flexion and extension movements. However, the cervical spine can return to the upright posture within a small average variation of 0.21° and 0.01° for real errors of flexion and extension and 2.36° and 2.50° for absolute errors of flexion and extension.

The results showed conflicting evidence for the hypothesis that time influences the repositioning ability of cervical joints, as the results demonstrated conflicting evidence on the effect of time on reposition errors of cervical joints.

The upper cervical joints demonstrated a larger amount of repositioning errors compared with that of the lower joints. This difference may be due to the different anatomy of the upper and lower cervical vertebrae.

Proprioception initiated from muscle spindles is an essential element in motor control and repositioning (Artz *et al.* 2015; Newcomer *et al.* 2000; O'Sullivan *et al.* 2003; Wang *et al.* 2017). Healthy controls demonstrated larger repositioning errors in the upper cervical joints compared with the lower ones (Study I). Anatomically, the upper cervical spine consists of more muscle spindles compared to the lower cervical region (Kulkarni, Chandy, and Babu 2001). In contrast, larger repositioning errors were shown in the upper cervical joints, which are in contrast with the larger amount of muscle spindles.

Treleaven *et al.* have also demonstrated larger reposition errors in the upper cervical region in neck pain patients (Treleaven *et al.* 2011). Thus, the upper cervical region demonstrated less repositioning acuity in both healthy controls and neck pain patients. Treleaven *et al.* suggested the repositioning errors in the upper and lower cervical regions should not be grouped, as grouping may reduce homogeneity. The larger repositioning errors in the upper cervical region were in line with the suggestion that the cervical spine should not be considered as a single unit, and that the cervical spine should be treated as a complex structure with multiple units of motion.

The real errors indicated that the cervical spine can return to the upright head and neck posture with only a minor error of on average 0.21 and 0.01 degrees. The small real reposition error is in line with the previous assumptions that the upright head and neck posture can return in healthy subjects. However, the absolute values in Study I showed that the cervical spine returns to the upright posture with an average absolute error of 2.36 and 2.50 degrees. Similarly, Artz *et al.* reported reposition errors after flexion and extension ranging from 1.61 to 2.25 degrees but considered the cervical spine as a single unit (Artz *et al.* 2015). The cervical spine was able to maintain the natural head and neck posture by compensating for large variation in other joints. The large variation in both real errors and absolute errors indicate that the results should be applied to the individual subject level with caution, and that cervical reposition error may not be suited for diagnosis.

The accuracy of upright cervical joint position sense in healthy controls is important, as the reposition errors may be reflected in dynamic cervical flexion and extension movements and in clinical conditions. The upright head and neck position is the position from which most movements begin (Walmsley, Kimber, and Culham 1996). The cervical joints can return to the initial position after flexion and extension movements with a variation of approximately 2.36 and 2.50 degrees (Study I). This raises the question as to whether the variation of the upright neck and head posture influences the cervical joint motion pattern throughout the entire flexion or extension movements.

Uneven distribution of the real errors suggested that the cervical spine counterbalanced flexion and extension movements with a resultant average error approaching zero. The counterbalance appears across multiple joints and serves to orient the head in a suitable position after flexion and extension.

No significant time effects were detected for real errors. The results were inconclusive for effect of time on absolute errors. Increased errors were found for longer time (340 s) compared with shorter time (20 s); however, this result was not demonstrated for 300 seconds when compared with 20 seconds. The results showed conflicting evidence on the effects of time on reposition errors, thus it is difficult to conclude that the reposition ability of the upright cervical spine position decreases

with time, although the magnitude of the error was larger as time increased. Therefore, it is necessary to conduct further studies to test the effect of time on joint position sense.

3.5 SUMMARY

Study I demonstrated that the position sense of all the cervical joints varies after flexion and extension movements and it has been influenced by time. The study may provide normal variation data for cervical spine upright position, which could be compared with patient for diagnostic purposes. This is the first investigation of single cervical joint repositioning errors. The study demonstrated in absolute values a variation of upright position of approximately 2.36 and 2.50 degrees for flexion and extension, respectively.

4 DYNAMIC CERVICAL INDIVIDUAL JOINT MOTION

The common clinical and scientific perception is that cervical joints move in curvilinear patterns and repeat their motions. However, new evidence shows that cervical joints move in convoluted patterns, with multiple changes of motion direction (Anderst *et al.* 2013a; Anderst *et al.* 2013; Wu *et al.* 2010). The new knowledge of cervical joint motion raises the question: Are dynamic cervical joint motion patterns repeated?

4.1 CERVICAL JOINT MOTION REPEATABILITY

The upright head and neck posture is the initial start position for cervical motions such as flexion, extension, axial rotation and lateral bending. Study I demonstrated that the cervical spine returns after full flexion and extension motions with an average variation of 2.36 degrees for flexion and 2.50 degrees for extension.

The repeatability of dynamic cervical joint motion is important for the understanding of cervical biomechanics. The question of repeatability is also of clinical importance as repeated examinations of cervical joint motion are used in spinal diagnosis and in assessment of treatment (Borghouts *et al.* 1999; Cleland *et al.* 2006; Fjellner *et al.* 1999; Strender, Lundin, and Nell 1997; Viikari-Juntura 1987). The motion pattern of the cervical spine has been assumed repeatable in clinical motion palpation examinations and other clinical examinations (Letícia *et al.* 2016; Overmeer *et al.* 2016; Pho and Godges 2004; Rebbeck *et al.* 2016). However, the assumed cervical motion repeatability has never been verified. In this thesis, cervical joint motion repeatability was investigated with a 20 s time difference (within-day repeatability) and a 1-week time difference (between-day repeatability).

Free and unrestricted cervical flexion and extension movements were repeated in Study II. The movements started and were repeated from the upright posture. Free and unrestricted cervical motion was chosen to mimic real-life motions. However, this was standardized with firm fixation of the upper thoracic spine, as upper thoracic motion is reported to influence the cervical spine motion (Edmondston *et al.* 2011; Katzman, Vittinghoff, and Kado 2011; Lau *et al.* 2010).

4.1.1 WITHIN-DAY REPEATABILITY

Comparisons of joint motion angles of cervical flexion and extension motions showed no significant differences in RM-ANOVA when repeated with 20s.

However, main effects of epochs for C1/C2 and C6/C7 were found in flexion. No further interaction effects were detected. For C1/C2, larger joint motion angles were shown for 10th epoch of flexion compared to 2nd and 7th epochs (Post hoc analysis, Tukey: P<0.04). For C6/C7, smaller joint motion angles were found between the 9th and 10th epochs of flexion compared to 2nd, 4th and 5th epochs of flexion (Post hoc analysis, Tukey: P<0.04) (Study II).

4.1.2 BETWEEN-DAY REPEATABILITY

Between-day cervical joint motion showed no significant differences for individual joints of flexion and extension motions. Significant main effects were found for epochs of C6/C7 during flexion, with smaller motions in the 10th epoch of flexion compared with the 1st, 2nd and 7th epochs (Post hoc analysis, Tukey: P<0.04) (Study II).

4.1.3 COMPARISON OF WITHIN AND BETWEEN DAY DIFFERENCES

The average within-day difference across all joints and epochs were 0.00° (SD 2.98°) and 0.00° (SD 3.05°) for flexion and extension, respectively. Likewise, the average between-day differences were 0.01° (SD 2.56°) and 0.05° (SD 2.40°) for flexion and extension, respectively (Study II). The within-day and between-day joint motion angle differences for each joint were presented in Table 3. In addition, the absolute within-day and between-day joint motion angle differences were presented in Table 4. No significant differences were found between measures of within-day and between-day repeatability for real or absolute joint motion angles (Study II). The results indicated that the repeatability of cervical joint motion was not influenced by time (20s vs 1 week).

Joint	Within-day		Between-day	
	Flexion	Extension	Flexion	Extension
C0/C1	-0.03° (2.95°)	0.01° (2.68°)	0.05° (1.76°)	0.19° (1.87°)
C1/C2	-0.15° (3.79°)	-0.16° (3.79°)	-0.12° (2.98°)	0.08° (2.61°)
C2/C3	0.01° (3.18°)	0.05° (3.81°)	0.08° (3.40°)	-0.01° (2.78°)
C3/C4	0.08° (2.59°)	0.04° (2.76°)	0.03° (2.52°)	0.08° (2.09°)
C4/C5	0.05° (2.93°)	0.08° (2.95°)	-0.13° (2.20°)	-0.02° (2.55°)
C5/C6	0.04° (2.53°)	-0.05° (2.65°)	0.09° (2.38°)	0.01° (2.45°)
C6/C7	0.00° (2.93°)	-0.01° (2.42°)	0.10° (2.38°)	0.03° (2.35°)
Average	0.00° (2.98°)	0.00° (3.05°)	0.01° (2.56°)	0.05° (2.40°)

Table 3. *The Mean (SD) in degrees of within-day and between-day joint motion angle differences of repeated flexion and extension movements. 'Average' indicates the joint motion angle differences across all the joints. The joint motion angle differences for flexion were presented in column 2 and 4 and extension were in column 3 and 5, respectively. Reused from Study II with permission (Wang et al. 2018a)*

Table 4. Within-day and between-day absolute joint motion angle differences

Joint	Within-day		Between-day	
	Flexion	Extension	Flexion	Extension
C0/C1	2.98° (4.02°)	2.71° (2.62°)	3.76° (2.92°)	2.43° (2.50°)
C1/C2	2.43° (2.37°)	2.53° (2.25°)	2.44° (2.92°)	2.71° (3.44°)
C2/C3	1.93° (1.64°)	2.17° (1.78°)	1.85° (1.47°)	2.58° (2.35°)
C3/C4	1.53° (1.09°)	1.70° (1.38°)	2.29° (1.72°)	1.74° (1.55°)
C4/C5	1.91° (2.37°)	1.72° (1.51°)	1.89° (1.49°)	2.11° (1.58°)
C5/C6	1.59° (1.37°)	1.77° (1.32°)	2.35° (2.23°)	1.82° (1.35°)
C6/C7	1.79° (1.68°)	1.74° (1.34°)	1.76° (1.36°)	1.69° (1.29°)
Average	2.02° (2.21°)	2.05° (1.84°)	2.33° (2.20°)	2.15° (2.17°)

Table4. *The Mean (SD) in degrees of within-day and between-day absolute joint motion angle differences of repeated flexion and extension movements. 'Average' indicates the absolute joint motion angle differences across all the joints. The absolute joint motion angle differences for flexion were presented in column 2 and 4 and extension were in column 3 and 5, respectively.*

4.2 DISCUSSION

Study II showed that cervical joints could repeat their full flexion and extension movements without influence of time delays. The hypothesis was confirmed on group level with average difference between repetitions from 0.00 to 0.05 degrees. The hypothesis was also confirmed on participant level with some limitation as the SD of the repetitions ranged from 1.76 to 3.81 degrees. The absolute repeatability differences for the cervical joints ranged between 2.02 and 2.33 degrees with the SD ranging from 1.32 to 4.02 degrees.

Interestingly, the results showed no effect of time on repeatability of cervical motions (20s vs 1 week). This result could indicate that cervical motor control was independent of time. However, further studies are needed to confirm the repeatability of cervical joint motions after longer time interval, as most of the

rehabilitation interventions last for several weeks. On group level, the repeatability differences were almost zero, the result suggested that the cervical spine repeats its motion accurately. However, the almost zero difference reflects that the data was normally distributed. Thus, the absolute repeatability differences were extracted to add this variance information to the motion repeatability.

A motor control with inherent variation and upright start position which also varies as documented in study I may contribute towards an explanation for the large SD of repeated motions reported in study II.

Biomechanically, cervical spine motion is commonly understood and modeled as a 'spring-like' structure (Haghpanahi, Haghpanahi, and Javadi 2012). Recently, many studies suggest the cervical joint moves with variable speeds and directions (Anderst *et al.* 2013b; Reinartz *et al.* 2009; Wang *et al.* 2017a; Wu *et al.* 2010). The complex motion patterns demonstrated in this thesis with changing motion directions and high variance of motion contributions between epochs do not support the 'spring-like' models of joint movements. (Anderst *et al.* 2013b; Reinartz *et al.* 2009; Wang *et al.* 2017a; Wu *et al.* 2010).

4.3 CLINICAL IMPLICATIONS

This is the first evidence to support the clinical assumption that flexion and extension of healthy cervical joints are repeatable, and the repeatability is not influenced by time delay. This result is important for clinical diagnosis and clinical examinations, as the result to some extent confirms the previous practice. The results support the assumption that healthy joint motions are repeatable. However, studies of cervical joint motion in patients with neck disorders are necessary to assess whether the variability in cervical joint motion patterns changes with neck pain.

The fluctuations and directions of cervical joint motion vary throughout flexion and extension movements, which contrasts with most surgeons' impression of cervical joint motion that the joint motion increases or decreases constantly through cervical flexion or extension. Thus, most surgeon's clinical and scientific understanding of repeated joint motions may not reflect the larger variance (SD) of results demonstrated in this study.

4.4 SUMMARY

The average difference between repeated joint motions approached zero. This result confirms the hypothesis that the cervical flexion and extension joint motions were repeatable. However, the results also show a variance in absolute differences with an average of approximately 2 degrees, this variance demonstrates a better motion repeatability for groups compared to single subjects. The repeatability of the cervical

joint motion pattern may provide background for future clinical and scientific investigations of the cervical motion pattern in different conditions.

5 QUANTIFICATION OF ANTI-DIRECTIONAL MOTION

5.1 ANTI-DIRECTIONAL MOTION

Anti-directional motion was defined as the motion opposite to the intended motion direction (Fig 7). Previously, anti-directional motion has been documented as reverse motion and inverse motion (Anderst *et al.* 2013c; Swartz, Floyd, and Cendoma 2005). Swartz *et al.* reported that C6 through C7 exhibited a brief anti-directional motion into extension during the neck flexion, followed by a brief anti-directional motion of C0 through C2 (Swartz *et al.* 2005). Similarly, Craine *et al.* concluded that the upper cervical segments of the lower cervical spine (C3-C7) flexed during neck extension, and vice versa (Craine *et al.* 1993). However, the distribution and quantity of the anti-directional motion during neck flexion or extension is unknown.

Real-time imaging of dynamic neck motion was used to investigate cervical joint motions (Anderst *et al.* 2013b; McDonald *et al.* 2010; Wu *et al.* 2010). Maximum joint ROM was reported before full flexion or extension (Bogduk and Mercer 2000). Anti-directional motion was observed during cervical spine flexion/extension (Anderst *et al.* 2015; Craine *et al.* 1993; Reinartz *et al.* 2009). One study demonstrated that some joints reached their maximum motions before the end-range position, and these joints must move anti-directional to some extent from their maximum ROM to reach the end-range position (Bogduk and Mercer 2000; Branney and Breen 2014). Anti-directional motion has likewise been reported before reaching full flexion and extension (Wu *et al.* 2010), and was found in asymptomatic subjects (Abbott *et al.* 2006). Brief anti-directional motions of C6/C7 during flexion were accompanied by anti-directional upper cervical motions (C0-C2) (Van Mameren *et al.* 1990). Anti-directional motions were also demonstrated for C0/C1 and C7/T1 during cervical flexion and extension (Anderst *et al.* 2015).

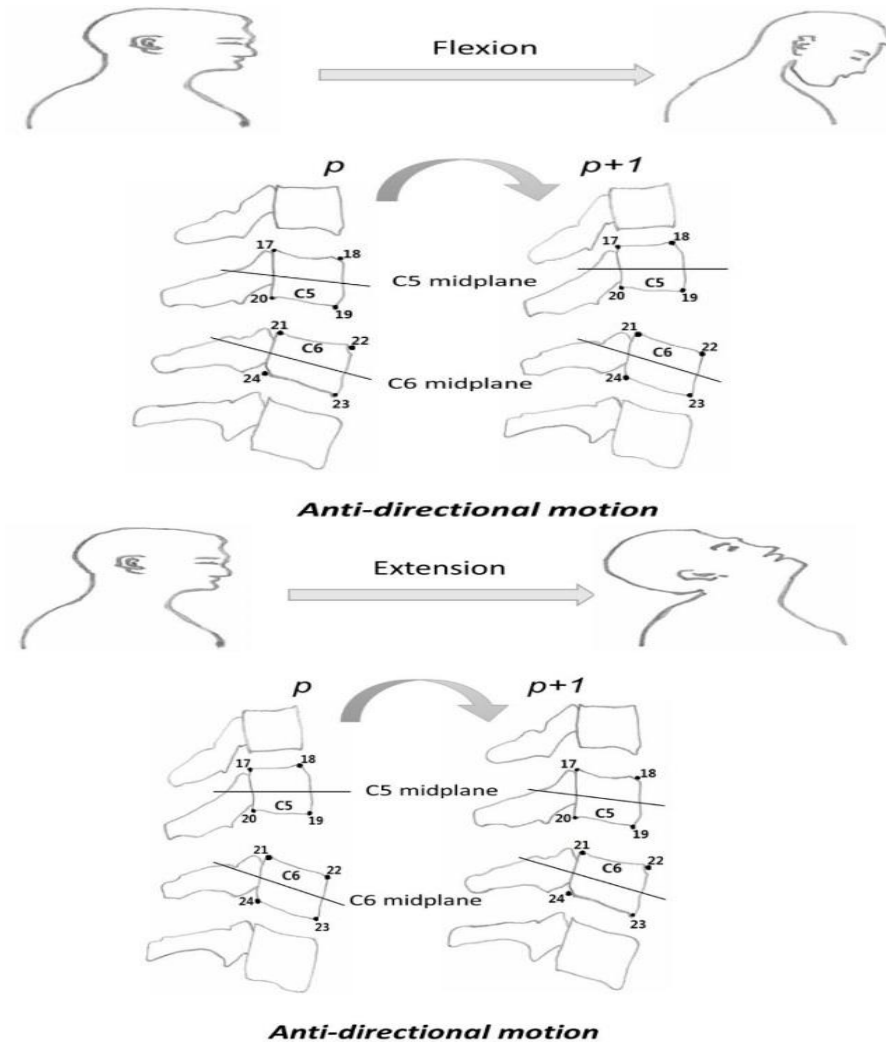


Figure 7. Illustrations of anti-directional motion with two drawings of cervical flexion and extension at the C5/C6 level. The figure shows C4 to C7 and the C5 is marked with marking points 17, 18, 19 and 20 and C6 is marked with 21, 22, 23 and 24. The midplane of each vertebra was determined from the midpoints of the two anterior and posterior points. The joint motion angle is calculated by subtraction of two adjacent joint angles. Joint angle was the angle between two adjacent midplanes. The joint motion changes in the drawings from p (left) to $p+1$ (right) of the joint C5/C6 represent the joint motion during cervical flexion (top drawing) and extension (bottom drawing). Anti-directional joint motion is defined as joint motion opposite the intended motion direction. For neck flexion each instance of extension

joint motion is anti-directional joint motion for the specific joint, and vice versa for neck extension.

5.2 JOINT MOTION DURING FLEXION AND EXTENSION

Cervical joint ROM has previously been investigated for individual joint ROM from static upright and end-range positions (Auerbach *et al.* 2011; Takeshima *et al.* 2002; Wu *et al.* 2010). However, static images of upright and end-range positions may not reflect the dynamic neck motion of cervical joints (Bible *et al.* 2010; Cobian *et al.* 2009).

The joint motion pattern of cervical flexion and extension is unclear; however, the motion patterns were reported to show great variances (Study III). Anti-directional motion is one component of dynamic cervical flexion and extension motions; however, the proportion of pro-directional and anti-directional is unknown.

Both flexion and extension motion demonstrated approximately 40 degrees of average anti-directional motion across joints (C0 to C7) (Study III). All joints demonstrated anti-directional motion, and the anti-directional motion was scattered throughout the dynamic cervical joint motions. The ratios between anti- and pro-directional motion were 42.8 (9.7) % and 41.2 (8.2) % for flexion and extension, respectively (Study III). Visual inspection of all joint motions showed that no joint motions demonstrated continuously pro-directional or anti-directional motions. During flexion, the upper cervical joints showed more anti-directional motions compared with the lower cervical joints. As for extension the C1/C2 and C2/C3 indicated larger anti-directional motions compared with C0/C1, C3/C4, C4/C5 and C5/C6 (Study III). Averaged anti- and pro-directional motions for each cervical joint were presented in Table 5.

Table 5. Mean (SD) anti- and pro-directional motion and the ratio at each individual joint through cervical flexion and extension movements

Joint	Flexion Movement			Extension Movement		
	Anti-direction	Pro-direction	Ratio	Anti-direction	Pro-direction	Ratio
C0/C1	6.78 (4.24)	9.83 (5.18)	0.67 (0.28) ☐ †	4.02 (3.38)	15.24 (6.67)	0.29 (0.10)
C1/C2	9.32 (7.04)	15.44 (6.59)	0.55 (0.22) #	8.54 (4.51)	15.56 (4.62)	0.61 (0.20) &
C2/C3	7.81 (4.04)	13.10 (3.76)	0.60 (0.18) #	7.90 (4.18)	13.77 (3.57)	0.58 (0.20) &
C3/C4	4.25 (1.86)	10.99 (2.73)	0.43 (0.15)	5.42 (2.41)	12.94 (4.09)	0.39 (0.16)
C4/C5	3.85 (2.45)	12.78 (2.73)	0.33 (0.16)	4.46 (3.26)	14.58 (4.26)	0.28 (0.15)
C5/C6	3.11 (1.78)	14.85 (3.66)	0.22 (0.10)	4.73 (2.22)	13.67 (4.49)	0.35 (0.18) ‡
C6/C7	4.82 (3.06)	14.86 (4.29)	0.30 (0.13)	5.18 (3.03)	11.74 (3.94)	0.45 (0.20) ‡
Sum	39.94 (14.32)	91.86 (16.25)	0.43 (0.10)	40.24 (10.84)	97.50 (15.22)	0.41 (0.08)

Table 5. The anti- and pro-directional motion were presented in degrees. The ratios between anti- and pro-directional motion for each joint were presented. 'Sum' indicates the anti-directional and pro-directional motion and ratios of all the cervical joints from C0/C1 to C6/C7. For the flexion ratios C0/C1 was larger than C3/C4, C4/C5, C5/C6 and C6/C7 (\sphericalangle , $P < 0.001$); C1/C2 and C2/C3 were larger than C4/C5, C5/C6 and C6/C7 ($\#$, $P < 0.02$). For the extension ratios C1/C2 and C2/C3 were larger than C0/C1, C3/C4, C4/C5 and C5/C6 ($\&$, $P < 0.03$). The C0/C1 ratio for flexion was larger than the extension ratio (\ddagger , $P < 0.002$). In contrast the C5/C6 and C6/C7 flexion ratio was smaller than the extension ratio (\ddagger , $P < 0.05$).

Figures 8 and 9 showed a representative sample of the diverse and irregular cervical motion patterns found in study III. The patterns were non-linear with large variations in pro- to anti-directional motions. The figures showed several joints with maximum motion occurring before end-range of motion. Almost all subjects demonstrated one or more joints where maximum ROM were reached before end-range. This diversity in motion patterns was not possible without the scattered anti-directional motion.

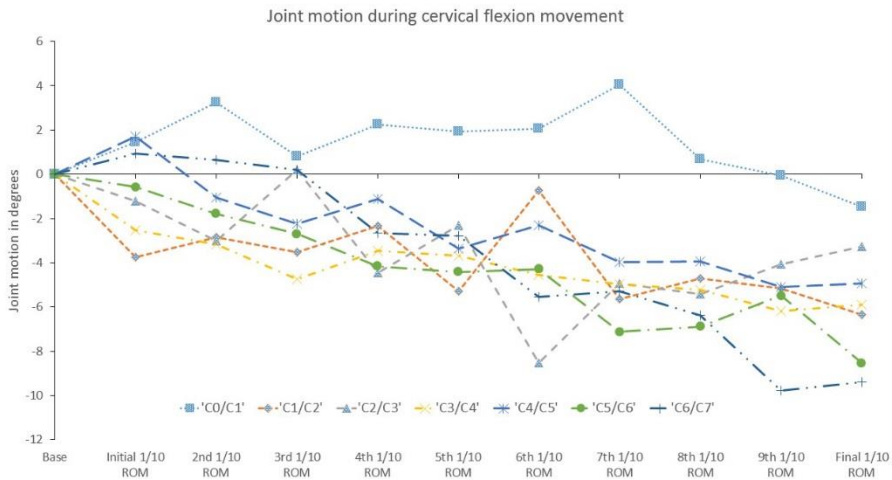


Figure 8. Neck flexion from one representative male subject. Pro- and anti-directional motion directions interchanged with occasional larger one-directional deviations. The maximum flexion C2/C3 motion was reached in the 6th epoch, and the maximum motion was 4.05°. Maximum flexion motions of C2/C3, C3/C4, C4/C5 and C6/C7 were reached before the end-range. Thus, the joints of C2/C3, C3/C4, C4/C5 and C6/C7 have to move anti-directionally before reaching end-range. The motions were analyzed in 10% epochs as illustrated in the figure, and epochs with

signs (-) opposite the intended motion direction (+) demonstrated anti-directional motion.

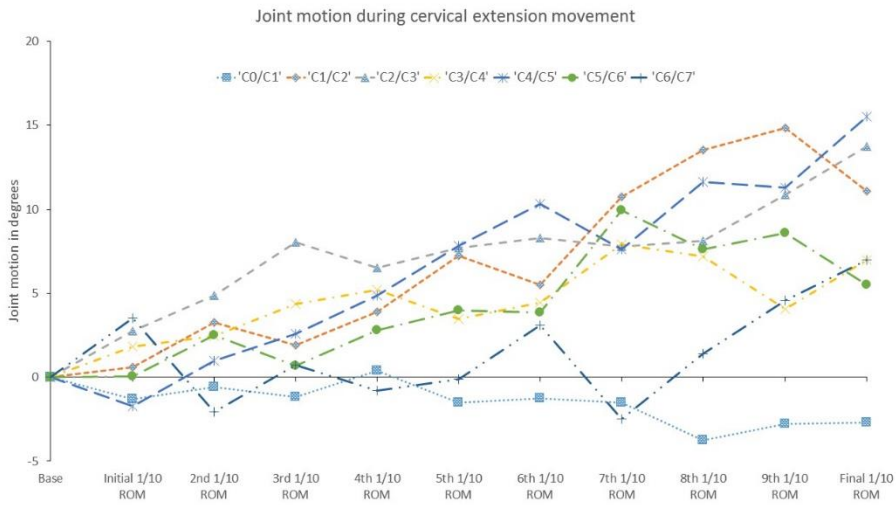


Figure 9. Neck extension from the subject in figure 8. Likewise, pro- and anti-directional motion directions interchanged with larger one-directional deviations. The maximum extension joint motion for C1/C2 and C5/C6 were reached before the end-range, and it was also noted that C0/C1 moves predominantly anti-directionally with maximum anti-directional motion in the 8th epoch. Anti-directional motion occurred when the joint motion in an epoch changed in a direction opposite to the intended motion direction.

Table 6 showed the average cervical joint ROMs across all subjects included in the thesis. Cervical joint ROM is the change in angle of an individual joint between the start position and the end position of the assessed motion. The table showed the largest flexion contribution from C5/C6, and the largest extension contribution from C0/C1 and C4/C5.

Table 6. Mean joint ROM (SD) in degrees of cervical flexion and extension movements		
Cervical Joint	Flexion Movement	Extension Movement
C0/C1	3.06 (4.39)	11.22 (8.37)
C1/C2	6.12 (6.27)	7.02 (5.50)
C2/C3	5.29 (3.80)	5.87 (4.77)
C3/C4	6.74 (3.43)	7.53 (5.00)
C4/C5	8.94 (4.21)	10.12 (5.06)
C5/C6	11.73 (5.23)	8.93 (5.51)

C6/C7	10.04 (5.34)	6.57 (4.68)
SUM	51.92 (9.28)	57.19 (12.16)

Table 6. Mean (SD) of cervical joint ROMs in degrees for all subjects included in the thesis. Left column indicates cervical joints and SUM presents the average ROM of the cervical spine. The middle column shows the joint ROMs between upright posture and end-range flexion. The right column shows the joint ROMs between upright position and extension. ROM indicates range of motion.

5.3 DISCUSSION

Study III investigated anti-directional motion of cervical joints after flexion and extension movements. The study demonstrated approximately 40 degrees of anti-directional motion for both flexion and extension movements. Sum of pro- and anti-directional motion was demonstrated separately for each joint. The results confirmed hypothesis 3 that all healthy cervical joints demonstrated anti-directional motions.

No individual joints showed continually increasing anti-directional or pro-directional motion through cervical flexion or extension. The anti-directional motion was intermittent and scattered through flexion and extension joint motion. The large proportion of anti-directional motion contributed to the variations of joint motion in the sagittal plane.

The cervical motion pattern of flexion and extension was subject-specific and diverse. Data were normally distributed and therefore group results contrasted with subject specific results. Group results were curvilinear and regular, and the group results resample the common perception of joint motion as continuous and linear.

The method may influence image acquisition. Branney and Breen reported a representative subject with the head and neck motion controlled by a pivot mechanism (Branney and Breen 2014). This subject showed smaller amounts of anti-directional motion in contrast to the free and unrestricted motions applied in this study and in another study by Reinartz *et al.* (Reinartz *et al.* 2009). The analysis method applied by Branney and Breen was semi-automated and included several iterations which were averaged. The averaging may also have smoothed the joint motion of the representative subject.

The ROMs of single cervical joints are proposed to provide more information on cervical spine motion compared to neck ROM (Puglisi *et al.* 2004; Wu *et al.* 2010). Joint ROM assessed from static flexion-extension radiographs or real-time videos enhances the understanding of cervical spine kinematics.

A previous study supports that C5/C6 contributes most to cervical flexion (Kowalski *et al.* 2005). The extension results are also in agreement with previous studies for C4/C5 (Wu *et al.* 2010). However, the C0/C1 is different from previous studies as these studies did not investigate the upper cervical joints (Anderst *et al.* 2013a; Anderst *et al.* 2013b; Auerbach *et al.* 2011; Wu *et al.* 2010). Frobin *et al.* calculated joint ROM from end-range flexion to end-range extension on radiographs for C0/C1 to C6/C7, where the largest motion occurred at C5/C6 in healthy males and C4/C5 in healthy females while the smallest motion at C2/C3 for both sexes (Frobin *et al.* 2002) (Table 6). With similar method Takeshima *et al.* documented the largest motion at C5/C6 and the smallest motion at C2/C3 (Takeshima *et al.* 2002).

5.4 CLINICAL IMPLICATIONS

It is widely acknowledged that pro-directional cervical joint motion occurs during cervical flexion and extension (Dvorak *et al.* 1992; Lind *et al.* 1989; Izzo *et al.* 2013). However, the anti-directional motion is commonly regarded as a rare healthy occurrence. The concept of healthy anti-directional motion conflicts with the clinical indication for potential biomechanical problems. The common clinical interpretations of cervical palpation and of functional x-rays do not include a high frequency of healthy cervical joints, which move intermittent anti-directionally. The study also demonstrated healthy joints with very reduced motion or anti-directional end range motion. This is in contrast to the common knowledge of joint motion (Gregory, Hayek, and Mann-Hayek 1998; Tanaka, Irikoma, and Kokubo 2013), where a joint moving anti-directionally or very little is an indication of a potential problem (Leach and Pickar 2005; Chau and Griffith 2005). This study indicates that new gold standards are necessary for the interpretation of cervical joint motions in order to accommodate the large amount of healthy anti-directional motions (Wang *et al.* 2017b).

5.5 SUMMARY

Healthy cervical joints move intermittent pro-directionally and anti-directionally during flexion and extension movements. The cervical spine and head reach the end-range of flexion or extension motion as a result of the combined anti- and pro-directional motions. Anti-directional motion is scattered throughout cervical flexion and extension motion. This study not only verifies the previous findings of anti-directional reports also demonstrates phases with anti-directional motion. The average flexion or extension joint motion contained approximately 40% of anti-directional motion with respect to pro-directional motion. These results enhance the understanding of cervical joint motion pattern in flexion and extension.

6 GENERAL DISCUSSION AND LIMITATIONS

This PhD work develops a novel method and technology to investigate cervical joint motion. The thesis proposes a new understanding of cervical joint motion. The new understanding improves the knowledge of joint motion by firstly clarifying the distribution of repositioning errors in the upright position and secondly showing that a similar variability to the upright position is maintained through the entire joint motion. The thesis further adds to the explanation for the variability of cervical joint motion by demonstrating a large proportion of anti-directional motion. The anti-directional motion explains part of the variance of motion direction found during the repetition study. Figure 10 gives a summary of the results and answers the questions raised in Figure 1.

The average neck and joint ROM found in the studies is largely in agreement with previous studies and the differences between studies can be explained by different stratification of subjects and different methods (Dvorak *et al.* 1992; Hole, Cook, and Bolton 1995; Hsieh and Yeung 1986; Reynolds *et al.* 2009; Salo *et al.* 2009; Whitcroft *et al.* 2010; Williams *et al.* 2010; Youdas *et al.* 1992). Joint ROMs were different between joints (C0/C1, C1/C2, C2/C3, C3/C4, C4//C5, C5/C6, C6/C7) and between movement directions (Flexion, Extension). The largest motion contributions came from C4/C5 and C5/C6 and these joints contributed three times as much as C0/C1 during flexion. These results suggested that the size of the joint contribution to a motion was not associated with size of the upright cervical joint reposition errors, the repeatability between cervical motions or the proportion of pro-directional respecting anti-directional motion.

Repositioning errors after flexion and extension movements were demonstrated for each cervical joint, and the average group repositioning errors were small with larger average absolute reposition errors of approximately 2.5 degrees. The results demonstrated larger reposition errors in the upper cervical regions after flexion and extension compared to the lower cervical regions.

The larger reposition error of healthy subjects in the upper cervical region may be a confounder in a previous study. That study found also larger repositioning errors in the upper cervical region in whiplash patients and attributed the larger reposition error to traumatic whiplash (Treleaven 2011). This result may indicate that the larger reposition errors found in the upper cervical joints may be attributed to the healthy variation and not to whiplash.

The repeatability of cervical joint motion has been assumed both in the clinic and in science; however, this assumption has never been tested. The thesis confirmed the

assumptions of repeatability with some limitations. The results demonstrated that cervical joints repeat their flexion and extension motions with an average variation of approximately 0.00 to 0.05 degrees in groups. The larger average variation of approximately 2 degrees in the absolute data shows that the repeatability for single joints was not as good as the group data. The small difference between group results can be explained by the normal distribution of the data.

Part of the variations found in the repeatability study could be attributed to anti-directional motions. The summed anti-directional motions across the cervical joints during flexion or extension movements were approximately 40 degrees and 40% of the pro-directional motions. Each individual cervical joint demonstrated scattered anti-directional motion through flexion or extension joint motion similar to the variation found in the repeatability study.

Previously, the anti-directional motion has only been identified (Anderst *et al.* 2015; Craine *et al.* 1993; Reinartz *et al.* 2009); however, it has never been quantified. The biomechanical mechanism underlying healthy anti-directional motion is unclear. Small oscillation motion in a few degrees is suggested to be undershoot and overshoot motions performed by the motor control system in order to follow a predefined motor control strategy.

Larger deviations of anti-directional motion may be influenced by the factors which also influence cervical ROM, such as sex, age, height, weight, anatomy, posture, position sense, cervical proprioception, motor control and most importantly the performed motion (Anderst *et al.* 2013b; Cho, Shin, and Kim 2014; Meisingset *et al.* 2016; Swartz *et al.* 2005; Wibault *et al.* 2013).

The thesis results challenge current spine surgeons' impression of cervical spine joint motion that conceptually joint motion is most often perceived as constantly increasing or decreasing through extension or flexion. In contrast, the thesis demonstrates great variability of cervical motion with intermittent pro-directional and anti-directional motions.

There were several limitations in the PhD thesis. The image marking error is the largest source of variation. Image distortion and magnification errors are well known X-ray confounders. Out-of-plane motion may also influence the motion outputs; to control this confounder, participants were asked to follow a vertical line to reduce out-of-plane motions. Blinding of the investigator during marking was not possible, as the procedures required marking of the initial image as a reference for subsequent images.

Control over thoracic movement during acquisition could not be too restrictive as the control may influence free and natural neck motion. Upright cervical spine

curvature (kyphosis, lordosis, normal curve) may also influence the cervical joint motion pattern.

ROM for the neck and cervical joint have previously been assessed with different methods. This thesis assessed neck and joint ROM for both sexes and from upright position to full flexion or full extension, without further guidance as to what full flexion or full extension was. Wu *et al.* applied similar fluoroscopy methods for joint ROM between C2 to C7 (Wu *et al.* 2010).

The ROM of the neck depends on the performed motions. An example is flexion with or without upper cervical retraction (localized forced upper cervical flexion) (Walmsley *et al.* 1996). Pilot data shows that retraction increases the motion contributions of the upper cervical joints. Likewise, other regional movements will increase the motion contributions from that region and the joints within the region. Stratification of healthy subjects into age, sex, height, weight and posture is likely to influence the cervical joint contribution to the performed motions (Dvorak *et al.* 1992; Malmström *et al.* 2006). Methodological difference in data acquisition also influences joint motion contribution to the examined neck motion. The motion contributions are different between continuous motion from full flexion to full extension or if the motions start from the upright position. The upright position includes the variance of that position; however, motions initiated from that position resemble the movement of daily living more than movement going from full flexion to full extension.

Age and sex are factors which influence cervical ROM, and probably also the individual joint motions within the ROM (Dvorak *et al.* 1992; Hwang and Jung 2015; Smith, Hall, and Robinson 2008). The participants in the studies were of both sexes between 20-30 years old and they do not represent all age groups.

Recurrence is a frequent feature of neck pain. Thus, the absence of neck pain within the last three months may not be a guarantee that the participants are healthy and without neck problems.

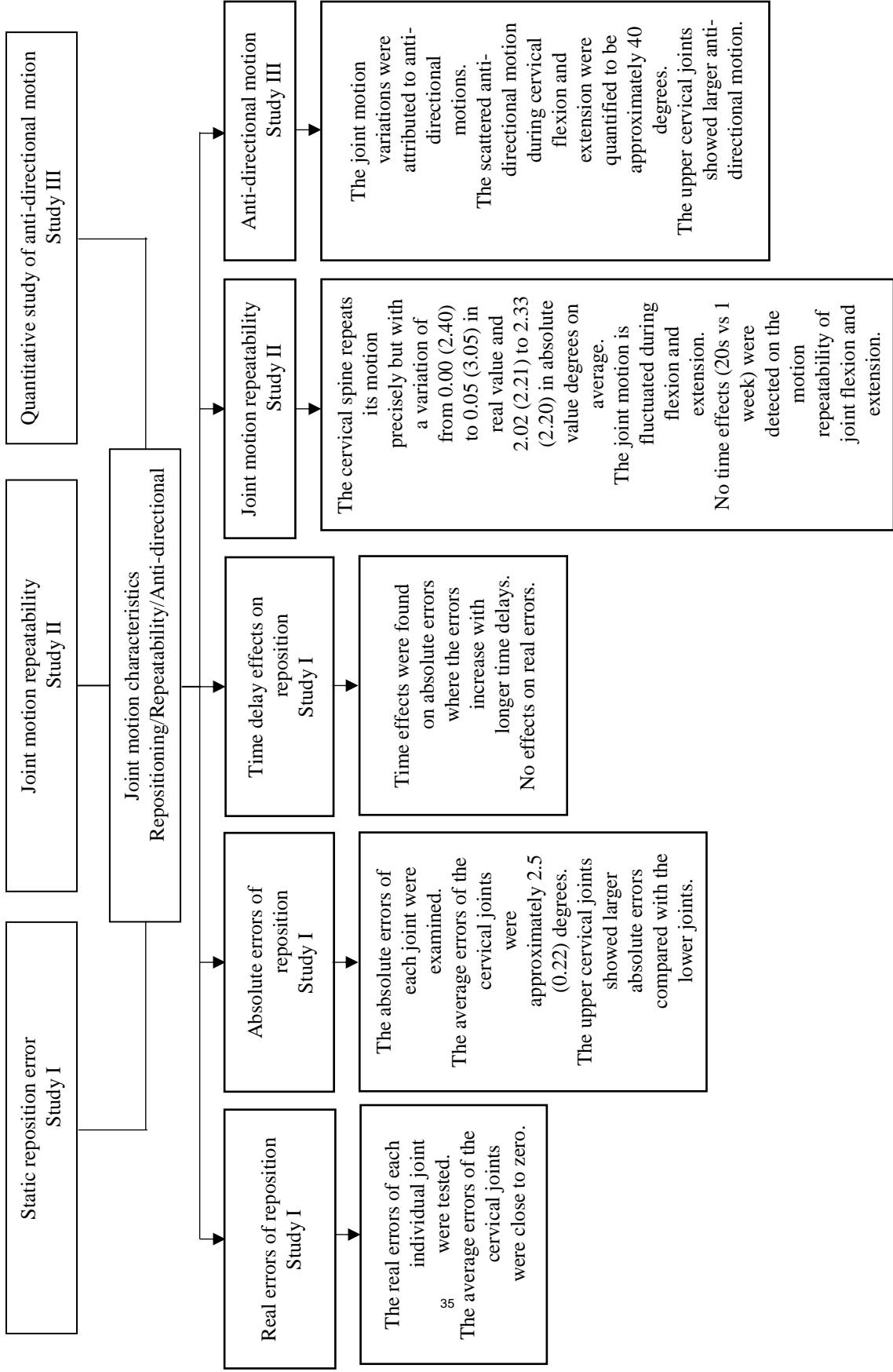


Figure 10. *The summary of the joint motion characteristics during sagittal cervical flexion and extension movements in healthy subjects. Static repositioning ability was assessed with real errors and absolute errors. The effect of time interval (long time vs short time) on repositioning acuity between different tasks were examined as time effects. Time effects on static and dynamic repositioning were investigated in Study I. Study II investigated repeatability of dynamic motion. Study III investigated anti-directional joint motion.*

7 FUTURE PERSPECTIVES

Normative studies of healthy joint motion stratified according to age, sex and spinal curvature are warranted. There is also a need for further exploration of healthy subgroups and other characteristics of normal or healthy joint motion.

The findings of the thesis have only been demonstrated for healthy subjects, and studies linking healthy results with pain conditions such as experimental muscle pain, experimental ligament pain, whiplash, and chronic neck pain will be necessary in future efforts.

Experimental muscle pain provides a method to study alteration in the cervical motion pattern under similar pain conditions. The method would allow investigations of the upright reposition error under short-term and similar pain conditions. Likewise, experimental pain would also allow investigations of dynamic cervical joint motions under similar pain conditions. The overall repositioning errors of the cervical spine under experimental pain conditions are expected to be larger compared with controls, and the variance in dynamic cervical motion is also expected to increase (Breen and Breen 2017).

Neck proprioception and motor control strategy were altered by chronic neck pain and whiplash (Misra and Coombes 2015; Treleaven 2011; Wibault *et al.* 2013). Impairment of deep cervical muscles have been documented in chronic neck pain and whiplash (Falla, Bilenkij, and Jull 2004; Johnston *et al.* 2008; Juul-Kristensen *et al.* 2013; Peterson *et al.* 2016; Stapley *et al.* 2006). The deep cervical muscles are the only muscles, which can control single cervical joint motions. The association between pain, deep cervical motor control and anti-directional motion is an interesting future research area.

8 CONCLUSION

This is the first dissertation, using a novel developed fluoroscopic video technology, to demonstrate individual cervical joint repositioning ability, motion repeatability and anti-directional motion during flexion and extension movements in healthy adults. This thesis developed a novel fluoroscopy video technology to test the repositioning ability of individual cervical joints after flexion and extension movements. The technology can also examine the repeatability of the dynamic motion and the anti-directional motion of individual joints. The healthy cervical spine demonstrated that i) the averaged upright posture repositioning variation after flexion and extension is approximately 2.5 degrees, ii) the upright reposition variations in the upper cervical spine are larger compared to the lower cervical spine, iii) the individual joint repeats its flexion and extension with an average variation in real values ranging from 0.00° to 0.05° and in absolute values ranging from 2.02° to 2.33° , iv) each individual cervical joint move pro-directionally and anti-directionally through flexion and extension. Additionally, the healthy cervical spine shows diverse increasing or decreasing joint motion pattern during flexion or extension.

Academically and clinically, the variation in the healthy cervical spine implies that i) the larger repositioning variation in the upper cervical spine may not indicate damage/injuries but healthy variations, and ii) the motion repeatability of the cervical spine provides the background and baseline data for further clinical and scientific investigation of cervical motion pattern, and iii) the results open the possibilities of ways for better understanding cervical biomechanics. Generally, this thesis concluded that the cervical spine, at the individual joint level, repeats its fluctuated motion pattern with a number of variations.

9 ENGLISH SUMMARY

Pain in the neck region is one of the most common medical conditions. Neck pain is a potential cause of altered neck proprioception and altered motor control. The cervical spine is a multi-joint unit, and the cervical spine has been studied extensively to assess the range of motion and repeated motions with associated repositioning ability for persons without and with neck problems. However, the repositioning ability and motion pattern of individual cervical joints have only been described minimally until now.

Individual cervical joints' upright posture repositioning ability (Study I), dynamic motion repeatability (Study II) and anti-directional motion (Study III) were examined in healthy subjects who were asked to flex and extend the cervical spine from an upright posture to an end-range position.

Most cervical spine movements are initiated from the upright cervical posture or postures closely related to this posture. Therefore, this posture is the baseline for the studies. The distribution of reposition errors showed larger errors in the upper cervical regions. The studies confirmed with some limitations the clinical and scientific assumption that cervical joint motion was repeatable.

Individual cervical joint repositioning and movement are essential to understand normal variations of the healthy cervical spine biomechanics. In the present work, the repeatability of single joint flexion and extension movements, including fluctuation of anti-directional joint motion (previously described as reverse motion in clinical studies, converse motion in biomechanical studies) were examined.

To investigate the individual cervical joints' repositioning ability, the subjects were asked to return to the upright cervical posture as precisely as they could after a cervical flexion or extension movement. A novel fluoroscopic video technology and Matlab based program analyzed the individual joint repositioning errors from C0/C1 to C6/C7. The repositioning errors were presented as real errors and absolute errors in degrees. Individual joint motion during flexion and extension was calculated in degrees. For detailed joint motion pattern analysis, the flexion or extension movement was evenly divided into ten epochs with respect to the C0/C7 ROM from upright posture to end-range position. Repeated flexion and extension movements were performed to examine the joint motion repeatability with long (1 week) and short (20 s) time intervals. Anti- and pro-directional motions were measured to reflect the variations during repeated joint flexion and extension.

The cervical spine returns to the upright cervical posture after flexion and extension, as it counterbalances the multiple joint motions within the cervical spine. The cervical joints returned after flexion and extension movements with positive or

negative joint repositioning errors. Despite the variations in the upright cervical posture after cervical flexion and extension movements, the variations through cervical flexion and extension movements were repeated with an error of approximately 2.5 degrees.

Cervical joints move repeatedly through flexion and extension with an average variation of 0.00° to 0.05° in real values, and an average variation of absolute values ranging from 2.02° to 2.33° . The movements include anti-directional motion, which contributes to the fluctuations of the flexion or extension of joint motions.

The average anti-directional motion of the healthy cervical spine was scattered throughout flexion or extension movements. Moreover, the upper cervical joints showed larger anti-directional motion compared to the lower cervical joints. The current thesis confirms that the anti-directional motion exists in free and unrestricted cervical flexion and extension movements with an approximately average of 40 %.

The results quantify the variations of cervical joint motion during flexion and extension movements, which may help to understand interventions directed towards improved joint motions. The variation of repositioning differences after flexion and extension suggests that this variation should be considered, when head and neck repositioning errors are applied in rehabilitation and in science.

10 DANSK SAMMENFATNING

Nakkesmerter er en af de mest almindelige sygdomme. Smerter kan være årsag til ændret sensorisk og motorisk kontrol af nakken. Halshvirvelsøjlen er en multifunktionsenhed, der er blevet undersøgt i vid udstrækning for at vurdere hvirvelsøjlenes bevægelser og repositioneringsevne hos personer med og uden nakkesmerter. Imidlertid er halshvirvelsøjlenes bevægelse og repositioneringsevne af enkelte hvirvelled kun beskrevet i begrænset omfang indtil nu.

Studie I undersøger individuelle halshvirvelleds repositioneringsevne, studie II undersøger reproducerbarheden af dynamiske halshvirvelleds bevægelser og studie III kvantificerer anti-direktionelle bevægelser. I studierne blev raske forsøgspersoner bedt om at bøje nakken forover og bagover fra den oprette stilling til fuld bevægelse af nakken.

De fleste bevægelser af nakken begynder fra den opretstående stilling eller stillinger tæt på denne kropsholdning. Derfor har nakkens oprette stilling været udgangspunktet for indeværende undersøgelser. Nakkens øverste led returnerede til udgangspositionen med større fejl end de nederste led. Undersøgelserne bekræftede med nogle begrænsninger den kliniske og videnskabelige antagelse om, at halshvirvelled gentager deres ledbevægelser.

Halshvirvelleds gentagne forover og bagover bevægelser hos raske blev undersøgt i dette projekt. Evnen til at gentage bevægelser af halshvirvelled er vigtig for at forstå normale variationer i nakkens biomekanik.

Forsøgspersonerne blev bedt om at returnere til den oprette stilling af halshvirvelsøjlen, så præcist som de kunne efter forover og bagover bevægelsen. En ny videoflouroskopisk teknologi har gjort det muligt at beregne de enkelte ledbevægelser mellem C0/C1 og C6/C7. Repositionsfejlene efter forover og bagover ledbevægelsen blev beregnet som reelle og absolutte fejl i grader. Forover og bagover bevægelserne blev opdelt i ti intervaller af led bevægelsen mellem C0 til C7 for analyse af nakkens fulde led bevægelse. Gentagne forover og bagover bevægelser blev udført for at undersøge reproducerbarheden af ledbevægelser med 20 sekunders og 1 uges mellemrum. Anti-direktionelle og pro-direktionelle bevægelser blev målt for at vise variationerne under de gentagne bevægelser.

Halshvirvelsøjlen returnerer til den opretstående stilling efter forover eller bagover bøjning med små repositionsfejl, idet større fejl af enkelte led kompenseres i andre led. Repositioneringsfejl angives som positive eller negative. På trods af de biologiske variationer i led bevægelsen returnerer halshvirvelsøjlen til den oprette stilling efter forover eller bagover bøjning af nakken med en middelfejl på ca. 2.5 grader.

Halshvirvelled reproducerer forover og bagover bøjningsbevægelser med en gennemsnitsvariation mellem 0.00° og 0.05° , og gennemsnitlige absolutte bevægelser mellem 2.02° og 2.33° . Led bevægelserne indeholder anti-direktionelle bevægelser (modsat rettede bevægelser), hvilket bidrager til variationerne i forover eller bagover bevægelserne.

De anti-direktionelle bevægelser var fordelt igennem forover eller bagover bevægelserne. De øverste halshvirvler viste mere anti-direktionel bevægelse end de øvrige halshvirvler. Afhandlingen viser, at anti-direktionel bevægelse forekommer i fri og ukontrollerede halshvirvelbevægelser med et gennemsnit på 40%.

Resultaterne kvantificerer de biologiske variationer af halshvirvelleds bevægelser under forover og bagover bøjning. Resultaterne kan bidrage til at forstå og forbedre behandlingen af nakkens biomekanik. Den biologiske variation af repositionsforskelle efter forover og bagover bøjning peger på, at denne variation bør overvejes, når repositionsfejl af hoved og nakke anvendes i rehabilitering og forskning.

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12 AUTHOR'S CV

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SUMMARY

Pain in the neck region is one of the most common medical conditions. Neck pain is a potential cause of altered neck proprioception and altered motor control. The cervical spine is a multi-joint unit, and the cervical spine has been studied extensively to assess the range of motion and repeated motions with associated repositioning ability for persons without and with neck problems. However, the repositioning ability and motion pattern of individual cervical joints have only been described minimally until now.

Individual cervical joints' upright posture repositioning ability (Study I), dynamic motion repeatability (Study II) and anti-directional motion (Study III) were examined in healthy subjects who were asked to flex and extend the cervical spine from an upright posture to an end-range position.

Most cervical spine movements are initiated from the upright cervical posture or postures closely related to this posture. Therefore, this posture is the baseline for the studies. The distribution of reposition errors showed larger errors in the upper cervical regions. The studies confirmed with some limitations the clinical and scientific assumption that cervical joint motion was repeatable.

Individual cervical joint repositioning and movement are essential to understand normal variations of the healthy cervical spine biomechanics. In the present work, the repeatability of single joint flexion and extension movements, including fluctuation of anti-directional joint motion (previously described as reverse motion in clinical studies, converse motion in biomechanical studies) were examined.

To investigate the individual cervical joints' repositioning ability, the subjects were asked to return to the upright cervical posture as precisely as they could after a cervical flexion or extension movement. A novel fluoroscopic video technology and Matlab based program analyzed the individual joint repositioning errors from C0/C1 to C6/C7. The repositioning errors were presented as real errors and absolute errors in degrees. Individual joint motion during flexion and extension was calculated in degrees. For detailed joint motion pattern analysis, the flexion or extension movement was evenly divided into ten epochs with respect to the C0/C7 ROM from upright posture to end-range position. Repeated flexion and extension movements were performed to examine the joint motion repeatability with long (1 week) and short (20 s) time intervals. Anti- and pro-directional motions were measured to reflect the variations during repeated joint flexion and extension.

The cervical spine returns to the upright cervical posture after flexion and extension, as it counterbalances the multiple joint motions within the cervical spine. The cervical joints returned after flexion and extension movements with positive or 40 negative joint repositioning errors. Despite the variations in the upright cervical posture after cervical flexion and extension movements, the variations through cervical flexion and extension movements were repeated with an error of approximately 2.5 degrees.

Cervical joints move repeatedly through flexion and extension with an average variation of 0.00° to 0.05° in real values, and an average variation of absolute values ranging from 2.02° to 2.33° . The movements include anti-directional motion, which contributes to the fluctuations of the flexion or extension of joint motions. The average anti-directional motion of the healthy cervical spine was scattered throughout flexion or extension movements. Moreover, the upper cervical joints showed larger anti-directional motion compared to the lower cervical joints. The current thesis confirms that the anti-directional motion exists in free and unrestricted cervical flexion and extension movements with an approximately average of 40 %.

The results quantify the variations of cervical joint motion during flexion and extension movements, which may help to understand interventions directed towards improved joint motions. The variation of repositioning differences after flexion and extension suggests that this variation should be considered, when head and neck repositioning errors are applied in rehabilitation and in science.