Clinical and statistical correlation of various lumbar pathological conditions

J. Michael Johnson [a], Mohamed Mahfouz [a,*], Nicholas V. Battaglia [a], Adrija Sharma [a],
Joseph S. Cheng [b], Richard D. Komistek [a]

[a] Center for Musculoskeletal Research, University of Tennessee, 301 Perkins Hall, Knoxville, TN 37996, USA
[b] Vanderbilt University, Department of Neurological Surgery, 1500 21st Avenue, South Suite 4340 VAV, Nashville, TN 37232-8618, USA

ABSTRACT

Current clinical evaluations often rely on static anatomic imaging modalities for diagnosis of mechanical low back pain, which provide anatomic snapshots and a surrogate analysis of a functional disease. Three dimensional *in vivo* motion is available with the use of digital fluoroscopy, which was used to capture kinematic data of the lumbar spine in order to identify coefficients of motion that may assist the physician in differentiating patient pathology. Forty patients distributed among 4 classes of lumbar degeneration, from healthy to degenerative, underwent CT, MRI, and digital x-ray fluoroscopy. Each patient underwent diagnosis by a neurosurgeon. Fluoroscopy was taken as the patient performed lateral bending (LB), axial rotation (AR) and flexion-extension (FE). Patient specific models were registered with the fluoroscopy images to obtain *in vivo* kinematic data. Motion coefficients, C_{LB}, C_{AR}, C_{FE}, were calculated as the ratio of in-plane motion to total out-of-plane motion. Range of motion (ROM) was calculated about the axis of motion for each exercise. Inter- and Intra- group statistics were examined for each coefficient and a flexible Bayesian classifier was used to differentiate patients with degeneration. The motion coefficients C_{LB} and C_{FE} were significantly different ($p < 0.05$) in 4 of 6 group comparisons. In plane motion, ROM_{LB}, was significantly different in only 1 of 6 group comparisons. The classifier achieved 95% sensitivity and specificity using (C_{FE}, C_{LB}, ROM_{LB}) as input features, and 40% specificity and 80% sensitivity using ROM variables. The new coefficients were better correlated with patient pathology than ROM measures. The coefficients suggest a relationship between pathology and measured motion which has not been reported previously.

1. Introduction

Low back pain (LBP) is a leading cause for physician visits in the United States, frequently ranked 2nd behind upper respiratory infections (Deyo et al., 2006, Hart et al., 1995). Costs associated with LBP exceed $100 billion annually (Katz, 2006), the majority of which are imaging expenses (Jarvik et al., 2003, Lurie et al., 2003). Numbers continue to rise as the population ages, as the prevalence of LBP increases with age (Woolf and Pfelger, 2003). It is difficult to treat LBP, as it is a non-specific symptom resulting from underlying etiologies which may be chemical, vascular, mechanical, or neural in nature.

In mechanical LBP, the symptoms are related to mechanical trauma or degeneration resulting from activities, including those of daily living. The spine is a mechanical system, with the various muscles, bones and tissues involved with motion becoming injured due to abnormal stresses leading to pain as a normal biological response to injury. Current clinical evaluations rely on static anatomic imaging modalities, which provide anatomic snapshots and a surrogate analysis of a functional disease. Clinicians are limited by the available diagnostic tools to determine treatment, including developing surgical plans based on pure anatomic imaging studies, such as CT, X-rays and MRI, showing anatomical changes which may not localize the abnormal stress and actual tissue injury. These images allow analysis at fixed moments in time, but fail to provide information regarding dynamic motion, making diagnosis of the functional problem or pain generator of the spine difficult.

Past efforts have used spinal kinematics and kinetics to understand the biomechanical factors associated with the clinical presentation of the patient. Previous methods used to quantify lumbar kinematics included ultrasound (Heneghan et al., 2009), goniometers (Lee et al., 2003), electromagnetic (Jordan et al., 1999), and optical tracking (Syed et al., 2007). Using these in vivo lumbar kinematic methods to measure the range of motion (ROM) in patients performing activities have been subject to reliability issues, and prone to errors due to placement or patient conditions. Most can be said to have questionable validity measures (Littlewood and May, 2007). More accurate optical

* Correspondence to: University of Tennessee, 307 Perkins Hall, 1506 Middle Drive Knoxville, TN 37996, USA. Tel.: +865 974 7668; fax: +865 974 6394.
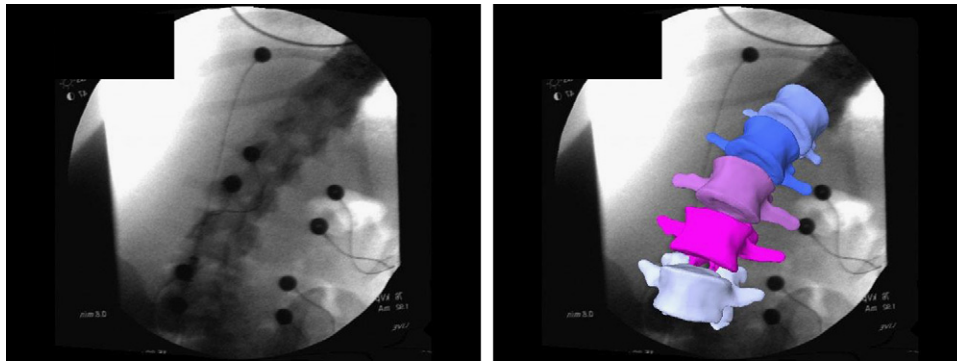E-mail address: mmahfouz@cmr.utk.edu (M. Mahfouz).

Fig. 1. Plot 2D–3D registration of patient specific vertebral models for kinematic analysis showing original fluoroscopy image (left) and models registered with image (right).

and electromagnetic tracking systems are becoming increasingly popular (Jordan et al., 2001), though these suffer from high expense and elaborate setup. In addition, while it has been shown that ROM is correlated with aging and decreased mobility (Castro et al., 2000), quantifying ROM is not a suitable measure for differentiating healthy and pathological patients (Esol, 1996, Nattrass et al., 1999). Previous results report only the motion in the direction of the activity being performed and ignore the effect of pathology on rotations and translations out of the plane of motion activity and the associated kinetics. Digital x-ray fluoroscopy offers the means to effectively track *in vivo* kinematics (Wang et al., 2008; Wong et al., 2006). Currently, it is believed tracking motion in a single plane is sufficient for kinematic diagnosis (Xia et al., 2010). However, the relationship of movement perpendicular to the sagittal plane with associated kinetics and spinal pathology has not been explored.

Our work tracks the *in vivo* kinematics of the L1–L5 vertebrae to calculate novel coefficients for differentiating between varying degrees of LBP pathology using different patient groups: healthy, healthy with LBP, degenerative and pre-operative spine patients. Our hypothesis is that motion of diseased or degenerated joints associated with low back pain is sporadic, displaying increased out-of-plane motion to minimize stresses on tissues and joints which are unable to move smoothly in the direction of the applied muscular force during motion. Using the *in vivo* kinematics of the vertebrae, the in-plane and out-of-plane motion can be quantified using a single coefficient for each activity. By examining the kinematics of various patient groups, some key measureable values may be identified which could differentiate low back pain patients with normally functioning joints, such as those with lumbar strain which will improve on its own, and those with pathological joints who need follow up medical care and treatment to address their symptoms.

2. Methods

2.1. Patient data

The study consisted of 40 patients. Each patient underwent fluoroscopic examinations as well as CT and MRI to assist in reconstructing the three-dimensional patient anatomy. Fluoroscopic examinations were performed at Vanderbilt University Medical Center. The fluoroscopic exam consisted of having the patient perform three activities, moving from the point of maximum flexion to maximum extension, lateral bending, and axial rotation. Patients were examined using a General Electric OEC 9800 or 9900 C-Arm type fluoroscopic unit (GE Healthcare, Waukesha, WI). Patients were diagnosed by a neurosurgeon. As decided by the surgeon, the patients were placed into one of four groups. The inclusion criteria for each patient group were chosen by the surgeon to represent clinically significant patient findings. The Healthy group included ten asymptomatic subjects with no radiological evidence of degeneration. The LBP group

consisted of ten patients with no radiological evidence of degeneration or defects of the lumbar spine, but had reported at least one episode of LBP within a year of the evaluation. The Degenerative patient group consists of ten subjects with radiological findings of lumbar degeneration and spondylosis, experienced pain prior to evaluation, and radiologically exhibited one or more of the following conditions: Schmorl's Nodes, disc bulging both with and without canal or foraminal stenosis, disc osteophyte complexes, decreased height and fluid signal in the intervertebral disc, or facet hypertrophy. Furthermore, the degree of degeneration was not considered severe enough to require surgery. Ten additional subjects with lumbar spinal stenosis and degenerative deformities were treated surgically with a single level decompression and fusion and volunteered for participation in this study. These patients were evaluated just prior to surgery and form the fourth patient group (PreOp). Mean ages for each group were 39.7 ± 13.2 for Healthy, 42.8 ± 9.64 for LBP, 40.1 ± 9.48 for Degenerative and 48.5 ± 10.3 for PreOp. Institutional Review Board approval was obtained as well as informed consent for all patients participating in this study (IRB ♯7393).

2.2. Kinematics

Patient specific bone models were segmented from CT scans for the L1–L5 vertebrae. The fluoroscopic images were digitized at a resolution of 640×480 pixels for use in the kinematic analysis. The bone models were registered with the fluoroscopy frames at 0%, 33%, 66% and 100% of the motion using a previously developed 3D–2D registration technique (Mahfouz et al., 2003). While the Mahfouz et al. study focused on the knee, the method was extended to and validated for the cervical spine in a cadaveric study by Liu with accuracy of 0.5 mm and 0.5° (Liu, 1997). The validation utilized optical tracking to verify the kinematics. Fig. 1 shows an example of a fluoroscopy frame before and after registration. Local coordinate system was assigned based on the Standardization and Terminology Committee of the International Society of Biomechanics (Li et al., 2009). The relative transformations between the bone models were recorded for each frame, as well as the overall path of motion. Euler fixed angles were calculated using an N3 > –N2 > –N1 > sequence, where N1 > represents lateral bending, N2 > represents axial rotation and N3 > represents flexion-extension. The axes are oriented so that flexion-extension, axial rotation and lateral bending are defined by the Euler rotations as seen in Fig. 2. Another software package was used to interpolate for the motion between successive vertebrae, to determine the
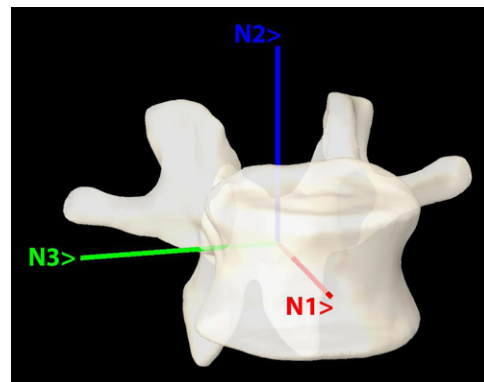

Fig. 2. Illustration of choice of axes orientation. Lateral bending is about N1 >, axial rotation is about N2 >, and flexion extension is about N3 >.

kinematics for the entirety of each activity. Interpolation was performed using shape preserving cubic Hermite polynomials so as not to over fit the data. The absolute values for the angular motion between successive vertebra and L1-L5 were recorded in the directions of flexion-extension (FE), lateral bending (LB), and axial rotation (AR). The overall motion was calculated as the sum of the relative motions. The absolute difference of angular motion was used to capture all out-of-plane motion, regardless of direction.

A coefficient of motion, C_M, representing the ratio between out-of-plane and in-plane motion, was calculated for each vertebra and type of movement as follows:

$$C_{AR} = \frac{A_{LB} + A_{FE}}{A_{AR}} \tag{1}$$

$$C_{LB} = \frac{A_{AR} + A_{FE}}{A_{LB}} \tag{2}$$

$$C_{FE} = \frac{A_{LB} + A_{AR}}{A_{FE}} \tag{3}$$

Here, A_M represents the sum of the absolute value of angular motion, during M, the motion for which C is calculated.

The other set of kinematic data examined in this work involved 3 range-of-motion (ROM) variables, ROM_{FE}, ROM_{LB}, and ROM_{AR}. This was considered to be equivalent to A_M, and represents the flexibility and overall motility of a patient during motion M.

2.3. Statistical analysis

To understand which variables provide the potential for differentiation between the patient groups, a Kruskal–Wallis test was performed for each of the 6 variables. The Kruskal–Wallis was chosen because the test avoids the assumption that the populations follow a normal distribution. A p-value of $p < 0.05$ was considered statistically significant. For variables having significant differences between patient groups, a multiple comparison test was used to determine between which patient groups the differences were. The method for the multiple comparison test was Tukey's least significant difference procedure, which is a reasonable test when the preliminary test shows a group significant difference for the variable. Additionally, the data was divided into two groups by combining the patients with normal radiological findings (Healthy and LBP) and those with degeneration. The overall means of these groups were compared using Kruskal–Wallis. The Jonckheere trend test was used to identify statistical significance of trends across all groups for each variable. Due to small sample size, no data was considered to be an outlier.

2.4. Classification

Classification was performed with the goal of differentiating patients without degeneration (Healthy and LBP) from those with pathology (Degen and PreOp). These groupings were considered clinically relevant, as differentiating symptomatic patients with normal findings from those with pathology is a common task for the clinician. Variables having significant differences per the Kruskal–Wallis test were used for classification. Additionally, one classification was performed using only the coefficient variables, one using only ROM variables and one using all six of the variables to determine the effect of using ROM and coefficient variables on the classification accuracy. The classifier was trained using the leave one out method. All features were normalized to zero mean, unit variance.

The classification technique was the flexible Bayesian classifier (John and Langley, 1995, Mitchell, 1997) which fits a Gaussian kernel for each observation. A new observation is classified by determining which class is most likely to contain the observation. This is done by maximizing the posterior probability that an observation belongs to its respective class of feature vectors (the kinematic measurements).

For the case of the lumbar data, the variables are not assumed to follow a normal distribution, and no assumptions were made about the mean or standard deviation of the measurements. The flexible Bayesian classifier was chosen because it has been shown to work well in diagnostic prediction (Kononenko,

2001) and because it is a good model for how a clinician might approach a problem. For example, given an observation—in this case, the *in vivo* patient kinematic data—determine the likely diagnosis. The probability of a diagnosis can be considered the posterior probability in the Bayesian framework, written as

$$Posterior\ Probability \propto Prior\ Probability \times Likelihood \tag{4}$$

For this work, the likelihood is the probability of the *in vivo* data (or features) given a diagnosis and the prior probability is the probability that a given pathology exists for a patient.

3. Results

3.1. Statistical results

The mean and standard deviations for each variable and data grouping can be seen in Table 1. The results of the Kruskal–Wallis test for each variable are presented in Table 2. The variables C_{FE}, C_{LB}, and ROM_{LB} had significant group differences. For these variables, a multiple comparison test using Tukey's least significant difference was performed. The results of this test are presented in Table 3.

Overall, C_{FE} and C_{LB} had a statistically significant difference between the most patient groups, 4 out of the 6 group comparisons. ROM_{LB} displayed a significant group difference, and was significantly different between the LBP and PreOp patient groups.

The mean for each of the ratio coefficients C_{FE}, C_{LB}, C_{AR} increased monotonically from Healthy to PreOp patient groups, as can be seen in Table 1. The trend of increasing means was significant ($p < 0.05$) for all coefficients according to the Jonckheere test. Only ROM_{FE} had a significant trend among other variables, though the change was not monotonic between group means. Figs. 3, 4, and 5 show 2D scatter plots of the coefficients for the data. Table 4 shows Kruskal–Wallis significance for each of the variables between the two groups. Of the six measured, C_{FE}, C_{LB}, ROM_{LB}, and ROM_{AR} had significant differences, with C_{FE}, C_{LB} having $p < 0.001$.

Table 2
Kruskal–Wallis results between 4 groups.

Variable	p-value
ROM_{FE}	0.104
ROM_{LB}	0.048
ROM_{AR}	0.107
C_{FE}	< 0.001
C_{LB}	< 0.001
C_{AR}	0.104
Age	0.282

p-values showing significance of each variable between all 4 patient groups (Healthy, LBP, PreOp and Degen).
Age was included to show it has no significance between patient groups. A p-value of $p < 0.05$ is considered sufficient for rejection of the null hypothesis.

Table 1
Means and standard deviations for coefficients and ranges of motion for various patient groupings.

	C_{FE}	C_{LB}	C_{AR}	ROM_{FE}	ROM_{LB}	ROM_{AR}	AGE
Healthy	0.237 ± 0.176	0.950 ± 0.342	2.507 ± 0.683	42.987 ± 10.572	40.612 ± 7.412	13.601 ± 3.425	39.74 ± 13.20
LBP	0.612 ± 0.137	1.400 ± 0.417	2.764 ± 0.688	43.016 ± 13.414	34.751 ± 7.142	14.570 ± 2.790	46.48 ± 9.64
Degen	0.977 ± 0.408	1.864 ± 0.308	2.775 ± 0.969	41.242 ± 10.365	47.233 ± 9.891	19.877 ± 6.935	40.13 ± 9.48
PreOp	1.350 ± 0.266	2.740 ± 0.673	3.790 ± 1.412	30.961 ± 10.660	43.153 ± 11.530	16.895 ± 6.727	48.53 ± 10.29
Healthy/LBP	0.425 ± 0.246	1.175 ± 0.437	2.635 ± 0.680	43.002 ± 11.755	37.681 ± 7.698	14.086 ± 3.081	43.11 ± 11.77
Degen/PreOp	1.164 ± 0.386	2.302 ± 0.679	3.282 ± 1.288	36.101 ± 11.512	45.193 ± 10.662	18.386 ± 6.824	44.33 ± 10.55

Table 3
Results of statistical test between each group.

	C_{FE}	C_{LB}	ROM_{FE}
Healthy vs LBP	N	N	N
Healthy vs Degen	Y	Y	N
Healthy vs PreOp	Y	Y	N
LBP vs Degen	N	N	Y
LBP vs PreOp	Y	Y	N
Degen vs PreOp	Y	Y	N

Results of Tukey's least significant difference test for the C_{FE}, C_{LB}, and ROM_{FE} variables. A "Y" indicates a statistically significant difference between the tested patient groups and is equivalent to a p-value of $p < 0.05$. A "N" indicates no statistically significant difference.
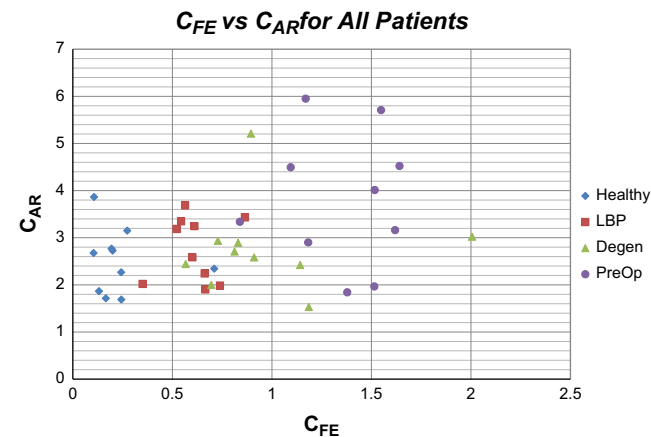

Fig. 5. Plot of C_{LB} vs. C_{FE} for all patients.

Table 4
Kruskal–Wallis results between 2 groups.

Variable	p-value
ROM_{FE}	0.074
ROM_{LB}	0.020
ROM_{AR}	0.040
C_{FE}	< 0.001
C_{LB}	< 0.001
C_{AR}	0.167
Age	0.807

p-values showing significance of each variable between patients having degeneration (Degen and PreOp) and those without (Healthy and LBP). A p-value of $p < 0.05$ is considered sufficient for rejection of the null hypothesis.

Fig. 3. Plot of C_{FE} vs. C_{AR} for all patients.

Table 5
Results of 2-class classification.

Features used	TN	FN	TP	FP	Sensitivity (%)	Specificity (%)
3 ROM's	8	4	16	12	80.00	40.00
C_{FE}, C_{LB}, C_{AR}	19	1	19	1	95.00	95.00
3C's, 3 ROM's	18	1	19	2	95.00	90.00
C_{FE}, C_{LB}, ROM_{LB}	19	1	19	1	95.00	95.00

Results of 2-class classification scheme using different features. All classifiers were trained and tested using the leave one out method.
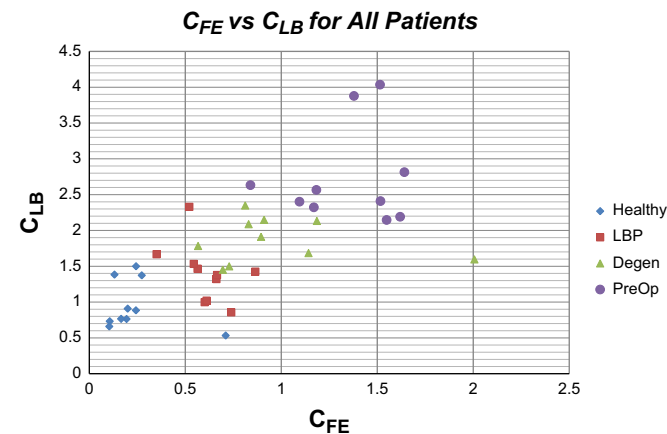

Fig. 4. Plot of C_{LB} vs. C_{FE} for all patients.

3.2. Classification analysis

The classification accuracy for each choice of input features is presented in Table 5. The highest sensitivity and specificity was 95%, achieved using the coefficients only as the input and using the variables having group differences as identified by the Kruskal–Wallis analysis. Using the coefficients as well as the ROM variables reduced classification accuracy slightly as compared to using the coefficients only as input. Using the ROM variables as input, the classifier achieved 80% sensitivity but only 40% specificity.
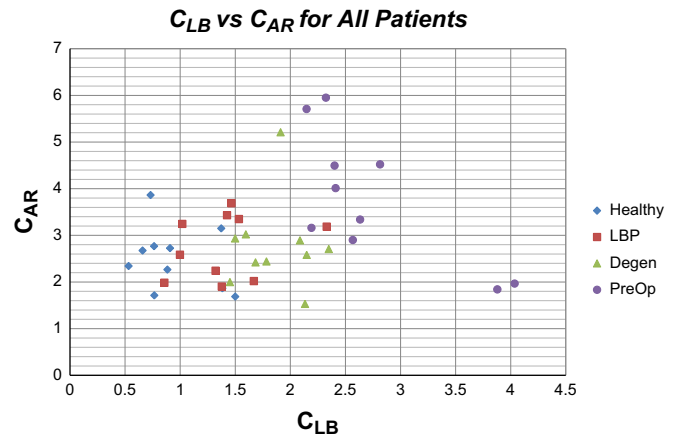
4. Discussion

This work assessed coefficients for quantifying lumbar motion in 4 groups of patients to determine if kinematics could differentiate between patients with normal findings and those with degenerative conditions. The results indicate that the coefficients showed statistically significant differences between various lumbar pathologies and may assist as a diagnostic technique in differentiating patients needing follow up using more expensive diagnostic and treatment methods. The trend of increasing coefficient values for increasing pathological severity, while not statistically significant between all tested patient groups, suggests the potential for these measurements for differentiating amongst symptomatic, but otherwise healthy patients, and patients with degenerative conditions. In the work by Nattrass et al., 1999 impairment and lumbar ROM were found to have no correlation, suggesting that using ROM is not sufficient for evaluating pathology. The presented coefficients, C_{FE}, C_{LB}, and C_{AR} are an extension of the ROM measurements made in previous work, and provide information which can be used to differentiate healthy and

degenerative patient groups. Esola et al., 1996 suggests that the pattern of motion is different in LBP and healthy patients, but fail to separate LBP patients needing follow up from those exhibiting degeneration. Our results suggest confirmation of those by Esol, while presenting a novel method for quantifying the different motion patterns.

In the classification portion of this work, the results confirm that ROM is not enough to distinguish pathological severity, as the accuracy was only 60%. Using only the coefficients, which quantify differing motion patterns, the classifier achieved 95% accuracy. Though ROM_{LB} displayed a significant difference between patient groups, it is not enough to distinguish pathological severity. In addition all ROM variables are subject to ambiguity in that decreasing ROM may be as much an indicator of age as pathology, with older patients unable to achieve the range of motion of younger patients. In addition, measuring ROM in the direction of motion does not allow quantification of the effect lumbar degeneration has on patient motion.

The relative weakness of C_{AR} as a distinguishing variable may be due to some biomechanical factors, but in this study, the more significant effect is likely due to experimental limitations. It is probable that the increased uncertainty for the axial rotation is due to the smaller ROM being measured for the axial activity (3–6° ROM for axial rotation, as opposed to 10–12° for other motions) and the resolution of the 3D–2D registration method, leading to increased variance. Also, measurement of the axial rotation is error-prone, as the images are acquired for frontal and lateral views, making small changes in the rotation difficult to detect. Still, the overall trend of increasing values with pathological severity still exists despite this limitation, suggesting that with improved measurement methods, C_{AR} should still be included in future studies. All measured coefficients imply a relationship between pathology and motion which has not been reported in literature, that the ratio of out-of-plane motion to in-plane motion increases with pathological severity. Additionally, if an approximation can be made of the coefficients in a clinical setting, then the potential to avoid unnecessary treatment may be realized.

The data presented in this work may also provide insight into which patient motions are affected by lumbar degeneration, providing a framework for researchers and clinicians to narrow the focus of kinematic studies, thereby preventing the patient from undergoing unnecessary, and often painful, movements. This work was limited by the small sample size, and does not accurately reflect the general population in terms of disease percentages, age, or ethnicity. Follow up studies should focus on increasing sample size to better understand the relationships between the measured coefficients. These studies should include measurement of the C_{AR} variable. Despite having no significant difference between patient groups, the variable suggests the same trend as the other two coefficients. Due to the smaller range of motion present in the rotation activity, it is suggested that the fluoroscopic images be acquired with improved resolution to reduce registration error. Also, the frames chosen for registration in this work represent large intervals of the motion, and it is known that the instantaneous helical axis (IHA) can migrate over large distances across even small intervals of motion (Haberl et al., 2004; Kettler et al., 2004; Mansour et al., 2004; Rousseau et al., 2006; Wachowski et al., 2009). The precision required for measuring IHA accurately in an *in vivo* setting is not feasible given current registration accuracy and frame rate. With this in mind, future studies of *in vivo* kinematics should register 3D models to smaller intervals of the activity, providing increased resolution of the motion in the time domain.

The mechanism which affects the motion is not fully understood, and more work should focus on analysis of MRI or CT to determine if the tissues involved in motion display differences between diseased and healthy patients. Also, classification may be improved by use of additional features, such as EMG readings, as the differences in patient motion may be identifiable by changes in muscle activation patterns. Any additional measurements which can compactly quantify patient motion could potentially be a useful feature as input into the classification scheme. In deciding which groups the data should be classified into, the binary classifier provides clinically relevant data from a pathological perspective. It could be of potential use to divide LBP and Healthy patients, to differentiate fraudulent claims of LBP, resulting in a 3-class classification scheme. There is little clinical motivation for differentiating Degen and PreOp patients, as they will undergo diagnostic imaging as part of the clinical evaluation for pathological patients.

Conflict of interest statement

There is no potential conflict of interest. None of the authors received or will receive direct or indirect benefits from third parties for the performance of this study.

Acknowledgments

References

Castro, W.H., Sautmann, A., Schilgen, M., et al., 2000. Noninvasive three-dimensional analysis of cervical spine motion in normal subjects in relation to age and sex: an experimental examination. Spine 25, 443–449.

Deyo, R.A., Mirza, S.K., Martin, B.I., 2006. Back pain prevalence and visit rates: estimates from U.S. national surveys, 2002. Spine 31, 2724–2727.

Esola, M.A., McClure, P.W., Fitzgerald, G.K., et al., 1996. Analysis of lumbar spine and hip motion during forward bending in subjects with and without a history of low back pain. Spine 21, 71–78.

Haberl, H., Cripton, P.A., Orr, T.-E., et al., 2004. Kinematic response of lumbar functional spine units to axial torsion with and without superimposed compression and flexion/extension. European Spine Journal 13, 560–566.

Hart, L.G., Deyo, R.A., Cherkin, D.C., 1995. Physician office visits for low back pain. Frequency, clinical evaluation, and treatment patterns from a U.S. national survey. Spine 20, 11–19.

Heneghan, N.R., Hall, A., Hollands, M., et al., 2009. Stability and intra-tester reliability of an in vivo measurement of thoracic axial rotation using an innovative methodology. Manual Therapy 14, 452–455.

Jarvik, J.G., Hollingworth, W., Martin, B., et al., 2003. Rapid magnetic resonance imaging vs radiographs for patients with low back pain: a randomized controlled trial. Journal of the American Medical Association 289, 2810–2818.

John, G.H., Langley, P., 1995. Estimating continuous distributions in Bayesian classifiers. In: Proceedings of the Eleventh Conference on Uncertainty in Artificial Intelligence.

Jordan, K., Dziedzic, K., Jones, P.N., et al., 1999. The reliability of the three-dimensional FASTRAK measurement system in measuring cervical spine and shoulder range of motion in healthy subjects. Rheumatology 39, 382–388.

Jordan, K., Dziedzic, K., Mullis, R., et al., 2001. The development of three-dimensional range of motion measurement systems for clinical practice. Rheumatology 40, 1081–1084.

Katz, J.N., 2006. Lumbar disc disordered: socioeconomic factors and consequences. Journal of Bone and Joint Surgery (American) 88, 21–24.

Kettler, A., Marin, F., Sattelmayer, G., et al., 2004. Finite helical axes of motion are a useful tool to describe the three-dimensional in vitro kinematics of the intact, injured and stabilised spin. European Spine Journal 13, 553–559.

Kononenko, I., 2001. Machine learning for medical diagnoses: History, state of the art and perspective. Artificial Intelligence in Medicine 23, 89–109.

Lee, R.Y.W., Laprade, J., Fung, E.H.K., 2003. A real-time gyroscopic system for 3-D measurement of lumbar spine motion. Medical Engineering and Physics 25, 817–824.

Li, G., Wang, S., Passias, P., et al., 2009. Segmental in vivo vertebral motion during functional human lumbar spine activities. European Spine Journal 18, 1013–1021.

Littlewood, C., May, S., 2007. Measurement of range of movement in the lumbar spine—what methods are valid? A systematic review. Physiotherapy 93, 201–211.

Liu, F., 1997. Theoretical modeling and experimental validation of in vivo mechanics for subjects having variable cervical spine conditions. Diss. University of Tennessee, Knoxville.

Lurie, J.D., Birkmeyer, N.J., Weinstein, J.N., 2003. Rates of advanced spinal imaging and spine surgery. Spine 28, 616–620.

Mansour, M., Spiering, S., Lee, C., et al., 2004. Evidence for IHA migration during axial rotation of a lumbar spine segment by using a novel high-resolution 6D kinematic tracking system. Journal of Biomechanics 37, 583–592.

Mitchell, T., 1997. Machine Learning. McGraw Hill.

Mahfouz, M.R., Hoff, W.A., Komistek, R.D., et al., 2003. A robust method for registration of three dimensional knee implant models to two dimensional fluoroscopy images. IEEE Transactions on Medical Imaging 22, 1561–1574.

Nattrass, C.L., Nitschke, J.E., Disler, P.B., et al., 1999. Lumbar spine range of motion as a measure of physical and functional impairment: an investigation of validity. Clinical Rehabilitation 13, 211–218.

Rousseau, M.A., Bradford, D.S., Hadi, T.M., et al., 2006. The instant axis of ration influences facet forces at L5/S1 during flexion/extension and lateral bending. European Spine Journal 15, 299–307.

Syed, F.I., Oza, A.L., Vanderby, R., et al., 2007. A method to measure cervical spine motion over extended periods of time. Spine 32, 2092–2098.

Wachowski, M.M., Mansour, M., Lee, C., et al., 2009. How do spinal segments move? Journal of Biomechanics 42, 2286–2293.

Wang, S., Passias, P., Li, G., Li, G., Wood, K., 2008. Measurement of vertebral kinematics using noninvasive image matching method-validation and application. Spine 33, E355–E361.

Wong, K.W., Luk, K.D.K., Leong, J.C., et al., 2006. Continuous dynamic spinal motion analysis. Spine 31, 414–419.

Woolf, A.D., Pfelger, B., 2003. Burden of major musculoskeletal conditions. Bulletin of World Health Organization 81, 646–656.

Xia, Q., Wang, S., Kozanek, M., Passias, P., Wood, K., Li G. In-vivo motion characteristics of lumbar vertebrae in sagittal and transverse planes. Journal of Biomechanics, 2010 July 20;43(10):1905-9. Epub 2010 April 9.