How Many Trials Are Needed to Estimate Typical Lumbar Movement Patterns During Dynamic X-Ray Imaging?

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Abstract

Dynamic biplane radiographic (DBR) imaging measures continuous vertebral motion during in vivo, functional tasks with submillimeter accuracy, offering the potential to develop novel biomechanical markers for lower back disorders based on true dynamic motion rather than metrics based on static end-range of motion. Nevertheless, the reliability of DBR metrics is unclear due to the inherent variability in movement over multiple repetitions and a need to minimize radiation exposure associated with each movement repetition. The objectives of this study were to determine the margin of uncertainty (MOU) in estimating the typical intervertebral kinematics waveforms based upon only a small number of movement repetitions, and to determine the day-to-day repeatability of intervertebral kinematics waveforms measured using DBR. Lumbar

spine kinematics data were collected from two participant groups who performed multiple trials of flexion–extension or lateral bending to assess the uncertainty in the mean estimated waveform. The first group performed ten repetitions on the same day. Data from that group were used to estimate MOU as a function of the number of repetitions. The second group performed five repetitions on each of two separate days. MOU was not only movement-specific, but also motion segment-specific. Using just one or two trials yielded a relatively high MOU (e.g., >4 deg or 4 mm), however, collecting at least three repetitions reduced the MOU by 40% or more. Results demonstrate the reproducibility of DBR-derived measurements is greatly improved by collecting at least three repetitions, while simultaneously minimizing the amount of radiation exposure to participants.

Introduction

Low back disorders (LBD) are one of the most significant causes of years lived with disability worldwide, ranking first amongst musculoskeletal disorders [1]. Although low back pain is complex and multifactorial, identification of abnormal kinematics is an accepted basis for clinical decision-making [2–5]. However, current kinematics-based metrics for diagnosis of lower back disorders are based primarily on static imaging modalities such as lateral X-ray images or supine MRI [5–8]. At best, these modalities provide linear, scalar, or discrete values such as end range of motion (ROM) and fixed center of rotation (COR) [9–12]. While useful, they remain inadequate to comprehensively capture nonlinear kinematic waveform patterns that occur during everyday movements and may differentiate between healthy and symptomatic cohorts [13,14].

Recent dynamic X-ray imaging-based studies have demonstrated the ability to directly and precisely measure continuous vertebral motion patterns during in vivo, functional tasks [13–19]. Further, they have also demonstrated the ability to reveal important kinematic pattern-related information during functional motion, particularly midrange motion, which cannot be captured with static imaging protocols, and could be critical for accurately assessing the nature and extent of the mechanical ~~mechanisms~~factors associated with lower back disorders [14,20–24]. These studies have raised the possibility of developing novel biomechanical markers for low back disorders based on dynamic motion rather than static metrics based on end range positions.

Some of the challenges to developing and standardizing such biomechanical markers lie in quantifying the variation in the measured waveform data with the appropriate statistical tools [25–27]. Beyond errors related to the measurement technique, one must contend with the variation inherent in human movement, even within the same individual performing the same overall task multiple times [28,29]. To address this issue, researchers routinely characterize a *typical* kinematic waveform as a mean function of the waveforms obtained from multiple trials, and then describe the variability therein. While, in general, more trials should improve the estimate of a *typical* waveform, conducting multiple trials within a radiographic measurement system proportionally increases radiation exposure. Hence, it is important to know, in advance, how many trials would be required to estimate a *typical* kinematic waveform with a known margin of uncertainty (MOU), and vice versa. A quantitative framework based on the as low as reasonably achievable (ALARA) principle to achieve such an optimal balance between reliability of dynamic X-ray imaging-based estimate, and additional radiation-

related risk is lacking. Furthermore, the day-to-day variability in kinematics waveforms measured by biplane radiography remain unknown. It is necessary to quantify these variations in movement patterns prior to integrating this technology into the clinical decision-making process.

Conventionally, linear metrics such as standard deviation, reliability coefficient [30], and interclass correlation [31] have been employed to quantify the uncertainty in a mean estimate. However, those methods are only applicable for estimating uncertainty in discrete points along a waveform. Although they can be adapted to continuous waveform data, if applied pointwise without considering the entire waveform simultaneously, such methods could yield *anticonservative* results: i.e., inferred confidence bands for the estimated typical waveform for a given significance level may be too narrow [32].

To account for this limitation, Degras (2017) [32] recently presented the concept of Simultaneous Confidence Bands, which is an approach for estimating the *typical* waveform—or mean function—and the variation therein by simultaneously considering the entire waveform, including the correlation between the data points constituting the waveform at various "time-points." The approach quantifies uncertainty in the estimate of the *typical* waveform based on limited trial data to enable simultaneous inferences on the whole waveform. The ability to assess a margin of uncertainty (MOU) for a typical waveform estimate with this approach, and a comparison to conventional pointwise approaches, was recently demonstrated for continuous time-series data involving plantar pressure during gait [33].

In the current study, we apply the method of Simultaneous Confidence Bands to identify MOU over multiple trials for the entire waveform of in vivo, lumbar kinematics data obtained from dynamic biplane radiography. The goals of this study were: (1) to determine the MOU in estimating the typical intervertebral kinematics waveforms based upon the number of repeated movement trials performed by individuals with chronic low back pain and (2) to determine the day-to-day repeatability in lumbar spine kinematics waveforms using biplane radiography.

Methods

Research Participants.

We recruited 20 (14 male, 6 female) participants ages 31 to 73 years (Table 1), and divided them into two groups. The first group of 10 individuals, recruited to assess the MOU of a typical waveform pattern from multiple repetitions, performed 10 repetitions of the same movement on the same day. Of these, five performed flexion–extension and five performed lateral bending movements. In the second group of 10 individuals, 5 performed flexion–extension and 5 performed lateral bending for 5 repetitions of the same movement on two separate days, with testing separated by 2 to 7 days. Participants were tested between 8:00 am and 12:30 pm. The mean (±95% confidence interval) difference in time of testing between day 1 and day 2 for each participant in the second group was 87 (±33) min. All participants reported chronic low back pain, defined as pain lasting longer than 12 weeks and a pain persistence of more than 50% of the time in the last 6

months [34]. Pain intensity scores were recorded based on PROMIS (patient reported outcomes measurement information system; scale 0–10) and VAS (visual analog scale; scale 1–100). Participants were excluded if they were younger than 30 years or older than 75 years, if they had a BMI greater than 34 kg/m^2, if they were pregnant, or if they had previous surgery on the lumbar spine. All participants provided informed consent prior to participating in this IRB-approved study (STUDY19120001).

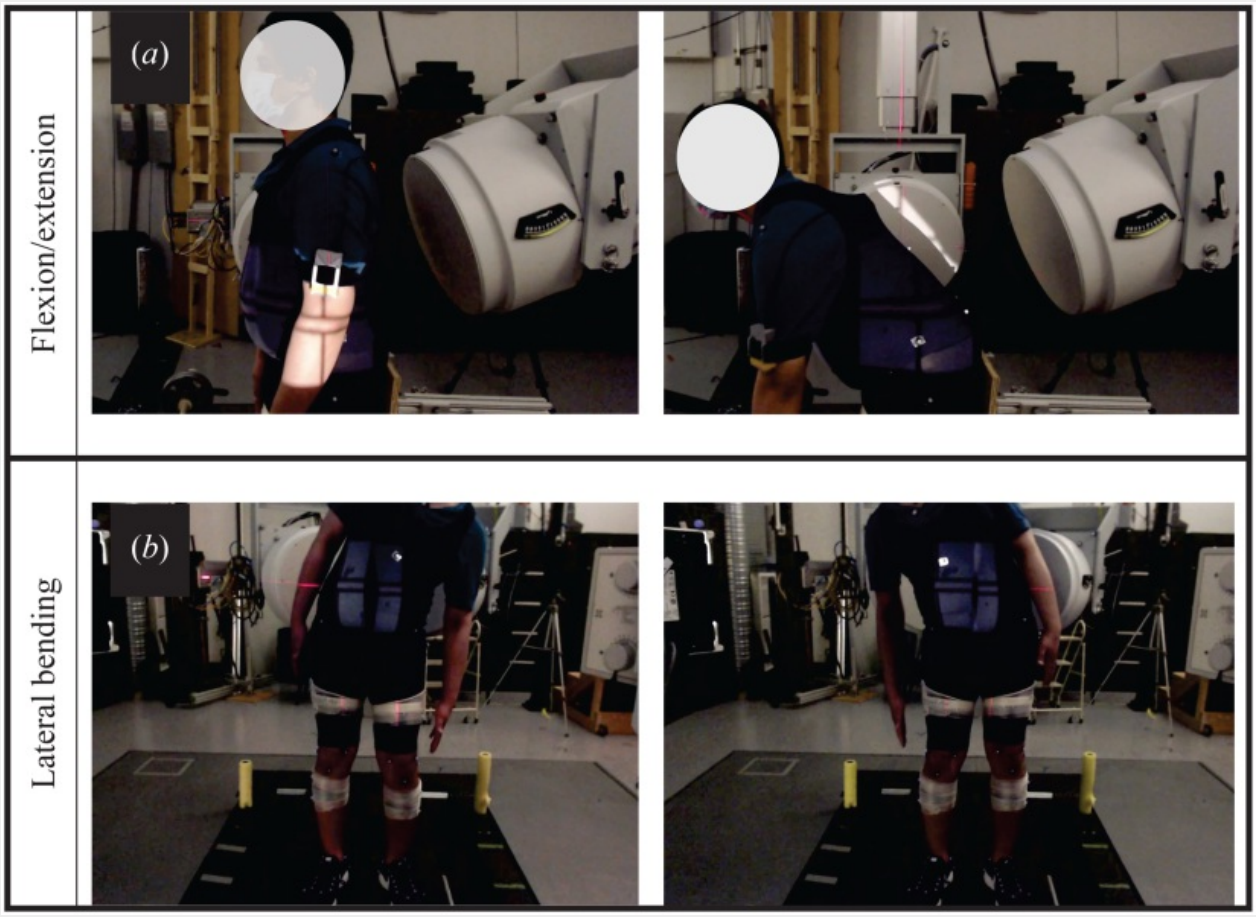
Table 1 Age, height, weight, and BMI of recruited participants. Mean (±standard deviation)

Age (years)	Height (cm)	Weight (kg)	BMI
52 ± 16	177 ± 8	89.5 ± 11.6	28.6 ± 3.2

Movement Tasks and Data Collection.

Participants were positioned with their low back centered within a biplane radiographic imaging system (Fig. 1). Starting from a standing, upright pose, participants performed continuous, repeated trunk flexion and extension (FE) movements (Fig. 1(*a*)) without any knee bending. For the lateral bending (Fig. 1(*b*)), participants slid their hand down the side of their leg while performing continuous sideways bending from left to right with explicit instructions not to rotate or tilt their pelvis.

Fig. 1 Photos showing two instants of the continuous flexion/extension (above) and lateral bending (below) movements performed within the biplane radiographic imaging system



Data acquisition occurred once the participant achieved a steady movement pace (usually the 2nd or 3rd continuous repetition). Synchronized biplane radiographs were then captured at 30 images per second for 2 s to obtain data for one trial (85 kV, 320 mA, 4 ms exposure per pulse). For the flexion–extension movement, images were captured during the extension portion of the movement and for the lateral bending movement, images were captured as the participant moved from their left to right. Ten such trials were recorded for each participant in the first group. Five such trials were recorded for each participant in the second group on each of their two test dates. Concurrently, conventional optical motion capture was used to obtain overall trunk motion (12-camera Vicon Vantage V5 system, Vicon Motion Systems Inc., Oxford, UK). Following successful data acquisition with the biplane radiographic system, a computed tomography (CT) scan of the participants' lumbar spine was obtained using a GE Discovery CT750 HD CT Scanner (GE Medical Systems, Waukesha, WI) with a slice thickness of 0.625 mm and an in-plane resolution of 0.305 mm x 0.305 mm. The original CT images were resliced to create 0.305 mm cubic voxels. Each vertebra was segmented from the resliced CT images to create 3D bone models using Mimics 24.0 (Materialise Inc., Ann Arbor, MI).

The maximum effective radiation dosage from the dynamic radiographic imaging was 6.4 mSv or 9.9 mSv for 10 movement trials of flexion/extension or lateral bending, respectively (estimated using pcxmc software, STUK, Helsinki, Finland), while the average effective radiation dose from CT was 20.5 ± 5.4 mSv.

Data Processing and Analysis.

Vertebral motion was tracked using a validated markerless volumetric model-based tracking system that matched digitally reconstructed radiographs created from subject-specific CT-based bones to the biplane radiographs (Fig. 2) with an in vivo-validated precision of 0.5 deg and 0.3 mm [14]. Anatomic coordinate systems were defined for each vertebra by three mutually orthogonal axes located in the center of the vertebral body. in vivo 6 DOF continuous segmental kinematics (three ordered rotations and three translations) were calculated from the tracked vertebral motion and expressed as the relative motion of the superior vertebra with respect to the adjacent, inferior vertebra for L12, L23, L34, and L45 motion segments. Multiple movement trials were synchronized based upon overall trunk-pelvis motion kinematics calculated in vicon nexus 2.11 (Vicon Motion Systems Inc., Oxford, UK). For the flexion–extension movement, the sagittal plane rotation (extension) and anterior-posterior (AP) translations for each segment were plotted against the overall trunk extension rotation. For the lateral bending movement, segmental lateral bending rotation and medial-lateral (M–L) translations were plotted against overall trunk lateral (left-right) bending.

Fig. 2 Data collection and data processing workflow. (*a*) Participants performed flexion/extension or lateral bending within the biplane imaging system. (*b*) Synchronized biplane radiographs were collected at 30 Hz. (*c*) Subject-specific 3D bone models of the lumbar vertebrae were created from high-resolution CT scan. (*d*) Landmarks were placed on the 3D bone models to establish an anatomical coordinate system. (*e*) A previously validated volumetric matching process was used to track 3D bone motion using an automated algorithm to maximize the correlation between the Digitally Reconstructed Radiographs (DRR) and the distortion corrected biplane radiographs. (*f*) Joint kinematics were calculated according to the anatomical coordinate systems and bone motion.

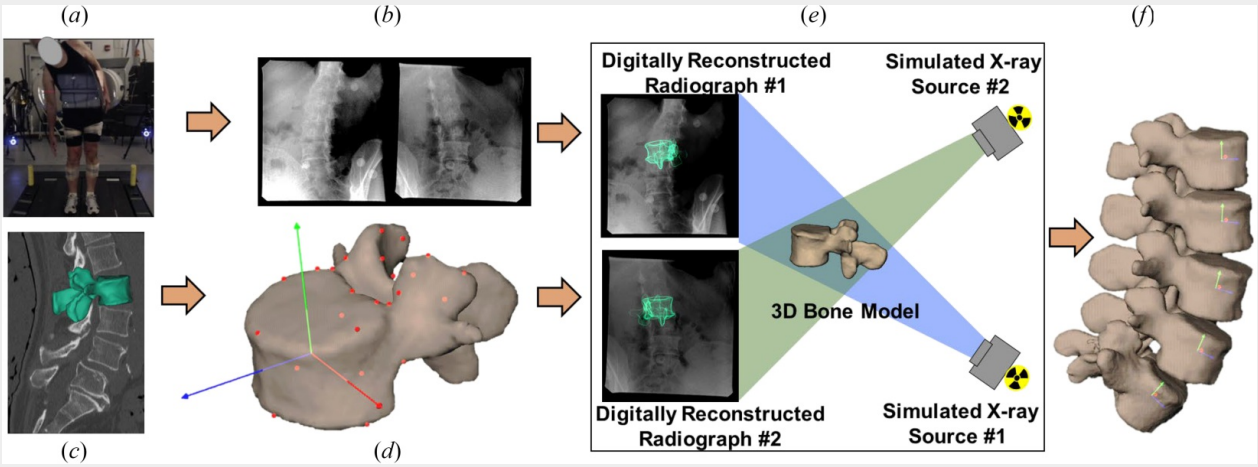
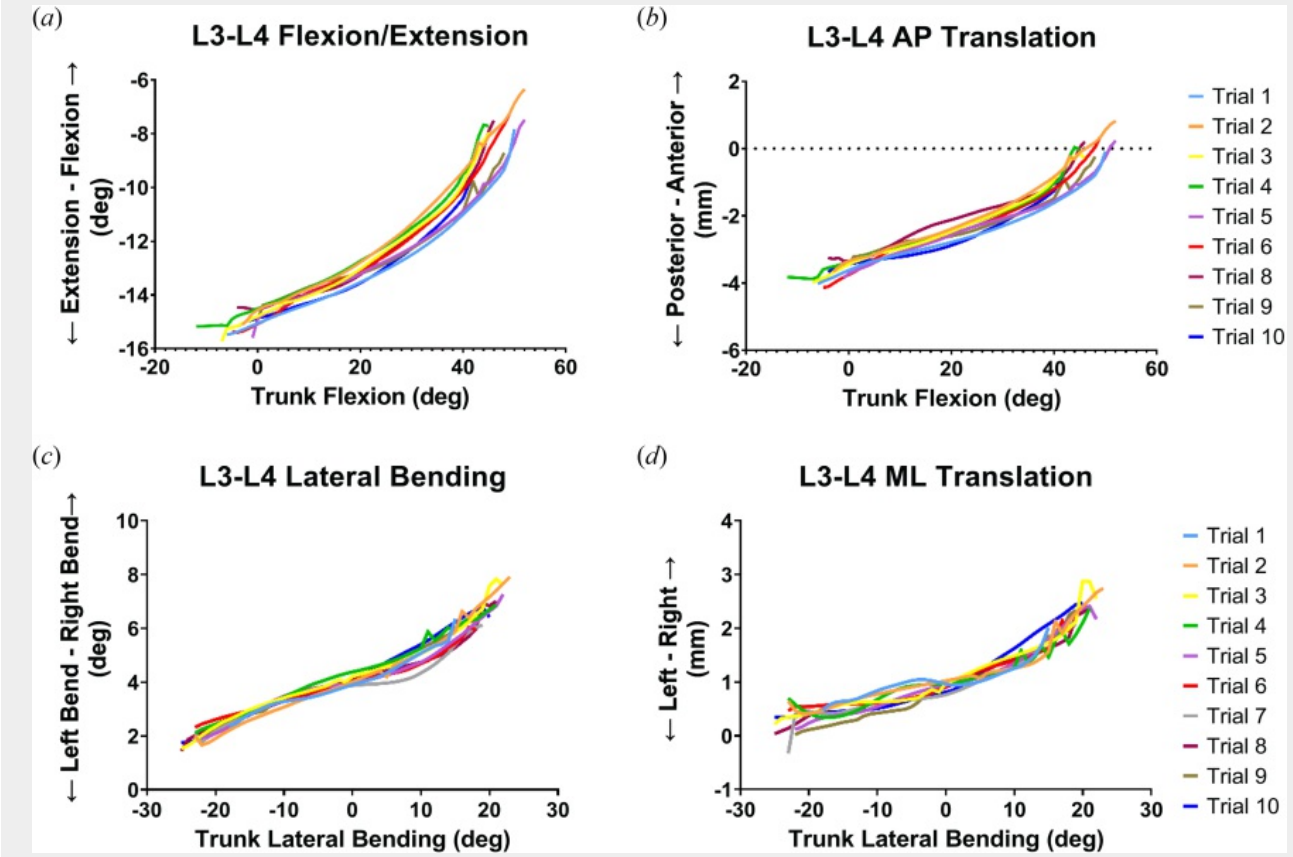


Fig. 3 Representative plots of a single participant's L34 segmental (*a*) flexion–extension, (*b*) AP translation, and another participant's (*c*) lateral bending and (*d*) ML translation, plotted against overall trunk extension ((*a*) and (*b*)) and lateral bending ((*c*) and (*d*)) movements. Note for (*a*) and (*b*): Data were recorded during the extension phase of the flexion–extension movement starting from trunk-flexed pose and continued until the participant reached the upright position, so movement proceeded from right to left along the horizontal axis, i.e., from ~50 deg trunk flexion toward ~0 deg trunk flexion. The "negative" intervertebral angle plotted on the vertical axis reflects the lordosis at the L3–L4 motion segment during the trunk flexion–extension movement.



Statistical Analysis.

A mean function, or typical waveform and its variation expressed as a confidence band, were constructed in the form of simultaneous confidence bands [32] separately for intervertebral extension and AP translation for the extension movement, and intervertebral lateral bending and M-L translations for the lateral bending movement for each of the lumbar segments: L12, L23, L34, and L45 as follows:

$$\text{Confidence band} = \hat{\mu}\left(t\right) \pm w \times \frac{\hat{\sigma}(t)}{\sqrt{n}}$$

where $\hat{\mu}(t)$ = mean; $\hat{\sigma}(t)$ = standard deviation of a waveform at time "t" estimated from "n" trials; w = percentile of a process accounting for the correlation among points of the waveform at different times.

Given "n" trials per subject, and defining $\tilde{\sigma}(t)$ as the pooled intrasubject standard deviation from the "N"subjects, the margin of uncertainty is then calculated as

$$\mathrm{MOU} = \max_t \tilde{\sigma}\left(t\right) \times \frac{w}{\sqrt{n}}$$

Thus, although the study intended to focus on intrasubject variability—occurring when a volunteer repeats the same prescribed motion *(n ≤ 10)*—it also implicitly considers the intersubject variability *(N = 5)*. The relationship between MOU and the number of trials (from 1 to 10) was calculated using simultaneous confidence bands. The calculation encompassed 50 deg of trunk extension, and 42 deg of trunk lateral bending. This range of motion was chosen for the analysis due to the variations in ROM among participants and included the common movement range across participants.

To assess day-to-day differences in kinematics waveforms, mean waveforms were calculated for each day using one trial, then two trials, and so on, up to five trials, using all possible combinations of trials for each day. The mean difference waveform between day 1 and day 2 was calculated for each possible number of trials (1, 2, …5) as the mean waveform of all possible combinations of differences for the given number of trials. Group means and standard deviations were then computed for these day-to-day differences.

Results

All 20 participants (5 that performed 10 trials of extension on the same day, 5 that performed 10 trials of bending on the same day, 5 who performed 5 trials of extension on two separate days, and 5 who performed 5 trials of bending on two separate days) completed the study. The mean (±95% confidence interval) day-to-day differences for the two measures of pain—PROMIS and VAS—were −0.39 (±1.22; *p*-value = 0.55) and 0.60 (±7.47; *p*-value = 0.88), respectively.

A total of 186 movement trials were included in this analysis. The 14 trials that were excluded due to poor image quality included all 10 trials from one participant, who performed 5 trials of extension on each of two separate days and 4 trials from 3 other participants. Table 2 shows the range of segmental extension and lateral bending recorded and analyzed for this study.

Table 2 Range of segmental extension and lateral bending across trials as participants performed 50 deg of trunk extension and 42 deg of trunk lateral bending

	Extension (deg)	Lateral bending (deg)
Lumbar segment	**Mean (± 95% confidence interval)**	
L12	5.9 (±0.5)	6.7 (±0.9)
L23	6.8 (±0.7)	5.7 (±0.9)
L34	7.3 (±1.0)	3.8 (±0.8)
L45	8.0 (±1.0)	0.6 (±0.1)

Figure 3 is a representative plot displaying kinematic waveform data from 10 trials for the L34 segment of one participant performing extension and another participant performing 10 trials of lateral bending.

The corresponding typical waveform, or mean function, along with the confidence band computed with data from the same-day trials are plotted in Figs. 4(*a*)–4(*d*), respectively. The lighter shaded, wider confidence band is based on three trials while the narrower, darker shaded band is derived from ten trials. Expectedly, availability of data from more trials narrowed the confidence band for the estimated typical waveform.

Fig. 4 Representative mean waveform estimate along with confidence bands of a single participant's L34 segmental (*a*) flexion–extension, (*b*) AP translation, and another participant's (*c*) lateral bending and (*d*) ML translation, plotted against overall trunk extension ((*a*) and (*b*)) and lateral bending ((*c*) and (*d*)) movements. Lighter, wider bands are obtained with data from three trials, while the narrower, darker shaded bands are obtained with ten trials. Note for (*a*) and (*b*): Data were recorded during the extension phase of the flexion–extension movement starting from trunk-flexed pose and continued until the participant reached the upright position, so movement proceeded from right to left along the horizontal axis, i.e., from ~50 deg trunk flexion toward ~0 deg trunk flexion. The "negative" intervertebral angle plotted on the vertical axis reflects the lordosis at the L3–L4 motion segment during the trunk flexion–extension movement.

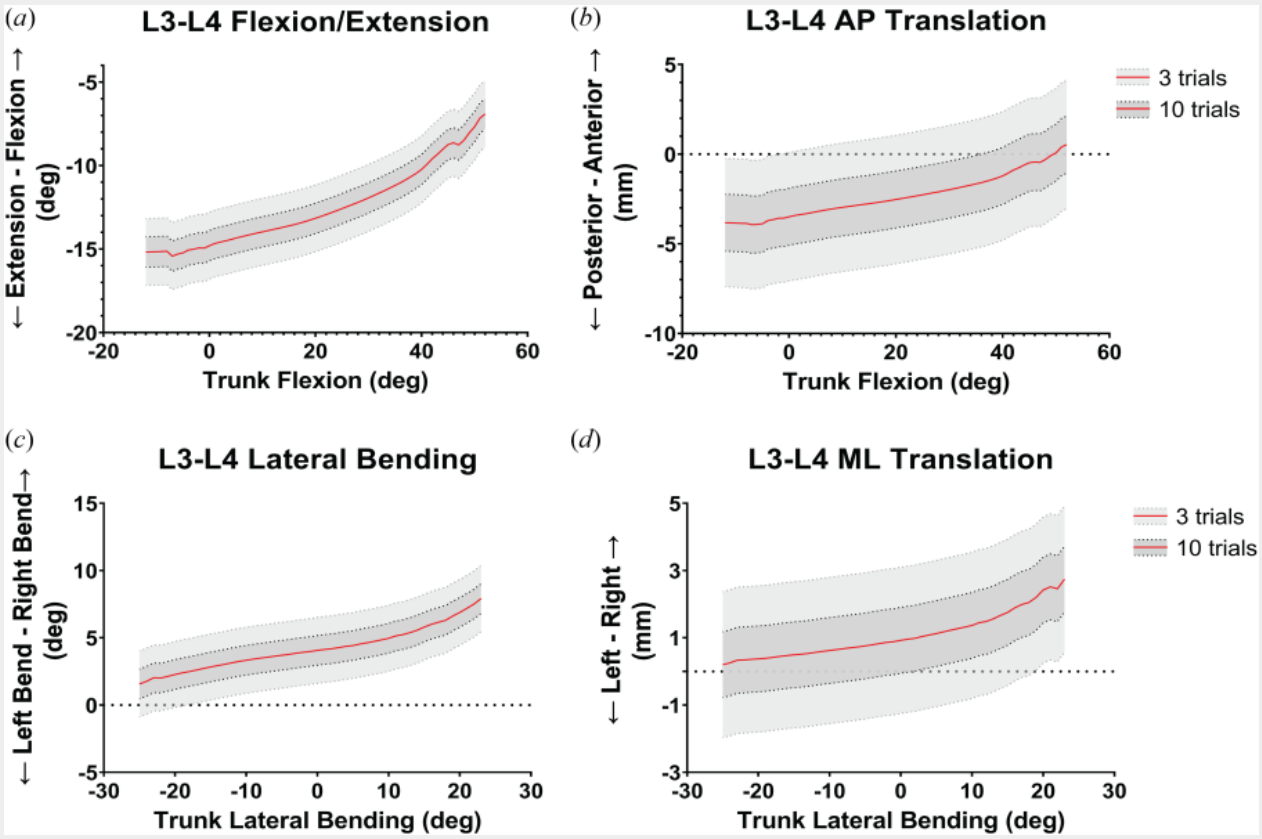


Figure 5 displays the variation of MOU with respect to the number of trials as continuous plots (Figs. 5(*a*)–5(*d*)) for each of the assessed intervertebral segments. Day-to-day differences in mean waveform estimates were less than the error in the measurement system when increasing the number of trials from one to five (Table 3).

Fig. 5 Variation of MOU with respect to number of trials for (*a*) segmental extension, (*b*) AP translation during extension, (*c*) lateral bending, and (*d*) ML translation during lateral bending.

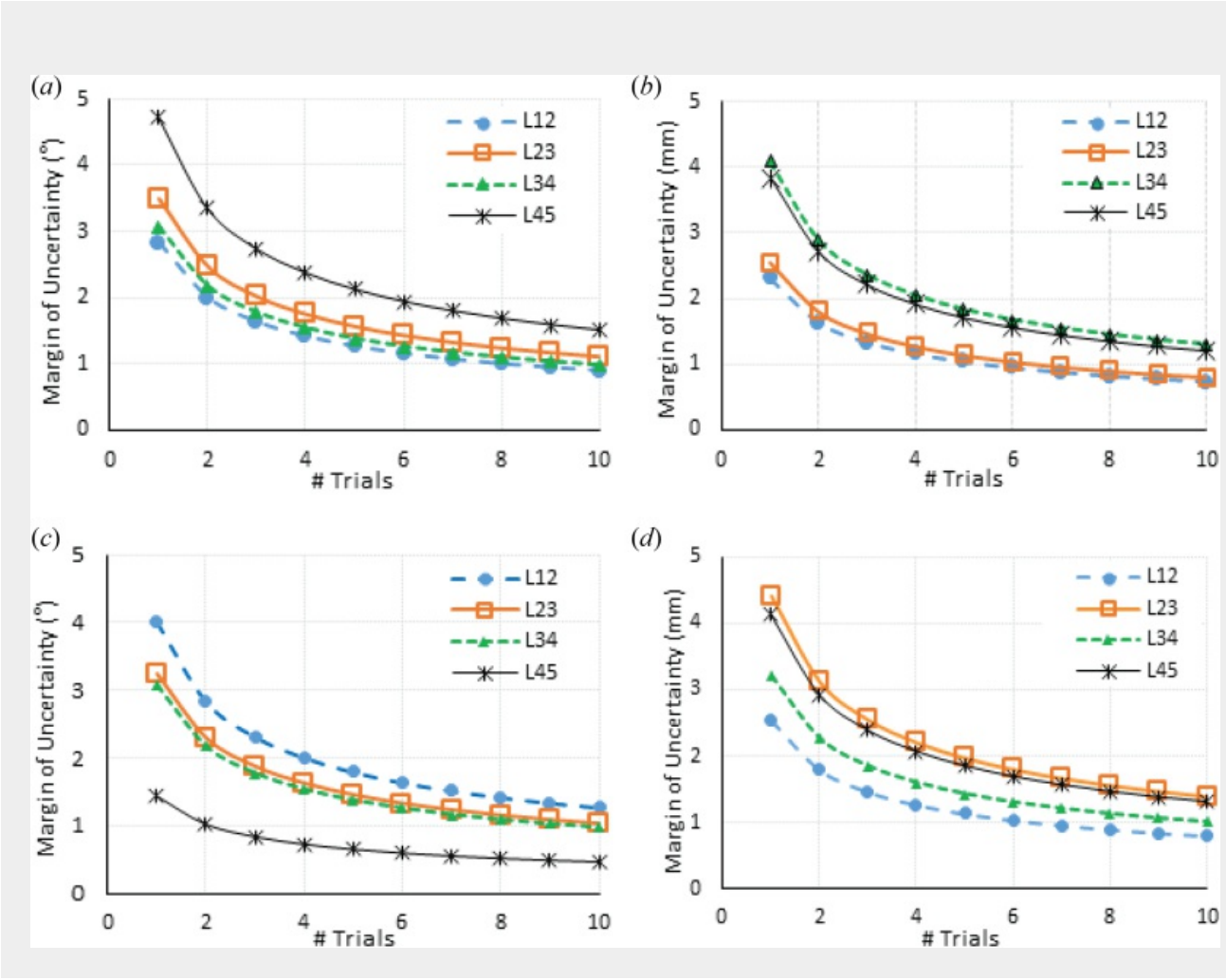


Table 3 Day-to-day differences in mean kinematic waveform estimates based on number of trials

		Cumulative # of trials				
Intervertebral segment	**Kinematic metric**	**1**	**2**	**3**	**4**	**5**
Extension movement		Mean (± standard deviation)				
L12	Extension (deg)	1.6 (0.8)	1.6 (0.8)	1.5 (0.8)	1.5 (0.8)	1.5 (0.8)
AP translation (mm)	0.8 (0.3)	0.8 (0.4)	0.8 (0.4)	0.9 (0.5)	0.9 (0.5)	
L23	Extension (deg)	1.9 (1.0)	1.8 (0.9)	1.7 (0.9)	1.8 (0.9)	1.7 (0.9)
	AP translation(mm)	0.9 (0.4)	0.9 (0.3)	0.8 (0.3)	0.8 (0.3)	0.8 (0.3)
L34	Extension (deg)	1.5 (1.1)	1.3 (1.0)	1.3 (1.0)	1.2 (1.0)	1.2 (1.1)
	AP translation (mm)	1.0 (0.6)	0.9 (0.6)	0.8 (0.6)	0.8 (0.6)	0.8 (0.6)

L45	Extension (deg)	2.1 (1.6)	2.0 (1.6)	1.9 (1.7)	1.8 (1.8)	1.7 (1.8)
	AP translation (mm)	1.0 (0.9)	1.0 (1.0)	0.9 (1.0)	0.9 (1.0)	0.9 (1.1)
Lateral bending movement		Mean (± standard deviation)				
L12	Lat bending (deg)	0.8 (0.3)	0.7 (0.2)	0.6 (0.2)	0.6 (0.2)	0.6 (0.2)
	ML translation (mm)	0.4 (0.3)	0.4 (0.3)	0.3 (0.3)	0.3 (0.3)	0.3 (0.3)
L23	Lat bending (deg)	0.8 (0.3)	0.7 (0.3)	0.6 (0.3)	0.6 (0.3)	0.6 (0.4)
	ML translation (mm)	0.4 (0.3)	0.3 (0.2)	0.3 (0.2)	0.3 (0.2)	0.2 (0.2)
L34	Lat bending (deg)	0.8 (0.4)	0.7 (0.3)	0.6 (0.2)	0.5 (0.2)	0.5 (0.2)
	ML translation (mm)	0.3 (0.1)	0.3 (0.1)	0.2 (0.1)	0.2 (0.1)	0.2 (0.1)
L45	Lat bending (deg)	0.6 (0.2)	0.5 (0.1)	0.5 (0.1)	0.4 (0.1)	0.4 (0.1)
	ML translation (mm)	0.4 (0.1)	0.3 (0.1)	0.3 (0.1)	0.3 (0.1)	0.2 (0.1)

Discussion

The current study was designed to assess the inherent variability in motion patterns of lumbar intervertebral segments during trunk extension and lateral bending movements over multiple trials, and to determine the day-to-day reliability in lumbar spine intervertebral kinematics in individuals with chronic low back pain. Variability over the entire kinematics waveform, rather than at discrete or specific time points within a movement, was assessed using the method of simultaneous confidence bands to quantify uncertainty in terms of margins of error (MOE). This metric provides a simple, but robust method to quantify the uncertainty in the kinematic waveform assessed from a limited number of trials beyond the otherwise known errors arising from the accuracy of the measurement technique. This method of simultaneous inference additionally provides better certainty that the estimated mean waveform lies within the estimated confidence band at *all* time points, compared to methods determining confidence bands based on pointwise inference, which does not guarantee such coverage [32].

Our study found that MOE decreased asymptotically with more trials. Within five trials, MOE decreased by more than 50% of the estimated MOU from two trials, and continued to decrease with increasing trials, albeit with progressively diminishing returns. This pattern was consistent for both the rotation as well as translation curves obtained from extension and bending movements. It does not appear that day-to-day differences are large enough to warrant gathering data from separate days, nor is the day-to-day repeatability improved appreciably by adding additional movement trials.

It is important to note that the measurement accuracy for capturing lumbar kinematics during in vivo functional tasks using dynamic biplane radiography itself has been previously validated to be better than 0.5 deg in rotation and better than 0.3 mm for translation [14]. In comparison, results from this study broadly reveal trial-to-trial variability in kinematic waveforms can be much larger and are significant enough that they must be explicitly considered while estimating typical kinematic patterns. More importantly, identifying markers for

diseases generally involves quantifying a deviation or "aberration" in comparison to a healthy or asymptomatic status. Hence, the inherent variability occurring within specific cohorts must be accounted for when identifying true changes in kinematic waveforms in the presence of pathology [14,19,24].

There was no consistent pattern across the assessed motions with respect to segment-specific MOU. For example, while the mean function could be estimated with a progressively *increasing* MOU from the most cranial to most caudal lumbar motion segment ($MOU_{L12} < MOU_{L23} < MOU_{L34} < MOU_{L45}$) from a given number of trials for extension (Fig. 4(*a*)), no corresponding segment-related pattern was observed for the MOU for lateral bending. For translation, the MOU *decreased* progressively during lateral bending movement from the most cranial to the caudal segment for ML translation ($MOU_{L12} > MOU_{L23} > MOU_{L34} > MOU_{L45}$). In the case of AP translation recorded during the extension movement, the two most caudal segments (L34 and L45) consistently had a larger MOU for a given number of trials compared to the more cranial L12 and L23 segments. This indicates that, for lumbar kinematics, the number of trials required to estimate a typical waveform with a given MOU is not only motion segment-dependent but also metric- and activity- dependent.

Most dynamic X-ray imaging-related studies on the lumbar spine have reported results based on a small number of repetitions (usually ≤ 2) [13–19,31]. This is understandable, given the important health-related constraint of limiting radiation exposure to the participants and the extensive amount of time required to process the data. In this regard, the uncertainty in estimating a typical motion pattern from just one or two trials can be much larger than the stated measurement accuracy of the measurement device or technique. More relevant for identifying disease-related biomechanical markers, limiting inferences to typical waveforms obtained from one or two trials may be insufficient to surpass thresholds for identifying significant differences or changes between healthy/asymptomatic and symptomatic/diseased statuses. However, adding just a few more trials could dramatically decrease the uncertainty (MOU). Such information, when available in advance, can help in designing more rigorous and reproducible studies while simultaneously keeping the radiation exposure to a minimum.

To our knowledge, only one other study has investigated repeatability of lumbar spinal kinematics obtained using dynamic radiation-based imaging [31]. Their results were based on a significantly larger cohort of 109 participants, albeit with just two repetitions per participant—one each on separate days. In contrast to our study, their results were limited to maximum range of motion rather than assessment of variations in continuous waveform patterns. Furthermore, repeatability and reliability were reported based on pooled datasets across all the measured intervertebral joints, either L2–L5 or L2–S1 for left-right bending and flexion–extension motions, respectively. The reported variations in repeatability—computed as minimal detectable change (MDC_{95})—ranged from 45% for anterior disk height measurements to 408% for motion sharing variability, seem larger than those reported in this study. According to our results, these differences may be due to only a single trial recorded each day in the previous study.

The study is not without limitations. Two of these—short interval for day-to-day testing and the radiation

doses—merit further discussion. Although we assessed "short-term" (i.e., several trials on a single day or a few days apart) fluctuations as a confounder of motion patterns, the results may not be easily extendable to quantify variations over longer, clinically relevant periods (e.g., several weeks to several months). This could be considered a limitation. However, the primary aim of this study was to understand how many trials must be recorded to estimate a typical movement pattern, when subjects are tested on any given day to assess their status at that time. This is, typically, the standard for a clinical visit or research study. We added the day-to-day variation, but deliberately limited it to a shorter interval to further investigate if any putative changes from day to day were significant enough to render single day assessments as less relevant, while minimizing effects of changes due to age, physical condition, or therapy. In this regard, the results appear to confirm that the standard of single-day assessments need not be altered. Nevertheless, natural variations over the longer term, if any, need to be better understood. This was, however, beyond the scope of the current study aims. As such, the results should be interpreted within this narrower perspective.

The relatively high radiation doses represent another limitation of the study, with the exposure from CT imaging being the predominant component. There are two aspects to this issue: (a) the necessity of biplane radiographs to improve accuracy of measured datasets for nominally uniplanar motion, and (b) the choice of imaging modality (e.g., CT versus MRI) for generation of the 3D model for subsequent 2D-3D coregistration. With respect to the first aspect, studies have shown that single plane imaging is inaccurate for measuring out of plane motion [35–37]. Although the instruction for our participants was to perform planar movements, it was possible that they might have moved out of plane due to pain or disability. Furthermore, the lumbar vertebrae are often noncollinear in the coronal plane, which leads to inaccuracy when making measurements in a single sagittal image. Ignoring these can increase the inaccuracy in the assessment of the primary degree-of-freedom. Biplanar radiography ensures maximum accuracy for the 6DOF kinematics. With regard to the second point, although CT imaging provides the most accurate 3D models for the coregistration step, other modalities such as MRI could be an attractive alternative. Nevertheless, several studies have demonstrated that bone models based upon MRI imaging do not match CT-based bone models [38–40]. Additionally, our registration process is density based, not silhouette based, so the bone density variation assists in improving the registration. Bone density is obtained directly from the CT scan after performing a slice-by-slice density correction based upon a bone density phantom. MRI sequences to accurately estimate bone density are still under development.

Further limitations are as follows. We did not explicitly assess the effects of health status, type of low back disorder or age in this study. Hence, the results for lumbar intervertebral kinematic waveforms for extension and lateral bending movements reported here may vary for different cohorts based on health status, pathology, and age. Although we recruited male and female patients, we did not explicitly assess the effect of sex as a variable on the inherent variability observed in the kinematic waveform patterns. The age (>30) and (slightly higher) BMI of the participants may not be fully representative of the general population, but they are representative of patients with chronic lower back pain [41]. Nevertheless, the study emphasizes assessment of variability in kinematic waveforms in this cohort, rather than claiming the reported kinematic patterns to be representative of this patient population. The latter claim would require a larger sample size of participants. Finally, the current results are specific to the joints—lumbar intervertebral joints—and movements—flexion–

extension and lateral bending—investigated in this study. Although the methodology is transferable, the procedure described here will need to be repeated for other cohorts, joints, and activities to identify the optimal number of repetitions needed to balance MOU and radiation exposure for those specific situations.

In conclusion, this study applies a recently described methodology [32,33] to quantify intrasubject variability in intervertebral kinematics waveforms while performing functional lumbar movements. The simple yet comprehensive parameter of margin of uncertainty (MOU), as obtained with the Simultaneous Confidence Bands technique, provides the researcher an objective metric to determine the relationship between the number of trials collected and the accuracy of the typical waveform estimate, and to balance the need for minimizing radiation exposure from the data acquisition process with a requirement for meaningful, clinically relevant datasets.

Margin of uncertainty in characterizing the typical kinematic waveform decreases significantly when results from more than two repeated trials are taken into consideration. The day-to-day variability observed in this study was small enough to accept data collected from a single day's trials as sufficiently representative of the motion pattern. From a clinical perspective, the MOU in estimating typical kinematic waveforms must be taken into account, in addition to the validated measurement system accuracy, when assessing the clinical impact of study results. For example, a given treatment or intervention may yield statistically significant differences in the estimated kinematic waveform, but the size of the effect must be evaluated within the context of the corresponding MOU.

Data Availability Statement

The datasets generated and supporting the findings of this article are obtainable from the corresponding author upon reasonable request.

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