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A Dynamic Optimization Approach for Solving Spine Kinematics while Calibrating
Subject-specific Mechanical Property

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4. Abbreviated title

Optimization to Solve Kinematics and Calibrate Property

A Dynamic Optimization Approach for Solving Spine Kinematics while Calibrating Subject-Specific Mechanical Property

Abstract-This study aims to propose a new optimization framework for solving spine kinematics based on skin-mounted markers and estimate subject-specific mechanical properties of the intervertebral joints. The approach enforces dynamic consistency in the entire skeletal system over the entire time-trajectory while personalizing spinal stiffness. 3D reflective markers mounted on ten vertebrae during spine motions were measured in ten healthy volunteers. Biplanar X-rays were taken during neutral stance of the subjects wearing the markers. Calculated spine kinematics were compared to those calculated using inverse kinematics (IK) and IK with imposed generic kinematic constraints. Calculated spine kinematics compared well with standing X-rays, with average root mean square differences of the vertebral body center positions below 10.1 mm and below 3.38° for joint orientation angles. For flexion/extension and lateral bending, the lumbar rotation distribution patterns, as well as the ranges of rotations matched *in vivo* literature data. The approach outperforms state-of-art IK and IK with constraints methods. Calculated ratios reflect reduced spinal stiffness in low-resistance zone and increased stiffness in high-resistance zone. The patterns of calibrated stiffness were consistent with previously reported experimentally determined patterns. This approach will further our insight into spinal mechanics by increasing the physiological representativeness of spinal motion simulations.

Keywords- Force-dependent Optimization, Kinematics redundancy, Parameter estimation, Spinal stiffness, Spine

INTRODUCTION

Evaluating human movement kinematics is essential in biomechanical analysis. Joint kinematics are also a primary input for most kinematics-driven models to compute joint loading and muscle forces⁶. However, although dedicated musculoskeletal models of the spine have been developed (e.g.,²), such analyses have only been used to a limited extent to analyze spine loading during movement. This is due to difficulties to measure accurate intervertebral motions caused by many degrees-of-freedom (DoF) of the spine as well as the relatively small motion of individual vertebrae.

Different approaches have been used to estimate spinal kinematics as accurately as possible. Medical imaging approaches are often regarded as gold standard as they can provide detailed geometric information. However, most imaging approaches are either limited by two-dimensional information (e.g., static X-rays and dynamic fluoroscopy ¹) or by restricted postures (e.g., CT, biplanar fluoroscopy and MRI), failing to capture three-dimensional (3D) dynamic motions (e.g., gait). Therefore, motion capture techniques combined with marker-based inverse kinematics (IK) are commonly used for estimating motions as these are non-invasive, flexible, and minimally interfering with activities of daily living. The IK method estimates the pose of the spine by minimizing the error between modeled marker positions based on a kinematic model and measured marker positions at each time frame (least square minimization). Given the high kinematic redundancy in the spine, accurate estimation of intervertebral joint kinematics is very challenging; space constraints on the spine prevent placement of sufficient reflective markers on the spine to capture all DoFs of the intervertebral joints. Skin artefacts during dynamic motions make it even harder to track the often small intervertebral joint displacements ³⁰. Therefore, to reduce the number of DoFs, constraints imposing constant ratios between lumbar kinematic variables have been suggested. In such approaches, the estimated intervertebral joint rotations are proportional to the overall lumbar rotations and coupled to another (IK + constraints), and translational DoFs are typically locked ³. However, these constraints represent an oversimplification as it is known from imaging studies that the distribution of total lumbar rotations over the different vertebral levels is motion-dependent as it changes with trunk rotation, lumbar posture, and loading ^{1, 23}.

IK methods only account for kinematic constraints, whereas optimization-based methods enable imposing additional dynamic constraints ²³. Marra *et al.* ¹⁴ proposed an approach called force-dependent kinematics to improve the estimation of secondary knee kinematics, i.e. the DoFs with a small ROM (e.g., knee translations). Secondary kinematics are iteratively updated until quasi-static force equilibrium between contact, muscle and ligament forces is reached. However, this method is not applicable for estimating both rotational and translational spine kinematics as both of them need to be determined ¹⁰. Shojaei *et al.* ²³ proposed an alternative optimization approach where the lumbar rotations are updated by minimizing the sum of squared lumbar muscle stresses, while neglecting lumbar translations.

However, the rotations are calculated based on a heuristic procedure that relies on multiple local optimization problems that each accounts for inverse skeleton dynamics and muscle force equilibrium for each spinal level independently. This approach does not guarantee **dynamic consistency in the entire skeletal system**. Another drawback of both above-described methods ^{14, 23}, as well as of most other optimization studies on spine kinematics (e.g., ¹⁰), is that they only account for static force equilibrium and thus estimate kinematics at each time frame independently. As a result, there is no **dynamic consistency over the entire time trajectory** which will influence kinetic analysis as it has been demonstrated that kinetic predictions and load-related calculations are sensitive to errors in static kinematic measurements ⁶. Finally, in previous studies (e.g., ^{10, 23}), the input information on bone positions for solving spine kinematics commonly originated from static medical images, therefore restricting evaluation of dynamic motion compared to marker-based measurements. To our knowledge, no studies analyzed the effect of accounting for dynamic consistency throughout the entire spine motion neither through marker-based nor medical imaging-based kinematic analysis.

None of the above-described methods for estimating spine kinematics account for the mechanical properties of the intervertebral joint, which play an important role in constraining spine motion. Given the high stiffness of the intervertebral joints, their mechanical properties largely determine joint kinematics ¹⁴. Moreover, these mechanical properties are highly subject-specific. In our previous work ²⁶, we already implemented physiological functional spinal units with comprehensive nonlinear stiffness properties into a rigid-body model of the full thoracolumbar spine, containing different parameter sets that account for differences in *in vitro* specimens. However, preknowledge of physiological conditions are not always available, thereby preventing a proper selection of stiffness parameter set. Petit *et al.* ²⁰ developed a method to calibrate stiffness properties. In their approach, the model's mechanical properties are adjusted to minimize the difference between simulated and measured spinal curvature angles during maximal voluntary lateral bending. However, this approach does not account for the dynamic properties of the movement and the high nonlinearity of intervertebral stiffness. Furthermore, stiffness calibration was limited to three sets of generic stiffness for all seventeen levels of the spine between T1 and L5. To

appropriately account for the influence of spine stiffness on intervertebral movement, there is a need for calibrated stiffness properties for each individual intervertebral DoF.

This study proposes a dynamic optimization approach to **estimate spine kinematics from trajectories of skin-mounted markers while simultaneously calibrating spine stiffness by enforcing the dynamic consistency of the movement**. As such, this study aims to improve the accuracy of estimates of dynamic spine motion based on 3D motion capture data by imposing dynamic equilibrium over the entire skeletal system and the entire movement cycle. **The estimated spinal kinematics were evaluated against kinematic estimations obtained from state-of-the-art IK methods, with and without generic kinematic constraints as well as standing bi-planar radiographs (gold truth) and published *in vivo* reference values.**

Materials and Methods

Measurements

Spinal motions of ten healthy subjects (three males, seven females) were measured by an optical tracking system (VICON, UK). The mean (standard deviation (SD)) age, height and weight of the subjects were 67.85 (6.95) years, 1641.4 (73.4) mm and 60.37 (15.45) kg respectively. Measured motions included (1) static neutral upright stance, (2) full range of spine flexion/extension (F/E) while seated, with hands crossed over the back of head to keep an upright upper trunk, and (3) full range of lateral bending (LB, from neutral to maximal left bending then to maximal right bending) while seated, with hands hanging on either side. Retroreflective markers (see FIGURE 1(a)) were positioned on the processus spinosus of the vertebrae (six asymmetrical three-marker-clusters²⁷ on T1, T3, T7, T11, L2 and L4; four single markers on T5, T9, T12, and L3; one cluster weights around 5-8 grams), left/right anterior/posterior superior iliac spine, and sacrum^{17, 18, 22}. Bi-planar X-rays (EOS Imaging, France) were also taken during neutral upright stance of the subjects wearing markers (FIGURE 1(b)) and used as gold truth. This study was approved by the institutional review board of UZ Leuven. All participants signed a written informed consent before the start of the experiment.

FIGURE 1. Illustrations of (a) the marker placement protocol on the spine, (b) the coronal and sagittal images measured by the Bi-planar X-rays system, and (c) the methods used to calculate sagittal joint orientation angles on X-rays. Two approaches were used to estimate the joint orientation. First, we determined the angles between the lines (being projected on sagittal plane) connecting the disc centers, which we manually indicated on the X-ray images. Second, we determined the angles between the lines connecting the center of geometry of the vertebral bodies and the corresponding disc center on X-ray. The results of both methods were averaged to reduce measurement errors.

Data processing

We used an existing musculoskeletal model (OpenSim , version 4.0) of a fully articulated thoracolumbar spine ² to process the collected experimental data. All 6-DoF of the intervertebral joints spanning from T1 to S1 were enabled, allowing three rotations and three translations in each joint. Based on our previous work ²⁶, we incorporated OpenSim ExpressionBasedBushingForce elements into the model to account for the stiffness originating from passive structures. Each bushing element (hereafter referred to as passive element (PE)) generates force as a function of the relative displacement of the two bushing frames connected to the articulating bodies. We used OpenSim's Scale tool to scale the generic model, non-pathologic male adult (25 years, 1750 mm, 78 kg), to the subjects' anthropometry.

The scaled model together with the measured 3D marker trajectories of motions were used to calculate the **IK** solution through running OpenSim's Inverse Kinematics tool (FIGURE 2). In addition, we also generated IK solutions while imposing linear kinematic constraints describing the relation between intervertebral displacements in different joints (hereafter referred to as '**IK-cons**'). The constraints imposed constant interpolation ratios for F/E, LB, and axial rotation (AR) individually at the different levels. The ratios were based on the reported values in literature: IK-cons1 refers to Christophy et al.³ (for lumbar F/E, LB, and AR), IK-cons2 refers to Bruno et al.² (for thoracic and lumbar F/E, LB, and AR), IK-cons3 refers to Shojaei et al.²³ (for lumbar F/E). Detailed ratios are listed in the supplementary table. Preliminary data analysis indicated that IK solutions with 6-DoF enabled for each intervertebral joint yielded unrealistic vertebral positions, as expected due to the excessive kinematic redundancy. Therefore, these results were excluded from further analysis and only IK and IK-cons solutions generated using a model with three-rotational DoF for each intervertebral joint (the common condition in most studies) were further analyzed.

Alternatively, we estimated spine kinematics by solving a dynamic optimization program (referred to as '**Opt-program**'). We solved for joint kinematics (positions and velocities of generalized coordinates) and stiffness parameters that minimized the difference between the modeled and measured marker trajectories as well as the intersegmental forces while satisfying skeletal dynamics. The **objective function** J in (1) is the weighted sum of a data-tracking term and a term penalizing large generalized active joint segmental forces (forces and moments):

$$J = \int_{t_0}^{t_f} \mathbf{w}_1 \|\mathbf{p}(\mathbf{q}) - \hat{\mathbf{p}}\|^2 + \mathbf{w}_2 \mathbf{F}_{Act}^2(\mathbf{q}, \dot{\mathbf{q}}, \ddot{\mathbf{q}}) dt, \quad (1)$$

where t is time, t_0 and t_f are the start and end time of the movement, $\mathbf{q}$ and $\dot{\mathbf{q}}$ are positions and velocities of the model's generalized joint coordinates, $\ddot{\mathbf{q}}$ are joint accelerations, $\mathbf{p}$ and $\hat{\mathbf{p}}$ are simulated and measured marker coordinates, respectively, where $\mathbf{p}$ are rigidly linked to the mounted body and thereby $\mathbf{p}$ is as a function of the coordinate positions $\mathbf{q}$, $\mathbf{F}_{Act}$ is the vector containing active joint segmental forces (in all 6-DoF) from T1 to sacrum, $w_1 = 1000$ and $w_2 = 10$ are weight factors determined heuristically to make the two cost terms of similar magnitude. The first tracking term ($\|\mathbf{p} - \hat{\mathbf{p}}\|^2$) minimizes the differences between the measured ($\hat{\mathbf{p}}$) and simulated ($\mathbf{p}$) marker positions. The second term ($\mathbf{F}_{Act}^2$) minimizes the sum

of squared generalized active joint segmental forces from T1 to sacrum, which are produced by muscles, and thus minimizes the muscle effort being used. This objective function was minimized subject to bounds and constraints. Upper and lower bounds for $\mathbf{q}$ were based on reported maximum RoM values in ^{21, 29} that were increased by 150%. Maximum deviation for $\mathbf{p}$ was set to 40 mm. **Dynamic constraints** impose that joint kinematics $\mathbf{q}$ and $\dot{\mathbf{q}}$ should be consistent with skeletal dynamics:

$$\mathbf{M}(\mathbf{q})\ddot{\mathbf{q}} + \mathbf{G}(\mathbf{q}) + \mathbf{C}(\mathbf{q}, \dot{\mathbf{q}}) + \mathbf{F}_{Act}(\mathbf{q}, \dot{\mathbf{q}}, \ddot{\mathbf{q}}) + \mathbf{F}_{PE}(\mathbf{q}, \mathbf{p}) = \mathbf{0}, \quad (2)$$

where $\mathbf{M}(\mathbf{q})$ is the system mass matrix, $\mathbf{G}(\mathbf{q})$ is the vector of gravitational forces, $\mathbf{C}(\mathbf{q}, \dot{\mathbf{q}})$ is the vector of Coriolis and centrifugal forces, and $\mathbf{F}_{PE}$ is the vector containing the corresponding passive forces generated by joint stiffness in response to joint displacement:

$$\mathbf{F}_{PE_i}(\mathbf{q}_i) = \mathbf{A}_i(e^{\mathbf{B}_i\mathbf{q}_i} - 1), \quad (3)$$

where vector $\mathbf{A}$ and $\mathbf{B}$ are static optimization variables (time-independent parameters) that were introduced as the coefficients of the nonlinear passive element, i indicates the vertebral level. The initial values of $\mathbf{A}$ and $\mathbf{B}$ were generic parameters based on fitting *in vitro* loading displacement of spinal intervertebral joints (for details, see our previous work ²⁶).

We used direct collocation method ⁴ to solve this dynamic optimization problem. Software Matlab and open-source software CasADi were used to formulate this nonlinear optimal control problem ⁸. Computation of skeletal inverse dynamics and the virtual marker positions were obtained through the OpenSim libraries. Finally, this nonlinear program is solved using IPOPT solver (Interior Point Optimizer). All computations were performed on an Intel Core i7-6560U 2.21 GHz processor with 16 GB RAM.

Evaluation of the kinematic results and calibrated stiffness

We first assessed the estimated spine alignment in upright neutral stance, i.e., the body positions and orientations of vertebral bodies based on measured 3D marker positions. FIGURE 2 gives an overview of the six different approaches we used to estimate joint kinematics during standing. We applied the inverse kinematic approach (IK) and the inverse kinematic approach with kinematic constraints (IK-cons), as well as the dynamic optimization approach described above (resulting kinematic solutions are referred to as ‘OptK’). More

specific, we compared OptK solutions where the stiffness parameters were simultaneously calibrated while optimizing the current motion (OptK_{PE=calibrated}), OptK solutions with predefined stiffness parameters, which were either the generic parameters (OptK_{PE=generic}²⁶) or parameters obtained from optimizing flexion/extension motion (OptK_{PE=F/E}), lateral bending motions (OptK_{PE=LB}), and a combined motion containing F/E and LB (OptK_{PE=F/E+LB}). We analyzed these different options as we assumed that the combined F/E and LB motion would contain more information resulting in more valid (i.e., representative of the subjects) parameter estimates⁷. In addition, we performed OptK without any forces generated by the PE (i.e., OptK_{PE=0}) to evaluate the effect between solely accounting for dynamic consistency and accounting for both dynamic consistency as well as passive contributions from PE. It should be noted that we used marker positions of stance from optical motion capture to scale the generic model, and marker trajectories of all bending motions were also from optical motion capture system.

Marker-based estimates of spine alignment were compared to spine alignments derived from X-rays, which is considered as the gold standard data source. The alignment curve was evaluated in terms of the 3D position of the centers of geometry (CoG) of the vertebrae bodies and sagittal joint orientations. We obtained the CoG by manually identifying the approximate center of vertebral bodies on X-rays. We determined joint orientation as the relative joint orientations between adjacent vertebrae on the sagittal plane (FIGURE 1 (c)). The alignment curve was derived from the marker-based kinematic estimates by connecting the midpoint between every two joint centers (approximated centers of discs) in the estimated pose of the model. We assessed the mean absolute error between marker-based and X-ray-based CoG positions (from T1 to L5) and joint orientations (from T7-T8 to L4-L5) across the ten subjects.

Additionally, we evaluated the kinematics distribution pattern for the different kinematic estimates based on motion sharing ratios (MSR)¹, i.e., a ratio of the joint angle of each lumbar intervertebral joint with respect to the motion of the entire lumbar spine at each time instant during motions. As initial and final postures were close to upright corresponding to zero joint angles in our model, we excluded the first and last 20th percent of the motion cycle from the analysis to avoid error due to dividing joint motions by small total rotations¹. The coefficient of multiple correlation (CMC)²⁷ was calculated to evaluate the similarity in MSR ratio between all subjects. The average MSR of F/E and LB of all subjects were compared to the published *in*

vivo data derived from medical-imaging or bone pine data during dynamic F/E and LB ^{5, 19, 21, 25}. In addition, the range of intervertebral joint rotation during F/E and LB calculated using all six approaches were compared to *in vivo* reference data for F/E ^{9, 25} (similar seated maximal F/E) and LB ^{5, 12, 19, 21} in literature.

We evaluated the calibrated PE parameters by comparing the calibrated stiffness values to a range of generic stiffness values modeled based on published data of healthy subjects of mean age around 50 years old ²⁶ and previously reported stiffness patterns in subjects with similar age as our test subjects. Due to the high nonlinearity of the functional spinal units, previous *in vitro* loading-displacements tests mainly focus on their neutral zones (over which a vertebra moves with minimal resistance ²⁴) and physiological ranges of motion under applied maximal external moments (high-resistance zone). Therefore, we calculated the F/E and LB bending stiffness values for all thoracolumbar levels at the neutral zones and high-resistance zones, corresponding to passive moments 0.1 Nm (assuming the vertebra were under minimal internal resistance against bending) and high momenets respectively. The high moments were determined based on the calculated main F/E and LB bending moments (see supplementary material).

As the proposed optimization workflow imposes additional constraints to enforce dynamic consistency as well as effects of mechanical properties, we evaluated to what extent the marker position errors between measured and simulated markers increased compared to IK where least-square minimization at each time frame was used. Therefore, the root mean square difference between measured and simulated marker positions was calculated (averaged over all frames of the motions) for the six approaches and compared that with IK.

FIGURE 2. A schematic showing different kinematic approaches of stance based on marker positions. IK- refers to kinematic solutions using Inverse Kinematics tool in OpenSim, and IK-cons- refers to IK solutions with kinematic constraints; OptK- refers to kinematic solutions using the proposed dynamic optimization program (Opt-program) where the forces of passive element (PE) generated by spinal stiffness are taken into account. PE=0 indicates that the PE does not generate forces, PE=generic indicates the generic values developed by Wang *et al.*²⁶ are used and not calibrated, PE=calibrated indicates the parameters are simultaneously calibrated while optimizing the current motion, PE=bending indicates the parameters are obtained from optimizing the other bending motions that include spine flexion/extension (F/E), lateral bending (LB) and a combined motion containing full ranges of both F/E and LB. Note that to compare the simulated spine alignment with X-ray data, we used extracted marker positions of stance on X-rays (FIGURE 1(b))¹⁸ as input motion for the above mentioned approaches to estimate spine kinematics (due to no optical motion capture system on when we took the X-rays), so the comparisons were based on the same posture.

Results

FIGURE 3 shows the boxplots of the mean absolute errors of the spine alignments derived from different kinematic solutions compared to X-rays. FIGURE 4 shows representative spine alignment curves of one subject. Among the different approaches, the spine alignment calculated by the Opt-program with calibrated PE were closer to the curve on X-ray than IK

and IK-cons solutions. The average errors of these OptK solutions over all subjects varied between 8.5 mm to 10.1 mm in CoG positions and between 3.29° and 3.38° in sagittal joint orientation angles. In contrast, for IK and IK-cons solutions, the average errors over all subjects were much larger, with a range of 15.2 mm and 24.3 mm respectively in CoG distances and a range of 4.04° and 6.08° respectively in joint orientation angles. In addition, differences were found among the alignment solutions of the Opt-program (FIGURE 3). The OptK_{PE=F/E+LB} solution (with PE calibrated from optimizing the combined motion of F/E and LB) showed best agreement in both CoG positions and joint orientations with X-ray (error=8.5 mm, 3.29°, respectively), but OptK_{PE=0} solution (without PE forces) and OptK_{PE=generic} solution (using generic PE parameters) showed least agreement (error=15.4 mm, 5.68°) and the second least agreement (error=12.1 mm, 3.50°), respectively. The errors of joint orientations by level are additionally presented in supplementary materials.

FIGURE 3. The mean absolute error of spine alignments of the ten subjects between different kinematic solutions and X-rays in vertebral body center in terms of (a) 3-dimensional position (T1-L5) and (b) sagittal orientation angle (T7-L5). Joint angles in the upper thoracic spine (T1-T7) were not compared due to the relative low quality of the bone geometry on X-ray. Also for healthy subjects the relative joint orientations on frontal plane of stance were too small to be excluded, as it might be too sensitive to measurement errors. Abbreviations are referred to FIGURE 2. OptK_{PE=generic⁺} and OptK_{PE=generic⁻} refer to OptK solutions using upper and lower limit of the generic stiffness. IK-cons1 refers to the

solutions using Christophy et al., 2012, IK-cons2 refers to the solutions using Bruno et al., 2015, IK-cons3 refers to the solutions using Shojaei et al., 2015.

FIGURE 4. Representative examples of the spine alignments from different kinematic solutions and X-rays for one subject, shown as the positions of the center of vertebral body from T1 (top) to L5 (bottom) in the sagittal plane (a) and in the frontal plane (b). Abbreviations are referred to FIGURE 2. Note that not all kinematic solutions are presented to save the clarity of the figure given the similarities of the predicted spine alignments of the other optimization methods, and here IK-cons2 refers to the solutions obtained using Bruno et al., 2015.

Each participant demonstrated a unique pattern of lumbar MSR. The CMC values of all the lumbar MSRs of the overall 20-80th percentile were 0.41 for F/E and 0.84 for LB, indicating that the similarity between subjects was low, especially for F/E. FIGURE 5 shows the average MSR pattern of all subjects (SD were shown as error bars) between the 20-80th percentile and also between smaller divided percentiles of the motion cycle: 20-40th percentile, 40-60th percentile and 60-80th percentile. In terms of the overall 20-80th percentile, the values of the MSRs and the overall decreasing pattern for F/E and LB from L1 to L5 were similar to *in vivo* studies^{5, 19, 21, 25} and the constraints ratios by Christophy³ and Bruno². For LB, the largest

ratios were seen at joint L2-L3 for all studies. The MSR patterns among the three small divided percentiles of the motion cycle were diverse for F/E, especially in L1-L2 and L5-S1, whereas a much closer agreement was found for LB.

The average lumbar intervertebral RoM of all subjects during F/E and LB are shown in FIGURE 6. The F/E RoM estimated with the opt-program were comparable to the literature^{9, 25} measuring maximal F/E while seated using medical images. In contrast, abnormal large RoM were estimated using IK. For LB RoM, all solutions fell within one SD of the average value of four reported references^{5, 12, 19, 21} except for joint L1-L2. For the thoracic spine, the F/E ROM using the OptK were in a reasonable range (less than 3.15°), which was consistent with the fact as the subjects were required to keep an upright thoracic spine during F/E movement. However, for IK solutions, the estimated F/E RoM were in a large and unrealistic range (9.38° and 63.42°). In addition, the average range of axial translations of each lumbar intervertebrae during F/E were from 5 mm to 12 mm, which is similar to the *in vivo* measurements (4 mm to 9 mm) by¹⁶.

FIGURE 5. The motion sharing ratio (MSR) of lumbar intervertebral joints during flexion/extension (F/E) and lateral bending (LB) over time, including the average MSR pattern of all subjects (error bars shown as their standard deviations) between the 20-80th percentile and also between smaller divided percentiles: 20-40th percentile, 40-60th percentile, and 60-80th percentile. Abbreviations are given in FIGURE 2.

FIGURE 6. The range of motion for the lumbar intervertebral joints in: (a) flexion/extension and (b) lateral bending. The model estimations were compared to *in vivo* measurements, where for flexion/extension the references measured similar maximal flexion in a seated pose while for lateral bending the reference data are averaged from literature by Rozumalski *et al.*²¹, Pearcy *et al.*¹⁹, Dvorak *et al.*⁵, and Li *et al.*¹². The error bars indicate the standard deviation of the data among the subjects. Note for brevity, only lower standard deviations for IK solutions are shown. IK-cons1 refers to the solutions using Christophy *et al.*, 2012, IK-cons2 refers to the solutions using Bruno *et al.*, 2015. As IK-cons3 by Shojaei *et al.*, 2015 generated abnormally large joint rotations (over 100°), they were not shown in these figures.

(a) Flexion/extension, high-resistance zone **(b) Flexion/extension, low-resistance zone**

(c) Lateral bending, high-resistance zone (d) Lateral bending, low-resistance zone

FIGURE 7. The calibrated stiffness values in the directions of flexion/extension and lateral

bending from T1-T2 to L5-S1. The upper and lower bounds refer to the nominal range of generic stiffness in ²⁶, considering stiffening effect of compressive follower load. External moments in the high-resistance zone were based on the main bending moments of the thoracolumbar spine in the optimized kinematic solutions (see supplementary FIGURE 2).

When optimizing the bending motion, mainly the PE parameters *A* and *B* (equation (3)) in the main bending directions changed from initial generic values (to a range of 0.4 to 4.57 times) while the parameters in the other rotational directions barely changed. The calibrated F/E parameters of OptK_{PE=F/E} and LB parameters of OptK_{PE=LB} were similar to those of OptK_{PE=F/E+LB} respectively. FIGURE 7 shows the changed values of the F/E and LB stiffness of the solution OptK_{PE=FE+LB}. In general, the stiffness values in low-resistance zone (neutral zone) tended to be smaller than generic stiffness, with the stiffness values of most intervertebral levels being below the lower bound of the nominal range. However, in the high-stiffness zone, a large number of the stiffness values changed to be greater than those in the low-stiffness zone. Most subjects showed stiffer values compared to the generic ones.

The average root mean square errors between estimated and measured marker positions during dynamic bending motions over all subjects were 4.8 mm and 7.7 mm for all the IK and OptK solutions respectively, with both solutions staying well below the error limit of 20.0 mm recommended by OpenSim. The computation time for a simulation of dynamic motion with 100 interval points varied between 2100s and 9210s. Rigid body assumption ²⁷ for the marker cluster was evaluated and - with variability of inter-marker distances being 0.27 mm (± 0.04) mm and relative variability being 0.58% ($\pm 0.1\%$)- confirmed.

400 The proposed dynamic optimization framework aimed to solve spine kinematics based on
401 3D skin-marker positions while simultaneously calibrating spine stiffness. Previously used
402 methods and models for solving spine kinematics are commonly static-based and are
403 constrained with strict kinematics bounds. Our proposed optimization approach enforces
404 dynamic consistency in the entire skeletal system and over the entire time-trajectories, as
405 well as the subject-specific nonlinear properties of joint stiffness. Thereby the approach
406 prevents unrealistic joint motions and kinematic inconsistencies caused by uncertainties in
407 body segment parameters and experimental measurement errors.

408 Our method estimated spinal alignment in stance from measured skin markers and
409 compared this with spinal alignment measured using X-rays-based methods. The estimates
410 using the developed optimization-based approach were better than the solutions of the state-
411 of-the-art IK and IK with constraints methods. In addition, the averaged FE and LB MSRs
412 matched the reported overall pattern, *in vivo* values reported in literature as well as the
413 constraint ratios by Christophy ³ and Bruno ². Compared to the abnormal high RoM in the
414 unconstrained IK solutions, both the estimated lumbar and thoracic joint rotations fell within
415 a reasonable and acceptable range when using the OptK solutions. **The similarities between**
416 **our estimations using the developed optimization-based method and published results**
417 **indicate that the estimations were in good agreement with the general physiological**
418 **pattern of spine movement, with our method outperforming standard IK methods when**
419 **solving the spine kinematics redundancy problem.**

420 Interestingly, our optimization method provides the possibility to account for subject-
421 specific variance in spine stiffness when solving the kinematics distribution problem. Using
422 this approach, we found diverse MSR pattern of the lumbar spine across all the subjects,
423 especially for F/E, with MSR pattern changing during the spine F/E movement. This confirms
424 large movement pattern variations among individuals during the movement cycle, as for
425 example reported in the video fluoroscopy study by Breen et al. ¹. Furthermore, the model
426 with generic kinematic constraints estimated reasonable lumbar joint RoM, but failed to
427 capture the subject-specific kinematic pattern, as reflected by the large errors between
428 estimated and X-rays-based vertebral body CoG positions (24.3 mm) and joint orientations

(6.08°) calculated using the IK-cons solutions. Due to the nature of changing kinematic relationships across spinal segments, **the generic joint kinematic constraints might be** capable of representing generic motion pattern of a group of measured population but **not be sufficient to account for subject- and movement-specific variation in spinal kinematic coupling. This suggests that the proposed optimization approach was more optimal than IK with generic kinematic constraints methods.**

In addition, the proposed method enables accounting for nonlinear passive element (PE) contributions to the spinal dynamic equilibrium on a subject-specific basis through subject-specific tuning based on an individual's dynamic motion pattern. As a result, the OptK solutions with calibrated PE showed better estimation of the spine alignment than the solutions without PE contributions and the solutions using different sets of the generic PE values (i.e., no calibration). Therefore, the results indicate that the subject-specific calibration of stiffness facilitates the reduced errors rather than higher or lower stiffness values. Solely using the optimization approach without PE contribution or calibration accounts for dynamic consistency, which helps estimating more smooth movement compared to IK and IK-cons. It however does not increase estimation accuracy compared to OptK solutions that account for PE contributions. Furthermore, increasing the amount of subject-specific information on spinal alignment by calibrating PE for the combined F/E and LB motion (OptK_{PE=F/E+LB}) showed the best agreement with alignment on X-ray, as the dynamic bending motion contains more information to provide valid (i.e., representative of the subjects) parameter estimates ⁷. Therefore, the increased accuracy in estimating spine alignment was related to the inclusion of PE contribution, the calibration of PE properties, and the amount of subject-specific information of spine motions.

Methods that non-invasively determine *in vivo* stiffness of individual functional spinal units are lacking. Nonetheless, we indirectly evaluated the effect of parameter calibration by comparing the calibrated stiffness values to a range of generic stiffness values ²⁶ and previously reported stiffness patterns in subjects with similar age as our test subjects. After parameter calibration, for most subjects spinal stiffness in the low-resistance zone (neutral zone) decreased, but spinal stiffness in the high-resistance zone increased. This phenomenon is consistent with studies on aging or spine pathology ¹⁵, where the reduced joint mobility but increased size of the neutral zone was related to aging or disc degeneration, thereby being

regarded as an indicator of clinical instability. Meanwhile, increased spinal stiffness and reduced flexibility in F/E and LB were observed in studies (e.g., ^{11, 15}) that assessed the mobility of degenerated spines. Although the subjects in this study were not considered as pathological subjects, natural spine aging can be expected especially given their age range. Therefore, we believe **the PE parameter calibration was reasonable and in agreement with physiological conditions of the subjects.** Moreover, **the improved accuracy of kinematic estimations when using calibrated PE yields another indirect confirmation of the effectiveness of the developed optimization-based approach.**

It should be stressed that the joint kinematics are optimized based on input kinematic information of truly measured marker positions. Therefore, the (relatively rough) maximal range of motion of the spine segment is known to a certain extent, and this can reflect the corresponding trunk mobility and therefore the joint stiffness. Although our indirect validation demonstrates that calibrating parameters improved the estimation of joint kinematics, it is likely that more accurate stiffness parameters can be obtained when using extended input data. For example, using ‘true’ kinematic data based on sophisticated measures such as 3D video fluoroscopy, as they can present the positions of vertebra during a continuous motion with high accuracy. In this case, the proposed optimization approach can solely calibrate stiffness without optimizing joint kinematics. Such independent calibration evaluation approach offers an avenue for further research.

Nevertheless, when using the OptK solutions, the F/E and L/B RoM of specific lumbar joints were slightly smaller than the mean *in vivo* values reported in literature. This could be caused by specimen variance, e.g., age and specimen physical conditions. For example, our subjects are much older than those in the referred studies (mean age around 27 to 40 years). In addition, the measured RoM could also be related to the test pose. Since for our measurements, the subjects were instructed to perform F/E and LB in a seated pose, and with their hands crossing behind their head during F/E. A review ²⁸ suggested that compared to free standing pose, reduced spinal RoM caused by constrained poses were seen in previous *in vivo* studies. The added values of imposing additional dynamic constraints and effects of mechanical properties (OptK solutions) did indeed result in slightly higher average differences between estimated and measured marker positions than IK solutions, the root mean square errors for all OptK solution were all within the recommended limit by OpenSim.

Limitations should be taken into account when interpreting the results. It should be noted that the measurement precision and skin movement artefacts could also affect the simulation accuracy. We used some custom-designed lightweight 3D-clusters (the cluster shape has been validated in ¹⁷). Our method implicitly accounts for potential skin artefacts and palpation errors by allowing a moderate deviation of the simulated marker coordinates with respect to measurement. Explicitly introducing additional constraints based on more sophisticated measures can be helpful to further enhance the accuracy of marker-based simulation. For example, Ma et al., 2008 ¹³ proposed a Bayesian prediction model that accounted for soft tissue errors by introducing boundary conditions of the initial and final spatial relationships between the vertebrae and sensors defined by the radiographic images, resulting in a mean error of intervertebral joint angles being 1.45°. Overbergh et al., 2020 ¹⁸ and Severijns et al., 2020 ²² who used the same spinal marker placement protocol as us aimed to further reduce palpation errors by correcting marker position based on extra information from radiography (see supplementary material). Future research aiming to improve the estimation effect might benefit from comparing kinematic solutions generated by different marker protocols to the ‘gold standard’ data of vertebra positions, collected using more sophisticated measures such as 3D video fluoroscopy, in order to determine the marker placement protocol with the least tracking errors.

In conclusion, we proposed a force-dependent dynamic optimization approach for solving spine kinematics and calibrating subject-specific mechanical properties. Marker-based estimations of spine kinematics were improved by accounting for the dynamic consistency of spinal movement. The ability to account for subject-specific stiffness measured non-invasively during dynamic motions drastically improved the current estimations of spinal alignment of the control subjects but may become even more relevant when studying subjects with adult spinal deformity. As such, this work is at the basis of enhanced insights into spinal mechanics through more physiologically-accurate biomechanical simulations in health and disease. Script of the proposed approach will be available upon acceptance in the online OpenSim repository (simtk.org).

Conflict of Interest statement

We have no conflicts of interest to disclose. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.

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References

1. Breen A. and A. Breen. Uneven intervertebral motion sharing is related to disc degeneration and is greater in patients with chronic, non-specific low back pain: an in vivo, cross-sectional cohort comparison of intervertebral dynamics using quantitative fluoroscopy. *European Spine Journal* 27: 145-153, 2018.
2. Bruno A. G., M. L. Boussein and D. E. Anderson. Development and Validation of a Musculoskeletal Model of the Fully Articulated Thoracolumbar Spine and Rib Cage. *J Biomech Eng* 137: 081003, 2015.
3. Christophy M., N. A. Faruk Senan, J. C. Lotz and O. M. O'Reilly. A musculoskeletal model for the lumbar spine. *Biomech Model Mechanobiol* 11: 19-34, 2012.
4. De Groote F., A. L. Kinney, A. V. Rao and B. J. Fregly. Evaluation of Direct Collocation Optimal Control Problem Formulations for Solving the Muscle Redundancy Problem. *Ann Biomed Eng* 44: 2922-2936, 2016.
5. Dvorak J., M. M. Panjabi, J. E. Novotny, D. G. Chang and D. Grob. Clinical validation of functional flexion-extension roentgenograms of the lumbar spine. *Spine (Phila Pa 1976)* 16: 943-950, 1991.
6. Eskandari A. H., N. Arjmand, A. Shirazi-Adl and F. Farahmand. Hypersensitivity of trunk biomechanical model predictions to errors in image-based kinematics when using fully displacement-control techniques. *Journal of Biomechanics* 84: 161-171, 2019.
7. Falisse A., S. V. Rossom, I. Jonkers and F. D. Groote. EMG-Driven Optimal Estimation of Subject-SPECIFIC Hill Model Muscle–Tendon Parameters of the Knee Joint Actuators. *IEEE Transactions on Biomedical Engineering* 64: 2253-2262, 2017.
8. Falisse A., G. Serranoli, C. L. Dembia, J. Gillis, I. Jonkers and F. De Groote. Rapid predictive simulations with complex musculoskeletal models suggest that diverse healthy and pathological human gaits can emerge from similar control strategies. *J R Soc Interface* 16: 20190402, 2019.

9. Hayes M. A., T. C. Howard, C. R. Gruel and J. A. Kopta. Roentgenographic Evaluation of Lumbar Spine Flexion-Extension in Asymptomatic Individuals. *Spine* 14: 327-331, 1989.
10. Ignasiak D., S. Dendorfer and S. J. Ferguson. Thoracolumbar spine model with articulated ribcage for the prediction of dynamic spinal loading. *J Biomech* 49: 959-966, 2016.
11. Kettler A., F. Rohlmann, C. Ring, C. Mack and H. J. Wilke. Do early stages of lumbar intervertebral disc degeneration really cause instability? Evaluation of an in vitro database. *Eur Spine J* 20: 578-584, 2011.
12. Li G., S. Wang, P. Passias, Q. Xia, G. Li and K. Wood. Segmental in vivo vertebral motion during functional human lumbar spine activities. *Eur Spine J* 18: 1013-1021, 2009.
13. Ma H. T., Z. Yang, J. F. Griffith, P. C. Leung and R. Y. Lee. A new method for determining lumbar spine motion using Bayesian belief network. *Med Biol Eng Comput* 46: 333-340, 2008.
14. Marra M. A., V. Vanheule, R. Fluit, B. H. Koopman, J. Rasmussen, N. Verdonschot and M. S. Andersen. A subject-specific musculoskeletal modeling framework to predict in vivo mechanics of total knee arthroplasty. *J Biomech Eng* 137: 020904, 2015.
15. Mimura M., M. M. Panjabi, T. R. Oxland, J. J. Crisco, I. Yamamoto and A. Vasavada. Disc degeneration affects the multidirectional flexibility of the lumbar spine. *Spine (Phila Pa 1976)* 19: 1371-1380, 1994.
16. Nagel T. M., J. L. Zitnay, V. H. Barocas and D. J. Nuckley. Quantification of continuous in vivo flexion-extension kinematics and intervertebral strains. *Eur Spine J* 23: 754-761, 2014.
17. Needham R., R. Naemi, A. Healy and N. Chockalingam. Multi-segment kinematic model to assess three-dimensional movement of the spine and back during gait. *Prosthet Orthot Int* 40: 624-635, 2016.
18. Overbergh T., P. Severijns, E. Beaucage-Gauvreau, I. Jonkers, L. Moke and L. Scheys. Development and validation of a modeling workflow for the generation of image-based, subject-specific thoracolumbar models of spinal deformity. *Journal of Biomechanics* 2020.
19. Pearcy M. and J. Shepherd. Is there instability in spondylolisthesis? *Spine (Phila Pa 1976)* 10: 175-177, 1985.
20. Petit Y., C. É. Aubin and H. Labelle. Patient-specific mechanical properties of a flexible multi-body model of the scoliotic spine. *Medical & Biological Engineering & Computing* 42: 55-60, 2004.
21. Rozumalski A., M. H. Schwartz, R. Wervey, A. Swanson, D. C. Dykes and T. Novacheck. The in vivo three-dimensional motion of the human lumbar spine during gait. *Gait Posture* 28: 378-384, 2008.
22. Severijns P., T. Overbergh, A. Thauvoye, J. Baudewijns, D. Monari, L. Moke, K. Desloovere and L. Scheys. A subject-specific method to measure dynamic spinal alignment in adult spinal deformity. *Spine J* 20: 934-946, 2020.
23. Shojaei I., N. Arjmand, J. R. Meakin and B. Bazrgari. A model-based approach for estimation of changes in lumbar segmental kinematics associated with alterations in trunk muscle forces. *J Biomech* 70: 82-87, 2018.
24. Smit T. H., M. S. van Tunen, A. J. van der Veen, I. Kingma and J. H. van Dieen. Quantifying intervertebral disc mechanics: a new definition of the neutral zone. *BMC Musculoskelet Disord* 12: 38, 2011.
25. Takayanagi K., K. Takahashi, M. Yamagata, H. Moriya, H. Kitahara and T. Tamaki. Using Cineradiography for Continuous Dynamic-Motion Analysis of the Lumbar Spine. *Spine* 26: 1858-1865, 2001.
26. Wang W., D. Wang, F. De Groote, L. Scheys and I. Jonkers. Implementation of physiological functional spinal units in a rigid-body model of the thoracolumbar spine. *Journal of Biomechanics* 109437, 2019.
27. Wang W., D. M. Wang, M. Wesseling, B. Xue and F. Y. Li. Comparison of modelling and tracking methods for analysing elbow and forearm kinematics. *Proceedings of the Institution of Mechanical Engineers Part H-Journal of Engineering in Medicine* 2019.

- 606 28. Widmer J., P. Fornaciari, M. Senteler, T. Roth, J. G. Snedeker and M. Farshad. Kinematics of
607 the Spine Under Healthy and Degenerative Conditions: A Systematic Review. *Annals of Biomedical*
608 *Engineering* 47: 1491-1522, 2019.
- 609 29. Wilke H. J., A. Herkommer, K. Werner and C. Liebsch. In vitro analysis of the segmental
610 flexibility of the thoracic spine. *PLoS One* 12: e0177823, 2017.
- 611 30. Zemp R., R. List, T. Gulay, J. P. Elsig, J. Naxera, W. R. Taylor and S. Lorenzetti. Soft tissue
612 artefacts of the human back: comparison of the sagittal curvature of the spine measured using skin
613 markers and an open upright MRI. *PLoS One* 9: e95426, 2014.

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SUPPLEMENTARY TABLE 1. Ratios of kinematic constraints and remaining degrees of freedom of the thoracic and lumbar spine

		Christophy et al., 2012			Bruno et al., 2015			Shojaei et al., 2015		
Spine	Level	F/E	LB	AR	F/E	LB	AR	F/E	LB	AR
Thoracic spine	T1T2/T2T3	-			1.00	1.08	0.74	-		
	T2T3/T3T4				1.00	0.93	1.15			
	T3T4/T4T5				1.00	1.54	0.87			
	T4T5/T5T6				1.00	1.12	0.89			
	T5T6/T6T7				0.80	0.73	0.95			
	T6T7/T7T8				0.84	0.64	0.83			
	T7T8/T8T9				1.00	1.32	0.92			
	T8T9/T9T10				1.00	0.80	0.92			
	T9T10/T10T11				0.67	0.89	1.04			
	T10T11/T11T12				0.75	0.79	2.02			
	T11T12/T12L1				1.00	1.04	2.63			
	T12L1/L1L2	-	-	-	0.62	-				
Lumbar Spine	L1L2/L2L3	1.10	0.75	0.93	1.21			0.75	0.94	0.62
	L2L3/L3L4	1.13	1.02	0.82	1.17			1.03	0.82	0.81
	L34/L45	1.10	1.35	1.00	1.44			1.35	1.00	0.70
	L45/L5S1	1.48	1.34	1.06	2.16			1.32	1.06	0.88
Degrees of freedom of the thoracic and lumbar spine		All 36 rotational DoFs in the thoracic spine; 3 rotational DoFs in the lumbar spine			3 rotational DoFs in the thoracic spine; 3 rotational DoFs in the lumbar spine			35 rotational DoFs in the thoracic spine; 11 rotational DoFs in the lumbar spine		

- ◆ In the manuscript, FIGURE 3 shows the boxplots of the range of errors on the vertebral positions and orientations calculated based on the following equation:

$$\begin{aligned}
 Distance_{IVD_level,subject} &= |Pos_{sim} - Pos_{Xray}| \\
 &= \sqrt{(x_{sim} - x_{Xray})^2 + (y_{sim} - y_{Xray})^2 + (z_{sim} - z_{Xray})^2} \\
 \text{Mean absolute error} &= \frac{1}{10} \cdot \frac{1}{17} \cdot \sum_{subject=1}^{10} \sum_{IVD_level=1}^{17} Distance_{IVD_level,subject}
 \end{aligned}$$

where Pos_{sim} and Pos_{Xray} are marker-based and X-ray-based CoG positions from $IVD_level=T1$ to $L5$. The joint orientation errors were calculated similarly across joint $T7-T8$ to $L4-L5$.

- ◆ To assess if the errors are random or systematic, we additionally evaluated the actual errors of joint orientations by level and presented the boxplots (see supplementary Figure 1). We evaluate the errors for three representative solutions: $OptK_{PE=F/E+LB}$, $OptK_{PE=0}$ and IK. We performed independent t-tests to evaluate if the joint orientation errors by spinal level are different than zero. The results of t-tests show that there is no significant difference between calculated orientation errors and zero ($p > 0.05$). Meanwhile, as shown in the figure the mean values of the orientation errors at each level are mostly around zero values. Therefore, we believe the errors are random instead of systematic.

(c) IK solution

SUPPLEMENTARY FIGURE 1. The errors of joint orientations by level for (a) OptK_{PE=F/E+LB} solution, (b) OptK_{PE=0} solution, and (c) IK solution. The positive or negative sign of errors refers to extension (+) or flexion (-) direction in the sagittal plane. Joint angles in the upper thoracic spine (T1-T7) were not compared due to the relative low quality of the bone geometry on X-ray. Abbreviations are referred to FIGURE 2.

- ◆ We evaluated the differences of the main bending moments during trunk F/E and LB between using the optimized and the generic stiffness (see Supplementary Table 2). The absolute F/E moments of the joints from T1-T2 to L5-S1 during trunk F/E were summed at the maximal range of trunk F/E, and similar calculation was performed for trunk L/B. The kinematics solutions using the optimized stiffness resulted in significantly smaller joint bending moments than the ones using the generic stiffness (paired t-tests, $p < 0.05$), with a mean difference of 57.53Nm and 20.53Nm for trunk F/E and LB, respectively.

SUPPLEMENTARY TABLE 2. Main joint moments of the thoracolumbar spine during trunk flexion/extension and lateral bending in different kinematic solutions across ten subjects.

Motion	Solutions using calibrated stiffness	Solutions using generic stiffness
Trunk flexion/extension	Mean: 76.57 Nm Range: 65.83 to 130.18 Nm	Mean: 164.07 Nm Range: 107.19 to 233.24 Nm
Trunk lateral bending	Mean: 40.90 Nm Range: 26.97 to 68.31 Nm	Mean: 61.43 Nm Range: 44.11 to 86.11 Nm

SUPPLEMENTARY FIGURE 2. The averaged main bending moments of each joint level during trunk flexion/extension and lateral bending in optimized kinematic solutions. The error bars indicate the standard deviations of the joint moments across ten subjects.

◆ Limitations due to the measurement precision and skin movement artefacts:

It should be noted that the measurement precision and skin movement artefacts could also affect the simulation accuracy. As an attempt to increase the simulation accuracy, we used some custom-designed lightweight 3D-clusters to obtain more information of the three-dimensional motion of vertebrae. In terms of the validation on the specific cluster shape, Needham et al., 2016¹⁷ reported that the 3D-cluster showed a high accuracy (expressed as a standard error of measurement that ranged between 0.17° and 0.35° against known reference positions of a mechanical frame). Additionally, our optimization method implicitly accounts for potential skin artefacts and palpation errors by allowing a moderate deviation of the simulated marker coordinates with respect to measured marker coordinates. We work from the assumption that increased simulation accuracy can be further added by accounting for skeletal dynamics and dynamic consistency. Still, there might be larger errors caused by skin movement and palpation especially during larger amplitude spine movement. Explicitly introducing additional constraints based on more sophisticated measures can be helpful to further enhance the accuracy of optical marker-based simulation. Ma et al., 2008¹³ proposed a method that accounted for errors due to soft tissue deformation in determine lumbar spine motion through probabilistic inference using the Bayesian belief propagation. They introduced boundary conditions of the initial and final spatial relationships between the vertebrae and sensors defined by the radiographic images, resulting in an overall mean error of intervertebral joint angles being 1.45° in neutral standing posture. Meantime, Overbergh et al., 2020¹⁸ and Severijns et al., 2020²² who used the same spinal marker placement protocol as us, aimed to further reduce palpation errors by correcting marker position based on extra information from radiography. Overbergh et al., reconstructed the spine model based on radiograph images and reconstructed the marker positions by delineating the iron beads inserted in the markers in radiograph planes, resulting in models with mean accuracy between 0.71-1.95 mm and 1.25 - 2.27° for vertebral positions and orientations. Severijns et al., used a polynomial function to fit through corrected marker positions based on obtaining offsets between makers and body positions on the radiograph, resulting in, for example, a root mean square error of estimated lumbar lordosis being 5.99° . Future research aiming to improve the kinematic estimation effect of marker placement might benefit from determining an optimal marker placement protocol, with a moderate number of single and cluster markers, which is

minimally affected by skin artefacts. Ideally, kinematic solutions generated by different marker protocols should then be compared to the 'gold standard' data of vertebra positions collected using more sophisticated measures such as 3D video fluoroscopy, in order to determine the marker placement protocol with the least tracking errors. In addition, the reference CoG positions on X-ray were estimated by hand by one inspector. Therefore, some DoFs including the frontal plane orientation angles and translations in stance were not evaluated.