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Bootstrap prediction bands for cervical spine intervertebral kinematics during in vivo three-dimensional head movements

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ABSTRACT

There is substantial inter-subject variability in intervertebral range of motion (ROM) in the cervical spine. This makes it difficult to define "normal" ROM, and to assess the effects of age, injury, and surgical procedures on spine kinematics. The objective of this study was to define normal intervertebral kinematics in the cervical spine during dynamic functional loading. Twenty-nine participants performed dynamic flexion\extension, axial rotation, and lateral bending while biplane radiographs were collected at 30 images/s. Vertebral motion was tracked with sub-millimeter accuracy using a validated volumetric model-based tracking process that matched subject-specific CT-based bone models to the radiographs. Gaussian point-by-point and bootstrap techniques were used to determine 90% prediction bands for the intervertebral kinematic curves at 1% intervals of each movement cycle. Cross validation was performed to estimate the true achieved coverage for each method. For a targeted coverage of 90%, the estimated true coverage using bootstrap prediction bands averaged $86 \pm 5\%$, while the estimated true coverage using Gaussian point-by-point intervals averaged $56 \pm 10\%$ over all movements and all motion segments. Bootstrap prediction bands are recommended as the standard for evaluating full ROM cervical spine kinematic curves. The data presented here can be used to identify abnormal motion in patients presenting with neck pain, to drive computational models, and to assess the biofidelity of in vitro loading paradigms.

1. Introduction

There is substantial inter-subject variability in intervertebral range of motion (ROM) in the cervical spine (Anderst et al., 2013a, 2013b; Dvorak et al., 1988; Frobin et al., 2002; Lind et al., 1989; Reitman et al., 2004; Wu et al., 2007). This makes it difficult to define "normal" ROM, and to assess the effects of age, injury, and surgical procedures on spine kinematics. Furthermore, because ROM is determined by only two maximal end range positions, analysis of ROM cannot identify differences in movement through the midrange positions that are most often encountered in activities of daily living (Bible et al., 2010; Cobian et al., 2009).

It would be beneficial to clinicians and to basic scientists if a range of "normal" intervertebral kinematics were defined for continuous, full ROM movements. For the clinician, it would be valuable to know if the kinematics of a patient fall into the "normal" range throughout their full ROM. This information could be used, for example, to target physical therapy to specific portions of the movement or to assess the effects of fusion on adjacent segments over the entire ROM. For the basic scientist, bounds defining "normal" continuous kinematics can be used to verify that the motion imposed by a loading device accurately replicates in vivo kinematics over the entire ROM, not just at the endpoints.

Boundaries defining the range of "normal" kinematics may be calculated using prediction bands. Prediction bands contain, with a pre-specified coverage probability, a new curve drawn from the same population as the training curves. In this way, clinicians and researchers can classify new subjects as belonging to the same population as that from which the training curves were collected (Lenhoff et al., 1999). The upper and lower boundaries defining the prediction bands for continuous kinematic curves are most often determined using point-by-point Gaussian theory intervals. In this case, the collection of separate point-by-point prediction intervals is used to form the upper and lower prediction bands. Prediction bands formed in this way have several shortcomings that have been described in detail (Duhamel et al., 2004; Lenhoff et al., 1999). Most notably, the true achieved coverage is much less than the desired coverage(Cutti et al., 2014; Duhamel et al., 2004; Lenhoff et al., 1999; Sutherland et al., 1996). As an alternative, prediction bands may be constructed using the bootstrap technique (Duhamel et al., 2004; Lenhoff et al., 1999; Sutherland et al., 1996). Bootstrapping is a non-parametric resampling technique that is computationally intensive and takes into account the correlation between points of a curve and the simultaneous nature of the inference required over points of the movement cycle (Cutti et al., 2014; Lenhoff et al., 1999). It has been demonstrated that the

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bootstrap technique is superior to the Gaussian point-by-point method in terms of providing the desired coverage when assessing gait and shoulder kinematic curves(Cutti et al., 2014; Duhamel et al., 2004; Lenhoff et al., 1999; Sutherland et al., 1996).

The objectives of this study were to use Gaussian point-by-point and bootstrap techniques to calculate prediction bands for the intervertebral kinematics of the cervical spine during three-dimensional, dynamic, functional motion in a group of healthy young adults, and to determine the true coverage probability of each technique.

2. Methods

2.1. Subjects

Following Institutional Review Board (IRB) approval, data were collected from 29 participants (15 M, 14 F; average age: 27.3 ± 4.4 yrs.; age range: 20–35 years) who provided informed consent to participate in this research study. All participants were healthy asymptomatic non-smokers, with no history of neck surgery, chronic neck pain, or diagnosis of osteoporosis.

2.2. Data collection

Subjects were seated, with their torso upright and unconstrained, within a biplane X-ray system and directed to continuously move their head and neck through their entire range motion for nine dynamic movement trials (flexion\extension (3), lateral bend (3), and axial rotation (3)), with a rest period provided between each trial. A metronome set at 40–44 beats per minute was used to assist the participants in moving at a continuous, steady pace to complete each full movement cycle in approximately 3 s. Biplane radiographs were collected simultaneously at 30 frames per second for 3.2 s for each dynamic movement trial (X-ray parameters: 70 KV, 160 mA, 2.5 ms X-ray pulses, source-to-subject distance 140 cm). For each participant, two trials of each dynamic movement were analyzed. The two trials were selected based on image contrast and the subject remaining in the field of view of both imaging systems. Additionally, three static neutral trials were collected with the participant motionless and looking directly forward. Four reflective markers placed on the head, and four placed on the torso, were tracked for each trial using a commercial motion analysis system (Vicon-MX, 60 Hz) that began data collection simultaneously to the biplane X-ray system. Finally, high-resolution CT scans ($0.29 \times 0.29 \times 1.25$ mm^3 voxels) of the cervical spine (C1–T1) were acquired from each participant (GE Lightspeed 16). The effective radiation dose for each dynamic motion trial was estimated to be 0.16 mSv (determined using PCXMC simulation software, STUK, Helsinki, Finland). The effective dose of a cervical spine CT scan has been reported to be between 3.0 mSv and 4.36 mSv (Biswas et al., 2009; Fazel et al., 2009).

2.3. Data processing

Bone tissue was segmented from the CT volume using a combination of commercial software (Simpleware, Exeter, UK) and manual segmentation (Thorhauer et al., 2010). A three-dimensional (3D) model of each vertebra was generated from the segmented bone tissue (Treece et al., 1999). Markers were interactively placed on the 3D bone models to define bone-specific anatomic coordinate systems (Panjabi et al., 2001). In vivo bone motion was tracked with sub-millimeter precision using a validated volumetric model-based tracking technique (Anderst et al., 2009; Anderst et al., 2011; Bey et al., 2006). For flexion\extension trials, all bones from C1 through T1 were tracked, while for lateral bend and rotation trials, only C3 through T1 were tracked due to the skull and mandible obscuring C1 and C2. A low-pass, 4th-order Butterworth filter was used to smooth the 6 DOF motion path of each bone (3 translations and 3 rotations). The optimal filter frequency for model-based tracking of bone motion (1.7 Hz for all flexion\extension trials and 1.5 Hz for all bend and rotation trials) was determined using residual analysis (Winter 2009).

After filtering the reflective marker data at 20 Hz, the movement cycle was partitioned into 4 sections according to head movement direction (positive or negative) and head orientation relative to the static neutral position (positive or negative). Intervertebral angles were determined using projection angles (P_{xj}, P_{yi}, P_{zi}) (Crawford et al., 1996) and were linearly interpolated at instants corresponding to each 1% interval of head ROM for each section of the movement cycle. A single intervertebral rotation versus percent of movement cycle curve was calculated for each subject by averaging data over the two trials for each subject. The average of the three static trials determined head orientation and intervertebral orientations in the static neutral position.

2.4. Prediction bands

Point-by-point 90% Gaussian prediction intervals were calculated for each 1% interval of the movement cycle by assuming a normal distribution ($\mu \pm 1.645^{*}\sigma$). The resulting points formed a 90% prediction band.

Ninety percent bootstrap prediction bands were formed according to the process described in detail by Lenhoff et al. (1999). In general, the bootstrap method performs sampling with replacement to generate a pseudo-sample from the given curves. The size of the pseudo-sample is equal to that of the original sample (in this case 29). The means and variability are then determined for the pseudo-sample. This process is repeated many times (e.g. 1000). The standardized distribution of the differences between the measured curves and the mean curve of each pseudo-sample is then determined. Specific to the current dataset, for each participant, the average kinematic curve was repeated to create a periodic waveform. Each curve was then represented as a finite Fourier sum. This allowed the bootstrap analysis to account for the correlation between points in the movement cycle curve. For the present analysis, an iterative process was used to determine that 18 Fourier coefficients were sufficient to extract an accurate parametric description of each waveform. Also specific to the present study, all bootstrap bands were constructed using 1000 iterations per band. Extensive details of the bootstrap technique may be found elsewhere (Lenhoff et al., 1999; Olshen et al., 1989).

2.5. Cross validation

Cross validation was performed on the full dataset of 29 curves (one average curve per participant) using a leave-one-out procedure (Lenhoff et al., 1999) in order to estimate the true achieved coverage for the bootstrap and point-by-point methods at a 90% limit. The cross-validation also served to confirm that the number of subjects was large enough to ensure that the achieved coverage was close to the desired nominal value when using the bootstrap technique.

2.6. Analyzed rotations

For the flexion\extension movement, the analysis was restricted to the flexion \extension angle at each motion segment from C1 to C7 because out-of-plane movement during flexion\extension is minimal (less than 3°) (Anderst et al., 2013a, 2013b). Head axial rotation and lateral bending induce "coupled" motion in the cervical vertebrae (Ishii et al., 2006; Lin et al., 2014), and therefore rotation and lateral bending angles were analyzed for each motion segment between C3 and C7 when the head performed either axial rotation or lateral bending movements.

3. Results

Inter-subject variability in the static neutral orientation was relatively high (Table 1). Within individuals, the static neutral position could be replicated with high precision (Table 2).

Table 1
Mean (± SD) static orientation in 29 young, healthy individuals. Flexion\extension, rotation and bend angles correspond to rotation in the sagittal, transverse and coronal planes, respectively. Average T1 flexion\extension orientation in space was 28.0 ± 8.4° (i.e. flexed 28° with respect to the horizontal plane).

	Flex(+)\ext (−) (deg)	Rotation (deg)	Bend (deg)
C1–C2	−13.9 ± 6.8	−2.1 ± 5.2	1.0 ± 2.4
C2–C3	−7.3 ± 7.3	0.7 ± 2.4	−0.1 ± 3.0
C3–C4	−4.0 ± 5.5	0.7 ± 2.8	0.1 ± 3.0
C4–C5	−2.0 ± 4.2	−0.1 ± 1.9	−0.4 ± 3.3
C5–C6	−2.0 ± 7.2	0.4 ± 1.8	0.6 ± 3.0
C6–C7	−3.7 ± 5.7	−0.2 ± 1.7	−0.1 ± 3.0
C7–T1	−7.4 ± 5.3	0.4 ± 2.4	−0.5 ± 2.6
Head–T1	−30.1 ± 11.2	−2.7 ± 3.0	0.9 ± 3.9

Table 2
Within-subject variability (SD) in static orientation determined using 3 trials in the static, neutral position.

	Flex(+)\ext (−) (deg)	Rotation (deg)	Bend (deg)
C3–C4	1.6	0.7	0.9
C4–C5	1.4	0.7	0.6
C5–C6	1.3	0.6	0.6
C6–C7	1.3	0.7	0.8
C7–T1	1.2	0.8	0.7
Head–T1	3.6	1.8	2.0