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ORIGINAL ARTICLE

ISSLS Prize in Bioengineering Science 2021: in vivo sagittal motion of the lumbar spine in low back pain patients—a radiological big data study

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Abstract

Purpose We investigated the flexion–extension range of motion and centre of rotation of lumbar motion segments in a large population of 602 patients (3612 levels), and the associations between lumbar motion and other parameters such as sex, age and intervertebral disc degeneration.

Methods Lumbar radiographs in flexion–extension of 602 patients suffering from low back pain and/or suspect instability were collected; magnetic resonance images were retrieved and used to score the degree of disc degeneration for a subgroup of 354 patients. Range of motion and centre of rotation were calculated for all lumbosacral levels with in-house software allowing for high degree of automation. Associations between motion parameters and age, sex, spinal level and disc degeneration were then assessed.

Results The median range of motion was 6.6° (range 0.1–28.9°). Associations between range of motion and age as well as spinal level, but not sex, were found. Disc degeneration determined a consistent reduction in the range of motion. The centre of rotation was most commonly located at the centre of the lower endplate or slightly lower. With progressive degeneration, centres of rotation were increasingly dispersed with no preferential directions.

Conclusion This study constitutes the largest analysis of the in vivo lumbar motion currently available and covers a wide range of clinical scenarios in terms of age and degeneration. Findings confirmed that ageing determines a reduction in the mobility independently of degeneration and that in degenerative levels, centres of rotation are dispersed around the centre of the intervertebral space.

Keywords Range of motion · Centre of rotation · Image registration · Flexion–extension · Instability

Introduction

The in vivo motion of the spine, and of the lumbar region in particular, has been a subject of investigation for decades. Building on pioneering studies in which parameters such as the range of motion and the centre of rotation of each motion segment were measured in vitro on cadaver specimens [1–3] as well as on the advances in motion analysis techniques [4], non-invasive technologies such as electrogoniometers, strain gauge-based devices and optoelectronic systems have been extensively used for a quantitative assessment of the spinal mobility in living subjects [5–10]. Although such techniques have been successfully used for a number of clinical applications [11], inherent limitations such as soft tissue artefacts restrict their accuracy and precision, restraining their use to cases

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in which measurement errors in the order of a few degrees are not critical or to the evaluation of the global motion of the whole trunk [4, 11].

Despite their invasivity due to the use of ionizing radiation, radiographic techniques do not suffer from these limitations, since they allow for the direct visualization of each single vertebra and thus for the precise determination of the movement of the individual motion segments. As a matter of fact, the use of radiographs in flexion–extension for the investigation of the spinal motion dates back to the 1930s [12, 13]; the successive decades have seen a conspicuous use of this technique both for basic research for the investigation of spine motion and the detection of abnormalities [14–16], and as a diagnostic tool for degenerative spinal disorders [17–20]. Besides the study of spine motion in flexion–extension, lateral bending and axial rotation have been extensively investigated by means of similar techniques exploiting simultaneous images acquired in the coronal and sagittal planes [21, 22].

As a matter of fact, the vast majority of the available radiographic studies addressing the motion of the lumbar spine included a relatively low number of subjects, typically in the range of a few dozen (e.g. [19]), up to one hundred [23]. A determinant factor for such small numbers, which are hardly representative of a whole population, is the considerable workload involved in the manual or computer-assisted measurement of the spinal motion, which requires many hours of work of one or more trained observers. Indeed, the largest study currently available exploited automated measurement software [24] for the assessment of the range of motion and centre of rotation in 658 motion segments. Besides reduced workload, such techniques provide improved repeatability and lower measurement errors, which have been shown to exceed 1.2° for the range of motion and 4 mm for the position of the centre of rotation when using standard techniques [25].

In this study, we investigated the flexion–extension range of motion and centre of rotation in a large population of 602 patients, corresponding to 3612 lumbar motion segments, suffering from low back pain and/or suspect lumbar instability, and we explored potential associations between lumbar motion and other parameters such as sex, age and intervertebral disc degeneration assessed on both radiographs and magnetic resonance imaging (MRI) scans of the lumbar spine. To this aim, we took advantage of purposely developed software allowing for a high degree of automation and repeatability of the measurement, as well as of the large imaging database of a major orthopaedic institute. The present work therefore constitutes the largest study to date aimed at the assessment of in vivo lumbar motion and is the first approaching the realm of big data.

Materials and methods

Patients and images

All radiographs of the lumbar spine in full flexion and extension acquired at IRCCS Istituto Ortopedico Galeazzi between 2016 and 2018, pertaining to subjects suffering from low back pain and/or suspect lumbar instability, were retrospectively collected. Images showing spinal instrumentation or vertebral fractures were excluded, as well as images with poor quality, with different magnifications among the flexion and extension images or with a field of view not covering the whole lumbar spine. In total, images of 602 patients were analysed. Age and sex were recorded for each patient.

In addition, the radiological database of the institute was searched for T2-weighted lumbar MRI scans of the same 602 subjects. Sagittal MRI images acquired in a time frame of 1 year with respect to the date of the study in flexion–extension, i.e. between 6 months before and 6 months after the radiographic examination, were collected. If the patient was operated after the flexion–extension study but before the MRI acquisition, the relevant MRI scans were not considered for data analysis. In total, MRI scans were retrieved for 354 of the 602 patients.

Image evaluation and processing

All spinal levels between T12-L1 and L5-S1 were analysed in the present study; therefore, 3612 levels from the radiographic images (i.e. six levels for each of the 602 patients) and 2124 from the MRI scans were investigated.

First, the degree of degeneration of each spinal level was graded on the original radiographs, taking into account both the image in flexion and the one in extension, based on the scheme published by Wilke and colleagues [26]. In brief, this validated grading system considers three distinct scores for three items which represent the most common phenotypes of disc degeneration which can be assessed on sagittal radiographs, i.e. disc height loss, osteophyte formation and diffuse sclerosis. The sum of the three scores is then used to determine an overall degree of degeneration, which can be either none, mild, moderate or severe.

As mentioned above, the degree of disc degeneration was also assessed on T2-weighted MRI scans whenever available, by means of the Pfirrmann scheme [27]. Such grading system includes the evaluation of the homogeneity of the bright area in the nucleus pulposus, the clarity of the distinction between annulus and nucleus, and the possible occurrence of collapse of the intervertebral space,

all assessed on the slice showing the mid-sagittal view of the intervertebral disc. By applying a simple algorithm, each disc is then graded in five classes, ranging from I (no degeneration) to V (severe degeneration with collapsed disc space, no homogeneous bright area, no distinction between nucleus and annulus).

For each couple of flexion–extension radiographs, the ROM and the position of the COR were then calculated for all levels between T12-L1 and L5-S1, by means of custom Python scripts allowing for a high degree of automation of the image processing workflow. In synthesis, after identifying the region of interest enclosing each vertebra in each single radiograph, standard image registration algorithms were used to: (1) rigidly transform the image in flexion so that the lower vertebra of the spinal level of interest is aligned to the same vertebra in the image in extension, considered as reference; (2) rigidly align the upper vertebra of the transformed image in flexion to the same vertebra in the image in extension; and (3) extract the ROM and COR from the matrix describing the Euclidean transformation in (2).

Data analysis

The calculated values of the ROMs were used to build box plots depicting the distribution of the ROM with respect to sex, spinal level and degree of disc degeneration, assessed both on the radiograph based on the Wilke scheme [26] and on MRI following Pfirrmann [27]. After assessing the non-normality of the distributions with the Shapiro–Wilk test, the statistical significance of the ROM differences between consecutive levels and degrees of degeneration was determined by means of the Wilcoxon rank-sum test with Bonferroni correction to account for multiple comparisons, assuming a significance level of 0.05. Scatter plots representing the distribution of the ROMs with respect to the age of the subject at the time of the examinations were also built.

In order to create standardized plots of the position of the COR with respect to the intervertebral space as well as probability heatmaps, a procedure aimed at transforming the actual coordinates of the COR in the radiograph (image space) to a normalized system of reference in which the intervertebral disc is simply represented as a square was developed (Fig. 1). This procedure took advantage of the methods used in finite element analysis for transforming coordinates in isoparametric quadrilateral elements; in particular, the solution of the inverse transformation problem from global to natural coordinates was exploited [28]. The geometric transformation from the image space to the normalized system of reference was calculated for each intervertebral disc with respect to the extension radiograph and then applied to the predicted coordinates of the COR in the image space to obtain its coordinates in the normalized space. Standardized plots of the position of the COR with respect to a standardized, idealized intervertebral disc could then be constructed.

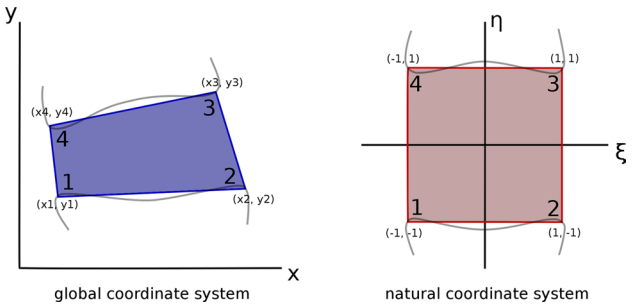

Fig. 1 In order to create standardized plots showing the locations of the centre of rotation independently of the shape of the intervertebral disc, a geometric transformation from the global coordinate system, or image space (left), to a natural coordinate system (right) in which the disc is simply represented as a square was developed exploiting methods used in finite element analysis [28]

Purposely developed Python scripts were used for all calculations and to create data plots, taking advantage of several free libraries and packages (StatsModels (https://www.statsmodels.org/), Plotly.py (https://plot.ly/python/), SciPy (https://www.scipy.org/) and Pycairo (https://www.cairographics.org/pycairo/)).

Results

The ROM in flexion–extension showed considerable variability among the subjects (Fig. 2). The median value of the whole population was 6.6°, with the first and third quartiles of 3.3° and 10.4° respectively, and extremes at 0.1° and 28.9°. A clear association between ROM and both spinal level and degree of degeneration was found, whereas no association with sex was observed (Fig. 2). A trend towards a ROM increase in the craniocaudal direction, between T12-L1 and L4-L5, was observed, with median values increasing from 5.2° to 7.8°. On the contrary, the ROM of L5-S1 was lower than that of L4-L5, with a median value of 7° ($p = 0.010$). A statistically significant difference between consecutive levels was also found between L2-L3 and L3-L4 ($p = 0.012$).

Disc degeneration determined a consistent reduction in the ROM in flexion–extension (Fig. 2), if assessed either on the radiographs [26] or on the T2-weighted MRI images [27]. By using the radiographic grading system, median values of 6.5°, 4.9° and 3.7° were determined for mild, moderate and severe degeneration, respectively, whereas non-degenerated motion segments had a median ROM of 8.2°. Statistically significant differences between consecutive degrees of degeneration were calculated between no and mild degeneration ($p < 0.001$), mild to moderate ($p < 0.001$)

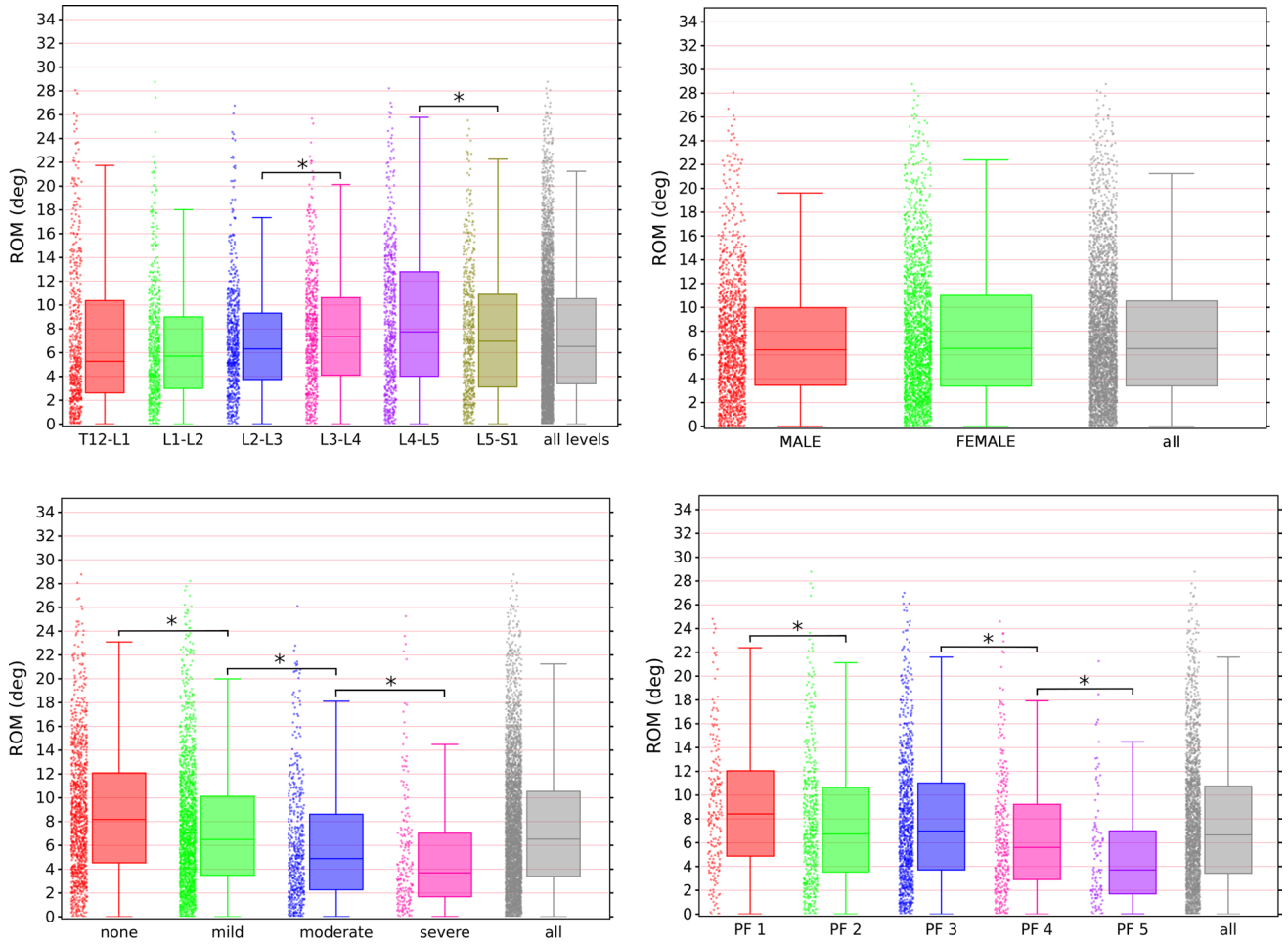

Fig. 2 Scatter and box plots showing the range of motion (ROM) for the different spinal levels (top left), for male and female subjects (top right) and for different degrees of degeneration assessed on radiographs [26] (bottom left) and on magnetic resonance imaging [27] (bottom right). "PF 1", "PF 2", etc.: Pfirrmann degree I, II, etc. Statistically significant differences between consecutive levels or degrees of degeneration are indicated by "*"

and moderate to severe ($p < 0.042$). Significant differences were also found between motion segments of grade I and II based on the Pfirrmann system ($p = 0.006$), with median values of 8.2° and 6.9°, respectively, whereas grade III did not show major differences with respect to grade II (median ROM 7.0°). More severely degenerated levels showed significantly lower motion (grade IV: median 5.6°; grade V: median 3.7°).

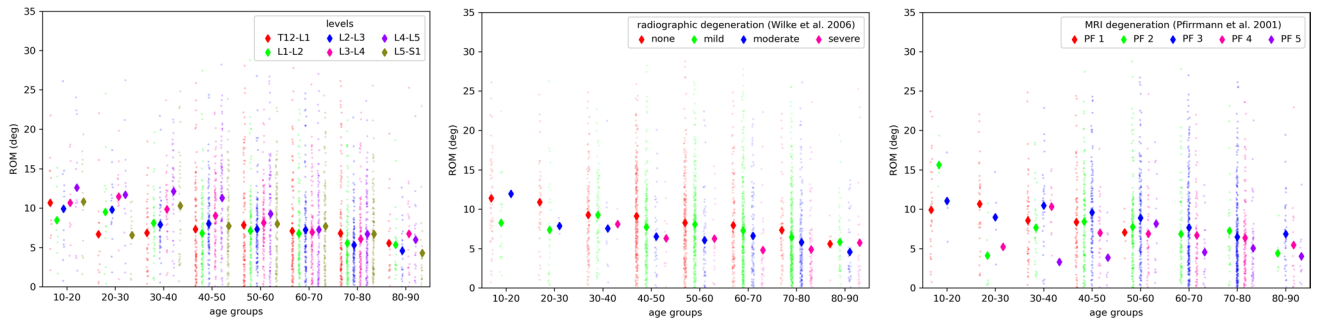

Fig. 3 Scatter plots showing the association between age groups and range of motion (ROM) subdivided by spinal levels (left), degrees of degeneration based on radiographs [26] (centre) and based on magnetic resonance imaging [27] (right)

The ROM was associated with the age of the subjects (Fig. 3). Lower ROMs were found towards the higher end of the age spectrum, consistently with the higher prevalence and severity of disc degeneration with increasing age. Interestingly, the ROMs clearly decreased with progressive ageing even when stratifying the motion segments by the degree of disc degeneration (Fig. 3).

No clear association between the position of the COR and the spinal level was observed (Fig. 4). In general, the most common COR position was approximately at the centre of the lower endplate of the intervertebral disc, or slightly lower, between L1-L2 and L4-L5. At L5-S1, the COR was located on average in the centre of the intervertebral space, whereas its position for the T12-L1 motion segment was distributed in a relatively large area, with the most common occurrences in the centre of the lower endplate of the disc.

Disc degeneration had an evident influence on the position of the COR (Figs. 5, 6). In case of non-degenerated discs or mild degeneration, as well as for Pfirrmann grades of I, II and III, the dispersion of the data around the most probable location was relatively low. On the contrary, moderate and severe disc degeneration assessed on both radiographs and MRI scans involved significantly larger variances of the COR position. The probability heatmaps did not show any clear preferential direction for the dispersion of the COR position in case of disc degeneration; indeed, the COR appeared to be distributed with random patterns around the centre of the intervertebral space.

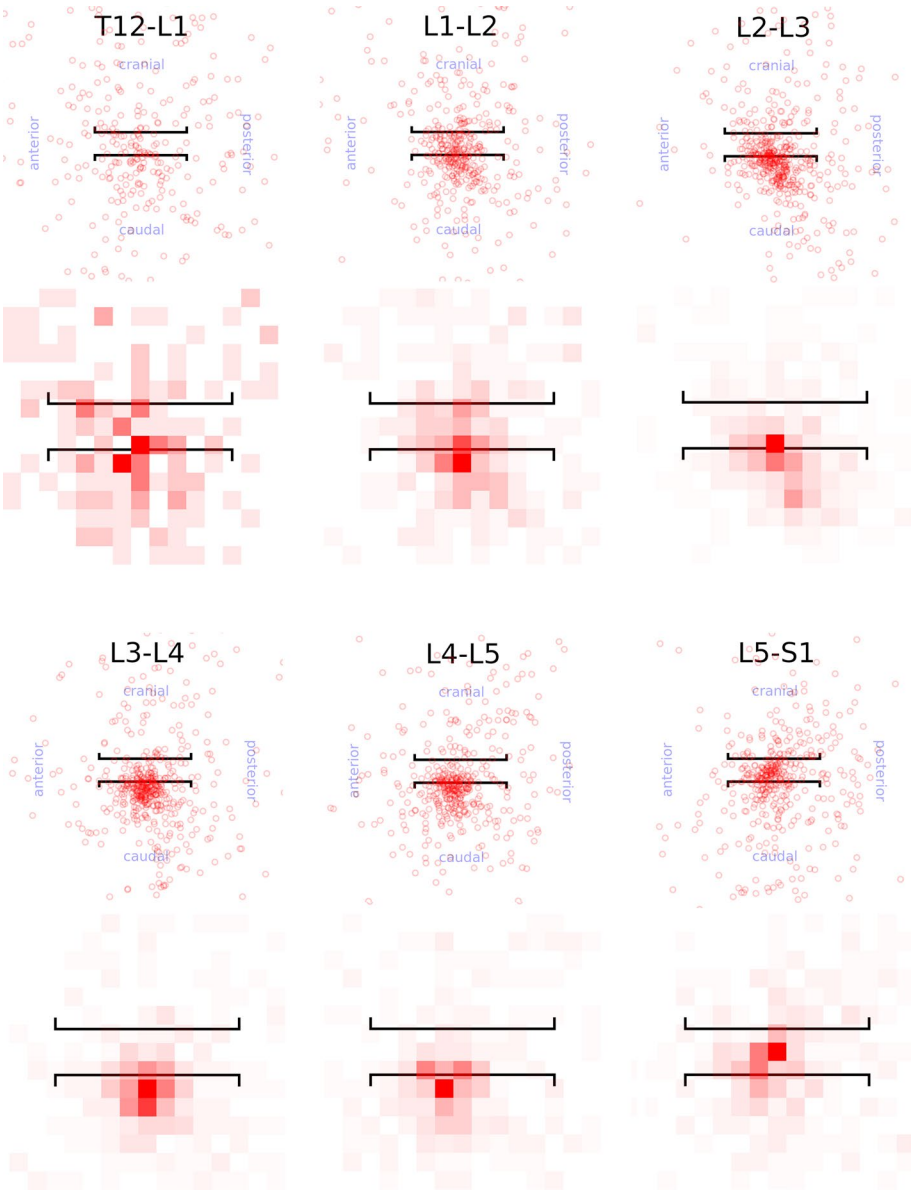

Fig. 4 Scatter plots (first and third rows) and probability heatmaps (second and fourth rows) indicating the location of the centre of rotation in the different spinal levels with respect to a standardized intervertebral disc

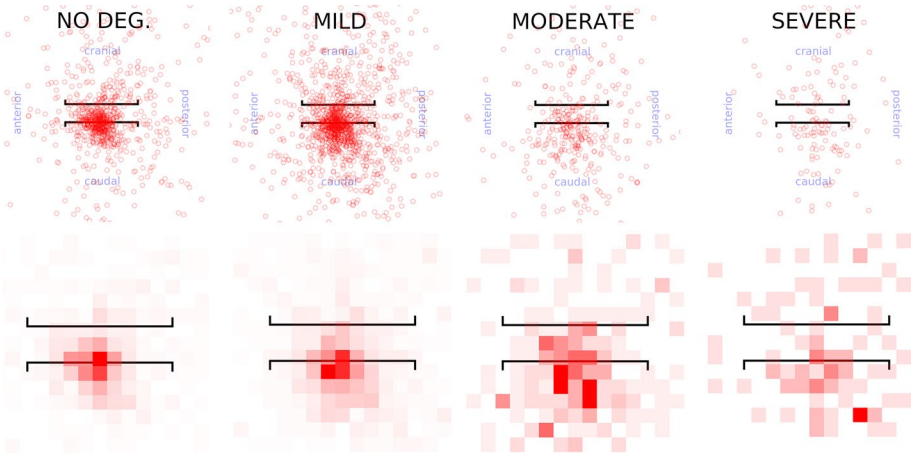

Fig. 5 Scatter plots (first row) and probability heatmaps (second row) indicating the location of the centre of rotation for the different degrees of degeneration assessed on the radiographs [26] with respect to a standardized intervertebral disc

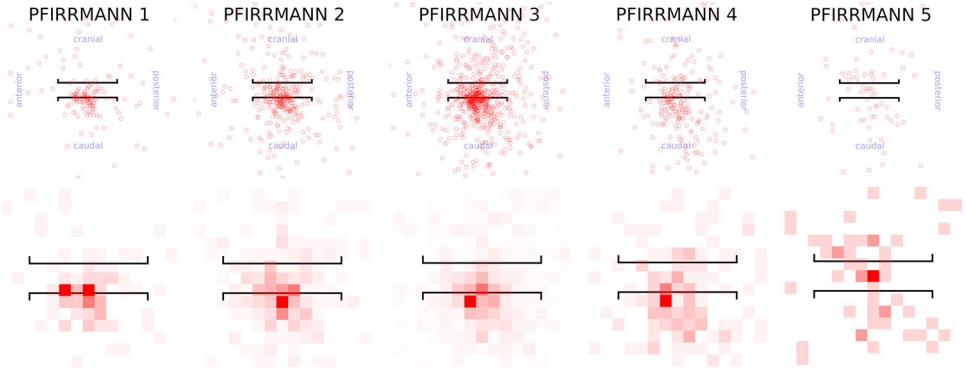

Fig. 6 Scatter plots (first row) and probability heatmaps (second row) indicating the location of the centre of rotation for the different degrees of degeneration assessed on magnetic resonance imaging [27] with respect to a standardized intervertebral disc

Discussion

In this study, we investigated the ROM and position of the COR of the lumbar motion segments in flexion–extension in 602 patients suffering from low back pain or suspect instability. The study constitutes the largest analysis to date of in vivo lumbar motion; such a *big data* analysis has been made feasible by the use of automated analysis methods and batch processing.

In general, the current results are in good agreement with the available literature. Staub and colleagues [24] investigated the ROM and COR position in 658 non-degenerated lumbar levels of asymptomatic individuals in the seated position and also found increasing ROMs in the craniocaudal directions between L1-L2 and L4-L5 and a decrease between L4-L5 and L5-S1. However, the mean values of the ROMs ranged between 11° and 14.5°, thus generally higher than those found in the present study, even in comparison with the non-degenerated segments (Pfirrmann I) which had a mean ROM of 9.1°. Another study, despite being conducted in the standing posture, found similar results in 11 young healthy volunteers [21]. These discrepancies should be attributed to the different populations under examination, i.e. low back pain and suspect instability patients seeking medical attention in this study versus asymptomatic, relatively young subjects in the previous works.

Nevertheless, a study in which patients with low back pain and disc degeneration were investigated also showed higher mean ROMs, ranging between 10.7° and 16.8° at the various levels, although with large standard deviations and based on a group of symptomatic subjects with relatively small size ($N=27$) [19]. We believe that age played a major role in determining the differences; indeed, the mean age of 40 years for the subjects with low back pain was considerably lower than that of the patients of the present work, which has a median value of 60 years. As a matter of fact, when considering only the subjects with age lower than 45 years and no degeneration, a median ROM of 13.9° was found in the present study; when including also the levels with signs of degeneration, the median ROM decreased to 12.12°, thus in complete agreement with the published observations [19]. It should therefore be concluded that ageing determines a decrease in the flexibility of the lumbar spine per se, independently of the presence of degeneration signs. This association between ageing and decreased ROM generally confirms the findings of a study conducted

on healthy volunteers [23], which, however, mostly covered the age range between 20 and 60 years.

The ROMs were also in good agreement with flexibility data measured in vitro by subjecting cadaver specimens to standardized loads such as pure moments in bending and torsion. Although such simplified loading conditions do not replicate in detail the in vivo loading environment, previous studies demonstrated that pure moments produce forces and moments in implants comparable with those observed in living subjects [29]. The present findings prove that also the ROMs measured in vitro are in agreement with the physiological ones, and thus further validate standardized loading conditions used in experiments. Indeed, Kettler et al. tested 203 specimens under a pure moment of ± 7.5Nm in flexion–extension and found an average ROM of 9° for non-degenerated levels and 6° for severely degenerated ones [30], which compare relatively well with the current observations (8.2°–3.7°, respectively). In another study, Mimura et al. subjected 47 specimens to pure moments of ± 10Nm, and observed ROMs between 12° and 9.5° depending on the degree of disc degeneration [31]. The lower ROMs observed in vivo for the degenerative segments may be attributed to pain and discomfort as well as fear-avoidance behaviour and anticipation of pain, which may add to the increased stiffness in reducing the segmental motion.

In the present study, the COR was found to be most commonly located approximately in the centre of the lower endplate of the intervertebral disc, independently of the vertebral level. This finding strongly agrees with previous observations [24, 32, 33]. On the contrary, the location of the COR in degenerated levels showed an apparently random dispersion around the centre of the intervertebral space, especially in case of severe degeneration or Pfirrmann V. Previous literature indicated that degeneration induces altered motion patterns in the lumbar spine, involving altered locations of the COR [34, 35]. However, to our knowledge, quantitative investigations of this issue have previously been conducted only in vitro on cadaver specimens [36–38] as well as with numerical models [39, 40]; the present study therefore provides a large-scale data set of in vivo COR locations in degenerated lumbar motion segments for the first time. The scarcity of available data reflects the technical difficulties typically associated with the time-consuming task of determining the COR location by means of manual and computer-aided methods [24, 32], which may result in low accuracy, precision and reproducibility. These limitations were overcome in the present study by the use of automated methods based on image registration, which allowed us to analyse thousands of motion segments in a robust and reproducible way in a relatively short time frame.

The importance of the COR as a metric to evaluate the alterations of the motion pattern due to degeneration, for example in case of degenerative instability, has been highlighted in several papers [36, 41, 42]. Besides, the COR location has been shown to determine the biomechanics of the motion segment, especially in terms of forces in the facet joints [37, 39, 43], which can in turn be implicated with the progression of degenerative disorders or deformities [44, 45]. Furthermore, knowing the in vivo location of the COR, in both healthy and degenerative conditions, provides valuable information for the design of implants aimed at restoring the physiological function of the motion segment, such as total disc replacements [38, 46]. We therefore believe that the data about COR locations here provided, taking into account the large number of subjects and the wide ranges of age and degrees of degeneration, constitute a valuable addition to the available knowledge about the motion of the lumbar spine in vivo.

The main limitation of the study reflects the choice of investigating the flexion–extension motion of the lumbar spine only by analysing the radiographs in full flexion and extension, thus neglecting valuable information about the dynamic behaviour of the different levels [47] as well as the instantaneous positions of the COR during the motion itself, which is commonly investigated in in vitro [1, 2, 37] and numerical studies [39, 40] and less frequently in vivo [33, 48, 49]. This choice has been determined by the availability of the images in the database of the institute; while a radiograph in the standing posture is typically available in addition to the dynamic images, it is normally acquired in a different session, thus with different magnification and possibly imaging parameters, resulting in poor performance of the image registration algorithm if used in combination with the flexion–extension radiographs. Other limitations pertain to the retrospective design of the study and to the broad inclusion criteria for the subjects. Indeed, we decided to employ such a study design, in which we excluded only the radiographs with poor quality, those exhibiting fractures, implants or insufficient field of view, in order to maximize the number of images to be processed. On the other side, this design did not allow us performing a stratification of the subjects in terms of symptoms and functional status.

In conclusion, the present data constitute the largest analysis of the in vivo motion of the lumbar spine in flexion–extension currently available, covering a wide range of clinical scenarios in terms of age and spinal degeneration. In general, an agreement between the novel and published data was found in terms of ROM and COR locations. Among the novel findings, we were able to demonstrate that ageing determines a reduction in the mobility of the lumbar spine independently of the presence of degeneration and that in degenerative levels, CORs are dispersed around the centre of the intervertebral space with no preferential directions. We also demonstrated that ROMs measured in in vitro experiments are in good agreement with those in vivo.

Availability of data and material

All range of motion and centre of rotation data are available from the corresponding author upon reasonable request. The radiographic data for this project are confidential.

Funding The study was partially supported by the Italian Ministry of Health ("Ricerca Corrente").

Code availability The code used to calculate the motion parameters is confidential.

Compliance with ethical standards

Conflicts of interest None.

Ethics approval The study has been approved by the Ethics Committee of Ulm University (no. 50/20).

Consent to participate All patients provided informed consent for the use of anonymized data for scientific and educational purposes.

Consent for publication All patients provided informed consent for the use of anonymized data in scientific publications.

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