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Title: Dynamic, Six-Axis Stiffness Matrix Characteristics of the Intact Intervertebral Disc, and a Disc Replacement

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ABSTRACT

Thorough pre-testing is critical in assessing the likely in-vivo performance of spinal devices prior to clinical use. However, there is a lack of data available concerning the dynamic testing of lumbar (porcine model) total disc replacements (TDRs) in all six axes under preload conditions. The aim of the present study was to provide new data comparing porcine lumbar spinal specimen stiffness between the intact state, and after the implantation of an unconstrained TDR, in six degrees of freedom.

The dynamic, stiffness matrix testing of six porcine lumbar isolated disc specimens was completed using triangle waves at a test frequency of 0.1 Hz. An axial preload of 500 N was applied during all testing. Specimens were tested both in the intact condition (INTACT), and the test repeated after the implantation of the TDR.

Sixteen key stiffness terms were identified for the comparison of the INTACT and TDR specimens, comprising the six principal stiffness terms, and ten key off-axis stiffness terms. The TDR specimens were significantly different to the INTACT specimens in twelve of these key terms including all six principal stiffness terms. The implantation of the TDR resulted in a mean reduction in the principal stiffness terms of 100%, 91%, and 98% in lateral bending, flexion-extension, and axial rotation respectively.

The novel findings of this study have demonstrated that the unconstrained, low-friction TDR does not replicate the stiffness of the intact specimens. It is likely that other low-friction TDRs would produce similar results due to stiffness being actively minimised as part of the design of low-friction devices, without the introduction of stiffening elements or mechanisms to more accurately replicate the mechanical properties of the natural intervertebral disc. This study has demonstrated, for the

first time, a method for the quantitative comparative mechanical function testing of TDRs, and provides baseline data for the development of future devices.

Introduction

The importance of pre-clinical testing to assess spinal devices prior to clinical use is well understood. However, there remains a lack of standardised test protocols for characterising the intact spine, or new spinal devices.[1, 2] As a result it is often difficult, or impossible, to quantitatively assess the likely in-vivo performance of new devices compared to the healthy spine.

TDR procedures emerged as a credible alternative to arthrodesis during the 1980s, and the Charité disc (DePuy Spine, Inc., Raynham, MA, USA) became the first TDR to be approved for clinical use by the FDA approximately a decade ago,[3] yet there remains limited data to suggest that TDR procedures offer clinically relevant improvements over the fusion procedures that they are designed to supersede.[4]

TDRs should allow motion at the operative level of the spine, whilst also being capable of withstanding the high loads present due to the weight of the head and/or upper body, and the action of muscles in providing stability and motion. If TDRs are to restore the kinematics and transfer of load through the spine, they should have similar mechanical properties to a healthy intervertebral disc (IVD).[5] However, the majority of TDR devices use low-friction ball and socket bearings. Such a design philosophy is at odds with the mechanical structure of the natural disc, and it is only with advances in materials and manufacturing techniques that biofidelic TDR devices have become more widespread.[6-9] This new generation of devices are currently entering pre-clinical and clinical trials, and as such there is limited data available about how they perform in-vivo in the mid- to long-term.

Pre-clinical performance testing is critical for all orthopaedics devices, but creates unique challenges for the testing of total disc replacements (TDRs), as these devices should be assessed in regard to how they restore the biomechanics of the natural IVD, which has six degrees of freedom (dof). Therefore, in order to replicate the in-vivo conditions as closely as possible, mechanical characterisation tests of the natural spine and efficacy tests of TDRs should be carried out in six axes, at a testing speed equivalent to normal activities, over physiological ranges of motion (ROMs), with an axial preload, and at a temperature and moisture condition representative of the in-vivo environment.[2] The stiffness of spinal specimens is significantly affected by the facets and posterior ligaments,[10] and this could result in a shielding effect when comparing the intact IVD with TDR devices.[11] Therefore, whilst the comparison to the in-vivo scenario may be reduced through the removal of the posterior elements of functional spinal units (FSUs) to create isolated disc (ISD) specimens, a greater understanding of the direct mechanical effect of a TDR compared to intact IVDs may be gained with such a testing protocol.

There are a number of studies that have compared spinal specimens with an intact IVD and after a TDR.[12-15] However, despite the stiffening effect of a physiological preload being well-documented,[10, 16, 17] there are few biomechanical studies of TDRs that have included the application of a physiological preload,[18-20] and no studies that have assessed a TDR dynamically, in all six axes, with a physiological axial preload.

The aim of this study was to compare the dynamic, six-axis stiffness matrices of porcine spinal specimens in an intact state and after the implantation of a DePuy In Motion TDR (DePuy Spine, Inc.). The mechanical function of the TDR was investigated in terms of how it was able to replicate the mechanical properties of the IVD in 6 dof.

Materials and methods

The In Motion device is a double ball and socket design, with two cobalt-chrome endplates and a lens shaped ultra-high molecular weight polyethylene (UHMWPE) sliding core with a circumferential flange to limit ROM and prevent dislocation (Figure 1). The endplates feature spikes for primary stability, and a textured titanium coating for secondary stability through bone in-growth. The In Motion device is an updated version of the well-established Charité disc replacement. The difference between the two devices is that the In Motion has a flat section on the outer faces of the endplates to aid implantation with the use of improved surgical instrumentation.

The design of the In Motion device is such that there is a variable centre of rotation (COR), with the variable radius of the core permitting relative translation between of the two endplates. The device used in the present study was medium in size, and comprised an inferior endplate with an angle of 0°, a superior endplate with an angle of 5°, and an 8.5 mm core.

Specimens were harvested from three pigs aged between eight and twelve months at the time of slaughter, with masses of approximately 60 kg. The dissection of FSUs from longer sections of spine (T12-S1) was undertaken on the day of procurement. The musculature and facets were then removed, leaving ISD specimens comprising the vertebral bodies, the IVD, and the anterior and posterior longitudinal ligaments (ALL and PLL respectively). Six porcine lumbar ISD specimens were prepared: two L1-L2; two L3-L4; and two L5-L6. Once prepared, the specimens were labelled, triple-sealed in plastic bags, and frozen at a temperature of -24°C until the day of testing.

On the morning of testing each specimen was left to thaw for three hours at room temperature in a sealed plastic bag to minimise moisture loss due to evaporation. During the last hour of thawing, the specimen was removed from the plastic bag, and three self-tapping screws were driven into the vertebral bodies at the cranial and caudal ends of the specimen to aid stability when potted in aluminium specimen holders using low melting point alloy (MCP75; Mining & Chemical Products Ltd., Northamptonshire, UK). Care was taken during potting to ensure that the IVD was aligned with the horizontal plane. Water-cooling of the specimen holders was used to prevent overheating of the specimen. The cranial end of the specimen was potted first, followed by the caudal end. The specimen was slowly lowered into the caudal specimen holder, which allowed the alignment to be finely adjusted prior to potting. Once the specimen was potted, it was sprayed with 0.9 % saline solution and wrapped in plastic food wrapping in order to maintain an adequate moisture level.

The specimen was then mounted in a custom-developed six-axis spine simulator[21] with the specimen in the neutral position and the centre of the IVD aligned horizontally and with origin of the displacement axes (Figure 2). All rotations and translations applied as part of the stiffness matrix tests were based on this fixed datum. A six-axis load cell was mounted between the caudal specimen holder and the baseplate of the spine simulator (AMTI MC3-A-1000, Advanced Mechanical Technology, Inc., MA, USA).

All testing was completed at room temperature (20±2°C). The ROM used for the stiffness matrices aimed to replicate normal ROMs, and was the same as used in previous in-vitro testing:[11, 21, 22] ±3 mm in anterior-posterior shear (TX); ±1.5 mm in lateral shear (TY); ±0.4 mm in axial compression-extension (TZ); and ±4° in lateral bending (RX), flexion-extension (RY), and axial rotation (RZ). All axes were tested using displacement control at a single test frequency of 0.1 Hz; this resulted in a testing speed of 1.6°/s in the rotational axes.

The determination of each stiffness matrix comprised six tests, one for each axis. For each test, one axis was cycled through five triangle waves, while the other five axes were held in a stationary position. Position and load data were acquired at 100 Hz for all tests using dSPACE ControlDesk software (Version 2.3, dSPACE Ltd., Melbourn, UK). For each specimen, stiffness matrix tests were completed first in the intact condition (INTACT), with the application of a 500 N axial preload via the actuator of the TZ axis and an equilibration time of 30 minutes. Following the completion of the stiffness matrix test, the specimen was removed from the spine simulator and the In Motion device was implanted. The specimen was again sprayed with 0.9% saline solution and wrapped in plastic food wrapping, re-mounted in the spine simulator in the same position, and the same stiffness matrix testing procedure undertaken.

The order of testing each axis within a stiffness matrix was randomised so as to minimise any residual effects of the previous test(s) on the results of any axis. During testing the axial position was adjusted between each test in order to maintain the preload of 500 N, if required.

The In Motion surgical instrumentation was not available for implantation. However, the operative technique was followed,[23] with the exception that the PLL was resected instead of being released to account for the smaller disc height of porcine discs compared to human discs. A spine surgeon demonstrated the disc replacement procedure on a porcine lumbar FSU prior to commencing the stiffness matrix testing for training purposes. This allowed the specimen preparation and device implantation to simulate the clinical situation.

The first two cycles of each test were considered as preconditioning cycles, and the last three cycles were used to calculate the stiffness at the centre of the superior vertebral body using rigid body transformations and the linear least squares (LLS) method over the entire cycle. The stiffness matrices were not assumed to be symmetric about the principal stiffness terms, resulting in a 6x6 matrix. Whilst infinitesimal motions would be expected to result in a matrix symmetrical about the diagonal of the principal stiffness terms ($k_{1,5} = k_{5,1}$, $k_{2,3} = k_{3,2}$, etc.), this is not the case over finite motions.[11, 20] However, half the terms were expected to be negligible due to sagittal plane symmetry of the specimens.[11, 24] For example, it would be expected that lateral shear forces, lateral bending moments and axial torque would be negligible as a result of anterior-posterior translation, anterior-posterior rotation, or axial compression-extension. The R^2 value for each term in the stiffness matrices was determined to assess the linearity.

For each term of the stiffness matrix a zero error (ZE) was calculated based on the noise floor of the load cell (±5 N and ±0.25 Nm), and the ROM for each axis. The noise floor was calculated based on the mean of a two second reading taken prior to testing each specimen. Stiffness terms with a value within the ZE were regarded as negligible.

Statistical comparisons were made between the stiffness terms of INTACT and TDR specimens using paired t-tests. All statistical comparisons were completed using SPSS (IBM SPSS Statistics 19; IBM Corporation, Armonk, NY, USA). In addition to the statistical analysis, the results were normalised and the difference calculated. In this method, the baseline stiffness terms were normalised to 0%, and an increase or decrease in stiffness as a result of the implantation of the TDR, and represented by a positive or negative percentage change respectively.[21, 25]

Results

All tests showed good repeatability during the three cycles over which the stiffness terms were calculated. Principal stiffness terms in INTACT specimens exhibited strongly linear relationships (R^2>0.78), with approximately half of non-negligible off-axis terms all exhibiting similar linear relationships. Though some terms exhibited symmetry about the principal stiffness terms, the matrices were generally asymmetric.

One specimen, when implanted with the TDR, exhibited impingement of the endplates with the outer flange of the mobile core, which was believed to be due an overly posterior positioning of the device. This produced greatly increased moments at flexion angles greater than 2 degrees. The off-axis stiffness terms related to the testing of the RY axis ($K_{1,5}$, $K_{2,5}$, $K_{3,5}$, $K_{4,5}$, and $K_{6,5}$) were assessed for deviation from the results of other specimens as a result of the misalignment. All five terms were comparable with other specimens, suggesting that the only term affected was the flexion-extension stiffness. Therefore, this specimen was removed solely from the calculation of the flexion-extension stiffness term ($K_{5,5}$), and from the associated statistical analysis between INTACT and TDR groups.
Significant differences were detected between the INTACT and TDR specimens in 18 of the 36 terms of the stiffness matrix (Table 1), including all six principal stiffness terms.

Eighteen terms of the 36 term stiffness matrix were expected to be negligible due to sagittal plane symmetry. This was the case for 11 terms, which were within the ZE in both the INTACT and TDR specimens. A further two terms ($K_{5,4}$ and $K_{4,5}$) were within the ZE for INTACT specimens, one term ($K_{3,6}$) was within the ZE for TDR specimens only, and four terms ($K_{3,2}$, $K_{5,2}$, $K_{4,3}$,and $K_{3,4}$) were non-zero in both INTACT and TDR specimens. There were significant differences between the INTACT and TDR specimens in six of the 18 terms that were expected to be negligible ($K_{2,1}$, $K_{6,3}$, $K_{4,5}$, $K_{1,6}$, $K_{3,6}$, and $K_{5,6}$).

Of the 18 terms that were not expected to be negligible due to sagittal plane symmetry, two were found to be below the ZE in both INTACT and TDR specimens ($K_{1,3}$ and $K_{6,4}$). There were significant differences between INTACT and TDR specimens in 12 of the remaining 16 stiffness terms. Five of the twelve significantly different stiffness terms were reduced to being within the ZE as a result of the implantation of the TDR ($K_{6,2}$, $K_{4,4}$, $K_{2,6}$, $K_{4,6}$,and $K_{6,6}$).

The mean R^2 values in the principal stiffness terms of INTACT specimens were greater than 0.78 in all cases, greater than 0.94 for $K_{3,3}$ and $K_{6,6}$, and greater than 0.99 for $K_{1,1}$ and $K_{2,2}$ (Table 3). Whilst the

R^2 values of non-principal stiffness terms were generally lower than the principal terms, and also demonstrated greater variability, key off-axis terms ($k_{5,1}$, $k_{4,2}$, $k_{6,2}$, $k_{1,5}$, $k_{3,5}$, $k_{2,6}$) did demonstrate strongly linear relationships (Figure 3).

The calculation of the normalised change in stiffness with respect to paired INTACT and TDR specimens demonstrated that the whilst the implantation of the In Motion device led to significant differences in all principal stiffness terms, the mean change was larger for the rotational stiffness terms (-100%, -91%, and -98% for $K_{4,4}$, $K_{5,5}$, and $K_{6,6}$ respectively) compared to the translational stiffness terms (-24%, +4%, and -9% for $K_{1,1}$, $K_{2,2}$, and $K_{3,3}$ respectively) (Figure 4).

Discussion

The aim of this study was to compare the stiffness matrices of lumbar porcine ISD specimens in the intact state, and after the implantation of an unconstrained low-friction TDR. This is the first study to assess the efficacy of a TDR dynamically, in 6 dof, with a physiological preload. It was found that the low-friction articulating design of the In Motion device led to significant differences in the majority of key stiffness terms.

Limitations

The operative procedure for the implantation of the In Motion TDR was modified to reflect the altered geometry of the porcine specimens. The surgical procedure for the implantation of the In Motion device calls for the ALL to be resected and the PLL to be released.[23] These ligaments were left intact for the testing of the specimens in the intact state but both were resected during the implantation of the In Motion disc. It has been shown that the disc height is a more important factor affecting ROM than whether or not the PLL has been resected,[26] and therefore the PLL was resected due to the smaller disc height of the porcine specimens.

Only one In Motion device was available in the present study. Whilst using a new device for each specimen would have provided a clearer understanding of the stiffness of a typical device, the authors believe that the results reliably reflect the low-friction articulating design of the In Motion device. Poor device positioning was reported to significantly reduce ROM and clinical outcomes in the FDA IDE study of the Charité TDR,[27] and it is probable that the positioning of the same device within individual specimens in the present study affected the results more than the mechanical differences between individual devices.

Dickey et al.[28] and Wilke et al.[29] have reported that porcine lumbar specimens exhibit mechanical behaviour similar to human cadaveric specimens, though the stiffness may be different in absolute terms. However, both these studies compared porcine and human cadaveric specimens using pure moment tests, without the application of an axial preload. Studies by Gardner-Morse and Stokes using porcine[10] and human cadaveric[24] FSU specimens, with preloads of 400 and 500 N respectively, reported similar values in the principal stiffness terms over small ROMs. Further testing using human cadaveric specimens would enable a direct comparison between the intact condition and TDRs, nevertheless, porcine spinal specimens provide valuable insight into the comparative mechanical function of spinal instrumentation due to the reduced inter-specimen variability compared to human specimens.[29]

The present study tested specimens at room temperature (20±2°C) after being sprayed with 0.9% saline, and wrapped in plastic wrap to minimise moisture loss through evaporation. Whilst this method meets previous recommendations for in-vitro spinal testing,[2] Bass et al.[30] have shown that the stiffness of the ALL is significantly higher at 21.1°C compared to 37.8°C. Therefore, it may be advisable in future studies to test specimens at body temperature.

The specimens in the present study were tested over ROMs representative of the normal physiological environment,[22] and so did not assess the comparative mechanical performance of the intact IVD with the TDR over the maximum physiological ROMs. It may be useful in future studies to assess ROMs at the extreme physiological range, in addition to the normal ROMs assessed in the present study. The R^2 values demonstrated that many of the key stiffness terms exhibited strongly linear behaviour; however, it is likely that the LLS method would be less applicable over maximum ROMs. The linearity of the stiffness terms of the INTACT specimens in the present study compare reasonably with previously published data of the principal stiffness terms of lumbar porcine spinal specimens over smaller ROMs,[10] particularly in regard to the principal stiffnesses in anterior-posterior shear ($k_{1,1}$), lateral shear ($k_{2,2}$), and axial rotational ($k_{6,6}$). Whilst it is a limitation that the stiffness terms were calculated using the LLS method over the entire load cycle of the last three cycles, it does provide a consistent manner to calculate all the terms of the matrix, has been adopted in previous stiffness matrix studies,[10, 11, 21] and provides an acceptable measure of the stiffness in many of the key stiffness terms.

The stiffness matrix method used a fixed COR, which may be a less physiological approach than pure moment tests, however, it does allow a comparison of the mechanical properties of different structures in 6 dof, with the addition of shear testing, which pure moment testing omits. Whilst the rotational tests occurred about a fixed point, the resulting off-axis shear forces were used to calculate the off-axis stiffness terms, and provide a quantitative comparison between the INTACT and TDR conditions. The variable COR of the In Motion device means that rotations should occur about the test datum without off-axis shear loads occurring, and the comparison of all stiffness matrix terms between the Intact IVD and the In Motion TDR provide a valuable measure of the ability of the TDR to replicate the mechanical properties of the IVD. However, the use of pure moment testing to quantitatively assess the effect of TDR implantation compared to the natural disc would also provide valuable data and should be considered for future tests.

Principal Stiffness Terms

Previous studies have compared intact IVD and TDR devices[12-15] but neglected to apply a physiological preload, which is known to significantly affect spinal stiffness. These studies also used FSU or multi-level spinal specimens, and it is possible that the facets and posterior ligaments will have shielded potential differences between the intact disc and the TDR. It is important to consider the stiffness and stability provided by the posterior elements, and in-vitro testing using FSU or multi-level specimens can provide valuable data regarding the effect of spinal instrumentation on the spine. However, the advantage of testing ISD specimens is that there can be a direct mechanical comparison between the IVD and a TDR device designed to replace the IVD. The completion of multi-axis testing using a variety of the above specimen types, combined with thorough clinical follow-up of the effects of TDR in 6 dof, will allow a greater understanding of what represents clinically significant differences when comparing natural structures of the spine, with spinal instrumentation, and the results of the present study provide a step toward that goal.

Five out of six principal stiffness terms were significantly reduced as a result of the implantation of the TDR in the present study, and the reductions were particularly large in the rotational stiffness terms. This was expected, as a key design feature of the In Motion TDR is to provide low-friction rotational motion. However, the axial preload led to instability, resulting in negative stiffness values, particularly in lateral bending ($K_{4,4}$). The muscles provide a great deal of stability to the spine, and it may be that the device would perform more favourably if the axial preload was applied using a follower load, or a system of simulated muscle forces. However, such alterations would be likely to affect the intact disc in a similar manner, providing increased stability, resulting in higher stiffness values for both the INTACT and TDR specimens.

The principal stiffness terms of the TDR specimens in translation ($K_{1,1}$, $K_{2,2}$, and $K_{3,3}$), though significantly different from INTACT specimens, were similar in magnitude. This can be seen most clearly in the normalised changes in stiffness, which were -24%, +4%, and -9% for anterior-posterior shear, lateral shear, and axial compression-extension respectively. Whilst current data make it difficult to define alterations in stiffness that are clinically acceptable due to the implantation of a TDR, the change in $K_{1,1}$, $K_{2,2}$ were within the expected variation of a patient population, which suggests that these terms may be within acceptable limits in the present study, though further data using cadaveric specimens would determine more fully if that is the case.

Off-Axis Stiffness Terms

Previous research by Gardner-Morse and Stokes[24] identified key off-axis stiffness terms associated with the stiffness matrix testing of spinal specimens. The present study identified the same terms as important in the mechanical evaluation of a spinal specimen in 6 dof, with the addition of the diagonal terms that were previously assumed to be symmetrical about the principal stiffness terms. This resulted in ten key off-axis stiffness terms, of which six were significantly different between the INTACT and TDR specimens (Table 2).

The term $K_{1,3}$ was found to be negligible by Gardner-Morse and Stokes.[24] The present study confirmed previous findings that $K_{1,3}$ and $K_{3,1}$ are not key off-axis stiffness terms. The present study found term $K_{1,3}$ to be negligible, and the diagonal term ($K_{3,1}$), whilst not below the ZE, was also low in magnitude.

Two further terms not necessarily expected to be negligible due to sagittal plane symmetry were within the ZE in INTACT specimens: The anterior-posterior shear force due to flexion-extension ($K_{1,5}$), and the lateral shear force due to lateral bending ($K_{2,4}$). That these terms were negligible in INTACT specimens suggests that the rotations were applied close to the natural COR. These terms were not below the ZE in TDR specimens, though the differences between the INTACT and TDR specimen were not significant for either term. Such comparisons provide useful data about whether a TDR has the capacity to replicate the COR of intact specimens. The results also confirm that whilst stiffness matrix testing forces rotation to occur about a fixed COR, which is less physiological than pure moment testing, the result of doing so can be detected and assessed through the associated shear forces.

Sagittal Plane Symmetry

The majority of terms that were expected to be negligible due to sagittal plane symmetry were within the ZE in both the INTACT and TDR specimens. Of the five terms that were not within the ZE with INTACT specimens, three may have been affected by the LLS method of calculating the stiffness ($K_{3,2}$, $K_{3,4}$, and $K_{3,6}$), and more specimens may be required to average out the asymmetry of individual specimens, and any misalignment during potting and mounting the specimens. Further studies using a larger number of specimens would provide a clearer understanding of the practical ZE for stiffness matrix testing in the spine simulator used in the present study.

There were six stiffness terms in the present study for which significant differences were detected in terms that were expected to be negligible ($K_{2,1}$, $K_{6,3}$, $K_{4,5}$, $K_{1,6}$, $K_{3,6}$, and $K_{5,6}$). In four of these terms ($K_{2,1}$, $K_{6,3}$, $K_{1,6}$, and $K_{5,6}$) the magnitude of both the INTACT and TDR specimens were below the ZE. This implies that the ZE was relatively conservative for these terms, as differences could still be detected. However, while the differences were significant, it is unlikely that they would be clinically relevant due to the low magnitudes of stiffness measured.

Conclusions

The lack of rotational stiffness found in the In Motion device is likely to be similar in many other ball and socket TDRs, due to the ball and socket working principle. Constrained ball and socket TDRs may also lead to increased off-axis loads as a result of a fixed COR that may not approximate the COR of the natural IVD. However, it has also been reported that constrained designs may reduce the shear forces at the facets joints compared to unconstrained ball and socket devices.[31]

Methods of introducing stiffness to the In Motion device have already been considered by DePuy in the form of a patent for a spring structure around the circumference of the device.[32] However, a critical aspect of any design modifications would be to provide rotational stiffness in all three planes, whilst maintaining the variable COR, which is a key feature of the In Motion device.

This study has demonstrated that dynamic stiffness matrix testing, in 6 dof, can be used effectively to compare spinal specimens in an intact state and after the implantation of a TDR. Sixteen key stiffness terms were identified for the mechanical function assessment of TDRs compared to intact specimens. The lack of stiffness and instability of the In Motion TDR led to 12 of these 16 terms being significantly different from the intact disc.

The low-friction ball-and-socket approach to total disc arthroplasty is unlikely to lead to the reproduction of the natural spine biomechanics. It is expected that the data from the present study will aid in the development of future TDR devices, ultimately leading to improved clinical outcomes for TDR procedures.

References

1. Goel VK, Panjabi MM, Patwardhan AG, Dooris AP, Serhan H. Test protocols for evaluation of spinal implants. *Journal of Bone and Joint Surgery-American Volume*. 2006; 88 Suppl 2: 103-9.
2. Wilke HJ, Wenger K, Claes L. Testing criteria for spinal implants: recommendations for the standardization of in vitro stability testing of spinal implants. *European Spine Journal*. 1998; 7: 148-54.
3. Food and Drug Administration. Summary of Safety and Effectiveness - Charité Artificial Disc. Rockville, MD, USA: Food and Drug Administration, 2004.
4. Jacobs WC, van der Gaag NA, Kruyt MC, et al. Total disc replacement for chronic discogenic low back pain: a cochrane review. *Spine*. 2013; 38: 24-36.
5. Costi JJ, Freeman BJ, Elliott DM. Intervertebral disc properties: challenges for biodevices. *Expert Rev Med Devic*. 2011; 8: 357-76.
6. McNally D, Naylor J, Johnson S. An in vitro biomechanical comparison of Cadisc-L with natural lumbar discs in axial compression and sagittal flexion. *European Spine Journal*. 2012; 21 Suppl 5: S612-7.
7. Mahomed A, Moghadas PM, Shepherd DE, Hukins DW, Roome A, Johnson S. Effect of axial load on the flexural properties of an elastomeric total disc replacement. *Spine*. 2012; 37: E908-12.
8. Pimenta L, Springmuller R, Lee CK, Oliveira L, Roth SE, Ogilvie WF. Clinical performance of an elastomeric lumbar disc replacement: Minimum 12 months follow-up. *SAS Journal*. 2010; 4: 16-25.
9. Reyes-Sanchez A, Miramontes V, Olivarez LMR, Aquirre AA, Quiroz AO, Zarate-Kalfopulos B. Initial clinical experience with a next-generation artificial disc for the treatment of symptomatic degenerative cervical radiculopathy. *SAS Journal*. 2010; 4: 9-15.
10. Gardner-Morse MG, Stokes IA. Physiological axial compressive preloads increase motion segment stiffness, linearity and hysteresis in all six degrees of freedom for small displacements about the neutral posture. *Journal of Orthopaedic Research*. 2003; 21: 547-52.

11. Holsgrove TP, Gill HS, Miles AW, Gheduzzi S. The dynamic, six-axis stiffness matrix testing of porcine spinal specimens. *The Spine Journal*. 2015; 15: 176-1884.

12. Daftari TK, Chinthakunta SR, Ingalhalikar A, Gudipally M, Hussain M, Khalil S. Kinematics of a selectively constrained radiolucent anterior lumbar disc: Comparisons to hybrid and circumferential fusion. *Clinical Biomechanics*. 2012; 27: 759-65.

13. Daniels AH, Paller DJ, Feller RJ, et al. Examination of cervical spine kinematics in complex, multiplanar motions after anterior cervical discectomy and fusion and total disc replacement. *The International Journal of Spine Surgery*. 2012; 6: 190-4.

14. Bauman JA, Jaumard NV, Guarino BB, et al. Facet joint contact pressure is not significantly affected by ProDisc cervical disc arthroplasty in sagittal bending: a single-level cadaveric study. *The Spine Journal*. 2012; 12: 949-59.

15. Cunningham BW, Gordon JD, Dmitriev AE, Hu NB, McAfee PC. Biomechanical evaluation of total disc replacement arthroplasty: an in vitro human cadaveric model. *Spine*. 2003; 28: S110-S7.

16. Stokes IAF, Gardner-Morse M. Spinal stiffness increases with axial load: another stabilizing consequence of muscle action. *Journal of Electromyography and Kinesiology*. 2003; 13: 397-402.

17. Wilke HJ, Claes L, Schmitt H, Wolf S. A universal spine tester for in vitro experiments with muscle force simulation. *European Spine Journal*. 1994; 3: 91-7.

18. Colle KO, Butler JB, Reyes PM, Newcomb AGUS, Theodore N, Crawford NR. Biomechanical evaluation of a metal-on-metal cervical intervertebral disc prosthesis. *The Spine Journal*. 2013; 13: 1640-9.

19. Crawford NR, Baek S, Sawa AGU, Safavi-Abbasi S, Sonntag VKH, Duggal N. Biomechanics of a Fixed–Center of Rotation Cervical Intervertebral Disc Prosthesis. *The International Journal of Spine Surgery*. 2012; 6: 34-42.

20. O'Reilly OM, Metzger MF, Buckley JM, Moody DA, Lotz JC. On the stiffness matrix of the intervertebral joint: application to total disk replacement. *Journal of Biomechanical Engineering*. 2009; 131: 081007.

21. Holsgrove TP, Gheduzzi S, Gill HS, Miles AW. The development of a dynamic, six-axis spine simulator. *The Spine Journal*. 2014; 14: 1308-17.

22. Stokes IA, Gardner-Morse M, Churchill D, Laible JP. Measurement of a spinal motion segment stiffness matrix. *Journal of Biomechanics*. 2002; 35: 517-21.

23. DePuy International Ltd. In Motion Lumbar Artificial Disc Surgical Technique & Product Catalogue. Leeds, UK: DePuy International Ltd., 2008.

24. Gardner-Morse MG, Stokes IAF. Structural behavior of human lumbar spinal motion segments. *Journal of Biomechanics*. 2004; 37: 205-12.

25. Costi JJ, Stokes IA, Gardner-Morse MG, Iatridis JC. Frequency-dependent behavior of the intervertebral disc in response to each of six degree of freedom dynamic loading - Solid phase and fluid phase contributions. *Spine*. 2008; 33: 1731-8.

26. Cakir B, Richter M, Schmoelz W, Schmidt R, Reichel H, Wilke H. Resect or not to resect: the role of posterior longitudinal ligament in lumbar total disc replacement. *European Spine Journal*. 2012; 21: 592-8.

27. McAfee PC, Cunningham B, Holsapple G, et al. A prospective, randomized, multicenter food and drug administration investigational device exemption study of lumbar total disc replacement with the CHARITE (TM) artificial disc versus lumbar fusion Part II: Evaluation of radiographic outcomes and correlation of surgical technique accuracy with clinical outcomes. *Spine*. 2005; 30: 1576-83.

28. Dickey JP, Dumas GA, Bednar DA. Comparison of porcine and human lumbar spine flexion mechanics. *Veterinary and Comparative Orthopaedics and Traumatology*. 2003; 16: 44-9.

29. Wilke H-J, Geppert J, Kienle A. Biomechanical in vitro evaluation of the complete porcine spine in comparison with data of the human spine. *European Spine Journal*. 2011; 20: 1859-68.

30. Bass CR, Planchak CJ, Salzar RS, et al. The temperature-dependent viscoelasticity of porcine lumbar spine ligaments. *Spine*. 2007; 32: E436-E42.

31. Huang RC, Girardi FP, Cammisa FP, Wright TM. The implications of constraint in lumbar total disc replacement. *Journal of Spinal Disorders & Techniques*. 2003; 16: 412-7.

32. Depuy Spine Inc., Moumene M, Masson M. Intervertebral disc prosthesis and associated methods. 2007; WO2007002602.

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Figures

Figure 1: The In Motion device comprising two cobalt-chrome endplates, and an UHMWPE sliding core, viewed from the anterior aspect in right lateral bending (left), the neutral position (centre), and left lateral bending (right)

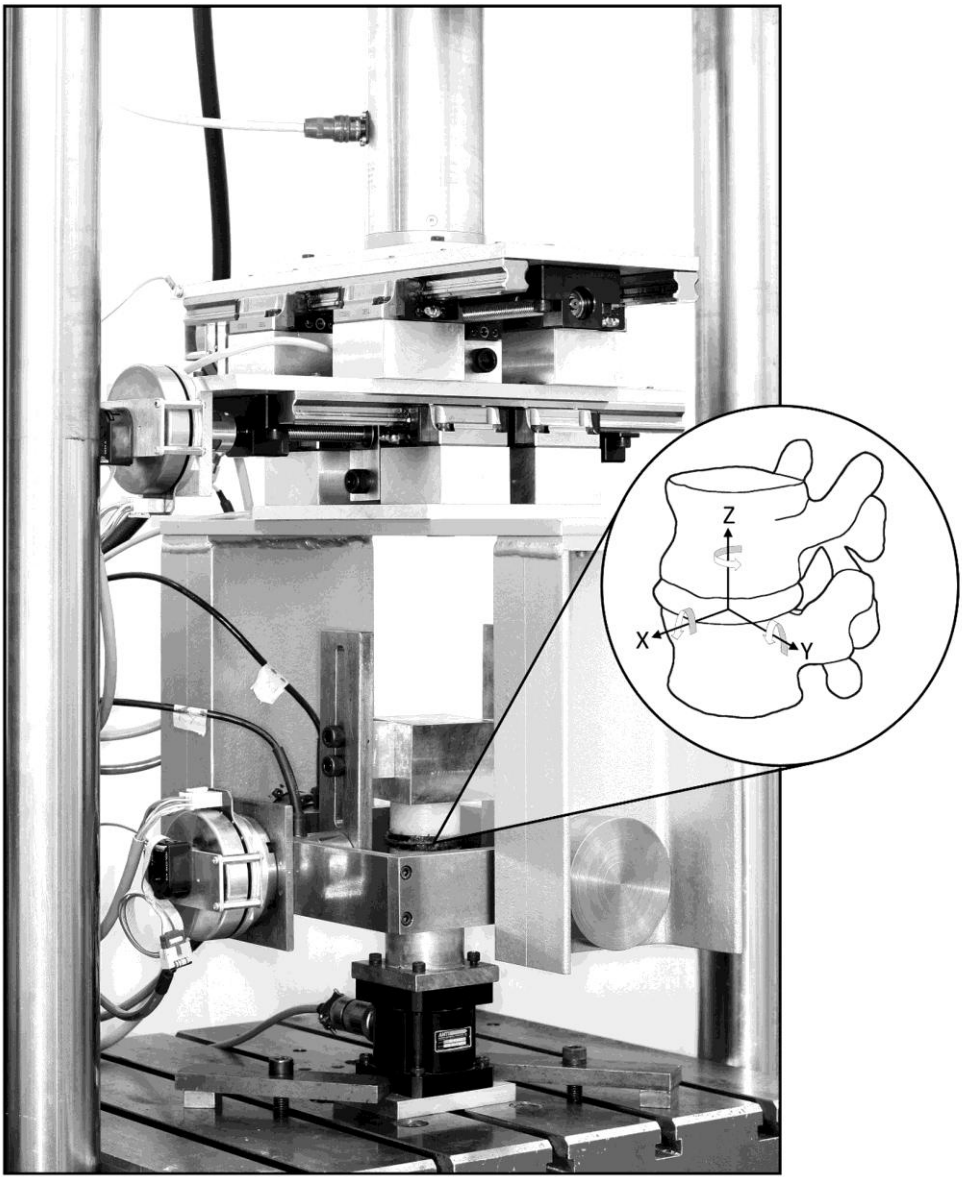

Figure 2: The spine simulator with an inset detailing the coordinate system for the application of translations and rotations about the centre of the IVD

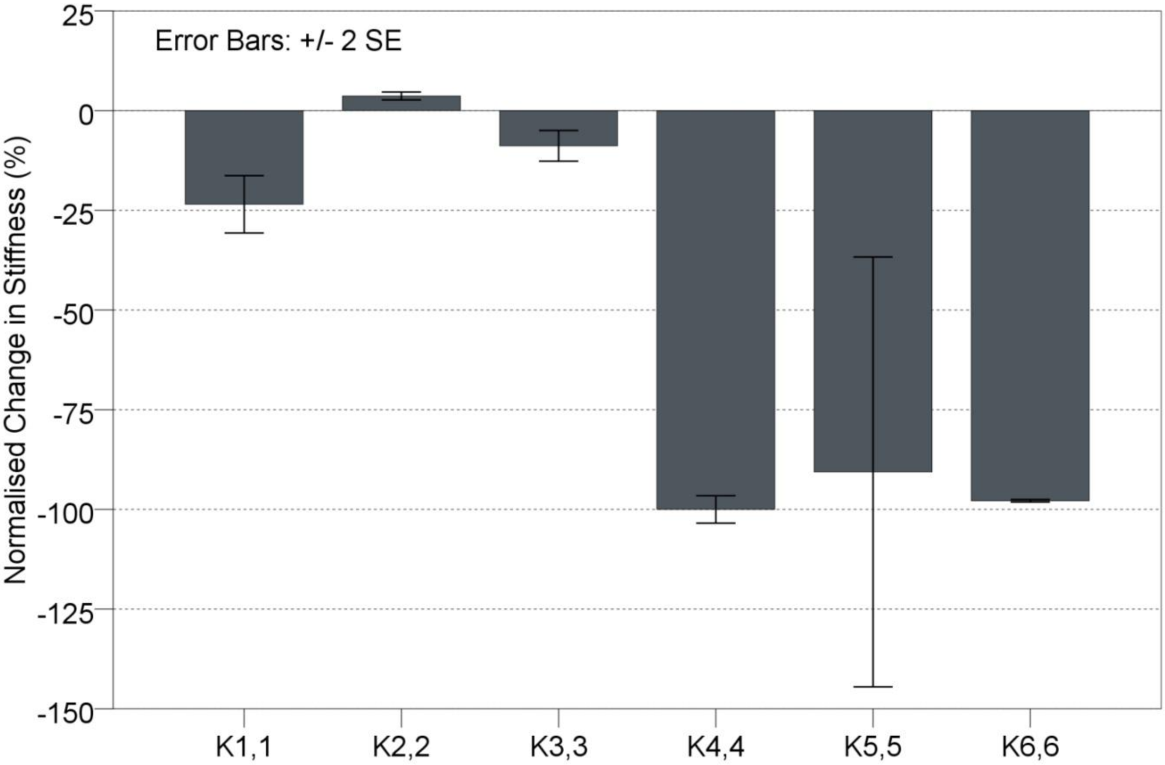

Figure 3: Representative load-displacement plots for a single INTACT specimen in anterior-posterior shear (top), lateral bending (centre), and axial rotation (bottom). Left-hand plots represent principal stiffness terms ($k_{1,1}$, $k_{4,4}$, and $k_{6,6}$ from top to bottom respectively), and right-hand plots represent key-off axis or coupled terms ($k_{5,1}$, $k_{2,4}$, and $k_{2,6}$ from top to bottom respectively)

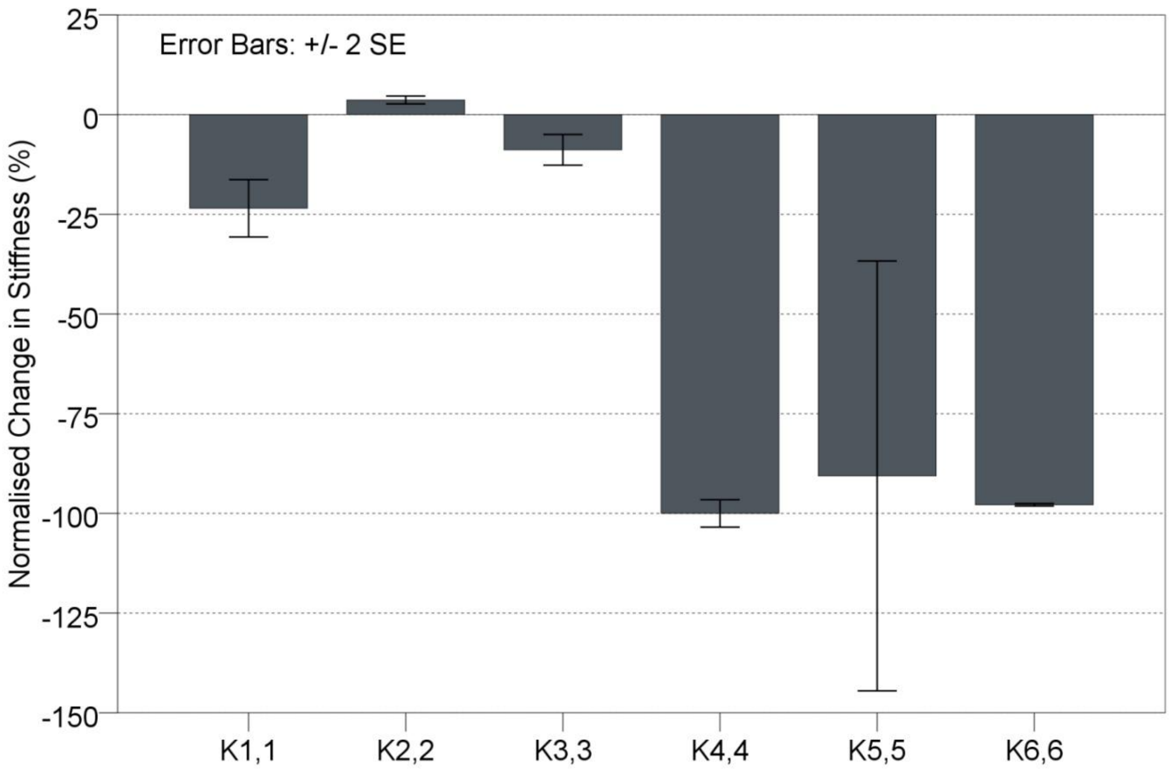

Figure 4: The normalised change in principal stiffness terms due to the In Motion TDR with respect to paired specimens in the intact condition

Tables

Table 1: Stiffness matrices with mean±SE of INTACT and TDR specimens. Asterisks denote significant difference ($p<0.05$), principal stiffness terms shown in bold, values below the ZE shown in italics

Load	Specimen	Test Axis					
		TX	TY	TZ	RX	RY	RZ
FX	INTACT	**33±1.0** *	*1.5±0.1*	*-6.1±10.1*	*23±21*	*1.8±64*	*44±13* *
	TDR	**25±1.5**	*1.5±0.2*	*-4.9±8.7*	*14±12*	-129±68	*3.0±11*
FY	INTACT	*-1.1±0.1* *	**38±0.4** *	*8.7±3.0*	*15±55*	*4.0±11*	374±27 *
	TDR	*-0.8±0.2*	**40±0.4**	*10.0±2.9*	112±26	*24±6.8*	*-0.7±30*
FZ	INTACT	17±5.3	5.8±3.1	**1,245±37** *	-1,741±424	-882±1,092 *	-202±70 *
	TDR	18±12	7.5±2.6	**1,135±34**	-2,200±332	2,504±809	*19±15*
MX	INTACT	*-78±29*	856±99	2,314±506	**65,000±13,986** *	*-969±2,541* *	8,651±475 *
	TDR	*-51±26*	946±62	2,035±696	***-184±1,184***	5,373±2,464	*265±803*
MY	INTACT	-989±119 *	-213±20	-1,304±1711 *	*1,584±3,031*	**27,982±7,271** *	*-3,466±809* *
	TDR	-619±75	-204±16	1,909±1,499	-5,846±2,424	**8,127±6,331**	*-581±351*
MZ	INTACT	*-46±11*	396±43 *	*-147±70* *	*-3,298±1,412*	*644±216*	**48,220±1,588** *
	TDR	*-53±12*	*-23±33*	*47±25*	-302±122	*302±134*	***969±59***

Table 2: Key off-axis stiffness terms, significance ($p<0.05$) denoted by an asterisk

Stiffness Term	Description	
$K_{5,1}$	Flexion-extension moment due to anterior-posterior shear	*
$K_{4,2}$	Lateral bending moment due to lateral shear	
$K_{6,2}$	Axial moment due to lateral shear translation	*
$K_{5,3}$	Flexion-extension moment due to axial compression-extension	*
$K_{2,4}$	Lateral shear force due to lateral bending	
$K_{6,4}$	Axial moment due to lateral bending	
$K_{1,5}$	Anterior-posterior shear force due to flexion-extension	
$K_{3,5}$	Axial force due to flexion-extension	*
$K_{2,6}$	Lateral shear force due to axial rotation	*
$K_{4,6}$	Lateral bending moment due to axial rotation	*

Table 3: R^2 values of stiffness matrix terms with mean±SE of INTACT specimens. Principal stiffness terms are shown in bold, values below the ZE shown in italics

Load	Test Axis					
	TX	TY	TZ	RX	RY	RZ
FX	**0.996±0.001**	*0.476±0.038*	*0.713±0.150*	*0.363±0.127*	*0.866±0.052*	*0.349±0.123*
FY	*0.520±0.120*	**0.996±0.000**	*0.436±0.134*	*0.688±0.081*	*0.195±0.076*	0.980±0.004
FZ	0.455±0.153	0.269±0.134	**0.946±0.005**	0.555±0.130	0.758±0.091	0.060±0.036
MX	*0.252±0.089*	0.831±0.060	0.655±0.131	**0.871±0.015**	*0.275±0.051*	0.582±0.052
MY	0.971±0.007	0.356±0.039	0.472±0.177	*0.268±0.124*	**0.780±0.098**	*0.233±0.074*
MZ	*0.875±0.018*	0.996±0.001	*0.616±0.138*	*0.739±0.146*	*0.390±0.117*	**0.967±0.002**