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Biomechanics of Artificial Disc Replacements Adjacent to a 2-Level Fusion in 4-Level Hybrid Constructs: An *In Vitro* Investigation

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AD 1,2 **Zhenhua Liao**
EF 3 **Guy R. Fogel**
C 2 **Na Wei**
B 4 **Hongsheng Gu**
AG 1,2 **Weiqiang Liu**

1 Department of Mechanical Engineering, Tsinghua University, Beijing, P.R. China
2 Biomechanics and Biotechnology Lab, Research Institute of Tsinghua University in Shenzhen, Shenzhen, Guangdong, P.R. China
3 Spine Pain Begone, San Antonio, TX, U.S.A.
4 Department of Orthopaedics, Shenzhen Second Hospital, Shenzhen, Guangdong, P.R. China

Corresponding Author: Weiqiang Liu, e-mail: weiqliu@hotmail.com
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Background: The ideal procedure for multilevel cervical degenerative disc diseases remains controversial. Recent studies on hybrid surgery combining anterior cervical discectomy and fusion (ACDF) and artificial cervical disc replacement (ACDR) for 2-level and 3-level constructs have been reported in the literature. The purpose of this study was to estimate the biomechanics of 3 kinds of 4-level hybrid constructs, which are more likely to be used clinically compared to 4-level arthrodesis.

Material/Methods: Eighteen human cadaveric spines (C2–T1) were evaluated in different testing conditions: intact, with 3 kinds of 4-level hybrid constructs (hybrid C3–4 ACDR+C4–6 ACDF+C6–7ACDR; hybrid C3–5ACDF+C5–6ACDR+C6–7ACDR; hybrid C3–4ACDR+C4–5ACDR+C5–7ACDF); and 4-level fusion.

Results: Four-level fusion resulted in significant decrease in the C3–C7 ROM compared with the intact spine. The 3 different 4-level hybrid treatment groups caused only slight change at the instrumented levels compared to intact except for flexion. At the adjacent levels, 4-level fusion resulted in significant increase of contribution of both upper and lower adjacent levels. However, for the 3 hybrid constructs, significant changes of motion increase far lower than 4P at adjacent levels were only noted in partial loading conditions. No destabilizing effect or hypermobility were observed in any 4-level hybrid construct.

Conclusions: Four-level fusion significantly eliminated motion within the construct and increased motion at the adjacent segments. For all 3 different 4-level hybrid constructs, ACDR normalized motion of the index segment and adjacent segments with no significant hypermobility. Compared with the 4-level ACDF condition, the artificial discs in 4-level hybrid constructs had biomechanical advantages compared to fusion in normalizing adjacent level motion.

MeSH Keywords: **Arthrodesis • Biomechanical Phenomena • Cervical Vertebrae • Total Disc Replacement • Two-Hybrid System Techniques**

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Background

As the criterion standard, anterior cervical discectomy and fusion (ACDF) has been successfully used for cervical disc disease treatment with satisfactory clinical outcome and a proven fusion range of more than 90% [1]. However, altered mechanics, such as higher stress and increased intradiscal pressures, occurred at adjacent levels. This has been associated with accelerated degenerative diseases at a rate of 2.9% per year within 10 years [2]. Moreover, the longer fusion would be faced with more significant risk. Multilevel arthrodesis, such as 4-level fusion, is more likely to result in adjacent segment degeneration, challenging fusion, and pseudarthrosis [3].

By preserving some amount of cervical motion and preventing overload of adjacent levels, artificial cervical disc replacement (ACDR) has become the alternative to fusion, with the potential to avoid the adverse effects of arthrodesis on adjacent levels [4]. Recent clinical studies reported that 1-level ACDR was an emerging technology with satisfactory effects as good as ACDF, at least in the short or medium term [5].

However, multilevel cervical spondylosis is not rare in clinical practice. Considering that multilevel segments fusion results in greater loss of mobility at instrumented levels, benefits for loads reduction at adjacent levels may be more important than single-level spondylosis [6], but more stringent indications and hypermobility also lead to the limitation of multilevel ACDR [7]. Hybrid surgery (HS), which combines ACDF and ACDR, may be a promising procedure by preserving segmental motion of the cervical spine and avoiding long-level fusion.

As a new combination procedure, HS still needs to be evaluated by biomechanical tests and clinical studies. Recently, some authors reported a few biomechanical experiments for 2-level and 3-level HS and found that HS may be a safe and effective operation for certain patients [8]. However, to the best of our knowledge, there is still little biomechanical research on 4-level HS. Aside from 4 levels of degenerative diseases at the same time, the 4-level hybrid construct may also be a rational alternative for symptomatic adjacent levels after prior 2-level cervical fusion, avoiding 4-level fusion.

Using an *in vitro* human cadaveric model, the objective of the present study was to investigate the biomechanical behavior of 4-level hybrid fusion and artificial cervical disc replacement compared to a 4-level anterior cervical fusion by measuring motion changes at instrumented levels and adjacent levels.

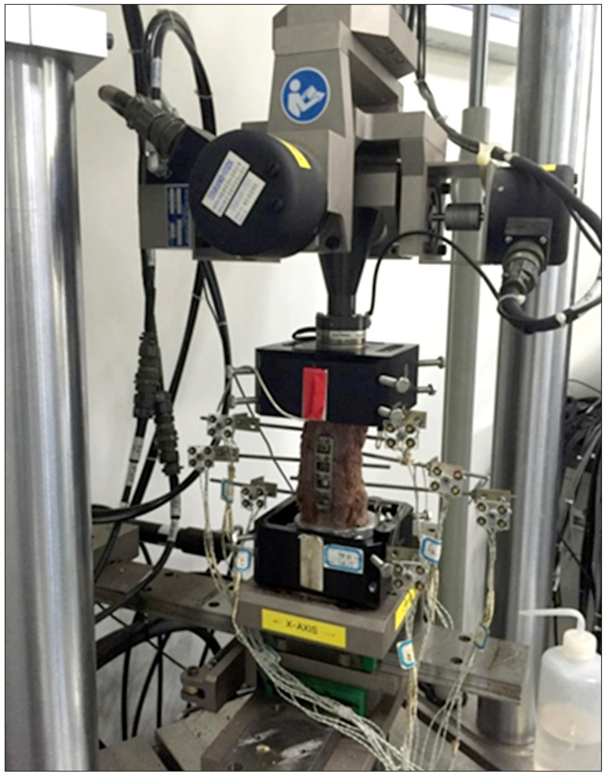

Figure 1. Testing set-up for in vitro biomechanical testing of cervical specimens.

Material and Methods

Specimen preparation

Eighteen intact fresh cadaveric cervical spines from C2 to T1 (age range, 42–68 years) were used for this study. These adult human cadavers were all obtained from Guangzhou Medical University in China. All cervical spines were evaluated for bone mineral density (BMD) using dual-energy x-ray absorptiometry scanning, and measured BMD values ranged from 0.57 to 0.74 g/cm^2. Before biomechanical testing, the musculature and fascia were carefully removed but the ligamentous structures were preserved. Specimens were excluded if fractures, traumatic pathology, bridging osteophytes, or other conditions existed as indicated by anteroposterior and lateral screening radiographs, because these conditions can significantly affect the biomechanics of the cervical spine. Once harvested, each cervical specimen was immediately conserved in a plastic bag and frozen at –20°C. In preparation for biomechanical tests, all required spines were thawed at 4°C for 12 h and at room temperature on the testing day. The proximal vertebra (C2) and distal vertebra (T1) were mounted in a cylindrical container separately using Wood's metal (melting point: 60~70°C), then the C2 was attached to the upper fixture and the T1 was mounted to the lower testing platform with screws. Plexiglas motion detection markers were fixed to the posterior aspects

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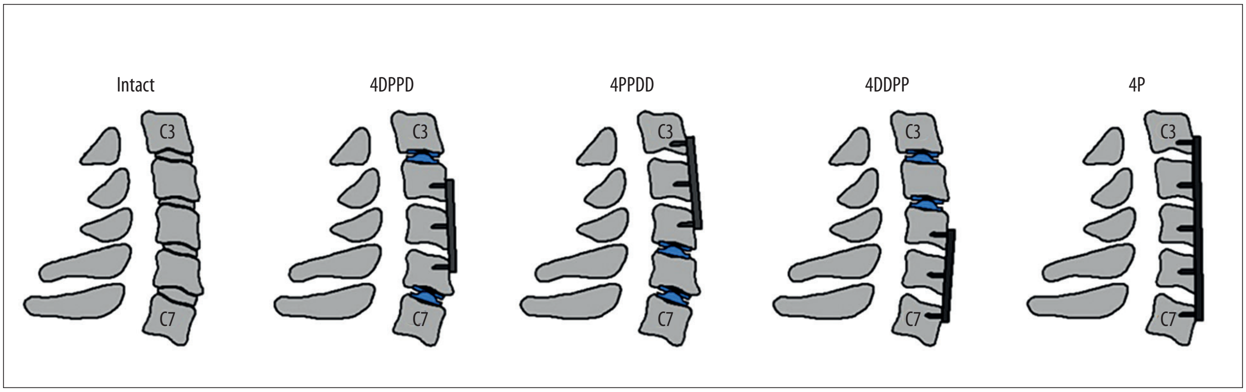

Figure 2. Testing conditions. Eighteen human cadaveric spines from C2 to T1 were divided into 3 groups (4DPPD, 4PPDD, and 4DDPP) and 4-level fusion (4P).

of each vertebra from C2 to T1. Every marker was equipped with 3 non-collinear light-emitting diodes so that it could be detected by an optoelectronics motion measurement system (Optotrak, Northern Digital Inc., Waterloo, Ontario, Canada).

Biomechanical tests protocol

Biomechanical testing was performed using a 6 degrees of freedom spine simulator equipped with modules for spine testing, consisting of a controlled (displacement) XY slide table assembly (MTS Bionix370.02A/T Systems Corp., Eden Prairie, MN, USA) (Figure 1). All biomechanical tests were performed under the hybrid testing protocol proposed by Panjabi, which includes pure moments for the intact condition and then total spinal motion replicated under displacement control for subsequent reconstructions [9]. Unconstrained intact moments of 2 Nm were used for flexion-extension (FE), lateral bending (LB), and axial rotation (AR) testing by measuring the operative- and adjacent-level range of motion (ROM). Each test was repeated for 3 loading cycles and the data from the third cycle were used for analysis. During the biomechanical tests, all cervical specimens were moistened with 0.9% NaCl physiologic serum spray to avoid tissue dehydration.

Reconstruction procedures

After analysis of the intact spines, 18 cervical spines were divided into 3 groups (A, B, and C). For each specimen, a simulated fusion and non-fusion construct was created between C3 to C7 and tested in the following conditions (Figure 2):

1. Group A: disc replacement (C3–C4), 2-level anterior fusion (C4–C6), disc replacement (C6–C7); 4-level disc plate disc (4DPPD).
2. Group B: 2-level anterior fusion (C3–C5), 2-level disc replacement (C5–C6; C6–C7); 4-level plate plate disc disc (4PPDD).
3. Group C: 2-level disc replacement (C3–C4; C4–C5), 2-level anterior fusion (C5–C7); 4-level disc disc plate plate (4DDPP).
4. All of the above A, B, and C: 4-level plate (4P).

In the biomechanical tests, the ACDR was a titanium alloy UHMWPE Cervical Disc (Discover Cervical Disc, Depuy Spine, Inc., Raynham, MA, USA). The ACDF was performed using an interbody cage (Telamon TM, Medtronic Sofamor Danek USA, Inc.) and an anterior cervical plating (ACP) system (OrionTM cervical plate, Medtronic Sofamor Danek, Memphis, TN, USA or DOC Cervical Plate, Depuy Spine, Inc., Raynham, MA, USA) (Figure 3).

Data and statistical analysis

The relative rotation at the C3–C7 corpectomy or adjacent level was normalized with respect to the overall rotation of the potted spine (C2–T1). For data analysis, the overall rotation of C2–T1 was set 15° in flexion and extension, as well as 12° in lateral bending and axial rotation, so that all tested cervical specimens could reach. One-way analysis of variance was used to analyze the differences between treatment groups, with a statistical significance of $P<0.05$.

Results

Motion changes at the 3 instrumented levels

At the instrumented levels, 4-level fusion (4P) resulted in significant decrease in the C3–C7 ROM compared with the intact spine in FE, LB, and AR ($p<0.05$). Compared to intact spines, almost 75% of motion was successfully restricted at C3–C6 fusion levels in flexion and extension, as well as 65~70% in lateral bending and axial rotation.

The 3 different hybrid treatment groups, 4DPPD, 4PPDD, and 4DDPP, caused only slight change in the C3–C7 ROM compared to intact except for flexion ($p>0.05$). No significant differences were observed between 4DPPD, 4PPDD, and 4DDPP in the C3–C7 ROM in FE, LB, and AR ($p>0.05$). The 4P condition was the stiffest. Significant differences were observed

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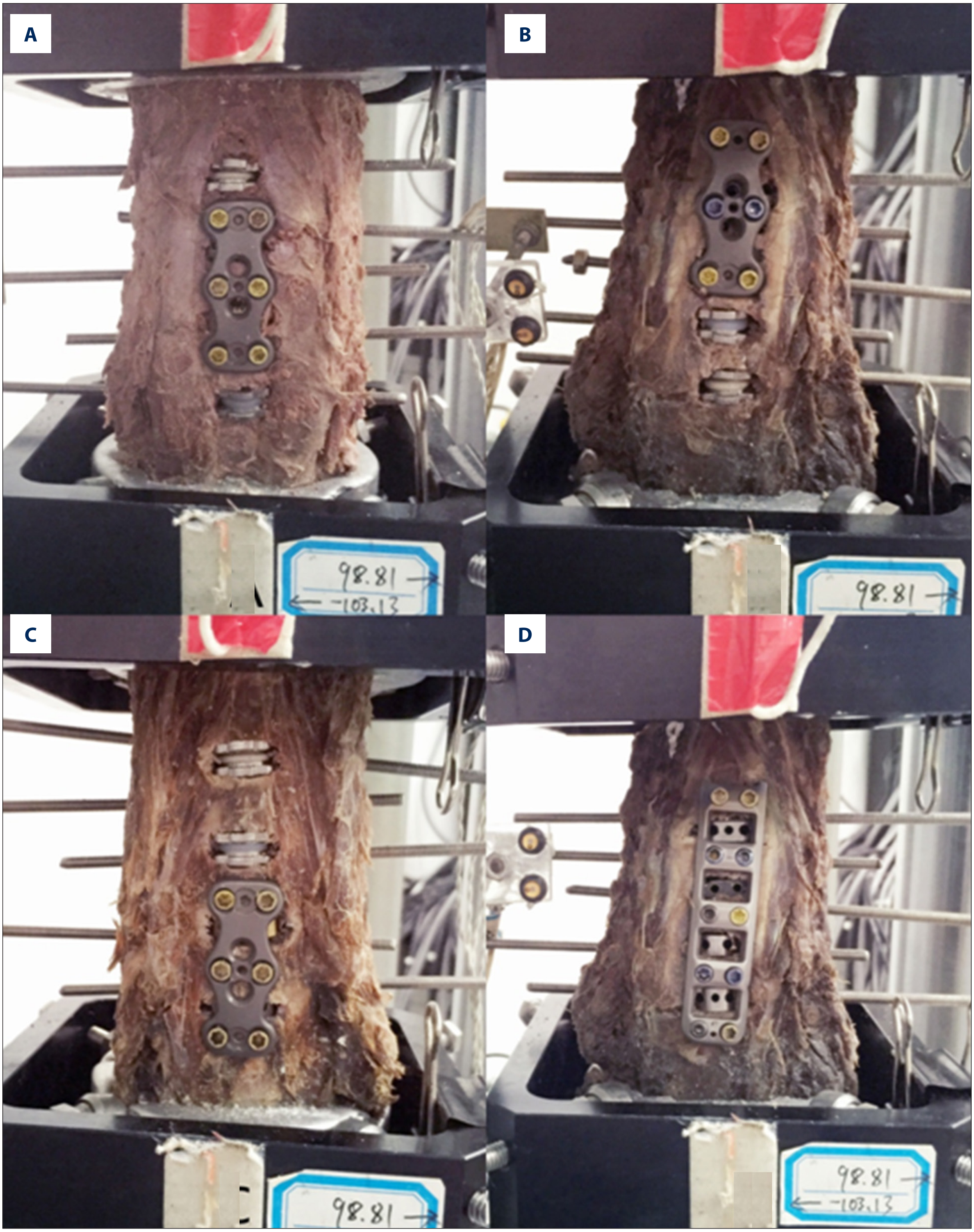

Figure 3. Instrumented cervical specimens: 4DPPD (**A**), 4PPDD (**B**), 4DDPP (**C**), and 4P (**D**).

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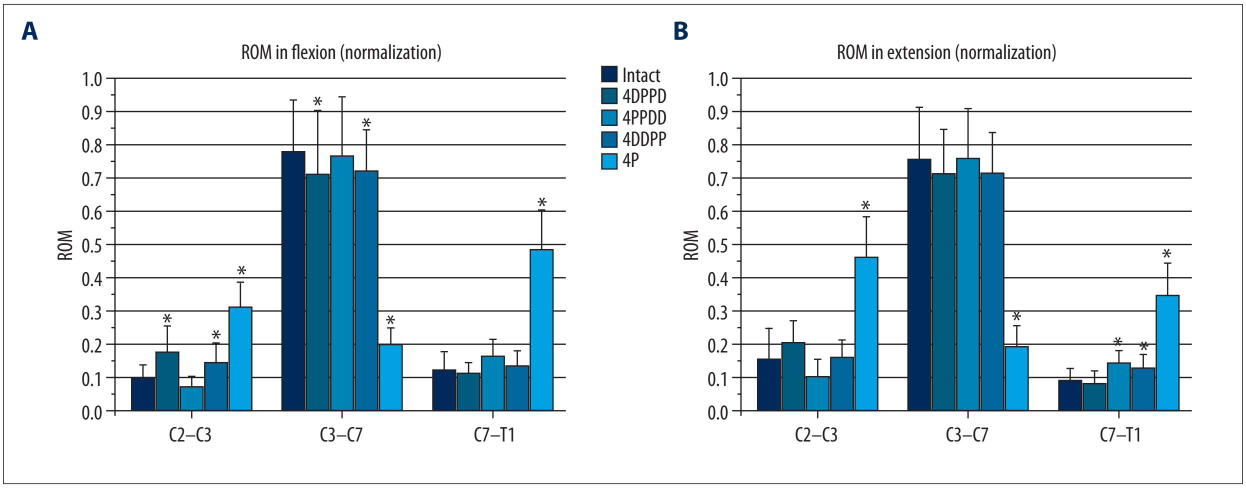

Figure 4. Segmental ROM relative to total C2-T1 ROM (15°) in flexion (**A**) and extension (**B**) (*: statistical significant difference, p<0.05, 4DPPD/4PPDD/4DDPP/4P *vs.* intact; I: Standard Deviation)

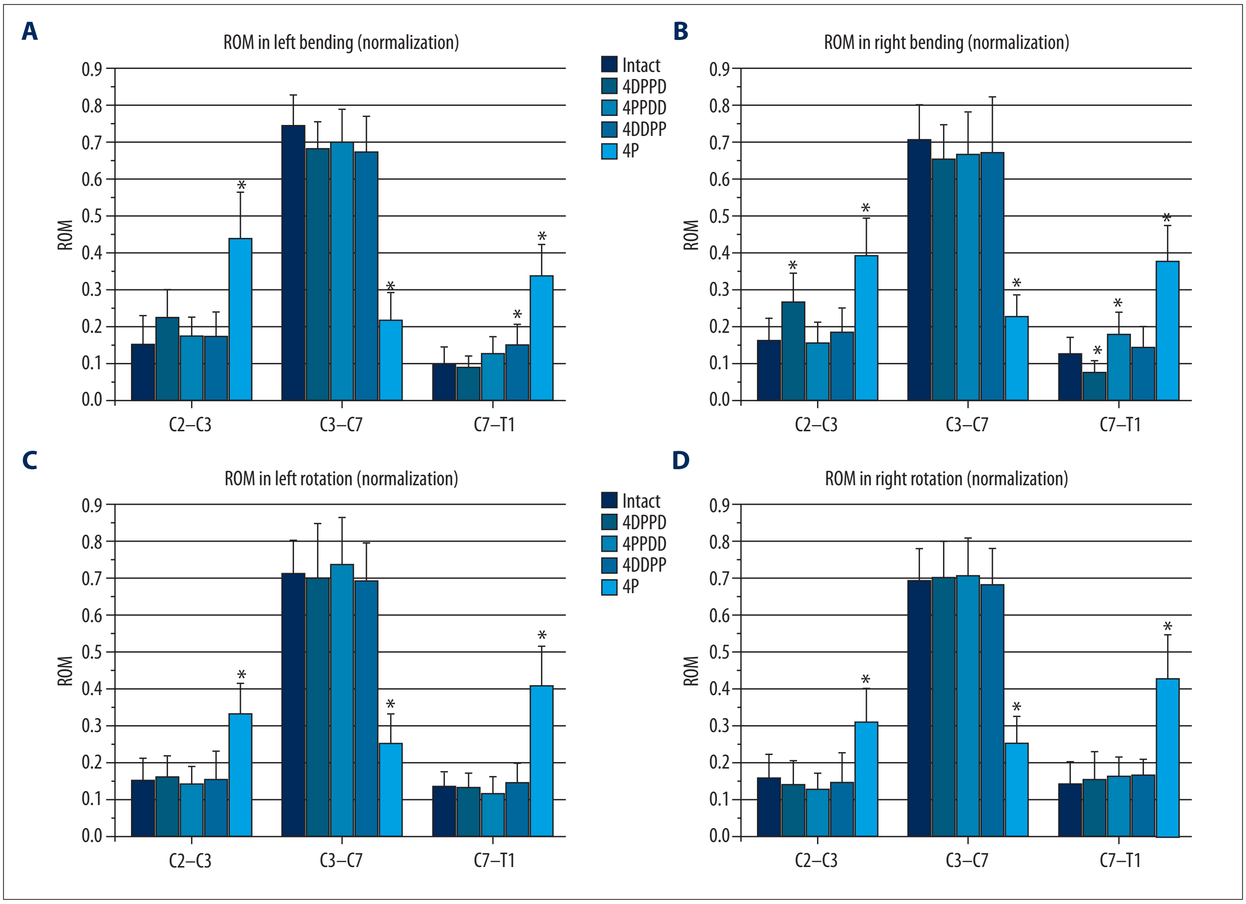

Figure 5. (**A–D**) Segmental ROM relative to total C2–T1 ROM (12°) in lateral bending and ROM (10°) in axial rotation (*: statistical significant difference, p<0.05, 4DPPD/4PPDD/4DDPP/4P *vs.* intact; I: Standard Deviation).

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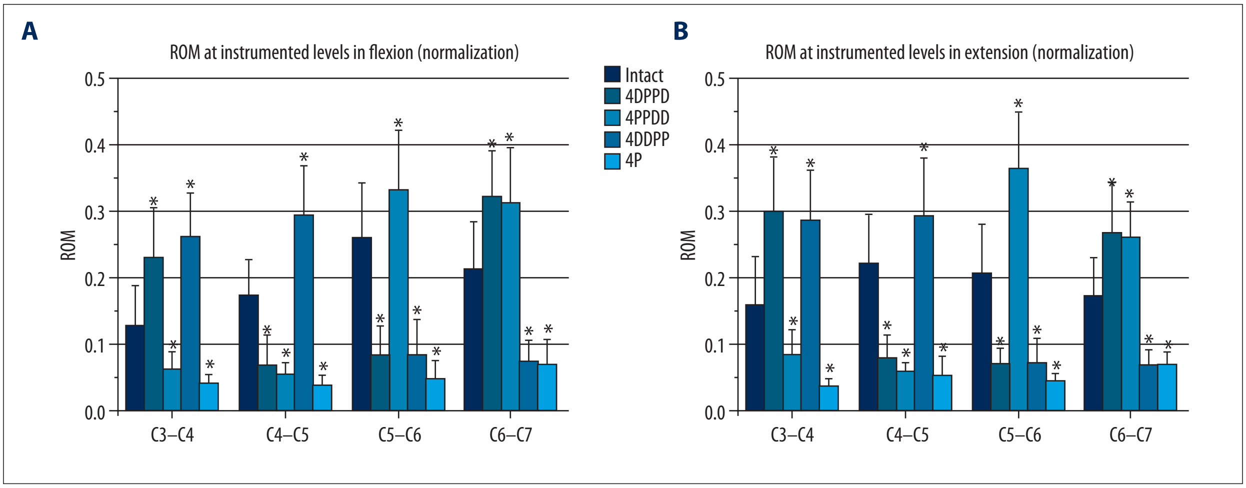

Figure 6. ROM at instrumented levels relative to total C2–T1 ROM (15°) in flexion (**A**) and extension (**B**) (*: statistical significant difference, $p<0.05$, 4DPPD/4PPDD/4DDPP/4P *vs.* intact; I: Standard Deviation).

between each hybrid treatment group and 4P in the C3–C7 ROM ($p<0.05$) (Figures 4, 5).

More normal motion with ACDR within construct

For each instrumented level, all 4DPPD, 4PPDD, and 4DDPP hybrid constructs caused reduction of ROM at the arthrodesis level and produced motion increase at the arthroplasty level compared to intact. All had significant differences ($p<0.05$; maximal variation of +90%) (Figure 6, Table 1).

Motion changes at adjacent levels

At the adjacent levels, 4-level arthrodesis resulted in a significant increase of contribution of both upper and lower adjacent levels in FE, LB, and AR ($p<0.05$; maximal variation of +340%). Concerning 4DPPD, 4PPDD, and 4DDPP hybrid constructs, significant changes of motion increase were only noted at the upper adjacent level in flexion and right bending, as well as at the lower adjacent level in extension and lateral bending ($p<0.05$; maximal variation of +70%) (Figures 4–6).

Discussion

The ideal procedure for multilevel cervical degenerative disc diseases (DDD) remains controversial. As a predominant surgical option, anterior cervical discectomy and fusion (ACDF) has been widely performed for radiculopathy and myelopathy from degenerative, inflammatory, and traumatic processes [10]. However, ACDF notably impairs normal cervical biomechanics, decreases motion at the instrumented levels, and alters mechanics at adjacent segments, resulting in higher stress and hypermobility. This has been associated with the acceleration of adjacent segment degeneration (ASD) [11]. Moreover, longer multilevel fusion is more likely to result in disk degeneration of the adjacent segments. In theory, when more cervical levels are fused, more compensatory motion and pressure occur at the adjacent levels, and the likelihood of ASD increases. Brodke et al. [12] reported that the fusion rate of 1-level ACDF was as high as 97%, whereas the fusion rate of 3-level ACDF decreased to 83%. Lee et al. [13] reported that 2-level fusion significantly increased compensatory pressure at adjacent intervertebral disks compared to intact. They also found that 2-level hybrid construct has relatively better biomechanical effects on the adjacent segment discs and facets when compared to fusion construct. Swank et al. [14] revealed that the likelihood of pseudarthrosis was 10% for 1-level surgery, 44% for 2-level surgery, and 54% for 3-level surgery.

Recently, artificial cervical disc replacement (ACDR) has been widely accepted as a surgical alternative, with the potential to preserve motion and maintain normal sagittal alignment and balance at the instrumented segments [15]. With surgical technology progress, ACDR has gained popularity. Ren et al. [16] evaluated the mid- to long-term clinical outcomes after ACDR and ACDF and reported that ACDR may result in better mid- to long-term functional recovery and a lower rate of subsequent surgical procedures compared to ACDF.

According to previous 1- and 2-level cervical disk diseases studies, the use of ACDR leads to satisfactory clinical and radiological outcomes [17,18]. Therefore, ACDR could be an attractive procedure for treating multilevel cervical disc diseases. Nevertheless, more than strict indications and hypermobility, multilevel ACDR may also lead to more rigorous surgical procedures and more arthroplasty-related complications. It is not always easy to find the ideal location for the implanted artificial disk prosthesis [19]. It remains unknown how the increased difference affects the normal physiological property

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Table 1. ROM at instrumented levels relative to total C2–T1 ROM (12°) in lateral bending and ROM (10°) in axial rotation: mean ± standard deviation (#: no statistical significant difference, p>0.05, 4DPPD/4PPDD/4DDPP/4P *vs.* intact).

	C3–C4	C4–C5	C5–C6	C6–C7
Left bending				
Intact	0.208±0.039	0.161±0.045	0.195±0.059	0.182±0.038
4DPPD	0.310±0.102	0.084±0.029	0.111±0.031	0.181±0.046#
4PPDD	0.106±0.031	0.097±0.012	0.290±0.043	0.206±0.052
4DDPP	0.254±0.035	0.255±0.029	0.083±0.026	0.084±0.017
4P	0.062±0.023	0.028±0.009	0.071±0.034	0.061±0.021
Right bending				
Intact	0.206±0.036	0.177±0.058	0.163±0.039	0.162±0.041
4DPPD	0.294±0.083	0.094±0.036	0.098±0.021	0.168±0.053#
4PPDD	0.106±0.027	0.102±0.039	0.245±0.058	0.212±0.034
4DDPP	0.225±0.030#	0.248±0.053	0.108±0.029	0.089±0.027
4P	0.071±0.019	0.052±0.026	0.044±0.023	0.062±0.018
Left rotation				
Intact	0.154±0.039	0.207±0.057	0.197±0.062	0.156±0.042
4DPPD	0.246±0.052	0.104±0.029	0.114±0.043	0.239±0.04
4PPDD	0.071±0.025	0.118±0.038	0.315±0.055	0.235±0.041
4DDPP	0.242±0.029	0.241±0.037	0.118±0.027	0.094±0.018
4P	0.079±0.017	0.054±0.024	0.047±0.019	0.075±0.031
Right rotation				
Intact	0.142±0.041	0.180±0.056	0.204±0.063	0.166±0.051
4DPPD	0.232±0.054	0.106±0.026	0.118±0.019	0.245±0.037
4PPDD	0.110±0.021	0.115±0.019	0.265±0.043	0.214±0.039
4DDPP	0.241±0.047	0.254±0.052	0.091±0.019	0.098±0.021
4P	0.075±0.020	0.059±0.015	0.044±0.016	0.078±0.023

of the cervical spine after multilevel ACDR [20]. Therefore, a rational surgical procedure for multilevel cervical disk diseases involving 3 or more levels needs to be developed.

Hybrid surgery (HS) combing arthroplasty and arthrodesis technique has been introduced to clinical surgery in recent years. HS can maintain segmental motion of fused levels and avoids the drawbacks of multilevel ACDF, as well as decrease possible complications of multilevel ACDR [21,22]. According to the current knowledge on HS for 2-level and 3-level constructs, HS demonstrates a biomechanical advantage and may be a safe and valid procedure for treating multilevel cervical disc diseases. Barrey et al. [23] found that 2-level ACDR and hybrid constructs showed better biomechanical properties than 2-level ACDF, and increased stress occurred only at the lower adjacent level, while 2-level ACDF caused ROM increase at both upper and lower adjacent segments. Faizan et al. [24] revealed that the spinal stiffness after HS was far closer to intact construct in all bending motions except extension, compared to 2-level fusion. Liu et al. [25] showed that 2-level hybrid surgery and ACDR did not alter ROM and minimally changed ICR at the adjacent levels compared to 2-level fusion. For 3-level cervical surgery, Ding et al. [26] stated that HS may be a rational alternative to ACDF for 3-level cervical disease due to the equivalent or improved early clinical outcomes, with less impact at adjacent levels. Kang et al. [19] suggested that HS should be a safe

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and effective alternative for multilevel cervical disk diseases involving 3 levels. Jia et al. [8] reported a systematic review of 8 biomechanical and 7 clinical papers and found some short-term evidence to support hybrid surgeries. Liao et al. [27] found that artificial cervical disc replacement in 3-level constructs normalized motion of its segment and adjacent segments.

However, to the best of our best knowledge, there is still only very low-quality evidence about 4-level hybrid surgery. The complications after 4-level fusion may be more serious due to longer-level arthrodesis [28]. Furthermore, it is common for patients to undergo a second longer revision fusion, such as 4-level fusion, due to ASD after previous 2-level fusion, which may more easily result in recurrent ASD. Four-level HS may be a promising procedure, but appropriate evidence for its use is currently lacking. Barbagallo et al. [29] reported that 2 patients underwent a 4-level HS procedure (arthroplasty at C3–C4, C4–C5; arthrodesis at C5–C6, C6–C7) with mean 24-month follow-up, and found that 4-level HS is as safe and reliable as 2-level and 3-level HS without revision. Considering the very low-quality evidence available, more *in vitro* biomechanical and *in vivo* clinical studies on 4-level HS should be developed. Thus, 3 general kinds of 4-level HS (4DPPD, 4PPDD, and 4DDPP), which are more likely to be used in clinic practice, were compared to 4-level fusion (4P) in this biomechanical study. The purpose of this *in vitro* research was to evaluate the kinematics of artificial disks next to a 2-level fusion by asking 2 questions: (1) Do artificial disc replacements adjacent to a 2-level fusion in 4-level hybrid constructs normalize motion at adjacent segments? and (2) Are artificial discs adjacent to a 2-level fusion subjected to a more challenging biomechanical environment that may result in hypermobility?

As expected, 4-level arthrodesis induced great reduction of ROM for 3 loading conditions (FE, LB, and AR). The limitation of motion was more marked in FE (mean reduction by ~75%) than in LB and AR (mean reduction by 65~70%). In contrast, although 4DPPD and 4DDPP induced significant reduction of ROM in flexion, 4DPPD, 4PPDD, and 4DDPP caused only slight change in the C3–C7 ROM compared to intact ($p>0.05$). No significant differences were observed between 4DPPD, 4PPDD, and 4DDPP in the instrumented levels, but significant differences were observed between each hybrid treatment group and 4P. At the adjacent segments, 4-level arthrodesis significantly increased the contribution of upper and lower adjacent levels to global ROM in FE, LB, and AR. However, for 4DPPD, 4PPDD, and 4DDPP hybrid constructs, significant changes of motion increase far lower than 4P at adjacent levels were only noted in partial loading conditions. Therefore, artificial disc replacements in 4-level constructs restored partly cervical kinematics at instrumented levels and also normalized motion at adjacent segments.

On the other hand, all 4DPPD, 4PPDD, and 4DDPP hybrid constructs produced significant motion increase at the arthroplasty level compared to intact (maximal increase by ~90%). In addition, 1 artificial disc did not affect the biomechanical behavior of the other implanted disc and there was little difference between 2 implanted discs in the same hybrid surgery. We did not observe destabilizing effect or hypermobility for 2 implanted discs in any 4-level hybrid construct. Nevertheless, artificial discs placed adjacent to a 2-level arthrodesis should face a more challenging biomechanical environment compared to a stand-alone disc [30]. Therefore, artificial discs used in such a clinical HS surgery should be able to accommodate more moment loads or undue wear during the expected lifespan.

This study has the limitations of any *in vitro* cadaveric biomechanical study of the cervical spine. We focused mainly on the extent of motion without considering the quality of motion. Another limitation of the current study was the lack of intradiscal pressures (IDP) measurement, which should contribute to further understanding of ASD. A more complete biomechanical evaluation of cervical kinematics after 4-level hybrid surgery should be developed by finite element methods or *in vivo* imaging techniques.

Conclusions

This study analyzed the biomechanics of artificial disc replacements adjacent to a 2-level fusion in 4-level hybrid constructs. Four-level fusion significantly eliminated motion within the construct and increased motion at the adjacent segments. For all 3 different 4-level hybrid constructs (4DPPD, 4PPDD, and 4DDPP), ACDR normalized motion of the index segment and adjacent segments with no significant hypermobility. Compared with the 4-level ACDF condition, the artificial discs in 4-level hybrid constructs had biomechanical advantages compared to fusion in normalizing adjacent-level motion.

Conflict of interest

None.

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