ELSEVIER

The SPINE JOURNAL

The Spine Journal 000 (2024) 1–10

Clinical Study

Prosthesis design and likelihood of achieving physiological range of motion after cervical disc arthroplasty: Analysis of range of motion data from 1,173 patients from 7 IDE clinical trials

Avinash G. Patwardhan, PhD[a,b,*], Robert M. Havey, MS[a], Frank M. Phillips, MD[c], Jack E. Zigler, MD[d], Domagoj Coric, MD[e], Richard Guyer, MD[d], Todd Lanman, MD[f], Muturi G. Muriuki, PhD[a]

[a] *Musculoskeletal Biomechanics Laboratory, Edward Hines Jr. VA Hospital, Hines, IL, USA*
[b] *Department of Orthopaedic Surgery and Rehabilitation, Loyola University Chicago, Maywood, IL, USA*
[c] *Department of Orthopedic Surgery, Rush University Medical Center, Chicago, IL, USA*
[d] *Center for Disc Replacement, Texas Back Institute, Plano, TX, USA*
[e] *Carolina Neurosurgery and Spine, Charlotte, NC, USA*
[f] *Cedars-Sinai Medical Center, Los Angeles, CA, USA*

Received 22 August 2023; revised 11 January 2024; accepted 22 January 2024

Abstract

BACKGROUND CONTEXT: The functional goals of cervical disc arthroplasty (CDA) are to restore enough range of motion (ROM) to reduce the risk of accelerated adjacent segment degeneration but limit excessive motion to maintain a biomechanically stable index segment. This motion-range is termed the "Physiological mobility range." Clinical studies report post-operative ROM averaged over all study subjects but they do not report what proportion of reconstructed segments yield ROM in the Physiological mobility range following CDA surgery.

PURPOSE: To calculate the proportion of reconstructed segments that yield flexion-extension ROM (FE-ROM) in the Physiological mobility range (defined as 5-16 degrees) by analyzing the 24-month postoperative data reported by clinical trials of various cervical disc prostheses.

STUDY DESIGN/SETTING: Analysis of 24-month postoperative FE-ROM data from clinical trials.

PATIENT SAMPLE: Data from 1,173 patients from single-level disc replacement clinical trials of 7 cervical disc prostheses.

OUTCOME MEASURES: 24-month postoperative index-level FE-ROM.

METHODS: The FE-ROM histograms reported in Food and Drug Administration-Investigational Device Exemption (FDA-IDE) submissions and available for this analysis were used to calculate

Work performed at the Musculoskeletal Biomechanics Laboratory, Edward Hines Jr. VA Hospital, Hines, Illinois, USA.

FDA device/drug status: approved (Cervical artificial Disc Prosthesis: ProDisc-C; PCM; Prestige; Bryan, Mobi-C; Secure-C; and M6-C).

Author Disclosure: ***AGP***: Stock Ownership: 3Spine (B); Consulting: 3Spine (None); Scientific Advisory Board/Other Office: 3Spine (None); Research Support (Investigator salary, Staff/Materials): 3Spine (F, Paid directly to institution/employer); Grants: Department of Veterans Affairs (F, Paid directly to institution/employer). ***RMH***: Nothing to disclose. ***FMP*** : Royalties: Nuvasive (F); SI Bone (F)Consulting : Nuvasive (E), Globus (C), Medtronic (C), Stryker (C), Spinal Kinetics (D), Spine Art (D)Advisory Board/BODs : Stock/Options – Nuvasive (<1%), SI Bone (<1%), Spinal Simplicity (<1%), Augmedics(<1%), Edge Surgical (<1%), Providence (<1%), Mainstay (<1%) ***JEZ***: Aesculap (D), Centinel Spine (E), K2M (B), Nuvasive (C), Spineway (C), ZimVie (A) ***DC***: Consulting: Globus Medical (C), Medtronic (D), Spine Wave (B), Royalties: Spine Wave (C), Accelus (E), Globus Medical (B), Medtronic (E), Stryker Spine (E), RTI (B), Spine Wave (F). Stock Ownership: Pressio (B), 3Spine (C), Premia Spine (5,000 Shares, 1%, <1%), Spinal Kinetics (C, 1%, Outside 24-Month Requirement), Spine Wave (50,000 Shares, 1%, ><1%).Scientific Advisory Board: Globus Medical Advisory Board (C), United Healthcare (B). Speaking and/or Teaching Arrangements: Globus Medical (C), Medtronic (B), Spine Wave (C), Stryker Spine (C). ***RG***: Aesculap (B); Centinel(B); NuVasive(B) ***TL***: Nothing to disclose. ***MM***: Grants: International Surgical SECZ (F, Paid directly to institution/employer).

*Corresponding author. Musculoskeletal Biomechanics Laboratory, Edward Hines Jr. VA Hospital, and Department of Orthopaedic Surgery and Rehabilitation, Loyola University Chicago 2160 S. First Ave, Maywood, IL 60153, USA

E-mail address: apatwar@luc.edu (A.G. Patwardhan).

https://doi.org/10.1016/j.spinee.2024.01.015
1529-9430/© 2024 Elsevier Inc. All rights reserved.

the frequencies of implanted levels with postoperative FE-ROM in the following motion-ranges: Hypomobile [0−4 degrees], Physiological [5−16 degrees], and Hypermobile [≥17 degrees]. The ROM histograms also allowed calculation of the average ROM of implanted segments in each of the 3 motion-ranges.

RESULTS: Only 762 of 1,173 patients (implanted levels) yielded 24-month post-CDA FE-ROM in the physiological mobility range [5−16 degrees]. The proportions ranged from 60% to 79% across the 7 disc-prostheses, with an average of 65.0%±6.2%. Three-hundred and two (302) of 1,173 implanted levels yielded ROM in the 0−4-degree range. The proportions ranged from 15% to 38% with an average of 25.7%±8.9%. One-hundred and nine (109) of 1,173 implanted levels yielded ROM of ≥17 degrees with a range of 2%-21% and an average proportion of 9.3%±7.9%. The prosthesis with built-in stiffness due to its nucleus-annulus design yielded the highest proportion (103/131, 79%) of implanted segments in the physiological mobility range, compared to the cohort average of 65% (p<.01). Sixty-five of the 350 (18.6%) discs implanted with the 2 mobile-core designs in this cohort yielded ROM≥17 degrees as compared to the cohort average of 9.3% (109/1,173) (p<.05). At 2-year post-CDA, the "hypomobile" segments moved on average 2.4±1.2 degrees, those in the "physiological-mobility" group moved 9.4±3.2 degrees, and the hypermobile segments moved 19.6±2.6 degrees.

CONCLUSIONS: Prosthesis design significantly influenced the likelihood of achieving FE-ROM in the physiological mobility range, while avoiding hypomobility or hypermobility (p<.01). Post-operative ROM averaged over all study subjects provides incomplete information about the prosthesis performance - it does not tell us how many implanted segments achieve physiological mobility and how many end up with hypomobility or hypermobility. We conclude that the *proportion of index levels achieving post-CDA motions in the physiological mobility range (5−16 degrees)* is a more useful outcome measure for future clinical trials. © 2024 Elsevier Inc. All rights reserved.

Keywords: Cervical disc arthroplasty (CDA); Clinical trials; Hypermobility; Hypomobility; Investigational Device Exemption (IDE); Physiological mobility; Range of motion (ROM); Total disc replacement (TDR)

Introduction

Several clinical studies have shown cervical disc arthroplasty **(CDA)** to be a viable alternative to anterior cervical discectomy and fusion for the treatment of radiculopathy and myelopathy [1−10]. The evolution of artificial cervical discs has resulted in sophisticated device designs using advanced biomaterials.

The functional goals of CDA are to restore enough range of motion **(ROM)** to reduce the risk of accelerated adjacent segment degeneration [9,11−13] but limit excessive motion to obtain a biomechanically stable index segment; herein termed "Physiological mobility range." Mobility and stability are two essential requirements which allow a spinal segment to function in harmony with its neighboring segments [14]. A concern with hypermobility is the potential for accelerated facet joint degeneration [15], which in turn may contribute to axial neck pain. Additionally, joint instability may initiate a self-stabilization (heterotrophic ossification) response. While clinical studies report average ROM after cervical disc replacement surgery (averaged over all study patients), they do not report what proportion of reconstructed segments yield ROM in the Physiological mobility range.

We hypothesized that prosthesis design will influence the likelihood of achieving FE-ROM in the Physiological mobility range, while avoiding hypomobility or hypermobility.

Methods

Patient sample

We analyzed 24-month post-CDA FE-ROM data from 1,173 patients reported in the single-level IDE clinical trials of 7 of the 8 FDA-approved cervical disc prostheses that were available in the public domain or made available for this analysis (ProDisc-C, PCM, Prestige, Bryan, Mobi-C, Secure-C, and M6-C) [16−22]. The 7 clinical trials had similar patient demographics (Table 1) and the inclusion and exclusion criteria were common across these trials. We analyzed postoperative ROM histograms to calculate what proportion of reconstructed segments yielded flexion-extension ROM (FE-ROM) in the Physiological mobility range.

Physiological mobility range

The range of physiological mobility was defined as 5−16 degrees. The 5-degree lower bound of the physiological mobility range was based on clinical observations of significantly reduced incidence of progressive radiographic adjacent level degeneration in patients with 5 degrees or greater ROM after CDA [12,13]. The 16-degree upper bound was based on laboratory data from 133 C5-C6 and C6-C7 segments from 102 cervical spines with mild-to-moderate degeneration evaluated in the biomechanical studies reported in the literature [23−25], which showed a

Table 1
Comparison of patient demographics and baseline functional characteristics among the pivotal IDE studies. Month / year refers to the date of FDA notice of approval.

Demographic Measures	ProDisc-C (12/2007)	Bryan Disc (05/2009)	Secure-C (09/2012)	PCM (10/2012)	Mobi-C (08/2013)	Prestige LP (07/2014)	M6-C (02/2019)
Male	44.7%	45.5%	53.6%	51.8%	47.6%	46.1%	51.3%
Female	55.3%	54.5%	46.4%	48.2%	52.4%	53.9%	48.8%
Age (years)	42.1±8.4	44.4±7.9	43.4±7.5	45.3±9.0	43.3±9.23	44.5±8.8	43.6±9.1
Age range (years)	–	–	24–60	–	21–67	23–78	22–68
BMI (kg/m^2)	26.4±5.3	26.6±4.8	28.9±5.5	28.2±4.6	27.3±4.4	28.5±5.6	27.2±4.8
Preop functional status							
F-E ROM (deg)	–	6.4	8.5±4.8	7.9±4.7	8.2±4.5	5.7±3.7	8.3±5.0
F-E ROM Range	–	–	0.1–23.3	–		0.3–18.1	–
Disc Ht (mm)	–	–	–	–	–	–	3.2±0.7
NDI	53.9±15.1	51.4±15.3	51.8±13.8	55.8±14.5	54.0±14.0	–	54.8±14.1
VAS neck pain	–	75.4±19.9	65.2±26.8	68.4±22.3	70.8±22.4	–	73±19
VAS L arm pain	–	71.2±19.5	45.1±37.4	51.2±33.9	46.7±36.5	–	46±37
VAS R arm pain	–	–	33.8±37.0	47.9±33.7	41.0±36.2	–	42±36
Treated levels							
C3-C4	2.9%	1.2%	3.3%	0.0%	0.6%	1.4%	2.5%
C4-C5	9.7%	5.0%	5.3%	14.2%	6.7%	7.5%	6.3%
C5-C6	56.3%	57.9%	49.7%	50.0%	56.1%	52.5%	51.3%
C6-C7	31.1%	36.0%	41.7%	34.9%	36.6%	38.6%	40.0%
Device heights							
5 mm	68.9%	–	–	–	76.5%	–	–
6 mm	30.1%	–	–	76.8%	21.2%	73.2%	–
7 mm	1.0%	–	88.9%	6.2%	2.2%	23.6%	–
8 mm	–	–	10.6%	17.0%	–	3.2%	–
9 mm	–	–	0.4%	–	–	–	–

ARTICLE IN PRESS

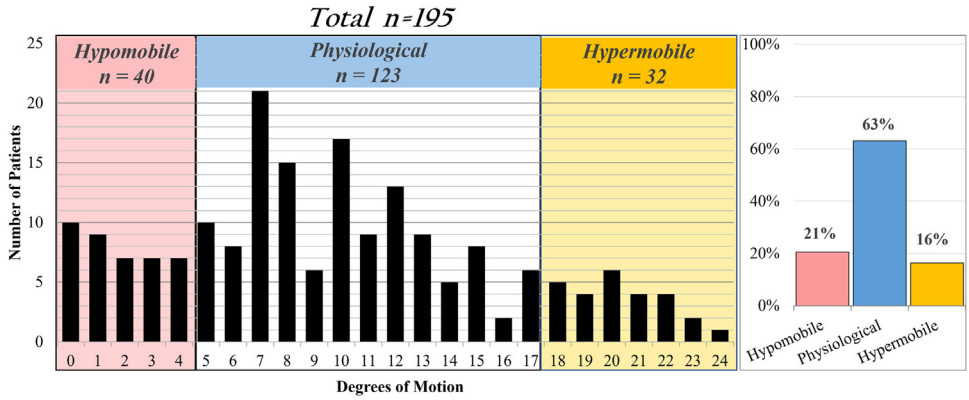

Fig. 1. An example of 24-month ROM histogram. Taken from the FDA document on the 1-level IDE clinical trial of the Secure-C disc [21].

mean FE-ROM of 12.1±4.0 degrees. The upper ROM bound was derived from the sum of the standard deviation and average range of motion of the 133 segments.

Analysis of ROM histogram data

Proportion of implanted discs in hypomobile, physiological, and hypermobile motion-ranges: The reported ROM histograms allowed calculation of the proportion of implanted levels with postoperative FE-ROM in the following motion-ranges: 0–4 degrees (hypomobility); 5–16 degrees (physiological range); and 17 degrees and higher (hypermobility).

Figure 1 is 24-month ROM histogram taken from the FDA document on the 1-level IDE clinical trial of the Secure-C disc [21]. It shows the number of patients having a given degree of FE ROM at the index level. In this clinical trial, out of the total of 195 patients, 123 patients, or 63%, had index level ROM in the 5-to-16-degree range (Physiological mobility group). 40 patients or 21%, had index level ROM in the 0 to 4-degree range (Hypomobile group), and 32 or 16% of patients had index level ROM of 17 degrees or higher (Hypermobile group).

Average ROM of hypomobile, physiological, and hypermobile discs: The ROM histograms also allowed calculation of the average ROM of implanted segments in each of the 3 motion-ranges. This was done by summing the products of ROM magnitude and the number of implanted segments having that ROM and dividing the result by the total number of implanted segments in that mobility range, yielding the average ROM for all segments that fell in a particular mobility range. This calculation was made for each of the three mobility ranges (hypomobile, physiological and hypermobile). For the histogram shown in Figure 1, there were 40 implanted levels with 2-year post-CDA ROM in the 0-4-degree range (hypomobile group). The average ROM for segments in this group was calculated as shown below:

Average ROM in the hypomobile group

$$= [(0 \times 10 + 1 \times 9 + 2 \times 7 + 3 \times 7 + 4 \times 7)/40]$$

$$= 1.8 \text{ degrees}$$

Standard Deviation [26]

$$= \left\{ \left[(0-1.8)^2 \times 10 + (1-1.8)^2 \times 9 + (2-1.8)^2 \times 7 + (3-1.8)^2 \times 7 + (4-1.8)^2 \times 7 \right] / (40-1) \right\}^{0.5}$$

$$= 1.5 \text{ degrees}$$

In the Secure-C clinical trial, the average ROM for the 123 segments with ROM in the 5-16-degree range (Physiological mobility range) was calculated to be 9.6±3.0 degrees, and for the 32 implanted segments whose ROM was 17 degrees or higher the average ROM was calculated to be 19.7±2.0 degrees. The overall average ROM considering all 195 implanted segments was calculated to be 9.7± 6.0 degrees.

Statistical analysis

Chi-square analyses [26] were performed to assess whether the prosthesis design had a significant influence on the proportions of implanted segments in the three postoperative motion ranges. Confidence intervals were used to decide whether a given prosthesis design was more likely than the cohort to lead to postoperative physiological mobility (ROM: 5–16 degrees), hypomobility (ROM: 0–4 degrees), or hypermobility (ROM ≥17 degrees).

Sensitivity analysis

Effects of changing the lower- and upper-bounds of the physiological mobility range on the results were systematically investigated. The baseline 5-degree lower-bound was lowered to 4 degrees to study the sensitivity of the results to the assumption of the smallest degree of postoperative ROM that yields a significant reduction in the incidence of adjacent segment radiographic degeneration. The 16-degree upper-bound was raised to 17 degrees, and 18 degrees, thereby defining hypermobility in a segment as an ROM of ≥18 degrees and ≥19 degrees, respectively.

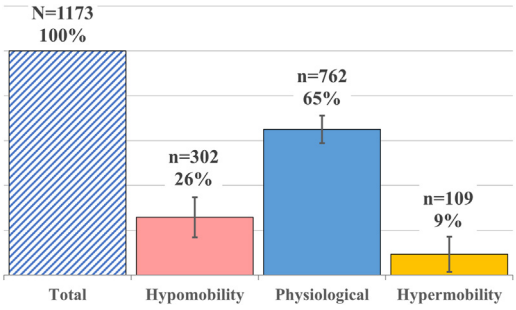

Fig. 2. Cohort averages: number and proportions of patients in the three mobility groups (hypomobility, physiological mobility, and hypermobility) at 2-years post cervical disc arthroplasty.

Results

Likelihood of achieving physiological motion

Cohort averages

Out of the total 1,173 implanted levels in the seven clinical trials, only 762 yielded post-CDA FE-ROM in the physiological motion-range (5–16 degrees). The proportions ranged from 60% to 79% across the 7 disc-prostheses, with a cohort-average of 65.0±6.2% (Figure 2). Three-hundred and two of the 1,173 implanted levels yielded ROM in the hypomobile range (0–4 degrees). The proportions ranged from 15% to 38% with a cohort-average of 25.7±8.9%. One-hundred and nine of 1,173 implanted levels yielded ROM of ≥17 degrees with a range of 2%-21% and a cohort-average of 9.3±7.9%.

Influence of prosthesis design

The frequencies of the implanted cervical disc to fall into the three mobility ranges (Table 2) were significantly influenced by prosthesis design ($p<.01$). The likelihood of achieving FE-ROM in the physiological mobility range (ROM: 5–16 degrees), thus avoiding hypomobility (ROM: 0–4 degrees) or hypermobility (ROM≥17 degrees) depended on the prosthesis design ($p<.01$) (Figure 3).

Three-hundred and fifty cervical segments had mobile-core disc prostheses (Mobi-C: 155, Secure-C: 195) implanted in them. Of these, sixty-five or 18.6% (65/350) yielded ROM greater than 17 degrees, twice the cohort-average of 9.3% (109/1,173) ($p<.05$) and comprised 61% (65/109) of the post-CDA hypermobile levels (Table 2). Mobi C yielded the highest proportion of hypermobile segments postoperatively (33/155 or 21.3%, $p<.01$).

Bryan and PCM disc prostheses yielded hypomobile segments with frequencies of occurrence of 34% (52/154) and 38% (68/178), respectively, significantly higher than the cohort average of 25.7±8.9% (302/1,173) ($p<.05$) (Table 2).

The M6-C prosthesis with design features that provided built-in stiffness (resistance to angular motion) yielded the highest proportion (103/131 or 79%) of implanted segments in the physiological motion-range, compared to the cohort-average of 65% ($p<.01$) (Table 2).

Average ROM in hypomobile, physiologically mobile, and hypermobile discs

Hypomobile segments moved an average of 2.4±1.2 degrees (Table 3). Segments with physiological mobility had an average ROM of 9.4±3.2 degrees, while hypermobile segments had an average ROM of 19.6±2.6 degrees. The average ROMs of implanted discs in the three motion ranges significantly differed from each other for individual prostheses as well as for the entire cohort of 1,173 patients ($p<.01$). Prosthesis design did not influence the ROM in each mobility range ($p>.05$) (Figure 4).

The ROM averaged over all patients in a particular IDE clinical trial (Table 3) was in the physiological mobility range (5–16 degrees) and was within 2 degrees of the average ROM of segments in the physiological mobility group for that prosthesis (Figure 4). This is also true of the entire cohort consisting of 1,173 patients from the seven clinical trials (average motion of segments in the physiological mobility group: 9.4°, ROM averaged over 1,173 implanted segments: 8.6°). It appears that the excess motion of the hypermobile segments was offset by the below-average motion of hypomobile segments, so that the overall average ROM over all implanted segments nearly equaled the average ROM of segments in the physiological mobility sub-group. This is seen in the example case of the Secure-C disc IDE trial [21]:

Table 2
The number of implants within an FDA submission that fall into each of the three postoperative motion ranges (0-4 deg, 5-16 deg, and 17 degrees and greater), and proportions of implanted segments falling into the motion ranges. Data calculated using public-domain data from IDE clinical trials. Data are shown for each prosthesis and for the cohort of 7 prostheses

Motion Range 24-month Postop	ProDisc-C	PCM	Prestige	Bryan	Mobi C	Secure-C	M6-C	All Prostheses	
	n1 (%)	n2 (%)	n3 (%)	n4 (%)	n5 (%)	n6 (%)	n7 (%)	N	Proportion
0–4 deg.	19 (20%)	68 (38%)	77 (29%)	52 (34%)	26 (17%)	40 (21%)	20 (15%)	302	25.7%±8.9%
5–16 deg.	61 (64%)	107 (60%)	175 (66%)	97 (63%)	96 (62%)	123 (63%)	103 (79%)	762	65.0%±6.2%
≥17 deg.	16 (17%)	3 (2%)	12 (5%)	5 (3%)	33 (21%)	32 (16%)	8 (6%)	109	9.3%±7.9%
Sub total	96 (100%)	178 (100%)	264 (100%)	154 (100%)	155 (100%)	195 (100%)	131 (100%)	1173	100.0%

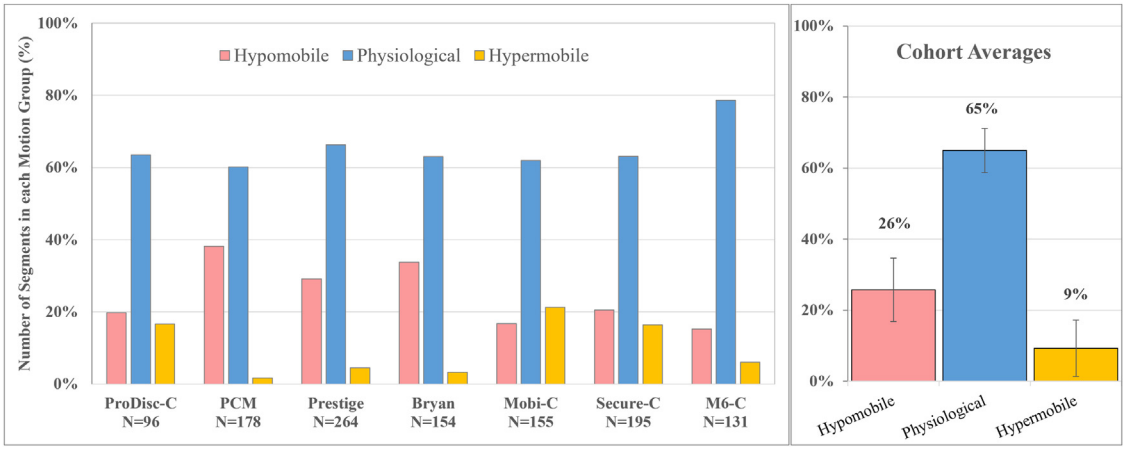

Fig. 3. Prosthesis design and likelihood of postoperative hypomobility, physiological mobility, and hypermobility at 2-year post cervical disc arthroplasty.

Below − average motion of hypomobile segments

$$= (1.8 - 9.7) \times 40 \text{ segments} = -316 \text{ degrees}$$

Above − average motion of hypermobile segments

$$= (19.7 - 9.7) \times 32 \text{ segments} = +320 \text{ degrees}$$

The below-average and above-average motions of hypo- and hypermobile segments nearly offset each other so that the average ROM of all 195 segments (9.7 degrees) nearly equals the average ROM of the 123 Secure-C segments that yield physiological ROM (9.6 degrees).

Sensitivity analysis

Changing the lower- and upper-bounds of the physiological mobility range did not affect the qualitative nature of the results. For example, changing the lower-bound of the physiological mobility range from 5 degrees to 4 degrees altered the definition of hypomobility range from 0−4 degrees down to 0−3 degrees. Yet, regardless of this change in the definition of hypomobility, the Bryan and PCM discs continued to yield greater likelihood of resulting in hypomobile segments postoperatively (Figure 5a).

Changing the upper-bound of the physiological mobility range from 16 degrees to 17 degrees or 18 degrees altered the definition of hypermobility range from ≥17 degrees to ≥18 and ≥19 degrees, respectively. Yet, regardless of this change in the definition of hypermobility, the mobile-core discs (Mobi-C and Secure-C) as a subgroup continued to yield greater likelihood of resulting in hypermobile segments postoperatively when compared to the cohort average (Figure 5b).

Finally, the combined effect of changing the lower- and upper-bounds of the physiological mobility range did not affect the relative findings of the influence of prosthesis design on the likelihood of achieving postoperative physiological mobility (Figure 5c). The M6-C prosthesis with design features that provided built-in stiffness to angular motion yielded the highest proportion of implanted segments in the physiological motion range, compared to the cohort average (Table 2).

Discussion

In this study, we attempted to answer the question: Do the specific design features of an artificial disc prosthesis play a role in restoring enough ROM to reduce the risk of accelerated adjacent segment degeneration but limit excessive motion to obtain a biomechanically stable index segment? The results demonstrate that prosthesis design significantly influenced the likelihood of achieving FE-ROM in the physiological mobility range, thus avoiding

Table 3
The number of implants within an FDA submission that fall into each of the three postoperative motion ranges (0-4 deg, 5-16 deg, and 17 degrees and greater), and average ROM (degrees ± 1 standard deviation) of the implanted segments falling into each motion range. Data are shown for each prosthesis and the cohort of 7 prostheses

Motion Range 24-month Postop	ProDisc-C n1 (ROM)	PCM n2 (ROM)	Prestige n3 (ROM)	Bryan n4 (ROM)	Mobi C n5 (ROM)	Secure-C n6 (ROM)	M6-C n7 (ROM)	All Prostheses N	All Prostheses ROM
0−4 deg.	19 (2.8±1.0)	68 (2.7±1.1)	77 (2.5±1.0)	52 (2.5±1.3)	26 (2.0±1.6)	40 (1.8±1.5)	20 (2.5±1.1)	302	2.4±1.2
5−16 deg.	61 (10.1±3.3)	107 (8.1±2.9)	175 (9.7±3.2)	97 (9.2±3.1)	96 (9.8±3.3)	123 (9.6±3.0)	103 (9.6±3.1)	762	9.4±3.2
≥17 deg.	16 (19.4±1.7)	3 (18±0)	12 (19.2±2.7)	5 (18.2±1.3)	33 (20.4±3.4)	32 (19.7±2.0)	8 (19.1±2.0)	109	19.6±2.6
Average ROM	**96 (10.2±5.7)**	**178 (6.2±3.9)**	**264 (8.0±4.9)**	**154 (7.3±4.6)**	**155 (10.7±6.5)**	**195 (9.7±6.0)**	**131 (9.1±4.6)**	**1173**	**8.6±5.4**

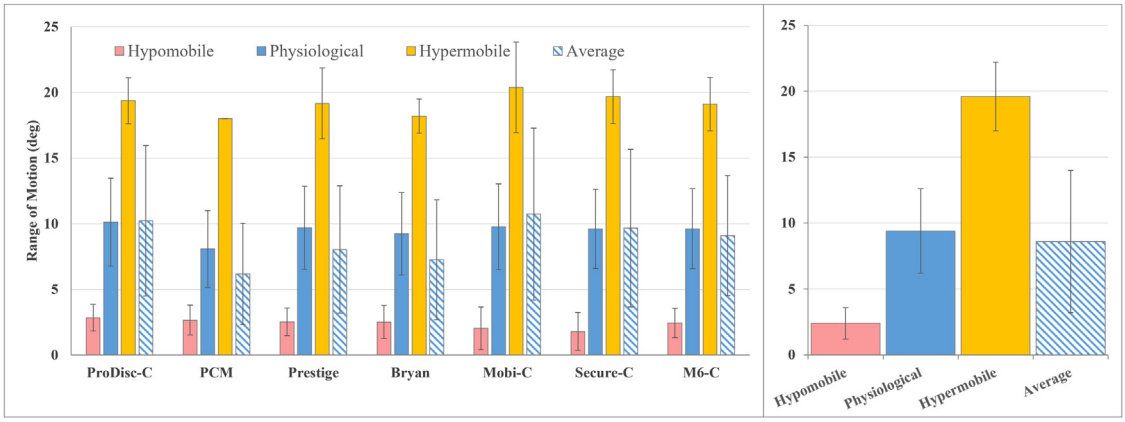

Fig. 4. Average ROM of segments in each of the 3 mobility groups (hypomobility, physiological, and hypermobility) per prosthesis type and over the entire cohort of 1,173 patients. ROM averaged over all patients in a prosthesis IDE clinical study are shown in hashed bars.

hypomobility (ROM 0–4 degrees) or hypermobility (ROM≥17 degrees) ($p<.01$). The overall 24-month postoperative average ROM of each prosthesis, which nearly equaled the ROM of segments in the physiological mobility range, was not significantly different for the seven different prostheses. Prosthesis design, however, significantly influenced how many implanted segments achieved physiological mobility and how many ended up with hypomobility or hypermobility two years after the disc replacement surgery.

All data presented in this work are from IDE studies of single-level cervical disc arthroplasty. Analysis of ROM contributions in multilevel arthroplasty was beyond the scope of this study but will be investigated in follow-up investigations. The vast majority of implantations were done at C5-C6 followed by C6-C7, and a small number at C4-C5 (Table 1). The available data did not allow assessment of the effect of arthroplasty level on the postoperative ROM results. The goal of this work was to report on all

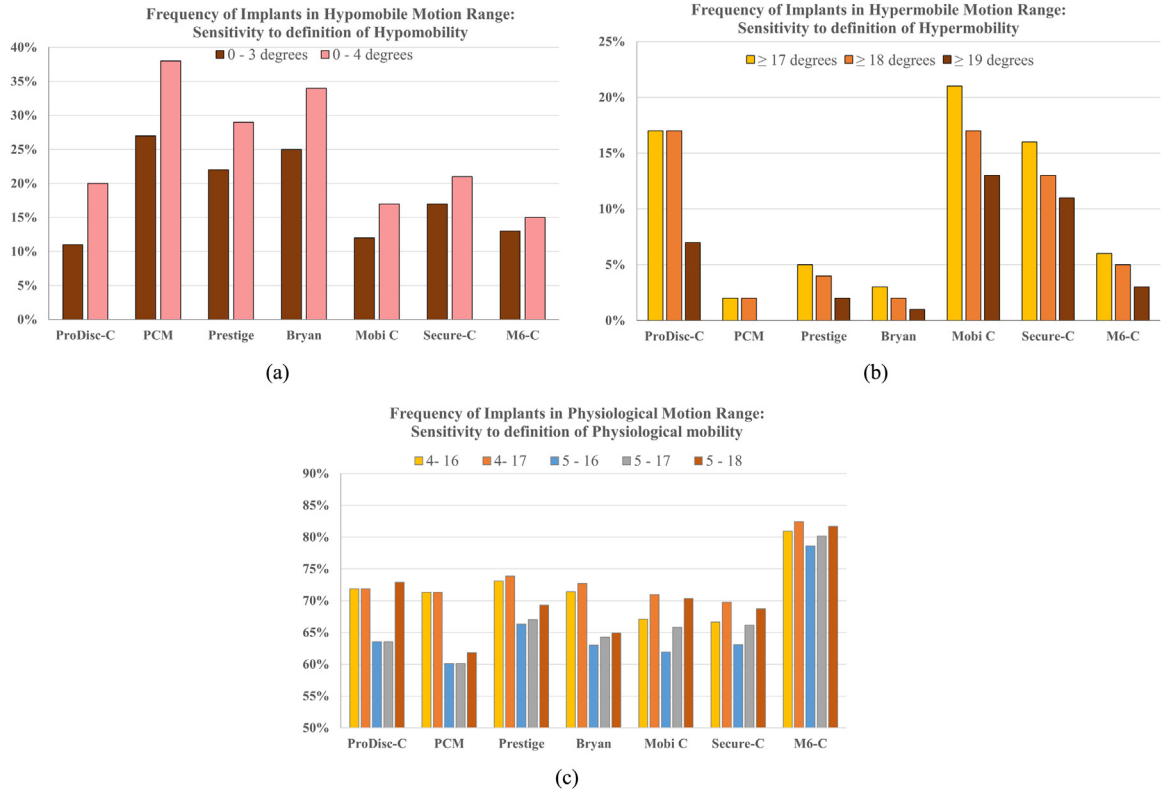

Fig. 5. Results of sensitivity analysis. (a) Frequency of implants in hypomobile motion range: Sensitivity to definition of hypomobility. (b) Frequency of implants in hypermobile motion range: Sensitivity to definition of hypermobility. (c) Frequency of implants in physiological mobility range: Sensitivity to definition of physiological mobility.

cervical disc prostheses designs that have been FDA-approved for use in US. Although some of the prostheses included in this analysis are no longer in clinical use in the U.S., the analysis provides useful insight into the effect of these designs on the likelihood of achieving physiological range of motion. The authors hope this information would be of benefit to designers of future generations of cervical disc prostheses. All devices approved for use in US are indeed included except one (Simplify® Cervical Artificial Disc). The ROM histogram data for study patients was not included in the IDE data reported to the FDA, only the averages were reported. The necessary data on the FDA IDE study was not available to the authors of this manuscript at the time of its submission to the Journal. As a result, the data from this prosthesis could not be combined with the data from other devices analyzed in this manuscript. Data generated from clinical studies of devices receiving FDA approval after the writing of this publication may be included in future updates.

In contradistinction to fusion, the disc prosthesis should limit adjacent level stresses by maintaining motion (or avoiding hypomobility). Logically, the next question addressed would be: Is there a minimum motion threshold that would mitigate the potential risk of accelerated degeneration at adjacent segments following CDA? Huang and colleagues [12] examined the relationship between ROM and adjacent-level degeneration 8.7 years after lumbar disc replacement in 42 patients and found that patients with at least 5 degrees of motion (n=13) had a 0% prevalence of adjacent-level degeneration, whereas those with less than 5 degrees of motion (n=29) had a 34% prevalence. These authors concluded the prevalence of adjacent-level degeneration at 8.7 years after disc replacement is higher in patients with motion less than 5 degrees. The minimum ROM threshold of 5 degrees may also be applicable to the cervical spine because of the similarity of disc mechanobiology between the two regions. Indeed, a recent study by Spivak et al. [13] supports setting the lower bound of the physiologic mobility range at 5 degrees based on their observations of significantly reduced percentage of patients showing progressive radiographic adjacent level degeneration 7-years after cervical disc replacement surgery if the patient had at least 4–6 degrees of ROM at the implanted level.

The disc prosthesis should ideally restore stability by limiting excessive motion (or hypermobility). The overall biomechanical stability of the reconstructed motion segment has theoretical implications when considering the neuromuscular control of spinal motion. Panjabi [27] postulated that an increased laxity, as demonstrated by a substantially decreased stiffness, would put increased demand on the spinal musculature to provide the stability needed during activities of daily living. Increased spinal muscle forces would, in turn, increase stresses in the spinal components and might contribute to pain. Hypermobility at the reconstructed segment caused by a lack of adequate stiffness during a portion of the arc of motion can disturb the harmony of segmental motion with respect to its neighboring segments in a similar way that hypomobility caused by excessive stiffness (i.e., fusion) would increase the burden of motion on adjacent segments [13]. Kerferd et al. [15] suggested that focal hypermobility can potentially lead to accelerated facet joint degeneration. Excessive stresses in the facets may contribute to axial neck pain. An upper bound of 16 degrees for the physiologic motion-range was arrived at based on laboratory data of one-hundred thirty-three (n=133) C5-C6 and C6-C7 segments from 102 cervical spine specimens of mild-to-moderate degeneration status reported in biomechanical studies [23–25], which showed an average FE-ROM of 12.1 degrees (one standard deviation=4.0 degrees). The upper ROM bound was derived from the sum of the standard deviation and average range of motion of the 133 segments.

The sensitivity analysis (Figure 5a-c) indicated that changing the lower- and upper-bounds of the physiological mobility range did not affect the qualitative nature of the results. The disc with the ability to offer built-in resistance to angular motion yielded significantly greater likelihood of achieving postoperative physiological mobility while avoiding hypo- or hypermobility. The mobile-core discs as a subgroup continued to yield greater likelihood of resulting in hypermobile segments postoperatively when compared to other prostheses designs in the cohort; and the Bryan and PCM discs continued to yield greater likelihood of resulting in hypomobile segments postoperatively compared to other prostheses in this cohort.

The total average FE-ROM in clinical trials, which tends to be the number that is reported, was similar regardless of the prosthesis design (Table 3, Figure 4). However, we contend that these averages, calculated using the whole patient cohort, are misleading: The supra-physiological motion contributed by the hypermobile segments was negated by the sub-physiological motion in the hypomobile segments, such that the total average ROM mostly reflected the motion of the segments that yielded physiological mobility (5–16 degrees), as borne out in Table 3. Postoperative ROM averaged over all study subjects provides incomplete information about the prosthesis performance - it does not tell us how many implanted segments achieve physiological mobility and how many end up with hypomobility or hypermobility. We conclude that the *proportion of index levels achieving post-CDA motions in the physiological mobility range (5–16 degrees)* is a more useful outcome measure for future clinical trials.

The preoperative ROM for individual patients is likely to influence the post-CDA ROM of the patient. However, preoperative ROM histograms were unavailable for 6 of the 7 prostheses included in this study. It is likely that there is significant interaction between preoperative ROM, preoperative disc height and disc-space distraction in influencing post-CDA ROM. A comprehensive database of pre-op and post-op radiographic and clinical outcomes is needed to better understand the interaction between pre- and post-

operative ROM and the cervical disc arthroplasty devices that are available for implantation. As disc technologies and understanding of kinematics evolve, we may be reaching a point where we start thinking about specific designs based on patient factors and types of pathology. There are now eight FDA-approved cervical arthroplasty devices in the US as of December 2021 with several more in FDA trials, with each having distinctive characteristics. These allow the clinician to select the best artificial disc for their patients considering the patient's preoperative FE-ROM and postoperative ROM goals.

Conclusions

The mechanical design of an artificial cervical disc prosthesis has a significant influence on the motion of the implanted segment after cervical disc arthroplasty. Furthermore, the disc design affects the likelihood of achieving FE-ROM in the physiological range (5−16 degrees) while also limiting excessive motion (>17 degrees). This comprehensive analysis of IDE clinical trial data suggests that the design features of cervical disc prostheses can potentially be matched to the patient characteristics to achieve the best postoperative outcomes of restoring physiological motion while maintaining biomechanical stability at the index segment. Further, the results suggest the proportion of index levels yielding post-CDA motions in the physiological mobility range (5−16 degrees) might be a valuable outcome measure for future clinical trials.

Declaration of competing interest

One or more of the authors declare financial or professional relationships on ICMJE-TSJ disclosure forms.

CRediT authorship contribution statement

Avinash G. Patwardhan: Conceptualization, Data curation, Formal analysis, Methodology, Investigation, Project administration, Supervision, Validation, Writing − original draft, Writing − review & editing. **Robert M. Havey:** Conceptualization, Data curation, Formal analysis, Methodology, Writing − review & editing. **Frank M. Phillips:** Investigation, Writing − original draft, Writing − review & editing. **Jack E. Zigler:** Conceptualization, Investigation, Writing − review & editing. **Domagoj Coric:** Conceptualization, Investigation, Writing − original draft, Writing − review & editing. **Richard Guyer:** Conceptualization, Investigation, Writing − original draft, Writing − review & editing. **Todd Lanman:** Conceptualization, Investigation, Writing − original draft, Writing − review & editing. **Muturi G. Muriuki:** Investigation, Methodology, Writing − original draft, Writing − review & editing.

Acknowledgments

Supported in part by funds received from the Department of Veterans Affairs, Washington, DC, USA. The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government.

References

[1] Pimenta L, McAfee PC, Cappuccino A, Bellera FP, Link HD. Clinical experience with the new artificial cervical PCM (Cervitech) disc. Spine J 2004;4:315S–21S.

[2] Sasso RC, Smucker JD, Hacker RJ, Heller JG. Artificial disc versus fusion: a prospective, randomized study with 2-year follow-up on 99 patients. Spine 2007;32(26):2933–40.

[3] Sasso R, Anderson P, Riew K, Heller J. Results of cervical arthroplasty compared with anterior discectomy and fusion: four-year clinical outcomes in a prospective, randomized, controlled trial. J Bone Joint Surg Am 2011;93:1684–92.

[4] Coric D, Nunley PD, Guyer RD, Musante D, Carmody CN, Gordon CR, et al. Prospective, randomized, multicenter study of cervical arthroplasty: 269 patients from the Kineflex C artificial disc investigational device exemption study with a minimum 2-year follow-up. J Neurosurg Spine 2011;15(4):348–58.

[5] Zigler JE, Delamarter R, Murrey D, Spivak J, Janssen M. ProDisc-C and anterior cervical discectomy and fusion as surgical treatment for single-level cervical symptomatic degenerative disc disease: five-year results of a Food and Drug Administration study. Spine 2013;38(3):203–9.

[6] Davis RJ, Kim KD, Hisey MS, Hoffman GA, Bae HW, Gaede SE, et al. Cervical total disc replacement with the Mobi-C cervical artificial disc compared with anterior discectomy and fusion for treatment of 2-level symptomatic degenerative disc disease: a prospective, randomized, controlled multicenter clinical trial. J Neurosurg Spine 2013;19(5):532–45.

[7] Gornet MF, Burkus JK, Shaffrey ME, Argires PJ, Nian H, Harrell FE. Cervical disc arthroplasty with PRESTIGE LP disc versus anterior cervical discectomy and fusion: a prospective, multicenter investigational device exemption study. J Neurosurg Spine 2015;23(5):558–73.

[8] Hisey MS, Zigler JE, Jackson R, Nunley PD, Bae HW, Kim KD, et al. Prospective, randomized comparison of one-level Mobi-C cervical total disc replacement vs. anterior cervical discectomy and fusion: results at 5-year follow-up. Int J Spine Surg 2016;10:1–10. https://doi.org/10.14444/3010.

[9] Derman PB, Zigler JE. Cervical disc arthroplasty: rationale and history. Int J Spine Surg 2020;14(s2):S5–13.

[10] Phillips FM, Coric D, Sasso R, Lanman T, Lavelle W, Blumenthal S, et al. Prospective, multicenter clinical trial comparing M6-C compressible six degrees of freedom cervical disc with anterior cervical discectomy and fusion for the treatment of single-level degenerative cervical radiculopathy: 2-year results of an FDA investigational device exemption study. Spine J 2021;21(2):239–52.

[11] Zigler JE, Blumenthal SL, Guyer RD, Ohnmeiss DD, Patel L. Progression of adjacent-level degeneration after lumbar total disc replacement: results of a post-hoc analysis of patients with available radiographs from a prospective study with 5-year follow-up. Spine 2018;43(20):1395.

[12] Huang RC, Tropiano P, Marnay T, Girardi FP, Lim MR, Cammisa Jr FP. Range of motion and adjacent level degeneration after lumbar total disc replacement. Spine J 2006;6(3):242–7.

[13] Spivak JM, Zigler JE, Philipp T, Janssen M, Darden B, Radcliff K. Segmental motion of cervical arthroplasty leads to decreased adjacent-level degeneration: analysis of the 7-year postoperative results of a multicenter randomized controlled trial. Int J Spine Surg 2022;16(1):186–93.

ARTICLE IN PRESS

[14] Patwardhan AG, Havey RM. Prosthesis design influences segmental contribution to total cervical motion after cervical disc arthroplasty. Eur Spine J 2020;29:2713–21.
[15] Kerferd JW, Abi-Hanna D, Phan K, Rao P, Mobbs RJ. Focal hypermobility observed in cervical arthroplasty with Mobi-C. J Spine Surg 2017;3(4):693.
[16] (ProDisc-C 1-level) https://www.accessdata.fda.gov/cdrh_docs/pdf7/p070001b.pdf Accessed 6 June 2021.
[17] (PCM 1-level) https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100012b.pdf Accessed 6 June 2021.
[18] (Prestige 1-level) https://www.accessdata.fda.gov/cdrh_docs/pdf9/P090029b.pdf Accessed 6 June 2021.
[19] (Bryan 1-level) https://www.accessdata.fda.gov/cdrh_docs/pdf6/P060023b.pdf Accessed 6 June 2021.
[20] (Mobi-C 1-level) https://www.accessdata.fda.gov/cdrh_docs/pdf11/p110002b.pdf Accessed 6 June 2021.
[21] (Secure-C 1-level) https://www.accessdata.fda.gov/cdrh_docs/pdf10/pdf10/P100003b.pdf Accessed 6 June 2021.
[22] (M6-C 1-level) https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170036B.pdf Accessed 6 June 2021.
[23] Patwardhan AG, Havey RM. Biomechanics of cervical disc arthroplasty—a review of concepts and current technology. Int J Spine Surg 2020;14(s2):S14–28.
[24] Phillips FM, Tzermiadianos MN, Voronov LI, Havey RM, Carandang G, Dooris A, et al. Effect of two-level total disc replacement on cervical spine kinematics. Spine. 2009;34(22):E794–9.
[25] Patwardhan AG, Tzermiadianos MN, Tsitsopoulos PP, oronov LI, Renner SM, Reo ML, et al. Primary and coupled motions after cervical total disc replacement using a compressible six-degree-of-freedom prosthesis. Eur Spine J 2012;21(5):618–29.
[26] Zar JH. Biostatistical analysis. 2nd edn. NJ, USA: Prentice-Hall: Englewood Cliffs; 1984.
[27] Panjabi MM. The stabilizing system of the spine. Part II. Neutral zone and instability hypothesis. J Spinal Disord 1992;5:390–6. discussion 397.