Biomedical Engineering Faculty Research and Publications

Biomedical Engineering, Department of

1-1-2014

Which Design and Biomaterial Factors Affect Clinical Wear Performance of Total Disc Replacements? A Systematic Review

Sai Y. Veruva
Drexel University

Marla J. Steinbeck
Drexel University

Jeffrey M. Toth
Marquette University, jeffrey.toth@marquette.edu

Dominik D. Alexander
Exponent, Inc

Steven M. Kurtz
Drexel University

Which Design and Biomaterial Factors Affect Clinical Wear Performance of Total Disc Replacements? A Systematic Review

Sai Y. Veruva

Implant Research Center, Drexel University, Philadelphia, PA

Marla J. Steinbeck

Implant Research Center, Drexel University, Philadelphia, PA

Jeffrey Toth

Department of Orthopaedic Surgery, The Medical College of Wisconsin, Milwaukee, WI

Dominik D. Alexander

Exponent, Inc, Boulder, CO

Steven M. Kurtz

Implant Research Center, Drexel University, Exponent, Inc, Philadelphia, PA

Abstract

Background: Total disc replacement was clinically introduced to reduce pain and preserve segmental motion of the lumbar and cervical spine. Previous case studies have reported on the wear and adverse local tissue reactions around artificial prostheses, but it is unclear how design and biomaterials affect clinical outcomes.

Questions/purposes: Which design and material factors are associated with differences in clinical wear performance (implant wear and periprosthetic tissue response) of (1) lumbar and (2) cervical total disc replacements?

Methods: We performed a systematic review on the topics of implant wear and periprosthetic tissue response using an advanced search in MEDLINE and Scopus electronic databases. Of the 340 references identified, 33 were retrieved for full-text evaluation, from which 16 papers met the inclusion criteria (12 on lumbar disc replacement and five on cervical disc replacement; one of the included studies reported on both lumbar and cervical disc replacement), which involved semiquantitative analysis of wear and adverse local tissue reactions along with a description of the device used. An additional three papers were located by searching bibliographies of key articles. There were seven case reports, three case series, two case-control studies, and seven analytical studies. The Methodological Index for Non-randomized Studies (MINORS) Scale was used to score case series and case-control studies, which yielded mean scores of 10.3 of 16 and 17.5 of 24, respectively. In general, the case series (three) and case-control (two) studies were of good quality.

Results: In lumbar regions, metal-on-polymer devices with mobile-bearing designs consistently generated small and large polymeric wear debris, triggering periprosthetic tissue activation of macrophages and giant cells, respectively. In the cervical regions, metal-on-polymer devices with fixed-bearing designs had similar outcomes. All metal-on-metal constructs tended to generate small metallic wear debris, which typically triggered an adaptive immune response of predominantly activated lymphocytes. There were no retrieval studies on one-piece prostheses.

Conclusions: This review provides evidence that design and biomaterials affect the type of wear and inflammation. However, clinical study design, followup, and analytical techniques differ among investigations, preventing us from drawing firm conclusions about the relationship between implant design and wear performance for both cervical and lumbar total disc replacement.

Introduction

Total disc replacement (TDR) was clinically introduced as an alternative to fusion to reduce pain and preserve segmental motion of the cervical and lumbar spine. TDR designs currently on the market may be classified as either fixed- or mobile-bearing analogous to large joint replacements. Of these designs, the most widely used in the market today include metallic endplates, which are fixed to the adjacent vertebral bodies and one or more articulations that involve

either metal-on-metal or metal-on-polymer bearing surfaces. The most commonly used lumbar disc replacements have relied on either cobalt-chromium (CoCr) alloy endplates articulating with a polymer core of ultrahigh-molecular-weight polyethylene (hereafter polyethylene) or metal-on-metal (MoM) bearings fabricated from CoCr alloys. In the cervical spine, a broader range of biomaterials has been used, including polyethylene, CoCr alloys, stainless steel, titanium (Ti) alloys, polyurethanes, polyetheretherketone, and Ti alloy-ceramic composites. In addition to the fixed- and mobile-bearing designs, a third "one-piece" classification of artificial disc design, in which an elastomeric polymer disc is fixed to metallic endplates, is currently undergoing clinical investigation. Thus, the field of artificial disc replacement includes a broad range of designs as well as heterogeneous assortment of biomaterials for lumbar (Table 1) and cervical regions of the spine (Table 2).

Table 1. Summary of contemporary lumbar total disc replacements

Device	Manufacturer	Classification	Biomaterials	Bearing design	IDE trial status (www.clincialtrials.gov)	Current regulatory status (as of January 2014)
CHARITÉ	DePuy Synthes Spine, Raynham, MA, USA	MoP	CoCr-UHMWPE	Mobile	Completed	FDA-approved but withdrawn from US/OUS market after DePuy Synthes merger, 2012
ProDisc-L	DePuy Synthes Spine, West Chester, PA, USA	MoP	CoCr-UHMWPE	Fixed	Completed	FDA-approved, available US/OUS
Activ-L	Aesculap AG, Tuttlingen, Germany	MoP	CoCr-UHMWPE	Mobile	Active; not recruiting	Available OUS
Mobidisc	LDR Spine, Troyes, France	MoP	CoCr-UHMWPE	Mobile	Terminated	Withdrawn
Maverick	Medtronic, Memphis, TN, USA	MoM	CoCr-CoCr	Fixed	Completed	Available OUS
Kineflex	Spinal Motion Inc, Mountainview, CA, USA	MoP	CoCr-CoCr	Mobile	Terminated	Withdrawn
Flexicore	Stryker Spine, Allendale, NJ, USA	MoP	CoCr-CoCr	Constrained	Not registered	Withdrawn
Baguera L	Spineart, Geneva, Switzerland	MoP	Diamolith-coated Ti-UHMWPE	Fixed	Not registered	Available OUS
CAdisc-L	Ranier Technology, Cambridge, UK	1P	1-piece polyurethane	One-piece	Completed	Available OUS

Device	Manufacturer	Classification	Biomaterials	Bearing design	IDE trial status (www.clincialtrials.gov)	Current regulatory status (as of January 2014)
Freedom	AxioMed, Garfield, OH, USA	1P	Ti plates and elastomer core	One-piece	Recruiting	Available OUS
eDisc	Integra Spine, Vista, CA, USA	1P	Ti plates and elastomer core	One-piece	Not registered	Available OUS
Physio-L	Nexgen Spine, Whippany, NJ, USA	1P	Ti plates and elastomer core	One-piece	Not registered	Available OUS
M6-L	Spinal Kinetics Sunnyvale, CA, USA	1P	Ti plates and polyurethane-UHMWPE fiber core	One-piece	Withdrawn	NA

IDE = Investigational Device Exemption; MoP = metal-on-polyethylene; MoM = metal-on-metal; 1P = one-piece; CoCr = cobalt-chromium; UHMWPE = ultrahigh-molecular-weight polyethylene; Ti = titanium; OUS = outside United States; NA = not available.

Table 2. Summary of contemporary cervical total disc replacements

Device	Manufacturer	Classification	Biomaterials	Bearing design	IDE trial status (www.clincialtrials.gov)	Current regulatory status (as of January 2014)
Prestige ST	Medtronic, Memphis, TN, USA	MoM	Stainless steel-stainless steel	Fixed	Completed	FDA-approved, available US/OUS
Bryan	Medtronic	MoP	Ti-PCU	Mobile	Completed	FDA-approved, available US/OUS
Prodisc-C	DePuy Synthes Spine, West Chester, PA, USA	MoP	CoCr-UHMWPE	Fixed	Completed	FDA-approved, available US/OUS
PCM	Nu Vasive, San Diego, CA, USA	MoP	CoCr-UHMWPE	Fixed	Completed	FDA-approved, available US/OUS
Mobi-C	LDR Spine, Troyes, France	MoP	CoCr-UHMWPE	Mobile	Completed	FDA-approved, available US/OUS
SECURE-C	Globus Medical, Audubon, PA, USA	MoP	CoCr-UHMWPE	Mobile	Active; not recruiting	FDA-approved, available US/OUS
Activ C	Aesculap AG, Tuttlingen, Germany	MoP	CoCr-UHMWPE	Mobile	Unknown	Available OUS
Kineflex/C	Spinal Motion Inc, Mountainview, CA, USA	MoM	CoCr-CoCr	Mobile	Terminated	Withdrawn
CerviCore	Stryker Spine, Allendale, NJ, USA	MoM	CoCr-CoCr	Constrained	Not registered	Withdrawn
DISCOVER	DePuy Synthes Spine	MoP	Ti-UHMWPE	Fixed	Active; not recruiting	Available OUS
Baguera C	Spineart, Geneva, Switzerland	MoP	Diamolith-coated Ti-UHMWPE	Fixed	Not registered	Available OUS
Prestige LP	Medtronic	CoC	Ti-ceramic composite	Fixed	Active; not recruiting	Available OUS

Device	Manufacturer	Classification	Biomaterials	Bearing design	IDE trial status (www.clincialtrials.gov)	Current regulatory status (as of January 2014)
NUNEC	Pioneer Surgical Technology, Marquette, MI, USA	PoP	PEEK-PEEK	Fixed	Recruiting	Available OUS
Freedom	AxioMed, Garfield, OH, USA	1P	Ti plates and polymer core	One-piece	Recruiting	Available OUS
NeoDisc	Nu Vasive, San Diego, CA, USA	1P	Silicone elastomer and textile	One-piece	Completed	Available OUS
CAdisc-C	Ranier Technology, Cambridge, UK	1P	1-piece polyurethane	One-piece	Not registered	Available OUS
Discocerv	Alphatec Spine Inc, Carlsbad, CA, USA	CoC	Ceramic-ceramic	Fixed	Terminated	Available OUS
ALTIA	Amedica, Salt Lake City, UT, USA	CoC	Ceramic-ceramic (silicon nitride)	Fixed	Not registered	Available OUS
CerPass	Nu Vasive	CoM	Ceramic-ceramic	Fixed	Terminated	NA
M6-C	Spinal Kinetics Sunnyvale, CA, USA	1P	Ti plates and polyurethane-UHMWPE fiber core	One-piece	Withdrawn	NA

IDE = Investigational Device Exemption; MoM = metal-on-metal; MoP = metal-on-polymer; CoC = ceramic-on-ceramic; PoP = polymer-on-polymer; 1P = one-piece; CoM = ceramic-on-metal; Ti = titanium; UHMWPE = ultrahigh-molecular-weight polyethylene; PCU = poly(carbonate urethane); CoCr = cobalt-chromium; PEEK = polyether ether ketone; OUS = outside United States; NA = not available.

Although the early developers of disc arthroplasty argued that the release of wear debris would not be a clinically relevant issue,[29] case studies have emerged in the literature over the past decade to illustrate the potential for not only wear debris-induced osteolysis in metal-on-polymer (MoP) TDRs, but also adverse local tissue reactions in MoM TDRs.[14] Compared with THAs and TKAs, little is known about the clinical damage modes for TDRs because the surgery to remove a malfunctioning artificial disc can be challenging, or even life-threatening, especially for the lumbar spine.[41] There has been one systematic review of complications in cervical disc arthroplasty[28] and previous (nonsystematic) surveys of retrieved total disc replacements,[21,24] but the authors are aware of no previous systematic approach to examine the effects of design and material selection on wear, corrosion, and tissue response around revised TDRs. Because

the biomechanical requirements for TDRs differ for the cervical and lumbar spine and are reflected in both the TDR design and material selection, studies on total disc replacements for each region of the spine should be considered separately.

We therefore performed a systematic review to evaluate which design and material factors are associated with differences in clinical wear performance (implant wear and periprosthetic tissue response) of (1) lumbar and (2) cervical total disc replacements.

Search Strategy and Criteria

This systematic review used the guidelines from the Cochrane handbook during the development of the study protocol and report.[7] To address the research questions posed in this review, studies were identified by searching the MEDLINE and Scopus electronic databases. An advanced search was performed in MEDLINE through PubMed by querying spine and arthroplasty MeSH terms along with title, abstract, and text word fields in the database. The following precise syntax was used for the search: ((((((((corrosion[tw] OR wear[tw] OR deform*[tw] OR degra*[tw] OR fracture[tw]))) OR (((adverse[tw] AND effects[tw]))))) AND ((((((spine[mh]) OR ((Spinal[tw] OR disc[tw] OR disk[tw]))) AND ((((((artificial[tw] AND prosthe*[tw]))) OR (((disc[tw] AND arthroplast*[tw]) OR (Disc[tw] AND implant) OR (Disc[tw] AND replace*) OR (Disc[tw] AND prosthe*)))) OR posterior fusion[tw]) OR (stabilization[tw])))) AND ((peek[tw] OR polyethylene[tw] OR polycarbonate urethane[tw] OR cobalt chromium[tw] OR prodisc[tw] OR freedom[tw] OR charite[tw] OR maverick[tw] OR kineflex[tw] OR activ[tw] OR mobidisc[tw] OR flexicore[tw] OR xl[tw] OR bryan[tw] OR prestige[tw] OR cadisc[tw] OR nubac[tw] OR secure[tw] OR discover[tw] OR nunec[tw] OR pcm[tw] OR dynesys[tw])))))))) NOT (finite element[tiab] OR biomechanical analysis[tiab] OR biomech*[ti] OR model[tiab] OR MRI[tiab] OR clinical outcome*[ti] OR ossification[ti]) AND "humans"[mh] AND ("2000/01/01"[pdat] : "2014/04/30"[pdat]) AND "English"[la]. The search was streamlined to specifically identify reports of wear, corrosion, and periprosthetic tissue response after spinal arthroplasty. Terms in the latter portion of the code were chosen based on the brand names of motion preservation devices currently in active use or under investigation.

Lastly, the search code excluded papers centrally themed around finite element analysis, biomechanical modeling, or strict clinical outcomes. PubMed filters further restricted results to human studies and reports published in English. Using the aforementioned criteria, 160 articles were obtained from MEDLINE published between January 1, 2001, and April 30, 2014. The same search strategy and filters were used for the Scopus database, yielding 180 articles, many of which overlapped the search results from MEDLINE. The precise syntax used in Scopus is provided (Appendix 1).

Of the 340 papers revealed by the search strategies, duplicates were removed and studies were then screened and assessed for eligibility to be included in the systematic review (Fig. 1). Screening of titles and abstracts revealed 55 articles with potential relevance for this review. Next, in vitro studies and review articles were excluded, narrowing the number of eligible papers for inclusion to 33. An additional three studies were located by searching bibliographies of key articles and identifying full-text articles by hand search. Further full-text assessment for eligibility led to the exclusion of papers without any semiquantitative analyses of wear, corrosion, osteolysis, or adverse local tissue reactions; this left 19 articles meeting the inclusion criteria for this systematic review consisting of 14 lumbar and seven cervical studies (with one overlapping study). The majority of clinical research was low-level evidence[19] and included a total of seven Level V case reports, three Level IV case series, and two Level III case-control studies. Case series and case-control studies, in general, were good-quality studies with mean scores of 10.3 of 16.0 and 17.5 of 24.0, respectively, on the Methodological Index for Non-randomized Studies (MINORS) Scale.[36] The main limitations to these studies included the lack of unbiased assessments, sufficiently long followups, and prospective calculations of study size. We did not grade study quality for the seven analytical reports because there is no suitable tool for this purpose.
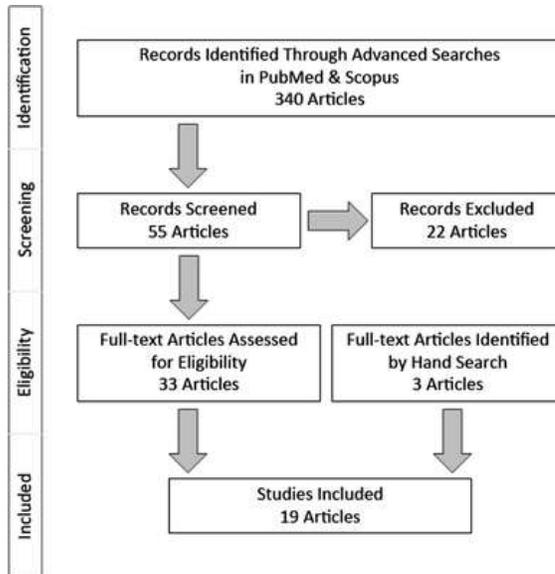
Fig. 1. A flow diagram demonstrates the systematic review protocol.

Each study was reviewed in detail by three authors (SYV, MJS, SMK). Data were extracted using a standardized form. The extraction form included study design, number of patients, patient demographic information, implantation type, disc design, biomaterials used, and outcome measures for device damage, wear, corrosion, metal ion levels, histology, and osteolysis. Some overlapping studies involving the same patients were included if the authors reported different outcomes or evaluated varying durations of followup.

For the systematic review, we summarized authors' evaluations of the removed artificial disc wear, corrosion, and/or periprosthetic tissue responses. We then classified these damage factors as absent or present in condensed cohorts to evaluate the impact of implant design and biomaterials on wear and corrosion performance. Given the methodological and analytical heterogeneity (i.e., between-study variation) between the studies included in this systematic review, the retrospective nature of the clinical series, and the absence of control groups in many of the studies we reviewed, we were unable to combine data across studies to perform a quantitative meta-analysis. Instead we sought to examine each study to glean the desired information about the associations among implant design, wear performance, and local tissue reactions in light of each study's strengths and limitations.

Results

Lumbar Total Disc Replacement

In MoP studies, the mobile-bearing designs, CHARITÉ (DePuy Synthes Spine, Raynham, MA, USA), Activ-L (Aesculap AG, Tuttlingen, Germany), and Mobidisc (LDR Spine, Troyes, France), demonstrated evidence of polyethylene surface damage, polyethylene wear debris, and innate periprosthetic inflammation; fixed-bearing ProDisc-L (DePuy Synthes Spine, West Chester, PA, USA) devices also evidenced endplate impingement and metal wear debris (Table [3]). A total of 49 mobile-bearing MoP retrievals with gamma-air-sterilized polyethylene were evaluated in two studies (48 from one report and one from a case study).[9,23] Impingement, typically between the polyethylene core and the metallic endplate, was observed in 34 of 49 (69%) of the retrievals in those two studies. In two separate studies that analyzed periprosthetic tissues from 22 of the 48 retrievals, one reported polyethylene wear and inflammation in 16 of 22 (73%) patients,[34] and the other identified a direct association among severe or moderate impingement, wear debris, and inflammation for 11 tissues around 11 impinged devices.[3] Despite the frequent observation of polyethylene wear, osteolysis was only reported in one of 48 (2.1%) implants.[23] For mobile-bearing designs with conventional cores, a single report on three retrievals found wear particle generation was two orders less than from gamma-air-sterilized cores.[2] Nevertheless, impingement, wear debris, and innate inflammation were observed in all three retrievals. For fixed-bearing designs, two studies reported burnishing in 11 of 19 (58%) and in one of one retrieval.[5,26] In a separate case report for a prosthesis removed as a result of migration, the presence of metallic debris was observed on the core.[37]

Table 3. Summary of findings from 14 published studies of retrieved implants, tissues, and fluids from lumbar total disc replacements

Classification	Bearing design	Device	Study	Mean implantation time (years)	Impingement	Periprosthetic debris		Inflammation		Osteolysis	Systemic metal ions measured (# of patients)
						Polymeric	Metallic	Innate	Adaptive		
MoP	Mobile	CHARITÉ; DePuy Synthes Spine, Raynham, MA, USA	David, 2005[9]	9.5	0/1	NR	NR	NR	NR	0/1	NR
MoP	Fixed	ProDisc-L; DePuy Synthes Spine, West Chester, PA, USA	Stieber and Donald, 2006[37]	0.1	NR	NR	1/1	NR	NR	NR	NR
MoP	Mobile	CHARITÉ; DePuy Synthes Spine, Raynham, MA, USA	van Ooij et al., 2007[40]	9.4	5/5	5/5	0/5	Y	N	1/5	NR
MoP	Mobile	CHARITÉ; DePuy Synthes Spine, Raynham, MA, USA	Kurtz et al., 2009[21]	8.50	34/48*	NR	NR	NR	NR	1/48*	NR
MoP	Fixed	ProDisc-L; DePuy Synthes Spine, West Chester, PA, USA	Choma et al., 2009[5]	1.2	1/1	1/1	0/1	N	N	NR	NR
MoP	Mobile	Activ-L; Mobidisc Aesculap AG, Tuttlingen, Germany; LDR Spine, Troyes, France	Austen et al., 2012[2]	1.9	3/3	3/3	0/3	Y	N	NR	NR
MoP	Mobile	CHARITÉ; DePuy Synthes Spine,	Punt et al., 2012[34]	10.0	NR	21/22	0/22	Y	N	NR	NR

Classification	Bearing design	Device	Study	Mean implantation time (years)	Impingement	Periprosthetic debris		Inflammation		Osteolysis	Systemic metal ions measured (# of patients)
						Polymeric	Metallic	Innate	Adaptive		
MoP	Fixed	ProDisc-L; DePuy Synthes Spine, West Chester, PA, USA Raynham, MA, USA	Lebl et al., 2012[26]	1.1	11/19	NR	NR	NR	NR	NR	NR
MoP	Mobile	CHARITÉ; DePuy Synthes Spine, Raynham, MA, USA	Baxter et al., 2013[3]	9.7	NR	11/11	0/11	Y	N	NR	NR
MoM	Fixed	Maverick; Medtronic, Memphis, TN, USA	Francois et al., 2007[12]	1.2	NR	NA	1/1	Y	Y	NR	NR
MoM	Fixed	Maverick; Medtronic	Zeh et al., 2009[42†]	3.1	NR	NA	NA	NA	NA	NA	15/15
MoM	Mobile	Kineflex; Spinal Motion Inc, Mountainview, CA, USA	Guyer et al., 2011[17]	1.7	NR	NA	2/2	Y	Y	NR	NR
MoM	Fixed	Maverick; Medtronic	Guyer et al., 2011[17]	3.1	NR	NA	1/1	Y	Y	NR	NR
MoM	Fixed	Maverick; Medtronic	Kurtz et al., 2012[24]	1.3	2/7	NA	1/1	Y	Y	NR	NR
MoM	Fixed	Maverick; Medtronic	Gornet et al., 2013[16†]	3	NR	NR	NR	NR	NR	NR	24/24

* This cohort includes retrievals from study performed by van Ooij et al.;[40] †these are metal ion clinical studies, not retrieval studies; MoP = metal-on-polyethylene; MoM = metal-on-metal; NR = not reported; Y = yes; N = no; NA = not applicable.

In MoM studies, both mobile-bearing Kineflex (Spinal Motion Inc, Mountainview, CA, USA) and fixed-bearing Maverick (Medtronic, Memphis, TN, USA) devices generated metallic debris accompanied by a mixed immune response. Based on a case report of two mobile-bearing retrievals, implant damage in one was negligible and

unreported in the second; however, tissues from both devices contained metallic debris.[17] Similarly, fixed-bearing implant analysis of tissues from two separate case studies[12,17] reported metallic debris. Furthermore, all tissue retrievals showed mixed inflammation. Two independent studies looking at systemic metal ions found elevated serum Co and Cr ion levels postoperatively between 0.25 and 49.4 years.[16,42]

Cervical Total Disc Replacement

In MoP studies, there were no reports on mobile-bearing designs; the fixed-bearing designs, ProDisc-C (DePuy Synthes Spine, West Chester, PA, USA) and Bryan Cervical Disc (Medtronic, Memphis, TN, USA), showed a high frequency of endplate impingement with polymeric wear debris and innate inflammation (Table 4). As observed in lumbar fixed-bearing designs, burnishing was consistent with metallic endplate impingement in 24 of 30 (80%) retrievals.[27] A separate case report noted one rare incidence of osteolysis.[38] In another study, impingement was observed in nine of 30 (30%) retrievals.[24] Tissues obtained from 15 of these 30 devices showed polymeric debris. Similarly, a separate case reported polymeric debris.[1] Metallic debris was infrequent to negligible in all but one of the cases.[11] An innate immune response was predominant in all tissues, although a few isolated regions of lymphocytic infiltration were noted.[24]

Table 4. Summary of findings from seven published studies of retrieved implants and tissues from cervical total disc replacements

Classification	Bearing design	Device	Study	Mean implantation time (years)	Impingement	Periprosthetic debris		Inflammation		Osteolysis
						Polymeric	Metallic	Innate	Adaptive	
MoP	Fixed	Bryan; Medtronic, Memphis, TN, USA	Anderson et al., 2004[1]	1.0	NR	2/2	0/2	Y	N	NR
MoP	Fixed	ProDisc-C; DePuy Synthes Spine, West Chester, PA, USA	Tumailan and Gluf, 2011[38]	1.3	NR	NR	NR	NR	NR	1/1

Classification	Bearing design	Device	Study	Mean implantation time (years)	Impingement	Periprosthetic debris		Inflammation		Osteolysis
						Polymeric	Metallic	Innate	Adaptive	
MoP	Fixed	Bryan; Medtronic	Fan et al., 2012[11]	8.0	NR	1/1	1/1	NR	NR	NR
MoP	Fixed	Bryan; Medtronic	Kurtz et al., 2012[24]	3.2	9/30	15/15	~0/15	Y	Y	NR
MoP	Fixed	ProDisc-C; DePuy Synthes Spine	Lebl et al., 2012[27]	1.0	24/30	NR	NR	NR	NR	NR
MoM	Fixed	Prestige; Medtronic	Anderson et al., 2004[1]	2.4	0/2	NA	2/2	Y	Y	NR
MoM	Mobile	Kineflex/C; Spinal Motion Inc, Mountainview, CA, USA	Cavanaugh et al., 2009[4]	~0.6	NR	NA	1/1	Y	Y	NR
MoM	Mobile	Kineflex/C; Spinal Motion Inc, Mountainview, CA, USA	Guyer et al., 2011[17]	1.2	1/1	NA	0/1	Y	Y	NR
MoM	Fixed	Prestige; Medtronic	Kurtz et al., 2012[24]	2.0	11/16	NA	15/15	Y	Y	NR

MoP = metal-on-polyethylene; MoM = metal-on-metal; NR = not reported; Y = yes; N = no; NA = not applicable.

In MoM studies, impingement was noted in one case study of a mobile-bearing Kineflex/C (Spinal Motion Inc) device; fixed-bearing Prestige Cervical Disc (Medtronic) devices evidenced impingement, metallic debris, and mixed inflammation. A case study on one mobile-bearing device reported no evidence of metal particles in tissues, but metallosis was pronounced.[17] In devices with fixed-bearing designs, impingement was evident in 11 of 16 (68.8%) retrievals, typically in anterior regions.[24] In addition, screw hole fretting and fretting adjacent to bone screws were observed. Focal metallosis was observed in all 15 (100%) patients with tissue retrievals; microscopic metallic debris was noted focally as well, but its distribution was not uniform. A separate study with an unreported bearing design also showed the presence of metallic debris in tissue retrievals.[4] Mixed inflammation was observed in all tissues from both designs.

Discussion

Although benefits of treating degenerative disc conditions with TDR include preservation of motion and limiting stress at adjacent vertebra, potential complications associated with wear debris remain a concern with the use of these devices. The aim of this study was to systematically review reports of wear, corrosion, and consequent biological responses for lumbar and cervical TDR. Additionally, we sought to determine which design and material issues are associated with the wear and corrosion behavior of these motion-preserving spinal devices. After analyzing reports from 14 lumbar and seven cervical studies (in 19 papers), we found that wear-associated complications may be specific to biomaterial selection for TDR in both regions of the spine. MoP devices typically produced polymeric wear debris, which was usually accompanied by an innate inflammatory response. On the other hand, MoM constructs tended to generate small metallic wear debris and metal ions, which activated an adaptive immune mechanism leading to adverse local tissue reactions in some patients.

The pool of studies in this review is very small. The clinical research on the topic is of mixed quality and included a small number of case-control studies that scored well on the MINORS quality scale that we used to grade the clinical research in this report. In the application of our inclusion and exclusion criteria, studies that did not report at least semiquantitative measures of wear were excluded, thus potentially eliminating studies with some important clinical information and patient outcomes in response to the use of certain implant designs/biomaterials. It is also important to note that all the studies that were included involved cases in which the primary revision reason was pain rather than an association with wear. Nevertheless, these criteria were necessary to report common endpoints and measurable findings that could be summarized and evaluated. However, variability in the reporting of wear and related damage mechanisms made it difficult to synthesize results as did the inclusion of data from case reports, which lack a representative comparison group. Standardized test methods for retrieval analysis of TDRs have only recently been developed;[24] thus, older studies included in this review typically relied

on visual characterization of wear. Tissue evaluations of wear debris and inflammatory responses were also limited.

Of the one lumbar and five cervical disc artificial disc designs that have been approved by the US FDA as of the time of this writing, only one is a MoM device fabricated from stainless steel (Table 2). MoM prostheses have been under heavy scrutiny by researchers/regulators given the high-profile concern of a previous recall and warnings of THA devices with Co-based alloy MoM bearings.[31] Metallosis and subsequent soft tissue reactions and pseudotumors have been reported in patients with CoCr MoM articulations, in which some cases showed aseptic lymphocyte-dominated vasculitis-associated lesion response associated with normal wear rate.[14,17] Metal hypersensitivity is also an issue with these CoCr designs,[4] although the relationship between delayed hypersensitivity and metallic debris remains unclear. Such a host response may also be triggered by tribochemical reactions in vivo, but to our knowledge, there have been no direct and standardized measurements of implant corrosion in TDRs. Fretting and corrosion products were observed in some cervical MoM TDRs,[1,24] but the extent of corrosive removal of metal in these devices remains unclear. Serum assays after lumbar TDR have revealed that there was an elevation in Co and Cr ions, thereby inferring corrosion, but it was later concluded that these levels were of a magnitude as those seen in successful MoM THAs.[16,42,43] Despite these biomaterial issues, using MoM designs have benefits that other bearing surface combinations do not. For instance, these devices are theoretically designed to achieve lower volumetric wear (mainly as a result of lower friction) in comparison to traditional MoP designs, thereby potentially reducing local inflammation and osteolysis. Also, it is worth noting that adverse local tissue reactions have been reported with all implant designs; thus, the small number of case reports for MoM studies exhibit important risks/complications of the technology. Further long-term followup studies are necessary to better understand the impact of such designs on long-term wear rates.

Unlike MoM devices, the central concern with the use of MoP devices is the generation of polymeric wear debris from bearing surfaces and innate inflammatory responses. Recent studies on MoP TDRs have revealed that tissue responses resulting from wear-related damage are indeed comparable to responses seen in total joint

arthroplasties (TJAs).[34] However, for THAs, polyethylene wear activates an innate inflammatory response that is associated with osteolysis and aseptic loosening, which is a fundamental cause of clinical failure.[20,22] Vertebral osteolysis, on the other hand, appears to be a rare phenomenon in the spine and has only been reported in one patient with lumbar mobile-bearing TDR and one patient with cervical fixed-bearing TDR in the retrieval studies we reviewed.[38,40] Explanations for the relatively low frequency of osteolysis may include the low ranges of motion (ROMs) in the anterior column of the lumbar spine and an absence of synovium compared with the hip and knee.[29] Furthermore, the particle concentration or cytokine levels are too low to directly cause osteolysis.[2] Despite the difference in wear debris concentrations, similar cytokines such as tumor necrosis factor-α, interleukin-1, and interleukin-6 are released by macrophages and giant cells in both tissue types; however, they appear to induce osteoclastogenesis in THAs and neuroinflammatory pain in TDRs.[13,35] For these reasons, the presence of wear remains a critical concern even in the spine.

This review consisted primarily of papers reporting on wear performance of MoP retrievals, particularly fixed- and mobile-bearing designs; of these reports, assessments of wear damage between these two designs were inconsistent, possibly reflecting the influence of bearing design. Mobile-bearing retrievals tended to have characteristic multidirectional scratches with adhesive/abrasive wear mechanisms at the dome (much like THAs) and microadhesive/microabrasive wear mechanisms at the rim (much like TKAs).[33] Whereas several fixed-bearing retrievals also had signs of scratches in the dome regions, a large percentage had characteristic metallic and endplate burnishing typically in the posterior region associated with impingement.[26] Also, fatigue-related rim damage and radial crack formation were only reported in gamma-air-sterilized cores of historical mobile-bearing retrievals, attributable to oxidative degradation.[9,23] Although this was not evident in gamma-inert sterilized fixed-bearing designs, the mobility of the core in designs may contribute to wear performance. Furthermore, the increased mobility and abnormalities in ROMs may also contribute to the number and type of wear debris generation. Although flexion/extension ROM was shown to be restored to physiological ranges by both designs,[15,30,44] mobile-bearing devices provide higher degrees of freedom (i.e., CHARITÉ; five degrees of

freedom) compared with fixed bearings (i.e., ProDisc-L; three degrees of freedom). The long-term consequences of the differing kinematics on wear debris generation and subsequent inflammation remain unclear.

Among papers identified by the systematic search, there were no studies of wear from one-piece retrievals, thereby highlighting a need for research on nonball-and-socket type designs to evaluate their effectiveness and resistance to wear/corrosion. Ball-and-socket articulating bearings were originally modeled from total joint arthroplasties, which raises the question whether they replicate the biologically and biomechanically different intervertebral disc. Ball-and-socket designs are typically rigid in the axial direction and are not designed to resist moments in bending or rotation like the natural and deformable spinal disc, which may lead to altered ROM, segmental lordosis, or overloading of facet joints.[6,8,32,39] One-piece designs typically incorporate compliant elastomer biomaterials to mimic the physiological six degrees of freedom.[18,25] Although the first one-piece model, known as the Acroflex (DePuy-AcroMed, Inc, Raynham, MA, USA) discs, was abandoned as a result of failure of elastic rubber,[10] newer designs have sought to improve the technology, including solving the issue of bonding elastic components to titanium endplates. Long-term followup studies are required to better understand the wear performance with these designs.

In summary, current TDRs have been developed using total joint arthroplasty models and thus comparable biomaterial issues have been observed. MoP devices raise a concern for the production of polymeric wear debris that initiates innate inflammation. MoM devices present the risk of generating small metallic debris, metal ion release, adaptive host responses, hypersensitive reactions, and pseudotumor formation. Increases in systemic metal ion levels have also been detected, raising the likelihood of responses in other tissues. Design factors such as mobile- and fixed-bearing or one-piece constructs may also influence wear performance of TDRs, but more research is necessary to better understand which models truly mimic the natural motions of the spine while minimizing wear. Additional analytical studies such as cohort and case-control designs would augment the existing body of literature and would facilitate a more formal quantitative assessment using standardized methodology. In addition,

future studies also need to address how design and wear of the various biomaterials impact neuroinflammation in the spine considering pain is the primary reason for revision of both lumbar and cervical TDRs.

Appendix 1. Search Syntax for Scopus Electronic Database

(((((TITLE-ABS-KEY(corrosion) OR TITLE-ABS-KEY(wear) OR TITLE-ABS-KEY(deform*) OR TITLE-ABS-KEY(degra*) OR TITLE-ABS-KEY(fracture))) OR (((TITLE-ABS-KEY(adverse) AND TITLE-ABS-KEY(effects))))) AND ((((((TITLE-ABS-KEY(spine) OR TITLE-ABS-KEY(spinal) OR TITLE-ABS-KEY(disc) OR TITLE-ABS-KEY(disk))) AND ((((((TITLE-ABS-KEY(artificial) AND TITLE-ABS-KEY(prosthe*))) OR (((TITLE-ABS-KEY(disc) AND TITLE-ABS-KEY(arthroplast*) OR (TITLE-ABS-KEY(disc) AND TITLE-ABS-KEY(implant)) OR (TITLE-ABS-KEY(disc) AND TITLE-ABS-KEY(replace*)) OR (TITLE-ABS-KEY(disc) AND TITLE-ABS-KEY(prosthe*))))) OR TITLE-ABS-KEY(fusion)) OR (TITLE-ABS-KEY(stabilization))))) AND ((TITLE-ABS-KEY(peek) OR TITLE-ABS-KEY(polyethylene) OR TITLE-ABS-KEY(polycarbonate urethane) OR TITLE-ABS-KEY(cobalt chromium) OR TITLE-ABS-KEY(prodisc) OR TITLE-ABS-KEY(freedom) OR TITLE-ABS-KEY(charite) OR TITLE-ABS-KEY(maverick) OR TITLE-ABS-KEY(kineflex) OR TITLE-ABS-KEY(activ) OR TITLE-ABS-KEY(mobidisc) OR TITLE-ABS-KEY(flexicore) OR TITLE-ABS-KEY(xl) OR TITLE-ABS-KEY(bryan) OR TITLE-ABS-KEY(prestige) OR TITLE-ABS-KEY(cadisc) OR TITLE-ABS-KEY(nubac) OR TITLE-ABS-KEY(secure) OR TITLE-ABS-KEY(discover) OR TITLE-ABS-KEY(nunec) OR TITLE-ABS-KEY(pcm) OR TITLE-ABS-KEY(dynesys))))))) AND NOT (TITLE-ABS-KEY(finite element) OR TITLE-ABS-KEY(biomechanical analysis) OR TITLE-ABS-KEY(biomech*) OR TITLE-ABS-KEY(model) OR TITLE-ABS-KEY(mri) OR TITLE-ABS-KEY(clinical outcome*) OR TITLE-ABS-KEY(ossification))) AND (PUBYEAR > 1999 AND PUBYEAR < 2015) AND (LIMIT-TO(LANGUAGE,"English"))

References

[1]Anderson PA, Rouleau JP, Toth JM, Riew KD. A comparison of simulator-tested and -retrieved cervical disc prostheses. Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2004. *J Neurosurg Spine.* 2004;1:202–210.

[2]Austen S, Punt IM, Cleutjens JP, Willems PC, Kurtz SM, MacDonald DW, van Rhijn LW, van Ooij A. Clinical, radiological, histological and retrieval findings of Activ-L and Mobidisc total disc replacements: a study of two patients. *Eur Spine J.* 2012;21(Suppl 4):S513–520.

[3]Baxter RM, Macdonald DW, Kurtz SM, Steinbeck MJ. Severe impingement of lumbar disc replacements increases the functional biological activity of polyethylene wear debris. *J Bone Joint Surg Am*. 2013;95:e751–759.

[4]Cavanaugh DA, Nunley PD, Kerr E Jr, Werner DJ, Jawahar A. Delayed hyper-reactivity to metal ions after cervical disc arthroplasty: a case report and literature review. *Spine (Phila Pa 1976).* 2009;34:E262–265.

[5]Choma TJ, Miranda J, Siskey R, Baxter R, Steinbeck MJ, Kurtz SM. Retrieval analysis of a ProDisc-L total disc replacement. *J Spinal Disord.* 2009;22:290–296.

[6]Chung SK, Kim YE, Wang KC. Biomechanical effect of constraint in lumbar total disc replacement: a study with finite element analysis. *Spine (Phila Pa 1976).* 2009;34:1281–1286.

[7]Cochrane Handbook for Systematic Reviews of Interventions. Available at: http://www.cochrane.org/training/cochrane-handbook. Accessed January 1, 2014.

[8]Cunningham BW, Dmitriev AE, Hu N, McAfee PC. General principles of total disc replacement arthroplasty: seventeen cases in a nonhuman primate model. *Spine (Phila Pa 1976).* 2003;28:S118–124.

[9]David T. Revision of a Charite artificial disc 9.5 years in vivo to a new Charite artificial disc: case report and explant analysis. *Eur Spine J.* 2005;14:507–511.

[10]Devin CJ, Myers TG, Kang JD. Chronic failure of a lumbar total disc replacement with osteolysis. Report of a case with nineteen-year follow-up. *J Bone Joint Surg Am.* 2008;90:2230–2234.

[11]Fan H, Wu S, Wu Z, Wang Z, Guo Z. Implant failure of Bryan cervical disc due to broken polyurethane sheath: a case report. *Spine (Phila Pa 1976).* 2012;37:E814–816.

[12]Francois J, Coessens R, Lauweryns P. Early removal of a Maverick disc prosthesis: surgical findings and morphological changes. *Acta Orthop Belg.* 2007;73:122–127.

[13]Gallo J, Raska M, Mrazek F, Petrek M. Bone remodeling, particle disease and individual susceptibility to periprosthetic osteolysis. *Physiol Res.* 2008;57:339–349.

[14]Golish SR, Anderson PA. Bearing surfaces for total disc arthroplasty: metal-on-metal versus metal-on-polyethylene and other biomaterials. *Spine J.* 2012;12:693–701.

[15]Gornet MF, Burkus JK, Dryer RF, Peloza JH. Lumbar disc arthroplasty with Maverick disc versus stand-alone interbody fusion: a prospective,

randomized, controlled, multicenter investigational device exemption trial. *Spine (Phila Pa 1976).* 2011;36:E1600–1611.

[16]Gornet MF, Burkus JK, Harper ML, Chan FW, Skipor AK, Jacobs JJ. Prospective study on serum metal levels in patients with metal-on-metal lumbar disc arthroplasty. *Eur Spine J.* 2013;22:741–746.

[17]Guyer RD, Shellock J, MacLennan B, Hanscom D, Knight RQ, McCombe P, Jacobs JJ, Urban RM, Bradford DS, Ohnmeiss DD. Early failure of metal-on-metal artificial disc prostheses associated with lymphocytic reaction: diagnosis and treatment experience in four cases. *Spine (Phila Pa 1976).* 2011;36:E492–497.

[18]Heuer F, Schmidt H, Klezl Z, Claes L, Wilke HJ. Stepwise reduction of functional spinal structures increase range of motion and change lordosis angle. *J Biomech.* 2007;40:271–280.

[19]Hujoel P. Grading the evidence: the core of EBD. *J Evid Based Dent Pract.* 2009;9:122–124.

[20]Jacobs JJ, Hallab N, Urban RM, Wimmer MA. Wear particles. *J Bone Joint Surg Am.* 2006;88:99–102.

[21]Kurtz SM, Steinbeck M, Ianuzzi A, Van Ooij A, Punt IM, Isaza J, Ross ERS. Retrieval analysis of motion preserving spinal devices and periprosthetic tissues. *SAS*. 2009;3:161–177.

[22]Kurtz SM. *The UHMWPE Biomaterials Handbook.* Burlington, MA, USA: Academic Press; 2009.

[23]Kurtz SM, MacDonald D, Ianuzzi A, van Ooij A, Isaza J, Ross ER, Regan J. The natural history of polyethylene oxidation in total disc replacement. *Spine (Phila Pa 1976).* 2009;34:2369–2377.

[24]Kurtz SM, Toth JM, Siskey R, Ciccarelli L, Macdonald D, Isaza J, Lanman T, Punt I, Steinbeck M, Goffin J, van Ooij A. The latest lessons learned from retrieval analyses of ultra-high molecular weight polyethylene, metal-on-metal, and alternative bearing total disc replacements. *Semin Spine Surg.* 2012;24:57–70.

[25]Lazennec J-Y, Even J, Skalli W, Rakover J-P, Brusson A, Rousseau M-A. Clinical outcomes, radiologic kinematics, and effects on sagittal balance of the 6-degrees-of-freedom LP-ESP® lumbar disc prosthesis. *Spine J.* 2013 Nov 19 [Epub ahead of print].

[26]Lebl DR, Cammisa FP, Girardi FP, Wright T, Abjornson C. In vivo functional performance of failed Prodisc-L devices: retrieval analysis of lumbar total disc replacements. *Spine (Phila Pa 1976).* 2012;37:E1209–1217.

[27]Lebl DR, Cammisa FP Jr, Girardi FP, Wright T, Abjornson C. The mechanical performance of cervical total disc replacements in vivo: prospective retrieval analysis of prodisc-C devices. *Spine (Phila Pa 1976).* 2012;37:2151–2160.

[28]Lehman R, Bevevino AJ, Brewer DD, Skelly AC, Anderson PA. A systematic review of cervical artificial disc replacement wear characteristics and durability. *Evid Based Spine Care J.* 2012;3:31–38.

[29]Link HD, Keller A. Biomechanics of total disc replacement. In: Buttner-Janz K, Hochschuler SH, McAfee PC, eds. *The Artificial Disc.* Berlin, Germany: Springer; 2003:33–52.

[30]McAfee PC, Cunningham B, Holsapple G, Adams K, Blumenthal S, Guyer RD, Dmietriev A, Maxwell JH, Regan JJ, Isaza J. A prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion: part II: evaluation of radiographic outcomes and correlation of surgical technique accuracy with clinical outcomes. *Spine (Phila Pa 1976).* 2005;30:1576–1583; discussion E1588–1590.

[31]Metal-on-Metal Hip Implants. US Food and Drug Administration. Available at: http://www.fda.gov/medicaldevices/productsandmedicalprocedures/implantsandprosthetics/metalonmetalhipimplants/default.htm. Accessed January 1, 2013.

[32]O'Leary P, Nicolakis M, Lorenz MA, Voronov LI, Zindrick MR, Ghanayem A, Havey RM, Carandang G, Sartori M, Gaitanis IN, Fronczak S, Patwardhan AG. Response of Charite total disc replacement under physiologic loads: prosthesis component motion patterns. *Spine J.* 2005;5:590–599.

[33]Punt I, Baxter R, van Ooij A, Willems P, van Rhijn L, Kurtz S, Steinbeck M. Submicron sized ultra-high molecular weight polyethylene wear particle analysis from revised SB Charite III total disc replacements. *Acta Biomater.* 2011;7:3404–3411.

[34]Punt IM, Austen S, Cleutjens JP, Kurtz SM, ten Broeke RH, van Rhijn LW, Willems PC, van Ooij A. Are periprosthetic tissue reactions observed after revision of total disc replacement comparable to the reactions observed after total hip or knee revision surgery? *Spine (Phila Pa 1976).* 2012;37:150–159.

[35]Scholz J, Woolf CJ. The neuropathic pain triad: neurons, immune cells and glia. *Nat Neurosci.* 2007;10:1361–1368.

[36]Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological Index for Non-randomized Studies (MINORS): development and validation of a new instrument. *ANZ J Neurosurg.* 2003;73:712–716.

[37]Stieber JR, Donald III GD. Early failure of lumbar disc replacement: case report and review of the literature. *J Spinal Disord.* 2006;19:55–60.

[38]Tumialan LM, Gluf WM. Progressive vertebral body osteolysis after cervical disc arthroplasty. *Spine (Phila Pa 1976).* 2011;36:E973–978.

[39]van den Broek PR, Huyghe JM, Wilson W, Ito K. Design of next generation total disk replacements. *J Biomech.* 2012;45:134–140.

[40]van Ooij A, Kurtz SM, Stessels F, Noten H, van Rhijn L. Polyethylene wear debris and long-term clinical failure of the Charite disc prosthesis: a study of 4 patients. *Spine (Phila Pa 1976).* 2007;32:223–229.

[41]van Ooij A, Oner FC, Verbout AJ. Complications of artificial disc replacement: a report of 27 patients with the SB Charite disc. *J Spinal Disord.* 2003;16:369–383.

[42]Zeh A, Becker C, Planert M, Lattke P, Wohlrab D. Time-dependent release of cobalt and chromium ions into the serum following implantation of the metal-on-metal Maverick type artificial lumbar disc (Medtronic Sofamor Danek). *Arch Orthop Trauma Surg.* 2009;129:741–746.

[43]Zeh A, Planert M, Siegert G, Lattke P, Held A, Hein W. Release of cobalt and chromium ions into the serum following implantation of the metal-on-metal Maverick-type artificial lumbar disc (Medtronic Sofamor Danek). *Spine (Phila Pa 1976).* 2007;32:348–352.

[44]Zigler J, Delamarter R, Spivak JM, Linovitz RJ, Danielson GO 3rd, Haider TT, Cammisa F, Zuchermann J, Balderston R, Kitchel S, Foley K, Watkins R, Bradford D, Yue J, Yuan H, Herkowitz H, Geiger D, Bendo J, Peppers T, Sachs B, Girardi F, Kropf M, Goldstein J. Results of the prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease. *Spine (Phila Pa 1976).* 2007;32:1155–1162; discussion 1163.