## Fundamentals of Mechanobiology and Potential Applications in Spinal Fusion

## MATTHEW SCOTT-YOUNG, MBBS, FRACS<sup>1,2</sup>; DAVID NIELSEN, MBBS, FRACS<sup>2</sup>; AND SUKHMAN RIAR, BSc<sup>1,2</sup>

<sup>1</sup>Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland, Australia; <sup>2</sup>Gold Coast Spine, Bond University, Gold Coast, Queensland, Australia

### ABSTRACT

**Background:** Mechanobiology can help optimize spinal fusion by providing insights into the mechanical environment required for bone healing and fusion. This includes understanding the optimal loading conditions, the mechanical properties of implanted materials, and the effects of mechanical stimuli on the cells involved in bone formation. The present article reviews the evidence for surface technologies and implant modification of spinal cages in enhancing spinal fusion.

**Methods:** Databases used included Embase, MEDLINE, Springer, and Cochrane Library. Relevant articles were identified using specific keywords and search fields. Only systematic reviews, meta-analyses, review articles, and original research articles in English were included. Two researchers independently performed the search and selection process. A flowchart of the search strategy and study selection method is provided in the article.

**Results:** The studies indicate that surface modification can significantly enhance osseointegration and interbody fusion by promoting cellular adhesion, proliferation, differentiation, and mineralization. Various surface modification techniques such as coating, etching, nanotopography, and functionalization achieve this. Similarly, implant material modification can improve implant stability, biocompatibility, and bioactivity, leading to better fusion outcomes. Mechanobiology plays a vital role in this process by influencing the cellular response to mechanical cues and promoting bone formation.

**Conclusions:** The studies reviewed indicate that surface technologies and implant material modification are promising approaches for improving the success of spinal cage fusion. Mechanobiology is critical in this process by influencing the cellular response to mechanical signals and promoting bone growth.

Focus Issue Article

Keywords: mechanobiology, mechanotransduction, spinal fusion, cages, surface technology

## INTRODUCTION

Mechanobiology and biomechanics are interrelated fields of study with different foci and approaches that often overlap in their research questions and techniques. These fields examine the mechanical properties and behaviors of biological systems using fundamental physics, engineering, and biology principles and aim to develop new strategies and technologies for improving health and performance.

Biomechanics studies the structural properties and mechanical behaviors of biological systems. In orthopedic biomechanics, our understanding continues to grow regarding behaviors of bone, articular cartilage, and soft tissues across different musculoskeletal regions. Innovative tools and analysis techniques have led to a better understanding of joint kinematics and tissue function during different activities. Mathematical modeling and improved engineering design of orthopedic implants have also progressed significantly. Biomechanical principles have been applied to address clinically relevant problems, improving patient treatments and outcomes through collaboration between bioengineers and orthopedic surgeons.<sup>1</sup>

Mechanobiology studies how cells sense mechanical stimuli and respond by altering growth, differentiation, and migration behaviors—a core principle known as mechanotransduction. It focuses on complex molecular machinery that regulates mechanical signaling pathways at cellular, tissue, and organ levels.<sup>2</sup> A deeper understanding of how mechanical stress regulates cells can contribute to the functional advancement of these technologies.<sup>3</sup>

#### Relevance to Spine Surgery

Low back pain is a prevalent ailment that frequently arises as a result of degenerative disc disease. It is a primary contributor to work absenteeism, disability, and diminished quality of life.<sup>4</sup> Chronic low back pain is primarily attributed to disc-related pain, followed by facet joint and sacroiliac joint pain.<sup>5,6</sup> The worldwide occurrence of low back pain is estimated to be around 60% to 70%, with significant variations observed

among individuals and regions. Young and middle-aged adults experience the highest occurrence of low back pain, resulting in prolonged disability, surpassing other ailments.<sup>7,8</sup>

Spinal fusion surgery alleviates chronic back pain, enhances spinal stability, and prevents further damage.<sup>9</sup> The success of this surgery depends on factors such as the spinal condition's severity, level of pain and disability, and overall health status. Spinal fusion surgery is usually recommended for patients with conditions causing instability<sup>10</sup> or chronic pain, including degenerative disc disease,<sup>11</sup> spinal stenosis, scoliosis,<sup>12</sup> or a spinal fracture that failed conservative management. The surgical goals are reducing pain, improving function, providing stability, correcting deformity, and obtaining fusion. Applying mechanobiology principles and techniques can assist significantly in achieving spinal fusion as it is a complex procedure involving physical forces and chemical processes that promote bone tissue growth and fusion.

Mechanobiology investigates how mechanical forces, such as tension, compression, and stiffness, are sensed and transduced into biochemical signals, which affect cellular behavior, gene expression, and tissue organization.<sup>13</sup> The extracellular matrix (ECM) communicates mechanical stimuli to cells through mechanotransduction, which generates different responses depending on the load's type, magnitude, duration, and location. Knowledge of mechanobiology can assist in creating innovative approaches and technologies for spinal fusion that take advantage of the mechanical environment of the spine and the response of bone cells to mechanical stimuli.<sup>14</sup> This can lead to the development of implants with enhanced biocompatibility and mechanical properties, including 3D-printed implants that mimic native bone architecture.<sup>15,16</sup> The feedback loop between surgeons and engineers can guide implant development and optimization, ultimately improving the success rates of spinal fusion surgery and the quality of life for patients with spinal disorders.

## METHODS

#### Search Strategy

This article reviews the impact of implant material and surface technology on osseointegration and interbody fusion in spinal cages, along with describing the role of mechanobiology and mechanotransduction in these processes. Databases used to search for eligible studies included Embase, MEDLINE, Springer, and Cochrane Library. The foremost vital terms were mechanobiology, mechanotransduction, spinal fusion, interbody cages, surface technology, and osseointegration. Search fields chosen for these terms were title, author keywords, and abstract. Boolean operators (OR and AND) combined the keywords and retrieved all relevant articles.

#### Literature Selection

Only systematic reviews, meta-analyses, review articles, and original research articles were included. Articles in languages other than English were excluded. Titles and abstracts of articles that met the inclusion criteria were screened, followed by the retrieval of the relevant articles in full text. The eligibility of full-text articles was assessed, and irrelevant articles that did not have data of interest or could not be retrieved were excluded. Two researchers independently performed the literature search to reduce errors. Figure 1 illustrates a flowchart of the search strategy and study selection process.

#### Basics of Mechanobiology

Force is essential to cell biology as it is crucial in physiological events such as cell division. Researchers have developed micro- and nanosensors to quantify cellular forces and measure the mechanical properties of cells, including the elastic modulus.<sup>17</sup> However, cells and tissues exhibit viscoelastic behavior and can store and dissipate mechanical energy over time, which can be characterized using rheological models such as the standard linear solid model.<sup>18</sup>

The ECM is a 3D structure that provides biochemical and biophysical signals to guide cellular functions. Cells can modify the ECM through synthesis, degradation, and chemical alterations. The characteristics of the ECM, such as stiffness and porosity, play a crucial role in maintaining tissue homeostasis and directing cell fate.<sup>19</sup> The ECM contains complex macromolecules and proteins, creating a unique microenvironment governing cell behavior. Cells can transduce mechanical signals from their surroundings through the adhesive binding sites on ECM components. However, the complexity of the native microenvironment makes it challenging to understand the mechanisms by which cells process these signals fully.

#### Research Techniques in Mechanobiology

Smart hydrogels, 3D culture systems, coculture systems, and microfabrication techniques are



Figure 1. Flowchart of the search strategy and selection process for this article.



Figure 2. Different techniques are available to investigate mechanotransduction pathways, including atomic force microscopy, microneedle manipulation, micropipette aspiration, acoustic tweezers, magnetic tweezers, twisting cytometry, and a uniaxial stretcher (left to right). Adapted from Mohammed et al<sup>3</sup> in accordance with Frontiers Creative Commons license. Copyright 2019 Mohammed, Versaevel, Bruyère, Alaimo, Luciano, Vercruysse, Procès, and Gabriele. Published by Frontiers Media.

promising alternatives to standard plastic dishes for cell culture.<sup>20</sup> Various techniques, including cell stretching, microscopy, bioreactors, genetic manipulation, computational modeling, and tissue engineering, are employed to study mechanobiology. These techniques provide insights into mechanotransduction mechanisms by manipulating cell adhesion patterns and applying well-controlled forces to living cells and tissues to measure signaling pathways.<sup>21</sup> Additional tools include optical and magnetic tweezers, micropipettes, and uniaxial stretchers (Figure 2).<sup>3,22</sup>

Integrins and transmembrane receptors connect adherent cells and the ECM. Mechanical signals are detected by focal adhesion sites, which trigger a biochemical response through the integrin signaling pathway, leading to actomyosin contractility. The mechanism by which mechanical signals are converted to biological responses is still under investigation. However, integrins are essential in mediating outside-in and inside-out signals (Figure 3).<sup>3</sup>

The cell adhesion process starts with actomyosin contractions of the integrin adhesions on the newly attached matrix. This causes them to adjust their size, strength, and dynamics in response to the applied forces and resistance of the matrix. Stiffer matrixes result in more extensive adhesions and more force-dependent signaling. Muscular adhesions activate the additional lamellipodial extension and retraction, leading to the next round of mechanosensing to evaluate matrix rigidity. Repeated patterns of cell edge activity, adhesion formation, and matrix testing determine the final cell morphology when it reaches a steady state.<sup>23</sup> Once the cell has attached, it spreads and flattens out on the surface of the ECM or neighboring cells (Figure 4). This process involves the reorganization of the cell's cytoplasm and the formation of new adhesion sites at the cell's leading edge.<sup>22,23</sup>

#### Challenges in Studying Cell Behavior

Studying cell behavior in vitro presents challenges due to various limitations of the experimental setup. These include the artificial laboratory environment, which may not accurately reflect the in vivo environment, and the lack of cell-to-cell interaction, which can influence signaling pathways and cellular responses. Cells in vitro may lose polarity and shape, particularly when cultured on flat surfaces, affecting their functions and behaviors. Additionally, in vitro experiments are often limited in timescale, making the study of long-term processes such as tissue development challenging.<sup>21</sup> Inadequate nutrients and oxygen in vitro can also affect cellular behavior and limit experimental outcomes. In vitro studies may produce models with limited predictive power due to artifacts from reagents, substrates, or experimental conditions that must accurately reflect the in vivo environment, leading to false or misleading results and complicating the interpretation of empirical findings.<sup>24</sup>

Scott-Young et al.



**Figure 3.** Illustration of force mechanotransduction (green) and cell-matrix signaling (purple) in a 3D fibrous matrix where a cell grows. Eukaryotic cells respond to external forces by modifying their migration, shape, stiffness, spreading, alignment, or adhesion behaviors. The extracellular matrix (ECM) presents several cues to cells, such as confinement, topography, rigidity, and biochemistry. Both types of mechanotransduction are facilitated by focal adhesion, which recruits transmembrane integrins. The nucleus converts mechanical signals (small arrows) into biological responses. Adapted from Mohammed et al<sup>3</sup> in accordance with Frontiers Creative Commons license. Copyright 2019 Mohammed, Versaevel, Bruyère, Alaimo, Luciano, Vercruysse, Procès and Gabriele. Published by Frontiers Media.

# The Relationship Between Mechanobiology and Spinal Fusion

The principles of mechanobiology can help surgeons optimize the mechanical environment to promote bone formation and fusion during spinal fusion surgery. Successful fusion depends on osteoblasts generating new bone tissue at the fusion site, and mechanical loading and stress are critical for successful bone healing and regeneration. An ideal graft material for spinal fusion should meet biological prerequisites, including osteogenic, osteoinductive, and osteoconductive factors and mechanical stability (Figure 5).<sup>25</sup> Understanding the complex bone healing process is crucial for spine surgeons to achieve successful fusion.

## DISCUSSION

Titanium (Ti), polyetheretherketone (PEEK), and tantalum (Ta) devices are commonly used in interbody fusion cages.<sup>29,30</sup> In their unmodified state, these materials have limited bioactivity. To achieve bioactivity,

the constituent materials of an orthopedic implant must elicit a specific biological response at the interface of the material, promoting the formation of a bond between the tissues and the implant. Surface treatments modify the interaction between the implant and the body, creating a bioactive layer that promotes osseointegration. This, in turn, results in a powerful implant-bone interface, providing structural, biochemical, and functional stabilities.

Cages can also be modified by utilizing additive and subtractive manufacturing techniques. Additive manufacturing involves building the spinal fusion cages layer by layer using materials like metal or plastic. This can be done using methods like 3D printing or stereolithography. Additive manufacturing allows for complex and customized shapes and designs that are impossible with traditional subtractive manufacturing techniques. Additionally, additive manufacturing can reduce material waste and lead time compared with subtractive manufacturing. On the other hand, subtractive manufacturing involves cutting, drilling, and shaping raw materials



Figure 4. A diagrammatic representation of the primary cycles underlying cell and tissue shaping. In most instances, activation of the motility process is initiated by intrinsic cell signals involving G proteins, kinases, and actomyosins. These structures alter cell morphology or stimulate neighboring cells to allow testing of the mechanical environment, consequently producing cellular responses that maintain cell morphology. Adapted from Wolfenson et al with permission from Annual Reviews. Copyright 2019 Wolfenson, Sheetz, Yang. Published by Annual Reviews.



Figure 5. The diamond model of bone healing interaction.<sup>25,27</sup>

like metal or plastic to create the desired shape of spinal fusion cages. This can be done using techniques like milling, turning, or grinding. Although subtractive manufacturing may be less precise and customizable than additive manufacturing, it is still widely used in the medical device industry due to its long-established manufacturing processes and familiarity.

#### Polyetheretherketone

PEEK is a high-performance thermoplastic polymer used in spinal fusion implants due to its excellent mechanical properties, biocompatibility, radiolucency, and lightweight properties.<sup>31–35</sup> The bioinert nature of PEEK restricts its osseointegration. It is hydrophobic in nature, which limits its interaction with biological fluids and tissues.<sup>36</sup> This limitation can be overcome through surface modification, structural modification, incorporation of bioactive materials, incorporation of growth factors, and microsurface texturing.

Surface modification techniques, such as plasma treatment, chemical etching, and coating with bioactive materials or metals, can alter the surface properties of PEEK to promote osseointegration.<sup>37</sup> Structural modification techniques, such as porous PEEK, fiber-reinforced PEEK, surface roughening, and interconnected channels, can improve osseointegration by altering the material's internal structure.<sup>38</sup> Incorporating bioactive materials and growth factors, such as hydroxyapatite (HA), calcium phosphate, bioactive glass, and bone morphogenetic proteins, can promote the attachment and growth of bone

cells and stimulate the formation of new bone tissue.<sup>39</sup> Finally, microtexturing techniques, such as laser ablation, microbead blasting, and electrospinning, can create surface features that enhance the attachment and growth of bone cells and promote the formation of new bone tissue.<sup>40</sup> Hydrophilic modifications can improve PEEK's wettability and surface energy, enhancing its interaction with biological fluids and tissues. This can lead to better cell adhesion, proliferation, and differentiation, essential for successful implant integration and long-term stability. Moreover, hydrophilic modifications can promote the formation of a mineralized layer on the surface of PEEK, which improves its osteoconductivity and osseointegration.

#### Titanium

Medical-grade titanium refers to a specific type of alloy composed of at least 99% titanium and small amounts of other elements, such as 6% aluminum and 4% vanadium. The exact composition of the alloy may vary depending on the specific application.

Titanium cages are commonly used for spinal fusion surgery because of their biocompatibility, strength, radiolucency, corrosion resistance, versatility, stability, and long-term durability.<sup>40</sup> However, the structural modification of these cages can enhance their mechanical properties, biocompatibility, or ability to promote bone growth and fusion (Figure 6).

Some common changes include surface roughening, coating, porosity, and geometry modification.<sup>41</sup> Surface



Figure 6. This diagram highlights the role of biologics, bulk modifications, and surface modifications in collectively improving the biocompatibility of metallic implants. Adapted from Bandyopadhyay et al<sup>28</sup> with permission from Elsevier. Copyright 2022 Bandyopadhyay, Mitra, Goodman, Kumar, and Bose. Published by Elsevier Ltd.

roughening involves creating a rough surface texture on the cage to promote bone growth and fusion. Coating the cage with materials like HA or bioactive glass can improve its biocompatibility and encourage bone growth. Porosity modification involves creating a porous surface on the cage to promote bone ingrowth and vascularization, which can enhance fusion. The porosity of titanium cages can be modified through several methods, such as plasma spraying, electrochemical etching, laser ablation, sintering, and 3D printing. Geometry modification involves changing the shape, size, or number of the cage's struts or adding features like spikes or anchors to improve fixation.

These modifications can help promote better bone growth, fusion, and fixation, allowing for customized implants that provide optimal support and stability for the spine. Ultimately, the structural modification of titanium cages can help improve the success of spinal fusion surgery by promoting bone growth and integration with the surrounding tissue.

#### Tantalum

Porous tantalum has been increasingly used in spine surgery due to its excellent biomechanical and biomaterial properties, including high porosity and anticorrosive surface oxide formation.<sup>42</sup> This allows for bony ingrowth and a closer modulus of elasticity to trabecular bone, reducing subsidence and stress shielding.<sup>43</sup> Studies comparing stand-alone porous tantalum cages to autograft and plating for anterior cervical discectomy and fusion (ACDF) have reported similar fusion and adjacent segment degeneration rates but lower maintenance of segmental lordosis with tantalum cages.<sup>43,44</sup> Different studies have found higher fusion rates for tantalum in lumbar spine fusions, but autograft had higher fusion rates in ACDF.<sup>26,43</sup> A retrospective study on single- and two-level cervical corpectomy using porous tantalum cages reported high fusion and low subsidence rates but no significant differences in postoperative cervical lordosis outcomes.45

## **PEEK vs Titanium**

In their meta-analysis, Tan et al<sup>46</sup> evaluated 11 articles, including 1 randomized control trial and 2 prospective studies, comparing PEEK and conventional titanium cages for cervical and lumbar fusion. When comparing surgery for noninfective conditions, titanium cages had a higher subsidence rate than PEEK. Regarding fusion rate, overall, they found no difference at 12 months or final follow-up. However, their lumbar fusion subgroup analysis showed higher fusion rates for titanium cages. In their 6-study meta-analysis, Seaman

et al<sup>47</sup> compared PEEK and titanium cages for ACDF and transforaminal lumbar interbody fusion (TLIF). They reported no differences in fusion rates, albeit with moderate heterogeneity. The subsidence was significantly higher for titanium cages, although their findings had moderate heterogeneity.

## ACDF: PEEK vs Titanium

A systematic review by Noordhoek et al<sup>48</sup> assessed 71 ACDF studies, reporting a mean subsidence incidence of 21%, with lower rates present in PEEK cages than in titanium cages.

Onyedimma et al<sup>49</sup> included 37 studies in their metaanalysis, comparing single- and two-level ACDF using stand-alone PEEK, titanium, and titanium cages. They reported no significant difference in fusion rate between PEEK vs titanium groups.

The meta-analysis by Li et al<sup>50</sup> included 4 studies (2 randomized and 2 nonrandomized) comparing PEEK and titanium cages for ACDF. They reported similar fusion rates and postoperative segmental angles but found that titanium cages had a higher subsidence rate (OR = 3.14 and I2 = 8%).

In their retrospective study of 154 patients undergoing single-level ACDF, Cabraja et al<sup>51</sup> compared PEEK and titanium cages. They reported similar fusion and subsidence rates and commented that subsidence rates were not affected by cage size or disc height.

In their prospective study of PEEK vs titanium cages for ACDF, Igarashi et al<sup>52</sup> found that PEEK cages had significantly less subsidence than titanium cages when the cage height was >5 mm but equivocal subsidence rates for cage heights <5 mm. The impact of cage height on subsidence was also noted by Yamagata et al<sup>53</sup> in their stand-alone titanium ACDF cage assessment. They reported a significantly higher risk of subsidence for cage heights of 6.5 to 7.5 mm than for cage heights of 4.5 to 5.5 mm.

Niu et al<sup>54</sup> prospectively evaluated 53 patients undergoing single- and two-level ACDF with PEEK and titanium cages. Similar levels of lordosis were achieved in both groups. However, the PEEK group had a significantly higher fusion rate and lower subsidence rate.

## Lateral Lumbar Interbody Fusion: PEEK vs Titanium

Amini et al<sup>55</sup> retrospectively analyzed patients receiving stand-alone lateral lumbar interbody fusion (LLIF) using PEEK and 3D-printed titanium cages. Fusion assessment with computed tomography (CT) revealed a higher fusion rate at their early timepoint (8.2 months) in the 3D titanium group, but at their late *t* (18.9 months), there was no significant difference between groups. In a separate publication, the same authors reported that stand-alone lateral interbody fusion with PEEK cages had a significantly higher subsidence rate than titanium (18.5% vs 3.0%).<sup>56</sup>

Campbell et al<sup>57</sup> performed a retrospective analysis of prospective data involving 113 patients under LLIF using PEEK and titanium cages. Following Marchi's criteria, they assessed subsidence on postoperative x-rays.<sup>58</sup> They found that the PEEK group had significantly higher subsidence rates at 2, 3, and 12 months postoperatively. A multivariate analysis identified age as a correlating risk factor for subsidence.

## PLIF/TLIF: PEEK vs Titanium

Khan et al<sup>59</sup> performed a retrospective registry matched-cohort study on 228 TLIF patients receiving PEEK or 3D-printed titanium cages. They reported significantly lower fusion rates and subsidence levels for PEEK cages than 3D-printed titanium (73% vs 90% and 40% vs 23.5%, respectively).

Massaad et al<sup>34</sup> performed a meta-analysis of 11 posterior lumbar interbody fusion (PLIF) studies comparing PEEK and titanium. They reported no difference in subsidence rates but noted a lower fusion rate in the PEEK group. However, a major confounding issue with this study is that their titanium group included both conventional and titanium-coated cages.

In their retrospective cohort of 137 patients undergoing single-level TLIF, Canesco et al<sup>60</sup> compared PEEK and titanium cages. They reported no significant difference between subsidence rate, fusion rate, or lordosis correction between the 2 groups at 12 months.

#### Cage Coating/Surface Modifications

## Direct PEEK Surface Modifications

Surface modifications to PEEK can be made directly without creating additional layers. Methods include wet chemical treatment, plasma, laser, ultraviolet, ozone, and accelerated atom beam surface treatments.<sup>61–65</sup>

#### Titanium Coating

Titanium coating aims to increase the bone-implant contact area, surface roughness, and osseointegration potential of biomaterials such as PEEK.<sup>66,67</sup> The development of titanium-coated PEEK (TiPEEK) cages has continued to increase.<sup>68,69</sup>

Different methods are available to achieve titanium coating on PEEK without damaging the material.

Low-temperature vacuum-plasma spraying can achieve roughened titanium coatings between 6 and 12 microns.<sup>35,70</sup> An alternative technique involves titanium oxide coating through arc-ion plating. An electron beam evaporator can achieve low-temperature deposition of a thin uniform titanium layer.<sup>71</sup>

In certain instances, however, adding surface modifications can lead to the formation of particle debris. Kienle et al<sup>72</sup> demonstrated that shear loading forces imparted during TiPEEK implant impaction could result in partial delamination of titanium coatings. The particles produced ranged in size from 1 to 191  $\mu$ m, with around half of the particles being nonphagocytosed because of the size (>5–10  $\mu$ m), thus raising concerns for causing potential inflammatory and osteolytic reactions. Similarly, Torstrick et al<sup>73</sup> compared TiPEEK with smooth and porous PEEK and found that impaction caused a significant loss of titanium coating.

#### HA Coating

HA  $(Ca_{10}[PO_4]_6[OH]_2)$  is a bioactive ceramic that is present in natural bone minerals. It has a long track record for use in orthopedic and dental implants, including evaluating optimal coating strategies.<sup>74–78</sup>

Compared with titanium-coated implants, some authors have reported better fusion rates and radiological outcomes when using HA-coated implants.<sup>79</sup>

Chin et al<sup>80</sup> retrospectively assessed single-level ACDF patients receiving PEEK vs HA-PEEK cages. They reported a trend toward earlier fusion at 3 to 5 months in the HA-PEEK on x-ray evaluation, although they did not comment on the statistical significance or final fusion rate.

#### PEEK vs Titanium-Coated PEEK

Godlewski et al<sup>81</sup> assessed 104 randomized patients receiving PEEK and TiPEEK for single- and multilevel ACDF. They found an overall subsidence rate of 21%, without significant differences between the groups. However, they reported that subsidence was associated with low implant-to-bone ratios.

In their prospective randomized study, Hasegawa et al<sup>82</sup> compared PEEK and TiPEEK in single-level open TLIF and PLIF. They assessed fusion according to the modified Bridwell classification, using serial CT assessments up to 12 months postoperatively. They reported earlier fusion for TiPEEK at 6 months, although at 12 months there was no significant difference in fusion rates between PEEK and TiPEEK. Subsidence rates between groups were not significantly different.

Schnake et al<sup>83</sup> performed a prospective randomized study comparing PEEK to TiPEEK in single- and two-level PLIF. Fusion was assessed with x-ray and CT at 6 and 12 months, using fusion criteria defined by McAfee<sup>30</sup> and Abbushi et al.<sup>84</sup> They reported no significant difference between groups for fusion rate through or around the PLIF cages.

Similarly, in their cohort of PLIF patients, Sakaura et al<sup>85,86</sup> reported that TiPEEK and PEEK cages demonstrated no difference in fusion rates when assessed using x-ray and CT.

The randomized pilot study by Rickertt et al<sup>87</sup> evaluated PEEK TLIF cages with and without titanium coating for single- and two-level fusions. They reported a fusion rate of 91.7%, with no difference in total or partial fusion rates between the 2 groups.

Singhatanadgige et al<sup>88</sup> compared PEEK with TiPEEK for single- and two-level minimally invasive surgery-TLIF in their prospective randomized study of 82 patients. They reported a significantly higher fusion rate in the TiPEEK group on initial 6-month CT. However, on the 12-month CT, there was no significant difference in fusion rate between groups.

Kashii et al<sup>89</sup> prospectively evaluated PEEK vs TiPEEK in 26 patients undergoing single-level PLIF. Their novel design saw each fusion level PLIF pairing receive 1 PEEK and 1 TiPEEK cage. On postoperative x-rays and CT, they assessed fusion rate, subsidence, and "vertebral cancellous condensation." They reported an 88% fusion rate on CT at 3 months, with persistent angular instability on dynamic x-rays at 12 months. The authors noted that TiPEEK had significantly higher rates of vertebral cancellous condensation than uncoated PEEK, suggesting the presence of bone on-growth.

## Titanium vs Surface-Modified PEEK

In their meta-analysis, Massaad et al<sup>34</sup> reported similar subsidence rates for TiPEEK cages vs titanium for PLIF. Still, they noted that fusion odds for TiPEEK cages were 0.62 times those of titanium cages.

Makino et al<sup>90</sup> studied 59 patients undergoing singleand two-level PLIF using TiPEEK and 3D-printed titanium. Using CT color mapping, they evaluated the amount of bone on-growth, following Walsh's method.<sup>67</sup> The presence of bone on-growth for TiPEEK and 3D-printed titanium increased from 6 (58.0% and 69.0%, respectively) to 12 months (63.5% and 75.0%, respectively). During that time, the grading of bone on-growth progressed in 3D-printed cages at both union and nonunion segments, as opposed to only in the union segments for TiPEEK. The same authors<sup>91</sup> later reported similar fusion and lordosis alignment between groups in a 63-patient cohort, although overall fusion rates at 12 months were notably low (75% TiPEEK and 83.3% 3D-printed titanium). They also noted that the 3D-printed titanium group had a significantly lower subsidence rate and vertebral endplate cyst sign formation.<sup>91</sup>

## CONCLUSION

Mechanobiology is a field that focuses on understanding how mechanical forces impact biological processes at the cellular and molecular levels. In the context of spinal fusion, the design and modification of implants play a crucial role in achieving successful outcomes. The principles of mechanobiology are fundamental in spinal fusion because the mechanical forces and stresses applied to implants can affect the surrounding bone tissue. In contrast, the mechanical properties of the implant itself can influence bone growth and fusion. Therefore, it is essential to optimize the mechanical properties of the implants and modify their surfaces to promote a conducive environment for bone growth and fusion while also ensuring that the implants can withstand patient-generated mechanical forces.

This field focuses on improving patient outcomes by understanding the interactions between mechanical forces and biological processes in spinal fusion. Engineers and surgeons are collaborating to develop implant designs that better mimic the natural mechanical environment of the spine, considering factors such as load distribution, stress transfer, and bone remodeling. By incorporating principles from mechanobiology into implant design, researchers aim to enhance bone healing and fusion rates, reduce complications, and improve the long-term stability and functionality of spinal fusion procedures.

Several trends can be observed in the current research. One trend is the use of advanced materials and fabrication techniques to optimize the mechanical properties of implants. For example, developing bioactive materials and surface modifications that promote bone growth and integration has shown promising results. Additionally, researchers are exploring using biodegradable materials that can gradually transfer the load to the surrounding bone, allowing for better integration and minimizing stress shielding.

Another trend is using computational modeling and simulation techniques to understand better implants' mechanical behavior and their interaction with the surrounding tissues. These models can provide valuable insights into the effects of different implant designs and loading conditions, allowing for virtual testing and optimization before clinical implementation. By combining computational modeling with experimental studies, researchers gain a more comprehensive understanding of the complex biomechanical factors involved in spinal fusion.

Overall, the current body of work in mechanobiology and spinal fusion highlights the importance of considering mechanical forces in implant design and modification. By leveraging principles from mechanobiology, engineers and surgeons are making strides in optimizing implant mechanical properties and surface characteristics to improve patient outcomes. Integrating advanced materials, computational modeling, and interdisciplinary collaborations between engineers and clinicians contribute to the advancements in this field. Nonetheless, it is essential to note that further research is still needed to fully elucidate the complex interactions between mechanical forces and biological processes in spinal fusion and effectively translate these findings into clinical practice.

### REFERENCES

1. Iorio JA, Jakoi AM, Singla A. Biomechanics of degenerative spinal disorders. *Asian Spine J*. 2016;10(2):377–384. doi:10.4184/asj.2016.10.2.377

2. Lim CT, Bershadsky A, Sheetz MP. Mechanobiology. *J R Soc Interface*. 2010;7. doi:10.1098/rsif.2010.0150.focus

3. Mohammed D, Versaevel M, Bruyère C, et al. Innovative tools for mechanobiology: unravelling outside-in and insideout mechanotransduction. *Front Bioeng Biotechnol*. 2019;7:162. doi:10.3389/fbioe.2019.00162

4. Kirkaldy-Willis WH, Farfan HF. Instability of the lumbar spine. *Clin Orthop Relat Res.* 1982;(165):110–123.

5. Manchikanti L, Helm S, Singh V. An algorithmic approach for clinical management of chronic spinal pain. *Pain Phys.* 2009:E225–E264. doi:10.36076/ppj.2009/12/E264

6. Bogduk N, Aprill C, Derby R. Lumbar discogenic pain: stateof-the-art review. *Pain Med.* 2013;14(6):813–836. doi:10.1111/ pme.12082

7. Wu A, March L, Zheng X, et al. Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the global burden of disease study 2017. *Ann Transl Med.* 2020;8(6):299. doi:10.21037/atm.2020.02.175

8. Chen S, Chen M, Wu X, et al. Global, regional and national burden of low back pain 1990–2019: a systematic analysis of the global burden of disease study 2019. *J Orthop Translat*. 2022;32:49–58. doi:10.1016/j.jot.2021.07.005

9. Beighley A, Zhang A, Huang B, et al. Patient-reported outcome measures in spine surgery: a systematic review. *J Cranio-vertebr Junction Spine*. 2022;13(4):378–389. doi:10.4103/jcvjs.jcvjs\_101\_22

10. Ravishankar P, Winkleman R, Rabah N, Steinmetz M, Mroz T. Analysis of patient-reported outcomes measures used in lumbar fusion surgery research for degenerative spondylolisthesis. *Clin Spine Surg.* 2022;35(6):287–294. doi:10.1097/ BSD.000000000001272

11. Patel MR, Jacob KC, Chavez FA, et al. Impact of postoperative length of stay on patient-reported and clinical outcomes after anterior lumbar interbody fusion. *Int J Spine Surg.* 2023;17(2):205–214. doi:10.14444/8414 12. Berven S, Baron M, Deviren V, Glassman S, Bridwell K, Verma K. The assessment of clinically significant differences in treating spinal deformity using the srs questionnaire: what is the threshold of change that is meaningful to patients. *Int J Spine Surg.* 2019;13(2):153–157. doi:10.14444/6020

13. Jansen KA, Donato DM, Balcioglu HE, Schmidt T, Danen EHJ, Koenderink GH. A guide to mechanobiology: where biology and physics meet. *Biochim Biophys Acta*. 2015;1853:3043–3052. doi:10.1016/j.bbamcr.2015.05.007

14. Zhang D, Feng M, Liu W, et al. From mechanobiology to mechanical repair strategies: a bibliometric analysis of biomechanical studies of intervertebral discs. *J Pain Res.* 2022;15:2105–2122. doi:10.2147/JPR.S361938

15. Makino T, Tsukazaki H, Ukon Y, Tateiwa D, Yoshikawa H, Kaito T. The biological enhancement of spinal fusion for degenerative spinal disease. *Int J Mol Sci.* 2018;19(8):2430. doi:10.3390/ ijms19082430

16. Laratta JL, Vivace BJ, López-Peña M, et al. 3d-printed titanium cages without bone graft outperform PEEK cages with autograft in an animal model. *Spine J*. 2022;22(6):1016–1027. doi:10.1016/j.spinee.2021.12.004

17. Shimamoto Y, Forth S, Kapoor TM. Measuring pushing and braking forces generated by ensembles of kinesin-5 crosslinking two microtubules. *Dev Cell*. 2015;34(6):669–681. doi:10.1016/j. devcel.2015.08.017

18. Baker BM, Trappmann B, Wang WY, et al. Cellmediated fibre recruitment drives extracellular matrix mechanosensing in engineered fibrillar microenvironments. *Nat Mater*. 2015;14(12):1262–1268. doi:10.1038/nmat4444

19. Annabi N, Tamayol A, Uquillas JA, et al. 25th anniversary article: rational design and applications of hydrogels in regenerative medicine. *Adv Mater*. 2014;26(1):85–123. doi:10.1002/ adma.201303233

20. Komor AC, Badran AH, Liu DR. CRISPR-based technologies for manipulating eukaryotic genomes. *Cell*. 2017;168(1–2):20–36. doi:10.1016/j.cell.2016.10.044

21. Chen CS. Mechanotransduction - a field pulling together. J Cell Sci. 2008;121(Pt 20):3285–3292. doi:10.1242/jcs.023507

22. Wolfenson H, Yang B, Sheetz MP. Steps in mechanotransduction pathways that control cell morphology. *Annu Rev Physiol*. 2019;81:585–605. doi:10.1146/annurev-physiol-021317-121245

23. Wang L, You X, Zhang L, Zhang C, Zou W. Mechanical regulation of bone remodeling. *Bone Res.* 2022;10(1):16. doi:10.1038/ s41413-022-00190-4

24. Chin IL, Hool L, Choi YS. A review of in vitro platforms for understanding cardiomyocyte mechanobiology. *Front Bioeng Biotechnol*. 2019;7(133):133. doi:10.3389/fbioe.2019.00133

25. Giannoudis PV, Einhorn TA, Marsh D. Fracture healing: the diamond concept. *Injury*. 2007;38:S3–S6. doi:10.1016/s0020-1383(08)70003-2

26. Patel MS, McCormick JR, Ghasem A, Huntley SR, Gjolaj JP. Tantalum: the next biomaterial in spine surgery? *J Spine Surg*. 2020;6(1):72–86. doi:10.21037/jss.2020.01.01

27. Rodriguez-Fontan F. Fracture healing, the diamond concept under the scope: hydroxyapatite and the hexagon. *Medicina (B Aires)*. 2022;82(5):764–769.

28. Bandyopadhyay A, Mitra I, Goodman SB, Kumar M, Bose S. Improving biocompatibility for next generation of metallic implants. *Prog Mater Sci.* 2023;133:101053. doi:10.1016/j. pmatsci.2022.101053 29. Dondani JR, Iyer J, Tran SD. Surface treatments of PEEK for osseointegration to bone. *Biomolecules*. 2023;13(3):464. doi:10.3390/biom13030464

30. McAfee PC. Interbody fusion cages in reconstructive operations on the spine. *J Bone Joint Surg Am.* 1999;81(6):859–880. doi:10.2106/00004623-199906000-00014

31. Reid PC, Morr S, Kaiser MG. State of the union: a review of lumbar fusion indications and techniques for degenerative spine disease. *J Neurosurg Spine*. 2019;31(1):1–14. doi:10.3171/2019.4.S PINE18915

32. Enders JJ, Coughlin D, Mroz TE, Vira S. Surface technologies in spinal fusion. *Neurosurg Clin N Am.* 2020;31(1):57–64. doi:10.1016/j.nec.2019.08.007

33. McGilvray KC, Waldorff EI, Easley J, et al. Evaluation of a polyetheretherketone (PEEK) titanium composite interbody spacer in an ovine lumbar interbody fusion model: biomechanical, microcomputed tomographic, and histologic analyses. *Spine J*. 2017;17(12):1907–1916. doi:10.1016/j.spinee.2017.06.034

34. Massaad E, Fatima N, Kiapour A, Hadzipasic M, Shankar GM, Shin JH. Polyetheretherketone versus titanium cages for posterior lumbar interbody fusion: meta-analysis and review of the literature. *Neurospine*. 2020;17(2):473. doi:10.14245/ns.2040058.029.c2

35. Han C-M, Lee E-J, Kim H-E, et al. The electron beam deposition of titanium on polyetheretherketone (PEEK) and the resulting enhanced biological properties. *Biomaterials*. 2010;31(13):3465–3470. doi:10.1016/j.biomaterials.2009.12.030

36. Briem D, Strametz S, Schröder K, et al. Response of primary fibroblasts and osteoblasts to plasma treated polyetheretherketone (PEEK) surfaces. *J Mater Sci Mater Med.* 2005;16(7):671–677. doi:10.1007/s10856-005-2539-z

37. Yu D, Lei X, Zhu H. Modification of polyetheretherketone (PEEK) physical features to improve osteointegration. *J Zhejiang Univ Sci B*. 2022;23(3):189–203. doi:10.1631/jzus.B2100622

38. Oliveira ÉR, Nie L, Podstawczyk D, et al. Advances in growth factor delivery for bone tissue engineering. *Int J Mol Sci.* 2021;22(2):903. doi:10.3390/ijms22020903

39. Koodaryan R, Hafezeqoran A. Effect of laser-microtexturing on bone and soft tissue attachments to dental implants: a systematic review and meta-analysis. *J Dent Res Dent Clin Dent Prospects*. 2021;15(4):290–296. doi:10.34172/joddd.2021.048

40. Warburton A, Girdler SJ, Mikhail CM, Ahn A, Cho SK. Biomaterials in spinal implants: a review. *Neurospine*. 2020;17(1):101–110. doi:10.14245/ns.1938296.148

41. Bobyn JD, Stackpool GJ, Hacking SA, Tanzer M, Krygier JJ. Characteristics of bone ingrowth and interface mechanics of a new porous tantalum biomaterial. *The Journal of Bone and Joint Surgery British Volume*. 1999;(5):907–914. doi:10.1302/0301-620X.81B5.0810907

42. Bobyn JD, Stackpool GJ, Hacking SA, Tanzer M, Krygier JJ. Characteristics of bone ingrowth and interface mechanics of a new porous tantalum biomaterial. *J Bone Joint Surg Br*. 1999;81(5):907–914. doi:10.1302/0301-620x.81b5.9283

43. Fernández-Fairen M, Alvarado E, Torres A. Eleven-year follow-up of two cohorts of patients comparing stand-alone porous tantalum cage versus autologous bone graft and plating in anterior cervical fusions. *World Neurosurgery*. 2019;122:e156–e167. doi:10.1016/j.wneu.2018.09.160

44. Wells JE, Clohisy JC, O'Keefe RJ. Treatment of intraarticular hip malignancy with extra-articular resection, preservation of the acetabular columns, and total hip arthroplasty. *Arthroplast Today*. 2018;4(4):431–435. doi:10.1016/j.artd.2018.07.007 45. Tome-Bermejo F, Álvarez-Galovich L, Piñera-Parrilla ÁR, et al. Anterior 1-2 level cervical corpectomy and fusion for degenerative cervical disease: a retrospective study with lordotic porous tantalum cages. long-term changes in sagittal alignment and their clinical and radiological implications after cage subsidence. *Int J Spine Surg.* 2022;16(2):222–232. doi:10.14444/8207

46. Tan JH, Cheong CK, Hey HWD. Titanium (TI) cages may be superior to polyetheretherketone (PEEK) cages in lumbar interbody fusion: a systematic review and meta-analysis of clinical and radiological outcomes of spinal interbody fusions using TI versus PEEK cages. *Eur Spine J.* 2021;30(5):1285–1295. doi:10.1007/ s00586-021-06748-w

47. Seaman S, Kerezoudis P, Bydon M, Torner JC, Hitchon PW. Titanium vs. polyetheretherketone (PEEK) Interbody fusion: metaanalysis and review of the literature. *J Clin Neurosci*. 2017;44:23. doi:10.1016/j.jocn.2017.06.062

48. Noordhoek I, Koning MT, Jacobs WCH, Vleggeert-Lankamp CLA. Incidence and clinical relevance of cage subsidence in anterior cervical discectomy and fusion: a systematic review. *Acta Neurochir (Wien)*. 2018;160(4):873–880. doi:10.1007/s00701-018-3490-3

49. Onyedimma C, Jallow O, Yolcu YU, et al. Comparison of outcomes between cage materials used for patients undergoing anterior cervical discectomy and fusion with standalone cages: a systematic review and meta-analysis. *World Neurosurg*. 2022;158:e38–e54. doi:10.1016/j.wneu.2021.10.084

50. Li ZJ, Wang Y, Xu GJ, Tian P. Is PEEK cage better than titanium cage in anterior cervical discectomy and fusion surgery? a meta-analysis. *BMC Musculoskelet Disord*. 2016;17(1):379. doi:10.1186/s12891-016-1234-1

51. Cabraja M, Oezdemir S, Koeppen D, Kroppenstedt S. Anterior cervical discectomy and fusion: comparison of titanium and polyetheretherketone cages. *BMC Musculoskelet Disord*. 2012;13:172. doi:10.1186/1471-2474-13-172

52. Igarashi H, Hoshino M, Omori K, et al. Factors influencing interbody cage subsidence following anterior cervical discectomy and fusion. *Clin Spine Surg.* 2019;32(7):297–302. doi:10.1097/BSD.000000000000843

53. Yamagata T, Takami T, Uda T, et al. Outcomes of contemporary use of rectangular titanium stand-alone cages in anterior cervical discectomy and fusion: cage subsidence and cervical alignment. *J Clin Neurosci*. 2012;19(12):1673–1678. doi:10.1016/j. jocn.2011.11.043

54. Niu CC, Liao JC, Chen WJ, Chen LH. Outcomes of interbody fusion cages used in 1 and two levels anterior cervical discectomy and fusion: titanium cages versus polyetheretherketone (PEEK) cages. *J Spinal Disord Tech.* 2010;23(5):310–316. doi:10.1097/BSD.0b013e3181af3a84

55. Adl Amini D, Moser M, Oezel L, et al. Fusion assessment in standalone lateral lumbar interbody fusion: 3d-printed titanium versus polyetheretherketone (PEEK) cages. *J Spine Surg.* 2022;8(3):323–332. doi:10.21037/jss-22-17

56. Adl Amini D, Okano I, Oezel L, et al. Evaluation of cage subsidence in standalone lateral lumbar interbody fusion: novel 3d-printed titanium versus polyetheretherketone (PEEK) cage. *Eur Spine J.* 2021;30(8):2377–2384. doi:10.1007/s00586-021-06912-2

57. Campbell PG, Cavanaugh DA, Nunley P, et al. PEEK versus titanium cages in lateral lumbar interbody fusion: a comparative analysis of subsidence. *Neurosurg Focus*. 2020;49(3):E10. doi:10.3171/2020.6.FOCUS20367

58. Marchi L, Abdala N, Oliveira L, Amaral R, Coutinho E, Pimenta L. Radiographic and clinical evaluation of cage subsidence after stand-alone lateral interbody fusion. *J Neurosurg Spine*. 2013;19(1):110–118. doi:10.3171/2013.4.SPINE12319

59. Khan I, Parker SL, Bow H, et al. Clinical and costeffectiveness of lumbar interbody fusion using tritanium posterolateral cage (vs. propensity-matched cohort of PEEK cage). *Spine Surg Relat Res.* 2022;6(6):671–680. doi:10.22603/ssrr.2021-0252

60. Canseco JA, Karamian BA, Patel PD, et al. PEEK versus titanium static interbody cages: a comparison of 1-year clinical and radiographic outcomes for 1-level Tlifs. *Clin Spine Surg.* 2021;34(8):E483–E493. doi:10.1097/BSD.000000000001201

61. Noiset O, Henneuse C, Schneider Y-J, Marchand-Brynaert J. Surface reduction of poly (aryl ether ether ketone) film: UV spectrophotometric, 3H radiochemical, and x-ray photoelectron spectroscopic assays of the hydroxyl functions. *Macromolecules*. 1997;30(3):540–548. doi:10.1021/ma960368+

62. Ha SW, Kirch M, Birchler F, et al. Surface activation of polyetheretherketone (PEEK) and formation of calcium phosphate coatings by precipitation. *J Mater Sci Mater Med.* 1997;8(11):683–690. doi:10.1023/a:1018535923173

63. Laurens P, Sadras B, Decobert F, Arefi-Khonsari F, Amouroux J. Laser-induced surface modifications of poly (ether ether ketone): influence of the excimer laser wavelength. *Journal of Adhesion Science and Technology*. 1999;13(9):983–997. doi:10.1163/15 6856199X00460

64. Khoury J, Kirkpatrick SR, Maxwell M, Cherian RE, Kirkpatrick A, Svrluga RC. Neutral atom beam technique enhances bioactivity of PEEK. Nucl Instrum Methods Phys Res. 2013;307:630–634. doi:10.1016/j.nimb.2012.11.087

65. Mathieson I, Bradley RH. Improved adhesion to polymers by UV/ozone surface oxidation. Int J Adhes Adhes. 1996;16(1):29–31. doi:10.1016/0143-7496(96)88482-X

66. Lim KM, Park TH, Lee SJ, Park SJ. Design and biomechanical verification of additive manufactured composite spinal cage composed of porous titanium cover and PEEK body. *Applied Sciences*. 2019;9(20):4258. doi:10.3390/app9204258

67. Walsh WR, Pelletier MH, Christou C, He J, Vizesi F, Boden SD. The in vivo response to a novel TI coating compared with polyetheretherketone: evaluation of the periphery and inner surfaces of an implant. *Spine J.* 2018;18(7):1231–1240. doi:10.1016/j. spinee.2018.02.017

68. Meers CMF, Verleye GBM, Smeets D, et al. Fine grained osseointegrative coating improves biocompatibility of PEEK in heterotopic sheep model. *Int J Spine Surg.* 2015;9:35. doi:10.14444/2035

69. Cheng BC, Koduri S, Wing CA, Woolery N, Cook DJ, Spiro RC. Porous titanium-coated polyetheretherketone implants exhibit an improved bone-implant interface: an in vitro and in vivo biochemical, biomechanical, and histological study. *Med Devices* (*Auckl*). 2018;11:391–402. doi:10.2147/MDER.S180482

70. Devine DM, Hahn J, Richards RG, Gruner H, Wieling R, Pearce SG. Coating of carbon fiber-reinforced polyetheretherketone implants with titanium to improve bone apposition. *J Biomed Mater Res B Appl Biomater*. 2013;101(4):591–598. doi:10.1002/ jbm.b.32861

71. Hoppe S, Albers CE, Elfiky T, et al. First results of a new vacuum plasma sprayed (VPS) titanium-coated carbon/PEEK composite cage for lumbar interbody fusion. *J Funct Biomater*. 2018;9(1):23. doi:10.3390/jfb9010023

72. Kienle A, Graf N, Wilke HJ. Does impaction of titaniumcoated interbody fusion cages into the disc space cause wear debris or delamination. *Spine J.* 2016;16(2):235–242. doi:10.1016/j. spinee.2015.09.038

73. Torstrick FB, Klosterhoff BS, Westerlund LE, et al. Impaction durability of porous polyether-ether-ketone (PEEK) and titanium-coated PEEK interbody fusion devices. *Spine J*. 2018;18(5):857–865. doi:10.1016/j.spinee.2018.01.003

74. Søballe K, Overgaard S, Hansen ES, Brokstedt-Rasmussen H, Lind M, Bünger C. A review of ceramic coatings for implant fixation. *J Long Term Eff Med Implants*. 1999;9(1–2):131–151.

75. Ban S, Maruno S, Arimoto N, Harada A, Hasegawa J. Effect of electrochemically deposited apatite coating on bonding of bone to the HA-G-TI composite and titanium. *J Biomed Mater Res.* 1997;36(1):9–15. doi:10.1002/(sici)1097-4636(199707)36:1<9::aid-jbm2>3.0.co;2-p

76. Allen MJ, Townsend KL, Bauer TW, Gabriel SM, O'Connell M, Clifford A. Evaluation of the safety of a novel knee load-bypassing device in a sheep model. *J Bone Joint Surg Am*. 2012;94(1):77–84. doi:10.2106/JBJS.J.00918

77. Spivak JM, Ricci JL, Blumenthal NC, Alexander H. A new canine model to evaluate the biological response of intramedullary bone to implant materials and surfaces. *J Biomed Mater Res.* 1990;24(9):1121–1149. doi:10.1002/jbm.820240902

78. Zhu C, He M, Mao L, et al. Titanium-interlayer mediated hydroxyapatite coating on polyetheretherketone: a prospective study in patients with single-level cervical degenerative disc disease. *J Transl Med.* 2021;19(1):14. doi:10.1186/s12967-020-02688-z

79. Qin J, Yang D, Maher S, et al. Micro- and nano-structured 3d printed titanium implants with a hydroxyapatite coating for improved osseointegration. *J Mater Chem B*. 2018;6(19):3136–3144. doi:10.1039/c7tb03251j

80. Chin KR, Gohel NN, Aloise DM, Seale JA, Pandey DK, Pencle FJ. Effectiveness of a fully impregnated hydroxyapatite polyetheretherketone cage on fusion in anterior cervical spine surgery. *Cureus*. 2021;13(8):e17457. doi:10.7759/cureus.17457

81. Godlewski B, Bebenek A, Dominiak M, Karpinski G, Cieslik P, Pawelczyk T. Subsidence following cervical discectomy and implant-to-bone ratio. *BMC Musculoskelet Disord*. 2022;23(1):750. doi:10.1186/s12891-022-05698-8

82. Hasegawa T, Ushirozako H, Shigeto E, et al. The titaniumcoated PEEK cage maintains better bone fusion with the endplate than the PEEK cage six months after PLIF surgery: a multicenter, prospective, randomized study. *Spine*. 2020;45(15):E892–E902. doi:10.1097/BRS.000000000003464

83. Schnake KJ, Fleiter N, Hoffmann C, et al. PLIF surgery with titanium-coated PEEK or uncoated PEEK cages: a prospective randomised clinical and radiological study. *Eur Spine J*. 2021;30(1):114–121. doi:10.1007/s00586-020-06642-x

84. Abbushi A, Cabraja M, Thomale UW, Woiciechowsky C, Kroppenstedt SN. The influence of cage positioning and cage type on cage migration and fusion rates in patients with monosegmental posterior lumbar interbody fusion and posterior fixation. *Eur Spine J.* 2009;18(11):1621–1628. doi:10.1007/s00586-009-1036-3

85. Sakaura H, Ikegami D, Fujimori T, Sugiura T, Yamada S, Mukai Y. Surgical outcomes after posterior lumbar interbody fusion using traditional trajectory screw fixation or cortical bone trajectory screw fixation: a comparative study between the polyetheretherketone cage and the same shape titanium-coated polyetheretherketone cage. *Clin Neurol Neurosurg.* 2021;209. doi:10.1016/j. clineuro.2021.106945 86. Sakaura H, Ikegami D, Fujimori T, Sugiura T, Mukai Y. Early fusion status after posterior lumbar interbody fusion with cortical bone trajectory screw fixation or traditional trajectory screw fixation: a comparison between the titanium-coated polyetheretherketone age and the same shape polyetheretherketone cage. *Clin Spine Surg.* 2022;35(1):E47–E52. doi:10.1097/BSD.000000000001237

87. Rickert M, Fleege C, Tarhan T, et al. Transforaminal lumbar interbody fusion using polyetheretherketone oblique cages with and without a titanium coating: a randomised clinical pilot study. *Bone Joint J.* 2017;(10):1366–1372. doi:10.1302/0301-620X.99B10.BJJ-2016-1292.R2

88. Singhatanadgige W, Tangchitcharoen N, Kerr SJ, et al. A comparison of polyetheretherketone and titanium-coated polyetheretherketone in minimally invasive transforaminal lumbar interbody fusion: a randomized clinical trial. *World Neurosurg*. 2022;168:e471–e479. doi:10.1016/j.wneu.2022.10.006

89. Kashii M, Kitaguchi K, Makino T, Kaito T. Comparison in the same intervertebral space between titanium-coated and uncoated PEEK cages in lumbar interbody fusion surgery. *J Orthop Sci.* 2020;25(4):565–570. doi:10.1016/j.jos.2019.07.004

90. Makino T, Takaneka S, Sakai Y, Yoshikawa H, Kaito T. Impact of mechanical stability on the progress of bone ongrowth on the frame surfaces of a titanium-coated PEEK cage and a 3d porous titanium alloy cage: in vivo analysis using CT color mapping. *Eur Spine J*. 2021;30(5):1303–1313. doi:10.1007/s00586-020-06673-4

91. Makino T, Takenaka S, Sakai Y, Yoshikawa H, Kaito T. Comparison of short-term radiographical and clinical outcomes

after posterior lumbar interbody fusion with a 3d porous titanium alloy cage and a titanium-coated PEEK cage. *Global Spine J*. 2022;12(5):931–939. doi:10.1177/2192568220972334

**Funding:** The authors received no financial support for the research, authorship, and/or publication of this article.

**Declarations:** This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors have no conflicts of interest to disclose.

**Corresponding Author:** Matthew Scott-Young, Faculty of Health Science & Medicine, Bond University, 27Garden St, Southport, Gold Coast, QLD 4215, Australia; swalter@goldcoastspine.com.au

#### Published 22 December 2023

This manuscript is generously published free of charge by ISASS, the International Society for the Advancement of Spine Surgery. Copyright © 2023 ISASS. To see more or order reprints or permissions, see http:// ijssurgery.com.