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Nano-Scale Surface Modifications to Advance Current Treatment Options for Cervical Degenerative Disc Disease (CDDD)

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Abstract

Degenerative Disc Disease (DDD) causes a nagging to severe back pain as well as numbing sensation to the extremities leading to loss of overall patients' height and weakness to leg muscles. Degenerative disc disease is often observed in aging patients as well as patients who have suffered from a back injury. Cervical Degenerative Disc Disease (CDDD) is a progressive condition that leads to the degeneration of the intervertebral discs supporting the cervical vertebral column. Anterior Cervical Interbody Fusion (ACIF) has been the longstanding treatment option for severe degenerative disc disease; however, ACIF presents various novel complications, necessitating numerous comparative device studies to reduce the negative effects of spinal fusion. Cervical disc arthroplasty, the recent focus of clinical attention, was one of the alternatives studied to mitigate the complications associated with vertebral fusion but presents its own disadvantages. These complications prompted further investigation and modifications that can be introduced into these devices. We will be discussing the nano-scale interactions between the implant and extracellular matrix play a crucial role in device integration and efficacy, providing an additional approach towards a device's overall success.

Keywords: Degenerative disc diseases; Nano-scale modification; Titanium implants

Abbreviations: ASD: Adjacent Segment Disease; ACIF: Anterior Cervical Interbody Fusion; BMPS: Bone Morphogenic Proteins; CDDD: Cervical Degenerative Disc Disease; CPTI: Commercially Pure Titanium; DDD: Degenerative Disc Disease; HRNS: Helical Rosette Nanotubes; MRI: Magnetic Resonance Imaging; NDI: Neck Disability Index; NSAIDs: Nonsteroidal Anti-Inflammatory Drugs; RNTS: Rosette Nanotubes; TNTS: Titanium Oxide Nanotubes; VAS: Visual Analog Scale.

Background and Introduction

Degenerative disc disease (DDD) mostly occurred in the lumbar, cervical, or thoracic region of the spine. DDD is described as the dehydration of the intervertebral discs, leading to calcification of the cartilaginous nucleus pulposus, as well as the degradation of the nucleus pulposus as patients' age [1]. The human vertebral column consists of the twenty-four vertebrae and twenty-three intervertebral discs protecting the spinal cord from trauma and injuries. The intervertebral disc is acting as shock absorbers, protecting the spinal cord from impact and pressure during physical activities exerted by the hosts. Other than providing height, the intervertebral discs also provide mobility [2]. The intervertebral discs are often likened to a jelly donut due to the gel-like outer ring of the discs, or annulus fibrosus, and nucleus pulposus, the inner portion of the discs. The main components of the nucleus pulposus of the discs are water, collagen, and proteoglycans [3]. DDD is one of the issues faced by the majority of the population after the age of 60 [4]. More than three-quarters of the adult population often suffer from back pain at some point during their lifetime [5]. DDD is often observed in aging patients and patients who have experienced a back injury. The loss of water content in the discs resulting in less shock absorbance, which causes back pain problems, especially as they get older. DDD may lead to a loss of overall patients' height and weakness to leg muscles [6].

Cervical DDD is a progressive condition that leads to the degeneration of the intervertebral discs supporting the cervical vertebral column and results in multiple symptoms that inhibit daily functional movements [7]. Patients often suffer from neck pain, muscle fatigue and weakness, paresthesia, stiffness of limbs, and radicular pain [8]. Some common symptoms of cervical DDD are neck pain caused by stiff muscles or soft tissue sprain, sharp nerve pain, or tingling of the extremities, such as arms or fingers [7]. Although there is no direct link between CDDD and neck

pain, it is thought that the degeneration of the discs may weaken the vertebrae, resulting in a slipped disc that applies pressure along the cord or the nerve root [7]. Aging is one of the many factors contributing to the degeneration of intervertebral discs. Other factors, including genetics and lifestyle, also influence the condition of intervertebral discs [9]. Regardless of other comorbid facts, as one ages, years of repetitive stress inevitably cause wear and tear to any regions of the spine, contributing to pain and loss of mobility to the patients. Cervical DDD can be diagnosed using different diagnostic tools such as magnetic resonance imaging (MRI) to provide a better diagnosis to the doctors and treatment plans to the patients. An MRI scan is able to reveal cervical DDD at its early stages and access the integrity of the intervertebral discs accurately [10].

Current Treatments and Limitations

There are many alternative treatment options for cervical DDD to surgery, such as the ACIF and arthroplasty, although surgery may still be required if these treatments fail. At its early stage, patients are generally advised to modify their lifestyle, such as incorporating exercises in their daily routine or be more aware of their overall posture as to not put unnecessary pressure on the spine [7]. A healthy, well-balanced diet, as well as hydration, is encouraged to all patients of all ages. Doctors can prescribe conservative treatments such as medication (NSAIDs and muscle relaxants) or steroid injection to patients who injured their neck or those who have been experiencing neck pain [5]. Some patients find relief from going to chiropractors or choosing from different options such as the electrical stimulation TENS unit, acupuncture, or massage therapy for pain management.

However, these pain management therapies and medications only relieve pain and do not cure cervical DDD. When the pain becomes too severe, and cannot be relieved by initial treatments and for those who have neurological deficits, different surgeries are often suggested as a method to alleviate the pain. The options will be provided based on the observation of the surgeons and are up to the discretion of the surgeon [5]. In the event that conservative treatment options are not sufficient, the surgical approach has shown dramatic success rates in improving all measured clinical outcomes [11]. These outcomes include the Neck Disability Index (NDI), Visual Analog Scale (VAS) for arm pain, and a short-form health survey SF-36 [12]. The success rate of surgical intervention is judged partly based on the statistically significant improvement in these scores from post-op, to multi-year follow-up evaluations. The two types of surgeries that will be discussed in this review in the following sections are the ACIF and arthroplasty.

Anterior Cervical Interbody Fusion (ACIF)

Conservative treatment options often fail due to the severity and progression of degradation within the disc. When these conventional methods fall short, surgical options such as ACIF and cervical arthroplasty are used due to their high success rates, based on clinical standards [13,14]. During the ACIF procedure, the patient undergoes anterior disc discectomy on the degenerated region. A cervical fusion spacer is then placed within the area between the two adjacent vertebrae where the disc has been removed. These spacers may act as autologous bone grafts or cadaveric allograft bone to encourage osteogenic growth between the two adjacent vertebrae. Once fusion is complete, the spacer will have achieved full osseointegration, and the two adjacent vertebrae are connected in a union [15]. ACIF may occur anywhere from a single level to triple-level fusion in reference to the number of discs being replaced with integrated spacers.

Anterior Cervical Interbody Fusion (ACIF) has long been considered the standard and is a highly effective treatment option for cervical DDD. Numerous clinical trials have demonstrated the efficacy of fusion as a treatment option, improving all clinical outcomes consistently over long-term patient surveillance [16,17]. In recent years, fusion as the standard practice has been questioned due to evidence suggesting that the procedure is biomechanically unsustainable and damaging towards adjacent segments of the spine. In short term clinical trials, pain reduction, and fusion are present in nearly all patients; however, long-term trials indicate progressive degradation of discs adjacent to the fusion site [18]. This degradation, termed adjacent segment disease, presents an adverse event tied directly into the biomechanically restricting nature of the procedure itself. Although fusion has been deemed successful by clinical standards, reduction of adverse event rates such as adjacent segment disease must be held at a high priority. This is especially true considering the variety of alternative treatment options in development on the market [19].

Arthroplasty

Another alternative surgical option for the treatment of cervical DDD is cervical arthroplasty. Arthroplasty is similar to fusion but differs in the device used for the insertion into the space between the vertebrae. Instead of fusing the vertebrae in one bony union, cervical arthroplasty replaces the degenerated disc with a synthetic polymer disc. This synthetic disc is most commonly capped with metal plates on each side to provide a site for osseointegration with the adjacent vertebral bodies [20]. Once fused with the bone, the synthetic disc acts as a healthy normal functioning intervertebral disc, restoring range of motion, and allowing degrees of freedom that standard ACIF would inhibit. Apart from segmental mobility, cervical arthroplasty also shows a relatively lower occurrence of adjacent segment disease, suggesting that this procedure is a better long-term solution to degenerative disc disease, especially in relation to the health of adjacent vertebrae and discs. Numerous devices for total disc arthroplasty and cervical fusion have been subjected to long-term clinical studies that confirm the efficacy and success of these treatment methods.

The success of both surgical procedures is based on the decompression of the spinal cord or nerve root being constructed by the myelopathy of the degenerating disc. Relief of signal interference by disc discectomy and replacement or vertebral fusion allows for restoration of essential function and reduction of all pain index scores. The degree of improvement of clinical outcomes is contingent upon the procedure that was chosen to treat cervical DDD. The surgical methods and long-term results of

cervical arthroplasty have been subject to a variety of comparative studies with cervical discectomy and fusion [21,22]. The benefits of arthroplasty, in contrast to fusion, depending on the return of a mechanically functional and realistic joint provided by the synthetic polymer disc. Cervical arthroplasty attempts to restore the natural range of motion and degrees of freedom to the joint space that would otherwise be fused and reduced to a single mass of bone [19]. This treatment method of DDD appeals massively towards the younger working force population that would be significantly inhibited by reducing the range of motion on a day-to-day basis. A return to the normal biomechanical function of the C3-C7 region of the spine is especially pertinent due to the highly mobile nature of the upper cervical region. In addition to this superiority in mechanical function, arthroplasty has been shown to reduce radicular/neck pain and restore natural muscle functions as effectively as fusing two vertebrae over the disc space [11].

Cervical arthroplasty has also been the center of recent debate surrounding the origin and factors related to the progression of Adjacent Segment Disease (ASD). In numerous studies investigating the long-term efficacy of fusion, there have been statistically significant findings regarding the rate of returning patients displaying symptoms of myelopathy in discs adjacent to the fused vertebrae [18,23,24]. ASD is caused when the biomechanical load of adjacent secondary discs shifts dramatically due to the fusion of vertebrae. This fusion causes stress to the surrounding discs that are greater than their normal load-bearing capabilities [25]. The reduction of mobility and an increase in stress on the adjacent segments of the spine have been the primary motivating factors that have shifted focus from fusion to arthroplasty and its treatment capabilities. Long term complications associated with cervical arthroplasty, however, have damaged the promise of overall superiority claimed by total disc replacement [26,27]. Short-term studies demonstrate the clear benefits of biomechanical restoration and propose a promising solution to the reduction of adjacent segment disease. However, long-term studies raise concerns regarding adverse events that are unique to arthroplasty, urging caution in the transition between ACIF and cervical arthroplasty. Heterotrophic ossification, infection, disc migration, and dysphagia are all adverse effects that have been noted in long term clinical studies using cervical arthroplasty devices [28]. The biomimetic nature of cervical disc replacement warrants further investigation into the improvements that can be made towards the devices and procedures that may mitigate many of these different adverse events. In order to establish a new gold standard method of cervical DDD treatment that restores biomechanical functions of the spine while significantly reducing the risk of short- and long-term adverse effects, further enhancements must be made to the current technologies available on today's clinical market.

Nanoscale Surface Modifications

Nano-surface modification for implants

Titanium (Ti) was discovered in the late 18th century and has been used widely as paint additives to obtain the color white. At the beginning of the 19th century, commercially pure titanium (cpTi) and Ti alloys have been widely used clinically as implants in the biomedical field, starting mainly in bone fusion and joint replacement surgery [29]. Ti has been proven to provide excellent corrosion resistance and has high biocompatibility with the human bones [30]. Ti has been proven to improve the osseointegration, and the stability of implants in the hosts [31-43] Their excellent mechanical properties and chemical properties are the main reason why they were chosen to play a critical role as artificial implants materials in orthopedic surgery [29]. Unfortunately, even with excellent chemical and physical properties of Ti as implants, surgeons and patients have been plagued by the underperformance of implants, causing the failure of the implants. Surgeons and researchers around the world have been trying to eliminate and decrease the incidence of bone-implant failures for decades. The reasons for failures could be associated with the lack of osseointegration [44] a significant difference in mechanical properties between the implant and the surrounding bones [44], general wear and tear around the surface of the bone and implant as well as bacterial contamination of the implants [45].

A study in 2004 found that bone tissues and bone-forming cells are accustomed to nanometer roughness, but the conventional synthetic metals implants only showed roughness in the micrometer scale and smoothness in the nanometer scale [46]. This means that the bone tissues and cells are not able to adhere to the implant properly when there is no rough surface in the nanoscale of the material, resulting in callus formation, which then encapsulates implants in bone with stratified scar tissues [44]. This led to various studies to prove that the roughness of nano-scale materials is essential to enhance osteoblast adhesion, decease fibroblast formation, and decrease endothelial cells lining that line the vasculature of the body [47]. Nano-scale materials, such as alumina nanofiber, carbon nanotubes, rosette nanotubes, or spherical particles of titania, were used in the studies [44] and were shown to be successful.

Since surface topography plays a vital role in osseointegration of the implants, many have tried different metals, metal alloys, plastics, and bone grafts to obtain the most successful implants that provide long term stability and least likely to acquire bacterial invasion. Titanium Oxide Nanotubes (TNTs) have been one of the most useful implant applications because it is easy to fabricate, and the size of the nanotube can be controlled precisely during assembly [48]. TNT has been shown to modulate the functions of osteoblast cells [49-53], Mesenchymal Stem Cells (MSC) [54-57], and endothelial cells [58,59]. Not only the nanotubes have a lower elastic modulus of 36-43 GPa, like natural bones, compared to conventional Ti implants, it also has better biomechanical properties as well [60]. While the biological performance of the TNT as implants was not well understood, it was found that nano-scale materials, regardless of size, would increase osteoblast functions. One study did find that cell activity, and cell functions work best when the size of the nanotubes is less than 15 nm [61]. Apart from TNTs, Rosette Nanotubes (RNTs) also have the potential to be used for implant applications in the future. Because these nanotubes are derived from DNA base pairs, the use of these

nanotubes is favorable compared to many implants that utilize inorganic materials. RNTs are known to be novel, biomimetic and biocompatible, and can self-assemble under physiological conditions.

Additional attention should be directed towards the novel advancements being made with respect to nanocomposites and scaffolds. Drug loaded nanoparticles, such as the RNTs, have serious utilization potential to enhance osteoblast adhesion, integration, and show promise to decrease the long-term failure rate of titanium implants. Nano-coatings have similar enhanced aspect ratio benefits compared to nano-etching and provide the additional option to load high concentrations of bone promoting factors integrated into these nanostructures. Many studies over the past two decades have been focusing on the promises of what and how RNTs could bring to the medical community [62,63]. Nanomaterial coatings, such as the helical rosette nanotubes (HRN), are highly sought after for their biocompatible, biomimetic, and biodegradable properties. Other than physical modifications on the TNTs and RNTs where the size of the implant materials was incorporated, chemical modification of titanium was also considered. Some studies showed that chemically modified titanium with the incorporation of ions, such as zinc (Zn), calcium (Ca), Chlorine (Cl), and Iodine (I), reduces biofilm formations from *E. coli* [60]. Although the mechanism of action of how anodic oxidation influences bacterial adhesion on the surfaces of the implant [64-66], an *in vitro* study has shown that bacterial counts ion-implanted surface decreased by 55-80% compared to cpTi [67]. On the other hand, the RNTs can be chemically functionalized with peptides to enhance cellular adhesion, migration, and differentiation after delivery. These nanotubes are formed from molecules derived from DNA base pairs self-assemble via hydrogen bond and stacked on each other via a robust pi-stacking interaction and can be measured up to 200-300 microns in length. The diameter of the nanotubes is approximately up to 3.5 nm, while the inner hydrophobic core of the nanotube can be about 1.1 nm in diameter.

Implant associated infections are one of the most severe complications in this industry and difficult to treat due to the need for additional surgeries leading to higher healthcare costs than expected. With the current global infection risk at 2-5% in orthopedic surgery [68], which is still high, this issue presents a significant burden to all the researchers, surgeons as well as patients [29]. Hospital-acquired infection, such as Staphylococcus *aureus (S. aureus*), is responsible for the infection that occurred during surgery from both skin and mucous membranes [69]. A series of disinfection and stringent aseptic surgical protocol, such as autoclave and ethanol immersion, is applied to decrease the bacterial contamination, but the bacteria could readily invade after surgery and cause infection on the nearby tissues. Typically, the adhered bacteria that caused the infection form biofilm on the implant, which makes it highly resistant to host defense and antimicrobial therapy [70,71]. In addition to that, surgical trauma can compromise the host defense. Thus, the implant insertion would increase the chance of bacterial invasion into the host. Many antiseptic surgical methods and protocols are applied because the removal of biofilm has been proven to be challenging. Researchers and manufacturers are aiming to optimize implants to minimize and eliminate the biofilm formation once and for all.

As mentioned previously, implants with TNTs materials are useful in combating the invasion of bacteria as well as increasing the rate of osseointegration of the bone cells with the implants. Due to its cylindrical nature, the nanotubes can act as drug carriers such as the growth factor as well as act as antibacterial agents like silver, Ag [72]. In addition to that, the nano-scale roughness of implants has been proven to be desirable for the bone cells to adhere quicker than conventional metal implants. Similarly, RNTs also show promising materials as nano-surface modifications for implants. Therefore, it is expected that both TNTs and rosette nanotubes can be used as materials for implants as joint replacement (arthroplasty).

Nano-surface modifications on Arthroplasty implants

Long term complications associated with cervical arthroplasty have damaged the promise of overall superiority claimed by total disc replacement [26,27]. Short-term studies demonstrate the clear benefits of biomechanical restoration and propose a promising solution to the reduction of adjacent segment disease. Overall, arthroplasty has shown statistically significant improvements in NDI and VAS scores over fusion, as well as a greater overall range of motion at the site of disc replacement [73]. C2-C7 range of motion improved in comparison to fusion groups while also showing lower rates of degradation in adjacent segments. Pain relief and functional recovery were superior in most patients undergoing arthroplasty in comparison to fusion. However, long-term studies have raised concerns regarding adverse events that are unique to arthroplasty, urging caution in the transition between ACIF and cervical arthroplasty.

Heterotrophic ossification, infection, disc migration, and dysphagia are all adverse effects that have been noted in long term clinical studies using cervical arthroplasty devices [28]. The biomimetic nature of cervical disc replacement warrants further investigation into the improvements that can be made towards the devices and procedures that may mitigate many of these different adverse events. In order to establish a new gold standard method of cervical DDD treatment that restores biomechanical functions of the spine while significantly reducing the risk of short- and long-term adverse effects, further enhancements must be made to the current technologies available on today's clinical market. The reduction of these adverse events can begin by focusing on the enhancement of the site of osseointegration. Decreasing the time necessary for vertebral attachment and osseointegration can, in turn, reduce the risk of disc migration and heterotrophic ossification. Disc migration often occurs due to instability in the joint space where implantation occurs, which in many cases, results in the significant anterior shift of the device [74]. This instability is primarily caused by the absence of an efficient and effective adherence design on the endplates of arthroplasty devices. Enhancements of the attachment site, such as TNTs formation, increases the rate of integration between bone and implant can then create a more

controlled environment for intended growth and attachment. An overall reduction in integration and recovery time may also result in the reduced risk of intervertebral disc shift.

Helical Rosette Nanotubes (HRNs), developed in the early 2000s, contain a lysine sidechain that have been shown to improve osteoblast adhesion when coated onto titanium samples suggesting an integral role in the increased protein activity between implant and external environment [75]. HRNs have also been shown to increase osteoblastic activity embedded within hydrogels simply by leaving a functionalized lysine group exposed and has also presented a decreased pHEMA polymerization time within injected hydrogels [76]. Additionally, hydroxyapatite (HA) loaded HRN has demonstrated similar results, including evidence suggesting nanoscale HA loaded onto these HRNs provide the best results regarding increased osteoblast adhesion and cytocompatibility [77]. The promise shown by drug-loaded HRNs encourages the conduction of further studies regarding the ideal titanium implant coating in relation to the implant location. Arthroplasty devices coated with drug-loaded nanoparticles may benefit from increased osteoblastic adhesion and anti-bacterial properties with the properly loaded nanoparticle such as JBNTs.

Implementing the concept of nano-surface modifications using an adequately studied method such as TNTs onto devices such as the Bryan Cervical Disc, ProDisc-C, or Prestige LP could help advance current fixation enhancement efforts in the clinical setting [78]. These three devices have shown varying degrees of promise through multiple variations in design; however, to our knowledge, no products on the market have utilized the antimicrobial and enhanced osseointegration benefits of TNTs or JBNTs. Many studies have demonstrated the superiority of these devices compared to traditional fusion practices, further noting the need for correctional measures to reduce the novel risks associated with disc replacement [79]. Enhancement in biomechanical restoration time and integrity may also assist in the reduction of adjacent segment disease incidents. Once these mechanical practicalities are established, cervical arthroplasty will be the most effective DDD treatment method to lower chronic pain and reduce adverse event risk post-surgery. Considering that there are no commercially available cervical arthroplasty products on the market that utilizes the benefits of the TNTs or JBNTs provide to other implants, it is logical to establish that the next step forward for this device is to introduce the application of TNTs or JBNTs to cervical arthroplasty implants. One of the conventional ways to avoid bacterial infection on implants is by coating the implant with antiseptics or antibiotics, such a Gentamicin, which is a commonly used antibiotic due to its broad antibacterial spectrum. Another way to avoid bacterial infection is to apply antibacterial drugs either locally or systemically by the surgeons after the surgery [80].

The TNTs, on the other hand, will be able to deliver drugs straight into the bone during the surgery and boost osseointegration instantly due to its nano-scale nature. A similar procedure of coating the implants with antibacterial agents can be done, but it is mainly as precaution step rather than prevention. It is also possible to incorporate growth factors such as bone morphogenetic proteins (BMPs) to promote bone growth into the nanotubes. When applied locally, different growth factors can influence bone cells' adhesion, proliferation, and differentiation. If BMPs can be incorporated into TNTs during the fabrication of TNT, it can enhance and improve the osseointegration of bones onto implants, which could decrease the time for vertebral attachment and decrease the chance of disc migration [81]. Similarly, JBNTs can be modified for the same purpose. Encapsulation of drugs or growth factors, such as BMP-7, with JBNTs, could stabilize proteins and enhance the bioavailability of a drug as well as improving osteoblast proliferation and functions [82].

TNTs or JBNTs could also be developed as a dual drug delivery carrier where antimicrobial and anti-inflammatory agents are incorporated into the channels of TNTs. The incorporation of the anti-inflammatory drug could prolong the longevity of the implants by abating the hosts' immune systems during and after the insertion of the implant. In addition to that, an antimicrobial such as silver (Ag), have been shown to release Ag+ ions that interfere with bacterial cell walls, and ultimately reducing bacterial adhesion, and viability [29] can also be incorporated into TNTs for further prevention of bacterial invasion. These drugs can be delivered instantaneously into the surgery site as soon as the implant came in contact with the cervical vertebral. While there are many successful studies *in vitro* for the TNTs in the past, there are not many studies that prove TNTs work as a drug carrier *in vivo*. Studies such as the protocols for drug formulation standardization, their ultimate dosage, the most suitable size of TNTs for the best drug, and the drug release activation needed to be investigated [75]. Furthermore, there have not been studies to show that TNTs or JBNTs would work as materials for cervical arthroplasty. However, TNTs and JBNTs as drug carriers are still encouraged in the field, with the hope of improving osseointegration time, minimizing bacterial contamination during and after surgery as well as increase the durability of the implant. Additional research and analysis are definitely encouraged to understand the application of TNTs as cervical arthroplasty implants.

Other than the incorporation of drugs into TNTs, many studies have also investigated their controlled local release into their surroundings after the surgery. It was understood that even though TNTs is one of the most promising local drug-delivery systems, a different drug release activation has been considered based on different surgery site [83,84]. Hence, it is still unknown if an internal (*in vivo*) or external activation system for drug release is needed for the application of cervical arthroplasty implant. The understanding of drug release for TNTs as cervical arthroplasty implants will provide new insights for prospective research. JBNTs show increased applicability to arthroplasty device nano-coatings due to their previously established slow drug release properties. JBNTs have been shown to successfully encapsulate and slowly release dexamethasone, a popular anti-cancer drug, within the *in vitro* setting [85]. Once translated to the *in vivo* setting, JBNTs would be an ideal candidate for arthroplasty device nano-coatings due to their previously established low cytotoxicity profile and slow-release properties. JBNTs loaded with osseointegration promoting factors and anti-bacterial agents could be incorporated

into the surface of cervical arthroplasty devices, causing increased integration and lower infection rates during the extended period of healing and ossification. Once the loaded drug has been released, natural biodegradation of the JBNTs will occur, leaving no toxicity profile to ensure the unaffected health of local tissue.

Although both ACIF and arthroplasty have advantages and disadvantages, both doctors and patients need to understand which option benefits them the most. Hopefully, TNTs and JBNTs can be integrated as the materials for the development of cervical arthroplasty implants in the near future.

Conclusion

Nano-surface modifications on titanium arthroplasty implants provide an opportunity to advance degenerative disc disease treatment. Drug loaded modifications (such as TNTs and JBNTs) can be easily be fabricated on the contact surface of implants, enhancing osseointegration, decreasing recovery time, and providing antimicrobial and anti-inflammatory agents directly to the site of activity. These enhancements provide solutions to the different adverse events associated with cervical arthroplasty, establishing superior performance outcomes over other DDD treatment options, such as anterior cervical interbody fusion. A nano-scale modification coated cervical arthroplasty device would establish a biomechanically functional and stable synthetic joint with significant relief of radicular pain, neck pain, muscle weakness, and fatigue caused by cervical disc degeneration.

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