SHORT REVIEW

Advances of Wear Reduction of Artificial Joints: Regenerative Cartilage Artificial Joints

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Abstract

The lifespan is a major concern for artificial joints when more younger patients are taking the total joint replacement operations. Wear is recognized as the main reason for the premature failure of implanted joints. So, lowering the wear is one of the most effective way to extend the lifespan, which has attracted much efforts in both academia and industry. This paper reviews some representative research progresses on reducing the wear of artificial joints. Development of new bio-materials is a main approach but

Introduction

Total joint replacement (TJR) is regarded as one of the most successful surgery operations in bio-medical area. American Academy of Orthopaedic Surgeons (AAOS) declares that more than 7 million Americans are living with an artificial knee (4.7 million) or hip (2.5 million) [1]. More importantly, it is generally recognised that an increasing number of people would take the joint replacement operations due to an ageing population and the demand for a contributes less in recent year. The research on surface roughness hasn't given a definite solution in directing the industrial practice. The surface texturing functions well in improving the friction and wear of artificial joints, but the working mechanism is still ambiguous. Cushion or buffering layer is a promising solution to introduce elastic contact between the bearing surfaces, but cannot totally avoid debonding or shear stresses currently. Latest progress on regeneration of articular cartilage makes it possible to form hyaline cartilage *in vitro* onto bio-implant surfaces to reproduce the original properties of healthy joints which is definitely the most promising way.

Key Words: Artificial joint; Bio-implants; Cartilage regeneration; Tribology; Wear

more active lifestyle [2,3].

Despite of the huge success in biomedical industry, it was widely reported that the orthopaedic implants generally only last 15-20 years after being implanted into the body [4,5]. This short *in-vivo* longevity means that a lot of patients need revision operations after a certain time of *in-vivo* service. For example, it was reported that approximately 10% of the patients underwent revisions within a 15-year lifespan [6,7]. Furthermore, due to the high cost

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of revision operation and the physical damages to patients, revision operation will lead to both economic and social burden to the entire society [8,9]. As a result, numerous efforts have been done to find a proper method to increase the longevity of artificial joints.

Wear is recognized as the main reason for joint implants failure, causing inflammatory reactions and osteolysis, which can lead to implant loosening [10,11]. So, it is widely acknowledged that lowering the wear is one of the most effective way to extend the lifespan of implanted joints, which has attracted much efforts both in academia and industry. However, for decades, most research are mainly focusing on the development of new applicable biomaterials for bearing combinations such as metal-on-metal (MoM), metal-on-polymer (MoP), ceramic-onceramic (CoC) and ceramic-on-polymer (CoP) [3,12-16]. Due to the more and more limited contribution along this pathway, in recent years focus has been converted to explore new possibilities to control the tribology and wear of the joint counterparts, such as micro-patterned surfaces to provide additional lubrication. However, all these attempts are still adopting the rigid prostheses and ignore an important fact that, in healthy joints, articular cartilage forms a natural elastic buffer layer which functions well in lowering the contact stresses and providing lubrication. The original working mechanism of human joints should does inspire us that this is a more promising way. But unfortunately, most endeavour are still proceeding along the conventional engineering route.

This mini review briefly highlights some representative works on developing the new types of artificial joints, especially on the micropatterned and elastic buffering artificial joints, and proposes a new possibility on developing the regenerative cartilage artificial joints, as (Figure 1) shows.



Figure 1) Illustration of main approaches to reduce the wear of artificial joints.

Development of materials

Since the advent of modern artificial hip joints in the 1960s, many efforts have been devoted on finding new biomaterials to improve the performance of bioimplants. New biomaterials are pursuing the reliable biocompatibility, high wear resistance, high corrosion resistance and some other improved mechanical properties related to achieve the desired lifespan [13]. Basically, metals, polymers and ceramics are three major categories in fabricating the artificial joints, and nearly all the commercial products are simply the combinations of these selected materials by forming solid and rigid parts. Metal-on-polymer (MoP), metal-onmetal (MoM), ceramic-on-ceramic (CoC) and ceramic-on-polymer (CoP) are the four main types adopted in practice to form the bearings, as shown in (Table 1). The metal-on-polymer is the standard material combination for current joint products due to the good long-term invivo performance and low fabricating cost. Three categories of metals are mainly used: cobalt-chromium-molybdenum (CoCrMo), titanium alloys (Ti4Al4V) and stainless steel (316L SS). As for the metal counterpart, the ultra-high-molecular-weight-polyethylene (UHMWPE) is the most conventional polymer used in fabricating bioimplants. In recent years, radiation-treated UHMWPE (XLPE) has also been used due to the increased wear performance. However, it was reported that the metal bearing surfaces was prone to being scratched (abrasion) by hard particles, which will lead to a higher risk in long-term service

TABLE 1 Advantages and wear features of typical materials combinations [11-29]

Bearing	Advantages	Wear Volume*	Wear Mechanism
МоР	 Good long-term results in elderly patients Standards for wear testing of other bearing articulations New applicable materials 	 CoCr-XLPE: 6.71 ± 1.03 mm³ Mc⁻¹[14] Ti6Al4V-UHMWPE: 38.8 mm³ Mc⁻¹[15] Stainless Steel-UHMWPE: 32.3 mm³ Mc⁻¹[15] 	AdhesionWeldingAbrasion
MoM	 Reduction in wear Improvement of range of movement Lower dislocation rate Good clinical results in small head MoM 	 CoCr-CoCr: 0.977-0.11913 mm³ Mc⁻¹[16] Ti6Al4V-steel: 0.35 mm³ Mc⁻¹[17] CoCrMo disk-Ti6Al4V pin: lubricated disk: 6.9 10⁻⁵ mm³/Nm, Ball:3.410⁻⁶ mm³/Nm [18] Ti6Al4V disk-Ti6Al4V pin: lubricated disk: 6.1 10⁻⁴ mm³/Nm, Ball: 2.010⁻⁵ mm³/Nm [18] Ti6Al4V disk-CoCrMo pin: lubricated disk: 6.5 10⁻⁴ mm³/Nm, Ball: 5.010⁻⁶ mm³/Nm [18] 	 Surface fatigue Tribochemical reactions
CoC	 Lower wear rate Lower osteolysis Higher survivor rate in long-term results Harmless wear particle to human body 	 Biolox®Delta -Biolox® Delta: 0.1 mm³ Mc⁻¹[19] HIPed Al₂O₃-HIPed Al₂O₃: 0.075 mm³ Mc⁻¹[20] ATZ-ATZ: 0.024-0.06 mm³ Mc⁻¹[21,22] ZrO₂-ZrO₂: 0.013 mm³ Mc⁻¹[16] ZrO₂-Al₂O₃: 0.014 mm³ Mc⁻¹[16] 	Surface fatigueAbrasive scratch
СоР	 Combine the advantages of both ceramics and polyethylenes Lower wear rate 	 Alumina-PE: 34 mm³ Mc⁻¹[23] ZTA-PE: 80 mm³ Mc⁻¹[24] Alumina-XLPE: 3.35 ± 0.29 mm³ Mc⁻¹[25] 	Surface fatigueTribochemical reactions

*These data are cited from some selected publications, which may vary much with respect of experimental conditions.

[12]. In this case, bio-ceramic is used to replace the metal bearing parts to improve the antiabrasion property. Due to the requirements of biocompatibility and mechanical properties, two main ceramics are used in the field of orthopedic implants: alumina (Al₂O₃) and zirconia (ZrO₂). As reported previously, the main failure mechanism of implanted joints is the bioactive reactions between polymer wear debris and surrounding tissues [11-14]. Hence, the idea of polymer-free bioimplants was introduced, MoM and CoC. As for MoM, although the wear performance is greatly increased, the potential chronic disease caused by the tribochemical reactions still hinders its application in largescale. The best tribological performance among the four-material combination is CoC, but the squeaking noise produced during the daily activity is unacceptable for most patients. Hence, the polymer-based bioimplants is still the number one choice in the orthopedic

industry, which includes MoP and CoP.

Although the evolving on materials benefits much on joint lifespan, saying around 90 percent of modern joint implants still function well until 10-15 years and some even last for 20-25 years (30,31), from the table above, it is clear that wear is always existing as a major concern behind the failure regardless of the materials.

Improvement of surface topography

Instead of using novel biomaterials to fabricate bioimplants for the purpose of increasing *in-vivo* longevity, another proposing way is to modify the surface topography without changing the properties of bulk materials. To be more specific, surface topography directly determines the contact and lubrication conditions of the artificial joints bearing areas. Two main pathways on investigating the surface modification involve surface roughness and surface micro-patterning.

Surface roughness

Surface roughness is an important topography parameter describing what forms on a bearing surface[32-35]. To be more specific, it can be used to characterize how asperities and troughs are distributed on a surface. Since both wear and friction are a product of asperity interactions after experiencing relative motion, surface roughness is widely used to characterize the tribological performance of a specific sliding system. The most commonly used roughness parameter in the literatures is the Ra, which is the arithmetic mean height of surface profile.

The correlation between surface roughness and tribological performance is still a controversial topic in the orthopedic industry. In industry, the standards for instructing the surface finish are relatively rough. For example, the ISO 7206-2:2011 standard suggests that for total hip prostheses, the surface roughness for the spherical articulating surfaces of metallic or ceramic components should have R_{amax} values not greater than 0.05 µm and 0.02µm respectively and the spherical articulating surface of the plastics acetabular components shall have an R_a value not greater than 2 μ m. Also, ISO 7207-2:2011 suggests the values for knee joint prostheses as $R_{amax} \leq 0.1 \ \mu m$ for metallic or ceramic components and $R_{amax} \leq 2$ µm for plastics components. It is still ambiguous if the critical surface roughness rule can be applied to the lubricated articulating joints in human body. However, regulations in these two ISO standards are different from the conclusions in the literatures, where most scholars claimed that the surface roughness of metal or ceramic bearing surface should have a Ra value smaller than 85 nm [13,36-39]. Meanwhile, some scholars opposed the idea of getting superfine surface finish due to the molecular-mechanical

effect [40,41]. Hence, more works should be carried out in the future to gain more knowledge regarding how surface roughness affects the tribological performance of bioimplants.

Surface texturing

Surface texturing is another way to improve the tribological performance of bioimplants without changing the properties of bulk materials. Technically speaking, surface texturing means that some specific manufacturing methods are used to fabricate designed micro patterns on the bearing surfaces [42-44], which include laser texturing [45], drilling/milling [46] and blasting [47,48]. The most common pattern shape investigated in the literatures is micro dimple. For example, Ito et al. firstly reported the improved tribological performance of dimple-CoCrMo-UHMWPE textured bioimplants in 2000, where they declared that a 16.9% decrease in coefficient of friction (COF) was achieved by laser textured micro-dimples (500 m diameter and 100 m depth). In recent years, due to the advances in fabricating technology, micro dimple with shallow depth (smaller than 20 m) becomes a popular research target due to its capacity to retain the viscosity of lubricant viscosity [49-51]. Another popular target pattern shape studied in the state-of-art is the micro-groove. Similarly, groove patterns with shallow depth are preferred by many scholars [52,53]. Besides, a comprehensive study conducted by Shen et al. revealed that the optimal pattern parameters of micro grooves in the field of bioimplant is: 500 m width, 4.5 m depth and 3 mm pitch distance [54]. Other shapes, like square, triangle and ellipse, were reported in [55]. Although most scholars agreed that surface texturing can benefit the tribological performance of CoCrMo-UHMWPE bioimplants, the experimental results from some scholars showed that the corresponding tribological performance would be deteriorated under some specific conditions [49].

As mentioned by some literatures [13,56], the working or failure mechanisms of surface texturing in bioimplants are still unclear. In the state-of-art, three theories were widely talked to account for the improved tribological performance of textured bioimplants. Firstly, pattern's ability to trap hard particles is universally believed by scholars that it can help reduce the chance of three-body abrasive wear [13]. Secondly, reserving lubricants has been proved that it can help avoid boundary lubricating condition [57]. Lastly, hydrodynamic pressure is widely discussed in the state-of-art, but scholars have different views regarding its role. Some believed that it is positively affecting the tribological performance of bioimplants [55,58,59] while others argued that its role can be neglected [60]. A recent comprehensive study conducted by Shen et al. proves that the slow sliding speed and low lubricant viscosity lead to the negligible role of hydrodynamic pressure in the tribological performance of textured bioimplants [61].

Cushioned artificial joints

Human joints are covered with soft layers of articular cartilage and lubricated with synovial fluid. These soft layers deform elastically while in contact with its counterpart, providing large contact areas, low contact stresses and what is believed to be a fluid film lubrication regime. The concept of using soft compliant materials similar in stiffness to that of articular cartilage to replace the polyethylene in conventional joint replacements has been discussed since the 1970s [60]. Further research has led to the understanding that during relative motion of the articulating surfaces, the contact between the soft material and a hard counter face can be separated by elastohydrodynamic and microelastohydrodynamic actions, which combined

with squeeze-film effects should provide fluid film lubrication similar to the natural joint with no wear [63,64]

Initial investigations into cushion bearing have manufactured from soft medical grade polyurethane layers adhesively bonded to polyethersulphone substrates [65,66]. Interface fatigue failure between the cushion layer and the substrate occurred in long-term durability tests where debonding was found to be initiated near the edge of the contact [67,68]. J Fisher, et al designed a composite cushion layer structure with gradually changing modulus from the soft surface layer to the substrate to relieve the stress concentrations at the interface, as shown in (Figure 2) [62,69]. This solution modified the stress distribution between the layers for hip joint but did very limited contribution to the stress distribution of knee joint [69]. JJ Elsner used a polycarbonate-urethane (PCU) acetabular buffer between CoCr shell and head, which indicated reduced wear rate, larger particle sizes and lower particle generation rate compared with the conventional CoCr-UHMWPE bearing, as (Figure 3) shows [70]. The only commercial hip system based on a PCU acetabular liner is the TriboFit® Hip System which consists of cushion-bearing components that are used for hip joint reconstruction. TriboFit has been implanted in more than 1,900 patients over 10 years, but few short-term (2-4 years) follow up reports are available, although it demonstrates excellent results by the Harris and Oxford hip scores [71]. Such soft compliant materials are even commercially used to mimic the function of the natural meniscus, such as the NUsurface[®] PCU implant [72], or used to replace the localized damaged cartilage such as the BioPoly® implant [73]. Synvisc-One® is a gel-like mixture made from a substance called hyaluronan that supplements knee joint fluid to provide the cushioning and improve the knee joint's natural shock absorbing abilities [74].



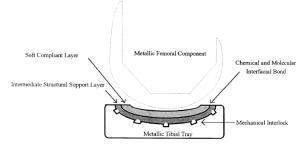


Figure 2) Composite cushion layer structure [60].



Figure 3) Configuration of PCU acetabular buffer [68]

The cushions are proved to function well in improving the lubrication condition and lower the local stress concentration so as to reduce the wear rate during the normal walk. However, for 95 percent of the time, people are not walking but standing still or moving slowly. Under such conditions, soft layer joint replacements must be designed to operate with thick elastohydrodynamic fluid films to provide some degree of protection as tribological conditions become severe, or alternatively incorporate alternative boundary or mixed lubrication mechanisms [54]. Furthermore, current cushion design only considered the elastic property of the layer to promote the lubrication condition by local deformation, which is not sufficient to approach the actual function of articular cartilage as the cushion cannot act exactly as the live soft bones. Besides deboning and high interface shear stresses, there is still great concern about the high level of friction and potential wear of soft layered bearings when they enter the mixed and boundary lubrication regimes. The high friction torque is also transmitted to the implantbone interface and may lead to joint loosening.

As this problem hasn't been solved effectively, there is only one commercial product available in the markets with very low implanting record.

Commercial products

Based on the summary of the state of the art above, it is clear that the major research in this area is still focusing on the development and adoption of new inorganic materials, either as bearing surfaces or cushion-like structures. The secondary major direction is the surface modification, including surface roughness optimization, surface coating, functional surface textures for enhanced lubrication. From the product catalogues of some leading manufacturers in artificial joints, it is easy to prove the above statements as well as we can see current products are mostly using the rigid parts with textured surfaces or additional articulation structure. Obviously, such product designs are still going along the traditional development pathway which introduce little buffering between the bearing surfaces so have very limited contribution to significantly reduce the wear rates further.

New development: regeneration of articular cartilage

Although it is widely acknowledged that elastic buffering structure helps much on improving the stresses distribution and lubrication, the very limited research is nearly all focusing on the compliant material layer design which inevitably brings the problem of debonding, additional interface shear stresses and accelerated wear of soft layers under boundary or mixed lubrication conditions.

Hyaline cartilage is an amazing substance that covers the joint bearing surfaces in humans and animals. It allows continuous and frictionless movement of the bony skeleton over a lifetime. Furthermore, the cartilage helps to transmit the load of the body to the underlying bone without causing any pain or discomfort. Obviously, mimicking or preproducing such a natural cartilage structure is more promising and effective on reducing the wear compared with the buffering structure solutions.

Although plenty of hard efforts have been devoted to mimic the function of hyaline cartilage, the majority of commercial artificial joints today are still using rigid components due to the lack of competent biomimetic products. Based on our best knowledge, no research has been found to regenerate articular cartilage *in vitro* onto artificial joints to reproduce the expected superior performance of natural hyaline cartilage. A key reason is that it was generally believed that the true articular cartilage regeneration is almost impossible in mammals, until recently the first success was made which demonstrated the possibility of this approach [75,76]

Regeneration of cartilage is not a new topic. Currently regeneration of cartilage is mainly used to repair small area of damaged articular cartilage locally for pain relief. For severe symptoms, total joint replacement is still the final option for pain management and regaining function in patients. Basically, there are three types of cartilage: hyaline, fibrous, and elastic cartilage. To treat osteoarthritis, a technique called microfracture (MF) surgery was developed in the 1950s and is still widely used today [77-80]. During MF surgery, the surgeon drills into the debrided chondral bone until the marrow cavity is accessed. A hematoma forms at the MF site that is resorbed and replaced with fibrous tissues. The resulting fibrous cartilage provides some symptomatic relief but has substantially reduced mechanical properties compared with those of normal articular cartilage [81]. By now, most of the cartilage regeneration results in the formation of fibrous cartilage, not hyaline articular cartilage. Until August 2020, Michael T. Longaker and Charles K. F. Chan made a publication in Nature Medicine providing a methodology to regenerate hyaline articular cartilage by activated skeletal stem cells (SSCs). The essential control strategy against formation of fibrous tissues, is to localize co-delivery of BMP2 and soluble VEGFR1 (sVEGFR1), a VEGF receptor antagonist, in a hydrogel skewed differentiation of MF-activated SSCs toward hyaline cartilage. This is considered as the first success in controlled regeneration of hyaline articular cartilage [76].

Furthermore, inspired by the autologous chondrocyte implantation (ACI) technology which has been successfully applied in local cartilage repair, the authors are developing a new technology to culture articular cartilage *in vitro* onto artificial joints to reproduce the properties of the healthy human joints. More outcomes will be published in later papers.

Summary

For long time it was generally believed that the articular cartilage regeneration is almost impossible in mammals, as nearly all clinical experiments can only get fibrous cartilage eventually. So, no idea has been proposed by now to develop articular cartilage on artificial joints. But the latest development of articular cartilage regeneration technology makes it possible. The authors first proposed the attempt to develop artificial joints with true articular cartilage to reproduce the original properties of the healthy joints. This will bring disruptive changes on the way of designing and manufacturing artificial joints. As no additional materials or layers are used, the problems of current cushion designs are effectively eliminated. This idea explores a new possibility to develop more endurable and patient-friendly solutions.

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