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In Vivo Degradation and Wear of Biomaterials in Total Joint Replacements

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Over a million of total joint arthroplasty (TJA) surgeries are performed annually to improve quality of life of the patients by relieving pain and offering increased mobility via restoration of joint functions. However, the TJA fails after few years causing pain, reducing the joint range of movements, and finally resulting in a revision operation. The main reasons for the revision are degradation and failure of implant biomaterials. This study aims at development of biomaterials for joint replacements being more successful. A preliminary evaluation of the wear-related failure of polyethylene glenoid components on the basis of the retrieval examination and wear simulations were performed. Degradation of implant materials was also assessed based on examination of the mechanical properties of the retrieved prostheses. Host response to the wear products was also discussed. The amount of wear was measured according to ASTM standards and volumetrically by using a laser scanning system. Furthermore, the implant surfaces were analyzed by scanning electron microscopy (SEM). The effect of the in vivo degradation on material properties was evaluated based on nanoindentation using of atomic force microscope (AFM).

The significant wear evidence was found in the present study. The volumetric wear rate varied from 6.9 to 30.4 mm^3/yr. The maximum linear wear rates exceed 0.2 mm/yr. Multidirectional scratches, flakes, pitting areas, and surface microcracks, which most likely result from subsurface fatigue, were observed in the SEM analysis. Based on the nanoindentation results, it was found that that the mechanical properties have changed due to degradation process of the polymeric implants.

From this study, it can be concluded that significant polyethylene wear and degradation do appear in TJA and may contribute to limited long-term survivorship of the implants.

Key words: *PE degradation, wear, debris, bone-implant interface, total joint replacement*

1. Introduction

Joint diseases, such as rheumatoid arthritis and osteoarthritis can result in pain and decreased functionality of human articular joints [13]. If non-surgical treatments are not successful, a joint replacement must be considered. This is a good treatment, as is demonstrated by the long-term results. However, complications can occur due to the mechanical and geometrical mismatch of the components and natural tissues. In artificial joint the load distribution is changed tremendously, many interfaces are introduced and the lubrication properties are decreased. These factors can cause implant failure, its wear, bone morphology adaptations and loosening of the components [13, 29, 39].

The main function of human joints is to provide a large range of mobility to fulfil 'Daily Living' tasks [15]. Doing these tasks can result in high joint loading and many interface motions, which in the long-term demand the most of these joints. For example, during down-hill walking the knee joint can undergo a contact force of 8 times body weight and it is estimated that a typical human joint experiences one million loading cycles each year [21]. A high strength material and contact area large enough must take care of high contact forces, whereas the amount of load cycles require good lubrication properties between the articulating surfaces and fatigue resistant, deformable materials.

Prostheses are designed to mimic the anatomical joint structure and function as much as possible using available engineering techniques and materials [31]. The affected and painful joint surfaces are removed and replaced by two components, which restore the concave and convex geometry of articulating surface of natural joint. The concave component material consists mainly of

the ultra-high-molecular-weight polyethylene (UHMWPE). For convex side of the artificial joint, the metal (CoCr alloys) or ceramic (aluminum ceramic) component is used. These components are equipped with short or long stems, which can be fixed to the trabecular bone by means of bone ingrowth to a porous surface with or without porous hydroxyapatite (HA) coating or by means of poly-methylmetacrylate (PMMA) cement [13]. To fixate the prosthetic components a surgeon has to remove not only affected and painful joint surfaces, but also lots of healthy bone. After insertion of a prosthesis a bone-prosthesis structure is a composite structure. This implies that it consists of separate substructures with different elastic and geometrical properties that are bonded to each other. These differences result in a change of load distribution in the artificial joint, as compared to the natural joint [13]. In natural joints the loads are distributed over the entire cross section of the proximal part of the bone (i.e. femur). In the case of an artificial joint, the load is partially transformed through shear across the bone/cement/prosthesis interfaces [13]. This altered load transfer leads to increased stresses at the cement/prosthesis interface and unloading of the bone away from the prosthesis. The interface shear stresses are further increased due to the stiffness ratio between the prosthesis and the bone, typically of the order of 10:1 and higher. In addition, the bending displacements in the bone surrounding the stem are reduced because of relatively high flexural stiffness of the prosthesis. The change in load distribution increases stresses in some regions and reduces them in others. Areas that see higher loads, may experience an increase in bone mass, while areas that see a reduction in load may experience a decrease. Moreover, when there is a inadequate proximal fit of the stem, either initially as an effect of bone preparation, or gradually postoperatively as the effect of stem subsidence, the proximal load transfer is bypassed in favor of distal load transfer. This "bypass" mechanism as well as stress shielding cause failure of the arthroplasty [13].

From comparing anatomical and artificial joints, it can be concluded that while healthy human joints are lubricated by fluid film, all current artificial joint with relatively hard bearing surfaces are lubricated by the boundary and mixed lubrication, which results in wear and wear debris from articulating surfaces [10]. Wear results in late loosening of prosthetic components [33, 39]. Wear particles from the articulating surfaces can arise due to the decreased lubrication properties, smaller contact areas and higher contact loads after a joint replacement. At the interfaces, wear is triggered by inter-

face debonding in combination with dynamical loading, where surface and material properties and the presence of other small particles determine the progressive character of the wear rates. The implant material subjected to very demanding conditions such as high stresses and high cycle loading coupled with aggressive body environment degrades in time, loosing its properties such as strength and wear and corrosion resistance.

This study aims at development of more succesful biomaterials for joint replacements. A preliminary evaluation of the wear related failure of polyethylene glenoid components on the basis of the retrieval examination and wear simulations were performed. Degradation of implant materials was also assessed based on examination of the mechanical properties of the retrieved prostheses. Host response to the wear products is also discussed.

2. In Vivo Wear

The investigation of in vivo wear of polyethylene in TJR was performed on the basis of the examination of the glenoid component retrievals.

Only few studies have been performed to assess the wear of glenoid components [7, 9] in comparison to plenty of studies concerning hip and knee replacements. From gross examination of retrieved glenoid components, Scarlat and Matsen [28] found that none had the same surface and shape as before implantation, even after 1 year of functioning in a patient body. Gills [7] and Gunther et al. [9] concluded that the abrasion, burnishing, pitting, and delamination were found as the most predominant modes of glenoid polyethylene wear. Moreover, some retrieved components were worn out completely and some of them were fractured [25]. All these studies have been mostly concentrated on the qualitative assessment of the polyethylene wear on the base of visual observations of retrieval implants. However, the quantitative assessment of in vivo wear performance of total shoulder replacement has not yet been reported.

This study aims to evaluate the wear related failure of polyethylene glenoid components on the basis of the retrieval examination.

Six glenoid components were retrieved and examined (five all-polyethylene and one metal-backed) (Fig. 1). All components were originally fixed with bone cement. A mean time of in vivo use for all components was about 10 years; with the shortest 7 and longest 14 yrs. Main reason for all revisions was glenoid component lucency.

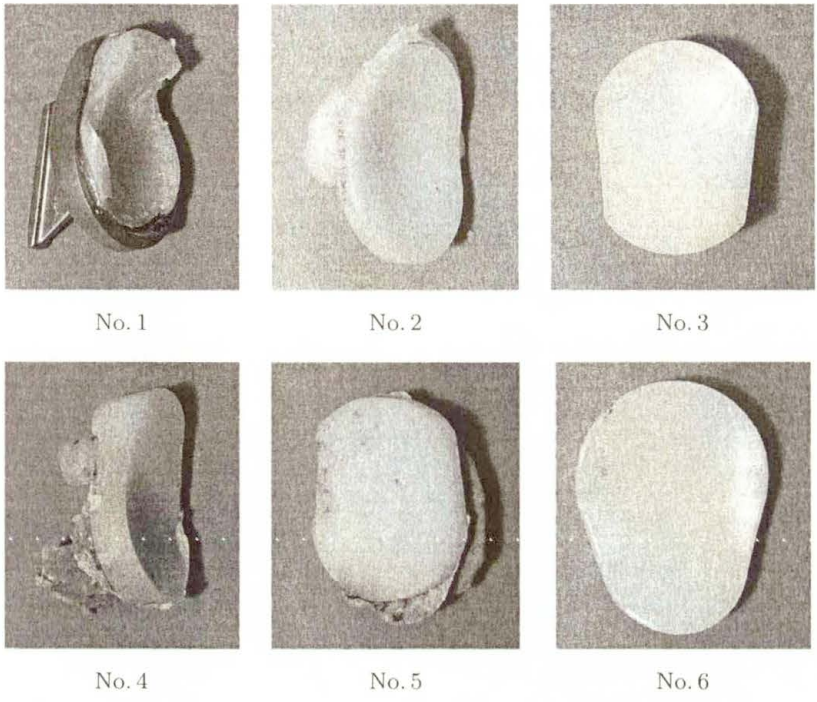
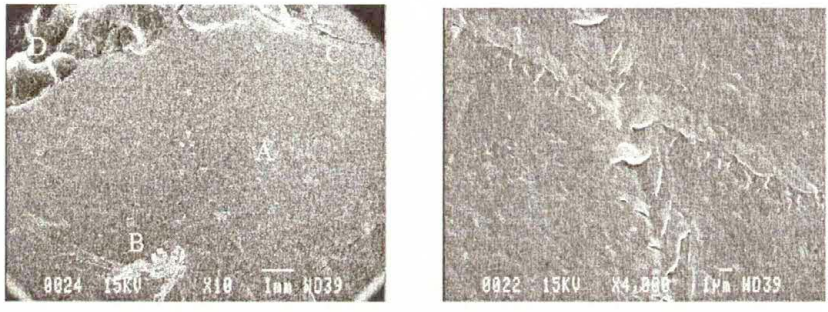


FIGURE 1. Retrievals of the glenoid components

To measure volumetric wear and wear depth of the retrieved components a laser scanning system was used. The articular surface of each component was scanned with accuracy of about $\pm 6\,\mu$m using a laser scanner LDi (Laser Design Inc, Minneapolis). The results of measurements have been used to generate geometrical models of the retrievals using CAD software—Pro/Engineer. These models have been subsequently used to determine the maximum depth and the volume of wear for each component according to method presented by Święszkowski et al. [30]. All six retrievals were examined using the scanning electron microscope (SEM). The retrievals were examined using this technique for analyzing wear scar locations, wear topography and stress-related gross microcracks. For SEM observations the surface of the components was sputter-coated with a gold film (20 nm). Observations were carried out, using various microscopes (Balzers SCD040, JEOL, Peabody, MA) at magnifications from 10 to 4000×.

Additionally, the components were evaluated visually for evidence of a polyethylene wear such as abrasion, pitting, scratching, burnishing and delamination, according to the method proposed by Gunther et al. [9].

It has been found in the present study that the volumetric wear rate varies from 6.9 to 30.4 mm^3/yr. The maximum linear wear rates for the analysed retrievals exceed 0.2 mm/yr. From the scanning electron micrographs of the exposed surfaces of the retrievals it was found that fine multidirectional scratches were dominant in all retrievals (Fig. 2). In addition to the scratches, flakes and rim erosion also are observed. Moreover, two implants had pitting areas and surface microcracks, which most likely result from subsurface fatigue.



(a) (b)

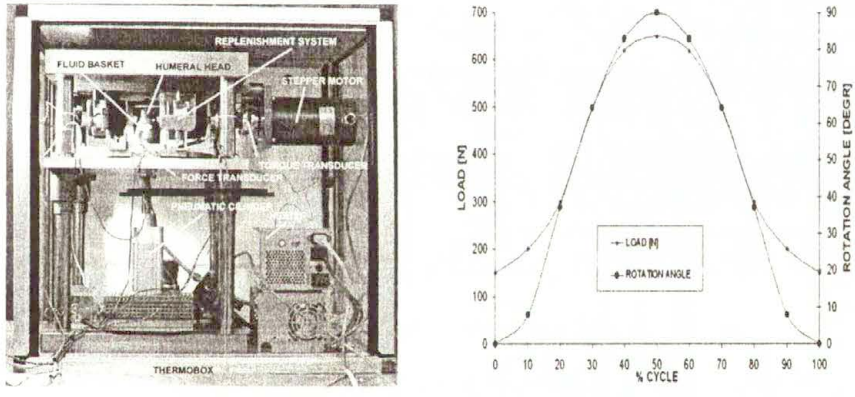
FIGURE 2. SEM of the retrievals No. 5 (a) and No. 2 (b) showing: multidirectional scratches (A), flakes (B), cracks (C) and rim erosion (D)

Polyethylene de-lamination was observed for metal backed component. The same component was completely worn out to the metal backing in some places. Yellow colour of polyethylene observed in this case gives indication of its extensive oxidation. It was found that the inferior parts of the all components had the highest damages (four from six components).

3. In Vitro Wear

There are many factors influencing the wear in total joint replacements, i.e. design-mechanical factors (the geometries of the prostheses, surface roughness and hardness, loading, motion and lubrication condition), the material factors (material properties, manufacturing process, sterilization method and atmospheric exposure that can lead to oxidative degradation), patient factors (weight, activity and bone properties) and surgical factors (positioning and fixation method). This study is mainly concentrated on effect of implant geometry on the PE wear since it is considered to be one of the major factors influencing the generation of wear debris [38].

To test in vitro wear performance of the total shoulder arthroplasty a newly designed shoulder joint simulator [32] was used (Fig. 3). In a preliminary test the wear performance of currently used glenoid and humeral components was tested in the shoulder wear simulator. The six examined prosthetic components were custom-manufactured from medical grade materials. Three humeral heads were made of 316L with a diameter of 44 mm, and surface finish Ra= 0.05 μm. Three glenoid components were made of UHMWPE (Chirulen1020, PolyHiSolidur GmbH, Vreden, Germany). The articular surfaces of the glenoid components have the following radius of curvature: 27, 24 and 22 mm. All components have the same thickness of 7 mm and the same roughness of Ra= 0.1 μm. Before testing, all UHMWPE components were treated by a gamma sterilization method with a radiation dose of 26.8 kGy. Additionally, the components were placed in container of deionised water for 3 weeks before testing to establish an equilibrated fluid absorption level.



(a) (b)

FIGURE 3. Shoulder wear simulator (a) and load and motion profiles for abduction/adduction obtained for the patient with a total shoulder prosthesis (b)

All tests were performed under physiological loads, with maximum force of 650 N, synchronized to the abduction/adduction movement. The tests ran for 3 million cycles. The cycling frequency was 1 Hz. During one cycle the head rotates from 0° to 90° and back to 0°. The tests were performed with newborn calf serum (Heclone®) as a lubricant. The temperature of the lubricant was maintained at 37° ± 3°. During the tests the frictional torque, applied load, rotation angle of the shaft and test environment temperature

were continuously recorded. After the tests were completed, the glenoid components were inspected for wear.

Wear rates were determined according to ASTM standard (ASTM F1714-96) [1]. This test protocol uses weight loss method for evaluating a wear performance of polymeric components of human joint prostheses. Every 250 000 cycles the glenoid component was removed from the simulator, cleaned, dried and weighed in order to determine mass loss. A soak control component was also used to correct the measured mass loss due to fluid sorption. During the test this control component was placed in the temperature conditioned chamber soaked with the same type of the lubricant. Afterwards a gravimetric wear of the test specimen was calculated from the following equation:

$$W_n = W_1 - (W_2 - (S_2 - S_1)) \tag{3.1}$$

where: W_1—initial weight of the tested component, W_2—final weight of the tested component, S_1—initial weight of control specimen, S_2—final weight of control specimen.

The gravimetric weight loss (wear) of the glenoid components as a function of the number of cycles is shown in Fig. 4. The weight loss of 38 mg was found for the first 27 mm glenoid component after 3 million cycles. For the conforming joint the PE wear of 54 mg was obtained after 3 million cycles (Fig. 4).

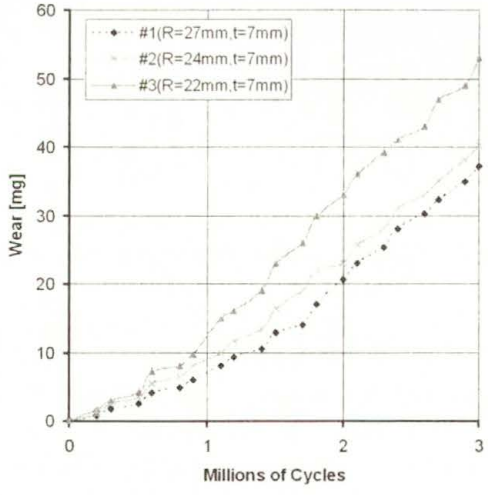


FIGURE 4. Gravimetric wear of the glenoid components during 3 million cycles of the tests for the 27 mm and 22 mm glenoid components

In this study, a significant (ranging from 38 mg to 54 mg), nonlinear loss of the weight was found. Assuming a polyethylene density of 0.946 mg/mm^3 and 1 million cycles as one year in vivo component use, the calculated volumetric wear rate is between 13.4 mm^3/yr and 20 mm^3/yr.

4. Degradation of UHMWPE

Although ultra high molecular weight polyethylene (UHMWPE) has been used for bearing surfaces in total joint replacements for over 30 years, during the last 10 years a large number of reports of failures have been published [34]. The major factor responsible for these failures is oxidative degradation induced by sterilisation with γ-irradiation. The irradiation results in generation of free radical in polyethylene. These free radicals may react with the oxygen that could diffuse into polyethylene during shelf storage and/or in vivo, causing the polymeric chain scission, in turn, this will lower the molecular weight of PE, increase the density, stiffness and brittleness, and reduce the fracture strength and elongation to failure. Any of these changes could dramatically affect the wear resistance.

The effect of the in vivo degradation on material properties was evaluated, based on nanoindentation using of atomic force microscope (AFM).

Traditionally, AFM has been used to measure the nanometer-scale topography of surfaces through direct contact between a sample surface and a probe tip mounted on the end of a cantilever microbeam. Development of the AFM's imaging capabilities has focused on the tip-sample interaction forces, leading to the utilization of the AFM as a surface force apparatus. In this mode, termed force mode, the AFM monitors the interaction forces as a function of the perpendicular distance traversed by the tip relative to the sample surface [34]. A plot of the tip deflection signal versus the vertical motion of the piezo-actuator, termed a force curve, contains information regarding the nanoscale response of the material to indentation.

The polyethylene samples were prepared from different regions of the retrieved glenoid component (Fig. 5). Nanoindentation was performed on the samples using the AFM diamond tip. The probe tip was lowered into the contact with samples. Triangular impressions were produced in the samples due to the triangular cross-section of the probe tip (Fig. 6). The distance from the apex to the base of each triangular impression was taken as a measurement of the plastic indent size. The force curves produced from each indentation were obtained (Fig. 7).

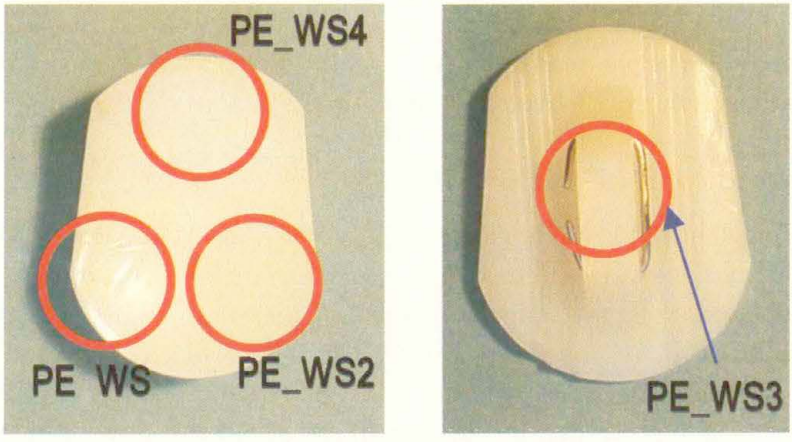


FIGURE 5. The glenoid component with the selected regions of samples acquisition

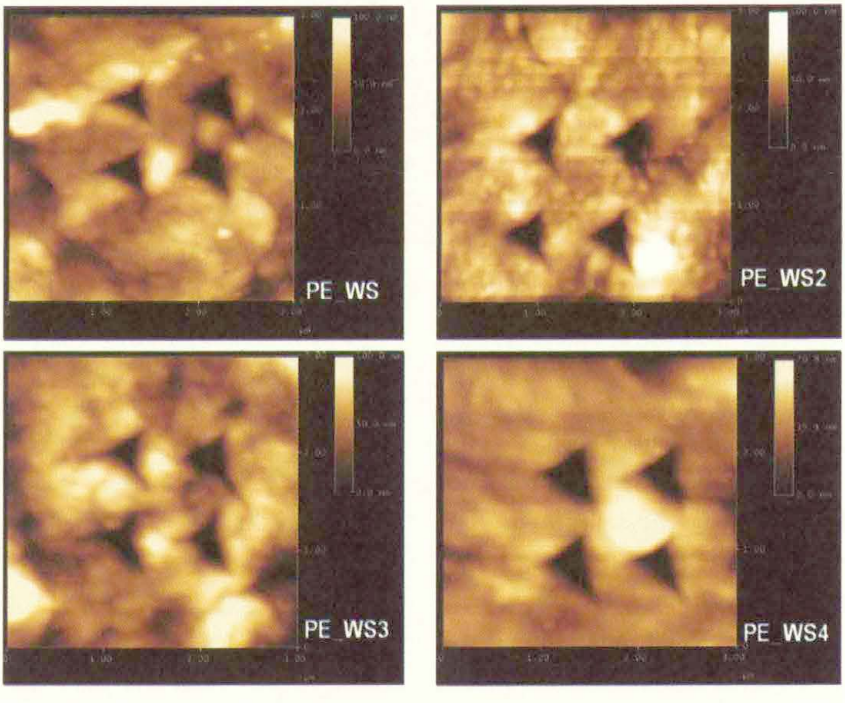


FIGURE 6. Triangular impression after nanoindentation for different samples

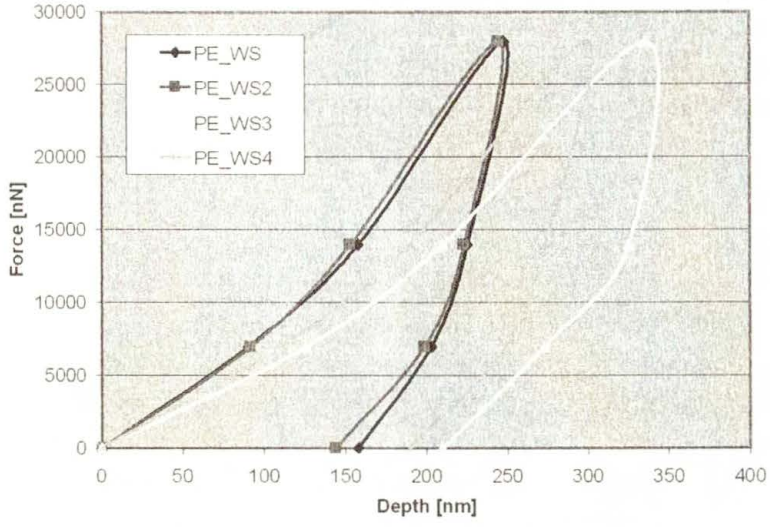


Figure 7. Force-displacement curves for different samples

Based on the force-displacement curves it can be concluded that the mico-mechanical properties of the polyethylene are different for different region of the implant after in vivo use. Material from the region of high wear evidence (PE_WS and PE_WS2) is stiffer than material coming from region showing less wear (PE_WS4 and PE_WS3). Generally, the stiffness of the implanted material after in vivo exploitation, increased. It can be results of the PE degradation due to its oxidation.

5. Host Response to Wear Particles of Biomaterials Used in Artificial Joints

5.1. Wear Particles: Small Size—Huge problem

Wear particles arise on the articulating surfaces of the artificial joint and also on the surface between bone and implant. They can migrate from these bearing surfaces into close contact with living tissues. The greatest number of particles isolated from periprosthetic tissue are less than 1 μm in the size [2, 5, 12, 23], so they are actually minute. The particles with small size are the most biologically active. It was shown, that particle between 0.3 to 10 μm can stimulate macrophages [8], what jeopardizes the stability of implant, beginning the cascade of inflammatory events.

Besides the size of particles, very important is also concentration of wear debris in tissues. It was experimentally verified that the number of 10^{10} particles per gram of tissue is related to the osteolysis [23]. This is a huge number, but when considered the mean size of particles, it is not so big.

5.2. Histology of Periprosthetic Tissue

Histological studies of periprosthetic tissues, obtained from patients who have had revision surgery due to aseptic loosening, have indicated a chronic inflammatory reaction. Dense fibrous tissue with signs of inflammation is often seen around loosened implants. Fibrous tissue with a huge number of wear particles, engulfed by macrophages and surrounded by multinucleate giant cells, is common characteristic event in periprosthetic tissue. Fibrous tissue, which arises around unstable implant, is composed of different cell types such as fibroblasts, macrophages and also lymphocytes (which migrate, when inflammatory reaction starts) (Fig. 8).

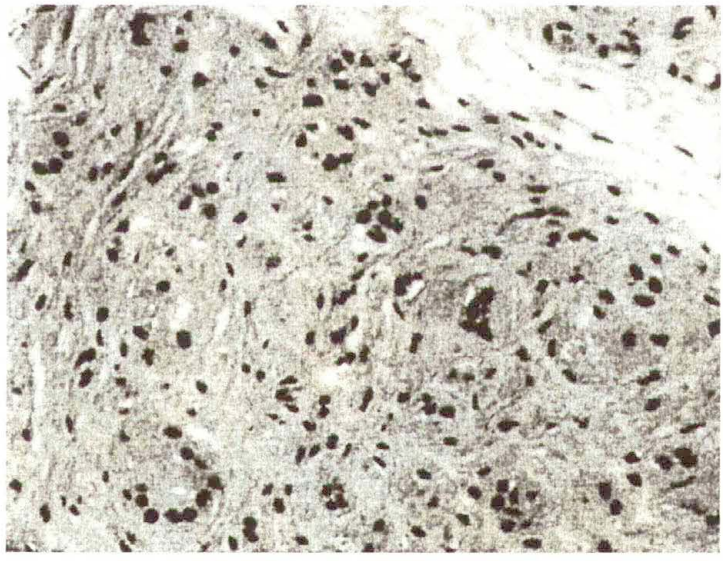


FIGURE 8. Microscopic examination of hematoxylin and eosin staining of tissue from a failed total hip replacement shows macrophages containing polyethylene wear particles that are seen as white fibers and flakes under polarized light (after T.M. Wright, and S.B. Goodman)[40]

5.3. Evoking Inflammatory Reaction

Wear particles in critical size and concentrations can lead to developing chronic inflammatory response. Wear particles are flowing in synovial fluid and with this fluid they can migrate. They are present between two surfaces of artificial joint (place where they are created), between human tissues and artificial joint pieces; therefore they can get in contact for example with synovial membrane, bone tissue and so on.

Wear particles, because of their small size, are able to evoke inflammatory reaction. Although the implant materials are biocompatible in the bulk form they may loose that feature when they are in the form of particles. When wear particles arise in tissue environment, they are treated by the host immune system as a foreign body. The body's defense system attempts, unsuccessfully, to digest the wear particles (as it would digest an organic molecule).

The appearance of wear particles around worn implant, contributes to migration of monocytes from blood to tissues which are under the influence of wear particles. Monocytes are white blood cells, which can defend the organism against foreign bodies. Monocytes can differentiate into macrophages, which have ability towards phagocytosis—the process of engulfing foreign bodies and digestion them inside macrophages. Therefore in case of presence of wear particles process of phagocytosis is used as well. Macrophages are able to phagocytose wear debris at the bone-implant interface [8], what was analytically confirmed using TEM [22]. Wear particles were observed inside the cells of macrophages, in the cytoplasm [22]. Macrophages are the key cells in the process of biological response to wear particles [22]. They start a cascade of events which leads subsequently to the aseptic loosening of implant.

Macrophages after phagocytosis of wear particles are able to more intensified synthesis of inflammatory mediators, such as IL-1, IL-6 and TNF [4, 8, 23, 33]. These cytokines are considered as the most significant for biological response to wear particles. They are involved in the first step of inflammatory process. These cytokines have influence on every cell type present in fibrous tissue. They act as mediators, transmitting the information about foreign bodies inside the tissue. They can activate other cell, stimulate cells to release other cytokines, other mediators, they boost inflammatory aggressive reaction.

The most undesirable and final consequence of the inflammatory reaction evoked by wear particles is osteolysis—intensive bone resorption around im-

plant. The continuously growing amount of wear particles appearing in the periprosthetic tissue can increase level of activated cells, contribute to intensified migration of monocytes from blood to the target tissue and lead to chronic inflammation. Activated cells occupy larger space at the cost of bone mass. They release larger amount of inflammatory mediators what can activate bigger amount of cells. The positive feedback is present and inevitable. Developing inflamed fibrous tissue precludes osseointegration. Implant surrounded by this tissue has no connection with bone, no support. Fibrous tissue cannot withstand stress and pressure to which it is exposed, therefore implant becomes unstable. Micromotion can lead to more intensify wear process, more aggressive chronic reaction and subsequently to necessity of revision.

5.4. Processes Contributing to Osteolysis

Wear particles may contribute to bone mass decrement by many modes, in direct or indirect way. The most important are: osteoclast activation and osteoclast differentiation, induction of matrix metalloproteinase synthesis and also inhibition of new bone formation.

Wear particles can directly or indirectly stimulate osteoclasts to active bone resorption what was confirmed by the level of ^{45}Ca release by the culture of mouse calvaria bone samples [37] after exposure to wear particles. Osteoclasts are able to engulf particles, which results in their activation [36]. Cytokines released after contact with wear particles can stimulate osteoclast survival and prevent them from apoptosis [14].

Wear particles as well can stimulate recruitment of osteoclast precursors and their differentiation into mature osteoclast, which can digest bone tissue directly and indirectly [6]. Macrophages which have had phagocytosed wear particles can differentiate into active osteoclastic cells (after addition of 1,25-dihydroxy-vitamin D3 into conditioning medium), which have the capacity of bone resorption [26, 27].

Many inflammatory mediators synthesized due to response to wear debris can induce production and activation of zymogens of matrix metalloproteinases. The matrix metalloproteinases (MMPs) are proteolytic enzymes that contain a zinc ion at their active sites. These enzymes can degrade collagen, elastins and other components of the extracellular matrix. Every kind of connective tissue consists of cells and big amount of extracellular matrix, which can be digested by MMPs. Also bone tissue on the bone-implant in-

terface can be destroyed by these enzymes. The degradation of bone matrix without a compensatory increase in bone matrix synthesis results in net bone loss.

Wear particle can have influence on osteoblasts—bone forming cells. Osteoblast can be affected by the cytokines which were released by other cells due to wear particles influence. The proinflammatory cytokines can inhibit procollagen mRNA expression and subsequently can lead to reduction of type I collagen synthesis [19], which is one of the most important structural proteins of the bone mass.

However wear particles can also have a direct impact on osteoblasts [17]. The osteoblast have been shown to have ability to internalize particles smaller than 1 μm, [11] which is the size of most wear debris. It was shown that wear particles can be phagocytosed by osteoblast [17,35] what can change its morphology, metabolic activity (inhibition of collagen synthesis). It was reported, that wear particles may decrease the growth rate of human osteoblastic cells in culture [18].

Inhibition of osteoblast ability to new bone deposition is not connected directly with osteolysis, but it contributes to net bone loss. Wear particles, what was shown earlier, promote bone digestion, when new bone cannot be synthesized appreciable bone loss is present. Osteoblasts cannot compensate the bone damage.

All these mechanisms contribute to osteolysis which, together with cyclic loading, leads to aseptic loosening of the implant.

6. Conclusions

This study shows that presently, it is not possible to replace the natural joints by engineering materials and designs with the same effectiveness. Complications occur within several years, as a result of the introduction of interfaces, decreased lubrication properties and a changed load distribution [21, 24]. The significant wear evidence of the implants was found in the present study. Multidirectional scratches, flakes, pitting areas, and surface microcracks, which most likely result from subsurface fatigue, were observed in the SEM analysis. Based on the nanoindentation results, it was found that the mechanical properties have changed due to degradation process of the polymeric implants.

Moreover, the wear process generates wear particles strongly influencing condition of the bone-implant interface. Biological response to wear debris is related to the size of the particles, the composition is not so important in general. It is more a size issue and a volume issue, than it is a material issue. Intensive bone loss without new bone production, intensive inflammatory fibrous tissue development in response to small wear particles lead to massive osteolysis. Wear particles remain one of the most important problems in total joint replacement. Many efforts were done to improve biomaterials features, reinforce wear rate. Despite technological efforts wear process is inevitable in artificial joint, where stresses are so high. Therefore we need to learn more about biological response to wear particles of different biomaterials. We should understand process which leads to osteolysis, implant loosening, and then we can try to weaken, modulate or subsequently stop this process.

From this study, it can be concluded that significant polyethylene wear and degradation do appear in TJA and may contribute to limited long-term survivorship of the implants. To improve total joint replacements in terms of long term component fixation and wear properties, future work should be concentrated on the design of advanced prosthetic materials, which will have better wear and degradation resistance and will better mimic properties of natural bone and cartilage tissues.

Acknowledgements

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