METALS FOR JOINT REPLACEMENT

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Contents

1. Introduction

1.1. Summary

This short overview provides first three different classifications of biomaterials in general, based on their composition, surface reactivity and production, which will help to put metals into context with everyday life. Not all metals can be used as biomaterials as their use in human body is tightly regulated; the general principles and specific EU standards reflect well the global status and trends in the regulatory field. Metal ions are held together by metallic bonds, which consist of relatively loosely

bound valence electrons. The positive metal ions are located in crystal lattice points, which are surrounded by electrons. This provides metals with special properties, such as good thermal and electrical conductivity, metallic lustre, but also their ductile and malleable properties, i.e. the ability to undergo plastic deformation without breaking. Unfortunately, most of the technically important metallic materials are thermodynamically not stable in the metallic state in air or in aqueous solutions. Instead, surface oxidation will take place (in which process metal looses electrons). The oxidized metal ions will either dissolve (corrosion), or form an oxide film on the metal surface (passivity). Surgical use of steel, titanium, cobalt-based alloys and tantalum are overviewed. Finally, some future trends like mini-invasive surgery, resurfacing implants, isoelastic implants, implant coating and osseointegrating implants are discussed.

1.2. Classification

Classification can be based on different premises. Biomaterials can be divided according to the chemical composition as follows:

1) Metals
2) Polymers
3) Ceramics
4) Composites and
5) Materials of biological origin

This chapter describes the use of metals in connection with joint replacements.

Biomaterials can also be divided based on their surface reactivity as follows:

1) Almost inert, with smooth surface
2) Almost inert, with porous surface
3) Chemically reactive surfaces and
4) Bioresorbable (bioabsorbable) materials

Metallic biomaterials in clinical use belong to group 1 or 2 according to their surface reactivity. Often the metal, e.g. stainless steel or cobalt-chrome, evokes a host response so that the implant is surrounded by fibrous tissue or capsule. If the biomaterial, however, is able to endure the effect of its biological surrounding, it is known as biotolerant. Some metals have an oxide layer on their surface, e.g. titanium, and can be in direct contact with the surrounding bone without causing any effects or reactions with its biological surrounding. They are bioinert materials. The group 3 surface reactive materials lead to tissue response, which can lead to a direct bonding to osteoid or bone. This has been demonstrated for example for calcium phosphate like hydroxylapatite, bioglass and glass ceramics. These materials are called bioactive and can be used for surface coating. Group 4 bioabsorbable materials are degraded and replaced by regenerating tissues either to full extent (for example polyglycolides) or partially (calcium phosphate).

It is also possible on historical basis to separate three different generations of biomaterials.

1) First generation: minimal tissue-biomaterial interactions, replacement of body parts with materials with an adequate functional performance, e.g. load bearing biomaterials
2) Second generation: control or induction of favourable host reactions, e.g. bioresorbable materials, which allow in-growth of host tissues
3) Third generation: emphasis on regeneration of impaired tissue, tissue engineering products, living cells used in combination with artificial materials

Metals or metal-based materials can belong to any of these, with whole metal implants belong to the first generation (Figure 1 A and B), bioactive-coated metal implants to the second generation and metallic scaffolds to the third generation.

2. Requirements for biomaterials

2.1. General requirements for biomaterials

The properties of materials that are planned to be used inside the body must meet the requirements concerning biofunctionality as well as biocompatibility. If the purpose of the material is to replace diseased tissue that, for instance, has had specific load bearing or optical properties, then the biomaterial also has to meet such requirements in order to be biofunctional. The main difference between biomaterials and other engineering materials is that the biomaterials and their products additionally need to be biocompatible and safe for the host.

The properties and production of biomaterials in the EU economical area are regulated by the European Union. The products have to be suitable for their purpose and they must attain the planned functionality and functional properties. The appropriate use of the products should not endanger the health of the patient, the user or any third person. The national regulations are based on European Union directives about active implants for medical use (90/385/EEC) and medical devices (93/42/EEC).

The risks caused by the use of biomaterials must be acceptable and compatible with the purpose of use from the point of view of health, security and high standards of the health care system. The manufacturer must recognise the risks associated with the biomaterials and must eliminate or minimise them. The user must be informed of the residual risk after this minimising procedure. All adverse effects have to be acceptable from the point of view of the planned use and properties of the biomaterial.

Planning of implants and properties of biomaterials are subject to regulation. The most important properties relate to chemical, physical and biological properties and infections or microbiological contamination. Special attention has to be paid to the selection of biomaterials and the compatibility of the biomaterials with tissues, cells and tissue fluids. The planned life in service of the implant has to be taken into account. Sterilising is subjected to its own requirements. The origin of biomaterials of biological origin is strictly regulated. The source material has to be traceable, but at the same time anonymity is required. Biomaterials of such origin has to meet particular requirements concerning modification, storage, testing and other handling, which all must be performed under optimal circumstances. Viruses and other infectious agents should to be removed or inactivated during processing. Biomaterials of human origin are developing rapidly.

The central standards regulating biomaterials have been published in the ISO 10993 series, which includes many standards. ISO refers to International Organization

for Standardization. Because the abbreviation of this organization would have been different in different languages, it was decided that a word derived from the Greek word “isos”, meaning “equal”, is used. Standards are referred below by using their original international ISO codes. The code EN refers to European standards created by CEN, CENELEC or ETSI.

2.2. Currently valid European Union standards, examples

BIOMATERIAL STANDARDS

ISO 10993-1 provides guidelines for the selection of tests required for the biological evaluation of devices and equipment used in health care.

ISO 10993-2 covers animal welfare requirements to be followed during biological testing of medical devices.

ISO 10993-3 covers evaluation of genotoxicity, carcinogenicity and reproductive toxicity. Genotoxic factors are able to cause mutations, chromosomal aberration and other permanent DNA effects. Because genes contain instructions for cellular behaviour, such changes can have disastrous effects, such as cancer or reproductive toxicity.

ISO 10993-4 regulates the selection of tests to determine hemocompatibility. Blood enables transportation of oxygen and carbon dioxide, defence against infectious pathogens and repair of injured tissues. These functions are of vital importance. Therefore, biomaterials coming into contact with blood have to be hemocompatible. Hemolysis or degradation of red blood cells can be caused by material itself or by mechanical injury caused by the use of the implant. Intravascular hemolysis leads to hemoglobinuria and kidney damage. Deleterious effects on white blood cells can impair defence against infectious agents. In deep granulocytopenia B-neutrophils < 0.5 x 109/l and risk for infections in e.g. skin or mucosa and even sepsis is high. In deep lymfocytopenia various intracellular viruses and tuberculous and atypical mycobacteria threaten. Blood contains many cascade systems of vital importance, such as complement, coagulation and fibrinolytic systems. The tests that are required for individual devices depend on the classification of that device and differ to for example blood vessel prosthesis, artificial heart valve, cardiac pacemaker, blood cannulas, stents and heart-lung machine.

ISO 10993-5 defines the test to be used for the determination of cytotoxicity in vitro. This is often done as the first test for planned medical devices to test their biocompatibility. This is because such tests can be rapidly performed, are well standardised, sensitive and cheap. Cytotoxicity testing correlates well with short-term implant fate. Cytotoxicity testing is so important that it has to be performed for all medical devices. Various cell lines, e.g. human colon adenocarcinoma cell line caco-2, can be used for cytotoxicity testing.

ISO 10993-6 provides guidelines how to analyze local effects after implantation. This standard describes experimental animal tests, tissues, follow-up times, implantation methods and estimation of the biological host responses. Usually the implant is

removed before the tissue samples are taken. Particular attention is paid to the interface between the implant and host.

ISO 10993-7 deals with residues produced as a result of ethylene oxide sterilisation.

ISO 10993-8 deals with the selection and qualification of reference materials for biological tests.

ISO 10993-9 provides framework for identification and quantification of potential degradation products.

ISO 10993-10 defines irritation and hypersensitivity tests. Biomaterial (and chemicals released from it) can cause irritation of skin, mucosa or eyes. Usually irritation leads to inflammation with redness, swelling, tenderness etc, which is roughly proportional to the concentration of the irritant. Numerous chemicals of biomaterial origin cause either immediate or delayed irritation. Some of the irritants are additives, which are used to facilitate production, whereas some are harmful contaminants. For example, devices, which have been sterilised using ethylene oxide gas, can contain residues, which lead to irritation if their concentration is high enough. In spite of numerous attempts to find *in vitro* tests, irritation is still mainly tested using animal experiments.

Hypersensitivity can arise, if the host is exposed repeatedly or for long time to biomaterials (or products thereof). Most of these hypersensitivities are delayed hypersensitivity reactions medicated by T lymphocytes. Immediate hypersensitivities mediated by IgE-sensitized mast cells are rarer. Therefore, these tests are usually performed using animal skin testing and epicutaneous or patch tests. Hypersensitivity leads to redness and swelling of the skin. In immediate hypersensitivity, an already hypersensitive individual can mount rapid responses when exposed to allergen. This can be tested using measurements of serum IgE antibodies or intracutaneous prick tests, more rarely using exposure (under controlled conditions). Hypersensitivity reaction is not proportional to the allergen, because even small concentrations of allergen can cause dramatic responses in hypersensitive individuals.

ISO 10993-11 deals with toxicity tests. Material released from the implant can cause systemic toxicity, which can affect the function of vital organs. Particularly liver, heart, kidneys and brain are considered important from this point of view. Toxicity tests are based on classical toxicological evaluation used for drugs and chemicals, which must be modified so that they can be applied to solid medical devices. This is particularly pertinent to corrosion products as the body has a limited capacity to secrete various metal ions released from metal implants, which may lead to an accumulation in vital organs. End stage kidney disease can form a contraindication for metallic implants.

ISO 10993-12 contains instructions for the preparation of samples and comparative materials. Test types, appropriate dissolvents and conditions and control materials are described. The standard recommends the use of medical device in its final composition, because the biological testing must cover all substances used for production of the device.

ISO 10993-13 provides help for the identification and quantification of degradation products produced from polymers, which in particular in totally replaced joints may cause a problem as a result of debris formation and foreign body reactions.

ISO 10993-14 deals with the characterization of materials.
Attention has to be paid to

a) Materials used in the production,
b) Additives, contaminants and residues,
c) Leachable substances,
d) Degradation products,
e) Other components and their interactions in the final product and
f) Properties and characteristics of the final products.

ISO 10993-15 deals with the identification and quantification of degradation products from metals and alloys.

ISO 10993-16 provides toxicokinetic study designs for degradation products and leachables.

ISO 10993-17 established allowable limits for leachable substance.

The principles behind individual standards can be exemplified using part eleven, systemic toxicity. It is based on seven main principles, which are:

1) Materials must be defined so that their composition and character, impurities and debris derived from them can be described and used as a basis for requirements for specifications.
2) Chemicals and degradation products derived from the materials have to be taken into consideration in the assessment of toxicity.
3) The tests planned used have to take into consideration exposure to materials produced from the implant, as a result of degradation or production by other means.
4) Testing has to follow good laboratory practise (GLP) principles and has to be performed by informed experts.
5) All test results have to be available for official government organizations.
6) If the material composition, production or purpose of use is changed, toxicity has to be re-evaluated.
7) All information available from non-clinical sources, clinical studies and post-marketing surveillance has to be taken into consideration in safety assessment.

CORROSION STANDARDS

ISO 17475:2005 "Corrosion of metals and alloys - Electrochemical test methods - guidelines for conducting potentiostatic and potentiodynamic polarization measurements" applies to corrosion of metals and alloys, and describes the procedure for conducting potentiostatic and potentiodynamic polarization measurements. The test can be used to characterise the electrochemical kinetics of anodic and cathodic reactions, the onset of localised corrosion and the repassivation behaviour of a metal.

ISO 11463: 1995 "Corrosion of metal and alloys - Evaluation of pitting corrosion" gives guidelines on the selection of procedures that can be used in the identification and examination of pits and in the evaluation of pitting corrosion.

ISO 11845: 1995 "Corrosion of metals and alloys – General principles for corrosion testing" contains the most important general guidelines for carrying out corrosion test under conditions of constant immersion.

ISO 12732:2006 "Corrosion of metals and alloys – Electrochemical potentiokinetic reactivation measurement using the double loop method (based on Cihal's method)" specifies the method for measuring the degree of sesitization (DOS) in stainless steel and nickel-based alloys using the Double Loop Electrochemical Potentiokinetic Reactivation (DL-EPR) test (based on Cihal's method).

ASTM standard G150-99(2004) "Standard test method for electrochemical critical pitting temperature testing of stainless steels" covers a procedure for the evaluation of the resistance of stainless steel and related alloys to pitting corrosion based on the concept of the determination of a potential independent critical pitting temperature (CPT).

HIP STANDARD (AS AN EXAMPLE OF A JOINT STANDARD)

SFS EN ISO 14242-1 covers the principle for the simulator testing of artificial hip joints, the specifications for the reagents and materials and apparatuses used in the testing and describes the simulator testing procedures and testing reports.

SFS EN ISO 14242-2 covers the measurement methods for the wear testing of artificial hip joints. The two methods described are the gravimetric method and the dimensional change method. The standard gives the principles for the testing methods, specifications for the reagents, materials and apparatuses used. Description of the preparation of test specimen, testing procedures and test reports are given.

3. Metals

3.1. Overview of metals

The most widely used metals in medicine are gold and other precious metals, surgical stainless steels, cobalt chrome alloys, titanium and its alloys and mercury-based alloys. Metals are divided to light and heavy metals with 5 g/cm^3 as the cut-off. Aluminium and titanium are light metals, whereas other metals mentioned below are heavy metals. Usually metals have a high chemical reactivity, except for the precious (noble) metals, which as a result usually occur as pure elements in nature. Many metals also contain various alloying elements and/or impurities, which are of importance for their physical and chemical properties, as well as for their biocompatibility. Biocompatibility refers to the ability of a material to appropriately interact (including inert behaviour) with the host in a specific location, e.g. in blood or bone.

Most metals have metallic lustre if not oxidized. Metals form positive ions in solutions and occur in metallic compounds only as positive ions. Metal oxides form hydroxides rather than acids with water. Due to their structure and chemistry, metals

are subjected to a special form of degradation, known as corrosion. However, when used in its broader sense, the word corrosion can refer to any environmental degradation of polymers, ceramics or polymers.

If the atoms of a material are organized into definite repeating pattern the material is called crystalline (in contrast to amorphous materials, Figure 2). The smallest repeating unit of a crystal is called unit cell. The orientation of the atoms in the unit cell defines the crystal structure. There are seven crystal systems defined by the geometry of the unit cell, i.e. by the lattice parameters. These systems can be combined with six different lattice centerings, i.e. adding symmetrical lattice points: no extra points, at the centre, centred on all faces or centred on two opposite faces (three options). In theory, there are 42 different combinations but in a closer inspection some of them are found to be identical with each other resulting in 14 different geometric arrangements (or Bravais lattices) into which all crystalline solids fit. The crystal structure is usually not perfect, but contains different defects, such as point, line and plane defects.

If the repeating pattern extends trough the entire piece of material it is called monocrystalline, whereas a material consisting of multiple (mono)crystals is called polycrystalline (Figure 2). The average size of the crystals in a polycrystalline material is called the grain size. If the long range order lacks completely from a material, it is called amorphous. Metals are usually polycrystalline materials and the most common crystal structures found in metals are body centred cubic (bcc), face centred cubic (fcc) and hexagonal close packed (hcp) with atomic packing factors of 0.68, 0.74 and 0.74, respectively (Figure 3). Packing factor refers here to the volume of space taken up by the metal atom spheres in a unit cell. The densest possible packing of equal-sized spheres is achieved with fcc and hcp structures, where the spheres occupy 74.05 % of the space.

Metals can be allotropic which means that they can exist in different crystal structures. E.g. iron has bcc (alpha-iron) structure at room temperature but exists in fcc (gamma-iron) between 900-1400 °C. Amorphous metals or glassy metals are a relatively new innovation and their full commercial potential is yet to be explored. These materials posses interesting physical properties such as high strength and they are used on e.g. surgical blades (Liquidmetal Technologies).

There are not enough electrons for the metal atoms to be covalently bonded to each other. In metallic bonds the valence electrons are relatively free, delocalized and only loosely held to the positive metal atom ion cores, which makes the bonds non-directional. There is a strong electrical attraction between the immobile positive metal ions and the mobile electrons, which makes the metallic bond.

Electrons can readily move in the crystal, so that metals conduct electricity which subjects them to galvanic corrosion. Because of the free electrons in metals, the thermal conductivity of the metals is usually higher than that of ceramics (although aluminium oxide has a high thermal conductivity) and of polymers, which are bonded by ionic and covalent bonds, respectively. For the same reason, metals feel cold. Melting point of the metals is, due to the strength of the metallic bond, usually quite high (e.g. Al 660 °C, Fe 1538 °C and Ta 3017 °C). However, mercury (MP -39 °C), caesium (MP 28 °C) and gallium (MP 30 °C) are liquid at room temperature and tin has a melting point of 232 °C.

Due to the non-directional metallic bonds neighbouring crystallographic planes can move relatively easily in relation to each other without causing a catastrophic failure of the material. This makes metals malleable and ductile (capable to undergo plastic deformation). However, cold working (or strain hardening, e.g. forging) deforms

individual crystals and introduces dislocations rendering the further formation of dislocations more difficult and the metal stronger.

Metals can also be strengthened by introducing impurities (or adding them intentionally to alloy), grain size diminution and precipitation. When adding alloying elements, substitutional replacement means replacing lattice atoms, whereas interstitial replacement means placing atoms between lattice atoms. Heat treatments, such as annealing and quenching, can be used to alter the grain size or to generate precipitates of a harder phase. In the latter case the harder phase acts as the disperse phase in composites, e.g. cementite (Fe_3C) in ferrite (α) iron matrix.

An alloy is a combination of two or more metals, or a metal and a non-metal with characteristics of a metal. Alloys are usually prepared by mixing the molten components and then cooling the mixture. If an alloy contains high percentage of iron then it is called ferrous alloy (compared to nonferrous metals/alloys that do not contain iron or contain it in relatively small amounts). Solid solution alloys are homogeneous mixtures of substitutional (e.g. $TiAl_6V_4$) or interstitial (e.g. C in steel) type. Substitutional alloys are made of two components with similar atomic radii (±15%) and bonding characteristics. In such alloys, one atom can substitute the other so that the solute atoms can take the positions of the solvent and occupy regular lattice sites. In interstitial alloys the smaller (usually a non-metal) of the two atoms has a radius of only approximately half of the larger one. Therefore, the smaller atoms fit into the spaces or interstices between the larger atoms and the solute occupies interstitial sites in the metallic lattice. The alloy produced is stronger than the pure metal. Steel is an interstitial alloy of iron and carbon, which contains up to 1.7% carbon. In contrast, heterogeneous alloys are non-homogeneous dispersions containing at least two different phases. An intermetallic alloys is, instead of being a solid solution, a compound formed of two different metals and has a definite chemical composition (e.g. $CuAl_2$). The chemical formula dictates the ratio of its components and its chemical properties and crystal structure are different from the parent metals. Naturally, an alloy can be a combination of the options mentioned above.

3.2. Biomechanical properties

From the materials science's point of view human implants are a very demanding but not a unique challenge and thus normal material testing methods yield useful information for their development. For example, most physical properties (Table 1) of a material are obtained simply by measuring its strain under stress (Figure 4). The stress is usually tension but also shear, torsion and compression is used. The latter is used especially with brittle ceramic materials.

Table 1. Mechanical properties of selected biomaterials

When the deformation is elastic, or "recoverable", the stress and strain are proportional, stress = $E \times$ strain. The coefficient E defines the *Young's modulus* or *modulus of elasticity* and its unit is Pa – the same as for the stress because in the formula the strain is relative. If the proportionality is not linear the coefficient has to be determined using e.g. tangent or secant modulus of the stress-strain diagram. The *modulus of elasticity* describes the materials ability to resist elastic deformation and can therefore be referred as the stiffness of the material. *Resilience* describes the materials maximum ability to store and release energy when loaded and unloaded to

the yielding point. Consequently, its unit is J/m^3 which can easily be derived to Pascal (Pa).

When the stress is so high that the material can no more reassume its original shape the material starts to yield and the deformation is plastic. For most metals the transition from elastic to plastic is gradual and therefore the exact starting point of yield is difficult to define. To overcome this problem a strain offset line parallel to the elastic part of the stress-strain curve is drawn so that the two curves intercept. Normally the offset sift is 0.002 towards higher strain. This level of stress – or more likely the material's ability to resist it – is called *yield strength*. For materials with nonlinear elastic stress-strain behaviour a certain value of strain (e.g. 0.005) is used to define the stress.

If the stress is further increased it reaches the point above which the structure can no more resist a rupture under continuous load. This point describes the *tensile strength* (*ultimate strength*) of a material. *Ductility* indicates the amount of plastic deformation at the point of fracture and is expressed either in terms of percent elongation %EL or percent area reduction %AR. The first one defines the percentage of strain whereas the latter defines the percentage reduction of the cross section due to the elongation. The opposite of *ductile* is *brittle* whereas *anelasticity* refers to time dependent recovery of elastic deformation. *Toughness* describes a materials ability to absorb energy before it breaks. To be *tough* a material should have both *strength* and *ductility* and thus *ductile* materials are often *tougher* than *brittle* ones.

Hardness is perhaps the most common way to obtain information on a material mainly because it is fast and easy to measure and because it gives valuable information for the testing of the tribological properties. Also, because *hardness* is another measure of a material's ability to resist plastic deformation it gives an indication of other mechanical properties. For example, for most steels the *tensile strength* is roughly 3.5 times the *Brinell hardness*.

The earliest way of determining the *hardness*, used mainly by mineralogists, was to compare which material could scratch others. Of such systems the best known is the ten step Moh's scale in which the hardest material that no other materials can scratch, diamond, is represented by number ten and the softest, talc, by number one. Since then numerous hardness scales based on the principle of making indentations have been developed. A probe of a known geometry is pressed with a constant force on the material under inspection and the size of the indentation defines the hardness. The most common hardness scales based on indentation are Shore, Brinell, Knoop, Rockwell and Vickers. A more sophisticated method used especially with thin films and hardest materials is the nanoindentation in which a hard, very sharp tip is pressed into substrate and the shape and the hysteresis of the load-displacement curve is recorded and the *hardness* is calculated. Sometimes these apparatus are combined to perform *nanoscratch* and *nanowear* measurements.

Fatigue testing gives information on a material's ability to resist cyclic loads. Such a load, preferably similar to real conditions, is applied on a test piece until it breaks. By repeating this experiment with different stress amplitudes a 'stress versus number of cycles to failure' (*S-N*) curve is obtained. The stress level below which fatigue failures do not exist is called *fatigue* or *endurance limit*. For example, for most steels this limit varies between 35 and 65 % of the tensile strength. However, there is usually a considerable amount of statistical variation involved in this kind of data. Also, some materials, such as aluminium and most other nonferrous alloys, do not have a *fatigue*

limit. Therefore, statistical methods are often used to define a suitably low failure probability (Callister 2000).

Good and versatile basic tools for evaluating, testing and screening of the tribological properties of new materials and their combinations are pin-on-disk and pin-on-flat testers. During testing a pin of known dimensions slides on a circular or reciprocating track chafing a flat specimen. Usually the pin is made of a harder material and its wear can be neglected. A typical implant related test arrangement would be a CoCrMo pin sliding on a polyethylene slab.

The load pressing the pin down, the sliding speed and the environmental parameters such as temperature, composition of surrounding liquid or gas, humidity of the surrounding gas etc. can be adjusted accurately. The number of cycles and the force needed to prevent the pin assembly from moving are recorded simultaneously during the test. The wear of the materials can be measured using several methods. The simplest and most straightforward method is to measure the physical dimensions of the wear track for example with a profilometer. The wear can also be measured using methods more common in simulators e.g. weighing the test pieces, filtering and analysing the surrounding liquid or, if the materials are hard and the wear is minute, measuring the profile of a marker scratch (Anttila *et al.*, 1999).

The data recorded before, during and after the measurement is used to calculate the contact pressure, friction, sliding distance, wear volume and wear factor. The wear factor, *k*, is obtained by dividing the wear volume with the load and the sliding distance and is normally expressed in terms of mm^3/Nm. It gives a relative number that can be used to compare the wear resistance of materials. However, when comparing materials a good testing practice is to use similar conditions for all the materials to avoid scale errors. For example, the contact surface area may change significantly if the wear is excessive biasing thus the results on the favour of less wear resistant materials.

The most important testing method for biomechanical components, apart from *in vivo* testing, is the use of implant simulators such as hip and knee simulators. The simulators mimic the movements of human joints and the loads associated with them providing tribological and endurance information simultaneously.

The human walking gait cycle was first described by J. P. Paul in 1967 (Paul 1967). It is still used as the basis of the ISO standard, which defines the cyclic loading used in hip implant testing. Paul gait curve and the simplified ISO standard are compared in Figure 5, which relates them to different phases of the gait cycle. With knee implants the loads are somewhat more complicated. The most important standards for knee and hip implant testing are ISO 14242 and ISO 14243.

3.3. Corrosion

Corrosion, gradual degradation of materials due to electrochemical attack, occurs in the electrolytic environment of the human body. Several forms of corrosion are recognized. 1) All metals in electrolytic solutions are subjected to certain amount of uniform attack or overall corrosion. However, the metallic materials typically employed for use in human body show a high resistance against active, uniform dissolution, as they spontaneously form thin but highly protective oxide layers (so-called passive films) on the metal surface. Such passive metals can be susceptible to special types of localized corrosion. 2) Crevice corrosion begins in narrow crevices containing fluid, e.g. between a screw and a plate. Local depletion of oxygen accelerates corrosion by impairing the passivating surface oxide layer (leading to

depassivation of the surface). Changes in the local electrolyte composition and pH also contribute to propagation of crevice corrosion. 3) Similar mechanisms are also active in pitting corrosion; however, in this case the pit initiation is a first step (which is not required in crevice corrosion, as the crevice already can be considered as a pit site). Pit initiation typically takes place at surface heterogeneities, such as inclusions, intermetallic particles, or precipitates. 4) Galvanic corrosion occurs between two different metals as electrochemical corrosion, due to a difference between their electrochemical potentials. 5) The same mechanism is also active in intergranular corrosion due to precipitations at the grain boundary. This leads to formation of internal galvanic couples between the bulk matrix and the surface in the vicinity of the grain boundaries, as depletion of alloying elements present in the grain boundary precipitates takes place. 6) Leaching is a form of selective corrosion, which occurs, not at the grain boundaries, but within the grains themselves. 7) Fretting corrosion refers to corrosion at *contact* areas between materials under load subjected to vibration and slip. 8) Tension corrosion (or stress corrosion) refers to corrosion of metal subjected to stress, e.g. bending. This will create electrochemical differences between the surfaces subjected to tensile vs. compressive stress. Corrosion is also accelerated if the tensile stress leads to a rupture of the passivation layer.

3.3 Corrosion testing

Since corrosion is an electrochemical process, it is usually studied by electrochemical methods. The most common and relatively simple electrochemical experiment used in the study of orthopaedic alloys is the potentiodynamic polarization curve. Potentiodynamic curves record the current related to the electrochemical reaction as a function of electrode potential impressed to the electrode. Potentiodynamic means that the electrode potential is changing linearly with time, so called sweep rate *dE/dt*, within the cathodic and anodic potential limit. Polarization curves are usually presented as current density (*j*) as a function of potential applied (*E*). To perform potentiodynamic curves one needs a potentiostat instrument and an electrochemical cell (Figures 6A and 6B). The behaviour of a metal in a certain solution depends on the thermodynamics and kinetics of both metal dissolution (anodic or oxidation reaction; $M \rightarrow M^{n+} + ne^-$, where M is metal in its elemental or zero valence state) and the balancing process (cathodic or reduction reaction; $X^{n-} + ne \rightarrow X$) (O'M Bockris and Reddy 2000). A typical anodic potentiodynamic curve is schematically presented in Figure 7.

Anodic potentiodynamic curves recorded for three most common orthopaedic alloys, titanium-based alloys, stainless steel and cobalt-based alloys in Hank balanced physiological solution are presented in Figure 8 (Milošev *et al.*, 2000a, Milošev and Strehblow 2000, Milošev and Strehblow 2003, Hodgson *et al.*, 2004).

Potentiodynamic curves give information about the susceptibility of a certain metal to corrosion and passivation, on the span of the passive region, transpassive oxidation, etc. Quantitative data on the corrosion potential and current density is obtained, although it is more convenient to get these data from the linear polarization measurement and Tafel plot. The latter are performed in the vicinity of the corrosion potential and are less destructive. Other electrochemical methods include potentiostatic (current measured as a function of time at constant potential), galvanostatic method (potential measured as a function of time at constant current), and electrochemical impedance spectroscopy. Electrochemical impedance is usually

measured by applying an AC potential to an electrochemical cell and measuring the current through the cell. The response to this potential is an AC current signal, containing the excitation frequency and its harmonics. This current signal can be analyzed as a sum of sinusoidal functions (a Fourier series) and provides parameters like corrosion rate, capacitance of the interface, etc. The advantage of the impedance technique is that is does not strongly change the electrochemical equilibrium, as only a small sinusoidal potential disturbance is applied to the sample, Therefore, this technique allows to monitor the corrosion of the sample as a function of time.

Several standards are available for performing the electrochemical measurements, for example: ISO 17475:2005 "Corrosion of metals and alloys – Electrochemical test methods – Guidelines for conducting potentiostatic and potentiodynamic polarization measurements", ISO 11463: 1995 "Corrosion of metal and alloys – Evaluation of pitting corrosion".

Corrosion testing can be performed also by non-electrochemical methods, i.e. weight-loss method, where the sample is suspended in a solution and weight of the sample is measured at regular intervals over a longer period of time (Pletcher and Walsh, 1990). Assuming that the change in weight represents only a loss of metal to the solution, it can be converted to mol/cm^2 (= rate) or a corrosion current in A/cm^2 can be calculated from the relation j_{corr}/nF = rate in mol/cm^2 (Pletcher and Walsh, 1990). Corrosion engineers usually express it in microinches/year. The data obtained from such a testing are rather limited and do not describe the corrosion mechanisms. Moreover, in the case of high corrosion-resistant passive materials the overall mass loss is quite small (as typically only localized corrosion will take place). This further limits the usefulness of weight-loss measurements.

4. Metals used in joint replacements

4.1. Surgical stainless steel

Pure iron (containing a maximum of 0.006 % carbon at room temperature), wrought iron (< 0.15% carbon) and cast (pig) iron (containing 2.1-4 % carbon) have at room temperature the bcc (α-iron, ferrite) crystal structure and they are (ferro)magnetic. They have poor mechanical properties and easily become rusty and corroded. Steel, an alloy of iron and carbon, contains maximum 1.7 % carbon, which at such concentrations increases strength. Carbon steel can be further processed to stainless steel to diminish corrosion. Stainless steel is an alloy of carbon steel and chromium as a major alloying element; stainless steel contains typically at least 12 % chromium. As a result of addition of the chromium, the surface of steel produces a thin and relatively durable passivating oxide layer, which protects against corrosion (rust). The passive film is highly enriched with Cr-oxide. Corrosion properties can be further improved by the addition of molybdenum and nickel. An addition of 2-6 % of Mo efficiently increases the resistance against pitting corrosion in NaCl-containing solutions. Nickel stabilizes the austenitic (γ-iron), face-centred cubic (fcc) phase microstructure of the steel (Fe-Cr steels are ferritic or α-iron). Austenitic steel is nonmagnetic, which eliminates movement of e.g. vascular stents and heating during magnetic resonance imaging (MRI), although metal-induced artefacts remain. The properties of steels can also, in addition to alloying, be modified by different type of heat treatments leading to microstructural changes. Hard martensite steel for e.g. piano wire is formed by rapid cooling (quenching) of austenite steel so it has the same

chemical composition but the atom spheres have arranged to a different tetragonal crystalline structure.

Due to this versatility, there are thousands of different brands of steel. At least 50 different types of steel are commercially available and approximately 20 of them are used as biomaterials. However, only some brands, for example American Iron and Steel Institute (AISI) austenitic stainless steel (AISI 316, 0.08 % carbon) and its low carbon derivative AISI 316L (<0.03 % carbon), are widely used.

Steel is relatively cheap compared to other metals. The iron and low-carbon alloyed, chromium (17-20 %) containing stainless steel used in medicine also usually contains 2-4 % molybdenum and 12-14 % nickel, and in addition small amounts of other elements. Corrosion has been minimized to minimize the release of these components as they could lead to toxic, allergic and various other symptoms. For example, nickel can cause toxic and allergic reactions. Iron release from steel can contribute to bacterial infections by acting as an iron source for bacteria. Iron is a reactive transition metal able to catalyse production of hydroxyl radicals in Haber Weiss–reaction. Wear debris formation increases the effective biomaterial surface, which increased corrosion. This can increase the iron burden of the body. Normally the body contains approximately 3-4 grams of iron. Clinical experience and accumulated knowledge suggest that human body tolerates relatively well leachables from surgical steel implants. Still, steel is mostly used in applications, which are temporary so that the implants are removed after use, or as coated implants. Typical applications are plates, medullary nails, screws, pins, sutures and steel threads and networks used in fixation of fractures. Use of steel in joint replacement has diminished since new cobalt- and titanium-based materials have been taken into use.

Production method and the microstructure of metal affect its mechanical properties. Regular AISI 316 has a relatively good yield point in traction, approximately 200-250 MPa. If a higher yield point is required, cold processing is used. Production defects and improper design increase the risk of fatigue fracture. Fatigue refers to a failure of an implant under repeated cyclic stress below the ultimate stress level. Metal implants usually fracture based on fatigue rather than mechanical overloading. For joint replacement of the large weight carrying joints the fatigue resistance during 10^7 cycle testing should be at least 400 MPa. Surgical steel has a relatively good fatigue resistance, approximately 350-400 MPa. Walking exposes a hip implant to approximately 10^6 walking cycles per year. The metallic stem of the total hip would easily last such loading. In reality, total joints are not subjected to such a high load. 400 MPa corresponds to 4000 kilograms/cm^2. Thus, in practise metallic stems should last indefinitely. Improper design, material defects, wear and corrosion can, however, diminish the fatigue resistance.

AISI 316L stainless steel has a relatively good corrosion resistance, but compared to cobalt- and titanium-based alloys is sensitive to crevice and pit corrosion. Therefore, steel implants should not have porous surfaces. Large surface area, i.e. porous surface or debris, increases leaching of implant components and additives.

AISI 316L steel is relatively heavy, its density being approximately 8 kg/dm^3. The coefficient of friction of steel against polyethylene is approximately 0.10, but under *in vivo* circumstances only 0.02. In a natural mixed mode lubricated joint the coefficient of friction has been estimated to be approximately 0.001-0.025 (0.001-0.01 for pressure film lubrication and approximately 0.1 for contact point lubrication). High coefficient of friction increases the formation of debris. In a gliding pair consisting of metal-UHMWPE (ultra high molecular weight polyethylene) the plastic polymer is naturally more easily worn than the hard metal. Sir John Charnley started to use steel

stems fixed with polymethylmethacrylate (PMMA) and cup produced from polyethylene. This configuration is still used as the golden standard in total joint replacements. Titanium- and cobalt-based alloys have better corrosion resistance. Therefore, titanium- and cobalt-based alloys for stem implants have largely replaced the AISI 316L stems.

Steel is approximately ten times stiffer than the cortical bone. Most of the steels currently used have an elastic modulus of approximately 200 GPa. When such stiff steel is used, load is carried by steel implant and the bone is not subjected to normal loading any more. Use of bone cement as an interface decreases this stress shielding effect, because the elastic modulus of bone cement is much lower than that of the steel and as the cement mantle forms an interface. Fixation of stiff steel implants is therefore done with bone cement. Use of steel implants can lead to periprosthetic osteoporosis and to pathological fractures. Stiffness of metal implants is also affected by their design.

Above the elastic limit has been reached, metals can after yield point undergo extensive plastic deformation under stress before (ductile) failure. Ductility is thus the maximum strain that a material can withstand before undergoing ductile failure. The non-discriminate nature of the metal atoms for neighbours makes it possible for them to change their relatively position under load, especially when dislocations are present. Therefore, they are ductile, not brittle like ceramics.

The corrosion resistance of steel is much improved by the passivation layer, which is 1-5 nm thick and has a low ion conduction capacity. This thin layer consists of hydrated oxides and contains more chromium compared to the composition of the bulk alloy. Corrosion and biological body fluids affect the composition of this passivation layer. The protective effect of the passivation layer is decreased by heterogeneities in the microstructure, for example at the site of chromium carbides and MnS inclusions. Defects in the passivation layer can lead to localized corrosion.

4.2. Titanium and its alloys

Titanium is named according to “Titans”, who were sons of the Earth Goddess Gaia in Greek mythology. $TiAl_6V_4$, which is a hcp-bcc alloy (hcp = hexagonal close packed, bcc = body-centered cubic), is now widely used in orthopaedics. Also commercially pure hcp titanium CPTi is used, particularly for dental implants. $TiAl_6V_4$ has a stress yield of approximately 900-1000 MPa and its fatigue resistance at 10^7 cycles is 600-700 MPa.

The elastic modulus of titanium is 110 GPa, which is only half of that of surgical stainless steel or cobalt-based alloys and five times that of cortical bone. This leads to more physiologically sound stress distribution in the peri-implant bone. Therefore, cement as an intermediate layer used for stress distribution in steel and cobalt-based implants, would not seem to be so important when titanium implants are used. To guarantee cementless fixation by bone in-growth and micromechanical interlocking instead, porous-coated implants are often used (Figure 9C). Pore size (e.g. 50-400 μm), pore interconnectivity (e.g. 75-150 μm), particle interconnectivity, volume fraction porosity (e.g. 30-40% for spherical beads), and the area coated (proximal part) are important for such a fixation. The other possibility is hydroxyapatite coating to allow direct chemical bonding (see under hydroxyapatite). Lately, a new titanium alloy, which also contains zirconium and niobium, has been developed (for example $TiZr_{13}Nb_{13}$). These alloys share a high strength and low elastic modulus (65-80 GPa). Nickel-titanium shape-memory alloy (Nitinol) implants can be deformed but return to

its original shape upon heating. Titanium-based biomaterials have better osteoconductive properties than cobalt-based materials. A titanium-based product (ReGenerex®) similar to tantalum Trabecular Metal® will enter the market in the near future.

Titanium is relatively light, its density being only 4.51 kg/dm^3. This is only approximately half of other biomaterial metals. Wear resistance of titanium is, however, not so good. This can be improved by eloxation (Eloxalverfahren, oxidation treatment), ion implantation and titanium nitride coating.

$TiAl_6V_4$ alloy has better corrosion resistance than cobalt-based materials and surgical steel. This is because a thin oxide (TiO_2 or titania) layer spontaneously formed on the surface of titanium-based implants protects it against corrosion. The TiO_2 passive film is very stable, and Ti and its alloys show a high resistance against pitting corrosion in NaCl-containing solutions. Wear may damage this protective oxide layer, but this loss is rapidly replaced with so called repassivation. This process produces so much oxide, that the peri-implant tissues gradually become dark black. This metallosis can be quite dramatic as seen in revision operation, but its biological effects are usually harmless, although it can induce necrosis in periprothetic tissue.

Another possible impact of the use of $TiAl_6V_4$ alloy is the fact that it contains aluminium. Aluminium is known as a cause of osteomalacia and has also been tentatively associated with dementia. However, aluminium and vanadium atoms are located randomly in titanium and do not form any particular aluminium-rich surface layer. Because corrosion resistance of titanium-based alloys is good and the bonding forces strong, no significant amount of aluminium is released. No reports of osteomalacia or dementia have been described upon use of titanium-based implants.

The main disadvantage of CPTi and to some extent also of $TiAl_6V_4$ compared to F75 Cobalt-based alloys is that it is relatively soft. Vickers Hardness number for F75 cobalt-based alloy is 300-400 compared to 120-200 for CPTi and 310 for $TiAl_6V_4$. The corresponding figure for the AISI 316L steel is 130-180.

4.3. Cobalt-based alloys

Cobalt comes from the German name “kobald” meaning “goblin” or evil spirit. Cobalt-based alloys contain usually 30-60 % cobalt and approximately 20-30 % chromium. Chromium has been added to improve corrosion resistance and molybdenum to increase strength. Cobalt-based alloys can also contain other elements, such as wolfram, iron, manganese and silicon. The main types are cobalt-chrome-molybdenum alloy, which is produced by casting, and cobalt-nickel-chromium-molybdenum, which is usually forged. In casting, molten metal is poured or pressured into a mould, usually with little pressure because the material is in a molten state. Following solidification, the article is removed by a process known as demoulding. Casting method has several different modifications, which can be named according to the mould (e.g. sand, investment/lost wax, shell, plaster, ceramic) or the force used to move the molten metal or perhaps some other feature of the casting method (gravity, pressure, rotatory, vacuum, squeeze, slip, rheocasting/thixocasting, which processes semisolid thixotropic metal etc). Forging utilizes ductility of metals, which makes it possible to apply heat and compressive force to metal to obtain plastic deformation to a desired shape.

The most widely used cast cobalt-based $CoCr_{29}Mo_5$ (F75 and F76) alloys have yield points (yield strengths) approximately 450-800 MPa and the nickel containing $CoNi_{35}Cr_{20}Mo_{10}$ (F-562) alloy 950 MPa. The fatigue resistances are approximately

200-950 MPa and 350-550 MPa for 10^7 cycles, respectively. As for other metals, production methods and micro-granularity modify their strength. The elastic modulus of cobalt-based alloys is usually 200-300 GPa. Therefore, PMMA bone cement has to be used for implantation of cobalt-based devices. The coefficient of friction between $CoCr_{29}Mo_5$ – polyethylene gliding pair is *in vitro* with the use of synovial fluid 0.16 and *in vivo* 0.04.

Cobalt-based alloys have a good corrosion resistance, although some corrosion occurs (Table 2). Accordingly, measurable cobalt and chromium ion concentrations have been observed in blood tests. International Agency for Research on Cancer ARC has classified cobalt to group 2B or possibly carcinogenic to humans. In contrast, trivalent chromium is an essential trace element (a daily uptake of 60 μg is necessary) and, therefore, chromium (III) and metallic chromium belong to group 3 and are not classified as carcinogens, although chromium (VI) compounds belong to group 1 and are carcinogenic to humans.

Table 2. Element concentrations in serum in patients with joint replacement implants.

Cobalt-based alloys are not sensitive for galvanic corrosion and e.g. titanium and cobalt can be used together. However, surgical steel should not be used in contact with cobalt-based implants, because the relatively poor corrosion resistance of steel leads to rapid galvanic corrosion. Titanium and titanium-based alloys have the best crevice corrosion properties and are in this respect better than cobalt-based alloys, which again are better than surgical steel. Cobalt-based implants have very good tension corrosion properties (a combination of tension and corrosion) in spite of the fact, that the body fluids contain quite a lot of chloride, which facilitates tension corrosion. In general, the corrosion resistance ranking order from the most resistant to the weakest is $TiAl_6V_4$, $CoCr_{29}Mo_5$ and AISI 316L (Table 3).

Table 3. Corrosion resistance of three commonly used implant metals

4.4. Tantalum

Tantalum (Ta) is a chemically very resistant metal. At low temperatures (< 150 °C) tantalum is almost completely immune to chemical attack. Only hydrofluoric acid, acidic solutions containing fluoride ions and free sulphur trioxide have a significant effect on it. Hence, tantalum is completely immune to body fluids and it is also a non-irritating metal (CRC 82nd). The biocompatibility and excellent osseointegration properties have augmented the interest on the use of tantalum on the bone-implant interface of cementless implants. Due to its high chemical resistance it can also serve as a supplementary corrosion barrier when new protective coatings are developed (Kiuru *et al.*, 2002).

Bulk tantalum exists normally in body centred cubic (bcc) α-phase and is ductile and relatively soft (HV 0.9 GPa) material that can be easily drawn into e.g. fine heating filaments. However, some deposition conditions of tantalum coatings can produce tetragonal β-phase that is thermally unstable and brittle and may cause coating failures (Matson *et al.*, 2000). Globally the main uses of tantalum are in electrolytic capacitors, vacuum furnace parts, nuclear reactors and military industry (CRC 82nd).

In medical industry the high melting point (2996 ºC) and somewhat elevated manufacturing costs of tantalum have restricted the use of bulk tantalum and led to alternative approaches. The most common tantalum-based material used in human implants goes under trade name Trabecular metal®. In its manufacturing process carbon foam is tantalum coated with chemical vapour deposition (CVD). The resulting 80 % porous trabecular scaffold consists of 99 % tantalum and 1% vitrous carbon. The modulus of elasticity is 3 GPa and the pore size 550 µm allowing the bone growth into the material (Levine *et al.*, 2006). According to the manufacturer it approximates the physical and mechanical properties of bone more closely than any other prosthetic material (Bobyn *et al.*, 1999).

4.5 Particle disease

Some of the particles formed from metal are so small that they are phagocytosed. Monocyte/macrophages try to digest the metal (or polymer) particles, but without success. This can lead to recruitment of more haematogenous monocytes to the site of inflammation, their maturation to macrophages and multinuclear giant cells and organization to foreign body granulomas. This so called foreign body reaction is associated with local production of pro-inflammatory cytokines, such tumour necrosis factor-α and interleukin-1β. Various proteinases, including matrix metalloproteinases and cathepsin K, are produced. Finally, growth and differentiation factors are produced. These include macrophage-colony stimulating factor and receptor activator of nuclear factor kappa B ligand (RANKL), which further enhance formation of both foreign body giant cells and osteoclasts. Osteoclasts mediate periprosthetic osteolysis and in the long-term loosening. Foreign body reaction or “particle disease” is considered to play a central role in aseptic loosening of total joint implants. Therefore, it has been suggested, that the toxicity of cobalt-chrome could be an advantage. Phagocytosis of cobalt-chrome particles can lead to apoptosis and necrosis of macrophages and fibroblast. This could have a moderating effect on the foreign body reaction.

4.6 Clinical success of metals used in joint replacement surgery, divided into "Surgical stainless steel", "Titanium and its alloys" and "Cobalt-based alloys".

Aseptic loosening is the most common mode of failure of a total joint arthroplasty (Malchau 1993). Therefore, success will in this paragraph be considered only regarding this particular endpoint.

Metals are predominantly used for bodies of artificial joints that are intended to be incorporated to the adjacent bone either by biological fixation or by means of polymethylmethacrylate (bone cement) anchoring. Contemporary articulating surfaces are constituted of a metal part articulating with a plastic polymer (UHMW polyethylene in most cases), but other types of bearings such as ceramic on polyethylene, metal-on-metal, and ceramic-on-ceramic are also widely used. The last two types are only used in total hip arthroplasties. Titanium alloys are also used for articulating surfaces, but more rarely seldom. Their use for this purpose is not recommended due to low wear resistance (Salvati 1993, Massoud *et al.*, 1997).

It is convenient to consider clinical performance of the metals in the prosthetic bodies separately from the metals for the articulating part as they have different relationship to implant failures.

All constituents of a total joint arthroplasty may be involved in the pathways leading to clinical failure and can be considered as links in a chain, the weakest defining the overall level of performance. Bearing couple usually presents the weakest link due to release of harmful particles that constitute the first step in the cascade of macrophage- or lymphocyte-mediated periprosthetic osteolysis and final failure.

Statistical problems with outcome studies

Although clinical success of various prostheses have been reported in literature for over 40 years it is still controversial which type of implant is best for which patient. A valid comparison between two prosthesis designs can be made only if the patient populations are similar, if the outcomes are the same and are measured in a similar fashion using a similar follow-ups or adequate statistical techniques. The confusion originates particularly from the shortage of head-to-head comparisons in long-term randomised clinical studies of new designs with the already established prosthesis. Further uncertainty stems from the large and continuously increasing variability of prostheses in use, the incorrect or incomplete data presentation together with the lack of independent assessment or conclusions from inadequate follow-up.

Early studies usually lacked adequate methods for survivorship analysis and subsequent studies have often used surrogate variables such as “radiographic loosening” rather than revision surgery as the primary outcome measurements due to relative shortage of early revisions. “Loose” has, however, been defined in various ways that has added to the confusion. As only a few authors have used confidence intervals, the overall impression of the published results may be too optimistic.

Stainless steel

With the introduction of high molecular weight polyethylene cup paired to already then well documented stainless steel stem, both fixed with cement, for total hip arthroplasty in November 1962 Sir John Charnley originated the modern era of artificial joints.

No prosthesis seems to have surpassed the cemented stainless steel Charnley in terms of length of service and universality of its use. Thus, the cemented Charnley design should represent the golden standard to which all other prostheses shall be compared due to its widespread use and consistent reports of its outcomes. The same applies for the material it was made of, namely stainless steel. Initially, “flat back” polished stem made of EN 58J stainless steel was replaced with high nitrogen content stainless steel (0.35-0.50 %, ORTRON stem; De Puy International, Leeds, UK) due to high incidence of stem fatigue fractures (Wroblewsky, 1982).

Despite the diversity of institutions and authors reporting, an amazing consistency is seen in that in many studies, as long as 15 years after the index surgery, about 90 % of the prostheses among the surviving patients were still in situ. Some reports with 20 years or more of follow up indicate that at 20 years, between 80 and 90% of the prostheses will be surviving (Wroblevski *et al.*, 1998, Ahnfelt *et al.*, 1990, Berry and Hamsen 1998, Joshi *et al.*, 1993, Hozak *et al.*, 1990).

Cobalt chrome alloy

Many cemented prostheses made of cobalt chrome alloy have come close to or in certain studies even surpassed the cemented Charnley. One of them was certainly the

T(trapezoidal)28 (Zimmer, Warsaw, IN), which at least for more than 60 years old patients reached 95% of surviving hips at 15 years, however, if "radiographic loosening" was considered as failures over 35% of older patients failed (Amstutz *et al.*, 1998). The Saint George Mark I and Mark II have reached similar longevity with less than 30% of failure rate after more than 20 years of follow up (Engelbrecht and Kluber, 1998). Lubinus SP II Link has also shown adequate performance according to Scandinavian hip registries and head-to-head comparisons (Havelin *et al.*, 2000, Jacobsson *et al.*, 1995**).**

Cobalt-chrome alloy has also been used in cementless fashion with variable success. It seems that surface finish determines the overall osseointegration potential and thus achievement (Sotereanos *et al.*, 1995). Porous coating (pore size among 50 – 400 μm) results in highest in-growth potential. Cumulative probability of survival reached 96 % at 12 years for patients more than 60 years of age. Osteolysis was however seen in 40 % off cases (including patients younger than 60) at 10 years follow-up (Engh 1998). Some systems like Tri-lock femoral stems (DePuy, Warsaw IN) and PCA (Howmedica, Rutherford, New Jersey) have reached nearly 100 % and 95 % survivorship, respectively, after 12-15 years of follow-up (Pellegrini 1998, Kawamura 2001).

Titanium alloy ($TiAl_6V_4$ or Nb)

Titanium (Ti) alloys are widely used for the manufacture of orthopaedic implants in total hip arthroplasty both for cemented and cementless prostheses. Three main types of Ti-alloys are in use: commercially pure titanium (CPTi), $TiAl_6V_4$ and TiAlNb. The former being mostly used for low-profile cementless cups, i.e. Bicon® (Plus Orthopedics), Allofit® (Zimmer) TOP acetabualr cup system® (Waldemar Link). The properties of Ti-alloys include good biocompatibility, low modulus of elasticity and their resistance to fatigue and corrosion (Kohn and Ducheyne 1992, Willert H-G 1996). Cementless stems are more resistant to osteolysis and mechanical failure when compared with similar cemented stems (Emerson *et al.*, 2002, Laupacis *et al.*, 2002, Head *et al.*, 1995).

Cementless fixation

Based on their ability to allow bone in-growth Ti alloys are the material of choice for cementless fixation. There are innumerable types of cementless Ti-alloy devices uniformly showing excellent performance. In Europe one of the most popular is the Zweymuller type (Variall®, Zimmer, SL Plus®, Plus Orthopedics) showing excellent survivorship (Table 4). In some recent publications a titanium alloy stem (Corail®, De Puy Warsaw Indiana) and Anatomic Hip (Zimmer, Warsaw, Indiana) showed no cases of aseptic loosening after an average 11.5 and 10 years of follow-up, respectively, with no distal osteolysis and no thigh pain in the former (Froimson 2007, Archibeck 2001).

Table 4. Some recent clinical experiences with titanium alloy total hip replacements.

Cemented fixation

In contrast to the good results obtained for cementless Ti alloy stems, the results for cemented Ti alloy stems are inconclusive and need a more detailed discussion. Cemented Ti alloy monoblock stems were introduced in the 1970s (Mc Kellop and Clarke 1988, Sarmiento and Gruen 1985) and the initial results were satisfying. The mid-term results for CoCr headed stems, such as Bicontact® (Eingartner *et al.*, 2001) and Ultima® (Bowditch and Villar, 2001), were also promising showing a survival rate of 97 % at 10 and 7.5 years, respectively. Straight Muller stems made of TiAlNb with a ceramic head showed the revision rate of 2.5 % at average 6 years follow-up (Rader 2000). Intermediate results depending on the cementation technique and head material were reported on long term (Kovac *et al.*, 2006). Good long term results with 87.3% survival at 20 years were reported with Ceraver – Osteal® polished and titanim oxide coated stems which, however, were too combined with alumina on alumina coupling (Hamadouche *et al.*, 2002).

On the other hand, Maurer *et al.* reported an increased loosening of cemented straight Muller stems made of $TiAl_6Nb_7$ alloy compared to CoNiCr alloy stems at a median of follow-up of 7.7 years (Maurer *et al.*, 2001). Unacceptable failure rates of 4.5 % (Tompkins *et al.*, 1994), 9 % (Jacobson *et al.*, 1995) and 11.5 % (Jergesen and Karlen, 2002) at 4.8, 5 and 5.5 years, respectively, were reported for Ti alloy cemented stems, too. The results for Capital® modular Ti-alloy stems with either CoCr or TiN coated titanium heads were poor with 16 % loose femoral components at a mean follow-up of 26 months (Massoud *et al.*, 1997).

Surface finish of the titanium alloy stem and its elasticity undoubtedly has an important effect on the performance of the prosthesis, with more polished surfaces and larger (less elastic) designs performing better than rough and more elastic models (Collis and Mohler 2002, Sporer 1999, Maurer *et al.*, 2001, Sarmiento *et al.*, 1998, Sedel *et al.*, 1990, Le Mouel *et al.*, 1998, Jacobson *et al.*, 1995, Massoud *et al.*, 1997, Janssen *et al.*, 2005, Agins *et al.*, 1988, Kärrholm *et al.*, 1998, Emerson *et al.*, 2002, Jergesen and Karlen 2002). Increased cement-stem interface motion and, accordingly, fretting wear at the interface depending also on their surface finish and elasticity (Mc Kellop *et al.*, 1990, Jacobson *et al.*, 1995) resulted in increased generation of wear debris leading to aseptic loosening (Salvati *et al.*, 1993, Witt and Swann, 1991, Agins *et al.*, 1988, Milošev *et al.*, 2001).

Metals used for articulating surfaces

Metal-on-metal (often abbreviated to M/M) articulating surfaces were introduced for THRs during the same time as metal-on-polyethylene (MP). However, MM implants were largely abandoned because of some early failures and excellent early results of Charnley's low friction arthroplasty at about the same time. Long term problems with MP articulating hips that developed serious osteolyses and consequent loosening due to polyethylene particles induced wear (Willert *et al.*, 1978), together with favourable long-term results with selected patients with first generation M/M coupling that showed virtually no osteolysis after more than 20 years of performance (Kreusch-Brinker *et al.*, 1998) resulted in development of second generation of M/M bearing couples. In the contemporary M/M bearings, most of the critical design parameters that seem to ensure clinical success, i.e. high carbon materials, proper clearance between components, surface finish and roundness, can be achieved with modern manufacturing techniques. Metals differ by the manufacturer; castings or forgings are used for processing in various fashions, like-on-like material combinations are used in a vast majority.

Second generation of metal-on-metal couples made of CoCrMo alloy originated in 1988 with the introduction of the Metasul bearing couples (Weber *et al.*, 1992) with the intention to achieve better long-term clinical results than conventional THRs by minimizing and possibly eliminating polyethylene wear as a cause of osteolysis and aseptic loosening (Weber *et al.*, 1992). All contemporary metal on metal couples are considered second-generation implants.

The manufacturers use $CoCr_{28}Mo_6$ alloys (ASTM F799 and ASTM 1537, ISO 5832-12) for the production of MM THRs. They differ in their content of carbon which might be clinically important. High-carbon alloys contain > 0.2 wt. % carbon, and low-carbon alloys < 0.07 wt. %. Metasul® for instance, is a high-carbon CoCrMo alloy, Sikomet SM 21® is a low-carbon alloy, whereas Ultima® is a combination of low-carbon head and high-carbon cup (Milosev *et al.*, 2005). Low-carbon and low-carbon-on-high-carbon combinations express higher wear rate (Firkins *et al.*, 2001, St. John *et al.*, 2004) and are related to higher number of particles released in the periprosthetic tissue being thus implicated in the development of osteolysis.

Use of M/M bearing in total hip surgery results in several advantages such as: 50 - 100 x decreased wear rate over conventional polyethylene in the laboratory tests (Mc Kellop 2001), 40 x decreased linear wear and 200 x decreased volumetric wear over conventional polyethylene *in vivo* (Rieker 2002, Rieker *et al.*, 2004), and possibly as a consequence of this, rare appearance of osteolysis (Milosev *et al.*, 2006, Park *et al.*, 2005). M/M bearing allows the use of large femoral heads with their improved stability, range of motion, and superior lubrication, concomitantly avoiding the risk of bearing fracture. With some exceptions (Bösch and Legenstein, 2004 , Park *et al.*, 2005, Milosev *et al.*, 2005), all involve low-carbon and low-carbon-on-high-carbon combinations, demonstrating excellent clinical results (MacDonald 2004).

There are disadvantages, too, including: biologic/carcinogenic concerns of metal ions elevations especially in patients with renal failure and in women in childbearing age (Milosev *et al.*, 2005, Ziaee 2007), that have been never confirmed but do not seem to exist with other bearings, and unclear but increasingly reported “deep” and partly local hypersensitivity to metals (Milosev *et al.*, 2005, Willert *et al.*, 2005, Hallab e*t al.*, 2001).

A summary of clinical results are presented in Table 5, which has been updated from our earlier paper in J Bone Joint Surg Am (Milosev *et al.*, 2006). It is reasonable to conclude that low-carbon M/M bearings produce inferior clinical results probably due to increased wear in comparison to high-carbon MM bearings.

Table 5. Literature analysis on clinical results obtained on metal-on-metal bearing hip implants. 5. Future trends

Resurfacing implants and mini-invasive surgery

Hip resurfacing arthroplasty was considered as an old unsuccessful orthopaedic concept that has undergone a resurgence of interest in the past decade with the advent of the second generation of M/M bearings in the 1990’. It is the most anatomical way of hip replacement, where the femoral head is not removed but instead we modelled, to allow the coverage with a low-profile resurfacing prosthesis ((Figure 10A, B, C and D). It provides superior stability for the hip joint and improved range of motion defined by individual head/neck ratio, normalized biomechanics while avoiding the problems of leg length inequality (as the sizes of the “ball” and the length of the

collum are anatomical). It conserves and preserves bone for a potential revision surgery.

The disadvantages besides those inherent to M/M bearings (MacDonald 2004, Milosev *et al.*, 2000, 2005, Hallab *et al.*, 2001) include demanding surgical technique not suitable for low-volume surgeon, increased exposure – more soft tissue releases, relatively small fixation area for the femoral component especially with tiny femoral heads, new potential modes of failure as avascular necrosis of the remaining bone and neck fracture (Shimmin *et al.*, 2005). The early and mid-term results seem promising at lest for a selected patient population (Amstutz *et al.*, 1998, De Smet 2005, Australian registry -http://www.dmac.adelaide.edu.au/aoanjrr/publications.jsp).

In the years after 2000, several articles emerged in the literature regarding minimally invasive hip and knee surgery (MIS). It can be performed from short incisions (Figure 9A), via which the femoral stem (Figure 9B) and a modular head (Figure 9C) are implanted. The issue became a major topic in contemporary orthopaedics with substantial media coverage that rose patient and surgeon interest. For all of the standard approaches a less invasive variant come into sight, each of them having its own propagators. Some were definitely supported and propagated by industry. In hip arthroplasty surgery mini anterior, mini anterolateral, mini direct lateral, mini posterior and a novel mini two incision (Berger 2003) dominated the literature. In the knee a mini subvastus, a mini mid vastus and a quad sparing approach were its counterparts.

The main advantages were claimed to be less or even no damage to soft tissues, a better cosmetic result, less blood loss and a quicker recovery after the surgery. The disadvantages included a potential of misplacement of the components and more tissue damage due to reduced vision and difficult extensibility of the approach when needed.

A special attention and extensive promotion was given to a novel two incision approach (Berger 2003, Berger 2004, Berry *et al.*, 2003). The authors claimed no muscle or tendon damage, rapid rehabilitation and even the potential for outpatient surgery. Soon after the early promotion heavy criticisms were published showing that no scientific data support the notion that two-incision approach is functionally better than other THA approach (Archibeck and White 2004). Cadaver work studies dispelled the belief that two-incision approach can be done without damaging muscle or tendon (Mardones *et al.*, 2005). The actual incidence of perioperative complications was dangerously high (Bal 2005, Pagnano *et al.*, 2005). In a direct comparison patients preferred other approaches when applied on the contralateral hip (Pagnano *et al.*, 2006).

Between conventional THR and resurfacing THR, there is a particular series of implants that require resection of the femoral head for the implantation but not the neck (Figure 12). Actually they are intended to be biologically fixed or in other words osseointegrated into the femoral neck bone. One of the first implants of this particular type was the Huggler-Jacob prosthesis in the eighties (Huggler and Jakob 1980). Today, there is a resurgence of this bone sparing designs. Among the most interesting are Gothenburg hip inspired by dental implants (Carlsson *et al.*, 2006a and b), DSP hip (Zimmer), the contemporary version of the Huggler implant (Jacob 2007) and Proxima and Silent hip (Johnson&Johnson). These short implants are bone friendly and very easy to implant even using the least invasive approaches (Santori *et al.*, 2005, Santori F *et al.*, 2006). On the other hand, they probably need a certain unloading period to allow integration. Their survival is very dependent on the proximal femoral bone quality. Even very limited osteolysis can be detrimental for

these types of implants. It is thus advisable to avoid polyethylene bearings with this particular design. There is some data regarding survivorship of these hips that show promising results that, however, can not compare to the best conventional hips.

Isoelasticity

Studies have shown that by increasing stiffness of the stem, either by stiffer material or by increasing cross sectional dimensions, the amount of load carried by proximal femur decreases, resulting in stress transfer and bone resorption in the proximal femur thus compromising the fixation of the proximal stem (Crowninshield *et al.*, 1980, Huiskes 1980, Lewis *et al.*, 1984). To overcome the mismatch between a stiff stem and the more elastic bone, the concept of isoelasticity was introduced in 1970s (Figure 11). This concept was based on the assumption that the implant and the bone should deform as one unit to avoid stress shielding.

Studies confirmed almost no loss of bone stock from the proximal femur or the acetabulum, even in cases that were clearly loose, with use of isoelastic implant (Niinimäki and Jalovaara 1995, Horne *et al.*, 1987). However, decreasing the stiffness excessively resulted in higher implant-bone or implant-cement motion leading to early debonding and failure (Trebše *et al.*, 2005). Computer-simulated models have proven high proximal stem/bone interface stresses, which may cause interface debonding and relative motions, possibly affecting implant loosening (Huiskes *et al.*, 1992, Burke *et al.*, 1991).

Thigh pain that occurs in different percentages in patients with bipolar THR is believed to be a result of stiffness mismatch between stem and bone. In one particular design (Anatomic Porous Replacement; Sultzer Orthopedics, Austin TX) the clinical incidence of thigh pain was significantly reduced after the stem was hollowed to decrease the stiffness below that of the bone (Dorr and Wan 1996).

Therefore, when introducing the concept of isoelasticity, one should aim for an optimal stem flexibility, to diminish stress shielding, but to keep interface stresses low enough. It is probably so that the optimal elasticity of an implant is different for every patient concerning bone quality, shape and dimensions; a task difficult to achieve even with a customized implant.

Coating of implants

Metal implants interact with their surrounding via their surface. The properties of the bulk can be fine tuned using specialized and purpose-designed coatings. Versatility and functionality has and will be extensively introduced to implants, which may have different functional domains, e.g. against bone or bone cement, and in an articular or modular gliding pair. One very promising approach is high quality amorphous diamond, rich in the sp3-diamond bonds, produced from industrial graffite using plasma acceleration in a pulse arc discharge setting. It basically eliminated formation of wear debris from the gliding surfaces and of corrosion products from implant surface in contact with body fluids (reviewed in Santavirta, 2003).

6. Aknowledgements

This study was supported and/or made possible by evo funds, Sigrid Jusélius Foundation, Finska Läkaresällskapet, COST 537 “Core laboratories for the improvement of Medical Devices in Clinical Practice from the Failure of the

Explanted Prostheses Analyses FEPA" and COST 533 "Materials for Improved Wear Resistance of Total Artificial Joints".

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