For submission to EU's 7th Framework Programme

**Surface modified Ti biocomposites for hip and knee joint replacements (SUMBIR)**

Programme objective: NMP-2007-4.2.3-1 Highly porous bioactive scaffolds controlling angiogenesis for tissue engineering

Hip and knee joint implants: visualisation

**Main output**

- New biocomposite materials for hip and knee joint replacements with increased capacity to fast tissue and bone resorption
- New fabrication technologies of biomaterials with highly porous surface layers
- Models of creation of composite structures, multiplex layers, and micro- and nanolayers
- Models of biochemical and biomechanical processes to occur in implant area
- Models of degradation of biomaterials caused by joint influence of mechanical stresses and human body environment during long term operation
- Computer tools for estimation of interrelations between surface microstructure, surface mechanical and physical properties, and human body environment
- New research procedures
- Expert system for lifetime prediction
Background

The endoprostheses of hip joint and knee joint are among the most popular implants. The titanium alloys have been applied for replacements of these two joints at early eighties but in clinical conditions an aseptic loosening of implants has been observed. As a result of this, the functional disturbances of bone - implant connections have occurred. This problem is still far from to be resolved and includes degradation of the implant, inflammation and degeneration of body surrounding implant, bone destruction, osteolysis and osteoporosis, aseptic loosening, improper biomechanical operation conditions. According to different reports, even in the U.S. a number of second total hip joint replacements comprises between 6% and 30%.

The majority of replacements is successful. However, the hip joints and especially knee joint implants have limited lifetime, which in first case may reach some 15-20 years, and in a second case - some 5-10 years. The another replacement of hip joint becomes very difficult for elderly patients and impossible in case of knee joint. That indicates for need to focus on research and development of new endoprostheses, of longer lifetime, more biocompatible and more resistant to all possible forms of degradation, with specific bioactive properties, exchanging stimuli with the surrounding tissue and inducing specific cellular reactions.

The better biocompatibility needs better both understanding of the processes occurring in human body in neighbourhood of the implant and implantation of special surface-structured endoprosthesis. The implant of the hip joint or knee joint must possess sufficient mechanical properties and chemical resistance and simultaneously to secure the efficient and fast biological binding of the implant, and bone and tissues, and appropriate biomechanical fitting. The possible solution may be an use of biocomposite implant with porous (scaffold) surface layer. The fabrication of such implant has not been successfully achieved yet and a number of possibilities is to be investigated.

The optimal implants are to be inspired by existing biological solutions of bone-tissue system. Therefore, the best solution, proposed here, is to design and fabricate the implant similar in structure and properties to such system: biological activity i.e. fast growth and high bond strength can be achieved by porous structure of the internal zone of surface layer (or the whole implant) and bioactive glass coating forming external zone of surface layer, i.e. sandwich construction with a contribution of scaffold (porous) layer. The further improvement of bioactivity and resulting strength can be obtained by composite dispersed structure of the layer, i.e. presence of hydroxyapatite inside the pores of metallic matrix (meshes of the scaffold). Finally, the external zone of metallic part needs modification by surface engineering or laser techniques in
order to also increase the biocompatibility and corrosion resistance. The use of composite metallic-ceramic implant seems the best idea to achieve also mechanical properties similar to those typical of bone materials of hip or knee joints.

The standard requirements for implants include: mechanical properties (yield stress, plasticity, Young modulus, fatigue strength etc.), physical properties (density, magnetic properties etc.), chemical properties (resistance to different forms of corrosion and wear degradation), biological properties (biocompatibility), and price. Thus, all the time one must take into account each of properties, and their interrelations. This problem is also unresolved, usually all properties are considered separately, no expert systems have been proposed to optimize the implant design and materials. The investigations of all possible factors which may affect the lifetime, together with response of human body, bone parts, tissues, and muscles, changing itself with increasing age, cannot be performed by normal procedures, needs more sophisticated approach by e.g. neural networks approach.

The behavior of an implant, its resistance to environmental degradation may be expressed as either chemical or mechanical degradation of oxide layer or dissolution of bulk of the alloy. The degradation rate of oxide layer mostly determines the dissolution rate of the bulk, i.e. metalosis rate. Therefore, corrosion of the alloy depends on structure, chemical and phase composition of the oxide layer, environmental factors like body fluid composition and temperature, and mechanical factors, like presence and forms of stresses and strains, the last associated with mechanical properties and thickness of the layer.

As to assess the possibility of mechanical or chemical dissolution of the oxide layer, one must take into account that it has properties of ceramic material. Such materials can be considered as relatively resistant to chemical dissolution, and prone only to some specific chemical reactions. The ceramics are also known as brittle species, with their resistance to brittle cracking extremely dependent on their thickness. Therefore, it is necessary to find a compromise between layer properties and its adhesion during long time of human existence, e.g. by FEM.

Dissolution of the bulk occurs as a consequence of a number of possible mechanisms of degradation/dissolution: mechanical damage of the layer resulted from wrong surgery procedure; mechanical breaking of the layer resulted from excessive strains; mechanical exfoliation of the layer resulted from decohesion at the interface layer-bulk, occurring at too thick layer and too weak layer-bulk bond strength; mechanical damage resulted from excessive wear; chemical reaction of some aggressive ions with titania layer (chemical corrosion); electrochemical corrosion resulted from unhomogeneity of the layer; wear-accelerated corrosion resulted likely from creation of chemical and electrochemical unhomogeneity; aging of ceramic oxide layer and formation of
short cracks; electrochemical and chemical dissolution of the metal bulk. There is again a number of factors which decide on dissolution rate in this area: dissolution kinetics of the bare metal, electrochemical characteristics of the surface, local environment, depolarization rates related to precipitation rate of corrosion products, oxygen or hydrogen ions’ diffusion etc., characteristics of corrosion tunnels, mechanisms and kinetics of diffusion of anions through crystal lattice, perfect and imperfect. Such factors and mechanisms are seldom discussed even if they decide on quantity of metal present in human body after many years.

After implantation, the internal human body is greatly disturbed, e.g. in distribution of blood to the bones and the ionic equilibrium. The presence of implant inhibits the defense mechanisms of the body leading to infection which can range from mild edema to chronic inflammation and alteration in bone and tissue structure. The direct response of the body to an implant is the development of a fibrous collagen sheath of low cellularity which encapsulates the implant and separates it from a normal body tissue. The capsule may contain an area of necrotic tissue adjacent to the implant surrounded by a region of chronic cellular infiltration. The thickness of the fibrous capsule depends on the corrosion resistance of the biomaterial, where the material producing the thinnest sheaths are the best tolerated by the human body. After implantation, elevated metal concentrations are often measured even in distant organs (e.g. liver, kidney and spleen), due to ionization, but also to the phagocytosing cells which circulate small metal and metal oxide particles. There are some basic issues associated with metal-ion release, namely: the amount of metal released from the implant, the site to which the metal is transported and the quantity that is transported, the chemical form of the released metal, and the pathophysiological consequences of such metal release. There is an increasing number of literature surveys concerning the first two issues however, but little is known about the patho-physiological consequences of metal release. The association between the release of metal ions from orthopedic devices and any metabolic, immunological, bacteriological, or carcinogenic toxicity is conjectural, and there is a need to discover and characterize such relations and phenomena.

The biomaterials made of Ti alloys, which are the main object of this project, are usually tested by procedures applied mainly for other materials. Some factors are modified, e.g. test temperature in tests is 37°C. There is also a few procedures proposed only for biomaterials and associated with their future application. However, the existing test procedures seem not fully relevant to real conditions met by long term implants, especially as regards corrosion fatigue (too high frequency, at which no corrosion effects can be observed and which does not fit frequency of joint operation), impact effect, long term corrosion, complex effects of various ions.
Societal/environmental objectives

- Increase in implant lifetime, patients comfort and safety, probability of only a single surgery
- New products, composite biomaterials, concurrent on the world market
- New fabrication technologies, concurrent on the world market
- Improved security and reliability of offered products

Principal Objectives and Sub-Goals

- Development of fabrication technology of porous metallic (Ti alloy) – ceramic biocomposite, both as:
  - a bulk product
  - as a gradient material, with scaffold or highly porous outer zone
- Development of technology of hydroxyapatite deposition within the pores of metallic matrix, either:
  - as a single phase
  - as a reinforced ceramics
- Development of new surface engineering techniques, including:
  - ion implantation
  - laser melting
- Development of adhesive layers on the whole area of metallic-ceramic composite
- Development of new testing procedures, including:
  - assessment of ion dissolution during long term exposure,
  - low frequency, low or high strain corrosion fatigue
- Development of mathematical tools of optimisation of properties of surface layers
- Development of mathematical tools of complex analysis of relations and interrelations of factors influencing the implant corrosion and lifetime in conditions of joint action of mechanical loads and human fluids` environment
- Development of expert systems to predict and to monitor the behaviour implant and status for a particular patient:
  - immediately after implantation
  - during long term activity

Preliminary Partners

Research centers and universities from:
- Germany
- Israel
- Italy
- Poland
Work packages; the Scientific Part

WP 1 - Fabrication of porous metallic (Ti alloy):
  1.1. Fabrication of bulk porous metallic alloys by powder metallurgy
  1.2. Fabrication of porous surface layer by selected methods
  1.3. Creation of scaffold layer on metallic alloy
  1.4. Investigations of microstructure, mechanical, physical, chemical and biological properties
  1.5. Analysis of results and choice of the fabrication technique

WP 2 - Development of new models of chemical, biological, mechanical and biological behaviour, new modelling procedures and new testing procedures:
  2.1. Development of new corrosion tests for extremely low corrosion rates and expected long lifetime
  2.2. Development of model describing the tissue - bone - implant interaction for porous (scaffold) structures during after-implantation time at various patients` age, activity, type of joint,
  2.3. Development of estimation method of mechanical properties for specific sandwich composites and volume composites
  2.4. Development of new low frequency, low and high strain fatigue and corrosion fatigue tests
  2.5. Development of mathematical tools for optimisation of properties of surface layers
  2.6. Development of mathematical tools of complex analysis of relations and interrelations of factors influencing the implant corrosion and lifetime in conditions of joint action of mechanical loads and human fluids` environment
  2.7. Development of biomechanical models describing the relations between mechanical stresses and strains, time after surgery, patients` age, activity, type of joint, time after surgery
  2.8. Development of expert systems to predict and to monitor the behaviour implant and status for a particular patient

WP 3 - Modification of properties of surface layer by selected techniques:
  3.1. Ion implantation
  3.2. Laser melting
  3.3. Chemical oxidation
  3.4. Electrochemical oxidation
3.5. Heat oxidation
3.6. Investigations of microstructure, mechanical, physical, chemical and biological properties
3.7. Analysis of results and choice of the fabrication technique

WP 4 - Deposition of micro- and nanoparticles of hydroxyapatite within the pores of metallic matrix (meshes of scaffold):
   4.1. Deposition by sol-gel method
   4.2. Deposition by biomimetic method in simulated body fluids
   4.3. Deposition of layer with various reinforcements
   4.4. Investigations of microstructure, mechanical, physical, chemical and biological properties
   4.5. Analysis of results and choice of the reinforcement

WP 5 - Creation of adhesive layers on the whole area of metallic-ceramic composite:
   5.1. Deposition of bioglass layer
   5.2. Deposition of thin HA layer
   5.3. Deposition of composite HA-base layer
   5.4. Investigations of microstructure, mechanical, physical, chemical and biological properties
   5.5. Analysis of results and choice of technique

WP 6 - Fabrication and evaluation of properties of new implant
   6.1. Computational implant design
   6.2. Fabrication of implant
   6.3. Microstructure investigations
   6.4. Internal stresses’ assessment
   6.5. Adhesion tests
   6.6. Corrosion tests
   6.7. Tribological tests
   6.8. Tribocorrosion tests
   6.9. Fatigue and corrosion fatigue tests
   6.10. Brittle cracking tests
   6.11. Assessment of physical properties
   6.12. Assessment of biocompatibility
   6.13. Analysis of the results

WP 7 - Project management and coordination
Biomaterials are nowadays essential for improving human health and quality of life. Originally foreseen with an aim to minimise rejection by the host organism, they have now entered a new stage in which they can be designed with bioactive properties, exchanging stimuli with the surrounding tissue and inducing specific cellular reactions. Bioinspired materials, on the other hand, take advantage of the knowledge that nature has been optimising over millions of years. Man-made material solutions can now take inspiration from the most complex naturally-organised chemical and biological structures (e.g. from the nanoworld of proteins to macroscopic structures of bone, shell and enamel). The main objective should be to achieve radical innovations in state-of-the-art biomaterials and to design highly performing bioinspired materials learning from natural processes.

**NMP-2007-2.3-1 Highly porous bioactive scaffolds controlling angiogenesis for tissue engineering**

Technical content/scope: In recent years biomaterials based on porous scaffolds have proved to be effective for bone and cartilage regeneration, showing that they are very promising for medical applications, in particular in the treatment of spinal disorders. However, existing biomaterials are not able to control cell differentiation and to achieve angiogenesis and cannot be adequately injected into the body. Therefore, there is the need to design highly porous but structurally sound bioresorbable tissue-engineered scaffolds able to be functionalized and to have direct influence on cells behaviour. Bioactive scaffolds are also required for the engineering of other complex tissues (e.g. nervous, ocular, visceral, nephrological-urological, vascular). The focus should be on advanced bioactive scaffolds enabling internal growth of tissue and the site specific delivery of bioactive signalling factors (temperature, pH, concentration, internal stimuli, etc). The approaches are expected to include issues such as delivery devices (e.g. injection), remodelling of large bone defects and improved tissue-biomaterial interfaces.

**Funding scheme:** Large scale integrating collaborative projects.

**Special features:** In line with the objectives of this topic, adequate industrial participation is recommended.

**Expected impact:** Medical applications (bones, joints, blood vessels etc.) improving health and quality of life, using biomaterials which are able to control cell differentiation and can be successfully injected into the body. Competitiveness of the European biomaterials industry.
### Contact

Andrzej Zielinski  
Gdansk University of Technology  
Faculty of Mechanical Engineering  
Department of Materials Science and Engineering  
Narutowicza 11/12, 80-952 Gdansk  
Poland  
phone: +4858.347.29.64, +48.501.329.368  
e-mail: azielins@pg.gda.pl, azielins@wp.pl  
fax: +4858.347.18.15

### Searched partners

- Universities and research centers from other EU countries, with experience in biomaterials
- Small or medium enterprise producing implants
- Hospitals or Medical Academies