швидкість виділення пухлинних клітин із крові обстежуваного хворого; виключення впливу фактора зовнішньої температури на результат дослідження.

Новими елементами пристрою в пропонованому винаході є застосування як камери для венозної крові скляного градуйованого циліндра, встановленого в прозорий пластиковий кожух, що має дві трубки, нижня з яких використовується для подачі підігрітою до температури + 36 °С води, а верхня – для виходу повітря з пластикового кожуха; встановлення на дні скляного градуйованого циліндра пластикової решітки з закріпленим на ній за допомогою металевого кільця каліброваним фільтром.

Більшість сучасних систем і технологій автоматизованого аналізу медичних мікроскопічних зображень потребує використання методів та алгоритмів подальшої обробки зображень, їх сегментації, визначення параметрів об'єкта, що визначаються в ручному режимі, що суттєво ускладнює їх практичне застосування в клінічній медицині внаслідок недостатньої кількості знань у медичного персоналу.

INTELLECTUAL MATERIALS IN BIO-MEDICAL ENGINEERING – THE MOST IMPORTANT COMPONENT OF THE «BIOART» PROJECT ACTIVITIES

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Among the multitude of materials that have found wide application in bio-medical engineering, intellectual (smart) bio-materials (hereinafter IBM) occupy a special place in manufacturing of implants, as they are capable of adequately reacting to environmental changes and self-improving their properties, repairing themselves or alternating their functional characteristics in the process of exploitation [1]. The BIOART project («Innovative Multidisciplinary Curriculum in Artificial Implants for Bio-Engineering BSc/MSc Degrees», ref. no. 586114-EPP-1-2017-1-ES-EPPKA2-CBHE-JP) envisages the modernization of the curricula for «Bio-medical engineering» speciality by implementing the most up-to-date disciplines, embracing such important contemporary research lines like implantology, bio-medical study of materials, mechanotronics, information systems and IT-technologies into the tuition process.[1]

Artificial mitral valves, tissue «plasters», contact lenses, artificial lenses and eye-lenses, artificial middle ear osselets, cochleae, joints, osteo-plates, internal osseous rods, bone cement, leather, urinary tracts, shunts for intracranial liquid, tooth fillings and dentures and the like are some of the many examples of the application of IBMs in bio-medical engineering.

Among metallic IBMs, an alloy possessing the memory effect, called «Nitinol» (an alloy consisting of nickel and titanium) has found a wide range of applications for bio-medical engineering, as devices based upon the phenomenon of super elasticity are simple in design and it is highly compatible with living tissues [2-4]. Such reaction of human organism-osse-integration is characterized by a reliable link of bone and implant, without formation of protective fibrous capsule. This discovery led to the creation of glue free fixation of artificial joints, made of Ti6Al4V alloy and tooth dentures, made of pure titanium.

As an example of non-metallic IBMs, we can mention the colour cement (a.k.a. glass-ionomeric) used in dentistry, having the same colour that adjoining teeth, acting at the same time as a source of fluorine, thus preventing further propagation of caries. Soluble surgery threads, made of polyactidic acid, that vanishes (it is solved in organism) after its function has been fulfilled is another example of IBM.

Introduction of some IBMs into bone tissues promotes formation of a new on their surface, causing the effect of healing the area of surgical operation. Synthetic hydroxiapatite, bio-active glasses and some types of glass ceramics are also examples of such IBM. Some proteins from the biological environment absorb on the surface of such material, that promote growth of bone cells, thus accelerating the process of recovery. In some IBM (like, for instance, bio-glass) it is preceded by reactions of ionic exchange on the surface of introduction and a layer of calcium phosphate emerges, promoting formation of direct chemical links between bio-glass and mineral phase of newly-formed bone tissue.

Phosphate-calcium ceramics possesses outstanding implanting properties among ceramic IBMs, as the mineral phase of bones is quite similar to hydroxiapatute [$Ca_{10}(PO_4)_6(OH)_2$], although it has a lower degree of crystallinity and has a whole set of phosphate micro-inclusions, like

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tricalciumphospahe, carbon apatite and other ionic admixtures of fluoride, magnesium and potassium.

Fluoride-apatite [$Ca_{10}(PO_4)_6(F)_2$], differing in chemical structure from hydroxiapatite is more stable at increased temperatures and more resistant to acids impacts. These materials are capable of forming a direct link with an alive bone, without formation of protective, fibrous tissue. Formation of chemical link between phosphate-calcium ceramics and bones is in partial solution of the surface layer of ceramics and formation of crystals of C03-apatite with inclusion of bio-molecules of surrounding liquid.

A new efficient way of increasing operating mechanical load for IBM is creation of a metal substrate, by means of plasma sputtering and deposition of a layer, consisting of ceramic calcium phosphate upon it [5], the metal substrate ensuring the specified strength, while the coating-ensuring a biological reaction of compatibility of the organism and the implant.

A new step in contemporary bio-science of materials is creation of IBM of the third generation –intellectual coatings [1]. Formation of a connecting tissue is a macro-process, that is regulated by the processes of nano-scale , while reaction of the organism to bio-material is determined by the peculiarities of its surface [6].

One of such methods is the chemical modification of the surface of biological materials for absorption of certain proteins, while another is implanting of biologically active molecules upon its surface. Peculiarities of surface bio-modification are determined by the character of the required reaction of the human organism. In case an implant undergoes an impact of bacteria, as it may happen with artificial vocal chords, for example, adhesion of cells is not desirable. On the contrary, for orthopedic implants adhesion is quite necessary. By specifying the factors determining the interaction of the implanted surface and cells, it is possible to modify deliberately the surface of IBM in order to gain control over bio-chemical reaction of the organism. Modified surfaces are capable of exerting influence upon the cell’s behaviour, thus controlling the nature of the protein layer that is formed on the surface in the biological environment. The cells can «feel» the implanted proteins thorough receptors. As a rule, implantation of certain cells upon the implanted surface is desirable, as well as their growth and quick division. Space alternation of chemical content seems to be quite an interesting line of development of living tissues. For example, deposited nitrogen containing polymers stimulate precipitation of nerve cells and neurons growth. The influence of the chemical composition of the surface upon precipitation of some cells can be used for gaining control over precipitation of the required cells in certain areas

Capabilities of biological modification of the surface of IBM implants can have many functions like anti-bacterial behavior, ensuring a reliable connection with bones and blood. Engineering of living tissues has become a new philosophy in the development of contemporary IBMs, as it is one of most quickly developed branches of bio-medical engineering. Its essence is in application of biological and technical methods of creation of functional tissues, either substituting or improving functioning of sore or pathological parts of the human organism. This idea is realized in practice by growing living cells upon biomaterial in presence of bioactive molecules. After that, the living cells and the extra-cellular matrix, produced by them including the substrate, are introduced into the organism as a single cell-bio-material structure.

Development of biologically modified IBMs seems to be a promising way for further research, their surface bearing certain data fro living cells, interacting with such surface. These data may consist of determining spots, where the cells should and should not be implanted and determining their orientation or differentiation [1].

The creation of truly intellectual substrates is a future task. In order to achieve it, further, joint, complex development of bio-science of materials, biology and medicine is required.

Development of new medical devices, biomaterials and especially IBM and artificial tissues is certain to play an ever more important role in treatment of illnesses. Further development of biomaterials is to be a result of joint efforts by material engineers, biologists and doctors. New IBMs are very likely to differ from biomaterials of the past. They will become much more intellectual, in the sense that they will interact with the biological environment, promoting recovery of physiological functions of the human organism and living tissues. The ultimate goal of treatment will be recovery of healthy tissue while simultaneous vanishing the remains of the implanted biological material [7].

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BIOMEDICAL ENGINEERING: ADVANCED TECHNOLOGIES FOR SMART ARTIFICIAL IMPLANTS

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Biomedical engineering (Bio-Eng.) is a multidisciplinary branch of science where engineering principles are applied in order to understand, modify or control biological systems. Bio-Eng. is a very broad field, encompassing many different areas [1]:

- Biomechanics, biomaterials, biosensors and biotechnology.
- Biomedical instrumentation, medical and biological analysis.
- Physiological modeling and bioinformatics.
- Clinical engineering and medical imaging.
- Rehabilitation engineering.
- Tissue engineering, prosthetic devices and artificial organs.

In particular, one very important area of Bio-Eng. is the design of artificial implants, i. e., artificial limbs, organs and other body parts to replace damaged / lost ones (due to illnesses, accidents or armed conflicts) or to improve the performance of the existing ones (either because their behavior has deteriorated or to enhance the natural human capabilities). In order to develop effective artificial implants, contributions from many different key fields are required:

- Biology and materials science (including biomaterials).
- Chemical and electrical engineering.
- Computational statistics and biostatistics.
- Computer science and machine learning (bioinformatics).
- Digital signal processing.
- Electronics.

Recent advances in these fields are allowing bio-engineers to develop *smart artificial implants* with enhanced capabilities. Some key contributions in this area are the following:

- Low-power microelectronics, advanced fabrication processes, and packaging for device miniaturization [2].
- Wearable sensors (including biosensors) that allow us to measure an ever increasing range of biosignals with a reduced burden for the user and an improved precision [3].
- Smart materials with the capacity of adaptively changing their