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Biomedical engineering for health research and development

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Abstract. – **Biomedical engineering is a new area of research in medicine and biology, providing new concepts and designs for the diagnosis, treatment and prevention of various diseases. There are several types of biomedical engineering, such as tissue, genetic, neural and stem cells, as well as chemical and clinical engineering for health care. Many electronic and magnetic methods and equipments are used for the biomedical engineering such as Computed Tomography (CT) scans, Magnetic Resonance Imaging (MRI) scans, Electroencephalography (EEG), Ultrasound and regenerative medicine and stem cell cultures, preparations of artificial cells and organs, such as pancreas, urinary bladders, liver cells, and fibroblasts cells of foreskin and others. The principle of tissue engineering is described with various types of cells used for tissue engineering purposes. The use of several medical devices and bionics are mentioned with scaffold, cells and tissue cultures and various materials are used for biomedical engineering. The use of biomedical engineering methods is very important for the human health, and research and development of diseases. The bioreactors and preparations of artificial cells or tissues and organs are described here.**

Key Words:
Biomedical engineering, Stem cells, Tissue engineering, Artificial cells and tissues.

Introduction

The biomedical engineering (BME) is a new area of medicine and biology research for health care and control of many diseases. It provides design concepts and principles to biomedical research for diagnostic and therapeutic purposes[1]. The biomedical engineering includes tissue engineering, genetic, neural, stem cell, chemical and clinical engineering and other areas solving health care of animals or humans by skills of engineering and medical and biological sciences[2] Biomedical engineering applications also include the development of biocompatible prostheses, several medical diagnostic and therapeutic devices which range from clinical equipments to microimplants, brain-imaging equipments such as MRI and EEGs, regenerative medicine, cells and tissue growth, artificial limbs, organs and urinary bladders, the pharmaceutical drugs and therapeutic developments. The tissue engineering is to make artificial organs from biological materials for patients who need organ transplants. The biomedical researchers have grown solid jawbones and tracheas from human stem cells[3] and artificial urinary bladders have been grown and transplanted into human patients (organs have been from patients own cells[4]. The hepatic assist devices that use human liver cells within an artificial bioreactor construct have been developed and a trial will begin for first artificial liver device using human cells[5]. The genetic engineering means genetic modifications or manipulations, gene splicing, recombinant DNA technology, and gene therapy for many diseases in humans. The genetic engineering utilizes modern methods and tools for molecular cloning and transformations to change the gene structure and characteristics of target genes for disease care. Not only for humans the genetic engineering is also used for animals and plant breeding for example, improving the genes for better dogs or more milk yielding cows and better crops of wheat, corn or barley by gene technology. For humans, synthetic insulin has been made through the modified bacterial genes for diabetes care, the erythropoietin was manufactured in hamster ovary cells, and oncomouse (cancer mouse) produced by new animal breeding experiments for human cancer research and development.

The neural engineering or Neuroengineering is a discipline that employs the methods of Biomed engineering to repair, replace or enhance neural cells or neurons in the brain or body of a patient. The neuroengineers or neuroscientists solve the

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genetic defects of neural cells or tissues living or non-living constructs. The pharmaceutical engineering includes drug engineering, new drug development, drug delivery targeting pharmaceutical technology. The drug analyses and unit operations of chemical engineering provide better drugs for treatment. The International Society for Pharmaceutical Engineering (ISPE) is an international organization that certifies new drugs for human health and disease care.

Medical Devices and Bionics

Medical devices include medical equipments and medical technologies. It also includes all health care products, chemicals, drugs, vaccines and tools which do not involve metabolism. The medical devices are used in diagnosis, mitigation, treatment or prevention of diseases. These examples include pacemakers, infusion pumps, heart-lung machine, dialysis machine, artificial organs and limbs, cochlea implants, eye lenses, facial prosthetics, dental implants, and others. The stereolithography is a medical modeling used to create physical objects, modeling of human organs and body by Biomed Engineering techniques are used for research and development, treatments and prevention of diseases and their careful monitoring[6] (www.ingentaconnect.com/content/klu/pharm/2006[7] Nanomedicine[8]. The Biomedical imaging is a part of medical devices. This includes ultrasound method of detecting embryo in uterus of a pregnant woman, magnetism, UV, radiology or other means. The MRI scans of head for brain imaging to see pictures of neuronal damage or diagnosis of disease, electrical engineering method and viewing animated sequence of slices. The equipments used are magnetic resonance imaging (MRI), fluoroscopy, positron emission tomography (PET) scans, and cranial tomography (CT) scans, nuclear medicine, ultrasound, optical microscopy and electron microscopy methods. The medical device of implants is to replace and act a missing biological structure or organ using biomedical materials such as titanium, silicone or other. The examples are artificial pacemakers, cochlear implants, and subcutaneous drug delivery devices as pills or drug-eluting stents. The artificial limbs, such as the right arm as prosthesis and left arm as myoelectric control. The prosthetic eye is an example of biomedical engineering application of mechanical engineering and biocompatible materials to ophthalmology[1]. The Bionics is the method of artificial body part replacements for the function of human body. The functions of eyes, ears, and other organs by improved cameras, TVs, Radio transmitters and receivers and several other tools.

Bionics methods can be used for available spare body parts of humans to replace the damaged or injured body parts by biomedical engineering.

The clinical engineering deals with implantation of medical equipment in hospitals or other clinical settings. The biomedical equipment technicians provide their services to observe working abilities with implants or medical devices of the patients. Clinical engineers execute the research and development of new implantation devices in humans and examine their proper functioning and usefulness everyday as well as to see the safety of engineering designs and precise procedures.

Tissue Engineering

Tissue engineering is the use of combination of cells, engineering materials, biochemical and physico-chemical factors and synthesis of tissues to improve, repair or replace the tissues for biomedical functions of human body[9]. These are bones, cartilages, blood vessels, cells, urinary bladders, skins, muscles, etc. which require proper functioning. The artificial pancreas, bio-artificial liver and other artificially-created systems are used. The regenerative medicine is synonymous with term tissue engineering but use of stem cells or progenitor cells, umbilical cord blood cells takes place to produce necessary tissues in human bodies. There are several examples of tissue engineering such as, bio-artificial windpipe, in vitro meat, bio-artificial liver utilizing living hepatocytes, artificial pancreas using islet cells to produce insulin for diabetes, artificial bladders, cartilage for knee repairs, scaffold free cartilage, heart in a jar, tissue airways and blood vessels, artificial skin construct from human skin cells embedded in hydrogel, artificial bone marrow, artificial bone, cardiovascular tissues and organs, oral mucosa and foreskin tissue engineering[9-12]. The principle of tissue engineering is as follows:

1. **1.** Cells of human body (by biopsy, taking of tissue under sterile conditions).
2. **2.** Cell isolation and cell cultivation in sterile tissue culture medium.
3. **3.** Cell proliferation and sterile cell culture.

4. Scaffold (formation of mesh of cells in groups in culture medium).
5. Tissue development (by cell proliferation, increase in cells and scaffold).
6. Adding of growth factor and mechanical stimulus for tissue development.
7. Implantation to human body for growth and repair of cells or organs under aseptic conditions.

The tissue engineering method utilizes living cells as starting material which includes fibroblasts from skin. Cartilages can be repaired by chondrocytes, telomeres producing immobilized cell lines, and culture of non-cancerous human cells and cancerous cells for research. The cells are extracted from body fluids such as blood (RBC and WBC) by centrifugation and apheresis method; the solid tissues are minced and then digested with enzyme, trypsin or collagenase to remove the extracellular matrix that holds the cells. The high temperature digests the tissue matrix faster but can do some damage to cells. Therefore, low temperature is safer when using collagenase enzyme for cell preparation.

Types of Cells Used for Tissue Engineering

Following types of living cells are used for the tissue engineering:

1. **Autologous cells:** These cells are obtained from the same person to whom those cells will be reimplanted. These cells have less rejection and pathogenic transmission. Autologous cells are not suitable for genetic diseases, elderly people, people suffering from severe burns to establish useful cell lines. The bone marrow cells, fat cells and mesenchymal stem cells are used because these can be differentiated into variety of cells. A large number of cells can be isolated from fat cells and used for bone repairs, cartilage, fat, and nerve cells.
2. **Allogenic cells:** These cells are obtained from the body of a donor of same species. These cells are dermal fibroblasts from human foreskin which are immunologically safe and a viable choice for tissue engineering of skin.
3. **Xenogenic cells:** These cells are isolated from individual of another species, particularly in experimental animal cells which are used for constructing cardiovascular implants.
4. **Syngenic or isogenic cells:** These are isolated from genetically identical organisms such as, twins, clones or highly inbred animal models for bio-medical research.
5. **Primary cells: These cells** are from a living organism and secondary cells from a cell bank.
6. **Stem cells:** These are undifferentiated cells with the ability to divide in cell cultures and produce various kinds of specialized cells. These are divided into two sources, adult cells which are multipotent, and embryonic cells which are mostly pluripotent and some cells are totipotent in early stages of embryo. There are some ethical issues to use umbilical cord cells from a woman to do embryonic cell cultures for the repair of diseased or damaged tissues in humans or to grow new organs from these stem cells.

Scaffold

Scaffold means the cells are implanted or seeded into an artificial structure capable of supporting three-dimensional (3D) tissue formation, and are critical in both in-vivo and ex-vivo conditions, and allow cells to influence their own microenvironment. Scaffold cells serve the following purposes: Allow cell attachment and migration, deliver and retain cells and biochemical factors, enable diffusion of vital cell nutrients and expressed products, and exert mechanical and biological influences to modify the behavior of cell phase[9]. The carbon nanotube (3D) structure is used for tissue engineering scaffold since these are bio-compatible and resistant to biodegradation and can function with biomolecules, but some toxicity with non-biodegradable nano-materials is also possible.

Materials Used for Tissue Engineering

Many natural or synthetic, biodegradable and permanent materials are used for tissue engineering. These are nylon sutures for surgery, collagen and polyesters and other nano-scale fibers. PuraMatrix®, is used as scaffold for clinical applications and life science research. The synthetic polylactic acid (PLA) material degrades within human body to form lactic acid and can be removed from body. Similar materials are olyglycolic acid (PGA), and polycaprolactone (PCL). The natural materials may also be used for scaffold from extracellular matrix which supports cell growth. Protein materials, such as fibrin or collagen and polysaccharides like chitosan[13] or glycosaminoglycans (GAGs) could be used for cell compatibility. Among GAGs, hyaluronic acid with cross linkage agent, glutaraldehyde, water-soluble carbodiimide, and others as scaffold. These are used to deliver small molecules of drugs to specific tissues in the human body. To improve in vivo like condition for 3D tissue via stacking layers of paper impregnated with cell suspension, extracellular matrix hydrogel which controls oxygen and nutrient gradients in 3D and analyzes molecular and genetic response described by Ratmir et al[14]. The different thickness of paper sheets and types of medium can support experimental environment in cell based high throughput screening and drug delivery[15].

Tissue Culture

To create functional and biological structures in vivo requires extensive tissue culture to promote growth, survival and function of cells. The basic requirements to maintain tissue cultures are oxygen, pH, humidity, proper temperature, macro- and micro-nutrients and osmotic pressure etc. The diffusion of nutrients and their metabolic transport are important for cell culture. The creation of capillary network within the tissue is also required for tissue engineering. The tissue culture stimuli and growth factors are important for function of cells. The growth hormones, specific nutrients, chemicals and physical stimuli and oxygen tension are required for normal development of tissues such as, chondrocytes require hypoxia, low oxygen for normal development. The endothelial cells respond to shear stress from fluid flow in blood vessels. The mechanical stimuli such as pressure pulses are important for cardiovascular tissues for instance heart valves, pericardium and blood vessels.

Bioreactors

The bioreactors are used for the cultivation of vascular grafts. These are small plastic cylindrical chambers used as bioreactor for 3D cell cultures. MC2 Bioteck is a bioreactor known as Proto Tissue that uses gas exchange to maintain high oxygen level for cell respiration and growth within cell chamber[16]. Bioreactor uses bioactive synthetic materials such as polyethylene terephthalate membranes to surround the spheroid cells in the environment that maintains high level of nutrients[17]. These are easy to open and close and the cells can be maintained at 100% humidity and could also be removed for testing purposes[18,19].

Generating Long Fibers

The laden fibers have been developed which are one meter long in length and about 100 μm in size[20]. Such fibers are created using a microfluidic device that forms a double coaxial laminar flow. Each layer of micro-fluidic device where cells are seeded in ECM, a hydrogel sheath and finally in calcium chloride solution. The seeded cells are cultured within hydrogel sheath for several days, and then the sheath is removed with viable cell fibers. The various cell types are inserted into the ECM core, including myocytes, endothelial cells, nerve cell fibers, and epithelial cell fibers. These fibers can be woven together to fabricate tissues or organs in a mechanism similar to weaving textile fibers. The fibrous morphology is an advantage because it provides an alternative to traditional scaffold design, and many organs, such as muscle cells are composed of fibrous tissues.

Conclusions

The biomedical engineering is very significant for the diagnosis, treatment, prevention and therapeutics of many human diseases. It can also develop artificial cells, tissues and organs needed for the repairs of many parts of diseased or injured organs in humans. Several types of cells and tissues are prepared and cultured by tissue engineering and various natural and synthetic materials are used to produce artificial cells and organs for disease control. Many equipments and techniques are described which are very useful for human health, as well as research and development. The stem cell technology for making blood vessels, nerve fibers or neurons, pancreas and liver cells, myocardiocytes or heart muscle cells and blood cells, etc. is the future of biomedical engineering. More research is needed for synthesis of blood cells, tissues and organs for control of human diseases.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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