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IMPORTANCE OF BIOENGINEERING IN PHARMACY

Subarna Mahanti, Dr. Dhrubo Jyoti Sen, Dr. Bankim Chandra Nandy, Dr. Falguni Patra, Dr. Khokan Bera and Dr. Beduin Mahanti

Department of Pharmaceutical Chemistry and Pharmaceutics, School of Pharmacy, Techno India University, Salt Lake City, Sector-5, EM-4, Kolkata -700091, West Bengal, India.

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Corresponding Author:
† Dr. Dhrubo Jyoti Sen

Email: dhrubosen69@yahoo.com

† Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake City, Sector-5, EM-4, Kolkata - 700091, West Bengal, India.

ABSTRACT

Biomedical engineering, or bioengineering, is the application of engineering principles to the fields of biology and health care. Bioengineers work with doctors, therapists and researchers to develop systems, equipment and devices in order to solve clinical problems. Examples of bioengineering research include bacteria engineered to produce chemicals, new medical imaging technology, portable and rapid disease diagnostic devices, prosthetics, biopharmaceuticals, and tissue-engineered organs.

KEYWORDS: Bioengineering, Drug discovery, Bioengineered Therapeutics, Importance of Sugar, *In-vitro* processes, 3D bioprinting, Organ-on-chip, Biosensors, Microtissue, Medical devices.

INTRODUCTION:

Bioengineering/Biological engineering/Bio-engineering is the application of principles of biology and the tools of engineering to create usable, tangible, economically viable product. Examples of bioengineering research include bacteria engineered to produce chemicals, new medical imaging technology, portable and rapid disease diagnostic devices, prosthetics device, biopharmaceuticals, and tissue-engineered organs. In general, biological engineer attempt to either mimic biological systems to create products or modify and control biological systems so that they can replace, augment, sustain or predict chemical and mechanical processes. Working with doctors, clinicians and researchers, bioengineers use traditional engineering principles and techniques and apply them to real-world biological and medical problems [1].

HISTORY:

Biological engineering is a science-based discipline founded upon the biological sciences in the same way that chemical engineering, electrical engineering, and mechanical engineering can be based upon chemistry, electricity and magnetism, and classical mechanics, respectively and it has the same fundamental attention to cost-effectiveness as all branches of engineering do.

Figure 1: Bioengineering scientist Heinz Wolff

Before WWII, biological engineering had just begun being recognized as a branch of engineering, and was a very new concept to people. Post-WWII, it started to grow more rapidly, partially due to the term "bioengineering" being coined by British scientist and broadcaster Heinz Wolff in 1954 at the National Institute for Medical Research. Wolff graduated that same year and became the director of the Division of Biological Engineering at the university. This was the first time Bioengineering was recognized as its

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own branch at a university. Electrical engineering is considered to pioneer this engineering sector due to its work with medical devices and machinery during this time. When engineers and life scientists started working together, they recognized the problem that the engineers didn't know enough about the actual biology behind their work. To resolve this problem, engineers who wanted to get into biological engineering devoted more of their time and studies to the details and processes that go into fields such as biology, psychology, and medicine. The first biological engineering program was created at University of California, San Diego in 1966, making it the first biological engineering curriculum in the United States. More recent programs have been launched at MIT and Utah State University. According to Professor Doug Lauffenburger of MIT, biological engineering has a broad base which applies engineering principles to an enormous range of size and complexities of systems [2].

BRANCHES OF BIOENGINEERING:

The branches of bioengineering are as following:

Medical engineering: Medical engineering concerns the application of engineering principles to medical problems, including the replacement of damaged organs, instrumentation, and the systems of health care, including diagnostic applications of computers.

1. **Agricultural engineering:** This includes the application of engineering principles to the problems of biological production and to the external operations and environment that influence this production.
2. **Bionics:** Bionics is the study of living systems so that the knowledge gained can be applied to the design of physical systems [3].
3. **Biochemical engineering:** This includes fermentation engineering, application of engineering principles to microscopic biological systems that are used to create new products by synthesis, including the production of protein from suitable raw materials [4].
4. **Human – factors engineering:** This concerns the application of engineering, physiology, and psychology to the optimization of the human–machine relationship [5].
5. **Environmental health engineering:** This field concerns the application of engineering principles to the control of the environment for the health, comfort, and safety of human beings. It includes the field of life support systems for the exploration of outer space and ocean [6].
6. **Genetic engineering:** Genetic engineering is concerned with the artificial manipulation, modification, and recombination of DNA or other nucleic acid molecules in order to modify an organism. The techniques employed in this field have led to the production of medically important products, including human insulin, human growth hormone, and hepatitis B vaccine [7].

BIOENGINEERING IN PHARMACEUTICAL AND MEDICAL MANUFACTURING INDUSTRY AND RESEARCH:

The pharmaceutical and manufacturing industry is focused on creating a variety of medicines and other health products that will improve the lives of people. The pharmaceutical industry is mainly known for its prominence in research and development (R & D) of new drugs.

- In this process testing of thousands of chemical compounds in the effort of finding a new drug is done by R& D departments.
- A large part of this is applied research, where scientific knowledge is used to develop a drug, targeted for specific use.
- The field of bioengineering encompasses the process of testing the millions of combinations to create new drugs, where engineering (genetic engineering, tissue engineering, fluids engineering) is required.
- A fundamental understanding of molecular cell and tissue biology has inspired the engineering of a promising new generation of drugs – BIOENGINEERED THERAPEUTICS.
- Bioengineered therapeutics development has three key areas - a) Design and discovery b) Delivery platforms c) Synthesis and manufacturing technologies.
- Bioengineering comprise native and engineered molecular scaffolds such as proteins, enzymes & antibodies as drugs, as well as macromolecular assemblies mimicking pathogens and cells as drugs, drug carriers and immune stimulants.

Role of sugar in human body: Exploring optimised version of biosynthesised proteins combined with chemically synthesised drugs could help the development of novel biomedicines and vaccines targeting. For example – Influenza [8].

Glycobiology, the structure and chemical reactions of sugars in the human body, can play a role in disease development. It is an emerging but complex field. In the SWEETOOLS project, Dr Milan Vrabel is supported by the European Research Council (ERC). The project is an attempt to combine chemical synthesis with bioengineering to build hybrid biochemical structures. Biologics are copies or optimised versions of human proteins which are engineered in laboratories. These genetically modified cells are grown to bind selectively to specific cell receptors. For example, they may be able to bind only to receptors of cancer cells, identifying and fighting specific abnormal cells without harming other healthy ones.

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Figure 2: Bioengineering

Such treatments could mean fewer side effects than are caused by their more established chemical counterparts, such as chemotherapy. Chemically synthesised drugs would still play a vital role in the process. These so-called small-molecule warheads can be used to deactivate targets (diseased cells, for example) rapidly and selectively. But for this to happen, Vrabel will need to develop a new class of bioconjugates – a chemical strategy to form a stable link between two molecules, at least one of which is a biomolecule – to be used as delivery systems that will bind the 'warheads' exclusively to sugar processing enzymes. This would enable researchers to further explore the role sugars play in both the development and treatment of disease. The research could help advance the engineering of novel therapies and vaccines for the targeted treatment of a wide range of diseases which currently have no effective cure [9].

METHOD, STRATIGIES, AND TECHNOLOGIES:

1. ***Organoids, Spheroids, and 3D Self - Assembled Tissue Cultures:***

Pluripotent stem cells and organ-specific progenitor cells cultured as 3D entities have been shown to differentiate into a collection of cell types that self-organize spatially into structures reminiscent of aspects of a specific organ and exhibit some functionalities associated with that organ [10].

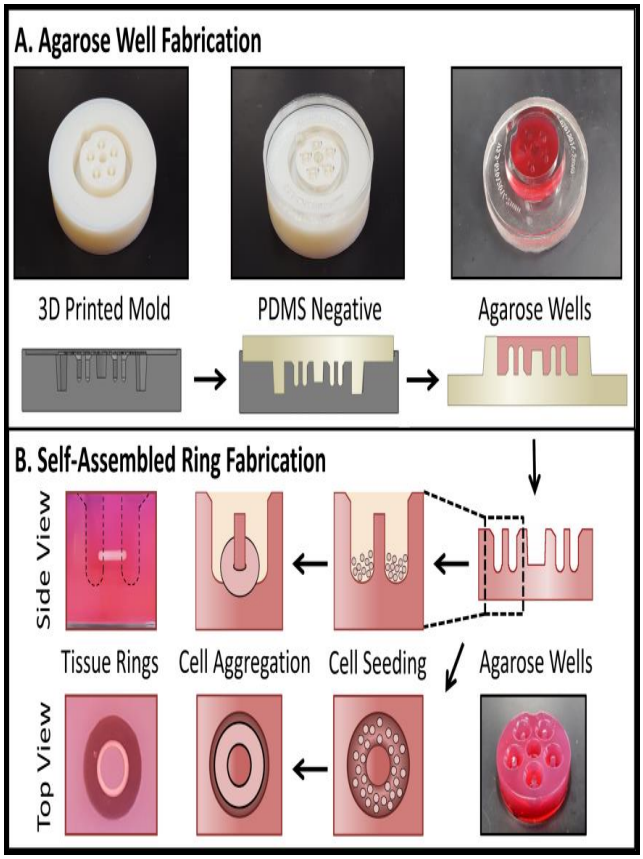

Figure 3: Tissue culture: Organoids & Spheroids

This approach has thus been broadly used as invitro investigative tool to gain insight into tumour biology and for drug screening studies [11].

2. Micro-tissues:

Micro engineered tissues, also termed microtissues, represent a new paradigm in the field of cell-based assays. They combine microfabrication and tissue-engineering, to provide in vitro models with tissue-like characteristics. Micro engineered human cardiac tissues, usually fabricated using cell-laden natural-based hydrogels casted on posts, or around a wire template are used in preclinical toxicology and drug screening assays.

This is a major drawback in the development of new therapies. Recently, arrays of lung microtissues suspended over multiple flexible micropillars that recapitulate the mechanical stiffening and contraction of alveolar tissue has been reported [12].

3. Tissue and Organ 3D Bioprinting:

The unique ability to precisely pattern cells and biomolecules in 3D structures has also provided an opportunity to tackle a paramount challenge in regenerative medicine and with *in-vitro* cultures. With few exceptions, cells typically exist in the body within 100–200 µm of blood vessels, beyond which nutrient and metabolite diffusion constraints can cause cell necrosis. Most approaches to produce 3D tissues models for *in-vitro* studies or *in-vivo* implantation do not provide a direct route to the incorporation of such vascular networks [13].

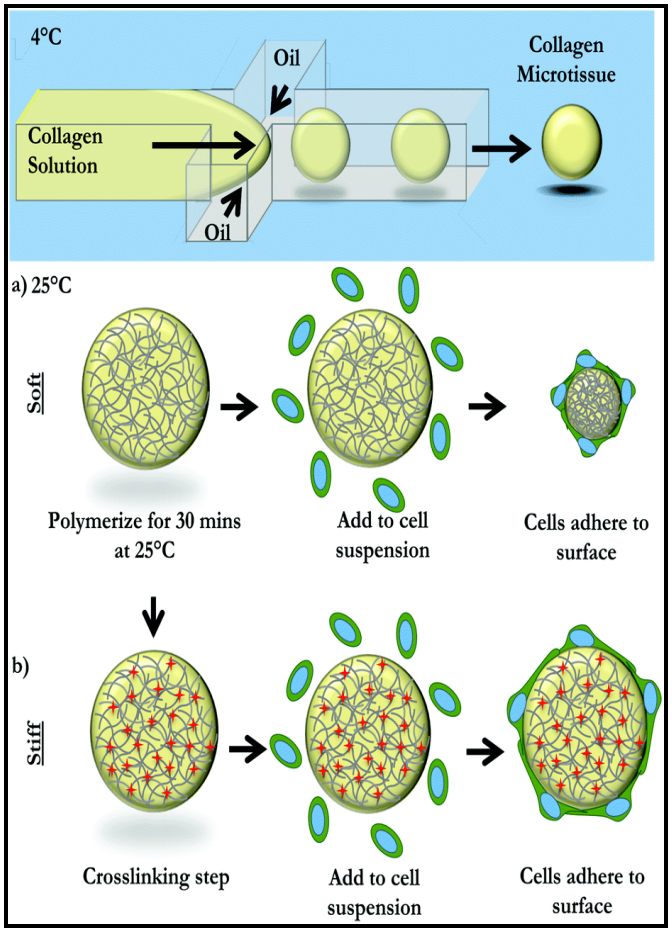

Figure 4: Tissue culture process of Micro tissues

4. *Organs-on a chip:*

The fundamental design philosophy behind the organs-on-a-chip (OOC) technology is the reduction of whole human organs and/or organ systems to minimal functional units capable of maintaining key aspects of the native tissue architecture and of the *in-vivo* physiology. The resulting micro engineered systems through a system of pumps, valves and filters, allow to precisely control the perfusion of microliter amounts of fluids through the microchannel network in a regime of laminar flow (i.e., microfluidics) [14].

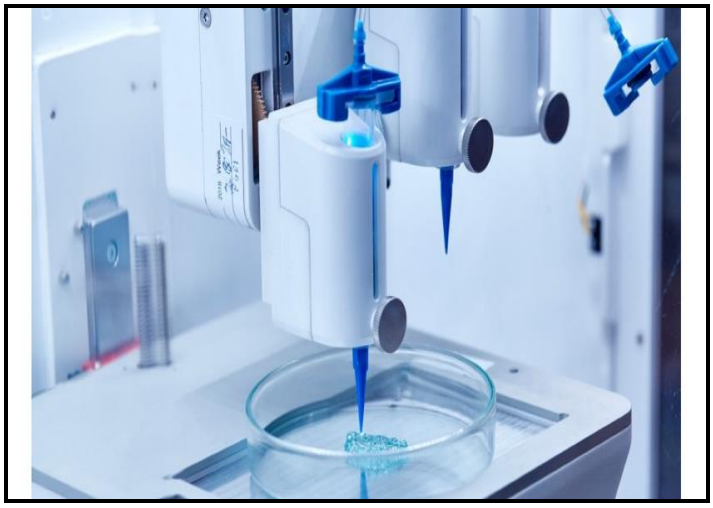

Figure 5: Organ 3D bioprinting

In this context, mechanical actuators that can generate different stress states (e.g., shear, compressive, tensile) to replicate the mechanobiology of living tissues have been integrated in microfluidic devices. In particular, the direct use of human cells not only promises to address the translatability challenges and ethical issues encountered with animal models , but is also expected to accelerate the development of personalized platforms for precision medicine and advanced drug screening in parallel with progresses in iPSC biology, finally used in OOC platforms to build personalized functional models for disease mechanisms and drug screening purposes. Other advantages of OOCs include (i) the ability of controlling environmental factors (e.g., temperature and gas concentration (ii) reproducibility, integration with other technologies (e.g., sensors for electrical, optical and biochemical readouts)

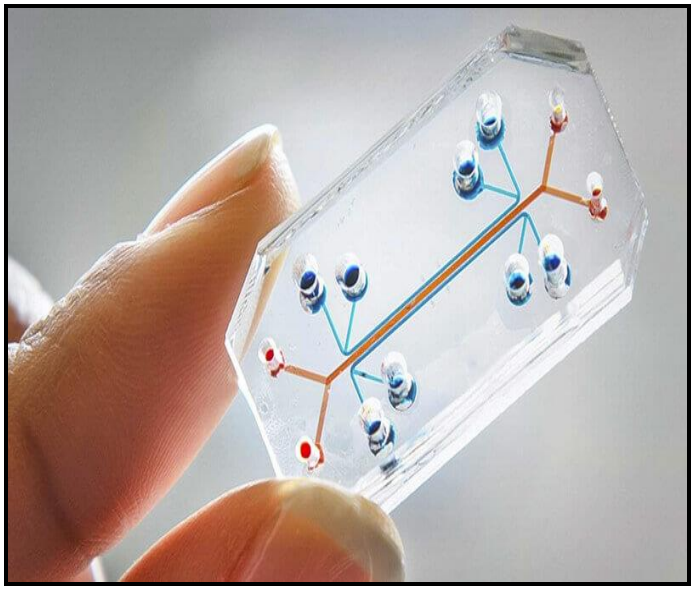

Figure 6: Organs-on-a-chip

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(iii) Advanced drug screening/discovery: bringing a new drug to market requires up to twelve years and more than 1.7 billion US dollars. In this context it has been seen particular interest because of recent advances in drug-delivery technologies for better pharmacological efficacy and bioavailability [15].

5. *Biomimetic in-vitro models*:

Vasculature, nephrons, mammary glands, gastrointestinal epithelium, hair-follicles, and corneal limbus are only some examples of tissue complex geometries in our body that researchers have been tried to reproduce in vitro employing a variety of biomimetic microfabrication strategies. For example, photolithography and replica moulding have been used to reproduce the wavy topography of the epidermal–dermal interface. It is accepted that epidermal stem cells lie in clusters specifically located in relation to this topography, but the relationship between their location and properties is currently unknown and can be investigated by reproducing the tissue architecture. Also, in skin tissue, the fabrication of 3D structures with the shape of the hair-follicle bulges has attracted a lot of attention. Micro moulding has been used to accurately create microwell arrays of self-assembling hair follicle germs able to generate spatially arrange hair follicles upon transplantation. Dermal papilla cells were then cultured on the microwells to promote the differentiation of human keratinocytes into specific hair follicle lineages and their physiological arrangement. Corneal limbus also has specific microstructures that serve as stem cell niches. Limbal architecture has been reproduced by electrospinning polymer fibres on micro moulds produced by stereolithography or by replica moulding on collagen gels. Regarding tubular structures, very recently an array of kidney tubules produced from a micro-moulded platform in collagen-matri gel gels. This platform allows for the modelling of kidney diseases such as cystic kidney disease and acute kidney injury as well as drug testing purpose. Finally, the small intestine crypt-villus morphology has also been reproduced by either replica moulding procedures and, more recently, by reaction-diffusion mediated photolithography. In all the cases, a significant improvement of the properties of the epithelial barrier on the 3D structures compared with the 2D monolayers was reported. Still, and despite the benefits reported [16].

1. Biosensors: Most of the reading outputs obtained from bioengineered in vitro models rely on imaging data. To advance these drawbacks, an excellent approach seems to integrate biosensors in the bioengineered platforms. Biosensors are analytical devices that rely on the molecular recognition capabilities of biological capture probes (antibodies, oligonucleotides, enzymes or even cells) to measure the concentration of analytes. These recognition events will be transduced to a signal that will be read-out. Biosensors can be used to continuous monitoring the critical parameters of cell microenvironment, and to study the response of the models to drugs over extended periods of time. Monitoring soluble biomarkers such as cytokines through integrated biosensors is also used as a reading output to monitor pathological processes in a non-destructive manner. In addition, electrical activity can also be a functional hallmark for cardiac, muscle, and nervous tissues. Electrical signal can be recorded by microelectrode arrays (MEAs), which can be easily integrated in micro physiological systems. Overall, online and/or integrated monitoring capabilities might be key in the future acceptance of bioengineered models as new valuable tools in drug development [17].

Improvement of medical devices:

1. Management and performance of breakdown, Maintenance biomedical equipments.
2. Management and performance of planned preventive maintenance of biomedical equipments.
3. Calibration, performance verification and certifications of biomedical equipments.
4. Utility certification: During installation of sophisticated equipments, Biomedical Engineers assess the utility needs of equipments viz. tonnage of AC, electrical power, drainage system required and generate feasibility report.
5. Planning and installation for all types of sophisticated Bio Medical Equipments.
6. Creation of Computerized database: dynamic software for maintaining work order, preventive maintenance schedule and technician time.
7. Pre-purchase evaluation and negotiation in procurement: Analysis of equipment characteristics in clinical environment ensures technical and clinical acceptability.
8. Incoming inspection of equipments: Using specialized testing and calibration of equipments for electrical safety, proper calibration and operational verification.
9. Management of maintenance contract: Analysis of equipment failure and assessment of repair cost, scheduling of repair /PM visit, documentation, monitoring equipment uptime, review maintenance contract in terms of quality and responsiveness of service provider to make decision on modification of service contract.
10. Equipment Retirement process: bioengineers also determines the optimal lifespan of healthcare organizations technology and its aging, out – modelled and inappropriate costly instrumentation is retired in accordance with a

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rational equipment replacement policy. Integral with this plan is the role in advising whether to shift to a newer, more innovative technology or to stay with the tired or true one.

11. Equipment Risk Management: This is an area, which is developing at a rapid place in western hospital. This tool allows the Bioengineers to deploy the technical resources in a cost-effective manner. In addition, to the direct economic benefits, safety gets enhanced as the more problematic equipment is identified, tagged with a higher risk rating and scrutinized more frequently [18].

A medical device is intended for use in:

- The diagnosis of disease or other conditions, or
- In the cure, mitigation, treatment, or prevention of disease.

Some examples include pacemakers, infusion pumps, the heart-lung machine, dialysis machines, artificial organs, implants, artificial limbs, corrective lenses, cochlear implants, ocular prosthetics, facial prosthetics, somatoprosthetics, and dental implants. Stereo lithography is a practical example of medical modelling being used to create physical objects. Beyond modelling organs and the human body, emerging engineering techniques are also currently used in the research and development of new devices for innovative therapies, treatments, patient monitoring and early diagnosis of complex diseases. Below figure, is a schematic biomedical instrumentation amplifier used in monitoring low voltage biological signals, an example of biomedical engineering application of electronic engineering to electrophysiology [19].

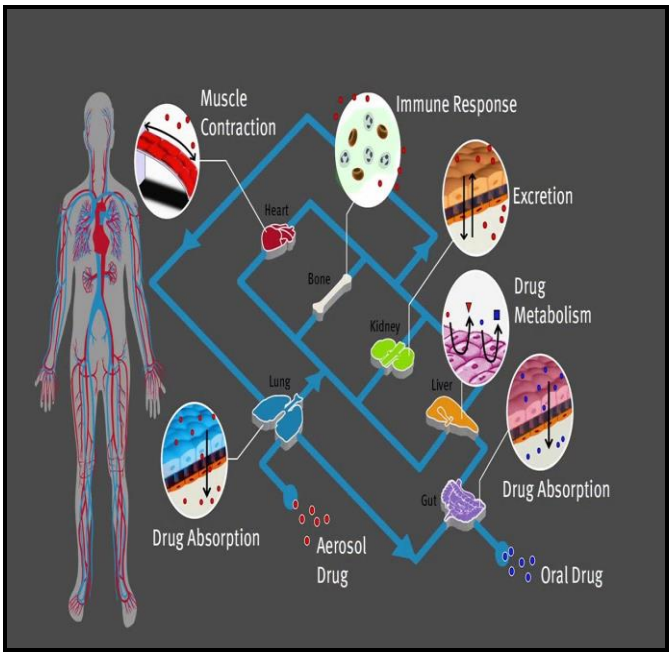


Figure 7: Biosensor

The required voltage signal for medical device can be obtain from the above amplification as express below:

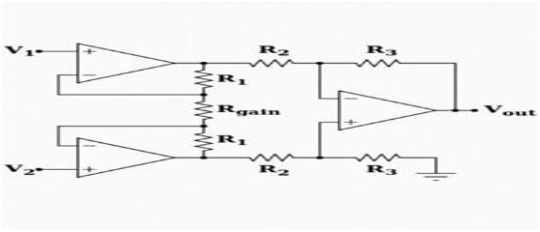
$V_1 = R_2 eqv (I_2+I_1)$.....(I)

$V_0 = I_1 R_{Smin}$ .....(2)

$V_{OUT} = I_1R_3+V_1-V_0$.....(3)

So, $V_{OUT} = I_1R_2 + R_2eqv(I_1+I_2) - I_1R_{Smin}$ .....(4)

$V_{OUT} = I_1R_3+[\{R_1R_2/(R_1+R_2)\}(I_1+I_2)] - I_1(R_{eqv}R_x/R_{eqv}R_x)$ .....(5)



Many particular electrophysiological readings have specific names:

- Electrocardiography – for the heart
- Electroencephlography – for the brain
- Electromyography – for the muscle
- Electroculography – for the eyes
- Electroretinography – for the retina
- Electroantennography – for the olfactory receptor for arthropods

MEDICAL IMAGING:

Medical imaging is a major segment of Medical Devices. This area deals with enabling clinicians to directly or indirectly view things not visible in plain sight (such as due to their size, and /or location). This can involve utilizing ultrasound, magnetism, UV, other radiology, and other means [20].

- Imaging technologies are often essential to medical diagnosis, and are typically the most complex equipment found in a hospital including;
- Fluoroscopy
- Magnetic resonance imaging (MRI)
- Nuclear Medicine
- Position Emission Tomography (PET) PET-CT scans
- Projection Radiography such as X-rays and CT scans
- Tomography
- Ultrasound
- Electron Microscopy

THE 10 MOSTS IMPORTANT BIOMEDICAL ENGINEERING DEVICES:

The most important biomedical engineering devices are those that save the most lives and/or improve the lives of the most people:

1. The X-ray machine images internal organs and thus discovers an internal abnormality and tumors in time to remove them.

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2. Computed tomography generates slice images of internal organs with improved contrast and spatial resolution.
3. Magnetic resonance imaging generates slice images of soft tissue and internal organs without radiation exposure.
4. The heart–lung machine oxygenates and pumps the blood to permit operations on the open heart to correct abnormalities and to replace diseased valves.
5. The artificial kidney extracts urea from the blood to extend the lives of those with end-stage kidney transplant
6. The electrosurgical unit makes tissue cutting easier to shorten surgical time and restores proper rhythm to many who otherwise would be invalids or die.
7. The cardiac pacemaker stimulates the dysfunctional heart and restores proper rhythm to many who otherwise would be invalids or die.
8. The ventilator permits operations on anesthetized patients and breathes for patients who have pulmonary crises.
9. The pulse oximeter noninvasively measures tissue oxygen saturation of anesthetized patients and breathes for patients who have pulmonary crises.
10. Artificial hips, knees, and other joints restore movement to those with mobility problems [21].

CONCLUSION:

The numbers of elderly and physically disabled in our communities are consequently glowing at a rapid rate and this is placing an ever-increasing demand on society to provide engineering and technical solution to help overcome their physical limitations.

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