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Role of Biomedical Engineering for Diagnose and Treatment

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ABSTRACT

Biomedical Engineering is the rising field in medical science by involving the knowledge of biology and medicine in combination with the principals of engineering to develop devices and procedures which can solve the greatest number of medical and health-related problems in this modern world. When technology merges with medicine it proceeds throughout healthcare from diagnosing, analysis for treatment and recovery as well as medical devices which were implemented such as artificial hips, pacemakers, prostheses (missing body parts replaced by artificial devices), medical information system and 3-D printing technology of biological organs. As the disease progress in time, the development of Biomedical Engineering application is well used to diagnose and treat the patients, therefore, the impact of biomedical engineering does not only improve the quality of life, however, it also saves lives. Additionally, industrial engineering and operations management methods are perfectly well-matched to solve the problems that arise from the health care system among patients, community groups, health professionals, industry, and governments.

The theme of this review article is to provide a standard information about Biomedical Engineering applications towards the healthcare by expressing its availability and its results which are up-to-date. The innovation also establishes how successful does it takes part in medical science and yet research to be done for unsuccessful cases.

Key Words: *Biomedical Engineering, Medical devices, Diagnostic, Therapy, Invasive technologies*

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1. INTRODUCTION

Biomedical engineering (BME) is defined as a discipline that advances knowledge in engineering, biology, and medicine as well as it improves the human health through cross-disciplinary activities that integrate the engineering sciences with the biomedical sciences and clinical practice [1]. By considering many terms such as biomedical engineering, biological engineering, bioengineering and medical/clinical engineer which are defined by the Bioengineering Education Directory and finally termed as bioengineering for the entire field [2]. Therefore, the overall applications of BME are medical imaging, artificial organs, biomaterials, tissue engineering, neural engineering and so on as it is mentioned in Figure 1.

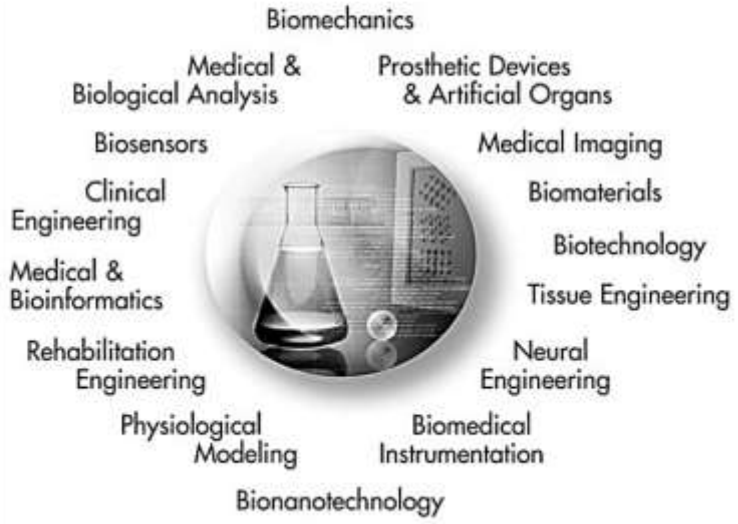

Figure 1: The world of Biomedical Engineering.

This review article is based on the role of BME which is used in diagnosing (e.g. body scanners) and treatment (radiation therapy and minimal access surgery) in order to prevent various diseases. Whereas BME is a successful emerging field of clinical application that is developed by in research of engineering information's, biology and medicine in addition of applying the development of new devices, systems, processes and algorithms which would progress healthcare distribution and medical practice into clinical disorders and biological systems which are known to be BME, it also differs from the general biological research therefore it searches solutions based on engineering principals [1]. Perhaps, the first step in biomedical engineering is to identify a latent problem in a physiologic system and then proceed with respective treatments [3].

BME is involved in diagnosis of most health-related issues which were exposed in this modern world through the fundamental aspects of device, software, design instruments and system analysis by introducing new procedures to solve clinical problems or to proceed with the research which would be a global improvement in the health care system [4]. Consequently, designing complications related medically would have a verity of large complex scale constructs such as hospital information analysis system, implementation of automated clinical laboratories and multiphasic screening facilities where acceptance of many tests to be conducted. As well as it includes the supplies of operating rooms, severe care units and emergency vehicles with the involvement of complications of remote monitoring and telemetry. Biomedical engineers are the challenging members of engineering profession where they apply the knowledge, concepts, and approaches of all the engineering academy such as electrical, mechanical and chemical engineering to solve particular health care-based issues and it also expresses the chances of interaction between the professionals of health care and engineers [2].

BME is involved in treatment of disease which are controlled to benefit greatly, so many healthy, injured or sick individuals are more accurately monitored and provided with effective treatments depending on for those who are acutely injured or who have chronic disease as well as having a tendency to reduce the required cost and aggressive treatment in the early stage [5]. Generally, treatments based on BME is done by using stem-cell-based technologies, devices, surgical tools and new drugs however many predictable treatments for humans are not the continuous solution of their respective injury and disease, therefore, they regularly processed with incomplete and temporary development in health, function or quality of life [6]. Therefore, biomedical engineers do have a huge responsibility to make sure the designs for medical practice, the techniques and technologies are prepared in a good manner based on the supportive of ethical principles, such principals include nonmaleficence, benefiting the patients, patient autonomy where the right to choose or refuse a treatment, dignified treatment of the patients, agreement of treatment based on a proper understanding of facts and medical information [7].

By combing progressive science engineering disciplines with the deep information of healthy and diseased cells, tissues and organs which allows the experts to transform medicine by progressing new methods for regenerating injured tissues and different treatments which would be constant and effective. For regenerative medicine the functional tissues are engineered by combining molecular, cellular, tissue and the whole organism's analysis, stem cells, microenvironmental effects (such as mechanical forces) and bioreactor technologies would qualify more advanced treatments on bioprocesses, 3D-printing, microfluidics and nanomaterial design through new technologies as well as it also improves treatments via surgical computer-assisted techniques and tools. Advanced treatment via pharmaceutical would be improved by considering drug-delivery system and new devices that depending on more accurate in assessing therapeutic targets, benefits and possible side effects of the new drugs [6].

2. HISTORY

2.1 Prosthetic device

Bioengineering is a practice of solving life science problems by using an engineering method. The design and production of medical devices as instruments engineered precisely to solve medical problems hence this includes prosthetic devices which were designed to replace the missing body parts. Therefore, 1000 years before any evidence was established in Egypt as shown in Figure 2, which was an artificial wooden toe of two collections of renovation varying in appearance and design. One extinguishes as artificial right foot big toe which was made up of cartonnage by using linen soaked layers with animal glue and coated with tinted plaster, in the time period of 600 BC and it is exhibited in Egyptian Galleries in the British Museum, UK.

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Figure 2: The image of an artificial right foot big toe. Is been exhibited in the British Museum, London and from the ancient Egypt it is meant to be Greville Chester artificial toe made from cartonnage (glue, plaster, and linen).

The second artificial toe in Figure 3 was made up of three pieces that consist complex series of laces joining three sections together was found attached in the right foot of the female mummy by means of a string in the time period between 710-950BC and this piece was exhibited in Egyptian Museum in the place called Cairo, Egypt.

Figure 3: The image of the wooden toe. It expresses the two pieces of dense hardwood and a third possibly leather of the artificial wooden toe of a female mummy who was buried near Luxor in Egypt.

At present, the known oldest prosthetic device would be the 300BC wealthy Roman burial in Santa Maria di Capua Vetere which was recused, it is a hollow wooden leg attached to a foot or metal rocking peg with holdup achieved by leather straps attached to a bronze waistband described by Bilquez whereas this bronze and wooden leg kept in The Royal College of Surgeons (London, England) was unfortunately demolished in the bombing attack of May 10/11/1941. Therefore, luckily in 1920, a detailed examination was undertaken by Sudhoff, the well-known medical historian and a paper were published by von Brunn of Rostock in 1926, these records permitted their construction of a replica, which is now displayed in the Science Museum (London, England).

Bliquez also reports on feet found in two European burial sites as initial examples of prosthetic. At Bonaduz, Switzerland, the artificial right foot dates to the 5th to 7th century AD and analyzed the leftovers and surrounding of the leather pouch that had been stuffed with hay or moss and by iron nails to assist stability a wooden base had been attached. Between 7th to 8th century AD, Frankish grave in Griesheim generated the second example made from wood and bronze, with the lower part of the left leg missing and the foot appeared to have a wood extension fixed as far as the knee. Czarnetzki et al.6 show how this device may have been strapped to the residual limb [8].

2.2 Biomedical engineering emerging as a field

Biomedical engineering as a field appeared after the World War II and then processed onwards while BME combines the knowledge in engineering with the knowledge of human biology and medicine in order to develop techniques and technologies for the patient care and health-care system. The field of BME which is very broad and covers up from the devices and tools used by a doctor to diagnose a patient’s condition to the modern technological machines that are able to extend the life of individuals in critical situations such as applications of ranging from molecular imaging to the construction of artificial hearts [7].

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In the time period of the 1700s, Luigi Galvani processed with a survey between animal physiology and electricity, whereas this lead to the study of our body usage of electrical impulses as diagnostic indications of health, such as in electro cardiology. At the beginning of 18th century, one of the students of Galvani named Alessandro Volta created the first battery which was immediately applied to electricity for therapeutic purposes.

Electrocardiogram (ECG)

In 1903 William Einthoven invented the first electrocardiogram (ECG) in Figure 4 and measured the electrical changes that arose during the beating of the heart while in the process, he finally predicted an ECG signal not much different from the "classic" one obtained with the string galvanometer. Einthoven initiated a new age meant for both cardiovascular medicine and electrical measurement techniques [9].

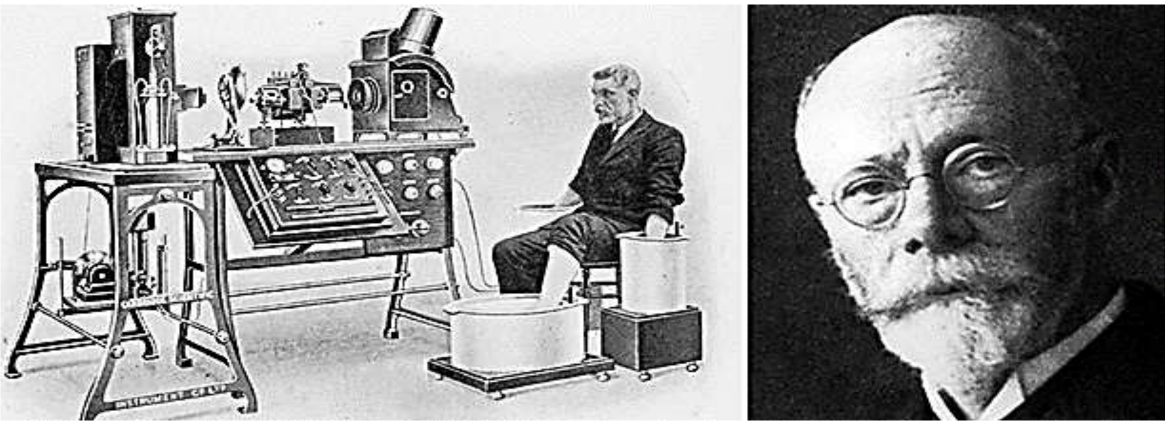

Figure 4: William Einthoven inventing the first electrocardiogram. The ECG a diagnostic and investigative tool that does not require to be introduced into the body, the cost is minimal and simple to record. In 1924 he was awarded the Nobel Prize in physiology and medicine, "for the discovery of the mechanism of the electrocardiogram".

Roentgen-rays known as X-rays

The most significant development in clinical medicine was the x-rays where Wilhelm Conrad Rontgen a German professor in Physics designated his first invention of electromagnetic radiation in a wavelength range, his experiments involved the electric current passing through the gases at extremely low pressure while he detected certain rays that were released during the transmission of the current through a well-covered discharge tube which was carried out in a room of dark and resulting in the production of rays which is illuminated in a barium platinocyanide covered screen. Then it appeared as fluorescent in the screen even though it was to be found in the path of the rays within 2m away from discharge tube. He, later on, continued his experiments capturing images of the objects by placing the photographic plate in the path of the rays therefore, he created the first "roentgenogram" by evolving the image of his wife's hand and evaluated the variable transparency as shown in Figure 5 that expresses her bones, flesh and her wedding ring [10].

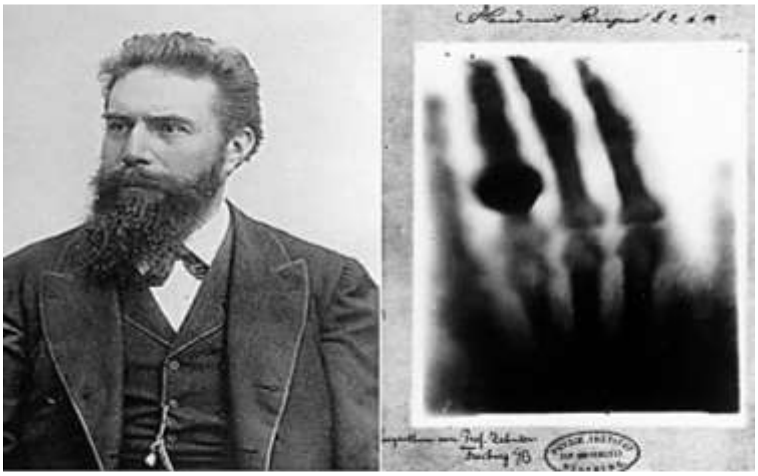

Figure 5: W.C. Roentgen was the initial person to discover the technique of X-ray. His wife holding out her hand and produced the first X-ray ever on the evening of 22nd of December in 1895 and he termed them as X-rays however, it is still acknowledged as Roentgen-rays as well. For the extraordinary achievement, he also received a Nobel Prize in Physics in 1901.

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By when the human body was opened for medical inspection as well as these x-rays were used for diagnosis of bone fractures and dislocations. X-ray machines were brought to the urbanist hospitals in the United States of this modern technology, while in the processes a distinct radiology department was established and influenced its activity with almost every department of medicine such as surgery, gynecology and so forth by advancing with the aid of this new tool. By the 1930s, x-ray imagining of nearly all the organ systems of the body as possible to examine by the use of barium salts and a wide variety of radiopaque materials [10].

2.3 Rest of the inventions

The introduction of drinker respirator and the first heart-lung bypass was held in 1927 and 1939 respectively and in 1940s cardiac catheterization and angiography which is the use of a cannula dye for the x-ray imagining of lung and heart vessels and valves were developed which was a beneficial for diagnosing accurately of congenital and acquired heart disease mainly the valve disorders due to rheumatic fever and a new period of cardiac and vascular surgery began.

Later on, the 1950s the electron microscope was discovered and entered the medical scene which provided significant advances in imagining relatively small cells. Whereas body scan detectors of tumors arose from the similar science that was implemented into societies reluctantly into the atomic age while these ‘‘tumor detectives’’ used radioactive material and became newly established departments of nuclear medicine in all hospitals [2].

In the following of 20th century, many unbelievable discovers existed under the union of chemical, mechanical and electrical engineering proceeded into the complex medical system, such systems included pacemakers and the artificial heart, dialysis, DNA testing and prosthetic devices which could response.

3. APPLICATIONS OF BIOMEDICAL ENGINEERING

In recent years, an important progress has been made in the expansion of biomedical microdevices which has a major role in diagnosis and therapy. The microelectromechanical systems (MEMS) technology has permitted the usage of advanced biomedical microdevices into a small medical device in the human body by the combination of electronics, sensors and actuators and other minimally invasive techniques. Human enhancement is the devices and procedures which were established by biomedical engineers that are typically designed to support therapy or diagnosis and also designed to improve healthy human individualities beyond a normal level, therefore, it has the probable of creating superhumans. If medicine were likely to participate in human enhancement, it would be beyond its traditional mission which is simply curative and preventive [7].

3.1 Electromagnetics for Biomedical Engineering

Description of Electromagnetism

Electromagnetism is created by the charges which can be either movable or immovable. Stationary charges (immovable) produces an electric field and moving charges (movable) produces magnetic fields, therefore both are part of the same force.

However, electromagnetic fields (EMF) can be used for medical purposes also. So, the interaction between biological structures and EMF might induce the heat deposition or the density of current and these communication modes might also induce both therapeutic and adverse effects, therefore, it is much more important to estimate the entity of the interaction [12].

For electromagnetic examination, the human body is an electrical conductor and a dielectric medium liable on the range of frequency and the estimated quantity such as electric field distribution or increased density of current. Although for the thermal analysis, it is the thermal conductor media, also noted that the biological tissues were not good electrical conductors due to lower conductivity and then with a high resistivity of a metal (few ten of Ωm versus 10-8 Ωm), nevertheless it is well known that the strength of the increased current can cooperate with the biological matter by causing some adverse effects like nerves and muscle stimulation or heat induction [13].

According to the research are of biomedical electromagnetics, it provides an innovative and more impact on scientific methods and structures that are progressed for certain illness to be diagnosed and treated as well as it has an important role in an inquiry. The human body contact of organs to various types of radiations has been a great concern, for example the scanning systems which include lasers, X-rays, and Magnetic resonance imaging (MRI), that have been an impact on medical diagnostics of various diseases and it also used in stroke diagnostics, breast cancer detection, microwave tumor treatment and localization of epileptic brain activity [14].

Diagnosing and treating Cancerous cells

The therapeutic application of the new model is microwave hyperthermia, in which cancerous tissues go through selective heating by focusing the energy in the microwave field of the targeted region is been broken to encourage apoptosis which is programmed cell-death of the diseased cells or to raise the effectiveness of radiotherapy and chemotherapy. In diagnostics application, one of the examples is the screening the functional and morphological changes for diagnosing early breast cancer, which feats the

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different responses of the microwave in the healthy tissues associated to the diseased ones, therefore to obtain the diagnostic information from the fields of the measure distributed by the anatomic region under investigation. It aims for the exposure conditions that are required to increase the effect of desire, the regulation of the radiant systems and synthesis as well as the methods developing for the process of data expected at the act of estimation in the diagnostic information [13].

In diagnosis, two issues are considered, the first issue is the progression of a new technique for the diagnosis of early breast cancer which uses nanomagnetic contrast agents that are able to concentrate cancerous tissues selectively. Appreciations to the human body of non-magnetic nature where the use of a contrast agent tolerates to summarize the occurrence of false positive and negative results with an understandable benefit in terms of quality and reliability of diagnosis. The second issue would concern the study of the differential use of microwave imaging procedures to monitor the development of the disease during a therapy.

Specifically, the concentration is on the monitoring of brain tissue that changes physiologically caused by the modifications of normal blood flow such as hemorrhage and ischemia or traumatic events such as hematoma. In view of both cases, research activities targeted at the design of devices that would be able to enhance the interaction between the human tissue and EMF in addition to advance the imaging methods of characterizing from properties of the electromagnetic multifaceted biological environments [15].

The therapeutic features are that the research reports on the growth of new procedures for the microwave hyperthermia and in specific execution and design of applicators that are capable of directing the electromagnetic energy in the diseased tissue, while the heating minimizes the surrounding tissues to avoid side effects. Consequently, the usage of proper optimization performances for the synthesis of the field and the correct arithmetical modeling propagation of the electromagnetic signal also its interface with biological structures visible are vital for the activity, which also make available for the necessary tools to an appropriate planning of detailed therapeutic treatments [16].

Magnets and electromagnetic therapy

About 1000 of years, medical treatments have used electricity and magnetism, whereas magnets and electromagnetic treatment are procedures of energy medicine. In between 10th-11th centuries of ancient China, acupuncture points were done by magnets to treat several other conditions and the qualities of natural magnetic with minerals termed as lodestones which were used. In the 19th century, it is mentioned: “the golden age of medical electricity” for the cause of many electrical devices and magnetic that was developed and encouraged [17].

The electricity and magnets are used to make both conventional which is usual medicine and unconventional which is unusual medicine. The conventional medicine which is predictable uses the electricity and magnets for the determinations of both diagnosis and healing, whereas the human body production of electric current was measured by ECG and Electroencephalogram (EEG) to detect the heart and brain situations, similarly, the MRI is been used with a high-powered magnet for imaging body parts. Newly, an advanced medical treatment is industrialized by using the electricity, for example, the people with other neurologic conditions and Parkinson’s disease have been treated by inserting small electrodes into the human brains.

Pulsed electromagnetic field therapy makes use of devices that produce magnetic fields at specific frequencies. It also has many possible uses that may encourage the bone fracture healing, ankle sprain swelling reduction, and healing of bedsores and joint issues [18].

Several suggestions were made by concerning the mechanisms in which magnets possibly will produce a therapeutic effect. Theoretically, a strong magnet near the spine can alter the neural action of the spinal cords to decrease the spasticity of the muscle and it is frequently appealed that in the body the less strong magnets can control the electrical imbalances which are supposed to cause the diseases. Hence, some devices are used for acupuncture points stimulation and are supposed to generate advantageous chemical changes in the body and some individuals also suggest that magnets possibly will change hormone levels, change the flow of electrically charged atoms or affect the immune system.

Magnetic therapy could support to recover the ache resulting from diabetes associated nerve injury and also in post-polio syndrome whereas, various reports results for the effects of low back pain and neck. A new area of research has been identified as stimulation of transcranial magnetic, which uses magnetic fields of high-intensity applied to the scalp, these fields pass through bone and stimulate the brain as well as some research recommends to treat many other circumstances such as depression and pain. Further research required to be directed and determine the effectiveness of these projected therapies due to the usage of strong magnetic fields and lack of long-term safety data, therefore, transcranial magnetic stimulation is specifically used in designated research centers [12].

Microrobots for Minimally Invasive Medicine

Minimally invasive procedures collaborate with a variety of patients related welfares extending from medical complications, a decrease of recovery time, postoperative pain to raise the quality of care, and infection risks as well as including preventative care. In the past period of time, these approaches have an effective history however, the zone has experienced two important advances [19]. Those are:

1. The first success is the Intuitive Surgical da Vinci of a robotic system, which is the minimally offensive surgical system.
2. The worldwide increasing of capsule endoscopy approval for gastrointestinal (GI) diagnosis.

Hence, both of the expansion demonstrates that the most important skill of surgeons is technical skills and cognitive ability which is required for dexterity and accuracy that can be frequently be delegated to suitable technology. Microrobots has the possibilities to achieve tasks that are mostly impossible or difficult and leading undoubtedly to the growth of therapies which are not yet considered.

To target the individual cells, medical nanorobots were used which are expressively smaller than the microrobots also classically intended as devices. Several projected nanorobots would be more like pharmaceuticals than machines, applying thoughts from synthetic biology and demanding great numbers of them to complete the task.

Some researchers are following electromechanical methods to design nanorobot nevertheless still illustrating and emerging the essential building blocks of future nanorobotic devices besides are not yet ready to manufacture a nanorobot which is proficient of performing a simple medical task [19].

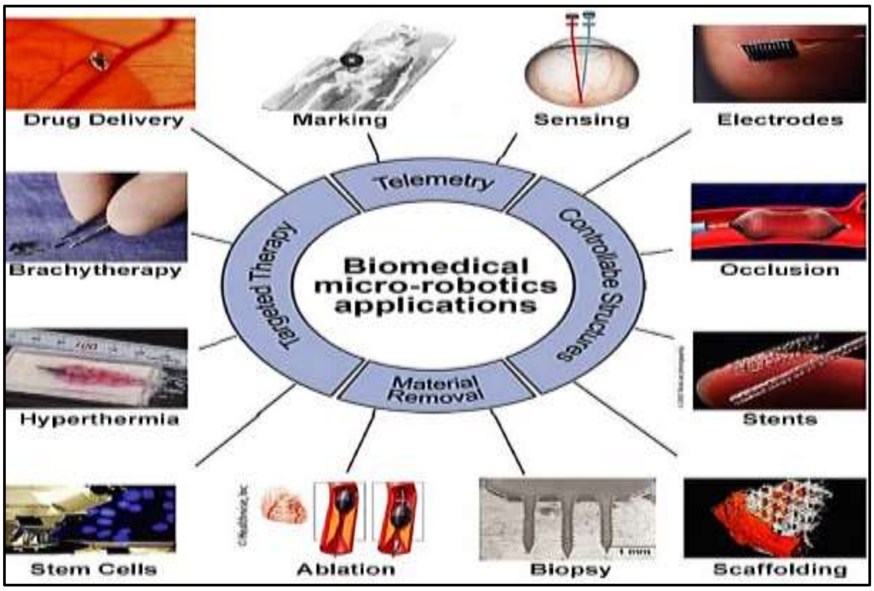

Figure 6: The usage of biomedical microrobots in various situations. Microrobots responsibilities in Medical that consist of therapy, material removal, controllable structures, and telemetry.

The advantages of microrobots are mentioned in Figure 6, such as:

- The targeted delivery of drugs will permit the therapies of improved effectiveness while minimizing side effects such as the microrobot is docked to a blood vessel as a planned therapy for retinal vein constrictions.
- Microrobots can also support to destroy tumors in brachytherapy by carrying seeds of radioactive.
- For hyperthermia therapy, a microrobot magnetic fields of time-varying used to increase the healing process.
- In vitro stem-cell examination is in the rapid progression, therefore, microrobots can make available of a method that implements these results in vivo.
- To remove undesirable tissue microrobots can accomplish ablation.
- For a biopsy, microrobots can also acquire tissue samples by using the devices which are designed for a miniature endoscopic robot.
- For tissue-engineering applications, microrobots can support as a framework. Whereas the image expresses a theory that consists of mineralized ingrowth into a scaffolding of polymer.
- Microrobots can act as stents which can be used to preserve the passages in open and it can function as obstructions in a situation where a passage required to be blocked.

- Microrobots can act or transmit as electrode implantations in the brain.
- Microrobot scan completes a wireless remote sensing by intraocular of oxygen sensor by which luminescence is a function of oxygen concentration.

A microrobot signals its own location which is used for localization. In this planned example, a microrobot prepared with a mechanical structure that is skilled with ultrasonic frequencies vibration which can be localized in the body by using receivers placed on the outside of the body.

The components in the human body such as blood and urine are used to distinguish certain diseases as well as under a wide variety of conditions procedures and medical tests are used to diagnose and treatments are held, so based on blood or urine the dielectric behavior is taken to consider under diabetes mellitus. It is presented in the measurements of the dielectric properties of glycosuria by using a coaxial probe at microwave frequencies at various temperatures and tried to tie the experimental results with Debye model. By considering the different glycosuria groups, it has been reported that the level of glycosuria rests on dielectric constant strongly in which the method can be connected to treat diabetic patients [14].

The chiral metamaterials are mainly used for sensing purposes apart from sensing diabetic troubles, urine infections, and hemoglobin of the blood optically, those metamaterials can be used for other biosensing requirements such as tracking of the temperature of marrowbone by applying microwaves. Interestedly, such microwave of biosensors may be appreciated for real-lifestyles events as through the modification of structural design depending on the frequency range of detection [20].

3.2 Ultrasound Enhanced Nanomedicine

Description of Ultrasound

An ultrasound scan which is also known as sonography is a test done by medical in which sound waves of high-frequency is applied to seizure live images of the cells from the inside of a human body which allows the doctor to observe any damages in the vessels, organs and tissues without demanding to make an opening in the body. Ultrasound is considered as safe, noninvasive, uses no radiation so it has minimal risks which vary from other imaging techniques such as X-rays or computed tomography (CT) scans, therefore, it is most preferred to be used for viewing a growing fetus during pregnancy. An ultrasound can also provide a view of the required internal view of the organ in case of any pain, swelling or any other symptoms. Consequently, it can be used to examine the brain of infants, eyes, bladder, gallbladder, liver, kidneys, pancreas, spleen, ovaries, blood vessels, thyroid, testicles, and uterus. It is also a supportive way to control the surgeons' movements throughout certain medical procedures, such as biopsies, diagnose heart situations, and measure the damage after a heart attack [21].

Ultrasound imaging is done by using a small transducer (probe) and ultrasound gel which is applied directly into the skin and then a high-frequency of sound waves were transmitted from the probe through the gel into the body. The transducer accumulates the sounds that reflect back and its computerized by using those sound waves to create an image. Ultrasound images are taken in real-time therefore, it can demonstrate the body's internal organs movement and the structure as well as the blood flowing through blood vessels [22].

Doppler ultrasonography (Doppler ultrasound) allows the physician to observe and estimate the blood flow through veins and arteries in the region of arms, legs, abdomen, neck and/or brain of infants and children or within several body organs by using special ultrasound performance. There are 3 various types of Doppler ultrasound, which includes Color Doppler, Power Doppler, and Spectral Doppler.

Color Doppler procedure is done by using a computer device to convert measurements of Doppler data into a collection of colors so that displays the speed and direction of the blood flowing through a blood vessel. Power Doppler is an advanced procedure which is more sensitive than Color Doppler and has the capability of providing more in detail of the blood flow, precisely when the blood flows minimally or less than the usual range. However, it not an advantage in the radiologist control of the blood flowing direction, which could be important in some circumstances. Spectral Doppler demonstrations the measurements of the blood flowing in graphically, by concluding the distance traveled / unit of time, as an alternative of color picture and it can also alter the blood flowing information into an individual sound that can be heard with each and every heartbeat. Hence, Doppler sonography is also performed by using the same transducer [21].

Ultrasound Microbubbles

Ultrasound imaging technology is the most common diagnostic modalities used in the health center. It varies applications from first-look investigations of the abdomen region and other soft tissues towards endosonographic by means of the esophagus or the female genital tract and also intravascular applications. Ultrasound investigations are generally achieved without any contrast agents besides the information of vascular derivative from color or power Doppler which is normally sufficient to figure out the accurate diagnosis. The microbubble is normally composed of a gas core even out by a cover comprised of proteins, lipids or

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polymers, however, microbubbles that are gas-filled act as intravascular contrast agents prove to be an advantage in some conditions such as,

- The liver lesions classification.
- The measurement of microcirculation in tumors and soft tissues.
- The therapy response assessment.

Microbubbles are usually used in myocardial perfusion estimation and functioning of the heart in addition to diagnosing vesicoureteral reflux. In past years the ultrasound device has been improved specifically and sensitively to detect the microbubbles. The progression of harmonic image technique permits the usage of microbubbles-specific scan modes such as pulse inversion methods or amplitude modulation methods hence, it is based on the comparison of soft tissues. Insolated microbubbles consist of stronger nonlinear response that is used to suppress the tissue background signals and detects the microbubbles.

Microbubbles for ultrasound has the difference of improvement usually has a diameter of between 1-4 mm even though molecular imaging is being limited to the vascular partition, the microbubbles with molecular ultrasound imaging are promising and affordable in generating targeted probes and determining detection procedures. Therefore, in this review article expresses the expansion of molecular ultrasound imaging onto the health center and the application of microbubbles for thrombolysis, for enabling drug and gene delivery beyond the biological barriers and for theragnostic applications [23].

In evaluation to disparaging microbubble (e.g., Doppler-based) detection techniques, there is no much involvement of the blood flow into the signal, mainly during the microbubbles that are used to diagnose cardiovascular diseases. As shown in Figure 7,

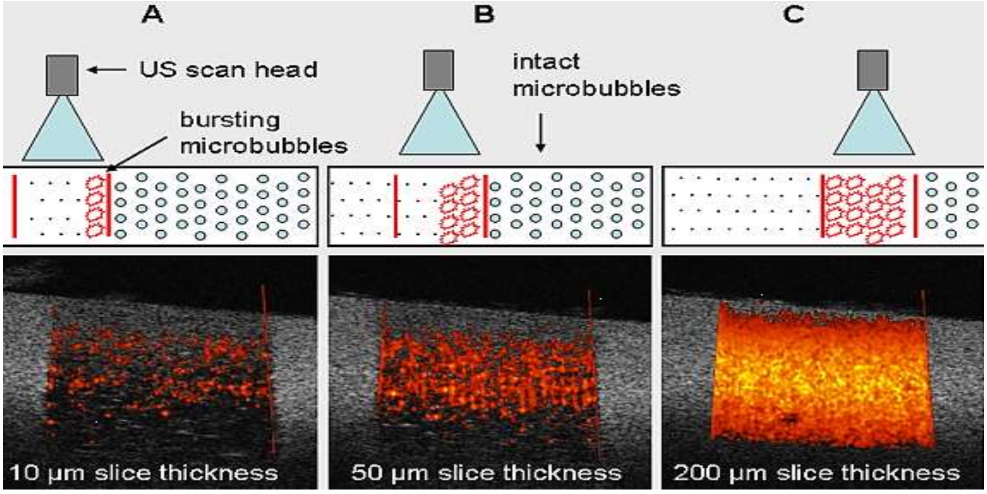

Figure 7: Sensitive Particle Acoustic Quantification (SPAQ).

SPAQ is a 3-dimensional scanning procedure with an image slice that is placed on top. For determination, the transducer or the scanned object was fixed with the servo-motor and moved in steps of micrometer during the progression of image acquisition and then an ultrasound energy pulse had the capability of expressing the microbubbles that have been applied already. During the first progress of disparaging of microbubbles image, it breaks in a broad slice and the quantification would be difficult to evaluate. However, after a shifting of micrometer-scaled between the object and the transducer a new microbubble in the non-overlapping distance will only be destroyed. Accordingly, the next and also all succeeding ultrasound scans will only take up the microbubbles from very thin excitation slices in which single microbubbles are identified [24].

Nanobubbles for enhanced ultrasound imaging of tumors

In the improvement of molecular imaging, the usage of important enabling technology for ultrasonic molecular imaging is the targeted contrast-enhanced ultrasound CEUS agent. Nevertheless, MBs are much larger (2–8 µm) related with the contrast agents for CT and MRI. Therefore, when ultrasound is used in diagnosis, the MBs may get trapped in the blood pool after intravenous injection and most of the exploration on targeted MBs has been controlled for studies concerning diseases of the cardiovascular system, for example, thrombus formation, inflammation, and arteriosclerosis. The MBs carriage severe restrictions in the tumor-targeted imaging due to its large diameters.

Recently, researchers developed nanoscale bubbles which are also called as nanobubbles [NBs], that are promising contrast agents for extravascular ultrasonic imaging. Nanoscale ultrasound contrast agents with several shells made out of polymers or phospholipids and cores of gas, liquid, or solid which have been made-up and expressed as good contrast improvement. So, based

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on some vitro and in vivo studies, the phospholipid-shell and gas-core of NBs have exposed optimum contrast enhancement capabilities though, the research on NBs is still in the early stage.

Furthermore, in vivo studies, it has been focused on the contrast enhancement facilities of these agents reacting towards normal organs or in tumors only and the inactive tumor-targeted potential is not yet being discovered. As well as the research on whether NBs can pass over the endothelial gaps of tumors and keeps a high imaging quality to be unknown. Therefore, in the experiment phospholipids were used as fabrication membrane formation of NBs in which then established an ultrasonic imaging capability that is comparable to that of MBs.

Scanning electron microscopy (SEM) were used to examine the morphological features of the NBs and in vivo experiments, it confirms the passive targeting capacity of NBs in tumor tissues. The NBs stored in the tumor area for an extended time period than MBs and a high imaging quality was noticed by using in vivo tumor ultrasound imaging. NBs of Red fluorescent dye-labeled were detected to be remained in tumor tissues, as it is assessed by using confocal laser scanning microscopy, and this discovery additionally supports the conclusion that NBs are passively targeted to tumor tissue [25].

Ultrasound-induced cavitation on human subcutaneous adipose tissue

In the viewpoint of clinical, the most effective tools for noninvasive fat reduction is done by using ultrasounds, through the generation of depression and compression series at a suitable frequency, it also causes cavitation singularities at the fat droplet of water-logged cytoplasm crossing point and ultimately adipocyte break and the triglyceride releases into the surroundings. Hence, ultrasonic energy can be distributed by both focused or unfocused waves. By means of the no focused mode, because of depth associated with ultrasound reduction, the superficial skin is visible to maximum energy intensity. By a difference of focused ultrasound which can be concentrated in a clear subcutaneous area to produce clinically related fat lysis while controlling the damages to blood vessels, connective tissue, nerves, and the primary organs. Still, the effects of thermal would be focused ultrasound energy that may value in adipocyte necrosis in the therapy area.

The devices for lipo-reductive determinations have been precisely designed to avoid undesirable injuries in tissue. a focused ultrasound emitter “Contour I (UltraShape, Yoqneam, Israel)” was initially established to accomplish the selective adipocyte lysis and appropriate drop in the volume of subcutaneous fat layer clinically, in the absence of important adverse effects. On the other hand, a different method of “Med2Contour (General Project, Montespertoli, Italy)” performance is done as it is constructed on two sides of angled transducers of nonfocused that would generate a focused ultrasound field which is weak within the subcutaneous fat pad at the point where the beams are overlapped [26].

Even with its certain clinical impact, the biological mechanisms depending on the detected of lipo-reductive properties are not studied fully in detail. Therefore, the adipose cell of cavities as shown in Figure 8 induces a vital alteration of the plasma membrane and the leakage of lipid, but then it is more likely to generate harmful effects of ultrasound on adipocytes and in other cell forms of the adipose tissue such as blood vessels, mast cells in addition to the nearby tissues also that were passed through the ultrasound beam like dermis and epidermis.

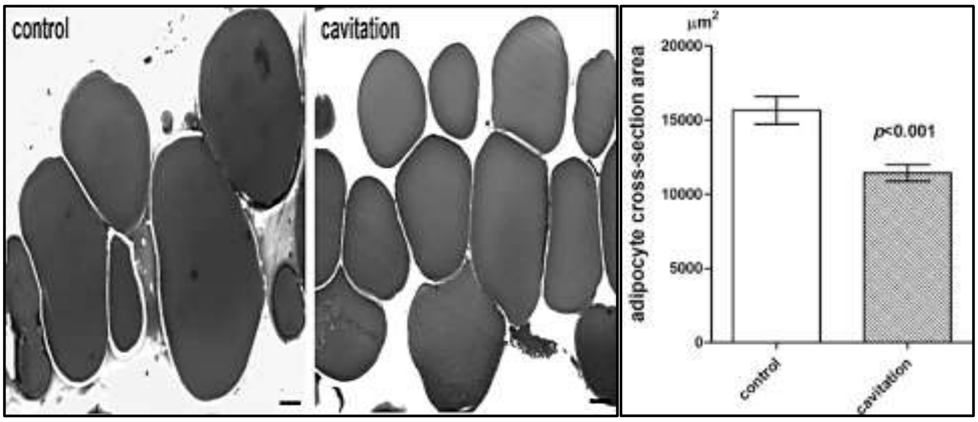

Figure 8: Ultrasound on human subcutaneous adipose tissue cavitation. Discoveries of subcutaneous adipocytes cavitation from ex vivo explants of the skin. Ultrasound cavitation causes a statistically important drop in the cross-section surface area of lipid vacuoles, related to adipocyte overall volume.

The recent study determines the ultrastructural changes of estimation and quantification made by ultrasound cavitation on the unlike cell components of the human subcutaneous fat layer in which it also includes adipocytes, blood vessel cells, upper skin tissues (dermal fibroblasts and epidermal keratinocytes) and perivascular mast cells as shown in Figure 9. For this reason, ex vivo full-thickness skin trials were reserved for a surgical procedure and subcutaneous biopsies of sham-treated as well as from individual patients the ultrasound-treated skin regions were also used [27].

Figure 9: Customizing treatment and the result of the Ul-therapy. It expresses the visual of pre-treatment and treatment after some days.

Ultrasound-mediated drug delivery for cancer treatment

The survival of cancer patients continued to be low till the implementation of chemotherapy drugs that react against the fast-dividing cancer cells whereas most of the dose get settled in the healthy tissues and causes rapid excretion or severe side effects. In tumors, the passage of drugs come across several physical barriers and the penetration of healing molecules is every so often heterogeneous and poor. Mainly in cancer, nanoparticles (NPs) has a great attention in diagnostics and drug delivery performance.

The application of drug-delivery with ultrasound depends on the collaboration between a biocompatible carrier and an acoustic wave. Therefore, the 3-D specificity of the release is recognized by focusing the zone of waves that need to be treated by using physical ethics and technologies established for a diagnostic and therapeutic ultrasound, for instance, lithotripsy or high intensity focused ultrasound (HIFU). The major task in ultrasound generated treatment is the design of the carriers that are both approachable to biologically active and ultrasound. So, these representatives would be able to transfer a large number of payloads and able to contact or even to gather differently within the tumor. The mechanisms by which ultrasound technique may release a payload and then define various drugs, nucleic acids or agents that have been released with ultrasound in the studies of pre-clinical. Whereas a recently published meta-analysis includes 117 reports of median 0.7% of the injected dose reached the tumor.

When focused ultrasound (FUS) combines with microbubbles (MBs) that emerges as a promising procedure for drug-delivery or the NPs to tumor tissues which can be developed in the non-invasive method. The mechanisms of the drug release through ultrasound procedure will be separated into both thermal and mechanical progressions as well as at times both in combination such as cavitation and radiation force [29]. Regardless of these developments, most of the inserted drugs are accumulated in the tissue of non-cancerous. Recently, a proposal was made to produce the drugs in-situ by initiating a chemical reaction by the release of ultrasound merged droplets. Therefore, by manipulating the strong hydrophobicity and lipophobicity of the perfluorocarbon (PFC) droplets composing and two of the prodrugs are isolated from each other up until the ultrasound-induced release, which also becomes a disorder for the presence of the active drug. Such a perception would assure that any pharmaceutical effects will be isolated within the specific ultrasound-induced drug-delivery zone [30].

As a multifunctional drug-delivery involving the polymeric NPs stabilized with MBs (NPMBs) to be applied in the FUS mediated and image-guided delivery of drugs has been developed as shown in Figure 10.

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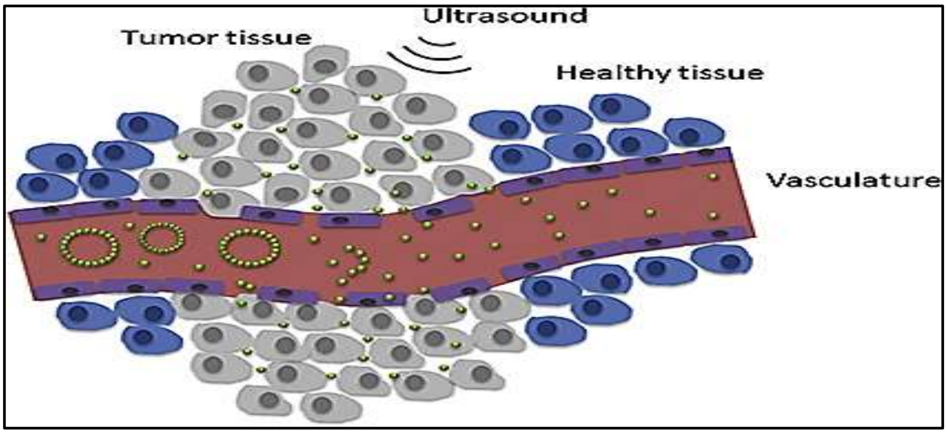

Figure 10: The diagram of ultrasound interacting with the tumor cells. The upgraded drug delivery to tumor tissue by using focused ultrasound (FUS) and nanoparticle-stabilized microbubbles (NPMBs) which is in green.

3.3 Biomedical Engineering for Cancer

Nanotechnology along with biomarker

Cancer is frequently diagnosed and treated in the final stage whereas the cancer cells have already occupied and metastasized into other body parts, for example, more than 60% of the patients with lung, breast, prostate, ovarian and colon cancer have concealed or unconcealed metastatic associations. Therefore, in this circumstance, the treatment modalities are limited in its effectiveness.

Nanotechnology in cancer is a developing field of research with the analysis of biology, medicine, chemistry, and engineering, in addition, major developments in cancer discovery, diagnosis, and therapy are done. The basic foundation includes polymeric particles, semiconductor, and metal that have an innovative electronic, magnetic, structural and ocular properties which are most of the time not accessible from individual molecules or collection of solids.

In the recent research, it has established the development of nanoparticles functioning in which are associated covalently with biological molecules such as nucleic acids, proteins, small-molecule ligands or peptides. Whereas in the other hand, medical applications have also developed a contrast agent for lymph nodes of “superparamagnetic iron oxide” nanoparticles that are used as prostate cancer recognition and then uses polymeric nanoparticles for targeted gene delivery to tumor vasculatures.

Significant prospects occur at the crossing point of the biomarkers and nanotechnology for diagnosing molecular cancer. On the complete cancer cells, the nanoparticle probes are used to quantify a group of biomarkers and in the samples of tissue by the involvement of traditional histopathology and molecular related materials. For the conjugation with multiple ligands a single nanoparticle is enough which would lead to greater affinity of binding and specificity through a multivalence effect so, these features are more important in identifying the cancer biomarkers which are available in small numbers of cells or low concentrations, as it is explained why biomarkers are needed in Table 1. Bio-conjugated particles and devices are also under an expansion of early cancer recognition in body fluids of serum and blood. Therefore, the devices of nanoscale are being controlled by the principles of selectively seizing cancer cells or proteins that are targeted by using the coated cancer-specific antibody sensors or other biorecognition ligands that yields in an electrical, mechanical, or optical signal for identification [31].

Table 1: The importance of biomarker in cancer

Use of Biomarker	Description
Risk assessment	To be used to help decide whether a person should undergo more intensive screening or take preventive measures
Screening	To help identify cancer at an earlier stage than would have happened without the test
Diagnostic	To help diagnose cancer, perhaps before it is detectable by conventional methods
Prognostic	To forecast how aggressive the disease process is and/or how a patient can expect to fare in the absence of therapy
Predictive	To help identify which patients will respond to which drugs
Monitoring	To determine how a patient is doing over time, either on or off therapy

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Targeted cancer therapy

Targeted cancer therapy is proceeded to deliver a high dosage of a drug which is anticancer, that is directly provided in the site of the tumor cells to improve the drug uptake by malignant cells and also to minimize the drug intake by the nonmalignant cells. The overall approach for sketching targeted cancer treatments are to design the drug-delivery system that could achieve the feature that is unique to tumor cells and tissues. Therefore, it is based on some characteristics of tumor microenvironment such as overexpressed of receptors in the cell surface, differences of intertumoral pH and leaky vasculature in addition to cell uptake process like endosomal pH. Due to some circumstances like the integral physiologic barriers, the particles which are used for targeted cancer therapy are mostly nanoscale that defines as nanoparticles hence, these particles are expressed to increase the delivery of drug to the malignant cells.

In the upgraded cancer research have been recognized receptors that are overexpressed in numerous types of cancer. The ligands binding which is overexpressed receptors have been effectively used as the targets of malignant cells and stimulates the polymer response that has also been technologically advanced to control the chemotherapy drugs release in response to environmental inducers.

With the combination of advanced biomaterials and nanotechnology have progression of targeted anticancer drug-delivery and moreover treating individual types of cancer cells along with minimal injurious side effects. The design of an effective targeted therapy will require optimization of both passive and active targeting mechanisms which are applied to develop the targeted delivery of drugs (Alexander-Bryant, Vanden Berg-Foels, and Wen, 2014).

Passive targeting

Solid tumors generally have a diffusion-limited maximal size of 2 mm^3 and settle until angiogenesis occurs (formation of new blood vessels), therefore permitting to access the circulation. A passive targeting mechanism proceeds with the properties of size and surface of drug delivery nanoparticles which need to be controlled to avoid the uptake by the reticuloendothelial system (RES). To induce the time of circulation and capability of targeting, the ideal size should be in diameter of >100 nm and the surface should be hydrophilic to avoid clearance by macrophages. A hydrophilic nanoparticle surface safety measures against plasma protein adsorption and accomplished through hydrophilic polymer coating otherwise by the use of block or branched copolymers.

An alternative passive targeting approach is done by using the tumor environment in an outline termed as “tumor-activated prodrug therapy” therefore conjugates the drug with a tumor-specific molecule and remains inactive until it reaches the target as shown in Figure 11.

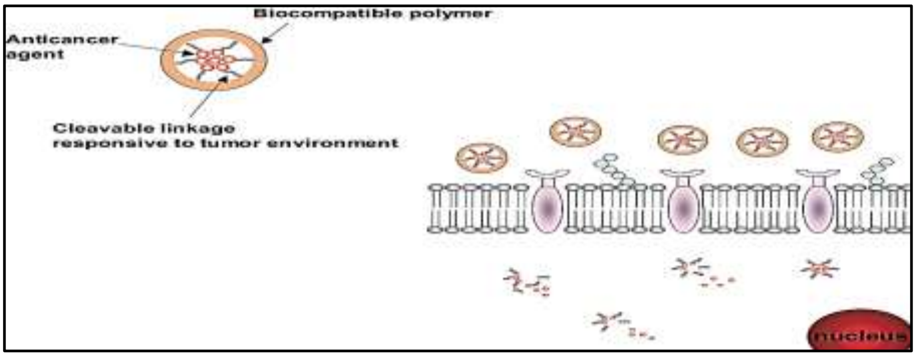

Figure 11: Tumor-activated prodrug delivery and targeting. The conjugation of anticancer agent with the biocompatible polymer is bounded by an ester bond therefore, the association is hydrolyzed by high or low pH at the tumor site or by cancer-specific enzymes, at which the nanoparticle releases the drug.

Another passive targeting technique which can be used is the direct local delivery of anticancer agents to the tumor cells, therefore, this approach has the benefit of not including the drug from the systemic circulation. Nevertheless, the administration would be highly invasive due to injections or surgical procedures and this technique is intolerable to use for some tumors which are not able to reach, such as lung cancers [34].

Active targeting

Active targeting technique is done by conjugating the nanoparticle with a targeting component that delivers a special nanoparticles accumulation in tumor-bearing organ / in the tumor itself / individual cancer cells / specific molecules in cancer cells / intracellular organelles. Therefore, this method depends on the association of ligand-receptor antibody-antigen, and lectin-carbohydrate (a classic example of targeted drug delivery for the whole organ which may harm normal cells). Lectins are proteins of

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nonimmunological derivation that have the ability of spotting and binding to glycoproteins expressed on cell surfaces as well as its interactions with certain carbohydrates are very specific. Moieties o carbohydrate can be used to target delivery of drug systems to lectins which would be the “direct lectin targeting” and lectins that are used as targeting moieties to target cell surface of the carbohydrates are known as “reverse lectin targeting”. Therefore, the targeting moiety is focused in the direction of specific receptors or antigens expressed plasma membrane or somewhere at the tumor site. The overreaction of receptors or antigens in human cancers provides an effective drug uptake via receptor-mediated endocytosis which is a cellular ingestion hence the glycoproteins cannot be removed by the conjugates of polymer-drug that have entered the cells through endocytosis so it activates the targeting mechanism by providing an alternative route for overcoming multidrug resistant-MDR [34].

3.4 Biomedical Material Engineering

Biomaterial is defined as “any substance other than a drug or combination of synthetic substances or natural in derivation which can be used at any time as well as it can be used as a whole substance or as a part of a system which could enhance, treats, or replaces any specific tissue, cells, organ or function of the body”. Academically, any material of natural or artificial which is a man-made can be a biomaterial that could assist for the specified medical and surgical purposes. As well as they are typically proposed to be in long-term interaction with biological materials such as intravenous catheters, prostheses, and reconstituted tissues. It also incorporates with the basics of biology, medicine, chemistry, physical, tissue engineering and materials science, however, the demand for biocompatible, biodegradable and bioresorbable materials has increased intensely subsequently from the last decade [35].

An ideal biomaterial should be biocompatible, biodegradable (which has the essential properties on biomaterials) and non-immunogenic which can be functionalized with bioactive proteins and chemicals. The achievement of any medical device or implantation rest on the types of biomaterial that are able to use and the synthesize materials like polymers, metals, and alloys, ceramics and carbons are also considered to have an important contribution in many traditional devices of medicine. Along with the principal status is the multilateral association between the processing methods, material properties, and design.

It is more important to have a detailed information of how cells interact with the materials and also its vital condition for the progression of new approaches to control cell-biomaterial and eventually tissue-biomaterial interactions [36].

Whereas in Table 2 defines the application of biomaterials in various field of medical industries and Table 3 describes biomaterials usage in different parts of body organs and the replacement of different parts for a living being.

Table 2: The uses of Biomaterials

Problem Area	Examples
Replacement of diseased or damaged part	Artificial hip joint, kidney dialysis machine
Assist in healing	Sutures, bone plates, and screws
Improve function	Cardiac pacemaker, intraocular lens
Correct functional abnormality	Cardiac pacemaker
Correct cosmetic problem	Augmentation mammoplasty
Aid to diagnosis	Probes and catheters
Aid to treatment	Catheters drain

Table 3: The uses of biomaterial in organs

Organs	Examples
Heart	Cardiac pacemaker, artificial heart valve, total artificial heart, blood vessels
Lungs	Oxygenator machine
Eye	Contact lens, intraocular lens
Ear	Artificial stapes, cochlear implant
Bone	A bone plate, the intramedullary rod
Kidney	Catheters, stent, Kidney dialysis machine
Bladder	Catheter and stent

The “vanadium steel” is the first developed metal alloy specifically for human usage which was applied to manufacture bone fracture plates such as Sherman plates and screws. Metals like chromium (Cr), iron (Fe), nickel (Ni), niobium (Nb), tantalum (Ta), cobalt (Co), molybdenum (Mo), tungsten (W) and titanium (Ti) were used to make alloys for the production of implantation where

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the body can only tolerate very tiny in amount. From time to time, the naturally occurring forms of metallic elements in the red blood cell function iron (Fe) or synthesis of a vitamin B-12 cobalt (Co) however, the body would not be able to tolerate in great amounts. The biocompatibility of the metallic implant is concerned mainly with the implants that can get rusted in an in vivo atmosphere. Whereas the significances of rusting break down the implantation material per seconds and leads to weakening, in addition, the injurious effect of corroded products with being presented on the surrounding of tissues and organs.

The most significant features which should take into consideration are non-toxic, non-allergic, non-inflammatory, non-carcinogenic, biocompatible and bio-functional in the host for its lifetime. Hence, ceramics are basically hard material and used in manufacturing implants can be classified into nonabsorbable which is relatively inert, bioactive or surface reactive which is semi-inert and biodegradable or resorbable which is non-inert. Examples like alumina, zirconia, silicon nitrides and carbons are inert bio-ceramics. Certain glass ceramics and dense hydroxyapatites are semi-inert (bioreactivity), and calcium phosphates and calcium aluminates are resorbable ceramics [37].

Nanomaterials for Bone Repair

Bioactive materials which are currently used in regenerative medicine is due to the predictable requirement for bone tissue regeneration as an effective way to recover the current medical practice of bone replacement. The composition of bone is a nanocomposite made up of inorganic and organic components with classified structure ranging from nano to macro scale. Usually, the clinical imperfections of bone modernization and repair are directed by using autologous and allogenic tissues as well as alloplastic materials which has its own functional restrictions. The properties of nanomaterials include the induced wettability and surface area which direct to the protein increased adsorption when related with conventional biomaterials [38].

Bone grafting (in Figure 12) is the 2nd most dominant transplantation surgery after blood transfusion whereas a various range of bone graft alternatives occurs in the biomedical field depending on the materials like ceramics, inorganics, and polymers. The most important role of nanomaterials is that they can correctly simulate the natural realistic dimensions of bone and collagen and as a result in a wide range of biomedical applications nanomaterials have been largely discovered, mainly in regenerative medicine.

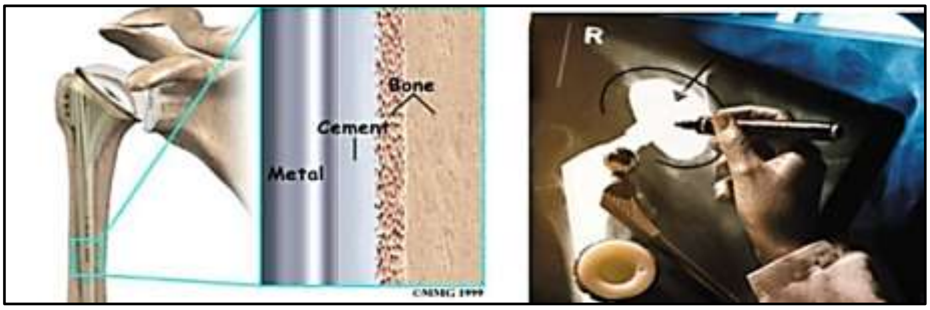

Figure 12: Using of biomaterials in bone grafting.

Biomaterials in dentistry

The known and experienced biomaterials are the dental materials that consider mercury compounds for dental fillings. A very important point is that these materials are sold very low in volume but at a high price and are considered as strategic products. The biomaterials along with technologies are not only for replacing damaged or missing tissues however it also initiates the tissue regeneration, as well as there, are many zones of research that both dental stem cells and biomaterials were used, therefore, it allows the possibility of tissue regenerating in periodontal ligament, dental pulp, dentin and even in the enamel. Similarly, the dental stem cells are being used as a source to facilitate the cell to repair of nondental tissues such as nerves and bone that has been presented. As the cellular mechanisms of tertiary dentin development are largely unknown and limited materials have been wisely designed to improve the rebirth of rootlike structures and also unravelling the cellular mechanisms-based dentin formation by pulp-derived stem cells and by using this information some other researcher might implement to design a new biomaterial that aims pulp-derived stem cells for stimulation of dentin formation [39]. The Figure 13, would express biomaterials interacting with dentistry.

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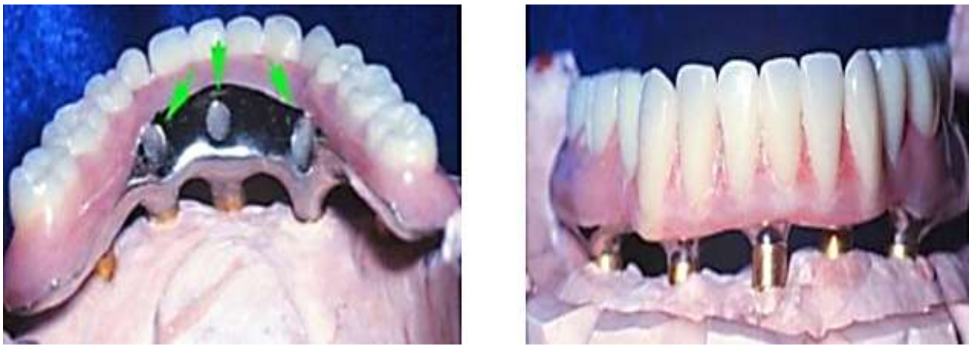

Figure 13: The application of biomaterials in dentistry.

3.5 Advanced Dental Science and Technology

Dental caries which is known to be an infectious and communicable disease that causes the tooth structure to get damaged by the bacteria of acid-forming in the dental plaque, an intraoral biofilm and in the presence of sugar components. Therefore, the outcome of the infection is in loss of tooth minerals that attacks the outer layer of the tooth and then continue to progress through the dentin to the pulp then eventually negotiate the strength of the tooth. From the past decades, observation of the infection is altered not only based on the occurrence of dental caries however by considering the distribution and outline of the disease population as well. Precisely, it is also detected in the distribution of dental caries on the surface of the tooth also changes and the lesion development rate through the teeth is moderately slow for most of the individuals.

Hence, the modification also plays a role in consequences for diagnosis and the management of emerging lesions also in expecting the risk of caries and by organizing the effective disease prevention and management programs for individuals and populations [40].

Analyzing the caries lesion in the early stage is much better because progression of the carious can be altered by the treatment of preventing so that the lesion would not be able to continue drilling into the pulp therefore, the balance can be controlled by adapting to diet, plaque control of enhancement and the use of fluoride properly.

Diagnosing by the usage of noninvasive quantitative technique should have the ability to detect the initial stage of the lesions and also monitor the changes that occur in lesion during the time in which preventive procedures could be initiated as well as by evading the premature of tooth treatment by restorations. Therefore, the caries detection methods include some primarily used procedure such as conventional methods that are classified into the visual-tactile examination and the international caries detection & assessment system (ICDAS) and novel diagnostic systems (based on physical signals that measures of the caries process).

Radiographic techniques

Radiographic procedures are also classified as conventional radiography, digital radiography and Digital subtraction radiography (DSR). Whereas in conventional radiography, initiates the application of bitewing as support for the clinical investigation that would allow more proximal sensitive detection and occlusal caries lesions in dentin-pulp. Also, it is a greater method for estimating the depth of lesion than in the photographic examination that carried out individually. Bitewing prognosis is a suitable radiographic technique for the detection of lesion caries and this technique necessitates a wing for the patient to bite with a film-holder.

Digital radiography presents the probable to increase the yield of diagnostic dental radiographs whereas expressed itself in subtraction radiography. This procedure consists number of pixels (each pixel has the range in between 0 and 255), with 0 indicating black and 255 expressing white as well as the values in between the range would indicate the shades of grey and proceed with digital radiograph with the probable of 256 grey points expressively with resolution of low than a conventional radiograph that encompasses millions of grey levels. Sensitivities and specificities of digital radiographs present lower than the systematic radiographs while measuring the small proximal caries. Nevertheless, a digital radiograph of images is developed by using a range of algorithms, so that some of which increase the white end of the grey scale and others with the black end. It establishes a decrease in radiographic dose and consequently suggests in additional benefits than diagnostic yield as well as with an ease the digital images can be archived and replicated.

DSR is an advanced technique of image analysis tools, therefore, the performance would express a small variation between succeeding radiographs, otherwise, it would have stayed constantly without observing due to the over-projection of structural anatomy or in the variation of density which is too small to identify by human eyes. Also, it has been used in the valuation of the progression, arrest, or regression of lesions caries.

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Enhanced visual techniques

Which is classified into fiber-optic transillumination (FOTI) and digital imaging fiber-optic transillumination (DIFOTI). In FOTI, photographic review of caries lesion depends on the phenomenon of spreading light. Whereas the sound enamel is embraced with the alteration of hydroxyapatite crystals that are so densely packaged and produces almost the transparent structure. The procedure is so simple, painless and noninvasive that can be applied repeatedly to the patient without any harm. It is also used to identify all surface of caries and mainly beneficial at proximal lesions. The study of FOTI is differentiated with the current review of a mean sensitivity of only 14 and a specificity of 95 in view of occlusal dentine lesions and 4 and 100% for proximal lesions respectively. In FOTI there are some restrictions which are required to be followed so that the system is subjective rather than objective and there are no continuous data outputted so it is not possible to record what is observed in an image, Figure 14 expresses the FOTI.

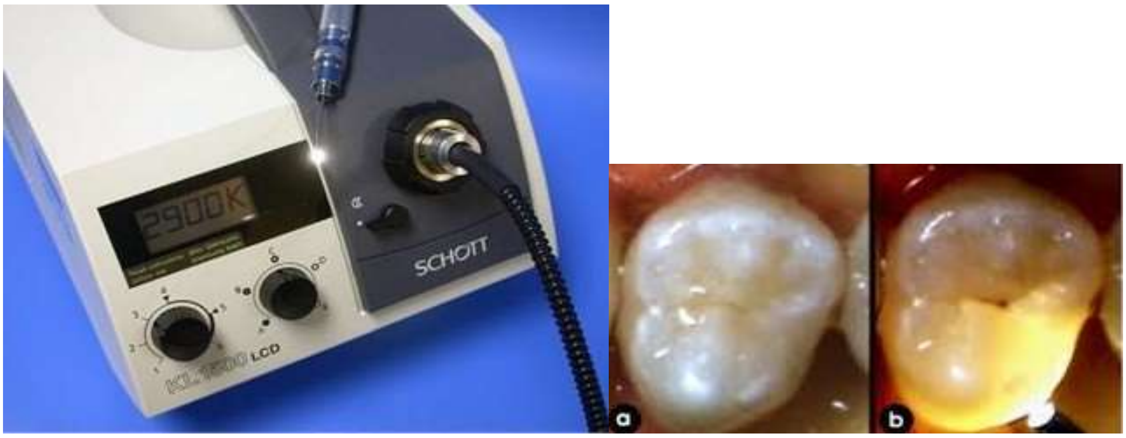

Figure 14: The image of FOTI and its application. The right side of the image expresses a normal clinical vision of the tooth and the other one with the vision using FOTI applicator.

DIFOTI is a procedure done by obtaining the images of teeth by using visible light through the support of FOTI. The images are developed by a charge-coupled device (CCD) camera or digital electronic (as shown in Figure 15), therefore DIFOTI may eradicate or decrease intra- and inter-observer differences, usually the emitting light from the optic fiber proliferates through the tooth to the non-illuminated surface are. Therefore, the image can be obtained by keeping the adjustment of control parameters of imaging number and then the collected data will be computerized for the analysis with algorithms in which it produces a digital image that can be seen by the patient and dentist.

Figure 15: The with digital imaging fiber-optic transillumination.

As well as this developed system can be applied for digital image processing approaches to improve the difference between sound and various tissues in addition to measure the features of emerging and secondary caries lesions smooth surfaces. It can also be applied to distinguish other variations in coronal tooth anatomy such as tooth fractures and fluorosis. Compared to the radiographic examination, DIFOTI presents higher sensitivity in recognition in early lesions and likely for monitoring numerically of selected lesions over a period of time. However, it does not provide the portion of lesion depth since the image obtained is from the surface or nearby the surface region. There is a failure to quantify the lesion progression although images can be associated over time and with the greater sensitivity and somewhat lower specificity there is a possibility of overdiagnosis.

There is some more application for detections are used which are fluorescent techniques (quantitative light-induced fluorescence-QLF), laser-induced fluorescence, based on electrical current measurement and by ultrasound techniques [41]. As in Table 4, the application in carried detection along with physical principle is summarized:

Table 4: The methods of caries discovery depending on their physical principles.

Physical principle	Application in caries detection
X-rays	Digital subtraction radiography Digital image enhancement
Visible light	Fiber optic transillumination (FOTI) Quantitative light-induced fluorescence (QLF) Digital image fiber optic transillumination (DIFOTI)
Laser light	Laser fluorescence measurement (DiagnoDent)
Electrical current	Electrical conductance measurement (ECM) Electrical impedance measurement
Ultrasound	Ultrasonic caries detector

4. CONCLUSION

Based on my review of this article, I conclude that biomedical engineering field does have a major role in this developing world and the applications are well designed in order to proceed without any harm. When science and technology combine to enhance the procedures for diagnosis and treatments which is an advantage for the health care system mainly for the cancer patients. Nevertheless, the research for certain health issues is still under study for a better outcome in the future.

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