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APPLICATIONS OF NANOROBOTS IN MEDICAL TECHNIQUES

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ABSTRACT: Nanotechnology is going to revolutionize the world. According to the National Nanotechnology Initiative (NNI), nanotechnology refers to the study of all particles in the range of 100 nanometers or less. One of the most important advantages of the smaller particle size is the ratio of surface atoms or molecules to the total number increases. That means they have large surface areas that lead to increase in surface activity and produce changes in their physical properties and biological properties. In the pharma-world, the applications of nanotechnology mean drugs containing nano-sized active ingredients. They are well used to cure HIV, Cancer and other harmful diseases; they can restore lost tissue at the cellular level, useful for monitoring, diagnosing and fighting sickness. The smaller drug delivery systems permit the deposition of medications in previously inaccessible areas of the body; it also has great importance in the treatment and diagnosis of certain diseases like cancer. A recent discovery in the field of drug delivery is target therapy, which improves the diagnostic tests and medical devices.

INTRODUCTION: Nanotechnology is a combination of chemistry, physics, materials science, and biology, to bring together the required collective expertise needed to develop these novel technologies [1]. Nanorobots are mainly the nano-devices that are used for providing protection or treatment against pathogens in humans. They are designed to perform a particular task or sometimes tasks with precision at nanoscale dimensions of 1-100 nm [2]. They are expected to work at atomic, molecular, and cellular levels in both medical and industrial fields.

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Advances in the areas of robotics, nanostructuring, medicine, bioinformatics, and computers can lead to the development of the nanorobot drug delivery system. Some of the examples are respirecyte nanorobots, microbivore nanorobots, surgical nanorobots, and cellular repair nanorobots. They have a diameter of about 0.5 to 3 microns and will be constructed out of parts with dimensions in the range of 1 to 100 nanometers.

The main element used in nanorobots is carbon because of its inertness and strength in the form of diamond and fullerene. They generally have an exterior passive diamond coating to avoid attack by the host immune system [3]. Techniques like Scanning Electron Microscopy (SEM) and Atomic Force Microscopy (AFM) are being employed to understand the molecular structure of the nanoscaled devices.

Fabrication and controls of the nanorobots are the main hurdles to develop nanorobots or nano-machine components. Such devices will operate in microenvironments, and their physical properties differ from those encountered by conventional parts.

Advantages of Nanorobots over Conventional Medical Techniques: Nanorobotics has aimed to overcome the following drawbacks of conventional medical techniques.

1. Incisions harm tissue layers, which take quite a long time to heal.
2. Painful anesthesia is used to limit the pain to a great extent, yet it is only for a short time.
3. Delicate surgeries such as eye surgery still do not have a 100% success rate.
4. In any of the invasive techniques, the patient's life is totally in the hands of the operator or surgeon or physician. It is risky, as one mistake could spell disaster.

Scientists and researchers are workings on a more robust, reliable, and bio-compatible approach. Instead of curing of the outside, they plan to defend the body from the inside. That is where medical nanorobots come in. The major advantages of this technology provide are

1. Minimal or no tissue trauma.
2. Considerably less recovery time.
3. Less post-treatment care required.
4. Continuous monitoring and diagnosis from the inside.
5. Rapid response to a sudden change.

Some added features of nanorobotics. Would also enable us to do the following:

1. It can store and process previous data, identify patterns, and hence, help to predict the onset of an ailment.
2. It can guide externally or as per program, targeting specific locations.
3. It has the ability to deliver payloads such as drugs, or healthy cells to the specific site.

They can navigate through natural biological pathways; hence it can be customized (and often more durable) to body cells manufactured externally.

Disadvantages of Nanorobotics:

1. When different nanorobots are inserted to cure different diseases, the clusters may be formed inside the body.
2. Installation cost is quite high.

Different Approaches to Nanorobotics:

1.1 Biochip: The combined use of nanoelectronics, photography and new biomaterials can be considered as a best possible way to enable the required manufacturing technology towards nano-robots for common medical applications, like surgical instrumentation, diagnosis and drug delivery [4-6] so, practical nanorobots should be integrated as nanoelectronics devices, which will allow teleoperation and advanced capabilities for medical instrumentation [7].

1.2 Nubots: Nubot is an abbreviation for “nucleic acid robot”. They are organic molecular machines at the nanoscale.

Biological circuit gates are based on DNA materials, which have been engineered as molecular machines to allow in-vitro drug delivery for the targeted region.

1.3 Positional Nano Assembly: Nano factory collaboration [8], founded by Robert Freitas & Ralph Werkle in 2000, is a focused ongoing effort that is developing positionally-controlled diamond mecha-nosynthesis & a diamondoid nano factory that would have the capability of building diamondoid medical nanorobots.

1.4 Bacteria Based: This approach proposes the use of biological microorganisms, like *E. coli* bacteria. Thus, the model uses a flagellum for propulsion purposes.

Ideal Characteristics of Nanorobots:

- They lie in the size range of 0.5 to 3 microns with 1-100 nm parts; else they can block capillary flow.
- Nanorobots prevent itself from being attacked by the immune system by having a passive, diamond exterior.
- It has the capability to communicate with the doctor by encoding messages to acoustic

signals at carrier wave frequencies of 1-100 MHz.

- It can produce multiple copies of it to replace worn-out units, a process called self-replication [3].

Some Types of Nanorobots:

Pharmacyte: The pharmacyte is a nanorobot of 1-2 µm in size. Depending on mission requirements, the payload stored in onboard tanks of nanorobotics system can be discharged into the proximate extracellular fluid or delivered directly into the cytosol using a transmembrane injector mechanism [9].

Respirocyte: It is an Artificial Oxygen Carrier nanorobot. The power is supplied by endogenous serum glucose.

This artificial cell is able to supply 236 times more oxygen to the tissues per unit volume than RBCs (Red blood cells).

Microbivores: It is an oblate spheroidal device for nanomedical applications with 3.4 µm in diameter along its major axis and 2.0 µm in diameter along its minor axis. The nanorobot can consume up to 200 pW. This power is used to digest trapped microbes.

Clottocytes: This is a type of nanorobot, with a unique biological capability: They generally deliver substances that help to promote coagulation [10].

Chromallocyte: The Chromallocyte would replace entire chromosomes in individual cells thus reversing the effects of genetic disease and other accumulated damage to our genes, preventing aging.

Inside a cell, this will first size up the situation by examining the cell's contents and activity, after that it will take action by working along molecule-by-molecule and structure-by structure; it will be able to repair the whole cell.

Components of Nanorobots: The substructures in a nanorobot include [11-15].

Payload: This is a void section that holds a small dose of drugs or medicine. It can transverse in the blood and release the drug to the site of infection or injury.

Micro Camera: The nanorobot may include a miniature camera, and it can be observed when navigating through the body manually.

Electrodes: The electrode mounted on the nanorobot could form the battery by the use of electrolytes in the blood. These protruding electrodes can kill the cancer cells by generating an electric current and heating the cells uzp to death.

Lasers: These lasers can burn the harmful material like arterial plaque, blood clots, or cancer cells.

Ultrasonic Signal Generators: These generators are used when the nanorobots are used to target and destroy kidney stones.

Swimming Tail: By propulsion, nanorobots get into the body. The motor is used for movement and manipulator arms or mechanical legs for mobility. They control design is the software developed for simulating nanorobots in an environment with fluids which is dominated by Brownian motion. The nanorobots have chemical sensors to detect the target molecules. The three main types of swarm intelligence techniques designed are ant colony optimization (ACO), artificial bee colony (ABC), and particle swarm optimization (PSO) [16]. Structurally it has consisted of molecular sorting rotor, propellers, fins, and nanosensors.

Bio-Nanorobots: Nanorobots designed by harnessing properties of biological materials (peptides, DNAs), their designs, and functionalities. These are inspired not only by nature but also by machines [17].

A. Introduction of Nanorobots into the Body: A viable robot has to be small and agile so that it can navigate through the human circulatory system, an incredibly complex network of veins and arteries. However, it is balanced against the fact that larger nanomachine more versatile and effective it is.

B. Movement of Device around the Body: Initially, the device is carried to the site of operation using normal blood flow. To reach the site of action, there should be a number of means for propulsion such as propeller, cilia, electromagnetic pump, jet pump membrane propulsion.

C. Direction of the Device: The defected tissues are identified by the sensors. The long-range sensors are used to navigate to the site of unwanted tissue. Short-range sensors are used to locate the tumor. Another purpose of using nanorobots is to locate the position of the microrobot in body [18].

It is possible to track the robot either by ultrasonic signal or by generating heat or infrared within the microrobot.

D. Control of the Device: There is mainly two types of sensors used. One for final navigation and another sensor is used for actual operation. It will guide the nanorobot to the tissue that is to be removed and away from the tissues that are not to be removed. The device is analyzed using a camera, spectroscopic technique, UHF (Ultra High Frequency) sonar for resolution.

E. Means of Treatment: The process can be done in different ways. The clump of substance can be broken to exert its action, and it gets eliminated afterward. They can be used to enhance other efforts.

F. Removal of Nanorobots After Treatment: The nanorobots introduced into the body to perform specific tasks need to be removed, after their task inside the human body. The problem is the exact opposite in case of semi-permanent introduction of the nanorobots in the bloodstream for maintenance purposes; the removal of nanorobots from the body is done deliberately. Another way of doing this is by using chemical sensors.

G. Powering of Nanorobots: The power required to operate the nanorobot can be obtained by two ways either power from a source of the body or getting power from the bloodstream. Or it can be obtained from an external source.

Medical Application of Nanorobots: Nanorobots are expected to enable new treatments for patients suffering from different diseases and will result in a remarkable advance in the history of medicine. The use of nanorobots may advance biomedical intervention with minimally invasive surgeries and help patients who need constant body functions monitoring, or ever improve treatment efficiency through early diagnosis of possible serious diseases.

Hemophilia: Nanorobots could travel to the spot and break it up. The robots must be able to remove the blockage without losing small pieces in the bloodstream, could travel elsewhere in the body, and cause more problem [21]. The robot must be so small enough so that it doesn't block the flow of blood itself assist in their healing process. One particular kind of nanorobot is the clottocyte or artificial platelet clottocyte; clotting could be up to 1,000 times faster than the body's natural clotting mechanism [19]. Clottocyte used to treat patients with serious open wounds.

Application of Nanorobots in Dentistry:

Nanorobotic Dentifrices (Dentifrobots): These when delivered either by mouthwash or toothpaste, can cover all subgingival surfaces, thereby metabolizing trapped organic matter into harmless and odorless vapors. Properly configured dentifrobots can identify and destroy pathogenic bacteria that exist in the plaque and elsewhere. These invisibly small dentifrobots are purely mechanical devices that safely deactivate themselves when swallowed.

Maintenance of Oral Hygiene: A mouthwash full of smart nanorobots could identify and destroy pathogenic bacteria while allowing the harmless flora of the mouth to flourish in a healthy ecosystem. Further, the devices would identify particles of food, plaque, or tartar and lift them from the teeth to be rinsed away. Being suspended in liquid and able to swim about, would be able to reach surfaces beyond the reach of toothbrush bristles or the fibers of floss. Sub occlusally dwelling nanorobots are delivered by dentifrice patrol. They prevent tooth decay and provide a continuous barrier to halitosis [21].

Cavity Preparation and Restoration: Multiple nanorobots working on the teeth in unison, invisible to the naked eye, may be used for cavity preparation and restoration of teeth. The cavity preparation is very precisely restricted to the demineralized enamel and dentin, thus providing maximum conservation of sound tooth structure.

Tooth Repair: Nanodental techniques involve genetic engineering, tissue engineering, and tissue regeneration procedures for major tooth repair. Nanorobots provide complete dentition replacement therapy, including both mineral and cellular components [20].

Dentin Hypersensitivity: Dentin hypersensitivity is a pathological phenomenon caused by pressure transmitted hydrodynamically to the pulp. Reconstructive dental nanorobots selectively and precisely occlude specific dentinal tubules within minutes, offering patients a quick and permanent cure from hypersensitivity [21].

Esthetic Dentistry: They are used for dentition re-naturalization procedures in esthetic dentistry. They excavate old amalgam restorations and remanufacture teeth with biological materials, in-distinguishable from original teeth.

Tooth Repositioning: Orthodontic nanorobots can directly manipulate the periodontal tissue, including gingiva, periodontal ligament, cementum and alveolar bone, allowing rapid and painless tooth straightening, rotation, and vertical repositioning within 3 min to hours.

Inducing Anesthesia: A colloidal suspension containing millions of active analgesic micron size dental nanorobots will be installed on the patient`s gingiva. After contacting the surface of the crown or mucosa, the ambulating nanorobots reach dentin by migrating into the gingival sulcus and pass painlessly through the lamina propria or through 1-3 µ thick layer of loose tissue at the CEJ. Upon reaching the dentin, they enter the dentinal tubules up to 1-4 µ depth and proceed towards the pulp guided by a combination of chemical gradient, temperature differentials and positional navigation under nanocomputer control. Thus, the migration of nanorobots from the tooth surface to the pulp occurs in 100 sec. Once installed in the pulp, they establish control over nerve impulse, analgesic nanorobots commanded by the dentist shut down all sensitivity in any particular tooth requiring treatment. When the dentist presses the handheld control, the selected tooth is immediately anesthetized. After the procedure is completed, the dentist orders the nanorobots to restore all sensation and egress from the tooth nanorobot analgesia offers greater patient comfort, reduces anxiety, no needles, greater selectivity, controllability of analgesic effect; fast and completely reversible action; avoidance of side effects and complications.

Application of Nanorobots in Cancer Treatment: Nanorobots with chemical biosensor (nanosensor) are used for detecting the tumors cells in the early stage of cancer development. This nanosensor will sense the presence of malignant cells in the body. Considering the properties of nanorobots to navigate as bloodborne devices, they can help with such extremely important aspects of cancer therapy. Nanorobots with embedded chemical biosensors can be used to perform the detection of tumor cells in the early stages of development inside the patient's body. Integrated nanosensors can be utilized for such a task in order to find the intensity of E cadherin signals.

Therefore, a hardware architecture based on nano bioelectronics is described for the application of nanorobots for cancer therapy. The scientists have genetically modified salmonella bacteria that are drawn to tumors by chemicals secreted by cancer cells. The bacteria carry microscopic robots, about 3 micrometers in size that automatically release capsules filled with drugs when the bacteria reach the tumor. By delivering drugs directly to the tumor, the nanorobot, which the team named bacteriobot, attacks the tumor while leaving healthy cells alone, sparing the patient from the side effects of chemotherapy [24-26].

DNA Nanorobotics:

- It is a type of nanorobot that is used to deliver the drug to the targeted cell only, not to the adjacent cell so no side effects damage to the healthy cells occurs.
- The aim of DNA nanorobotics is the design and fabrication of dynamic DNA nanostructures that perform specific tasks via a series of state changes.
- State changes can be done from the hybridization/denaturing of a single base to the hybridization/denaturing of entire strands.
- These state changes can be effected autonomously, in which case the system switches state without external intervention while in other cases precise amounts of specific species, such as DNA strands or enzymes, are introduced to enforce state changes [22].

- It should be noted that different copies of the nanostructures might be in different states at the same time, and we are generally interested in the overall average behavior system. The two halves of the hexagon are latched together to form the vessel where the payload (*i.e.* the drugs) will be placed [23].

Components of DNA Nanorobot:

DNA Origami: The term origami refers to the Japanese folk art of folding paper into a special shape. The method is called DNA origami since one long strand of DNA is folded to produce the desired structure with the help of smaller staple strands. The origami folding process is the method is based on the folding of the large ssDNA (usually the 7.3 kilobase genome of the M13 bacteriophage) with an excess of smaller complementary strands (typically 32 bases).

These small strands are called "staple" strands and are complementary to at least two distinct segments of the long ssDNA. Long ssDNA and an excess of staple strands are then heat-annealed in a specific buffer with a high concentration of magnesium to form the origami [24-26].

How Does a DNA Nanorobot Reach the Target: A major challenge in nanotechnology is to precisely transport a nanoscale object from one location on a nanostructure to another location following a programmable path. DNA has been explored as an excellent building material for the construction of both large scale nanostructures and individual nanomechanical devices. The successful constructions of two dimensional DNA lattices and one dimensional DNA arrays made from DX molecules [27], TX molecules [28], rhombus molecules [29] and 4 × 4 molecules [30] provide the structural base for realization of the above goal.

However, the existing DNA nanomechanical devices only exhibit localized nonextensible motions such as open/close [31-34], extension/contraction [35-37] and reversible rotation motion [38, 39].

Applications of DNA Nanorobot in Treatment of Cancer: DNA nanorobot can be used as a targeted drug delivery system to improve medical treatments. There are many chemotherapy drugs that are designed to kill fast-dividing cells. But the actual fact is fast-dividing cells not only include cancer cells but also include stomach lining, hair follicles, blood cells, *etc*. As chemotherapy drugs attack all of these fast-dividing cells, they usually lead to various side effects like nausea and vomiting, hair loss, low blood cell counts, *etc*. So, this is the main drawback of chemotherapy drugs. It can be overcome by

- By stimulation of death receptors causing apoptosis.
- Destruction of cancer cells by targeted delivery of anti-cancer drugs.
- By direct damage to the cancerous cells [41].

Targeted Drug Delivery System: Nanorobot is made from DNA, and is in the shape of a hexagonal barrel to carry a variety of payloads. It is held together by two "locks" comprising DNA aptamers, which are short strands and can bind to antigen targets. The locks get opened when they encounter antigens on the surface of certain cells, and the robot exerts its action [40].

DNA Nanorobots as Biosensors: The technology of nanosensing is also under development. For sensing certain analytes, genetically engineered versions of pore-forming proteins like *Staphylococcus aureus* alpha-hemolysin are also being studied. Efforts to detect biological warfare agents like cholera toxins by utilizing their ability to bind to a bilayer membrane in the presence of gangliosides are another example. Light sensors could be made using certain photoreceptive polypeptides containing azobenzene or spyropyran units as they respond to light or dark environmental conditions by undergoing conformational change, for example, the transition from random coil to a helix. An optical DNA biosensor platform has been reported using etched optical fiber bundles filled with oligonucleotide functionalized microsphere probes. Finally, work is in progress to develop sensors for brain implantation, which would foretell the development of a stroke and be useful for perioperative online monitoring during coronary by-pass surgery [42].

Delivery of Therapeutic and Imaging Agents for Cancer Therapy: Medical nanorobotics holds great potential to deliver drugs with a higher degree of precision and speed when compared to passive diffusion methods. In tumor therapy, the released drug can be externally triggered, allowing the nanorobotic platform to distribute a high amount of the therapeutic agent in a localized area of the tumor [43]. Biohybrid nanorobots can be used for targeted delivery of payloads inside living animals. Magnetotactic bacterias, which naturally produce magnetic iron oxide nanoparticles, have been coupled with liposomes loaded with therapeutic payloads *in-vitro*. More recently, these modified bacteria have been guided in a study using an external magnetic field to deliver the drug-loaded liposomes *in-vivo* to a mouse tumor site [44].

Robots in Nanogene Therapy: A medical nanorobot is capable of treating genetic diseases by comparing the molecular structures of both DNA and proteins within the cell to known or desired reference structures. Any abnormalities can be corrected, or modified there. Floating inside the nucleus of a human cell, an assembler-built repair vessel works for genetic maintenance. The molecular structures of both DNA and proteins are compared to information stored in the database of a larger nanocomputer positioned outside the nucleus and connected to the cell-repair ship by a communications link. The repair vessel would be smaller than most bacteria and viruses, yet capable of therapies and cure [45].

Nanorobots in the Diagnosis and Treatment of Diabetes: Nanorobot architecture based on Nanobioelectronics can be well used for diabetes. A computational approach with the application of medical Nanorobotics for diabetes is simulated using clinical data. In the proposed 3D prototyping, a patient can be well informed to avoid hyperglycemia.

A practical medical Nanorobotics platform can be made for *in-vivo* health monitoring [46]. In the medical Nanorobot architecture, the significant measured data can be then transferred s to the mobile phone carried by the patient [47]. At any time, if the glucose achieves levels beyond 130 mg/dl as a target, that indication is displayed or alarmed through the mobile phone [48, 49].

Bypass Surgery: People with coronary artery disease are treated by doing heart bypass surgery. This is done to increase the flow of blood to the heart muscles. More than one artery may be bypassed during the operation, but this method is not devoid of side effects. Instead, a nanorobot can be used to operate. The nanorobot is containing two regions an outer region and an inner region is attached with an electric motor for its circulation. Along with with the electric motor an artery thermometer, a microprocessor, a camera, and a revolving needle is incorporated into it. The microprocessor will control the complete operation [20, 50]. Radioactive material is infused into the outer region to trace the movements of the nanorobot.

This can be switched anytime using a magnetic switch. The induced nanorobot can cut out the plaque and grind them into microparticles [51]. After the action is over it is removed by directing the nanorobot to anchor to a blood vessel that is easily accessible from outside.

Nanorobots in Kidney Disease: Nanorobots can be used to break the kidney stones by ultrasonic shocks. Kidney stones cause excessive pain and large stone formed does not pass out in the urine. Nanorobot works to break the stones in small pieces, which can pass out through urine [51].

Nanorobots in Gout: 52 Gout is a condition where the kidneys lose the ability to remove waste from the breakdown of fats from the bloodstream. Nanorobots provide relief from the symptoms by breaking up the crystalline structures at the joints, though they aren't able to reverse the condition permanently.

Tissue Reconstruction: Nanoparticles with nano-robots can be designed in such a way that it resembles the bone structure. An ultrasound is performed on existing bone structures, and then bonelike nanoparticles are created using the results of the ultrasound. When they arrive at the fractured bone, they assemble to form a structure that becomes part of the bone. So, such applications will helpful in case of bone fractures, arthritic conditions *etc.* [53]

Nerve Regeneration: Another application of nanorobots is in the treatment of injured nerves. Scientists are working on it, and in the near future it will be an effective tool to cure spinal injuries, neurons, *etc.* [54, 55]

Delicate Surgeries: Immense risk is involved in the delicate surgeries of eyes, and they require a steady hand and strong constitution. Microsurgery of the eye, as well as surgeries of the retina and surrounding membranes, will be performed using nanorobots. Also, instead of injecting directly into the eye, nanorobots could be injected elsewhere in the body, and that will be guided to the eye to deliver drugs, if necessary. Another example of delicate surgery is fetal surgery. It is risky due to the high mortality rate of either the baby or the mother. It will achieve a 100% success rate as nanobots can provide better access to the required area inducing minimal trauma [56].

Future Scope: In the present world most of the treatment which is required for curing problems inside the human body is done through surgical operations. Thus the use of nanorobots helps us to cure all those problems without surgery. Comparing with the surgical methods, using nanorobots provides more controlled medical treatment. In the case of cancer treatment using nanorobots to destroy the cancer cells helps in replacing chemotherapy.

As the future scope, medical nanorobots can be utilized in the area of eye surgery. The nanorobots will make surgical procedures and medical treatments safe for all the patients and will be an effective tool for targeting the source of dreadful diseases. The dimensions of nanorobots are made smaller to prevent the damages caused to the tissues. Another future scope of nanorobotics in the field of biotechnology where it mainly focuses on information delivery, not on the medicine. It will be programmed in such a way that it will deliver the data to the brain.

CONCLUSION: Nanorobots monitoring a nutritional concentration in three-dimensional workspaces is a possible application of nano-robotics in the medical field than any other biomedical problems. Nanorobotics has a strong potential to dominate healthcare, to treat diseases in the future. Consequently, they change the shape of the industry, broadening product development. Nanorobotics has made great development, but the disadvantages related to it make it less important. Hence we need to improve the techniques to such an extent that we could hope nanorobot with all its challenges and opportunities will become part of our future.

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