



IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203




Human Journals

Review Article

October 2017 Vol.:10, Issue:3


© All rights are reserved by Sambhaji Patil et al.

Nanotechnology Used in Treatment of Cancer Disease and Heart Surgery



IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203



Sambhaji Patil*, Pankaj Ombase, Nikita Patil, Nikita Pandare, Rutuja Patil, P. S. Kore

*Rajarambapu College of Pharmacy, Kasegaon
Taluka: Walwa Dist: Sangli 415404*

Submission: 22 September 2017
Accepted: 3 October 2017
Published: 30 October 2017



HUMAN JOURNALS

www.ijppr.humanjournals.com

Keywords: Nanorobot, Cancer therapy, Cancer diagnosis, Nanocarriers, Targeting molecules

ABSTRACT

Nanotechnology is such a field which is changing vision of Medical science. Nanotechnology is advanced technology used in medical field for treatment of various diseases. Nanorobots are useful in treatment of diseases such as cancer and heart surgery. The treatment of various diseases by using nanorobot is mostly useful. This nanotechnology was first used by scientist Richard Feynman. Nanorobots are generally hair like structure. In treatment of cancer, they are most useful. Because; oldest therapy such as chemotherapy is not completely suitable for treatment of cancer. It is also used in the treatment of heart surgery. But by using nanorobot technology the disease can be completely destroyed. This technology has high accuracy and less time is required. It is less costly Nanorobot therapy, fast and biodegradable. In heart surgery, a single cluster of three nanorobot is guided using magnetic field. Researcher says the technology could help break up blocked coronary arteries in human. Nanotechnology is a field of research at the crossroads of biology, chemistry, physics, engineering, and medicine. Design of multifunctional nanoparticles capable of targeting cancer cells, delivering and releasing drugs in a regulated manner, and detecting cancer cells with enormous specificity and sensitivity are just some examples of the potential application of nanotechnology to oncological diseases. In this review, we discuss the recent advances in cancer nanotechnology with particular attention to nanoparticle systems that are in clinical practice or in various stages of development for cancer imaging and therapy.

INTRODUCTION:

Nanorobots are tiny machine used to cure diseases in human or in any organism. They perform task at Nanoscale organism dimensions. A nanorobot is a specialized Nanomachine designed to perform a specific task repeatedly and precision Nanorobots have dimension on the order of nanometer. It is three microns about maximum size for blood born medical nanorobots, due to capacity passage requirement. Nanorobot can inject into the body by means of the one centimeter cube needle.

Nanorobots are useful in treatment of cancer and heart surgery. The nanorobots are small in size 0.1to 0.3nm in size. The treatment on disease by using nanorobot is mostly useful. This nanotechnology was first used by scientist Richard Feynman. Nanorobots are generally hair like structure. In cancer type of disease, they are most useful because other therapies cannot completely kill cancer. But by using nanorobot technology the disease can be completely cured. Chemotherapy is the general therapy on cancer disease but in these therapies, the medicine can affect other parts of body. Many side effects are arrived like damaging the hair cells, blood cells and negative anemia. Features of nanotechnology are as follows:

- Specific action on disease.
- As compared with other treatments it requires less time.
- It is very fast. No, any side effect.
- Biodegradable and optimal.



Structure of nanorobot:

- Manipulator gripper
- Biomolecular sensor
- Acoustic sensor
- Dipole antenna
- Link up connector
- Locomotion flagella

- NMG machine
- Camera
- Capacitor

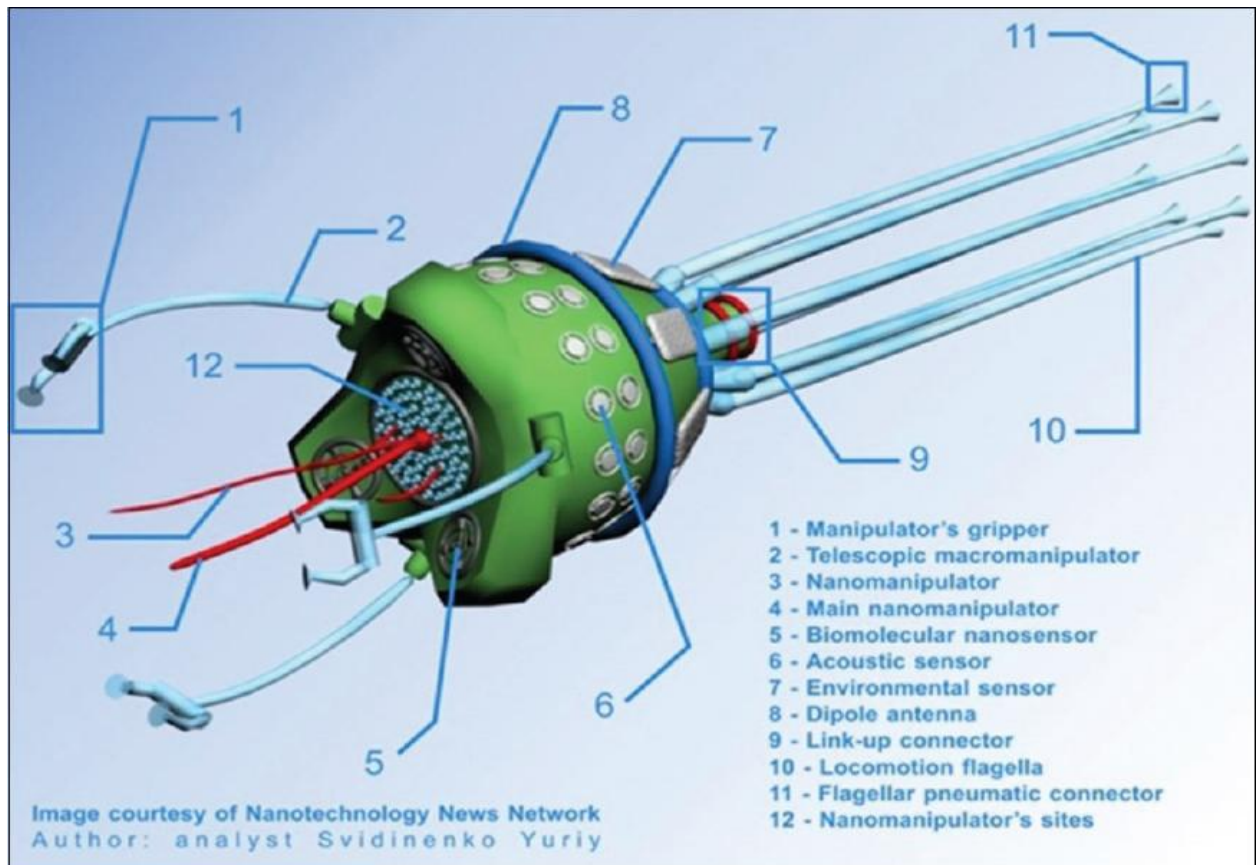


Figure 1: Structure of nanorobot

Mechanism:

1) Cancer

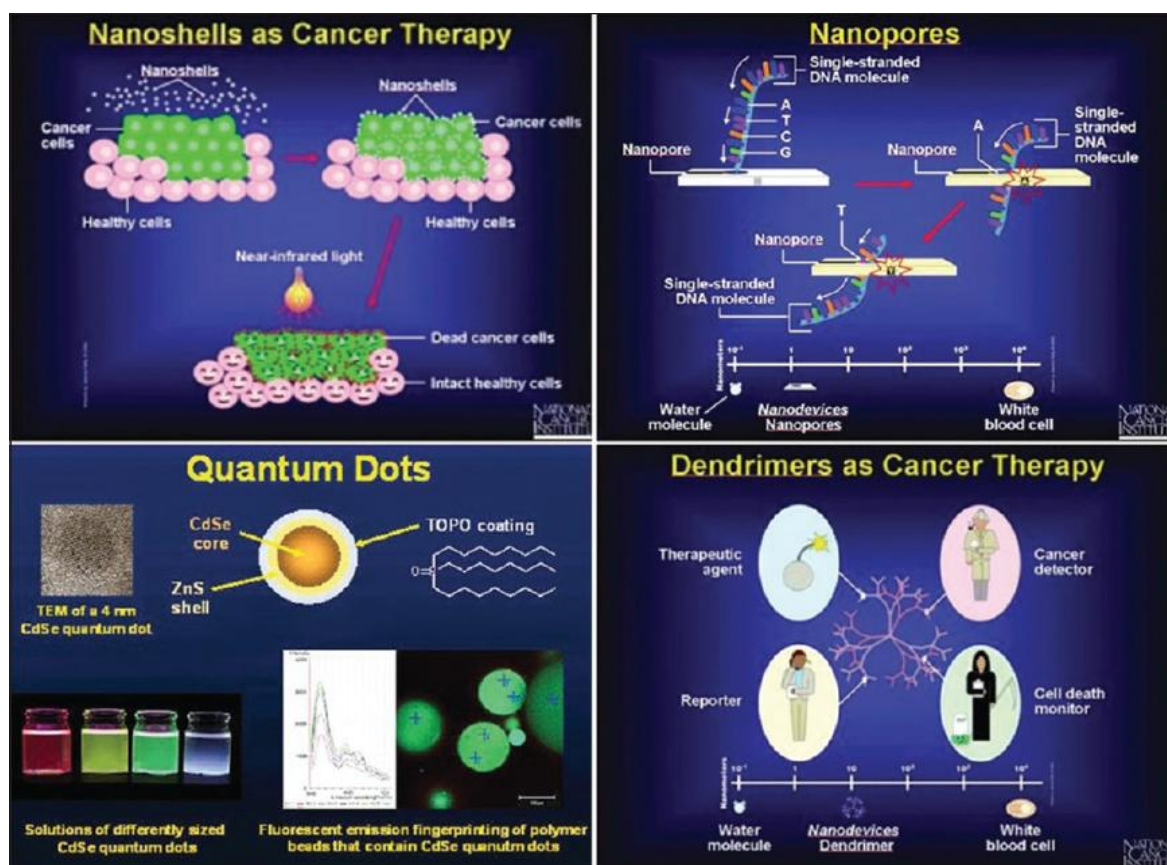


Figure 2: Mechanism of nanorobot

Chemical signal inside the body:

Chemical signals and interaction with the bloodstream is a key aspect to address the application of nanorobots for cancer therapy. The nanorobot sensing for the simulated architecture in detecting gradient changes on E-cadherin signals is examined. To improve the response and bio-sensing capabilities, the nanorobots maintain positions near the vessel wall instead of floating throughout the volume flow in the vessel an important choice in chemical signaling is the measurement time and detection threshold at which the signal is considered to be received. Due to background concentration, some detection occurs even without the target signal. After the first nanorobot has detected a tumor for medical treatment, it can be programmed to attach on it. Then, beyond attracting a predefined number of other nanorobots to help for incisive chemotherapeutic action with precise drug delivery above the tumor, the architecture permits it to use wireless communication to send accurate position for the doctors informing that a tumor was found.

Power supply

The use of CMOS for active telemetry and power supply is the most effective and secure way to ensure energy as long as necessary to keep the nanorobot in operation. The same technique is also appropriate for other purposes like digital bit encoded data transfer from inside a human body. Thus, nanocircuits with resonant electric properties can operate as a chip providing electromagnetic energy supplying 1.7 mA at 3.3 V for power, allowing the operation of many tasks with few or no significant losses during transmission. Radiofrequency (RF)-based telemetry procedures have demonstrated good results in patient monitoring and power transmission with the use of inductive coupling using well-established techniques already widely used in commercial applications of radio frequency identification (RFID). The energy received can be also saved in ranges of $\sim 1 \mu\text{W}$ while the nanorobot stays in inactive modes, just becoming active when signal patterns require it to do so.

Data transmission

The application of devices and sensors implanted inside the human body to transmit data about the health of patients can provide great advantages in continuous medical monitoring. Most recently, the use of RFID for *in-vivo* data collecting and transmission was successfully tested for electroencephalograms (EEG) For communication in liquid workspaces, depending on the application, acoustic, light, RF and chemical signals may be considered as possible choices for communication and data transmission. Chemical signaling is quite useful for nearby communication among nanorobots for some teamwork coordination. Using integrated sensors for data transfer is the better answer to read and write data in implanted devices. Teams of nanorobots may be equipped with single chip RFID CMOS based sensors. CMOS with sub-micron SoC design could be used for extremely low power consumption with nanorobots communicating collectively for longer distances through acoustic sensors. For the nanorobot, active sonar communication frequencies may reach up to $20 \mu\text{W}$ 8 Hz at resonance rates with 3 V supply.

System implementation

The nanorobot architecture includes integrated nanoelectronics. The nanorobot architecture involves the use of mobile phones for, e.g., the early diagnosis of E-cadherin levels for smart chemotherapy drug delivery and new cancer tumor detection for cancer treatments. The

nanorobot uses a RFID CMOS transponder system for *in-vivo* positioning using well-established communication protocols, which allow track information about the nanorobot position. This information may help doctors on detecting tiny malignant tissues even in initial stages of development. The nanorobot exterior shape consists of a diamondoid material to which may be attached an artificial glycocalyx surface that minimizes fibrinogen (and other blood proteins) adsorption and bioactivity, ensuring sufficient biocompatibility to avoid immune system attack. Different molecule types are distinguished by a series of chemotactic biosensors whose binding sites have a different affinity for each kind of molecule. These sensors can also detect obstacles which might require new trajectory planning. A variety of sensors are possible. For instance, chemical detection can be very selective, e.g. for identifying various types of cells by markers. Acoustic sensing is another possibility, using different frequencies to have wavelengths comparable to the object sizes of interest.

Nanorobot Simulation

As a result from the advances on nanoelectronics, nanorobots may be considered a promising new technology to help with new treatments for medicine. The nanorobots are inside the vessel, they can be either observed in 3D real time with or without the visualization of red blood cell. Glucose carried through the bloodstream is important to maintain the human metabolism working healthfully. The simulated nanorobot prototype model has embedded Complementary Metal Oxide semiconductor [CMOS] bioelectronics. The nanorobot computation is performed through embedded nanosensor; for pervasive computing, performance requires low energy consumption. The nanorobot is not attacked by the white blood cells due to biocompatibility. In the medical nanorobot architecture, the significant measured data can be then transferred automatically to the mobile phone.

Nanorobots in cancer detection and treatment

The development of nanorobots may provide remarkable advances for diagnosis and treatment of cancer. Nanoparticles (NPs) play a key role in developing new methods for detecting cancer. Detection of cancer in an early stage is a critical step in improving cancer treatment. Various NPs used are cantilever, nanopores, nanotubes and quantum dots. These are being briefly described here in the literature.

Cantilever

As cancer cells secrete its molecular products, the antibodies coated on the cantilever fingers selectively bind to these secreted proteins. The physical properties of the cantilever change in real time and provide information about the presence and also the concentration of different molecular expressions.

Nanopore

Another interesting device is nanopore. Improved methods of reading the genetic code will help researchers in detecting errors in gene that may contribute to cancer. Nanopores contain a tiny hole that allows deoxyribonucleic acid (DNA) to pass through one stand at a time making DNA sequencing more efficient.

Nanotubes

Nanotubes carbon rods about half the diameter of a molecule of DNA will not only detect the presence of altered genes but also pinpoint the exact location of those changes. A multidisciplinary team at the Massachusetts Institute of technology has developed carbon nanotubes (CNT) that can be used as sensors for cancer drugs and other DNA damaging agents inside living cells.

Quantum dots

Quantum dots are tiny crystals that glow when they are stimulated by ultraviolet light. When injected into the body, they would drift around until encountering cancerous tissue. The dead cells would latch onto a special coating on the glowing dots. The light particles would serve as a beacon to show doctors where the disease has spread. Nanorobot could be very helpful for therapy of patients since current treatments like radiation therapy and chemotherapy often land up destroying more healthy cells than cancerous ones. From this point of view, it provides a non-depressed therapy for cancer patients. The nanorobots will be able to distinguish between different cell types that are the malignant and the normal cells by checking their surface antigens this can be accomplished by the use of chemotactic sensors keyed to the specific antigens on the target cells. Using chemical sensors they can be programmed to detect different levels of E-cadherin and beta-catenin in primary and metastatic phases. Medical nanorobots will then destroy only the cancerous cells. There are

ongoing attempts to build micro-electromechanical system [MEMS]-based microrobots intended for *in-vivo* use. For example, the “MR – Sub” project of the nanorobotics Laboratory of Ecole Polytechnique in Montreal will use a magnetic resonance imaging system as a means of propulsion for a microrobot in the blood vessels. Application of the first generation prototype might include targeted drug release, the reopening of blocked arteries, or taking biopsies. The project is gathering the necessary information to define design rules for this type of microrobot, with a long-term goal “to further miniaturize the system and to create a robot made up of nanometric parts,” making it possible to carry out procedures in the blood vessels which are still inaccessible. Gordon's group at the University of Manitoba have also proposed magnetically controlled “cytobots” and “karyobots” for performing wireless intracellular and intra-nuclear surgery, respectively.

The nanorobots may enable drug delivery and are loaded with therapeutic chemicals avoiding cancer to advance further. Dendrimer and nanoshells, liposomes, NPs, micelles are used for drug delivery.

Dendrimers

These are spherical, highly branched and synthetic macromolecules with adjustable size and shape. A single dendrimer can carry a molecule that recognizes cancer cell, a therapeutic agent to kill those cells, a molecule that recognizes the signal of cell death. Dendrimer NPs have shown promise as drug delivery vehicles capable of targeting tumors with large doses of anti-cancer drugs.

Nanoshells

Nanoshells have a core of silica and a metallic outer layer. By manipulating the thickness of the layer, scientist can design beads to absorb near infra-red light, creating an intense heat that is lethal to cancer cells. The physical selectivity to cancer lesion site occurs through a phenomenon called enhanced permeation retention.

Liposomes

Liposomes have a long history as drug carrier systems because of their easy preparation, acceptable toxicity and biodegradability profiles. Drug loading in liposomes can be achieved through (1) Liposome formation in an aqueous solution saturated with soluble drug; (2) the

use of organic solvents and solvent exchange mechanisms; (3) the use of lipophilic drugs; and (4) pH gradient methods.

Polymeric NPs

These are delivery devices made from biodegradable polymers and are an attractive option as carriers of therapeutic drugs in cancer therapy. Polymeric NPs, which include nanospheres and nanocapsules, are solid carriers ranging from 10 to 1000 nm in diameter made of natural or artificial polymers which are generally biodegradable and in which therapeutic drugs can be adsorbed, dissolved, entrapped, encapsulated or covalently linked to the polymer backbone by means of a simple ester or amide bond that can be hydrolyzed *in-vivo* through a change of pH. When systemically administered, NPs are generally more stable than liposome but are limited by poor pharmacokinetic properties that is, uptake by the reticuloendothelial system [RES]. As with liposomes, the surface of NPs can be coated with molecules or intercalated into their structure to increase pharmacokinetics and even enable targeting for delivery and imaging purpose.

Micelles



Polymeric micelles are biodegradable spherical nano-carriers with a usual size range of 10-200 nm. Micelles are considered ideal drug delivery vehicles because they provide a set of important advantages. The hydrophobic core can be used to carry pharmaceuticals, especially lipophilic drugs, which are solubilized and physically entrapped in the inner region with high loading capacity. Polymeric micelles can simultaneously co-deliver two or more therapeutic agents and are capable of releasing drugs in a regulated manner. The encapsulated drugs can be released through erosion of the biodegradable polymers, diffusion of the drug through the polymer matrix, or polymer swelling followed by drug diffusion. External conditions such as change of pH and temperature can also induce drug release from micelles. Moreover, the surface modification of micelles with ligands such as antibodies, peptides, or other small molecules can be used for targeted delivery and uptake of these nano-carriers, thereby reducing their systemic toxicity and improving their specificity and efficacy.

1) Heart surgery

Blood vessels play an important role in supply a blood to all parts of the body. Due to the fatty deposition on the walls of blood vessels, blood will not move freely to all parts of the

body these leads to heart attacks and damage the vital organs. In general, the most common methods of surgery used for heart attacks is

- By-Pass surgery
- Angio Plaster

NANOROBOTS IN HEART SURGERY

Both of the above methods are risky and number of side effects. As a result, patient becomes very weak. But a surgery-using nanorobot is very simple one. Doctors do their treatment even without touching the body.

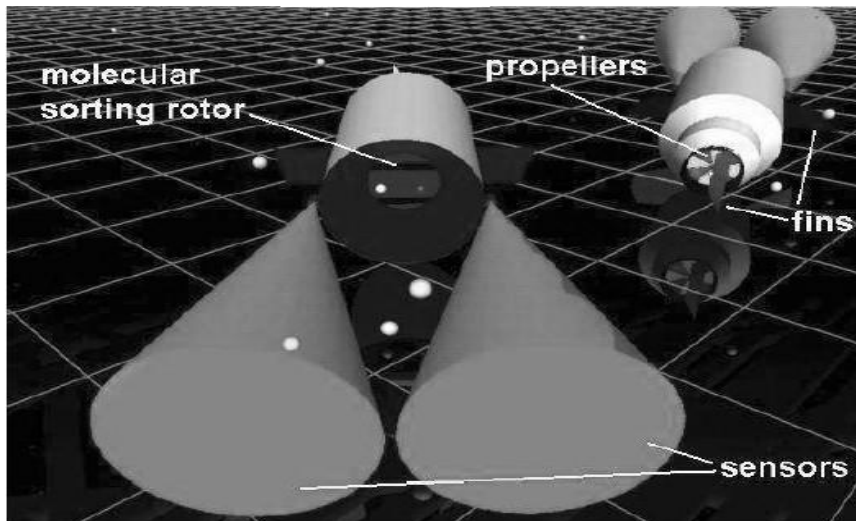


Figure 3: Structure of Nano Robots

The above figure shows the structure of the nanorobots. It is constructed with various nanomechanical devices and nanosensors like.

- Molecular sorting rotors
- Propeller
- Fins
- Sensors

Types of Sensors

1. Chemical sensors: To find the fatty deposit.
2. Microwave generated sensing: To generate movement.
3. Chemotactic sensors: To find cancer cells.
4. Acoustic sensors: To guide the nanorobots

MOLECULAR SORTING ROTORS

It is made up of carbon nanotubes. Simply a sheet of carbon atom forms a carbon nanotube. A roll having only one sheet of carbon atoms thickness is known as single walled carbon nanotubes (SWNT). Thus the electrical properties of SWNT's can be used to generate mechanical motion from electrical energy. One of the main advantages of these SWNT's is, operating at the molecular level. Nanotube substitutes with nanogears with axle used for changing the direction of movement.

PROPELLOR

The word propeller in ship is used to drive forward the device against water. Like that in nanorobots, it is used to drive forward against the bloodstream. Fins are fitted along with the propellers which are used to propel the device. Sensors are fitted externally and internally with the nanorobots to receive the signal for correct guidance. There are several techniques to do the heart surgery with the nanorobots. We have to know how to inject nanorobots into our body, how to move it to the destination place, how to control and remove the device after surgery.

INJECTION OF NANOROBOTS

We have to find a way to introduce nanorobots into the body for surgery and allowing it to do the operation without ancillary damage. So nanorobots should be made smaller than the blood vessels thus making it travel. Femoral artery in the leg is considered to be the largest artery in our body. So we inject the nanorobots through this artery.

NAVIGATION

Every living thing needs area to move. Like fishes are moved in water, nanorobots use blood flow for its movement. It must be able to guide the device which makes use of the blood flow. The devices used for navigation are propeller, fins, jet pump, and electromagnetic pump. In order to move the nanorobots in blood flow, following things are very important

- Speed of blood
- Get through the heart without stuck
- React with changes in blood flow rate
- Able to change the direction according to the bloodstream

To satisfy the above consideration we have to make the nanorobots with electric motors turning propellers.

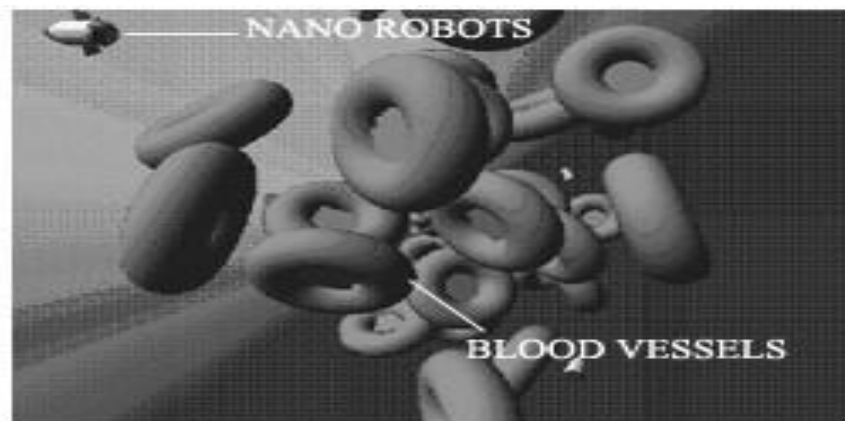


Figure 4: Navigation of nanorobots into blood vessels

POSITIONING

To know the location of nanorobots where it goes we use ultrasonic technique. Nanorobots must be able to produce ultrasonic waves by passing a signal to piezoelectric membrane, which is inbuilt with the device. Several signals processing techniques are used to track this ultrasonic signal and finding the location at any time. Instead of ultrasonic wave, we use infrared ray for signal processing.

DETECTION

To locate a blood clot (or) deposit of arterial plaque we use sensors of different types. Already preplanned route is available to reach operation site. With the help of preplanned route, we reach the fatty deposited area. To control the nanorobots as per our wish, we fit the TV camera in the nanorobots and transmit its picture outside the body to a remote control unit. Solid-state television camera sensors are used to receive the signals from the remote station and do the operations according to signals send by remote control unit. There are preprogrammed microchips available to give appropriate signals so that nanorobots are initiated externally through a computer.

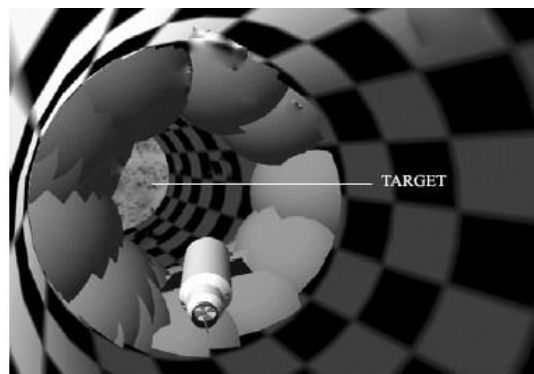


Figure 5: Nano Robots towards a destination

DESTRUCTION

The fatty deposits (or) clots are removed using special blades fitted with nanorobots. Continuous (or) pulse signal is used to activate the blades. These blades physically separate the deposits from blood vessels. Care should be taken in removing the fatty deposits. Small deposits of these fatty materials without removing lead to big problem in future

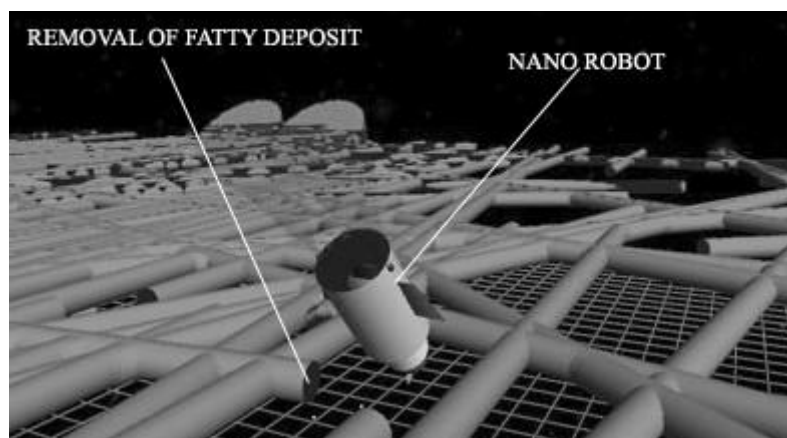


Figure 6: View of nanorobot removing the fatty deposit

Production of power is very important for every operation to most efficient one in magnetic induction. Our body is full of magnetic field. Rotation of nanorobots cuts this magnetic field, produce power based on *Faraday's law*. To take nanorobots from the body we use two methods one is retrace our path upstream another is making small surgery to remove.

CONCLUSION

Nanorobot is good option on chemotherapy. It needs for every type of disease. Size of nanorobot should be maximum small. As per our aim, we have proposed the usage in heart surgery. Due to this, number of risks and side effects are reduced. The same technique is used in various treatments like cancer, breaking kidney stones, breaking liver stones, parasite removal only with slight modification. Automated robots used in medicine delivery has evolutionary characteristics such as mutation, crossover, chromosome selection and combination of these automated robots with genetic engineering takes over world to new revolution. Within ten years several advancement technologies should be made by researchers from this nanorobotics.

Acknowledgement:



We are very thankful to our Principal Dr.C.S.Magdum and Vice-Principal Dr.S.K.Mohite for guiding us for publication of review article.

REFERENCES

1. Emanuel, E. Schwartz, "The Biological Basis of Radiation Therapy" in, Philadelphia: J.B. Lippincott Company, pp. 210-216, 1966. Show Context Radiation's effect on individual cells is a probabilistic process [1]
2. D.W. Roberts, "Stereotactic Technology in Tumor Surgery: Concepts and Principles", *Journal of Neuro-Oncology*, vol. 28, pp. 1-4, 1995. Show Context CrossRef Stereotactic technology, which has been applied to neurosurgery since the early nineties [2], recently has been applied to radiation treatment of tumors, particularly brain tumors.
3. F.A. Calvo et al., "Stereotactic Radiosurgery with Linear Accelerator", *Rays*, pp. 462-85, Jul-Sep. 1998. Show Context Stereotactic technology, which has been applied to neurosurgery since the early nineties [2], recently has been applied to radiation treatment of tumors, particularly brain tumors [3].
4. S.D. Chang et al., "Clinical Experience With Image-Guided Robotic Radiosurgery in the Treatment of Brain and Spinal Cord Tumors", *Neuro Medico journal*, pp. 7W.7, Nov. 1998. Show Context Interactive image-guided radiation therapy is very new [4].
5. A. S. Lubbe, C. Alexiou, C. Bergemann, "Clinical applications of magnetic drug targeting", *Journal of Surgical Research*, vol. 95, pp. 200-206, 2001. Show Context CrossRef The key problem with current chemotherapy is not that the drugs are not effective, existing cancer-treatment drugs do successfully kill growing tumor cells, but that the rest of the body cannot tolerate the drug concentrations required to eliminate the cancer cells [5].
6. V.S.W. Chan, "Nanomedicine: An unresolved regulatory issue", *Science direct*. Show Context CrossRef It also provides materials for controlled drug delivery by directing carriers to a specific location [6].

7. S.P. Leary, C.Y. Liu, M.L.I. Apuzzo, "Toward the emergence of nanoneurosurgery: Part III Nanomedicine: Targeted nanotherapy nanosurgery and progress toward the realization of nano neurosurgery", *Neurosurgery*, vol. 58, no. 6, pp. 1009-1025, Jun. 2006. Show Context CrossRef Particularly interesting are biomedical engineering applications [7][8], where nanorobots and nanoscale-structured materials inside the body provide significant improvements in diagnosis and treatment of disease [9][10].
8. P. Couvreur, C. Vauthier, "Nanotechnology: Intelligent design to treat complex disease", *Pharmaceutical Research*, vol. 23, no. 7, pp. 1417-1450, Jul. 2006. Show Context CrossRef Particularly interesting are biomedical engineering applications [7][8], where nanorobots and nanoscale-structured materials inside the body provide significant improvements in diagnosis and treatment of disease [9][10].
9. R. A. Freitas, "Nanomedicine", *Vol. I: Basic Capabilities Landes Bioscience 1999 "Nanomedicine" Vol. IIA: Biocompatibility Landes Bioscience 2003*. Show Context Particularly interesting are biomedical engineering applications [7][8], where nanorobots and nanoscale-structured materials inside the body provide significant improvements in diagnosis and treatment of disease [9][10].
10. *National Institutes of Health Roadmap: Nanomedicine*, 2003. Show Context Particularly interesting are biomedical engineering applications [7][8], where nanorobots and nanoscale-structured materials inside the body provide significant improvements in diagnosis and treatment of disease [9][10].
11. C. Montemagno, G. Bachand, "Constructing nanomechanical devices powered by biomolecular motors", *Nanotechnology*, vol. 10, pp. 225-231, 1999. Show Context Cross Ref For example, ongoing development [11][12] of molecular scale electronics, sensors and motors provides components to enable nanorobots [13].
12. Cavalcanti Adriano, Waren W. Wood, Luiz C. Kretly, Bijan Shirinzadeh, "Computational Nanomechatronics: A Pathway for Control and Manufacturing Nanorobots", *IEEE CIMCA Int'l Conf. on Computational Intelligence for Modelling Control and Automation IEEE Computer Society*, November 2006. Show Context For example, ongoing development [11][12] of molecular scale electronics, sensors and motors provides components to enable nanorobots [13].
13. A. Cavalcanti, R. A. Freitas, "Nanorobotics Control Design: A Collective Behavior Approach for Medicine", *IEEE Transactions on NanoBioScience*, vol. 4, no. 2, pp. 133-140, June 2005. Show Context View Article Full Text: PDF (1300KB) For example, ongoing development [11][12] of molecular scale electronics, sensors and motors provides components to enable nanorobots [13].
14. R. Weiss, T. F. Knight, "Engineered Communications for Microbial Robotics", *Proc. of Sixth Intl. Meeting on DNA Based Computers (DNA6)*, 2000. Show Context Demonstrations of programmable bacteria [14] can produce computation capability for nanodevices.
15. M.J. Zhang, C.L. Sabharwal, W. Tao, T.J. Tarn, N. Xi, G. Li, "Interactive DNA sequence and structure design for DNA nano applications", *IEEE Transactions on Nanobioscience*, vol. 3, no. 4, pp. 286-292, Dec. 2004. Show Context View Article Full Text: PDF (1762KB) The development of nanosystems for control of nanorobots to perform specific tasks in medicine may also enable improvements for nanotechnology automation [15].
16. K. Eric Drexler, "Nanosystems: Molecular Machinery Manufacturing and Computation" in, NY: John Wiley & Sons, 1992. Show Context. These control signals are provided by external acoustic, electrical, or chemical signals that are received by the robot arm via an onboard sensor using a simple "broadcast architecture" [16][17] a technique which can also be used to import power. the biological cell may be regarded as an example of a broadcast architecture in which the nucleus of the cell send signals in the form of mRNA to ribosomes in order to manufacture cellular proteins.
17. R.C. Merkle, "Design-Ahead for Nanotechnology in Markus Krummenacker James Lewis eds. Prospects in Nanotechnology: Toward Molecular Manufacturing" in, New York: John Wiley & Sons, pp. 23-52, 1995. Show Context .These control signals are provided by external acoustic, electrical, or chemical signals that are received by the robot arm via an onboard sensor using a simple "broadcast architecture" [16][17] a technique which can also be used to import power. the biological cell may be regarded as an example of a broadcast architecture in which the nucleus of the cell send signals in the form of mRNA to ribosomes in order to manufacture cellular proteins.
18. J.W. Bryson et al., "Protein Design: A Hierarchic Approach", *Science*, vol. 270, pp. 935-941, 1995. Show Context CrossRef Assemblers are molecular machine systems that could be described as systems capable of performing molecular manufacturing at the atomic scale which require control signals provided by an onboard

nanocomputer This programmable nanocomputer must be able to accept stored instructions which are sequentially executed to direct the manipulator arm to place the correct moiety or nano part in the desired position and orientation, thus giving precise control over the timing and locations of chemical reactions or assembly operations [18].

19. R.C. Merkle, R.A. Freitas, "Theoretical analysis of a carbon carbon dimer placement tool for diamond mechano synthesis *Nanosci Nanotechnol* 2003", vol. 3. Show Context Making complex nanorobotic systems requires manufacturing techniques that can build a molecular structure via computational models of diamond mechanosynthesis (DMS) [19].

20. A.S.G. Curtis, M. Dalby, N. Gadegaard, "Cell signaling arising from nanotopography: implications for nanomedical devices", *Nanomedicine Journal Future Medicine*, vol. 1, no. 1, pp. 67-72, June 2006. Show Context CrossRef In the 3D workspace the target has surface chemicals allowing the nanorobots to detect and recognize it [20].

21. *Nanorobot Communication Techniques: A Comprehensive Tutorial*. Show Context Thus they can be employed effectively for treating cancer [21].

22. R.A. Freitas, "Nanomedicine" in *Basic Capabilities Landes Bioscience, Georgetown, TX.*, vol. I, 1999. Show Context Phagocytes could also tag target cells with biochemical natural defensive or scavenging systems, a strategy called "phagocytic flagging" [22].

23. A. Grakoui, S.K. Bromley, C. Sumen, M.M. Da Vis, A.S. Shaw, P.M. Allen, M.L. Dustin, *Science*, vol. 285, no. 221, 1999. Show Context .Seeding the outer wall of a target cell with phosphatidylserine or other molecules with similar action could activate phagocytic behavior by macrophages, which had mistakenly identified the target cell as apoptotic substances capable of triggering a reaction by the body [23] Phagocytes would be capable of carrying up to approximately 1cubicmeter of pharmaceutical payload stored in onboard tanks that are mechanically offloaded using molecular sorting pumps operated under the control of an onboard computer [24].

24. R.A. Freitas, "Nanomedicine" in *Basic Capabilities Landes Bioscience, Georgetown, TX.*, vol. I, 1999. Show Context Seeding the outer wall of a target cell with phosphatidylserine or other molecules with similar action could activate phagocytic behavior by macrophages, which had mistakenly identified the target cell as apoptotic substances capable of triggering a reaction by the body [23] Phagocytes would be capable of carrying up to approximately 1cubicmeter of pharmaceutical payload stored in onboard tanks that are mechanically offloaded using molecular sorting pumps operated under the control of an onboard computer [24].

25. *Nanomedicine Volume II: Biocompatibility Landes Bioscience Georgetown TX*, 2003. Show Context The nanorobots might then be recharged, reprogrammed and recycled for use in a second patient who may need a different pharmaceutical agent targeted to different tissues or cells than in the first patient [25].

26. D. Murphy, B. Challacombe, M.S. Khan, P. Dasgupta, "Robotic Technology in Urology", *Postgraduate Medical Journal*, vol. 82, no. 973, pp. 743-747, Nov. 2006. Show Context CrossRef Laparoscopy has some different robotic systems currently in use [26].

27. E.J. Hanly, M.R. Marohn, S.L. Bachman, M.A. Talamini, S.O. Hacker, R.S. Howard, N.S. Schenkman, "Multiservice laparoscopic surgical training using the daVinci surgical system", *The American Journal of Surgery*, vol. 187, no. 2, pp. 309-315, Feb. 2004. Show Context CrossRef As an example, the daVinci Surgical System [27] has been responsible for the huge surge in the number of robotic procedures performed in the past 5 years.