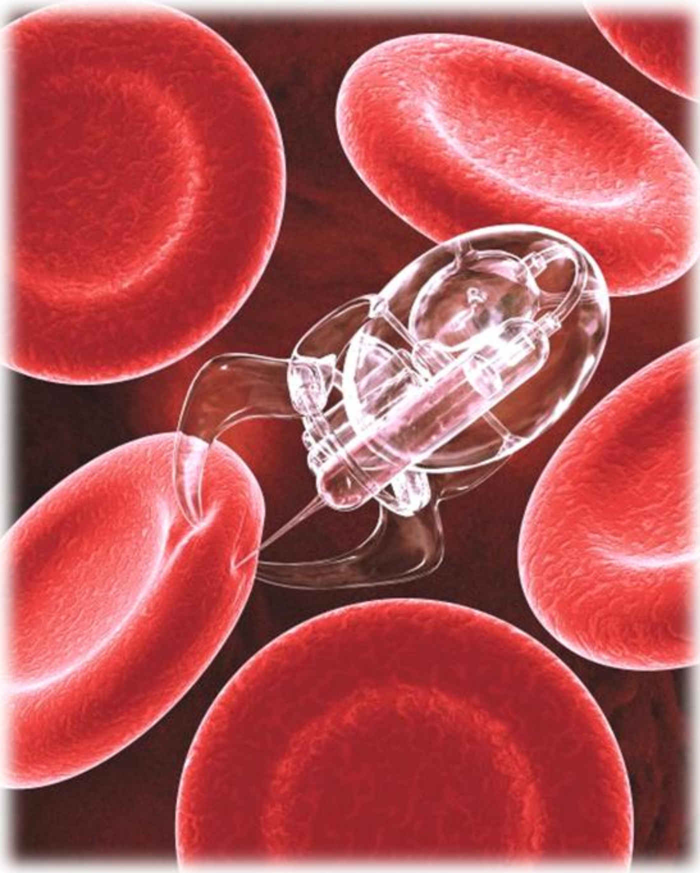
NANOTECHNOLOGY: APPLICATIONS IN THE DIAGNOSTICS AND TREATMENT OF CANCER



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RESEARCH PAPER
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ABSTRACT
This paper considers the use of nanotechnology in the treatment of cancer as an alternative to chemotherapy, radiotherapy, biopsies and some of the other conventional diagnostic and therapeutic tool employed by doctors to treat this disease. Nanotechnology is the manipulation of components at an atomic or molecular level, usually structures between 1 and 100 nanometres and through the use of quantum dots, gold bullets, nanopores and dendrimers, I propose an innovative way to control and prevent cancer in the future.

Introduction:

What is NT? Nanotechnology is the manipulation of components at an atomic or molecular level, usually structures between 1 and 100 nanometres. A nanometre is 10^{-9} m or 1 billionth of a metre long and working at such a small scale is ideally suited to medicine, enabling scientists to design and engineer new products that open up the horizons for diagnosis and treatment. Nanotechnology is about building from atoms attempting to copy nature in its *'bottom up' approach* – the most complex molecular machinery structures made from the most simple, small (DNA), using weak bonds.
Below figure 1 gives a point of comparison for objects down to nano-scale:

History and development of Nanotechnology:

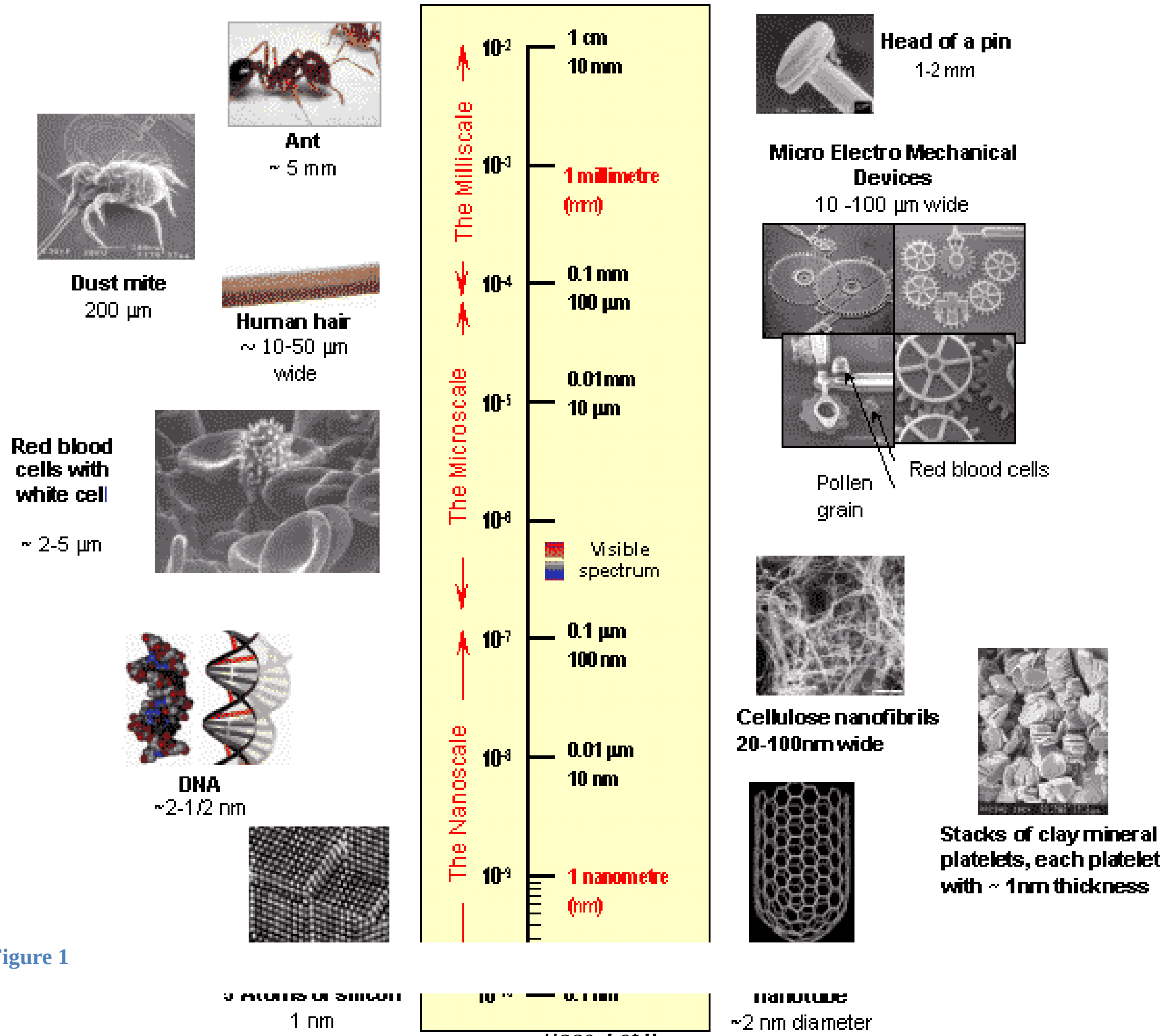


Figure 1

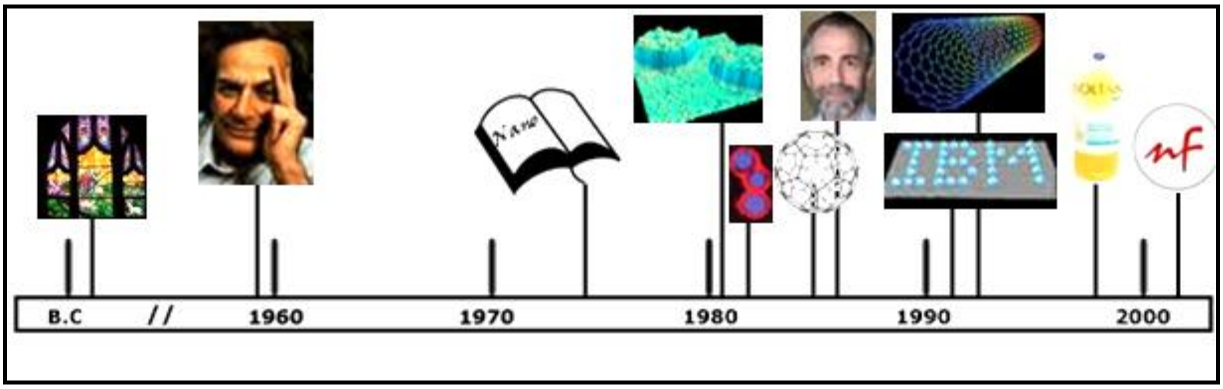


Figure 2

Figure 2 is a pictorial representation of the timeline given below detailing the milestones in nanotechnology:

Ancient Romans were, unknowingly, the first users of by adding gold chloride to molten glass when making red stain glass windows. The gold nanospheres absorbed and reflected light giving the window their brilliance.

In 1959, Feyman started the idea of molecular machinery with his famous lecture, *'There's Plenty of Room at the* Bottom'; knowing that there was huge potential, he encourage scientists to construct devices at atomic scale – essentially nanotechnology.

It wasn't until 1974 that the term 'nanotechnology' was coined by Prof. Taniguchi as *'the processing of separation, consolidation and deformation of materials by one atom or one molecule'*.

The Scanning Tunnelling Microscope (STM) was invented by Binniung and Roher in 1981, allowing scientists to see regions of high electron density and therefore deduce the positions of individual atoms and molecules.

In the 1980s Quantum Dots were discovered by Dr.s Brus, Efros and Ekimov; so intriguing was there discovery because a material at different sizes displayed different physical properties (ie. colour). Also in this period, Drexler explored the definition of nano-technology in greater depth than anyone before.

Towards to the end of this decade and the start of the next, a new form of carbon was discovered, named after architect that came up with the geometric dome that now makes the shape of the *modern* football buckminsterfullerene aka fullerene or buckyballs . To add to this were nanotubes – essentially rolled sheets of graphite, only 100 times stronger than steel and one-sixth of steel's weight, with semi-conducting or conducting capabilities. With the discovery of these carbon structures, new possibilities for drug delivery systems were envisaged (for example, oral treatment of diabetes, protecting the insulin from stomach acid and other substances that would destroy the drug, until it reaches its destination) and for many of them there is ongoing research into the potential benefits.

Furthermore, in 1989, scientists in the United States created a motor, using Atomic Force Microscopic (AFM) and laser tweezers to manipulate individual atoms. The motor is 250 times smaller than a human hair and consists of a gold blade attached to an axle made from a carbon nanotube. The ends of the nanotube are anchored to two silicon dioxide electrodes that conduct electricity to rotate the blade, controlling its speed, direction and. So small, the motor can be imbedded in a silicon chip. More tolerant of wider temperature ranges, the motor can operate in a vacuum and cope with harsh environments; Oxford scientists are now trying to develop new drug delivery systems, through comparison to flagellum on bacteria to the motor as a propeller.

Outside the information technology industry, microfabricated impact sensors, used as triggers for airbags in vehicles, were the first nanotechnological breakthrough. Based on the same technology as computer chips, the sensors were smaller, 100 times cheaper and more efficient than their alternatives and so, upon introduction in 1995, took the world market in a matter of months. The success of products such as these highlighted the potential for the production of cheaper, more accessible and effective treatments for patients.

Following this, nanoscale electronics has made rapid progress due to competing approaches based on carbon nanotubes – led by Dekker– and nanowires so by the end of the 90s, consumer products such as car wax, sports equipment and clothing were available, as well as medically-significant products, for example, wound dressings and sunscreens – simply because of small particle size.

Current Applications, Ongoing Research and Future Implications in Medicine

Nanotecnology in medical practices offers some exciting possibilities, there is a huge range of uses all either visualised, at various stages of testing, whilst others have made it through clinical trials and are in use today. There are applications of nanoparticles currently under development, as well as longer-term research to produced nano-robots (nanobots) to make repairs at a cellular level.

Drug Delivery

Nanotechnology will enable the use of specific cell targeted medication, involving drugs, heat or light to specific sights of disease; this will reduce the damage to healthy cells in the body but has not yet made it to clinical trialling. This theory is known to many scientists as the *'golden bullet'*, nano-containers that are triggered to release its products by chemical receptors on the 'bullet's' surface , thus limiting the side effects on other body parts and so the possibilities of using stronger drugs, considered too toxic for the rest of the body, are endless.

Nanotechnology has also been discovered as a way to treat diabetes, without insulin injections; Prof. Desai (2009) found that implanting pancreatic cells, that secrete insulin into nanocapsules, could in effect, act as an artificial pancreas. This would mean that high blood sugar flow into the nanocapsule would stimulate insulin production and release into the blood at a steady rate to control sugar levels, while the nanopores of the capsules mean that the body's antibodies cannot get into the capsules to attack the cells. This ensures that insulin is always at an optimal level, unlike insulin injections that are not only unpleasant but flood the body with insulin at intervals and not steadily as needed.

Therapy Techniques

In the future buckyballs could be used in the trapping of free radicals during an allergic reaction; for example, the radicals that release histamine during an asthma attack could be trapped and so stopped from causing inflammation. Further discussion and investigations have been conducted into the use of nanofibres to stimulate the re-growth of cartilage in joints and the use of nanoparticles to fight respiratory viruses in the future.

Diagnostics and Imaging

Iron oxide particles have been very useful in improving the MRI images of cancerous tumours, coated in peptides to bind to cancerous tumours and in so doing enhancing the magnetic properties of the iron oxide enhances the images used in diagnosis. In addition, 'Bar code' DNA assay techniques using magnetic nanoparticles have been introduced as well as non-invasive in-vivo (in a living creature) imaging, which could possibly be used in the future as a diagnostic tool for cancerous tumours.

Cell Repair

The void for scaffolding made with nanoparticles to support broken bones or prosthetics was filled by Israeli scientists, led by Rousso and Fazit in 2010. Nanotubes and sphere are stiffer and stronger than steel, yet much lighter, therefore promoting quicker and more successful healing. Possibilities for cell repair include specially programmed nanobots to repair specific cells in a similar way to the action of our antibodies and the repair of damaged implantable devices, such as pacemakers, by communicating with external monitoring devices.

However, the creation of such machines that assemble themselves from individual atoms, running on the energy from glucose and oxygen in the blood, on such a small scale raises the question are they reliable enough to work on their own? Is there the possibility that they could malfunction an instead of patrolling the body and aiding its defences, attacking it instead? If so, how would create nanobots to repair malfunctioning ones when there is a risk that they could malfunction too? And to add to dilemma, being so small, how would we remove them once treatment has been completed?

The newest, up-and-coming nanotechnology applications are now dominating the medical and pharmaceutical industries' research and could revolutionise diagnostics and treatment of damage and disease to the human body; disease is the malfunctioning at cellular scale and so investigations into the use nanomachines in diagnosis and surgery as a form treatment is ongoing. A problem with many conventional drugs are the unwanted side effects and so by developing nanotechnology into effective and efficient therapy could potentially affect only the affected area of cells.

In the future, nanotechnology is likely to be used in post-operative care, for example a small drug release chip could maintain the health of a patient in a localised manner, over a longer period of time, reducing the risk of any long term complications.

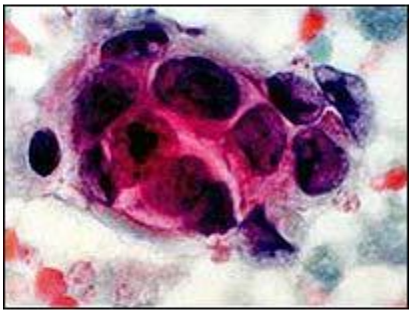
However the most exciting prospect for the use of nanotechnology in medicine is the use of tissue repair and regenerative medicine, working with the body to encourage its own recovery and repair mechanisms to treat diseases such as diabetes, osteoarthritis and degenerative disorders of the central nervous system.

However, my aim to of this paper is to explore the possibilities of nanotechnology in cancer diagnostics and treatment.

Discussion:

What is cancer?

Cancer is the uncontrollable mitosis of cells in the body, starting as a tumour that acts as a parasite, using the body's nutrients, placing pressure on the body and interfering with normal cell function. Tumours are caused by mutations in a person's DNA however it is the number of specific mutations that increases the chance of chance occurring. Furthermore with increased age, there is a greater chance of an older person contracting a mutation that causes a malignant tumour. Only malignant tumours cause cancer as benign tumours cannot metastasise, migrating to other parts of the body; malignant tumours, on the other hand, are invasive and can perform metastasis, making surgery more difficult and worsening the prognosis.



Diagnosis

Currently, the earlier cancer is diagnosed the better the prognosis; the key is to detect the cancer before the cells multiply and spread to other parts of the body. Currently, there are two methods used in the diagnosis of cancer: the extraction of tissue samples for a biopsy examination and the second is non-invasive in-vivo imaging.

- Biopsy: A suspected malignant tumour has to be confirmed through the histological examination of a pathologist. These tissues would be extracted either through biopsy or surgery
- Non-Invasive in-vivo imaging: here a patient would have to orally or intravenously take signal amplification agents. Radioactive elements, chemical dyes and or protein molecules, to help produce distinctive images of diseased tissue.

However, these methods have a low sensitivity in detecting single cancer cells, therefore, missing key opportunities to diagnose early. Non-invasive in-vivo imaging, in particular, employs the use of some radioactive elements that have to be administered at high does as because of their poor specificity to the target cancer cells. These disadvantages, as well as the possibility that some of the organic dyes used will lose colour glow very quickly due to photo-bleaching, make both methods of detection rather impractical.

Alternatively, I propose Quantum dots (qdots) to identify tumours, then nanowire biosensors to analyse tumours to ascertain if they are malignant or benign. Highly luminous nanoparticles, the crystals will glow under UV (different colours correspond to crystal size) therefore if one were to fill beads with qdots of the same size then design them so that different colours correspond to different levels of mutation by binding to specific DNA mutations. In so doing different DNA mutations could be detected and also, more than one could be detected at any one time.

Figure 3 -Solutions of different sized quantum dots

The use of qdots, could eliminate the use of biopsies, cutting costs within the NHS, much to the delight of the government, and qdot imaging permits high resolution imagery that will prove very useful in detecting even the smallest tumours.

However, as mentioned earlier not all tumours are malignant and so tumours discovered will need to be analysed using nanowire biosensors.

Nanowire biosensors allow the early detection of more than one analyte – the substance being found in the analytical process – contained in a single chip. The biosensor would be made of a receptive tissue or cell receptor and a transducer that will measure the change in the data collected by the biosensor and converted into quantative data that can be easily interpreted.

Adjacent is a table showing how a transducer would use the data collected by biosensors to produce data that a definitive diagnosis can then be made from.

Biosensor	Measures the change in
Piezoelectric	Mass
Electrochemical	Electric distribution
Optical	Light intensity
Calorimetric	Heat

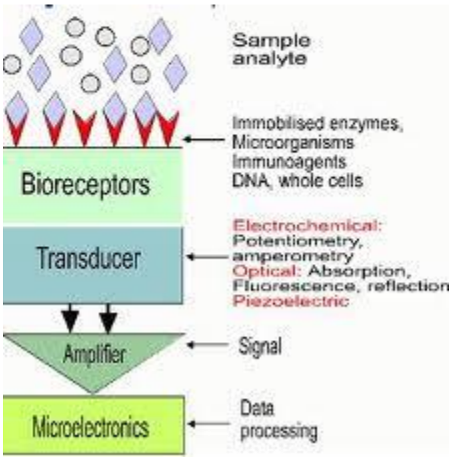


Figure 4

By using nanotechnology and coating the nanowires with protein complimentary to the glycoproteins on the surface of carcinogenic cells, you can change the shape of our protein shapes which also aid the detection of more than one strain of cancer simultaneously. By creating such detailed technology that will examine at such a minute-scale, we may be able to discover more about cancer and its development with new versatility and as mentioned earlier, decrease time needed to detect cancer so that treatment can start earlier. Figure 4 to clarify data processing by the biosensor.

Treatment

Can is currently treated by a combination of aggressive surgery, chemotherapy, radiation therapy, as well as other methods; the choice of treatment is dependent on location and the grade of the tumour and the stage of disease, as well as the strength of the patient to withstand potential surgery. Treatment aims to remove the entire tumour, however current diagnostic tools mean that we cannot identify single cancerous cells so cancerous cells can be left behind to reoccur. Another disadvantage of current methods is the use of radiation on the neighbouring healthy cells of a tumour, damaging the neighbouring cells' genetic material. Also the use of cytotoxic medication, that affects the growth of all fast growing cells, causing hair loss and extreme nausea.

To combat the shortfalls of current treatment, I propose the introduction of 'gold bullets' as non competitive inhibitors, attaching to glycoproteins, first to stop the replication of any more cancerous cells. Secondly, X rays can be transmitted to the gold bullets to replace radiotherapy and burn the tumour. The non competitive inhibitors would have to be in a complimentary shape to the glycoproteins of the various cancerous cells and when taken, time would be given to allow the bullets to travel round the body and attach to the cancerous cells. This also opens doors for and oral treatment of progressive cancer that has spread throughout the body; the bullets small size make the treatment particularly suited to the dispersal within a tumour and their engineering to hit specific target cells rather than the whole body. Furthermore the gold nanoparticles have an increased chemical and heat resistance to survive in hostile environments such as the acidic stomach.

Finally, after the destruction of the tumours, ongoing monitoring of the body could be maintained through installing nanopores throughout the previously affected area; being so small, there would be no issue of rejection and they could be used o to monitor genetic codes for malignant change. What's more if this malignant change proves to be reoccurring, dendrimers could be sent in to correct genetic mutations.

The advantage of my proposed treatment is principally the lack of invasive surgery and the cost-cutting potential as well as the reduced levels of trauma to the patients from nausea, post-operative pain and perhaps hair loss too.

In conclusion, nanotechnology has a promising future in terms of contributions to the medical field; however, I do feel that the potential for controversy is great: the potential to be seen as unnatural interference with the design of the body and the possibility that it may not be back by the National Health Service, thus potentially introducing a two tier healthcare system. Yet, I still believe that the potential successes of nantotechnology outweigh the conservative views of some sceptics in society. The use of quantum dots, biosensors, nanopores and dendrimers could prove invaluable to formulating a cure for cancer so that it does become a disease of the past.

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