

**THE APPLICATION OF NANOTECHNOLOGY IN
DIAGNOSTIC MEDICINE**

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Abstract

Nanotechnology is developed from the manipulation of matter at the atomic scale; this gives the particles remarkable properties which will revolutionise modern society. There are many possible applications of the technology, particularly in medicine. A key feature of medicine is diagnosis. Diagnostic methods are under continual improvement aiming to be more accurate and much quicker. The application of nanotechnology could implement this improvement and shall be discussed in this paper. However there are many factors that should be accounted for if nanotechnology is to be successfully ingrained into society. If diagnosis was improved nanotechnology could fundamentally save lives.

Introduction:

Research into nanotechnology has developed extensively in recent years however nanotechnologies have always been ingrained within the natural world, for instance the enzyme ATP synthase is actually a tiny rotary motor attached to a nanoscale nickel bar magnet. Through observing nature we can synthesis these particles to enhance new or existing products, opening countless avenues in medicine particularly diagnosis.

Nanotechnology deals with particles at the atomic scale of 1×10^{-9} m. In order to manufacture nanomaterials a 'bottom up' approach is used where smaller components are built into larger assemblies using tools such as the scanning tunnelling microscope which was invented by Gerd Binnig and Heinrich Rohrer at IBM in 1981. Nanotechnology has so far only enhanced existing products such as self-cleaning glass. However currently in the USA more money is invested in nanotechnology than the budget for NASA, which means that soon nanotechnology will bring about a significant change in society. I believe the self-cleaning properties of glass could be replicated into medicine. Self-cleaning surgical tools could transform sterilisation. Similarly self-cleaning door handles could minimise the spread of pathogens decreasing the spread of deadly hospital-bound infections such as MRSA. Already antimicrobial properties of nanocrystalline silver are being used in wound dressings in the USA. Nanotechnology can be used in preventative medicine as well, for instance in sunscreen nano-titanium dioxide can absorb and reflect UV light. The pigment is also present in paint but due to the particle size being between 10-20nm it does not scatter visible light as in paint so appears transparent.

At nanoscale, the properties of materials are strikingly different. This fundamentally alters the optical, electrical and magnetic behaviour of the material. The surface area to volume ratio increases; this leads to the atoms being more reactive on the surface than at the centre, meaning nanoparticle based materials are a good catalyst for reactions. An example of this is that nanogold melts at a much lower temperature than solid gold metal. However Brownian motion within fluids means that the nanoparticles will constantly be bombarded. Due to this 'nanobots' which replicate themselves inside blood vessels are currently impractical as they would be broken apart by all the other particles. Similarly inertia is negligible and viscosity dominates. Also the forces which hold surfaces together become very strong due to the influence of the strong force. This is a disadvantage for 'nanobots' as they would stick to the first surface they contacted. Aggregation, the grouping together of particles, could overcome this as it would lower the surface to volume ratio; this could lead to the potential for nanoparticles to be used as vehicles for gene and drug delivery. The nano-forces could lead to elegant self-assembly systems. Soap molecules use self-assembly to capture water in structures such as films and bubbles.

Nature uses nanoforces to its advantage; Geckos can hang upside down from a flat sheet of glass due to the nanoforces created by the extremely fine hair on their feet. A team of German

and Swiss scientists led by Andrew Martin from the Institute of Technical Zoology and Bionics calculated that nanofibres allow spiders to carry more than 170 times their own body weight (see reference 9). The complex quantum effects can cause difficulties when designing new technology however if scientists can harness them and overcome the problems, the potential of nanotechnology creating novel structures, devices and systems within the human body is infinite. A nanoparticle material that will be highly useful in the near future is nanocrystalline zirconium oxide as it is strong, lightweight, resistant to corrosion and inert; this makes zirconium oxide a good material for medical implants.

Within medicine diagnosis plays a fundamental role. Diagnosis is the process of identifying diseases from exhibited symptoms. It is implied that 90% of medicine is diagnostic; this includes patient history, examinations and tests. Lack of diagnosis will lead to a lack of sufficient treatment, and could harm the patient; a form of medical malpractice. Advancements in nanotechnology could lead to a firmer diagnosis. More precise tests would lead to a more reliable diagnosis. Also new investigative techniques could allow for a quicker and earlier diagnosis, which is essential in diseases such as cancer. According to Cancer Research UK 'there are around 298 000 new cases of cancer diagnosed each year in the UK'. Therefore improvements in cancer diagnosis through nanotechnology would be a valuable investment and research area. Early detection of cancer is essential before any anatomic anomalies become visible; this would lead to a much more effective, less painful and less stressful treatment for the patient.

Discussion:

Mammography is a type of imaging that detects breast cancer by using a low-dose x-ray system. A Mammogram examination is a central part in early detection of breast cancer as it detects the tumours before Doctors and Physicians can feel the lump. However for accurate clinical diagnosis this current technique requires more than a million cells, which is still an established tumour. Nanoparticles are being developed which recognise proteins produced only by cancer cells. The proteins are from each individual cancer cells plasma membrane, the proteins are on the outer edge of the membrane and have carbohydrate chains attached, hence their name; glycoprotein's. Glycoproteins are important in cell recognition, which is the body's ability to recognise whether a cell is foreign or self. However cancer cells can hide their glycoproteins so the body does not often detect them as a foreign cell. Nanotechnology can be used to detect the proteins instead; this would theoretically replace the need for mammography and other medical imaging devices. Quantum dots are a form of nanotechnology which could do this by acting as tiny beacons or markers that can watch and track cells, genes, proteins and other small molecules. Electrons in the core of a quantum dot become excited when a beam of light is shone on them. This means the electrons move into higher energy levels within each atom. As the electrons lose energy, and consequently fall back down to a lower energy level, energy is emitted as light. The wavelength of the light depends on the size of the core of the quantum dot. By altering the size of the core researchers can fine-tune quantum dots to emit light at a variety of wavelengths producing multicoloured markers which can then be detected by a machine. The advantage to quantum dots over conventional dyes is that they are a thousand times brighter and last much longer. By adding other molecules to the quantum dots they can be targeted to specific cells. The quantum dots could be targeted to the glycoproteins on cancer cells, they would only be able to emit light if they were attached to the specific glycoprotein. This will enable the diagnosis of cancer when the tumour is only 100-1000 cells, compared to the current technique of

mammography which for an accurate diagnosis needs around a million cells. Quantum dots will revolutionise medical diagnostic imaging.

Unlike quantum dots nanoshells absorb or scatter the energy. Gold nanoshells have a core of glass and an outer case of gold; they are an example of a nanoparticle fullerene or buckyball. The origins of nano-sized fullerenes was in 1996 when Sir Harry Kroto, Rick Smalley and Robert Curl won the Nobel prize for their synthesis of a new form of carbon, C₆₀, which they named buckminsterfullerene, hence the name 'Buckyballs' as they are shaped much like a football. The properties of Buckyballs are remarkable; when fired at a steel plate at 15000mph they bounce back, and when compressed to 70% of their original size they become twice as hard as a diamond. However the property that is useful in medical diagnosis is that their chemistry can be manipulated, this means that adding extra molecules changes the fullerenes optical properties. The same can be said for nanoshells. This could be applied in a variety of areas of medicine, for instance quick blood tests could be created using nanoshells coupled to molecules that detect disease-associated proteins, the change in the nanoshells optical properties when they bind to the target could easily be detected. Quicker blood tests would obviously save time and money. However it would also transform diagnosis as the results could quickly be found without having to send a sample to a laboratory. This would cut down patient waiting time, and increase patient satisfaction. Quicker blood tests would also save lives as the Doctor would be able to start a course of treatment more quickly and efficiently. Similarly this idea could be applied in pregnancy testing kits, drug tests and in HIV detection.

Endoscopy and Colonoscopy could also be improved by nanotechnology techniques. Currently they are invasive and quite distressing for the patient, many people fear them. The use of Nanotubes could change this. In 1991 Nanotubes were first discovered by Japanese researcher Sumio Iijima and also by Al Harrington and Tom Maganas of Maganas Industries. Nanotubes are a tube-like structure made from carbon, which like many other forms of nanoparticles (as previously mentioned) has fascinating properties; they are at least 100 times stronger than steel but only one-sixth as heavy. They also conduct heat and electricity far more effectively than copper. The aspect that could be captured in improving Endoscopy and Colonoscopy however is through the tube being hollow. The inside could be covered with pure nanoparticle glass. A form of fibre-optic cable would be created. Many of the nanotubes could be grouped together so that an image could be created. However the nanoparticle fibre-optic cable would be much smaller in diameter than the current optical fibres used, so the overall instrument would be smaller. It could potentially have better resolution which would create a clearer image.

Other forms of nanotechnology that can improve diagnosis are nanowires which are similar to nanotubes but are thread like structures less than 50nm wide. Research into nanowires is based around the early detection of precancerous and malignant lesions from biological fluids. Japanese scientists have used nano-needles 100nm wide to deliver materials to very specific points in the cell. The potential of this in medicine is vast, one example being direct drug delivery. The use of a nanowire is much less invasive and decreases the chance of infection; this improves the patients' chance of recovery. Similarly nanotubes can be used to deliver drugs without other pathogens entering the body as the tube is so narrow. Future developments in science, particularly molecular science, will allow for more developments in nanotechnology and so more potentially diagnostic medical products will be available.

Conclusion:

Social influences in the future will decide whether consumers wish to have nanotechnology within diagnosis. Society may condemn nanotechnology through fear of a cyber world. Consumer demand can make or break a product, for instance the hugely popular iPhone compared to the unpopular Segway transport, one reason for the divide in the popularity of these products was marketing. The manufacturers of the iPhone, Apple, have a huge marketing scheme throughout the company however the manufacturers of the Segway did not advertise effectively. Some products create a public controversy, when GM foods hit the market in the UK there were huge debates and they were banned, however in the USA GM food products are consumed by customers as they are seen as advantageous. Nanotechnology must be marketed as a desirable product; this will make patients more willing when using diagnostic nanotechnology devices.

Environmental impacts of nanotechnology are unknown, it is often impossible to see the impact on the environment for a decade or more. With nanoparticles being so tiny they could easily travel through air and water, and spread through the environment, it would be difficult to detect and stop the polluting. When asked of nanotechnologies will affect the environment, Mr Doug Parr, Chief Scientific Advisor of Greenpeace, said;

'They definitely will. But at the present it's hard to tell whether the effect will be good or bad.'

Here Greenpeace, which is a non-profit global campaigning organisation, is remaining impartial; they are not condemning nanotechnology or promoting it. In order to determine the effect of nanotechnology on the environment more research is needed. Professor Mark Welland, the Director of the Interdisciplinary Research Centre for Nanotechnology and the Nanoscience Centre at the University of Cambridge states this in his comment;

'Technologies in general do. Nanoparticles could potentially have a toxic effect. We need to understand the pathways through which they move into the environment. At the moment, the quantities being made are tiny, but they could be greater in the future as people start to scale-up production.'

In addition to research into the effect on the environment, trials will have to be run that focus on living organisms. In recent years the effect of plastic on aquatic animals has been found to be dangerous and life-threatening, this is one of the reasons for a large recycling campaign. Some research has found that buckyballs can harm fish, but this was at very high concentrations and with very few fish, however changing chemicals within the buckyballs changes their properties so a generalisation cannot be made. The effect of nanotechnology must be assessed in all areas of life, from the effect on patients, to the long and short term on the environment, to the effect on other animals.

As well as the concerns after production on the environment there are many safety issues when producing the nanoparticle products. This is because the properties at nanoscale of the materials are remarkably different, so little is known about safety measures that should be implemented during manufacture. One route that nanoparticles could enter our body is through the skin. This is dangerous as they could interfere with the function of glycoproteins or be absorbed by our cells and interfere with organelles or intercellular molecules. Another way of nanoparticles entering our bodies is through the lungs; this would lead the

nanoparticles directly into the bloodstream and to be transported around our body. This could be advantageous in other areas but if the nanoparticle was toxic it is a safety issue. Nanoparticles could cause inflammation within the lungs. Carbon nanotubes especially are a cause for concern as they resemble asbestos fibres which have now been shown to cause cancer in workers who inhaled them. Safety measures within the workplace would have to be assessed and adjusted with the backing of firm research in order for nanoparticles to be manufactured and accepted by the public.

Research into these presented issues will have to be non-bias and follow all scientific regulations in order for it to be scientifically valid and accepted.

The inevitable cost of nanotechnology could be another burden for a cash-strapped NHS. Even if the new technology was made available on the market, hospitals throughout the UK within the NHS might not be able to afford it. The new technology will be seen as a risk as it could be replaced quickly, thus outdated it and also it does not have the vast number of clinical years as the 'old' technology does to show that is as effective. Even if relatively the cost of materials is low due to the nanosize, if made in small amounts as a batch production instead of a continuous mass production the cost will be high. Also the machinery used to make the nanotechnology will be very expensive. This will reflect into the cost of the product. This could lead to the diagnostic devices only being available within private hospitals or more economically developed countries (MEDCs) which would heighten global inequalities. However, if made available to less economically developed countries (LEDCs) the technology could allow the LEDC to revolutionise its society and bypass the outdated technology it could previously only afford. The profit gained from the nanotechnology within the LEDC would allow other areas within the country to be improved, for instance living conditions, working conditions and overall healthcare. Also many LEDCs are in dept to MEDCs, through trade the LEDC could pay off its debts. The UN Millennium project stated that;

'Nanotechnology is likely to be particularly important in the developing world, because it involves little labour, land or maintenance; it is highly productive and inexpensive; and it requires only modest amounts of materials and energy.'

Nevertheless within modern society the biggest problems could be tackled with the technology we already possess, so nanotechnology is not a direct solution.

Nanotechnology has been seen to have many possible avenues in diagnostic medicine. The properties of the nanoscale instigate this; however the unusual properties also require us to proceed with caution highlighting the potential safety and environment issues. Ethical issues also must be considered and public opinion taken into account. Also economic factors will influence the path of nanotechnology. If we want a society in which diagnostic methods are enhanced through nanotechnology we must work together collectively to overcome the barriers that will be presented. Fundamentally through doing so the time taken for diagnosis will be shortened, patients' welfare will be improved and lives will be saved.

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