

# THE APPLICATION OF NANOTECHNOLOGY IN DISEASE DIAGNOSTICS

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Interest in Nanotechnology has increased dramatically over the past couple of years as its huge potential has finally been recognised. We wanted to look at the potential to use nanotechnology in the medical and veterinary industries, and how in the not too distant future, it may be hugely affecting our lives. We have focused purely on diagnostics and the treatment of cancer as there has been a lot of research into this area. We believe it to be of huge relevance as, at this day in age, it is affecting a huge proportion of the population in one way or another. In this report, we've touched lightly on ideas and treatments that have undergone a great deal of research and testing, to give an insight into what may soon be available to the public. Like with any scientific development, there are of course concerns and disadvantages to using the nanomaterials. Despite some of the drawbacks mentioned, we believe the advances nanotechnology could provide hugely outweigh the possible side effects.

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The ability for us to work at the nano-scale opens a window of new opportunities for the manipulation of existing materials that will in time revolutionise medicine and veterinary science. This paper will focus on nanotechnology being used in diagnostic techniques and cancer treatment, although other applications for nanotechnology involve using nanoparticles as a drug delivery system and in asthma detection.

When referring to nanotechnology, we essentially mean anything smaller than 100 nanometers in dimension (this is equivalent to  $1 \times 10^{-7}$  metres). It enables us to work at atomic, molecular and supramolecular levels to manipulate materials, creating new structures and such devices with entirely new properties. Ocheke et al (2009) summarised the concepts of nanotechnology and applications being researched at the present time.

The future possibilities of nanotechnology are huge, which is why the National Institute of Health is continuing to fund research at eight Nanomedicine Development Centres. Such research is allowing us to further understand and work with material at the nano-scale with increasing ease.

Nanotechnology is particularly crucial to medicine as it allows us to isolate specific cells within the body, which was previously a physical impossibility. Cells are incredibly small – about 10,000nm – but with nanotechnology we can engineer the structures inside a cell to improve treatment techniques and our knowledge and understanding of diseases.

Recently, devices have been engineered to help in a variety of medical fields, one such example are Nanobots, which can potentially perform functions inside the body - including procedures such as cell repair and implanting devices – building the necessary structures inside the body. Nanotechnology may also be able to aid cancer treatment as it can target purely the undesirable cancer cells and not the healthy cells in the surroundings; resulting in minimal damage to the body. There is also the prospect of being able to detect and destroy the cells before they develop into tumours.

Cancer is an increasing issue within the medical world today, with more than 1 in 3 people developing cancer at some point in their lifetime [Cancer Research UK]. The ability for us to use nanotechnology to not only treat cancer cells, but also improve our diagnostic techniques could severely reduce the number of deaths seen from cancer each year.

Firstly, nanotechnology could help provide individual therapies for personalised medicine. Using nanotechnology for diagnostics, doctors can target specific molecules that help distinguish the different types of cancer and one patient's cancer type another. One highly researched method is known as Q-dots – Quantum dots – which are tiny nanocrystal structures that express specific proteins on their surface which allow them to attach to distinctive proteins on cancer cells. They produce high-resolution, coloured images of the molecules moving within individual cells. These can be collected over time to generate an insight into the tumour stage and type. Another method uses Iron oxide nanoparticles, to help enhance images produced from MRI scanning.

Furthermore, several techniques have been developed to give a 'targeted' chemotherapy, where only the cancer cells are affected.

Work on the nano scale is so suited to medical testing because its tiny size enables it to respond to much smaller amount of substances such as bacteria and virus. The high surface area to volume ratio of nanoparticles also increases the reactivity, which means they have the scope to be used in areas such as drug delivery (such as for cancer treatments).

Overall there are many exciting prospects for the future of nanotechnology, which will hopefully be readily available to the majority of the population, in the near future.

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Using nanotechnology for diagnostic imaging has the potential to be highly successful because it means detection of things such as tumours and infections can be more precise, therefore administration of treatment can be more accurate. An example of where this concept is being used is in the detection of pneumonia using silver nanorods.

Existing ways of detecting pneumonia involve taking blood tests or doing x-rays on the patient's chest. The disadvantages of using blood tests is that the results can take a few days to process and therefore the pneumonia has time to progress within the patient as well as spread to other people, potentially becoming more difficult to treat. X-rays however, provide quick, easily visible results but the procedure can be lengthy, expensive and inconvenient for the patient. Excessive levels of radiation for the patient must also be taken into consideration.

Research has been undertaken at the University of Georgia where scientists have developed a way of testing for pneumonia that significantly reduces the diagnosis time from a few days to a few minutes. [Rapid diagnostic test for common type of pneumonia uses silver nanorods <http://www.nanowerk.com/news/newsid=19439.php>]

Duncan Krause conducted this research and the procedure happens in the following way: Firstly, silver nanorods are extended out in a brush-like formation at specific angles. The silver nanorods are then combined with an existing technology called 'surface enhanced Raman spectroscopy', which allows single molecules to be detected when they are absorbed by a surface. The silver nanorods and surface enhanced Raman spectroscopy (SERS) are then combined, resulting in a technique that is safe and effective. Although it is possible to produce silver nanorods in a variety of ways, one common to this technique is to use seed-mediated growth. One way of doing this is to react twinned decahedrons to a trace of a salt, such as NaCl, under the protection of Argon. [Tang, X., Tsuji, M. Synthesis of silver nanowires in liquid phase].

Another way can be to carry out a reduction reaction between a copper chloride and the twinned decahedrons. The secondary example has oxygen present in the reaction and there had been research to show that this reduces the yield of silver nanorods formed because the oxygen can be absorbed by the silver surface and block any sites the silver atoms would react with. For large-scale production of silver nanorods, silver 'nano-seeds' are formed in a chemical reaction, in which Silver Nitrate is reduced by an acid whilst surrounded by the nanoseeds and other substances such as NaOH to achieve synthesis of the silver nanorods. By altering the amount of silver nitrate present in the reaction, the length of nanorods can be altered.

The main advantage to using nanotechnology in this procedure is that it will allow diagnosis to become faster and therefore the pneumonia can be treated faster and more effectively. It is also hoped that, eventually, the equipment will be able to fit in a suitcase (due to the microscopic size of the nanoparticles the overall size of the testing equipment will be

reduced) [Rapid diagnostic test for common type of pneumonia uses silver nanorods <http://www.nanowerk.com/news/newsid=19439.php>] which means it can become portable, allowing more people to be easily tested for pneumonia and the spread of the disease monitored more closely.

A disadvantage of developing this technique of testing for pneumonia is going to be the cost of research and production. There is currently a large amount of funding into this information by the U.S. Army Research Laboratory and the National Science Foundation. [UGA researchers develop rapid diagnostic test for common type of pneumonia [http://www.eurekalert.org/pub\\_releases/2010-12/uog-urd121510.php](http://www.eurekalert.org/pub_releases/2010-12/uog-urd121510.php)]. Despite already receiving funding, if this diagnostic tool is to eventually be the standard pneumonia test due to its efficiency and portability, more funding will be required to cover costs from other organisations and governing bodies.

Issues surrounding the use of nanotechnology in diagnostic testing are common to other areas of scientific development as well as being specific to this. For example, the nano particles will either have to be released into the atmosphere where they could potentially build up in rivers or the soil, or recycled/dumped in a landfill because they are part of fixed machinery (as in the testing for pneumonia). Either way, the problems are not fully understood.

Another problem that some people have with nanotechnology is whether it is socially responsible to manipulate particles on a nano scale, which has the potential to blur the lines between biological and physical science. As well as destroying some well-respected boundaries, nanotechnology has the scope to remove other ethical issues. These include the ability to produce cells rather than obtaining them (such as in stem cells), which is considered morally and ethically wrong by some organisations, particularly those who campaign for human and animal rights.

As mentioned before, the main funding for nanotechnology research is coming from the government and that runs the risk of not everyone's interests being represented. It means that whilst nanotechnology may be used to develop things such as nuclear weapons and tracking systems, smaller companies with interests in diagnostics maybe not get an insight into newly available technology. Ultimately, this means nanotechnology will become more 'exclusive' and therefore more expensive and less available for the majority of the population.

An important aspect of the nano-scale technology is how it is being regulated and monitored. Currently, the limitations on nanotechnology are more physical than implemented by the law. Organisations such as the Environmental Protection Agency, the Food and Drug Administration (U.S.) and the Health and Consumer Protection Directorate of the European Commission have been researching the potential risks of nanotechnology, although no specific legislation has been put in to place. One of the reasons the danger to society that nanotechnology poses is being looked into is that small nano scale particles have the potential to penetrate the human skin due to their tiny size. This means, they could

cause problems within body as they are highly reactive, which is because they have a high surface area to volume ratio.

Although the current risks and benefits of nanotechnology in human and veterinary medicine are unknown as of yet, many scientists are clearly interested in its development. At a time when experts globally are on the brink of developing a cure for cancer, one of the top killers in animals and humans alike, the new concept of working at “nano” level means that new methods of detection and treatment of the disease are currently in the pre-development stage.

As with any disease, rapid detection is a must, to increase the chance of a successful recovery. Some types of cancer can be notoriously hard to detect, for example: cancer of the lungs or brain. Often once the disease has been discovered; it may be too late for any effective treatment.

MRI (Magnetic Resonance Imaging) scanning can be used in the diagnosis of some types of cancer, although Computerised Tomography can also be beneficial. MRI scanning involves the use of magnetism to give an internal image of anatomical parts. They give a cross-section view of the body, and fairly clear images can be obtained.

However, sometimes it can be hard to distinguish between benign and malignant tumours, which would lead to a false negative/false positive result. This is where the development of nanotechnology in human/veterinary medicine comes into light.

As previously mentioned, MRI scanning relies on magnetic properties. If a magnetised compound were present in the area concerned, this could enhance the image greatly, and distinguishability of the cancerous nature of tumours would be more straightforward.

Iron Oxide is a comparatively safe magnetic compound to use in humans/mammals, in relatively small doses. Iron oxide nanoparticles could be coated in a peptide, before insertion into the target area. The peptide would bind with the (cancerous) tumour. Once bound, the magnetic properties of the iron oxide should cause a vast enhancement of the Magnetic Resonance Image. This theory has been tested in a small animal model, to detect a pancreatic tumour.

To develop beyond this technology that is within the realms of feasibility for progression within the next decade, I wish to explore further the possibilities of nanotechnology within diagnosis of disease.

If a molecule of Iron oxide can be coated in a peptide in order to bind with a tumour, then surely there could be a goldmine of prospects for the binding of nanoparticles to peptides or other polymer chains such as polypeptides or proteins? Rather than coating a compound to aid diagnosis of the cancer, an antibody could be coated in an amino-acid polymer. This antibody could be used to target a specific type of cancer. As with the MRI use for nanotechnology, the peptide would bind with the tumour, and then the antibodies would be used to kill the cancer cells.

However, the key issue with current cancer treatment options (radiotherapy, chemotherapy etc) is that they kill normal body cells just as readily as they kill cancer cells. This is what causes patients to experience many negative side-effects, a common one being hair loss.

This reveals a huge flaw in the concept of coating an antibody in a peptide, as spread of the antibody could not necessarily be contained, and may result in the destruction of other non-cancerous body cells.

The only method of defeating cancer that can be hugely successful, would be one where the means of destroying the cancerous cells were inserted directly into the cells concerned, so as to bypass all other normal body cells.

Within nanotechnology, several solutions to this matter have been produced:

An example is a technique that attaches the drug to a gold nanoparticle enabling it to be 'hidden' from the immune system. It is therefore able to make its way through the blood stream without being destroyed. Another method being trialled uses the concepts of heat theory to destroy tumours. Similarly the iron oxide nanoparticles are transported by the bloodstream to the site of the tumours; where they accumulate and focus the infrared light to destroy purely the cancerous cells.

A "micro-scalpel" (laser) could produce a fast, high-energy pulse of light. This would be able to kill an individual cancer cell, and the process would be so rapid that other normal body cells in the vicinity would be completely undamaged.

Another method of targeting individual cells is aided by the use of "nanobubbles" – formed from lasers. Short laser pulses could be used to strike gold nanoparticles, which would be able to produce a nanoscopic bubble of such a size that it would be of the right size so that it could cause the cell to burst, therefore destroying it. The size of the nano-bubble could be altered by changing the power of the laser, therefore suitable for different cell sizes accordingly.

Obviously extensive testing will be necessary before this sort of technology can be considered in modern medicine, but it is a hugely promising step forward for doctors and vets alike, with a wish to push the boundaries of the current fields of diagnostic imaging and cancer eradication.

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It is evident that in the future, nanotechnology will be a vital part of medicine and veterinary science, and this may well include diagnostics, drug delivery and treatment of several killer diseases. Despite the massive potential that working on the nanoscale allows, nanotechnology can still be deemed relatively new, and therefore many questions that are opposed to it are left unanswered. Before using nanomaterials on a large scale we need to consider their effect on the environment, their ecological consequences and whether they present any health and safety risks in consumer goods.

The National Research Council recently released a report stating that “[Nanomaterials] can have unknown and possibly negative impacts, such as unexpected toxicological and environmental effects ... EHS research published to date has provided some data indicating the potential for risks to laboratory animals exposed to nanomaterials and has show that much more work is needed to assess the potential risks involved”. This alone indicates that we are only at the start of uncovering the true effects of using nanotechnology, and as a relatively new idea, the long term effects will go unknown for many years to come.

However, several problems have already been uncovered, which include: the release of waste products during the manufacture of nanomaterials; implications for biological processes in animals and social implications of their production. Due to their small size they can penetrate animal cells or – due to the large surface area – may even be absorbed by macromolecules in animals. The nature of the nanoparticles can hinder biological processes, which means the nanomaterials can present a danger to living organisms. While considering the primary effects of nanomaterials, we must also look at the bigger picture and acknowledge the secondary effects of the nanomaterials.

As mentioned above, the social implications of nanotechnology will be huge as the materials produced can replace natural substances. This could result in agricultural/industrial job losses, as farmers and factories are dependent on the production and distribution of the natural substances that the nanomaterials can replicate.

A mass introduction of the materials will lead to huge financial loss in certain areas, although on the other hand, the mass production of nanotechnology may in fact lead to a creation of thousands of jobs and counter balance the loss.

It is evident that there is still a demand for research before we can put to use our findings of nanotechnology. For example, the effect of nanoparticles on the environment and society has had relatively little research put into it. Before we can use nanotechnology in application it will have to be pumped with funding to ensure its safety before finally being trialled on humans or non-testing animals.

Overall, we can see that the possibilities involving nanotechnology are huge, and in time, it may lead to extraordinary medical advances that we once did not believe possible. And so, if the possible problems associated with nanotechnology could be overcome, or perhaps justified, then using nanotechnology for medical work will subsequently be hugely advantageous to the treatment of millions of patients and vital to the progression of the medical and veterinary world.

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