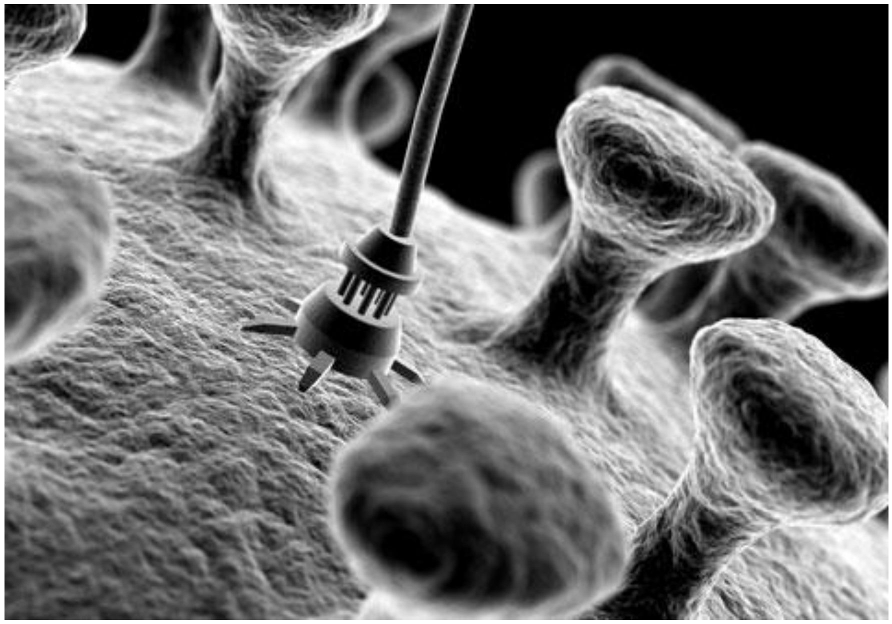
Exploring the Recent Advancements, and Future Potential Developments in the Application of Nanotechnology in the Field of Medicine, and the Ethics



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Abstract

For centuries the human body has suffered with incurable disease, malfunctions and cellular degeneration. This can change. Nanotechnology is a rapidly developing science, and this manipulation of matter on an atomic scale has the potential to repair the body, whatever the problem.

This paper argues for the mass employment of advanced applications of nanotechnology in the field of medicine, to account for the failed attempts of other known medical drugs and procedures to remedy the human body in the face of ailment or disease. This paper firmly believes and concludes that given the right funds, focus, and scientific attention, nanotechnology wields the invaluable potential to cure cancer, to replace nervous tissue with functional artificial tissue, and to restore vision to the blind.

INTRODUCTION

In 2003, Peter Singer wrote in his tutorial Mind the gap: science and ethics in Nanotechnology: **"As the science leaps ahead, the ethics lags behind [12]."** In this paper, we will explore this exactly; what advancements have been made, the potential of future developments, and the ethics underlying the field of nanotechnology.

The fundamental concept of nanotechnology is very simple, yet the mechanism behind the notion is far more complicated. This continuously developing branch of science deals with structures on the order of 100nm (a billionth of a metre, or 10-9m), or less. Now imagine the implications of being able to directly manipulate matter on an atomic scale – we would be able to target the most specific region with such a high degree of precision and deftness, without affecting the majority of the body. As a result, nanotechnology is now at the exciting forefront of advancements in the field of medicine, introducing new and innovative prospects.
This can be applied to the continuous battle to cure cancer. Presently, standard chemotherapy does not distinguish between cancerous and healthy cells, but destroys both (causing hair loss, anaemia, degradation of immunity etc...). However, the current outlook on nanotechnology is teeming with possibilities in both diagnosis and destruction. For example, Professor Shan Wang of Stanford University (2006) believes nanoparticles that are ultra-sensitive to magnetism [6], could be utilised to detect potentially cancerous cells. According to his publication: "Wang's specialty in magnetism is particularly important in medical applications because a magnetic field stands out like a flare in the night sky in magnetically neutral biological settings". This is of particular importance as magnetism stands out more than fluorescence (the current detection for signalling cancer-related protein). This means that if cancer proteins can be made to somehow trigger a magnetic response, detection will be more sensitive, leading to a better diagnosis and earlier knowledge of whether a particular treatment is working or not. The work of Ehud Shapiro of the Weizmann Institute of Science in Israel (2001) provides further breakthroughs in nanotechnology, where he actually used deoxyribonucleic acid (DNA) as bio-molecular nanocomputers in rudimentary ways to diagnose cancer. The four bases of DNA, Adenine, Guanine, Cytosine and Thymine actually replace the two bases (1s and 0s) of binary computing and by doing so we can also assess the concentration of specific cancer-related strains of mRNA in a desired region. Nanotechnology also holds the potential to destroy cancerous cells. This can be done in many ways. One of which is by inserting carbon nanotubules (microscopic synthetic rods), very precisely into cancerous cells or tumours, and then focusing an infrared laser beam onto the affected area. This heats the carbon nanotubules very efficiently; as they have a thermal conductivity of nearly 3500 $Wm^{-1}K^{-1}$ (copper only has a thermal

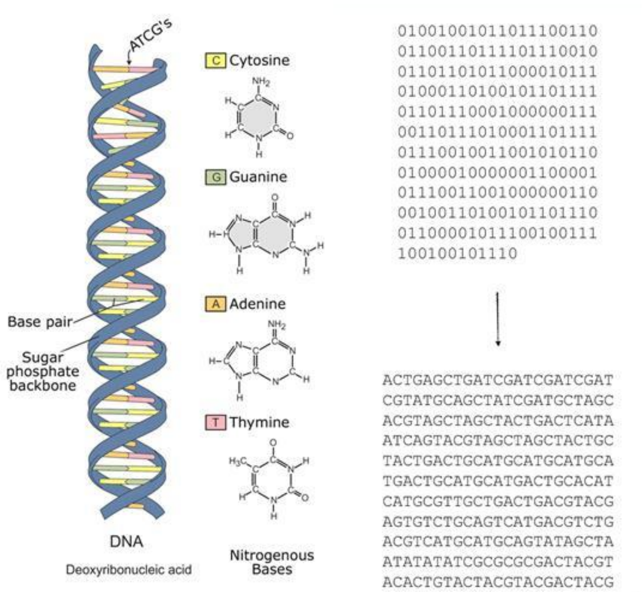

Figure 1 – In DNA computing, the four bases of DNA, AGCT, replace the 1s and 0s of binary computing [4]

conductivity of 401 $Wm^{-1}K^{-1}$) [18]. This is because carbon nanotubules have a unique property in that they conduct heat by ballistic conduction [3] - the unimpeded flow of charge or energy. In fact, nanotechnology is projected to make detection of cancer much simpler and more effective in years to come. ‘Non-invasive’ procedures involving the use of ultrasound-radiating microchips are currently in development which can detect metastases and circulating tumour cells in the bloodstream [5], in their early stages have even been patented and can identify and isolate tumour cells. This would be an incredible innovation, as it would help identify and remove cancerous tumours a fraction of the size of those diagnosed today. As a result, action can be taken against the disease much earlier and survival rates are likely to multiply. There has already been much headway made in experimental data that showed that “the CTC microchip successfully identified CTCs (circulating tumour cells) in the peripheral blood of patients with metastatic lung, prostate, pancreatic, breast and colon cancer in 115 of 116 (99%) samples” [8 and 17] in tests by the Surgical Services and BioMEMS Resource Centre, Massachusetts General Hospital, Harvard Medical School, and Shriners Hospital for Children, Boston, Massachusetts. This tool can be used in conjunction with treatment and to monitor the progress of a cancer, as there is a known correlation between CTC abundance in blood and the size of cancer tumours. Successful trials have taken place with this technology in Spain and Boston, USA. Larger scale testing is due to begin in the near future.

Quantum dots [11 and 15], which are fluorescent semiconductors, are another advanced nanodevice which holds promise to extremely high-resolution cellular imaging. Quantum dots can be encased within a shell tailored to imitate organic receptors within the body, and emit light when exposed to energy (e.g. UV light), effectively lighting up the desired area (as opposed to the conventional organic florescent dye used). Additionally, quantum dots have a large surface area to volume ratio, leaving ample space to attach other entities on the dot surface (apart from the required receptors). This includes various drugs for treating a disease the dots have been tuned to find. Quantum dots have an energy output of almost 100%; enriching the already vast arsenal of imaging tools and advanced drug delivery systems available through use of nanotechnology. Other already developed drug delivery systems include nanobots (which can also be used to measure blood sugar levels), and buckminsterfullerene, which is composed of 60 carbons bonded to make a spherical shape.

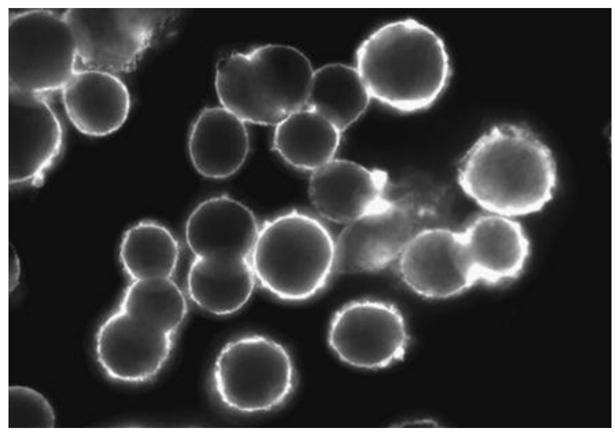

Figure 2 - These breast cancer cells are labelled with a quantum dot conjugate

The applications of nanotechnology extend further, however. We know today that proteins are produced by the triplet code (codons) which process the base pairs which are bonded in DNA. The specific orders of the bases affect the specific protein that is produced. Recently, it has been discovered that we can manipulate the base pairs to produce nucleic structures that we can use in the future to benefit medicine; eventually even replacing human tissues completely. These can form junctions with arms or ‘crossover’ junctions of DNA which have many useful properties. These structures can be used to form the aforementioned nanotubes which have been used to develop cures for the cancer by destroying tumour cells. Nanoarchitecture has advanced thanks to work in this field; to the point where we can spell out words in 3D with particles and more importantly, this means applications in use for molecular electronics can succeed as we can successfully manipulate particles. Nanomechanical devices can also be built due to DNA complexes that are formed; they can modify molecules and even react to act as buffers in resisting pH change; which is important to human reactions. Therefore the use of nucleic acid and editing DNA for medicinal benefit is almost boundless.

Dr Andreas Schatzlein from the School of Pharmacy, London has recently used gene therapy selectively kill off cancer cells [10]. Schatzlein and his team investigated chain-like molecules called dendrimers and then mixed them with DNA molecules or cancer drugs, forming microscopic balls called 'nanoparticles'. For reasons unknown to man, these particles are highly attracted to tumours – the reason is thought to be because of the nature of blood vessels that lead to cancers. The nanoparticles also tend to build up and become concentrated in tumours, making them even more effective.

DISCUSSION:

"As the science leaps ahead...

Nanotechnology has a lot of potential for treating and curing cancer, simply because of the difficulty that other approaches face in distinguishing the difference between a healthy cell, and a cancerous one - a feat that our own complex and intelligent bodies cannot do. This paper has carefully considered the recent advancements in nanotechnology, and offers the following suggestions on possibilities for more advanced diagnosis and treatment in the future:

i) **Cancer**

Building on Dr Andreas Schatzlein's work in the introduction, instead of inserting genes that kill off cancer cells, what could be engineered is that for genetically recessive diseases such as cystic fibrosis, one could place the 'correct' gene into the cancerous cells in order for them to regain their normal function. This could be useful in terminal patients in order to provide temporarily better quality of life, and even extend their life expectancy. In the future, small tumours in sensitive areas could be treated using minimally invasive surgery, by injecting a series of carbon nanotubules filled with radioactive substances such as Iodine-131 or Iridium-192 [2 and 16]. This will act as a nanoscale type of brachytherapy which works on the principle that rapidly dividing cells are highly sensitive to damage by radiation. This method has been proved to work in the past on larger scales than I have suggested, and still prove to be cost-effective and also provides a lower overall dose of radiation to the body than external irradiation.

Leading us into the discussion about genetics, people who have previously had cancer are susceptible to getting it again, as cancer is due to the accumulative effects of minor mutations to proto-oncogenes, tumour-suppressor genes and DNA repair genes. If cancer is treated in one of these patients, one can safely place a bet that some, if not all of the above genes have mutations in and may not function properly. I propose that we use gene therapy to give ex-cancer patients the correct allele for such genes, mainly the DNA repair genes, in order to decrease the likelihood of the cancer re-developing after. This can be done by adenoviruses, which contains double-stranded DNA, which inserts the DNA straight into the host cell, but not into the chromosomes, providing a temporary boost in the body's own defences against cancerous tumours reforming shortly after treatment. A long term solution would be to use retroviruses [7], which will contain the RNA for the proteins above that we would like to insert into the DNA. This is done by an enzyme in the virus called reverse transcriptase which turns the RNA into DNA, and then by the enzyme called integrase, which integrates the DNA into the chromosome of the patients' cells. This will provide a more permanent solution as this new DNA will be replicated into future cells, but also carries with it the risk of insertional mutagenesis, which happens when this new DNA is inserted into part of another gene, breaking up the gene and causing it not to function. Having said this, there are methods in order to reduce said risks.

ii) Genetics

Additionally, this paper goes to the extent of suggesting that current developments in nanotechnology could be tailored to repair individual genetic disorder. The previously mentioned idea of manipulating codons in the DNA could be extended further, to manipulating individual nucleotides in the DNA sequence. If a single nucleotide was deleted near the start of a gene, then all subsequent triplets in the sequence would be altered (leading to a different subsequent codons). As a result the proteins synthesised will consist of the wrong amino acids, changing the function of the protein dramatically. For example, if the nucleotide sequence was originally CTC-GGT-CAT-CCC.., and the "T" nucleotide was deleted, then the mutated nucleotide would be CCG-GTC-ATC-CC… This may lead to the wrong synthesis of amino acids, eventually leading to hereditary disease such as phenylketonuria, or cystic fibrosis (in which three consecutive nucleotides are lost from the gene for CF). The basis to my solution to this stems from the work of Kuroiwa, Yoshimi, Tomizuka, Kazuma, Yoshida, Hitoshi, Ishida, and Isao (2009) titled "Artificial human chromosome containing human antibody a light chain gene" (1), I believe the same methods used could one day develop into a powerful sure - should ethics allow it. If a chromosome can have genes added to it, then sufferers from recessive diseases could then have their germ cells or one-cell embryo changed in such a way that the 'correct' allele for the genetic disorder is added onto both strands of a chromosome, meaning that their children will always have a dominant, correct allele. The potential for this is not to eradicate lots of diseases, but to make their effects nullified. Although the disease allele will still exist and influence the body slightly, the presence of the 'correct' allele will ensure that the phenotype for the disease will not be shown.

iii) Tissue reconstruction

It may be possible in the future to completely reconstruct degenerative body tissue using nanotechnology, or to even construct artificial tissue to replace the previously irreplaceable. My premise for this is based on the work of Samuel Stupp and John Kessler at Northwestern University in Chicago, in which they succeeded in making tiny rod like nanofibers called amphiphiles which can capped with amino acids or other chemical. If these amphililes could somehow to be engineered to tail Dr Andreas Schatzlein's previously mentioned nanoparticles (dendrimers mixed DNA), then it may be possible to cap the amphilies with Talcum powder [(9)], (a chemical which stimulates the production of healthy cells to produce a substance known as endostatin. This slows the spread of cancer cells) and apply this to the site of the tumour. Additionally, it may be possible to spur the growth of neurons and prevent scar tissue formation, effectively closing in on an answer to ending SCI (spinal cord injury) and myelopathy.

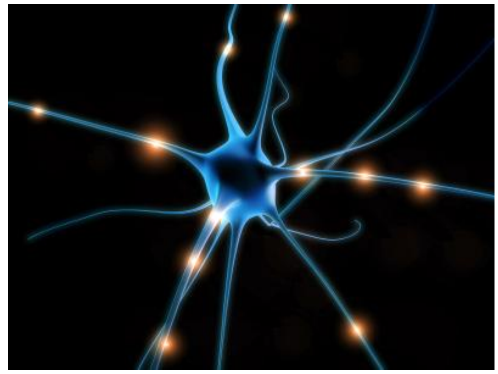

Figure 2 – Nerve cells stop dividing at an early age, leading to permanent damage if injured. There are currently two research fronts that look promising to offer a solution: one being nanotechnology, the other being stem cell research

…the ethics lags behind."

However, whilst nanotechnology certainly opens the path to advances that can help cure illnesses we never before understood, it also opens the door to many questions about how ethical and practical it is to introduce nanotechnology and to allow it to influence our lives. Over recent years, there has been advanced research and large grants and funds dedicated to nanotechnology in order to develop new technologies which can improve living conditions for people worldwide. However, there has been much less interest or care shown for researching or studying the ethics of nanotechnology. As such, the scientific world risks falling far behind and being unable to utilise future nanotechnology to benefit society due to a lack of any specialised legislation or structured authority. This would prevent proper administration or distribution whilst the public's lack of exposure to the issue could cause a general backlash and rejection of such unfamiliar treatments. Ethical questions held by patients left un-discussed would only be raised in the future halting potential treatments which could save or drastically improve lives.

As a starting point, any scientist would have to consider what sample of the public to test their nanotechnological prototypes on. Is it safe to inject nanoparticles into an ill person? There is evidence of nanoparticles collecting in subjects' cells and bloodstreams, the effects of which are as yet uncertain but could include respiratory problems. The use of nanotechnology requires intrusive procedures to plant the nanoparticles into the correct area of the body. These can become very intimate and invasive and could possibly be uncomfortable for patients who may feel that their usual privacy is thus breached. It must be questioned whether it is correct to do this to patients and whether the majority would even be comfortable enough to agree to such treatments. Therefore research into the general public opinion is very advisable as an unpopular new treatment would be ineffectual, uneconomically viable and a source of immense frustration to researchers. Use of nanotechnology in patients can be to collect data, storing even the most minuscule data about patients. But at which point is this information too intrusive? Could this lead to an over-cautious society where we store excessive and on the most part, useless data? This is a potential scenario which needs to be considered seriously as storing such data leads to various problems; firstly how can we facilitate all this information? Hospitals are already struggling to store information on patients today; the potential for much more collected from within the body would mean a shortage of computers to hold such information. To provide more computer systems could cost billions and would be extremely difficult to raise funds for due to the current weak economic climate and also a lack of public awareness of the issue making it a less attractive project to governments.

Furthermore, with the storage of so much more information there is so much more liability on medical professionals who would handle plenty more confidential information. This could well lead to a legal minefield where medical treatment is restricted by legislation and medical professionals find themselves more often handling paperwork than helping patients. After development of new nanotechnologies and hopefully beginning to use them there is also the difficult question of how frequently they will be used. Nanotechnology, based on future research, could be used in the future as regularly as vaccines are used and it is questionable whether this would be a good thing or may lead to over-dependence on technology. In the event of disasters or crises, the whole structure could collapse due to the almost inevitable overuse of new technologies.

There is also the long-standing question which stem-cell researchers have struggled to solve for years that manipulating nature and changing the way things are may not be ethically correct. For years, this discussion has slowed down the progress of medical research and caused cuts in funding, which could also become a problem for developing nanotechnology as it manipulates fine details of organisms. A compromise or common ground must be found between all sides in order to allow the continued success of nanotechnology research so that it doesn’t come against the same obstacles as past research.

Unfortunately, the potential for nanotechnology also increases the potential for damage to the local environment and its inhabitants [(14)]. In fact, the risk of harm is unknown as scientists as yet do not fully understand the affects of nanoparticles and the consequences of them collecting in the atmosphere and buildings. Speculated consequences include lung disease [(13)], DNA genetic mutations and toxicification of wildlife habitats. In 1986, scientist Eric Drexler warned that if tiny nanobots used were to escape into the environment they could consume the entire biosphere. Especially considering the adverse affects of pollution that society is attempting to deal with today this is a serious problem which requires further research and a better understanding to find out what could occur and how to prevent or handle it. There are also concerns over how nanotechnology may be used, or conversely, abused. As with many of today’s innovations, it may be a tool for rich, economically-developed countries to widen the financial gap between themselves and poorer nations. By developing nanotechnology themselves, richer countries can use them cheaply and sell them to other countries at much higher rates, plunging others into serious debts just as they have before with other products, such as weaponry. Even so, nanotechnology may still be very inaccessible to the poorer population and become exclusive to merely the rich and those who are able to afford high fees. The newfound strength of having nanotechnology to strengthen governments’ positions may cause them to become less cooperative and play ‘hardball’ with counterparts as a result of this new found makeweight that they would have. Many people, and doubtless governments, hold concerns over the future use of nanotechnology for military purposes, especially in the wrong hands. We have already seen chemical terrorism in the 21st century with anthrax attacks in the USA however similar attacks using nanotechnology could have much more destructive and widespread results.

Overall, each factor considered, in our opinion the benefits of nanotechnology well outweigh the drawbacks and so any research and funding should be further increased and encouraged. This, however, must be balanced with consideration for its future implementation in society; the public need to be exposed to the subject and legislation drawn up for administration and legal purposes. If this is done sufficiently and the science continues to flourish we may benefit for decades or even centuries to come.

CONCLUSION

As mentioned in the introduction, nanotechnology has already found many uses in today's medicine. This is achieved because of the huge diversity of molecules that can be made on such a small scale, giving it the ability to affect almost any part of the fundamental building blocks of human life - cells. From ultrasound radiating microchips helping to identify smaller cancers using minimally invasive techniques, to the ethically controversial grounds of gene therapy, nanotechnology has shown modern day medicine that it can be implemented into a diverse range of fields. However, a minority of issues surrounding the notion of nanotechnology remain problematic and unexplored in publications on this topic. For example, environment issues can be of concern; what happens to nanomaterials once they enter the environment, and what are the effects? The U.S. Environmental Protection Agency (EPA), is currently exploring these potential environmental concerns; "There are always possibilities for environmental or health harms", said Barbara Karn, EPA official (19). Additionally, some avenues of research into nanotechnology discussed involve the use of artificial machines or even cells into the human system, arguably negating the gap between man and machine, human and robot. Will this be acceptable in the eyes of society? And further, will man realise his limits ones he finally reaches them? All is to be discovered.

To conclude, this paper firmly believes that our current scientific understanding of nanotechnology is very much still in the early development stages; with each new discovery leading to a myriad of new and previously unthought-of possibilities. Although surrounded by a host of ethical and scientific dilemmas, nanotechnology is still teeming with promise and potential, and hopefully one day, given the correct funds and the correct attention, we will be able to remedy any disease in the field of medicine via advanced application of nanotechnology.

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