How can Nanotechnology be used in the Detection and Diagnosis of Stage I Cancers?

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Abstract

Nanotechnology has become an increasingly popular method of diagnosing and treating cancers. Being difficult to detect in the early stages, nanotechnology has widened the window of hope for cancer patients by allowing for more efficient and effective treatment. In this paper we plan to discuss how nanotechnology can be used to detect and diagnose a cancer in stage I, why it's more suitable than current systems already in practice and the issues surrounding these new techniques.

Introduction

Nanotechnology is the development and engineering of devices so small that they are measured on a molecular scale. [Figure 1] The advantages of having these tiny devices can branch to many different sections of industry but have been cornered by many scientists for their possible use in treating diseases; this is due to their ability to travel anywhere in the body. Their size is 100-1000 x smaller than the cells in our body and can therefore be used in an incredibly diverse way. [1]

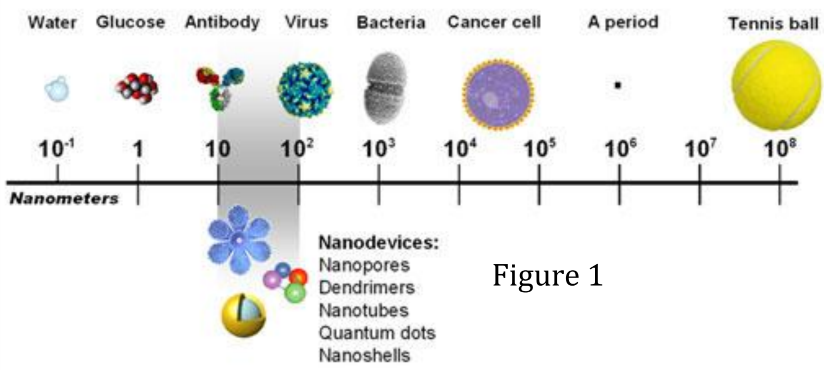

Figure 1

One of the diseases that this technology has great possibility to help is cancer. Cancer is described as 'a group of diseases characterized by uncontrolled growth and spread of abnormal cells.' [2] It is a viscous disease that has been predicted to rise to 11 million deaths in 2030. [3] The risk of dying from a secondary form of cancer - the metastases - is much higher than a primary and is responsible for around 90% of all cancer-related deaths. [4] It's not only the emotional and physical burden that worries many but also the financial cost; at the moment cancer care is costing the NHS around 5% of their overall budget, which, with cancer incidence rising at 1.5% per annum, will steadily increase also. [5]

Classification of cancers allows doctors to make a full prognosis of a patient's individual situation. There are several systems employed by medical physicians to assess fully the depth and breadth of the disease. One of the simpler systems is by staging them from I to IV, stage I being the earliest stage and stage IV being advanced. [6] By staging cancers the patient is given an idea of the progression of their cancer. Stage I cancers have the least progression in terms of size and spread of the tumour and are the hardest to detect both with physical symptoms and using current imaging techniques. But nanotechnology holds the key to detecting cancers in this very early stage when they are much easier to treat and to prevent them reoccurring.

As already identified, cancers are the production of an uncontrollable growth of cells; this is brought about by both genetic and environmental factors.

This is because the cancer is a growth of one's own body cells, brought on by the interaction between how one lives their life and one's genetic code. Usually the body would fight back with the immune system but cancer cells do not trigger an immune response. As the body does not do anything to control this growth, the cancer continues to invade the body's systems and override them. This is why it is so difficult to detect cancer at an early stage, as it is only just developing. When the immune system is triggered, the normal process would cause our body's response in the form of a physical symptom, if the illness hasn't already. As the immune system is not triggered and the 'intruder' does not give particularly noticeable symptoms then we do not know anything is wrong. This allows the cancer to develop further till symptoms are far more noticeable. Only then may the cancer have been recognised, by which point the cancer may have progressed past stage I and sometimes already into stages III and IV. [7]

This paper aims to discuss the new detection techniques that are able to detect cancer at a very early stage, before it has spread and begun to cause too much damage to the body. These advances in medicine will not only increase the survival rate but also decrease the financial funding needed to support the cost of cancer.

Current techniques include Magnetic Resonance Imaging (MRI), Position Emission Tomography (PET) scanning, Computer tomography (CT) scanning and ultrasound. These are used worldwide to detect the presence of any unidentified masses within the body, but they are not accurate and not very detailed. [Figure 2] Techniques for particular cancers have been effectively developed for their screening processes, these include, breast, cervix, colon and rectum cancers. [8] One of the effective screening processes is mammography for breast cancer. It is a low dose x-ray that uses radiation to create an image of the breast and any unusual masses within the breast. [9] This is where nanotechnology can offer a screening process for a far wider range of cancers that cannot be detected so early.

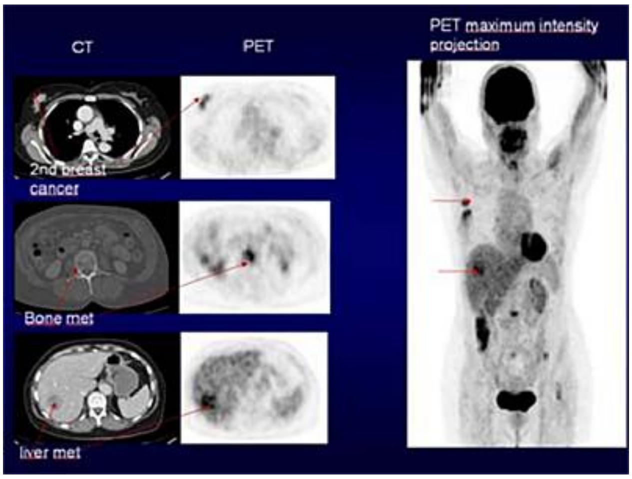

Figure 2
Comparing CT scans and PET scans of various tissues in the body. The images are barely distinguishable between tissue and tumour.

Discussion

There are several new advances incorporating nanotechnology in the field of cancer research. These can either be used in the detection or the diagnosis of early stages of cancer. These include nano barcoding, magnetomotive photoacoustic imaging, and the use of nanowires and nanocrystals.

An experimental imaging process has been found to detect effectively even the smallest cancer cells using nanomolecules and combining it with the usual screening methods in use already. Magnetomotive photoacoustic imaging is a new branch of cancer imaging which uses tiny molecules of iron oxide, coated in gold. These can be injected into the body where they can penetrate into soft tissue. The iron oxide core is magnetic and will react to an external magnetic field (see below); the gold absorbs the magnetic waves effectively and causes the magnetic core to vibrate as the energy is transferred. This vibrating causes heat energy to be produced and radiated out into the soft tissue. [10] An ultrasound can then externally pick up this heat as sound waves due to pressure variation, detecting the location of even the smallest tissues. [11]

Two different magnetic fields can be used to produce the excitation of the nanoparticles. In one instance, the wave can be continuous where the vibrations occur at a predetermined frequency and allow for filtration of other sources of tissue motion. The other variation is using a pulsed wave, this can be used over a shorter time span and also creates less heat within the body, and because of this it can produce images of tissues much deeper in the body with less harm to the patient. [12]

Figure 3

Coating tiny droplets of water in gold and then removing the water using freeze-drying methods is the current method for producing the nanomolecules. These 'droplets' of gold are then used to surround and coat the iron oxide core. [13] [Figure 3]

The possibilities are seemingly endless when you combine this technique with the idea of adding functional and biomechanical properties to the particles, enabling a way for them to bind onto specific cell surface proteins found on cancer cells. This can be done by adapting the nanomolecules to have multifunctionalites attached to their outside; markers allow the molecules to travel to specific sites, such as cancer cells. These markers are made of proteins and can be in the form of monoclonal antibodies. These antibodies have a binding site used normally by the immune system to destroy any invading microorganisms, but in this case adapted to attach to proteins on cancer cells such as high affinity folate receptors or luteinizing hormone releasing hormone. [14] As researchers and scientists uncover other molecules in the form of cell surface proteins and DNA or gene sequences, nanoparticles that target the specific tumor and supporting endothelial cells of the cancer will become the method of choice for finding cancer.

Another new detection system is being used more specifically in the detection of cancer that may recur. This is called nano barcoding. Nano barcoding is the use of nanometer-sized disks, made from gold and nickel, which can hold specific information. Like a barcode, the nanodisks can form patterns which can be associated with a unique response to a stimulus, such as electromagnetic radiation. The stimulus to which the disk responds depends on what type of molecule you 'decorate' the disks with. An example of the 'decoration' of the nanodisks is a dye that emits a unique light spectrum when illuminated with a laser beam. This means that these disks could be used as biological labels in DNA detection and even the detection of cancer cell markers; these are known as chromophores. [15]

In current studies undertaken by Chad Mirkin and his research team, nano disk arrays as long as 12 micrometers have been successfully achieved, on which 10 pairs of disks can be incorporated. These 10 disk pairs alone can produce a massive 287-nanodisk codes. His work has focused on the reoccurrence of prostate cancer; already he has been able to prove with now around 450 patients, that everybody has a baseline level of Prostate-Specific Antigen (PSA) post-prostatectomy. And you have two groups of people: those that will never be detectable with conventional tools—these are effectively cured—and then we have those that might have PSA levels that gradually rise with time, in those people, cancer is going to recur.

The possibility that these chromophores hold for early cancer detection is brilliant. It gives the doctors a conclusive ability to say whether or not your cancer will recur. If the answer is no, then all the better for the patient; if it's a yes, then they can be directed on to a programme where the cancer can have the most effective treatment that will result in a better outcome than it might previously have done with conventional methods. [16]

Detection of the abnormal cell growth is only half the process. The follow up diagnosis for many is more important as it gives the patient a better understanding, where they feel more in control of their disease. A diagnosis will include whether or not the cell mass is malignant or benign and what variety of cancer it is and therefore being able to move onto a prognosis and a more productive treatment plan.

One such diagnostic tool is the use of Quantum dots. Quantum dots are nanocrystals of a semiconductor material that act as "molecular light sources", light sources that can be coupled with an antibody or DNA functional group. They can then seek out cancer markers and act as visual beacons that light up when a bond with the DNA sequence that they are seeking out is made.

So far this hasn't been taken much further than the laboratory where samples are taken from the patient and then analysed *ex situ*. The light source can appear as different colours depending on the size of the crystal. Because of the multitude of colours they can emit, they can be used to detect a number of different markers. In one example, researchers were able to detect and simultaneously measure levels of breast cancer marker Her-2-actin, micro fibril proteins and nuclear antigens. [17]

How can we expand on these advances?

By increasing the sensitivity of the nano particles, crystals and barcodes it allows scientists to progress to catch cancer earlier, with more precision and speed. Some developments go as far as to interact with the DNA of cancer cells so diagnosis can be taken a step further, knowing exactly what cancer it is and building up a database so our knowledge of one of the least understood diseases can increase.

This development uses cantilevers, nanoscale, flexible beams, resembling a row of diving boards. They are coated in molecules which have the ability to bind with specific substrates. These cantilevers can detect a single molecule of DNA or protein. The antibodies covering the cantilever fingers selectively bind to the proteins that are secreted by the cancerous cells and these bindings change the physical properties of the cantilevers. These changes can express to a researcher not only the presence of a molecule's DNA but also the concentration of said molecule. Overall, nanoscale cantilevers are a sensitive construction for the rapid detection of cancer molecules. [18]

Very similarly nanowires are very selective and specific by nature. The nanowires are laid across a microfluidic channel. The molecular make-up is detected by the nanowires when particles flow through the channel. The information that is collected is then directed through electrodes. Nanowires can detect the presence of mutated genes which are associated with cancer and so may enable researchers to locate the exact site of the mutation. By finding the source of mutation we can understand how that mutation occurred in the first place. [19]

The Ethics of Nanotechnology Research

Like any other medical advancement, nanotechnology detection systems have to be trialled before they can be used on humans. To be able to conclude definitively that these processes work effectively, more so than current processes, is one such reason for testing. The only way to do this, however, is to test them on animals before being trialled on humans. Animals used for testing, such as mice, have been found to contain a very similar nervous system to human beings and therefore it has been concluded that they must also feel pain like we do. This proves a strong argument that animal testing inflicts pain unnecessarily on another creature. This can be strengthened through religious reasoning; animals are to be cared for by humans, not taken advantage of. As humans have the ability to make moral decisions a growing consensus seems to be that animals should not be harmed for any reason. [20]

On the other hand scientists must decide whether the benefits of testing on animals outweigh the risks of causing pain and sometimes even death. To take a new idea and test it on humans straight away would obviously hold many more moral and ethical issues. Humans have free thought, speech and have the freedom of life. Without knowing the potential risks of a new development, how can researchers potentially know the benefits? Without testing on animals many of the everyday products we use would not be in use today, let alone products used in medicine. We would never have any sense of progression; pushing the boundaries of science to ultimately create new theories.

For this particular development, the researchers cannot say how harmful the use of nanotechnology may be on humans. Nanoparticles are such a completely different advance in medicine, much of it cannot be related to other systems similar in use, as there aren't any. Therefore testing must be done on animals; it is the only way that nanotechnology in medicine can be pushed to the limit so it can finally become commercial.

Health and Environmental risks

Nanotoxicology refers to 'the study of the interactions of nanostructures with biological systems.' Toxicological tests will allow scientists to build up a database producing a general groundwork for the basis of risk assessment. Instruments have been specifically designed to allow scientists to assess the risks involved with the production and use of nanotechnology. In particular these instruments are used for detailing the composition, size and surface area of nanomolecules and making sure that the benefits really do outweigh the risks.

Research is being done into the effect that the particles bonded onto the surface of nanoparticles have on the tissues they infiltrate. [21] The processes themselves are minimally invasive; the particles are all naked to the human eye, less of them are needed for a greater effect and it is only the imaging itself that could potentially cause any harm. At the present time the benefits achieved by using ultrasound and other similar scanning processes are greater than the risks. Of course the patient will always know the risks they are taking, because of the preliminary consultation.

Environmental impact should also be considered. The discussed detection and diagnostic tools take less energy to produce than conventional detection and diagnostic tools. Their incredibly small size reduces the amount of energy and materials required to accomplish a desired task. Nanotechnologies are already adapted for society's need for cheaper and quicker manufacture giving them a much smaller carbon footprint then you would expect.

The Cost of Nanotechnology Research

One of the most desirable aspects of nanotechnology for medicine is the reduced cost involved in its sector. In most processes we have discussed only small concentrations of the particles are needed and their make-up isn't too complicated. Their ability to interact with current techniques already in place reduces the cost of having to produce new machines to read signals and produce images of the tumours. And now, because the field of nanotechnology is so broad, more jobs are available for researchers. If the cost of their manufacture decreases then more people can be employed, increasing the speed of getting the technology being trialled into hospitals.

Conclusion

There are many reasons why nanotechnology has been chosen for the next step into biological research. Nanotechnology possesses several attributes that make it perfect for such engineering. Firstly the nano devices are good signal amplifiers, making it possible to place a small molecule deep in the body and still pick up a signal effective enough to produce quality imaging. No other screening process so far has worked well enough to achieve this. What makes this more special is that it means only a few of these molecules are needed for an incredibly rich signal. Secondly they have a large surface area for what they are, this allows many markers onto just one molecule so the possibilities are increased dramatically. To have just one molecule with several properties reduces the cost of having to produce one molecule per function. Another property of nanotechnology is that it can be used with other conventional methods, allowing for the practitioners involved in using the technology not to have to learn a great deal more before conducting the imaging. Lastly, and one of nanotechnology's more important attributes, it is a versatile sector that can be applied through many other areas of industry, such as biochemistry, because its properties are transferrable. Just within the research of one disease it can be used in detection, diagnostics, treatment and prevention. If the power of nanotechnology can be utilised further, it is believed nanotechnology will become a part of our everyday lives.

It is ground breaking technology like this that could change our whole perspective on cancer. The few new advances in nanotechnology we mentioned can branch out further into cancer treatment and even prevention of cancer. This research isn't limited to cancer, but many other diseases that require in depth screening processes and diagnostic tools. This is just the beginning of a new revolution into molecular level engineering which holds the possibility of changing medicine rapidly in the next decade.

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Figure 2
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Figure 3
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Figure 4
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