Quantum Dots: A Potential Screening and Diagnostic Method for Pancreatic Cancers

By
Minhal Zar

PASS

RESEARCH PAPER
BASED ON
PATHOLOGY LECTURES
AT MEDLINK 2010

ABSTRACT

Pancreatic cancer is extremely difficult to diagnose as sufferers only develop symptoms after having the cancer for months. By then any tumours formed would most likely have metastasised and treatment would not be very effective. Current scanning methods for early stage pancreatic cancers are not very effective as sharp images of cancerous cells or tumours cannot be obtained. However in the development of nanotechnology, semiconductor nanocrystals known as quantum dots have been found to fluoresce brightly when excited by photons or ultraviolet light. By binding them to various antibodies, the exact position and size of tumours can be found within the body. This dissertation will explore the advantages and disadvantages of quantum dots as a means of scanning for pancreatic cancers and further developments that could be made into this field.

INTRODUCTION

The development of nanotechnology mainly occurred during the 20th century, with its original definition by Professor Nerio Taniguchi of Tokyo Science University in 1974[1] still standing:

"'Nano-technology' mainly consists of the processing of separation, consolidation and deformation of materials by one atom or one molecule."

Eric Drexler further developed the idea of nanotechnology in his book 'Engines of Creation: The Coming Era of Nanotechnology' published in 1986 by discussing the idea of molecular manufacturing and how it would be possible if specific groups were placed together with atomic precision, which could then lead to nano-machines. He is considered as one of the first people to have specifically described engineering in nanoscale, where one nanometre is equivalent to one billionth of a metre, as opposed to Taniguchi's general term.[2] Although his theoretical ideas were ground-breaking, they could not be tested then, however upon the discovery of buckminsterfullerene in the 1990s by Smalley et al., it became apparent that it is possible to manipulate matter by individual atoms.

As medicine has developed, the understanding of the importance of individual cells and how they are affected by molecules in nanoscale has increased. By controlling these substances that are used in cell signalling, it is possible to prevent damage to the cells and help heal them. This would help find, prevent and cure diseases which would otherwise be extremely difficult to treat.

Cancer can be extremely difficult to locate, particularly pancreatic cancers as symptoms do not show until the cancer has been present for several months. By this time a tumour may have developed and even metastasised, which lowers the chance of the patient surviving.[3] However by using nanotechnology it can be possible to locate specific cancerous cells that would not be seen using current methods, which would then aid in the treating of the cancer. Engineering and manipulating individual atoms and molecules to create nanomachines allows the opportunity for specific dangerous cells to be found and destroyed.

DISCUSSION

Cancer is a huge obstacle in modern medicine, with increasing numbers of patients and limited diagnostic and preventative methods. It is not easy to diagnose as the patient's own body cannot recognise the cancerous cells as dangerous, allowing a tumour to form which can be benign or malignant. Diagnosing the cancer early makes it easier to cure and improve the outcomes for the patient; however this is extremely difficult especially for pancreatic cancers.

Although it is not one of the more common cancers, approximately 7800 people are diagnosed with it each year within the United Kingdom and it is the fifth most common cause of cancer deaths.[4] Cancer Research UK states that 270 000 plus cases of pancreatic cancer were diagnosed in 2008, with around 266 000 people dying from it in the same year.[5]

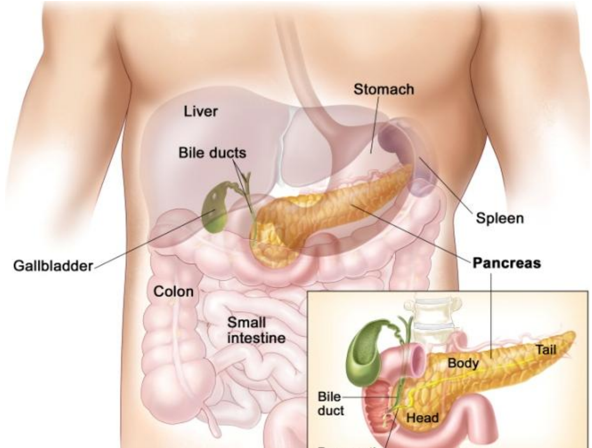

Figure 1

The pancreas is essential for the production of enzymes and hormones in the body, but due to its location behind the stomach deep within the abdomen as shown in Figure 1, it is difficult to access. Pancreatic cancers are more likely to develop in people over 50 years of age, however they do not often cause its sufferers any symptoms or pain until it has grown for months or even years - at this advanced stage it is usually too difficult to treat. The screening methods for pancreatic cancers include various techniques from CT scans, MRI scans and angiograms (using fluoroscopy to obtain an X-ray image of the blood vessels) to needle biopsies (passing a long needle through the skin into the pancreas to take a tissue sample). However, these are normally ordered when the cancer has already developed into its advanced stage. [3]

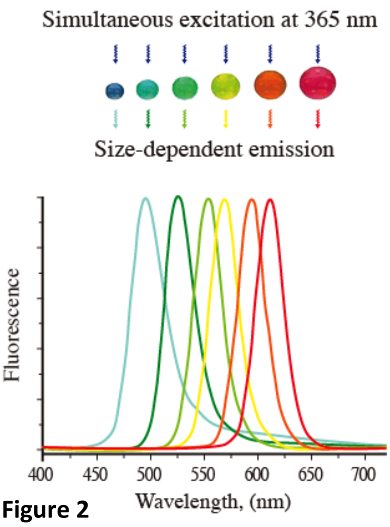

Figure 2

Development into nanotechnology has made it possible to create molecular machines or 'nanobots' which can be injected or ingested into the body to perform a certain function. The production of quantum dots has provided the potential to transform diagnostic techniques. Quantum dots are fluorescent nanocrystals which can be utilised to help aid the diagnosis of pancreatic cancer. According to their size, they emit a different colour light far brighter than organic dyes when UV is shone on them (see figure 5), even though they all are excited by the same wavelength as Figure 2 displays.[7]

Shuming Nie, Director for Nanotechnology and Bioengineering at the Winship Cancer Institute, has been working on encapsulating quantum dots with protective polymer coatings to allow them to enter the body without causing damage. By attaching these quantum dots to antibodies which detect certain antigens on cancer cells, they can be used as biomarkers to show the doctors where the exact location and nature of the cancer cells. Nie's polymer coating (shown in figure 3) improves the solubility of quantum dots in water which not only protects the dots from the environment, but also provides functional groups for bonding with the probe molecules. [7]

By combining different coloured quantum dots with different antibodies, it is possible to find out precisely what kind of cell is present in biopsies, which can be extremely useful for diagnosing specific cancers. The combination of the different colours in varying amounts on the cell surface would inform the doctor with the exact nature of the cell and even which specific cancer it is. By using this idea of "multiplexing", the doctors would only have to look at an image of the biopsies and process the different colours present to find out which cancer it is, how advanced it is and what treatment is needed.

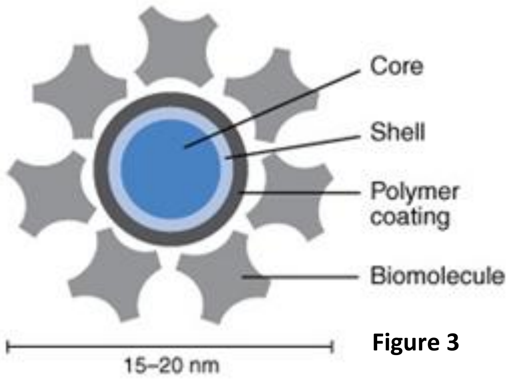

Figure 3

The use of quantum dots provides better imaging than organic dyes due to their bright optical characteristics (see figure 5) and as they would be specific, the images would be more precise and accurate. In the long term quantum dots would also be cheaper to use as they would not be broken down due to their inert polymer shells, so they would not continuously need to be added.[8]

Although quantum dots have only been applied in biopsies so far, research has involved the injecting of quantum dots into live mice which have then tracked down tumours, shown by Figure 4. These dots were able to be seen with a simple mercury lamp, so dangerous UV radiation wasn't needed. After more research into any hazards into the use of quantum dots inside live organisms, it can be possible to diagnose cancer without a biopsy being needed.

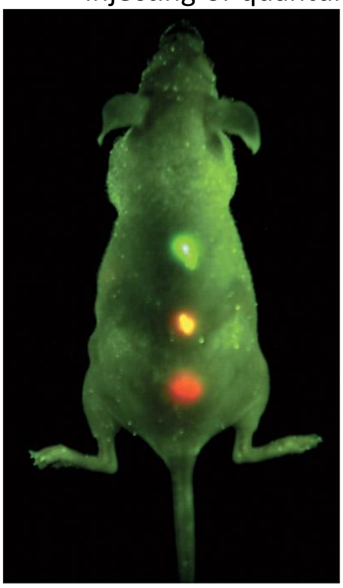
Figure 4

Due to the present difficulty in screening and diagnosing pancreatic cancers, I believe that quantum dots can be further developed to be applied in vivo. This would help aid in diagnosing pancreatic cancer and perhaps even be used for early screening processes. At the moment biopsies are often taken of the pancreas when testing for cancers however it is very difficult to conduct many tests on a limited sample - the multiplexing quality of quantum dots removes this obstacle.

However there are a few issues surrounding the use of quantum dots in vivo, particularly considering the long term effects that they may have inside the body. Due to their inert coating quantum dots cannot be broken down by the body and instead may build up within blood vessels or in the liver. There are also some concerns as to whether the continuous fluorescence of the quantum dots may cause mutations or denaturing of cells and that they may otherwise disrupt normal cell function.

Alternatively, by remaining in circulation within the body quantum dots can be used in regular screening to check for the development or the status of any cancerous cells present. Quantum dots may even be developed so that they repel each other slightly, reducing the risk of their accumulation. There may also be further discrepancies of its effect in the body, so further research is required into their application and usage.

CONCLUSION

Pancreatic cancer remains a leading cause of death worldwide. The outcome depends on the stage at which it is diagnosed. The best chance of survival is in patients where it is detected at a very early stage when it has not yet spread to other organs and also has not grown large enough to involve local vessels and lymph nodes. The new generation of CT scans, MRI and PET scans has improved the diagnostic accuracy but remain far from ideal. Many patients either present too late or even if are considered operable on current scanning techniques, at the time of surgery are found to be inoperable.

In order to improve the survival in patients with pancreatic cancer, we need to develop techniques which can detect the cancer at a very early stage in the at-risk population and have the ability to clearly define the extent of the cancer. It is hoped that difficulties in screening and diagnosing pancreatic cancers can be overcome in future with the use of quantum dots. Their unique optical properties and their ability to be combined with biomolecules such as antibodies means that they can provide exact details of cancer cells.

Figure 5

As the likelihood of developing cancer of the pancreas increases for those over 50 years and those with family history of cancer, it may be possible to use an in vivo dose of quantum dots associated with specific ‘ pancreatic cancer-seeking’ antibodies, early stage pancreatic cancers can be found and dealt with instead of only finding them at a late stage. The quantum dots can then remain in the body and be used to regularly monitor the status of the cancer and to identify recurrence after treatment.

With further research, quantum dots can be developed to deliver therapeutic drugs such as in chemotherapy to target and destroy the cancer cells. Such a targeted therapy can ensure that only the cancerous cells are destroyed without damage to normal tissue. It can also seek out micro-metastases and potentially reduce the risk of recurrence at a future date.

The quantum dot technology promises to open new avenues in the management of pancreatic as well as other cancers. However, much more research is needed before the technique will become available for clinical application. The possibility of adverse events from any residual nanoparticles left in-situ side at the end of treatment will need to be considered. Perhaps in future we may be able to develop a technique through which the quantum dots can be extracted from the body once they have delivered the desired clinical effect as we learn to control and manipulate these nanoparticles.

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Figure 2 (page 3)
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Figure 3 (age 4)
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Figure 4 (page 4)
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Figure 5 (page 5)
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