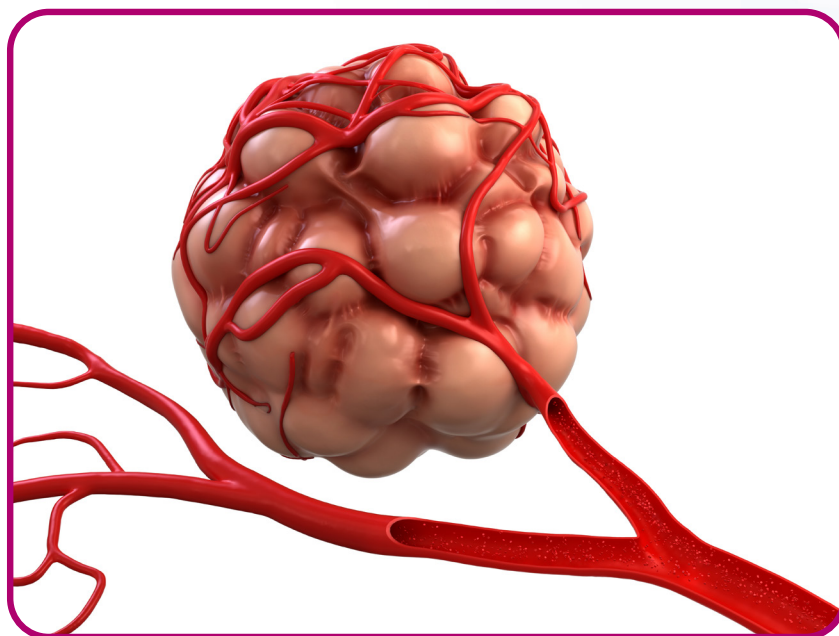


Fighting Cancer with Maths



Cancer is the second biggest killer after heart disease, causing almost 30% of all deaths in the UK. Unfortunately, cancer is an extremely complicated disease which can be difficult to both diagnose and treat. Mathematicians at the University of St Andrews have developed important new models of how cancer spreads, thereby enabling clinicians to have a better understanding of how to provide more effective treatment for patients.

Angiogenesis Research

When a solid tumour reaches around 2mm in diameter it starts to form its own structure of blood vessels, in a process called angiogenesis. This system of blood vessels allows the cancer to develop its own supply of blood, providing it with additional nutrients (such as oxygen) thereby enabling it to keep on growing, and it also allows cancerous cells to escape into the patient's blood stream. This can lead to secondary tumours forming in different parts of the human body, making it very difficult for the patient to be treated.

The structure of blood vessels which forms around a tumour is made up of microcapillaries which are so small that they can't be seen using conventional scanning techniques. The lack of imaging techniques is a difficult problem for doctors, as they want to deliver chemotherapy drugs to the tumour via the system of blood vessels. Sometimes the blood vessels are poorly formed and are leaky, meaning that the chemotherapy drugs don't work effectively, because they "get stuck" in the blood vessel network or diffuse out into the tissue and therefore don't reach the site of the cancer.

"Mathematicians at the University of St Andrews have developed important new models of how cancer spreads"

Doctors need a better image of the structure of the blood vessels attached to a tumour, to be able to optimise the dose of chemotherapy drug and target the tumour more effectively.

The mathematicians at St Andrews have worked on developing a model of how the network of blood vessels grows towards the tumour. Modelling how a cancer grows is extremely difficult – its growth is controlled by multiple factors, and it is very difficult to predict. Modelling cancer has often been compared in complexity to modelling the weather – there are so many controlling factors that the system becomes what is known as non-linear, meaning that it is inherently unpredictable over long times scales. Recent improvements in computing power have however meant that increasingly

complicated mathematical models can be used, opening up many new possibilities for modelling cancer.

The system of blood vessels which supply a tumour is in many ways like a system of pipes. For a long time there has been a lot of mathematics which can effectively describe how fluids flow through pipes. Microcapillaries are in fact much more complicated – they are so small that the flow of blood cells causes stress on the walls of the blood vessels – leading to the formation of new vessels. This complicated feedback situation, where the flow of blood itself creates new vessels has been incorporated into the mathematical models. These models are now helping cancer researchers to understand how cancerous tumours form a network structure of supporting blood vessels and it is hoped that in the future that this will lead to significant advances in how cancer is treated using chemotherapy.



**Institute of
mathematics**
& its applications

Solid tissue modelling

Another line of research is focusing on how a solid tumour grows and changes shape. As a cancer becomes more aggressive, some of the cancer cells stop adhering to the main tumour and start to behave independently. When a patient is scanned before a round of radiotherapy or surgery, the scanning process will be unable to detect these tiny breakaway cancer cells. This means that the breakaway cancer cells can later grow and develop into new, independent tumours, causing the treatment to fail. This is where the mathematical models can help – they are able to predict where a cancer is likely to spread to, enabling more of these individual cancer cells to be killed using radiotherapy in addition to the surgical removal of the main tumour.

Gene Regulatory Networks

The researchers have also investigated the underlying causes of cancer, modelling the processes which happen within a cell itself. Most cancers start at a genetic level – genes inside a cell make proteins which tell a cell to die or multiply. When this process goes wrong, it can be the start of cancer. The mathematicians have developed new mathematical models which model how the concentrations of these important controlling proteins oscillate within a cell. They have focused on modelling what happens within a healthy cell. Cancer scientists can then use this information to help understand what happens when the process goes wrong and cells start to form cancerous tumours.

Future Developments

The research at St Andrews focuses on a type of cancer called carcinoma. Around 90% of cancers fall into this category, meaning that this research is extremely useful and wide-ranging. Currently the mathematical models describe a generic solid tumour, but in the future the

researchers hope to hone their models to apply to specific cancers such as breast, lung or colon cancer. The mathematical models which have been developed are extremely adaptable enabling them to be used in many different areas of cancer research.



TECHNICAL SUPPLEMENT

In order to model the growth of a solid tumour the researchers used what are known as Partial Differential Equations. These equations describe how the density of cancer cells changes over time, which is very useful in describing how the main body of a tumour might grow. However, when it comes to cancer cells, even one or two cancerous cells could lead to the spread of the tumour. Therefore it is important for researchers to keep track of individual cancer cells, which is difficult to do when you are only talking about tracking overall concentrations of cancer cells.

This is why the mathematicians have used a process, called discretisation, which means that they solve the Partial Differential Equations on a

2D spatial grid, enabling them to find out how many cancer cells lie at each point within the grid. They are then in a position where they can start to track the behaviour of each individual cancer cell and the endothelial cells of the blood vessels.

Each cell will move with a certain probability up down, left or right through the grid. The movement of individual cells can then be modelled over time within the grid. In order to determine how likely a cell is to move in a certain direction, the researchers look at the concentrations of what are known as Tumour Angiogenesis Factors (TAF), which are chemicals which stimulate the growth of cancerous cells, and matrix degrading enzymes (MDE) which

degrade the surrounding tissue and facilitate invasion.

The model studies the movement of cancer cells on a 2D grid. However this is a good approximation for how cancers spread through layers of tissue. The Researchers have also extended their model to work in a 3D environment.

Expert

Professor Mark Chaplain,
University of St Andrews

Links & References

<http://www.cancerresearchuk.org/health-professional/cancer-statistics/mortality>

The IMA would like to thank Professor Mark Chaplain, for his help in the preparation of this document.