The Future of Radiation Oncology

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Researchers have long recognised that although termed the same way, each individual cancer is distinct and unique. For oncologists, the quest to personalise treatments is more important than ever.

In the ideal future state of radiation therapy treatment, a newly diagnosed cancer patient would first undergo a tumour radiosensitivity assay to estimate the tumour's response to radiation. Based on the patient's intrinsic tumour radiosensitivity, the calculated dose required to achieve an optimal cure will be prescribed. After that, the radiation oncologist should have easy access to the wide array of radiotherapy treatment technologies available.

Ideally, selecting the right radiation particle and technology could be as simple as selecting the X-ray energy used for conventional radiation therapy. So what treatment options would future patients have? In this feature, we look at the various tools oncologists are beginning to utilise in the ongoing war against cancer.

Radiotherapy – a weapon with proven success

The curability of a patient can be attributed to various treatments. Of cancer patients who experience full remission, curability can be attributed to: surgery (49%), radiotherapy (40%) and chemotherapy (11%). Despite its therapeutic importance, it represents only 5-10% of all cancer-related health expenditure in the U.S. and is under-represented in clinical trials. But things may be changing.

Radiotherapy delivers high-energy ionising radiation (such as photons or protons) which causes double-stranded DNA breaks that lead to the destruction of cancer cells. Knowing the sensitivity of the patient's cancer cells will help the radiation oncologist customise the dose and intensity of radiation to deliver to the tumour. Imaging these cells accurately allows for more focused targeting.

Focused targeting is achieved by technological advancement in beam shaping and, more recently, the use of heavy-particle therapy. Together, these advances are pushing the envelope of cancer treatment, giving rise to new possibilities that may transform the oncology landscape.

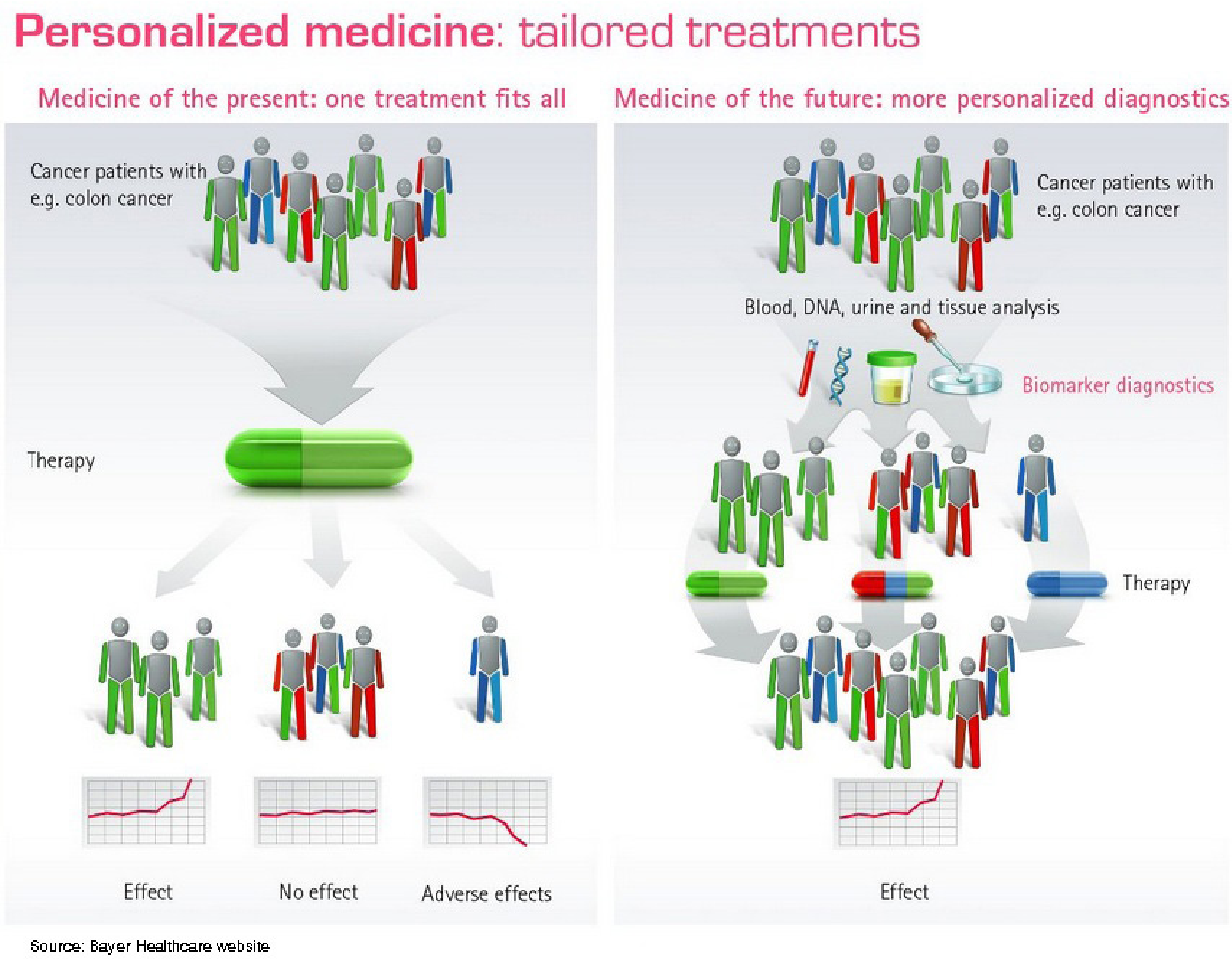
Radiogenomics – giving physicians a map on the battlefield

Radiogenomics is the study of genetic variation associated with response to radiation therapy. This is a step forward in delivering Precision Medicine, which tailors treatments to a patient's individual genetic makeup. In current clinical settings, patients are offered uniform radiation therapy doses without due consideration given to factors such as genetic variations of the patient's cancer and how they affect the tumour's response to radiation. This ultimately impacts treatment outcomes and side effects.

A recent study conducted at Moffitt Cancer Centre derived a genomic-adjusted radiation dose (GARD) value using gene-expression-based radiation-sensitivity index and the linear quadratic model. (Source: Lancet Oncology, 2016)

The GARD value was then used to predict the therapeutic effect of radiotherapy on specific tumour types. The findings suggest that radiotherapy doses should be adjusted according to individual patients' and their tumours' intrinsic radiosensitivity in order to maximise efficacy and minimise toxicity.

Being able to tailor a radiation dose to the individual would



(Source: http://pharma.bayer.com/en/innovation-partnering/research-focus/oncology/personalized-medicine/)

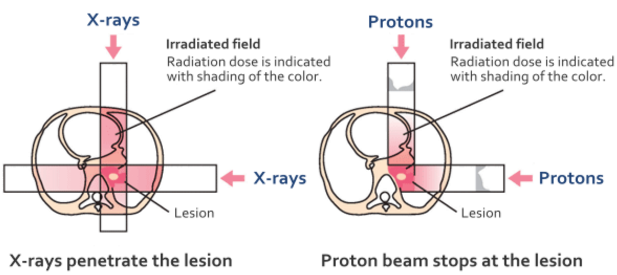
be a game-changer with regards to achieving maximum cure and minimal toxicity, as patients now receive standard radiation doses that were empirically determined decades ago.

Heavy-Particle Therapy – a variety of weapon systems, each with unique advantages

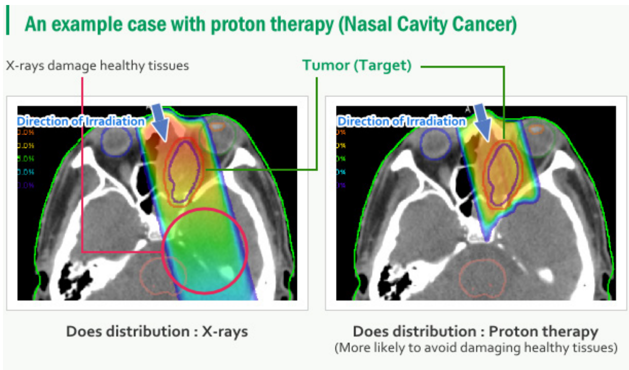
Beams other than X-rays have been considered for use in cancer treatment because of their unique properties, which can potentially enhance patient outcomes. However, expensive infrastructure is needed to generate heavier particles. This increases the final cost of treatment, raising issues of cost-effectiveness . Some newer particles have shown great promise, and are awaiting introduction into mainstream treatments. As developmental costs for these expensive technologies are reduced over time, one can anticipate a time when radiation oncologists mix and match beams of various properties to individualise the best treatment beam for each patient.

Proton Beam Therapy – a sharper, more focused beam

Proton Beam Therapy (PBT) is touted as the most advanced form of targeted radiation therapy available for treatment today. Proton beams enter and travel through tissue with minimal dose deposition until the end of their paths, where a peak of energy deposition called the Bragg peak occurs. Beyond that, the dose falls practically to zero. This distinct property, unlike X-rays which release energy throughout their path, allows most of its energy to be deposited into the tumour, and leads to around 60% reduction in stray radiation doses to the neighbouring organs.



Comparison of radiation dose between X-rays and Protons delivered to the same lesion. (Source: http://w3.ai-hosp.or.jp/_en/ptc/what_ptc.html)



(Source: http://w3.ai-hosp.or.jp/_en/ptc/what_ptc.html)

This advanced therapy is particularly useful for paediatric and brain cancer patients, where stray radiation outside the tumour must be kept to the minimum. Like conventional radiotherapy, PBT is also delivered on an outpatient basis, which is more convenient for patients as the time spent in the hospital is reduced. However, because of the high cost of construction, PBT is not readily accessible to most patients.

PBT can be arranged across borders thanks to telemedical technology. One such example can be seen through Singapore-based Asian American Radiation Oncology's collaboration with Japan-based Aizawa Hospital. Through this initiative, patients can have seamless access to PBT treatment based on international protocols and techniques in Japan, generating cost savings for the patient.

Carbon-Ion-based treatment – a more powerful beam

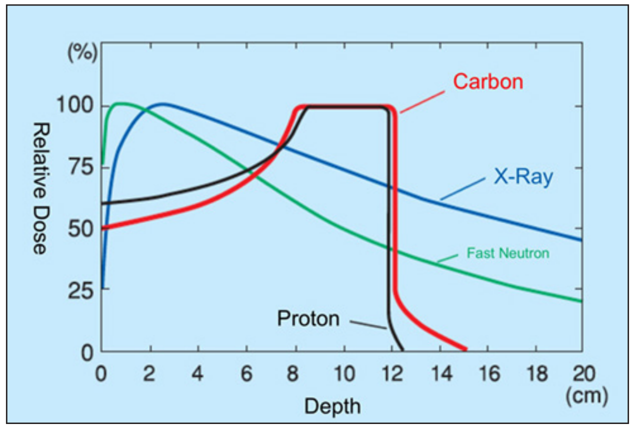
Carbon-ions are heavier particles than X-ray photons or protons. This allows carbon-ions to deliver a higher dose of radiation with a sharp energy deposition precisely within the tumour.

Carbon-ions are also associated with an enhanced radiobiological effect, meaning that they kill cancer cells in a tumour more effectively than a similar dose of conventional X-rays. This is especially beneficial for deep-seated hypoxic and radioresistant tumours that are often untreatable, and can potentially achieve the same therapeutic effect in fewer fractions. In recent years, researchers have gained increasing clinical experience and understanding of this powerful beam (Ebner and Kamada, 2016).

Boron Neutron Capture Therapy – a beam that selectively detonates tumour cells

Boron Neutron Capture Therapy is a complex binary therapy that involves low-dose exposure to thermal or epithermal neutrons, which by themselves are relatively harmless to the body. To eliminate cancer cells, neutron beams are selectively captured by boron-labelled bio-molecules (these are inert and harmless) which are administered separately to the patient and taken up by rapidly growing tumour cells. When a boron atom absorbs a neutron, a nuclear fission reaction creates a high-energy alpha particle and a lithium ion, which have ranges of around 10 micro meters – around the diameter of a single cell – thus detonating extremely targeted radiation at the cellular level and sparing non-tumour cells.

Thanks to developments in cancer genomics and radiation



Properties of different particles showing their energy deposition within the patient. (Source: http://journal.frontiersin.org/article/10.3389/fonc.2016.00140/full)

technologies, we are now entering an era of personalised radiation oncology. Every day, we are a step closer to our promise of delivering patients the right treatments with the right dose, at the right time and with the right beam.

About the Author

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Dr Daniel Tan is Consultant Radiation Oncologist and Medical Director at Asian American Radiation Oncology (AARO), Gleneagles Hospital Singapore. He has trained under leading experts in the field both locally and in North America, specialising in the application of stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) in the treatment of brain metastases and oligo-metastasis. Dr Tan was instrumental in the development of the Novalis Brain Radiosurgery programme while he was at NCCS and started the Novalis Spine SRS programme upon his return from HMDP.

From 2012-2015, he was national project coordinator for the International Atomic Energy Agency's (IAEA) RCA project 6065 on 'Strengthening the application of SBRT to improve cancer treatment'. This project involved efforts to train and develop SBRT in countries within the Asia-Pacific Region. He was Course Director for the first regional training course in SBRT in 2012 and in 2014 he was invited to IAEA in Vienna as an expert consultant for preparation of phase 2 of this regional project.