21st Century Cancer Warfare:

A Glimpse into the Operations of a Modern Radiotherapy Unit

Harnessing technology to save lives

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Introduction

Modern warfare has become highly complex over the past century, driven by advancements in strategies and technology as well as nations' incessant drive to stay ahead of the game.

In a similar fashion, the war against cancer has reached new heights in the 21st century. However, unlike the zero-sum game in human conflict, the cumulative pool of scientific discovery coupled with technological development has resulted in greater cures and improved the quality of life for cancer patients.

Still, these are small victories and the outcomes are only the beginning of what could potentially be better things to come for cancer patients. One of our goals in the medical community is to see the effects of cancer whittled down to such an extent that they are comparable to those associated with less threatening ailments such as hypertension - significantly more manageable despite a certain degree of inconvenience. With a growing armamentarium of treatment options and methods, cancer treatments are increasingly individualized, minimally invasive and much less disruptive to lifestyles.

Radiotherapy

Like the three services of defense forces (Land, Air and Sea), cancer therapy requires a combination of approaches – in this case, surgery, radiotherapy and chemotherapy – to be effective [Figure 1].

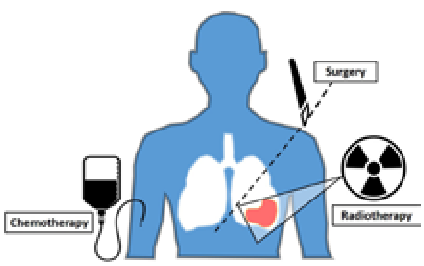

Figure 1: A combination of surgery, radiotherapy and chemotherapy in use for effective cancer therapy

As in warfare, where the enemy's stronghold has to be neutralized and the remaining insurgents flushed out, the primary tumor has to be destroyed, and the remaining and runaway cells sterilized and mopped up to ensure complete victory and prevent a 'resurgence' (recurrence).

Surgery physically cuts off the visible tumor, while radiotherapy and chemotherapy act at the cellular level to eradicate microscopic tumor that cannot be seen or felt. Both exert their effects by targeting the DNA of the cells.

In the case of radiation therapy, high-energy X-ray beams are produced by a machine and directed towards the area suspected of harboring renegade cells. These high energy X-rays contain particles of energy called photons, which strike the DNA of the cancer cell directly to cause double-stranded breaks or, indirectly through an oxidation process, and renders the cell incapable of further reproduction, thus killing it[1] [Figure 2].

It is in fact a 'physical' therapy, which is non-invasive and yet able to eradicate internal tumor by directing the beam toward it.

The Evolution of Radiotherapy

X-rays were first discovered in 1895 and soon after recognized to have therapeutic properties, although their mechanism was not well understood[2]. Initial treatments made use of radioactive sources and low energy X-ray machines that were unable to penetrate beyond superficial tumors.

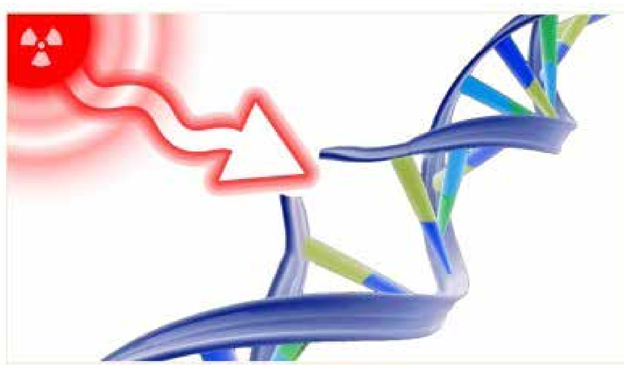

Figure 2: Double-stranded breaks in cellular DNA caused by photons

The development of cobalt machines and medical linear accelerators after World War II enabled the production of higher energy X-rays to target deeper tumors. Up to the early 80s, radiation therapy was delivered by directly irradiating the surface of the body overlying the tumor using coarsely shaped fields, which were significantly larger than the tumor itself[3].

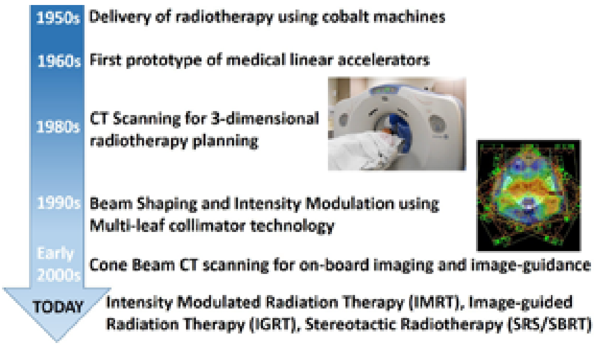

Figure 3: A brief timeline on the evolution of radiotherapy

Due to the limitation of imaging and beam shaping ability, significant excess tissue had to be irradiated to avoid missing the target. Using military analogy, the lack of sophisticated reconnaissance and targeting capabilities meant that carpet-bombing was necessary to destroy the enemy. This resulted in significant collateral damage, which contributed to the negative impressions that many people have about radiation therapy, especially in relation to radiation burns and mucosa ulcerations [Figure 4].

A few key developments took placed which changed the entire scene of radiotherapy within a span of 20 years.

First, CT scanning technology was incorporated into the radiotherapy planning process in the 1980s. This ushered in the three-dimensional conformal radiotherapy era. The tumor could now be mapped and radiation doses calculated more accurately than before[4].

Figure 4: Radiation burns sustained during carpet bombing of the olden era from cobalt treatment machines

Next, radiation beam delivery became more conformal with the advancement of multi-leaf collimator technology on modern linear accelerators in the 1990s. These enabled beams to be shaped according to the tumor contour and were used to vary the strength of the radiation dose delivered, ushering in the era of intensity modulated radiation therapy (IMRT)[5] [Figure 5].

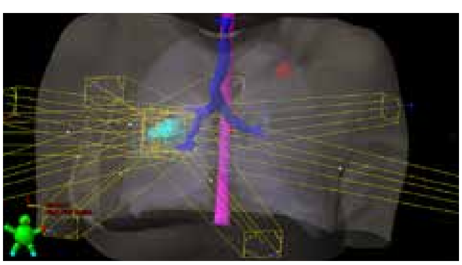

Figure 5: A tumour contour in 3-dimensional view, with planned radiation beams shaped around the tumour

Third, by the early 2000s, CT scanning was incorporated onto the linear accelerator in the form of the cone beam CT. This enabled the location of the tumor to be verified when the patient was lying in the treatment position. Such a development ushered in the era of image-guided radiation therapy (IGRT)[6]. This meant that radiation oncologists were able to 'see what they treat and treat what they see' almost in real-time [Figure 6].

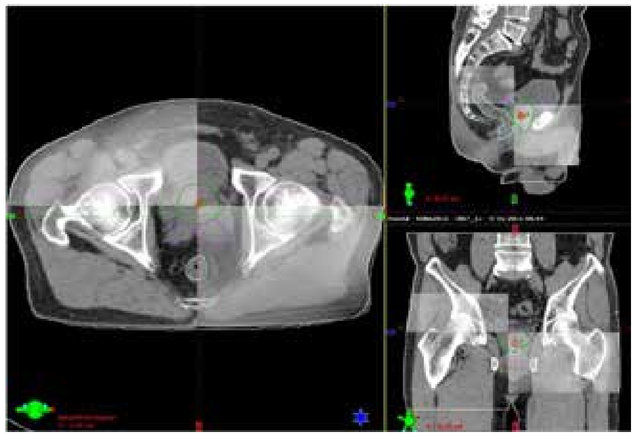

Figure 6: On-board imaging used for IGRT- On-board Cone Beam CT images are registered onto planning CT scan to calculate shifts which are then applied onto the patient's couch to achieve perfect targeting

These technology-enabled advances brought about new possibilities in tumor targeting. Doses could be increased, now that accurate targeting and beam shaping reduced the collateral damage.

Radiosurgery, a form of radiotherapy that uses extremely high dose radiation and pin-point targeting to destroy tumors in a single session, could now be performed on targets within the body[7]. Previously, this was only possible for targets in the brain using the gamma-knife system where a navigation metal frame was screwed onto the patient's skull to identify the tumor location, and radiation was delivered using its proprietary beam-shaping helmet.

The war against cancer thus entered a new era with better reconnaissance, targeting capabilities, and a new range of weaponry that was more potent and targeted. This meant a new range of possibilities in cancer strategy not unlike the use of UAVs to take down high-value targets without having to put boots on the ground. Likewise, some primary tumors could now be destroyed 'remotely' using radiosurgery, instead of invasive surgery.

The Radiation Delivery Process

Behind a successful tumor-targeting operation is a dedicated team of healthcare professionals who ensure that the entire radiation delivery system and chain is integrated and battle-ready. This requires regular machine checks and maintenance, as well as constant training and coordination between team members.

1) First, the treatment strategy is deliberated and formalized by a team of specialist doctors representing all disciplines within oncology. The role and sequence of radiotherapy is decided andthe team proceeds to prepare for their tasks.

2) Next, the patient is carefully positioned and immobilized on the treatment couch in a treatment position, which best exposes the tumor to accurate targeting while keeping the patient comfortable.

3) A planning CT scan called a simulation scan is performed. This scan becomes the photographic representation of the patient and the team uses this dataset to identify tumor targets and non-target 'civilian' zones. It is also used to design the required radiation beams and dose [Figure 7].

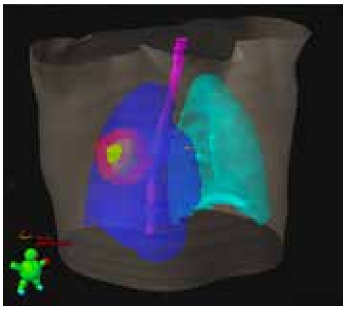

Figure 7: 3-dimensional view of the delineated tumor targets (red) and non-target zones like lungs (blue and cyan), and spinal cord (magenta).

4) A tedious process of target identification proceeds in the back room, where the radiation oncologist carefully carves out the targets and avoidance structures on the patient's CT scan using treatment planning software, and assigns radiation dose prescriptions and limits to both the tumor and normal organs.

5) Medical Physicists and Dosimetrists then use the treatment planning software to design the radiation beams direction and intensity to achieve the prescriptions assigned. Multiple iterations are made until the plan is fully optimized and approved by the radiation oncologist [Figure 8].

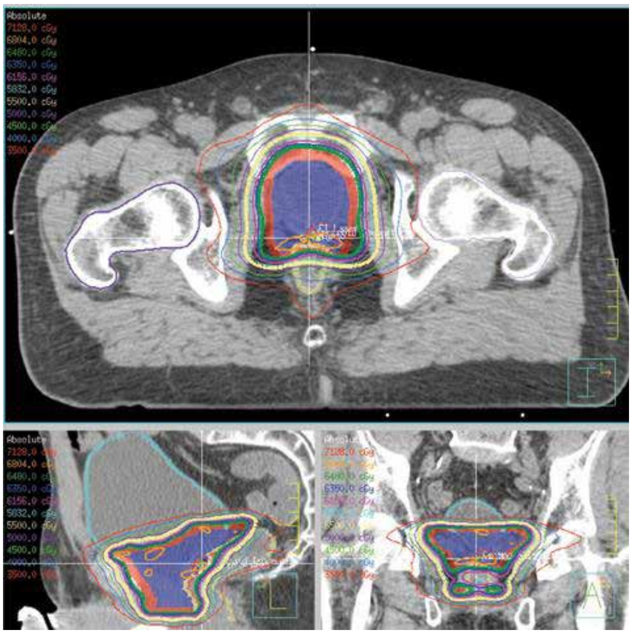

Figure 8: An Intensity Modulated Radiation Therapy plan for prostate cancer demonstrating high dose to the prostate and lower doses to the bladder and rectum

6) The treatment data is then transferred to the linear accelerator (radiation delivery machine) where a dry run, and mock irradiation, is done on a phantom to verify that doses delivered on set are as planned.

7) The patient arrives on the treatment day, and the whole team sets into action to position the patient as designed, before running an on-board CT scan to obtain a final image of the tumor, which is then registered to the planning CT scan to calculate minute shifts which are then applied to the treatment couch so that the patient and his tumor are now in the exact location where the beams were designed to target.

8) Then everyone leaves the radiation bunker. With the doors shut and the delivery arm of the linear accelerator in position, radiation therapists perform their final checks, with verifications read out. Then the button is pressed, and the beams are switched on.

Figure 9: Patient receiving modern radiotherapy with close monitoring throughout the treatment process

9) All this while, music is played in the background and the patient is looking at beautiful scenery projected onto the ceiling of the treatment room, while the radiation therapy team monitors the treatment process in the control room through CCTVs and the treatment console. There is no pain or smell, just the beeping sound of the machine to indicate that the beams are firing.

10) The whole process takes only a few minutes, after which the room is filled with activity again as the patient gets up to go back home, while the therapists are busy returning their immobilization device to the rack and preparing for the next patient's treatment.

On the Patient Front

The better the radiation team, the more seamless the treatment process for the patient. Modern oncology standards dictate that the patient maintains a high quality of life with as much normalcy as possible during the course of his treatment. A team of healthcare staff ensures this by maintaining a holistic focus on the patient's needs.

This is the reality of modern cancer warfare: the battle rages intently, the combat units execute their orders with skill and clinical precision, and the war zone shows little signs of being attacked, except where the offending target is located.

A Memorable Battle

Mdm Low was a lady in her mid-50s who had metastatic sarcoma to her right lung. A few years ago, the primary tumor at her right armpit was surgically removed and further treated with radiation to prevent a local recurrence. This was successful but unfortunately the cancer returned in her right lung.

It was thought at that time that since the upper half of the right lung had received some stray doses of radiation from her right armpit treatment, further radiation would damage the surrounding structures and thus she was only left with chemotherapy for the metastasis.

Unfortunately her tumor was not sensitive to the chemotherapy and continued to grow. It soon filled up her right thoracic cavity, compressing her right lung. She was oxygen-dependent at rest and on the verge of death.

A colleague who had heard of advanced radiation capabilities asked me to review her. Indeed, her tumor was huge, spanning more than 20cm in diameter and abutting closely to critical structures, which were sensitive to high radiation doses.

However, utilizing the capabilities described above, we were able to deliver extreme high doses of radiation within the tumor while maintaining a moderate dose at its circumference, which was safe for its neighboring structures. Using image-guidance, we were able to target the tumor accurately with tiny margins to keep collateral damage to the minimum.

Her treatment was delivered over five sessions according to the process described above. Over the next three months, the tumor stopped expanding, a huge contrast to her condition in the past when the tumor doubled in size every six weeks.

Over the following three months, it began to shrink to 50% of its original size and the previously compressed lung re-expanded. She became less oxygen-dependent and only needed supplementation on strenuous activity. She was able to walk again and returned to her daily routine.

For the following year, she was able to make several trips abroad to tour places she wanted to visit with her husband. Sadly, after a year, the tumor grew again in several places and she eventually passed on due to complications. Before she departed, she and her family were grateful for the extra year of life that the use of technology made possible.

Conclusion

Advances in radiation oncology have opened possibilities to many conditions previously thought to be untreatable. They have also blurred the lines between modalities, such as in the field of radiosurgery where patients no longer need open surgery to remove their tumors but can expect instead to be treated in an outpatient, non-invasive setting.

Tumors of the brain, spine, liver, lung and prostate can now be treated with advanced techniques with better outcomes and fewer side effects. Across the disciplines of oncology, similar advances are being made. Immuno-oncology is yet another stealth development which holds much promise.

The modern war on cancer will rely less on individual heroics and more on a well-integrated team of professionals, harnessing advancements in technology to achieve greater precision and minimize patient downtime.

Patients are only beginning to reap the benefits of this technological revolution as these capabilities require advance equipment, training, experience and, critically, team integration. The radiation oncologist and his team are but one unit amongst the entire force in this endeavor. We are privileged to live in these exciting times.

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About the Author

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Dr Daniel Tan is Consultant Radiation Oncologist and Medical Director at Asian American Radiation Oncology (AARO). 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 oligometastases. 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.