Minutes of the Sixth Ordinary Meeting

Held on Thursday 2nd February 2017

'Stereotactic Radiotherapy – Where Can The Robots Help Us?'
Dr Karen Venables, Head of Radiotherapy Physics, Mount Vernon Hospital

Dr Venables was introduced by the LMI President, Mr Derek Machin.

Dr Venables studied physics at Durham University and went on to undertake an MSc in Medical Physics in Aberdeen. She followed that with her Part I training in clinical practice within the Merseyside Training Consortium with her radiotherapy placement being at Clatterbridge. She was then appointed as a radiotherapy physicist in Bristol where she undertook Part II training. She moved to Mount Vernon Hospital and studied for a PhD prior to undertaking her current role of Head of Radiotherapy Physics.

By way of an introduction, Dr Venables gave a brief overview of radiotherapy. She described how Wilhelm Roentgen's discovery of X-rays in 1895, Henri Becquerel's discovery of radioactivity and the isolation of radium by the Curies lead to using beams of radiation to treat disease. The first recorded use of X-rays in this way was by Grubbe in 1896 to treat skin cancer and, in 1906, patients with pituitary cancers were reported to being treated. The phrase "stereotactic radiosurgery" (S R S) was coined by Lars Leksell in 1951 when he described "the non-invasive destruction of intracranial…..lesions that may be inaccessible or unsuitable for open surgery". Leksell went on to pioneer radiosurgery with particle beams and linear accelerators. S R S was usually given as a single fraction of radiation dose, often limited to brain lesions.

Stereotatic [body] radiotherapy (S [B] R T) was also being developed to treat tumours outside of the brain utilising multiple dose fractions (typically 1 to 5). The rationale behind fractionation is that it gives healthy tissue time to repair, noting the superior ability of non-cancer cells to repair between each fraction. Modern conventional radiotherapy is usually delivered in many fractions (typically 25 or more) and this can take several weeks. The dose delivered at each fraction is typically 2 Gray (Gy). So what is the rationale behind treating tumours with much higher radiation doses but with these higher doses being delivered during each of a smaller number of fractions?

Before discussing possible explanations, Dr Venables outlined the "5 Rs" of radiobiology (***r***epair; ***r***epopulation; ***r***edistribution; ***r***eoxygenation & ***r***adiosensitivity). The conventional mathematical model used to predict tissue response from ionising radiation is the "linear quadratic model" and this predicts a lesser effect on late responding tissues (i.e., normal tissue) and a greater effect to the same radiation dose on early responding tissues such as tumours. The Biologically Effective Dose (BED) is crucial in developing treatment regimes and BED is a derived quantity used to compare the effect of different treatment schedules.

To support the notion that a smaller number of higher dose fractions is clinically acceptable, Dr Venables gave as an example of a dose fractionation regimen for lung tumours. She cited published data showing little difference (within the limits of clinical data) of the tumour control probability for single doses, a few small number of S [B] R T fractions and conventional radiotherapy. So why do higher doses per (fewer) fraction work? She suggested among other reasons, improving image guidance and the ability to more accurately shape radiation beams, that the linear quadratic model may not be an accurate predictor of cell killing at high doses; that classical radiobiology does not predict the anti-tumour effects at high doses and also that many tumours are not hypoxic so do not benefit from the presumed reoxygenation between fractions.

Turning to current delivery systems for stereotactic radiotherapy, she described the four available (Gammaknife®; Tomotherapy®; systems based on linear accelerators (linacs) and Cyberknife®).

The Gammaknife® was originally introduced in 1968, initially having 179 cobalt-60 sources (later 201 sources) in a hemispherical array for treating brain tumours in a single dose of radiation. The Tomotherapy® system was developed in the 1990s and the first patient was treated in 1994. This

machine used a small megavoltage (MV) source, mounted on a rotating gantry with the patient moving through the gantry. Beam modulation was achieved by multi-leaf collimators (MLCs) and, with image guidance provided by a MV CT imager, there was the ability to achieve complex beam shapes.

Linac-based systems were introduced in the 1980s and they originally used metallic cones to shape the radiation beams. These were replaced with MLCs, e.g., the BrainLAB manufactured by Novalis. In these, the beam delivery system rotated around the patient (as with conventional linacs) and the patient moved on a sophisticated couch capable of 6-dimensional movement with a positional accuracy of less than 0.7 mm.

Dr Venables continued her talk with a detailed description of the Cyberknife® delivery system. Mount Vernon Hospital has been fortunate in having one of these systems, provided by a private benefactor. It was installed about 6 years' ago and there a dedicated Cyberknife® team of four consultant oncologists, physicists, radiographers and others.

The Cyberknife® system (manufactured by Accuray) was designed in 1994 by John Alder, a radiosurgeon based in Stanford. The original production run incorporated an industrial robotic system manufactured by FANUC in Japan but later models of the Cyberknife® incorporate a German robotic system manufactured by KUKA. The robotic arm is capable of six axes of motion and this flexibility provides an unparalleled radiation beam directionality which allows for maximum dose weighting and optimal dose conformity which is especially useful for complex lesion shapes. Dr Venables showed a video of the robotic arm moving and the audience was able to fully appreciate the flexibility of the motion in firing its radiation beam into the patient from a large number of directions. The advantage of this robotic delivery arm was that it is able to deliver radiation from many different directions without the need to move the patient. However, Dr Venables did note that having the ability to send a radiation in any direction did require the treatment room to be well shielded in all directions, something that some conventional radiotherapy treatment rooms would lack. Therefore, if a hospital was intending to replace a conventional radiotherapy machine with one of these robotic systems, complete room shielding would need to be considered if not already in place. Dr Venables showed an intriguing slide of an industrial plant with several similar robots manufacturing motor vehicles.

The Cyberknife® system has a positional reproducibility of the direction of the radiation beam of 0.12 mm. The radiation beam at Mount Vernon is produced by a 6 MV linac and is currently capable of delivering 600 centiGray (cGy) per minute but the model currently being manufactured by Accuray is capable of 1000 cGy per minute. The radiation beam is collimated using fixed tungsten "cones" which produce circular radiation fields. The system at Mount Vernon can generate radiation field sizes from 5mm up to 60 mm. Additionally, variable aperture collimators of prismatic tungsten elements can generate variable size dodecagon radiation fields and this eliminates the need to change the fixed collimators. Imaging is crucial to delivering the planned radiation dose. Imaging is provided by two ceiling-mounted X-ray tubes and two receptor plates, giving an image resolution of 1024 x 1024.

Imaging frequency is determined by the radiographers. Patient movement is relayed to the robotic arm and the radiation beam direction can be changed automatically. If there is significant patient movement (taken as ± 10 mm in any direction or ± 1^{o} pitch & roll or ± 3^{o} yaw), the treatment is paused and the patient repositioned.

Treatment planning is based on combining a model-based auto contouring; image fusion using CT, MR (and PET) images; and one of two algorithms (based on either a library of beam designs or a Monte Carlo calculation). Dr Venables showed a typical treatment plan for an intracranial lesion with 21 Gy in one fraction or 27 Gy in each of three fractions. She also showed a typical vertebral body treatment giving 27 Gy in three fractions. She also described the use of implanted gold fiducial markers, typically inserted one week prior to the CT image for a prostate treatment plan. She showed a typical prostate plan highlighting the clear benefit in beam accuracy and surrounding normal tissue sparing.

The question of correcting for normal internal movement of a tumour was described. She described the use of implanted gold fiducial markers, typically inserted one week prior to the CT image, for monitoring prostate motion. An alternative solution for motion correlated to breathing is to fix optical markers on the patient's skin, transmit light via fibre optic cables and detect the external movement of the patient, correlating this with X-ray images to give the internal motion of the tumour. Dr Venables then described the manner in which the normal breathing pattern of the patient (which will affect the spatial position of a tumour located in the lung) is accounted for. The Cyberknife® system can compensate for lung expansion and contraction (and therefore tumour displacement) during normal breathing and this ensures that the radiation beam is always directed to the tumour.

Dr Venables concluded her discussion of clinical aspects of radiation treatment regimens by discussing a detailed table of particular organs at risk during treatment. Among other sites, she talked about dose constraints in CNS and GI treatments. She noted several clinical sites that have mandatory dose constraints (typically 10 Gy – 16 Gy) for radiosensitive organs within the brain for a single fraction, increasing to 30 Gy to 40 Gy for the same organs with eight fractions.

Dr Venables described some of the necessary quality assurance procedures needed to ensure optimum system performance.

In concluding her talk, Dr Venables pondered the future of stereotactic radiotherapy. She noted that there are many trials currently underway to assess clinical benefit against conventional treatment regimens and the outcome of these is awaited. She also noted the technology was moving forward quickly and that new developments were in place, such as tracking of lung tumours with mutl-leaf collimators, implanted radiofrequent beacons and surface mapping may reduce or eliminate the need for tumour imaging. In addition, she commented on the fact that a much lower number of fractions (and therefore outpatient hospital visits) was convenient and popular with patients.

At the end of Dr Venables's presentation, Mr Machin invited questions and Dr Venables responded to several questions for the audience.

Dr Harold Stockdale (IOP Branch member and IOP link to the LMI) thanked Dr Venables for her entertaining and informative talk. That the question session lasted about 20 minutes showed the level degree of interest and enquiry generated by the talk. The audience showed its appreciation of Dr Venables talk in the usual manner.

Harold Stockdale
Institute of Physics