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EDITORIAL

Technical know-how in stereotactic ablative radiotherapy (SABR)

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With the sophistication of present day technology, we are now able to deliver stereotactic ablative radiotherapy (SABR), entailing delivery of ablative individual doses in a very precise and accurate fashion to extracranial tumours, a feat which was unimaginable in the past. SABR is virtually a spin-off of intra-cranial stereotactic radiosurgery (SRS) and has been used to treat primary tumours of the lung, the liver, the kidney, and the prostate, and oligometastatic and oligoprogressive disease.[1–3] In order to minimise any collateral damage to surrounding normal parallel tissues like lung and liver or adjacent serial organs such as the oesophagus or spinal cord, highly conformal radiation isodose distribution and very tight margins are used. For tumours that move with respiration, manoeuvres accounting for respiratory motion are necessary to avoid inadequate coverage of the tumour being treated. To facilitate safe and effective delivery of SABR, the technical requirements are very stringent and their importance cannot be overemphasised.

The SABR process can be divided into: (1) Proper selection of patients; (2) Immobilisation; (3) Respiratory motion control; (4) CT simulation; (5) Delineation of target volume and organs-at-risk (OARs); (6) Treatment planning; (7) Pre-treatment verification; and (8) Treatment delivery and intra-fractional monitoring.[1–3] The subsequent sections will discuss all the above components individually.

Proper Patient Selection

Eligibility criteria vary among different trials or centres for each disease site or condition.[1] However, there are some general stipulations to be met in order for the patient to be eligible for SABR. Firstly, the patient must be able to derive benefit from the procedure either in terms of durable control of the target tumour or symptomatic relief. In other words, there must be a set goal for therapy for the patient. Secondly, the patient must be able to tolerate lying still in the immobilisation device for the SABR treatment. If a robotic radiosurgery system is used, the treatment delivery time can easily exceed 1 hour. However, if a linear accelerator (LINAC)-based system is used and when volumetric modulated arc therapy (VMAT) and beam-flattening filter-free feature are available, the treatment delivery time can be dramatically reduced. Thirdly, the target to be treated must be clearly visualised on imaging as typically, there is very little or no margin expansion around the gross tumour volume (GTV) with SABR.

Immobilisation and Respiratory Motion Control

A robust immobilisation is of utmost importance in the SABR process as very tight margins are set around the GTV and in many cases, such as in spinal metastasis,

there are critical OARs in the proximity. Immobilisation can be achieved either by the use of rigid external immobilisation devices, by active motion detection and compensation during treatment delivery and by fast treatment delivery. Depending on the treatment machine used and the body site to be treated, different immobilisation devices should be considered.[1–3] Among all, spinal SABR requires the most robust immobilisation, especially when a LINAC-based system is used. Li et al. has demonstrated that the dual vacuum system (BodyFIX; Elekta AB) is superior to other immobilisation devices in terms of set-up accuracy and can keep the set-up variation to 2 mm or less with intra-fractional adjustment.[4] However, colleagues from VU University Medical Center in the Netherlands showed that based on pre- and post-fraction X-ray imaging during fast lung SABR, simple support devices can result in spine stability that is comparable to that reported with rigid external immobilisation.[5] When a robotic radiosurgery system is used, the near real-time tracking capability renders semi-rigid immobilisation unnecessary and the patient can simply be immobilised using a regular vacuum cushion or body cradle.

With regard to respiratory motion control, there are 3 broad strategies, namely, motion dampening, gating, and tracking.[1] The 2 most common ways of achieving motion dampening are abdominal compression and active breathing coordination (ABC). The abdominal compression device is frequently a built-in feature of some commercially available stereotactic bodyframes. The patient needs to be able to tolerate tight abdominal compression and it is important to check to ascertain that the patient does not have an abdominal aortic aneurysm, which is at risk for rupture with application of pressure. Gating entails tracking of the tumour's range of motion during respiratory cycles and the radiation beam is switched on only during a specific segment of each cycle. Tracking involves the moving of the radiation beam in a near real-time fashion based on the respiratory motion of the tumour utilising surrogate markers such as fiducials. When none of the above approaches are used, an internal target volume (ITV) can be constructed based on a 4-dimensional CT (4DCT) to account for the tumour position in all respiratory phases.

Regardless of the manoeuvres used to account for respiratory motion, the acquisition of treatment planning data should incorporate the same considerations. All breathing motion compensation strategies above are in clinical routine use and have achieved excellent outcome. To date, no study was able to confirm superiority of one particular strategy over the others.

CT Simulation and Delineation of Target Volume and Organs-at-Risk (OARs)

Patients are immobilised in a reproducible setup for CT simulation. Contrast injection can enhance the visualisation of the gross tumour and facilitate delineation of OARs, especially those close to vascular structures. In many centres, when contrast injection is planned, another set of non-contrast CT is done for treatment planning in order to eliminate any uncertainty in dose computation caused by the contrast. Depending on the method of respiratory motion control, a free breathing or a deep expiration CT can be used as the primary image set for treatment planning. If fiducial markers are used, the deep expiration CT will be more suitable as the primary image set as the image of the markers will be blurred out in a free breathing CT, render tracking or gating based on the markers very difficult. The slice thickness should be no greater than 1–3 mm. For the treatment of tumours that move with respiration, a 4DCT is obtained and fused with the primary CT set regardless of the method of respiratory control used. A maximum intensity projection can be used to generate an ITV. Sometimes, for liver tumours that are hypodense on CT, a minimum intensity projection may be more useful than a maximum intensity projection for ITV generation.

Other imaging modalities can be fused to the treatment planning CT to assist in delineation of the target volume and OARs. A positron emission tomography (PET) fused with the treatment planning CT can be very useful for lung, liver and adrenal tumours. For tumours (such as liver, spinal and prostate tumours) or OARs (such as spinal cord) not very well visualised on CT, the fusion of appropriate sequences of magnetic resonance imaging (MRI) with treatment planning CT can facilitate more accurate target volume and OAR delineation. A CT myelogram can be fused with the treatment planning CT to facilitate delineation of the spinal cord in the scenario where the artifacts from metallic spinal hardware obscure the visualisation of the contents of the spinal canal. Contouring atlases for OARs are available through the Radiation Therapy Oncology Group (RTOG) website (https://www.rtog.org/CoreLab/ContouringAtlases.aspx).

Treatment Planning

The treatment planning techniques commonly used for LINAC-based SABR include 3-dimensional conformal radiotherapy (3DCRT), intensity modulated radiotherapy (IMRT), and VMAT. Fitzgerald et al. reported their

experience with 3DCRT and VMAT at this journal issue.[6,7] The CyberKnife (Accuray, Sunnyvale, CA) system has a unique treatment planning system based on robotically directed beam delivery. If the tumour is in a location where there are no critical OARs, an attempt is usually made to create an isotropic isodose distribution. On the other hand, when the tumour is in close proximity to a critical OAR such the spinal cord as in spinal metastasis, great efforts are made to steer the radiation dose away from the structure utilising inverse planning to avoid catastrophic toxicities.

The importance of the use of an optimal treatment planning algorithm, particularly in the thoracic region, cannot be overemphasised. Multiple studies have demonstrated that the use of a suboptimal treatment planning algorithm will result in inaccurate dose estimation that can lead to inadequate tumour coverage.[8] The Imaging and Radiation Oncology Core (IROC) at M.D. Anderson Cancer Center has included a list of approved treatment planning algorithms for lung targets and they are approved for use in RTOG SABR trials for lung tumours (http://rpc.mdanderson.org/RPC/home.htm). A recent study based on data obtained from anthropomorphic thorax phantom for RTOG credentialing showed that even with advanced treatment planning algorithms such as convolution/superposition and anisotropic analytic algorithm (AAA), the dose that was delivered to the lung target was overestimated. Only Monte Carlo algorithm agreed with measurement within 0.6%.[8] OAR constraints have been established in prospective trials and developed in single-institutional studies, facilitating safe delivery of SABR. However, prospective validation of these tolerance doses is needed in the future.

Pre-treatment Verification, Treatment Delivery and Intra-fractional Monitoring

Before SABR is delivered, the pretreatment verification of set-up accuracy is paramount. In the early days of technical development, orthogonal ports were used. At present, with the availability of advanced on-board imaging technologies, stereoscopic X-rays, conebeam CT (CBCT) or megavoltage (MV) CT (as used in Helical TomoTherapy; Accuray) can be used to verify the set-up with higher degree of set-up certainty.[1] All in-room verification imaging technologies need to be consistent with treatment planning imaging regarding breathing motion compensation.The mode of treatment delivery depends on the treatment machine being used. In general, a modern LINAC-based system takes a much shorter time than a robotic radiosurgery system (CyberKnife; Accuray) for radiation delivery. To ensure that the patient remains in the same position during radiation delivery, a midway CBCT or megavoltage CT (MVCT) can be performed and adjustments can be made if the patient's position changes.[1] The combination of digital tomosynthesis and triangulation also allows for monitoring of spine position with sub-mm accuracy and precision.[9] The CyberKnife system tracks the tumour or target using bony landmarks or fiducial markers in a near real-time fashion throughout the treatment.

Conclusion

SABR adds to the armamentarium against cancer and is a very exciting therapeutic opportunity for cancer patients. Its technical requirements have to be very stringent as the therapeutic margin is narrow. When all the principles are followed, it is possible to deliver SABR to extracranial tumours safely and effectively. Further development of SABR across the globe is under way and the expansion of its applications in various oncological settings is anticipated.

Conflict of Interest

Simon S. Lo has received honorarium and travel support for previous educational symposia from Varian Medical Systems and Accuray and has also received research support from Elekta AB. Ben Slotman has received speaker honorarium and travel support from Varian Medical Systems. Matthias Guckenberger has received speaker honorarium, travel and research support from Varian Medical Systems and Elekta AB. Daniel Tan has received speaker honorarium and travel support from Varian Medical Systems and Brainlab AG. Arjun Sahgal has received honorarium for previous educational seminars for Medtronic Kyphoplasty division, Elekta AB and Varian Medical Systems and has also received research grants from Elekta AB. The other authors have no other relevant disclosures.

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