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CyberKnife Image-Guided SABR System: Volumetric Image-Guided or Real-Time Tracking SABR Systems, Treatment Delivery, Image Guidance, and Technical Considerations for Proton Therapy

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Abstract:

In recent years, stereotactic ablative radiation therapy (SABR), also known as stereotactic body radiation therapy (SBRT), has gained a lot of attention as a potential alternative to surgical resection for certain patients with early-stage non-small cell lung cancer (NSCLC) or patients who cannot tolerate it. When it comes to early stage NSCLC, data from many clinical trials and retrospective studies show that SABR/SBRT is a safe and effective treatment that can compete with surgical resection. Compared to less harsh fractionation methods, the toxicities caused by ablative radiation doses are far more severe and difficult to tolerate. In view of these facts, it is essential to take into account a number of factors in order to accomplish high-quality treatment. The correct selection of patients is based on solid published evidence. The treatment is carefully planned to reach enough tumour coverage while avoiding organs-at-risk. The ablative radiation is delivered with care, using reliable immobilisation, accurately targeting the tumour, and verifying the dose delivery precisely.

Keywords: CyberKnife, Real-Time Tracking SABR Systems, Treatment Delivery, Image Guidance, Technical Considerations for Proton Therapy

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Introduction

A new and potentially life-saving option for patients with early-stage nonsmall cell lung cancer (NSCLC) is stereotactic ablative radiotherapy (SABR), also known as stereotactic body radiation therapy (SBRT). This treatment is ideal for patients who cannot undergo surgical resection and may even be able to forego surgery altogether in certain cases. One of the most fruitful and satisfying applications of SABR is the treatment of intrathoracic tumours. By utilising several radiation beams that converge on the area harbouring neoplastic cells, stereotactic area-based radiation therapy (SABR) is able to provide extremely high radiation doses to the tumour target in a relatively small number of fractions, often five or less. Because it is quick, easy, and doesn't require general anaesthesia or an invasive operation, the treatment has become increasingly popular with radiation oncologists and patients since its launch. An essential aspect of contemporary stereotactic radiation therapy is the development of supplemental methods [1, 2] to fine-tune the dose distribution to millimetre precision. These methods include intensity modulation and volumetric arcs. By using these methods, normal structures are spared the harmful effects of radiation because the ablative doses go off sharply beyond the target treatment volume. The reason why SABR has proved so effective in treating early stage (T1-2 N0) NSCLC is that this illness mainly affects older people who have smoked for a long time. What this means is that patients typically have a higher-than-average burden of comorbidities and a performance status that is below average. Even with early detection, patients who were considered medically inoperable for lung cancer often had limited treatment options. Traditional fractionated radiation was a possibility, but the results were terrible, with local control rates of 30–50% and long-term survival rates of 10–30%. The fact that toxicities hindered dose escalation, making it impossible to administer a dose that was actually tumoricidal, probably influenced our findings. Conventionally fractionated regimens have a biologically equivalent dose (BED) limit of about 80 Gy before toxicities become intolerable; nevertheless, this level is never high enough to reliably eradicate gross disease in NSCLC. Recent advances in stereotactic therapy and hypofractionation [3, 4] have made it possible to safely achieve a BED of 100 Gy or greater without causing severe toxicity. Several studies have shown that SABR can produce local control rates of 70-98% in early stage NSCLC, which is a significant improvement over traditional fractionation's dismal results. Ninety percent of patients have shown local control after undergoing SABR with BED (100 Gy to target volume). Medically inoperable patients with early stage NSCLC are now being approached differently due of the significant difference in results between conventionally fractionated radiation and SABR. But when it comes to quality control and technical knowledge [5-7], SABR is among radiation oncology's most challenging fields. Two crucial aspects raise the stakes significantly. There is a direct correlation between the quality of treatment and the likelihood of a fatal outcome in early stage non-small cell lung cancer (NSCLC), which is both deadly and, in most cases, still curable.

Various Approaches to Treating Early Stage Non-Small Cell Carcinoma

Two features of lung cancer patients have motivated the enthusiastic and widespread adoption of SABR for NSCLC; first, a poor performance status; and second, the fact that, when administered correctly, SABR gives final treatment for these patients. First, non-small cell lung cancer patients tend to be older, with a median age of 71 years. This means that many of these patients also have other chronic conditions. Second, smoking increases the likelihood of developing lung cancer and a host of other systemic illnesses, such as COPD and coronary artery disease. Surgical intervention for individuals with lung cancer is dangerous due to their advanced age and medical comorbidities [8, 9]. The perioperative mortality rate for lobectomy, the gold standard surgical procedure, increases from 2-3% for an average male patient over 65 years old with mild to moderate comorbidities to about 20% for the worst surgical candidates, according to numerical data from prospective trials and statistical models. The latter group of high-risk individuals are the ones for whom SABR has the greatest potential. Peripheral lung tumours can be safely ablated using SABR with acceptable toxicity, even among poor surgical candidates, as long as the lesion is placed distant from important structures.

Treatment by Surgeon

Until phase III evidence disproves the lack of randomised trials comparing SABR with surgery, lobectomy is the gold standard for treating early stage NSCLC. Therefore, it is important to determine if the patient is a good candidate for

this operation before proceeding. The Goldman Index, Detsky's Modified Cardiac Risk Index, Eagle's Cardiac Risk Assessment, Lee's Revised Cardiac Risk Index, the Thoracoscore Model, and others can be used to estimate the worldwide operative risk of a patient before surgery. Although the first three models were designed to be applicable to any type of surgery, the last one was specifically trained on data from thoracic surgeries, making it ideal for lobectomy risk assessment. The Thoracoscore Model calculates the risk of death while hospitalised based on a number of variables, such as age, sex, comorbidities, performance status, dyspnea severity, and ASA score. Although there is no one-size-fits-all risk threshold that would make surgery impossible [10-11], these calculators, along with clinical gestalt, can help both patients and surgeons assess the pros and cons of the procedure to decide if it is worth the risk. Focusing on pulmonary function, the physiologic measure primarily influenced by the procedure, is a simpler and more typical way to assessing the pros and cons of lobectomy. There is no universally accepted risk threshold for lobectomy; however, in our institution, patients are considered to be candidates if (a) their forced expiratory volume in 1 second (FEV1) is at least 75% of their predicted volume, or 1 litre (l), and (b) their lung's diffusion capacity for carbon monoxide (DLCO) is at least 60% of its predicted capacity. A Xenon study is conducted to forecast postoperative pulmonary function in circumstances where these criteria are unclear. With a predicted postoperative FEV1 of less than 35% (or less than 0.8 litres), the likelihood of mortality increases. Similarly, the likelihood of surgical complications increases when the projected DLCO is less than 40% after the operation. In order to lower the risk of coronary events or to prevent thrombosis after coronary stent placement, an increasing number of patients with lung cancer at presentation will be on chronic aspirin or thienopyridine therapy, such as clopidogrel. This is due to the high correlation between lung cancer and cardiovascular disease. In cases where a drug-eluting stent has been implanted, elective procedures may need to be postponed for up to a year [12, 13]. Myocardial infarction or death can occur from discontinuing aspirin or thienopyridine medication before surgery. A cardiologist should be involved in the decision-making process when it comes to specific patients about the discontinuation of antiplatelet therapy in order to undergo lobectomy. Presently, sublobar (wedge) resection and SABR are alternatives to supportive therapy for patients who are not lobectomy candidates. Although there is no agreement on the relative efficacy of these methods, as will be seen in the clinical outcomes section, historical evidence reveals that although both methods are similar in terms of survival, SABR seems to provide superior local control. Technical, anatomical, and physiological factors all play a role in determining potential SABR candidates. The use of particular thresholds for FEV1 and DLCO is disputed, because physiological candidature is not as strict as surgery [14-17]. Predicting greater toxicity following SABR and triaging patients to appropriate supportive care or systemic therapy is done at some centres using a FEV1 of less than 0.2 litres. Patients with tumours outside of the chest wall, in the periphery, typically have less complications than those with tumours closer to the rib cage, the superior sulcus, or central mediastinal structures.

Standard Radiation Treatment

The treatment was restricted to 60-66 Gy in 1.8 or 2.0 Gy segments to honour the dosage limitations of normal tissues. Overall survival rates were 10-30% and local control rates were 30-50% after 5 years, with some patients achieving a cure. Conventional radiation therapy did enhance survival rates compared to observation in a SEER study of patients treated from 1988 to 2001, even if the treatment did not cure the disease. The safety and effectiveness of SABR has led to its removal from consideration as a first-line treatment for early stage NSCLC in conventional radiation therapy.

Ablation with Radiofrequency

Electrode placement at the tumour location allows for the delivery of high-frequency electrical currents in radiofrequency ablation (RFA). By coagulating the surrounding tissue, the heat produced by RFA ablates the tumour. The main benefit of RFA is that treatment just requires one session and does not require hospitalisation. As the electrode is guided percutaneously to the tumour site using CT imaging, accuracy is achieved. Patients whose tumours are less than 4 cm in size are eligible for RFA. There is a larger danger of catastrophic harm when tumours are less than 1 cm away from major airways or veins, making them relatively contraindicated. Because blood flow may carry heat away from the tumour, rendering the operation ineffective, it is best to avoid treating central tumours with RFA. When performed by trained professionals, the technique rarely causes side effects. Pneumothorax, haemorrhage, sepsis, and skin and/or lung infections are among the most serious side effects of RFA. Although self-limited pneumothorax is the most common complication, the literature shows that it occurs in anywhere from 5% to 60% of RFA treatments. Due to the small sample sizes of the trials conducted and the fact that RFA has historically only been

used on patients who either refused surgery or were medically deemed inoperable, there is insufficient evidence to determine whether or not it is effective for patients with early stage NSCLC. In their study, Simon et al. treated 75 patients with stage I non-small cell lung cancer (NSCLC) [20-23]. They found that patients with tumours less than 3 cm had a progression-free survival rate (PFS) of 47%, while those with larger tumours had a PFS of 25%. The RAPTURE RFA trial showed encouraging results with a 2-year overall survival rate of 75% in a small cohort of 13 patients with stage I NSCLC. Among 19 patients with stage I non-small cell lung cancer (NSCLC), Hiraki et al. found a 3-year overall survival rate of 74%, whereas Pennathur et al. found a 2-year overall survival rate of 68%. According to another study conducted by Ambrogi et al. (2006), there was a full response rate of 59.5%, an average local recurrence interval of 25.9 months, and a median overall survival of 33.4 months in medically inoperable stage I non-small cell lung cancer (NSCLC) patients with tumours less than 5 cm in size. The American College of Surgeons Oncology Group (ACOSOG) Z4033 is an ongoing trial that will shed light on the safety and effectiveness of radiofrequency ablation (RFA) in a larger group of patients with early stage non-small cell lung cancer (NSCLC). One interesting possibility is to combine RFA with external beam radiation, where SABR is more effective on the periphery (because of hypoxia and necrosis at the centre) and thermal ablation is most effective in the centre (because of heat dissipation at the periphery). This method is still in its early stages [24, 25] of development. Though RFA shows potential for some patients, many hospitals choose SABR because it has increased overall survival rates in bigger, prospective trials. One benefit of SABR is that radiotherapy may be applied more consistently and evenly than heat, which means there's less chance of local failures due to inadequate treatment. The local control rate seems to be better with SABR if BED is 100 Gy, while there is no direct comparison between RFA and SABR. Investigating RFA's function as a salvage treatment following SABR would be an intriguing prospect.

The Role of Technology

Technical factors will be the main emphasis of this section. Here are four questions that the radiation oncologist needs to answer before SABR can be started. (1) Is it possible to immobilise and place the patient? (2) Is it possible to account for tumour movement in treatment planning? (3) Will the targeted area be treated while avoiding nearby vital structures? (4) Is it possible to check the radiation's accuracy while the patient is being treated?

The Patient's Position and Immobilisation

Using SABR on lung tumours requires careful positioning and immobilisation. There is no "second chance" due to the biological properties of radiation, therefore if the tumour target is geographically missed, there is no chance for a cure. Thus, it is crucial to utilise multiple reference points to ensure that the patient's body posture can be reproduced with great accuracy. In order to shield their arms from radiation, patients are usually asked to raise them and hold onto an indexed T-shaped bar. A vacuum immobilisation bag that stretches from the skull to the pelvis can be used to lay the patient flat on their back and reduce the amount of movement between the various parts of the body. But based on their own experiences [26-29], several institutions may deploy immobilisation devices in different ways. While specialised masks are usually unnecessary, they can be made to immobilise the neck and head in order to treat apical tumours.

Next, modelling to compensate for tumour motion

Lung tumours can undergo translation, translation along any axis, stretching, and deformation as part of the breathing cycle. Modern techniques have made it possible to overcome the challenge of capturing the complete tumour in the radiation field, despite its many axes of motion. We suggest using a state-of-the-art four-dimensional (4D) CT planning system to outline the full trajectory of a tumour during a respiratory cycle. Obtaining spatially oversampled CT data while monitoring the patient's respiration is the usual method for obtaining these 4D data. Images are captured for more than one respiratory cycle at each CT couch position and then divided into about ten phases according to when they occur in relation to the overall cycle. The relative position of these phases is usually expressed as a percentage, with 0% representing full inspiration, 50% end-expiration, and 90% the phase just before full inspiration again. Compiling matching phase data from each couch position allows for the creation of a comprehensive reconstructed three-dimensional (3D) CT dataset for each phase. Playing these 3D phase reconstructions in order allows one to create a 4D map of the tumor's location [30-34] with respect to nearby structures during the whole

respiratory cycle. Whether treatment should be administered during free-breathing, respiratory gating, or breath holding depends on the properties of the 4D image and the patient's ability to control or hold their breath.

Slicing the Target Away from Healthy Tissues

The treatment planning station allows for considerable leeway in specifying the tumour volume that will be treated after the simulation pictures have been uploaded. Contouring the tumor's envelope during the respiratory cycle is the most cautious approach for tumours that move around a lot. The internal gross tumour volume (iGTV) is a volume that can be obtained from the various CT phases in various ways (Chang et al. 2008b). As an example, (a) in every respiratory phase add up all the gross tumour volumes (GTVs), (b) in the 0% and 50% phases of the respiratory cycle add up all the GTV contours, (c) in every respiratory cycle define the GTV contour as the maximum intensity projection (MIP) at each voxel, and (d) in every respiratory phase use the MIP technique to modify the contours as needed with visual verification. Methods (b) and (c) have been shown in published data to have a tendency to understate the amount of tumour coverage. Using the MIP with some visual tweaks helps us strike a good mix between speed and precision. Lung window contouring is necessary for GTV [35-38]. If the lesion is near the bronchial tree and major arteries, intravenous contrast-based simulation may be considered. An expansion of 5-8 mm for the clinical target volume (CTV) and an expansion of 3-5 mm for the planning treatment volume (PTV) are added to the iGTV to compensate for set-up error and to cover microscopic illness. However, these extensions should be resized in a way that doesn't expose normal tissues to too much radiation, and they should also consider other organs that are at risk. Instead of using a CTV expansion, several centres including the Radiation Therapy Oncology Group (RTOG) produce a PTV straight from the iGTV. There are three further cases that necessitate careful examination. When dealing with tumours that are closer to the surface and have less than 5 mm of motion, a conventional static planned treatment volume expansion can be used at any point in the respiratory cycle as long as the PTV expansion is more than the range of motion that has been seen, which is approximately 5-8 mm beyond the CTV expansion. Secondly, the mediastinum can be evacuated by using breath-holding on tumours that are close to central tissues. At the simulation, the patient usually wears specialised goggles that show them how far their diaphragm goes when they inhale deeply. In order to maintain the same level of respiratory support during therapy as during simulation, the patient wears his original eyewear. Finally, patients with severe lung disease, like emphysema or interstitial fibrosis, may not be able to achieve adequate inspiration due to their underlying illness, and using ITV techniques could lead to an unacceptable decline in pulmonary function. This could make breath-holding a challenge for these patients. When this occurs, respiratory gating might be employed [39-41]. This technique allows the radiation oncologist to precisely target the tumour at a specific point in the respiratory cycle, such as at the end of inspiration. The radiation is then administered in pulses that are timed to match the patient's breathing, ensuring that treatment is administered exclusively during the designated respiratory phase.

Potential Problems with Dosimetry and Treatment Scheduling

Selecting an appropriate dose distribution that covers the tumour well while avoiding normal tissues and is physically possible is a challenging task in SABR dosimetry, which requires navigating through multiple dichotomies. Here we'll look at a few of these dichotomies as they pertain to SABR. The use of homogeneous vs heterogeneous modelling, coplanar vs non-coplanar beams, margined versus unmargined blocking, and finally, forward-planned versus inverse-planned 3D conformal intensity-modulated radiation are all factors to account for. Sharp dose gradients, high-precision localisation, and a high dosage per fraction in extracranial sites are typically achieved by combining numerous beam angles (6-12 beams) in SABR. It is recommended to utilise analytical anisotropic algorithm (AAA) or Monte Carlo for precise dosage calculations. The dosage prescription is the following factor to be considered. One possible explanation for the discrepancies in local control rates found in clinical trials [42, 43], according to retrospective assessments, is that different approaches to dose prescription planning are used. A recent analysis by Senan et al. 2011a of the Netherlands highlighted the fact that dosing a tumour from within can lead to insufficient dosing of the lesion's periphery and poorer local control. Consequently, a dose that is outside of the target should be prescribed using an isodose line. The standard of care is to target the whole tumour with radiation at a biologically effective dose (BED) higher than 100 Gy. With 54-60 Gy administered in three fractions or 48-50 Gy administered in

four fractions prescribed to the 60-90% isodose line, this dose level can typically be achieved if the lesion is peripherally located and at least 2 cm from critical normal structures. This was confirmed in a retrospective review of a multi-institutional study in Japan, which indicated that 5 year local recurrence rates improved from 8.4 to 26.4% when comparing patients treated to \100 Gy BED to those treated to at least 100 Gy BED. It may be necessary to adjust the dosage and fractionation in order to avoid serious problems if the lesion is located in the centre. The body is considered a homogenous medium with a density of water in conventional methods for calculating dose distributions in tissues. Given that lung air has a density far lower than water, this causes issues in the thorax. Tissue heterogeneity correction techniques, which substitute CT Hounsfield units for tissue electron density, provide a mathematical explanation for this disparity. There has been a lot of debate regarding [44-47] whether these corrections are really necessary for conventionally fractionated thoracic radiation programmes because there is a lot of correlation between the corrected and uncorrected versions. However, due to the use of fewer fractions and extremely high dosages, the effect of heterogeneity correction in SABR is significant. Few studies have compared SABR target plans that have been developed homogeneously and those that have been calculated heterogeneously. Based on a review of treatment plans that were submitted to the RTOG 0236 stereotactic body radiotherapy protocol, it was found that the planning target volume receiving 60 Gy was reduced by 10.1% on average when heterogeneity corrections were applied. This means that 54 Gy was actually delivered instead of 60 Gy in 3 fractions. Based on these results, we suggest using heterogeneity corrections while planning SABR. When designing a SABR plan, the ideal arrangement of beams should take into account both the need to cover tumours and spare healthy tissue. Currently, arc therapy, multiple static noncoplanar beams, and multiple static coplanar beams are the three most used beam combinations. When comparing the two static options, non-coplanar beams have a few advantages. One is that they can achieve higher conformality around the PTV. Another is that they typically have steeper dose gradients. Skin dosage is lowered. And in some situations, they can even effectively spare the entire contralateral lung.

Nevertheless, patients suffering from a heavy load of concomitant lung disease may not be able to tolerate the increased volume of lung getting low doses in noncoplanar designs. Because of the need to adjust for couch and gantry changes, treatments with non-coplanar beam configurations can take more time overall. At the low dosage level, there is a variation in lung exposure between the coplanar and non-coplanar designs for the same patient. The SABR plan's dosimetric profile can be affected by the blocking method as well. The treatment volumes are typically more uniform when using conventional forward-planned 3D conformal plans, which call for blocks to be positioned at a margin beyond the PTV. While this strategy could potentially enhance SABR dose homogeneity, it comes at the expense of increasing normal tissue exposure, which can lead to violations of organ dosage restrictions when utilising typical block margins. Hence, in the penumbra zone, forward-planned SBRT blocks are usually positioned along the PTV's edge. There is more variability within the tumour mass because more monitor units are needed to guarantee tumour coverage [48-51] at the periphery when this blocking method is applied. Since greater dosages within the tumour may lead to better therapeutic impact, this is not necessarily hazardous. VMAT is a relatively new technique that shows potential for optimising conformality and tissue sparing without necessitating non-coplanar treatment administration. In this technology, the gantry speed, MLC leaf position, and dose rate are continually varied during delivery. It can cut treatment delivery time in half while still correctly and efficiently delivering radiation doses with improved conformality. Compared to static coplanar beam configurations, VMAT appears to lower skin and lung dosage in early single institution investigations. The treatment delivery time is reduced from 20 minutes for the maximal dose when 8-12 non-coplanar beams were utilised to ~3 minutes when VMAT is delivered in flattening-filter-free mode. Lastly, when it comes to designing and delivering SABR for lung tumours, a few of centres have moved away from forwardplanned 3D conformal radiation treatment and towards intensitymodulated radiation therapy (IMRT). Structures of the chest wall and the theoretical framework for preventing both immediate and future problems. Reducing the likelihood of rib fracture and chronic neuropathy is one of the most often mentioned applications of this approach, which involves limiting peripheral dosage within the chest wall. Although conformality has several benefits, there are a few things to remember when using IMRT.

First, patients who need to hold their breath throughout treatment or who have trouble staying comfortable in the supine position owing to medical issues may not be able to complete their therapy as planned because of the considerably lengthier treatment durations. Secondly, the collimator leaves and tumours interact in IMRT, which might lead to radiation delivery that deviates from the planned dosage distribution. These differences are typically less

noticeable at 30–40 fractions in traditionally fractionated programmes. However, because SABR plans only use three or five fractions, errors in any one fraction can have far-reaching effects on patient care. Because of this, it is much more important to have good motion management and quality assurance throughout the whole SABR process when using IMRT. Finally, unless otherwise stated, IMRT optimisation algorithms are typically tuned to favour more homogeneous doses [52-55], which means that the amplified central tumour dose resulting from 3D conformal dose heterogeneity may not be delivered when plans are created using IMRT. This is not an inherent feature of IMRT, but it does happen. By optimising MU (decreased modulation), this can be largely mitigated in VMAT (RapidArc). The question of whether this loss of tumour heterogeneity has any therapeutic relevance remains unanswered.

Verifying the Precision of Dose Administration via On-Board Imaging

Because incorrect administration of SABR may induce castrotrophic repercussions, geometric verification at the time of treatment is vital and should not be overemphasised. Metastatic seeding of a locally curable disease can occur due to a geographic miss, and injury to organs at risk can be life-threatening if treated accidentally. In order to guarantee patient safety and oncologic efficacy, it is not suggested to use portal films before each treatment and compare them to digitally reconstructed radiographs based on skeletal architecture as the only method of geometric verification. We instead recommend that you be able to see the lesion clearly when you treat it. Technologies like cone-beam computed tomography and CT-on-rails, which provide three-dimensional imaging in real-time, are at your disposal. After treatment has started, some linear accelerator systems can supplement positional precision with real-time orthogonal radiography. Both before and during SABR treatment, these tools can ascertain the patient's and lesion's position. We may be able to further reduce the PTV size to help spare important normal tissues as these technologies enhance accuracy and precision. Two on-board imaging systems that are currently in use are detailed below.

Spectral-Axis-Based and/or Time-Resolved SABR Methods

The importance of 4D CT image-guided SABR treatment planning in considering intrafraction tumour movements has already been mentioned (Chang et al. 2008b). Furthermore, it is important to resolve the uncertainties surrounding the migration of tumours in interfraction, changes in anatomy, and setup. For daily tumour site verification, the most precise method is cone-beam CT or CT on-rail-based volumetric image-guided distribution [56-58]. As its foundational configuration, megavoltage cone-beam CT (MVCBCT) imaging systems use therapeutic megavoltage X-rays and EPIDs installed on linac gantries. Several kV radiographs are generated as the gantry spins in kilovoltage cone-beam CT (kVCBCT) imaging. For soft tissue target delineation, kVCBCT images are preferable to MVCBCT images because of the higher contrast provided by the lower kV X-ray energy. A great platform for high-precision, image-guided radiation therapy is an integrated treatment unit, such the Varian Trilogy or the Elekta Synergy Unit. High-precision stereotactic radiosurgery and stereotactic radiotherapy can be delivered using the BrainLab AG with Exac Trac integrated IGRT system, which is part of the Novalis Body SystemTM from BrainLAB AG in Heimstetten, Germany. The device also allows for target localisation and setup correction. The two imaging subsystems used for image guidance are a kV stereoscopic X-ray imaging subsystem and an infrared (IR) tracking subsystem that operates in real-time. To track the location of infrared-reflecting markers—either on the patient's skin or on the treatment couch's reference frame—two infrared cameras are positioned on the ceiling. The first step in setting up a patient for a couch shift is automatically generated when the marker photos are compared to stored reference information. Additional visual feedback on the patient's position is provided by a video camera system. Following this, the X-ray imaging guidance system handles internal target alignment using implanted fiducial markers or bone landmarks. The optical tracking system (IR) and the fluoroscopic X-ray imaging system can collaborate to track the target's position and execute therapy interventions during treatment administration. Adaptive gating of the therapy beam and real-time correction of target offset are two possible treatment interventions that can be carried out utilising a 6D robotic couch. The True Beam accelerator, developed by Varian Medical Systems, is state-of-the-art technology that combines imaging, beam delivery, and motion control in a synchronised system. It offers efficient and precise targeting and delivery with the use of volumetric image guiding and VMAT. New technology is also in the works to treat the tumour as it moves by following its trajectory with the multi-leaf collimator's (MLC) moving leaves. Initial results suggest that such MLC-based devices have a fast enough response to accurately deliver the targeted dosage.

The CyberKnife SABR System with Image Guidance

Positioning of Fiducial Markers

When employing the CyberKnife to treat tumours that move with breathing, dynamic target tracking is essential. To facilitate image-guided tracking, this procedure necessitates the insertion of metallic fiducial markers into or near the tumour. A variety of methods exist for delivering markers before the first simulation, such as endovascular delivery, CT-guided percutaneous needle implantation, or a bronchoscopic operation. While remaining in close proximity to the lesion to be treated, the fiducial markers should be positioned such that their projections from the perspective of both in-room X-ray pictures are distinct, meaning they do not overlap and are well separated (by about 1 cm). While it's true that three markers are all that's needed for precise spatial localisation, it's common practice to use four or five markers just in case. Another method has been detailed, which involves implanting and monitoring a single marker located in the tumor's core. Using fiducial markers can be difficult due to the invasive nature of the implantation procedures. To be more specific, implantation-related pneumothorax is the most common acute complication of CyberKnife-based SABR for lung tumours. Pneumothorax is most likely to occur during the CT-guided percutaneous technique. When using bronchoscopic techniques, the risk of pneumothorax can be decreased.

Therapy Routines

The utilisation of inverse optimisation is a unique aspect of the CyberKnife treatment planning system. This enables "dose painting," the practice of simultaneously prescribing different dosages to high- and low-risk locations, such as those corresponding to microscopic and gross tumour extension, as well as simultaneous conformal targeting and normal tissue avoidance. The user can choose the settings, such as the size and number of collimators, and the structures that are excluded from beams. By utilising dynamic tracking, the CyberKnife is engineered to counteract target motion caused by respiration. Bear in mind that a breath-hold CT scan can be used to construct a tumour tracking plan. To avoid geometric misses during therapy delivery, the robotic manipulator tracks the route of the implanted fiducial markers. While the static plan may show one dose to normal structures in the area, in practice, this need not be the case. In the presence of 4D CT simulation, the treatment planning system can estimate the dynamic dose distribution by calculating the dosage on all 4D CT data set phases using dynamic fiducial tracking and then deformably propagating the doses to the reference phase. Traditional algorithms for calculating doses have a flaw in their modelling of dose accumulation and penumbra caused by lateral electron scatter as radiation beams pass across interfaces of materials with very differing densities. A pencil-beam (electronic path length, EPL) model generates precise dose distributions for targets in homogeneous density regions like the brain, according to the CyberKnife treatment planning system's standard dose calculation methodology. On the other hand, it produces very inaccurate results when applied to areas with very steep density gradients, as the air sinuses in the brain or the area immediately around the liver. You can choose to include Monte Carlo dose computation as an extra in the treatment planning system. It models the interactions produced by individual photons to generate correct dose distributions when simulating several events. Discrepancies in the calculated dose (covering a specified volume of the target) between the EPL and Monte Carlo algorithms for lung tumour treatment range from 10-20% in most cases to more than 80% in extreme cases; the biggest discrepancies are observed for small tumours encircled by air-filled lung parenchyma. Without conducting a comparable calculation, it is impossible to generalise or forecast the degree of error in the EPL computation, which constantly overestimates the tumour coverage. Consequently, definitive treatment of thoracic tumours should be seen as requiring the Monte Carlo module.

Treatment Administration and Visual Aids

The robotic manipulator is used to compensate for the target's motion caused by breathing by adjusting the linac position. I proceeded to use the Synchrony Respiratory Tracking System to begin the dynamic marker-based tumour tracking. The optical camera's signal determines the timing of a series of 10-15 X-ray photos that are taken before treatment begins. These images sample the internal marker coordinates from different parts of the breathing cycle. Using the coordinates of the exterior markers, a correlation model is constructed to constantly determine the location of the interior fiducials' centres of mass. The dynamic beam tracking is based on this computed or anticipated position. The acquisition of intermittent X-ray images is maintained throughout the delivery, as is the case with each beam. The correlation error is determined by comparing each new measurement of the position of the internal markers to the corresponding projected position. Assuming the correlation error stays below a user-specified threshold—often 3

mm—treatment will continue. Therefore, this cutoff serves as a rough upper limit for the system's tracking inaccuracy. If it is discovered to be exceeded, therapy is halted, further photos are obtained, and the correlation model is, if needed, reconstructed using the new images. Additionally, the XSight Lung Respiratory Tracking System offers an optional marker-less tracking capability for the treatment of certain lung tumours. The in-room X-ray images are automatically segmented in real-time according to the tumor's contrast, allowing for tumour localisation. Therefore, the system is most effective for lesions that are large enough (at least 1.5 cm) and situated on the periphery of the lung, away from other dense anatomical structures like the heart, diaphragm, and spine, so that they can be clearly seen on both of the in-room X-ray images. Consequently, only a small subset of lung tumours may be amenable to marker-less tracking at this time. Moreover, there has been no thorough clinical validation of its accuracy yet [59], and the only publications on the subject so far have focused on measuring its performance in artificial settings. However, there is indirect evidence of its accuracy from early clinical reports of favourable tumour control using this method, and the updated Xsight version may make it possible to treat more patients with this option. Since around 100-200 non-coplanar beams are administered sequentially, a standard lung tumour SABR plan takes 60-90 minutes to complete. The significance of a competent and caring treatment team is not diminished by the fact that the CyberKnife system's automatic image-guided motion adjustment is its most distinctive feature. The allure of letting the therapy session run autonomously with minimal user intervention is a possible stumbling block. To guarantee that treatment is administered correctly, it is essential to manually review the displayed images during the procedure and to interrupt for reimaging as needed, as mistakes can and do happen in automatic image analysis, such as fiducial marker extraction. Technical correctness and quality of treatment are ultimately determined by the therapy team and treating physicians, not by the technology itself.

Using Protons for Localised Imaging

The potential for serious toxicity to healthy tissues, such as the lungs, heart, oesophagus, and spinal cord, is a major obstacle in the treatment of non-small cell lung cancer patients. While photons inflict ionising damage all along the beam path, especially in the exit dose path, proton therapy has the ability to reduce radiation-induced toxicity by penetrating tissue and concentrating their energy at a specific depth, the Bragg peak, which is determined by the initial energy of the protons and the density of the tissue along the beam path. Proton radiation shows potential for protecting vulnerable organs from damage due to its depth-dose distribution, which is defined by dose deposition in a well defined target and limited exit dose. For patients with little lung capacity, this aspect of proton treatment might be life-saving.

Details to Think About When Doing Proton Therapy

The clinical value of a single-energy proton beam is limited due to its small Bragg peak. A spread-out Bragg peak is required to encompass the full tumour volume. This method generates a sequence of Bragg peaks by delivering many proton beams of varying energy. When added together, these peaks provide a consistent dosage distribution that encircles the target volume without reaching distant structures. Cobalt-Gray equivalents (CGE) are a measure of the dose given in proton beam therapy. This is because a conversion factor is required to find the amount of protons that would have the same impact as photon radiation dose prescriptions. The RBE is the ratio of the photon radiation dose needed to produce a certain biological effect in an experimental system to the proton radiation dose needed to produce the same biological effect. It is that simple. The RBE is typically believed to be 1.1 for proton therapy. At this time, there are two different approaches to proton treatment. Using 3D treatment planning tools, passive-scattering proton therapy (PSPT) delivers a conformal dose distribution. To shape the distal edge of the beam and limit the perimeter of the radiation field, a compensator is utilised during therapy. In contrast, scanning beam proton therapy treats the tumor's constituent "spots" (voxels) one by one by employing pencil-beam scanning with varying energies. An inverse planning method known as intensity-modulated proton therapy (IMPT) is usually used to develop pencil-beam scanning plans. In order to ensure that each of the hundreds of voxels within the tumour volume receives an adequate radiation dose, IMPT optimises the pencil beam's intensity and energy at the same time using an objective function. While pencil-scanning techniques, such as IMPT, provide superior conformality than passive-scattering techniques (PSPT), both of which limit dosage to normal structures by means of the Bragg's physical features. Still, there's less room for error with IMPT's higher precision, which can be a major drawback for mobile targets like early stage NSCLC.

Results in Clinical Practice with Proton Beam Therapy Photon-based SBRT is typically sufficient to accurately and safely treat the lesion in the majority of peripheral tumours. Patients whose tumours are situated superiorly near the brachial plexus or other sensitive central structures may benefit from hypofractionated proton treatment, which aims to improve the toxic-therapeutic ratio. Few clinical studies have examined the use of proton therapy in patients with early stage NSCLC because using photons to deliver the ablative dose-fractionation schemes described above can cause serious complications including severe pneumonitis, oesophageal ulceration, severe pneumonitis, tracheal or great vessel rupture, oesophageal ulceration, and spinal cord myelopathy. Using real-time fluoroscopy to confirm patient posture without taking any particular measures to account for breathing movements, Bush et al. (2004) administered 51-60 CGEs in 10 fractions to 68 patients. In this trial, the 3-year rates of local control and cause-specific survival were 74% and72%, respectively, despite the use of an older method and a BED below 100 CGE. Additionally, no patients had early or late oesophageal or cardiac toxicity, acute radiation pneumonitis, or any other side effects. A local control rate of 95% was reported at 24 months by Nihei et al. (2006), who treated 37 patients with 60 CGE administered in 6 portions. Their approaches included 3DCT modelling, respiratory gating, and real-time digital radiography for position verification. In 2007, Hata et al. administered 50 or 60 CGE in 10 fractions to 21 patients with stage I NSCLC; after 2 years, the overall survival rate was 74% and the cause-specific survival rate was 86%. The toxicity profile was encouraging, with no grade 3 or higher reactions, and the investigators reported that all irradiation tumours were controlled throughout follow-up, with the exception of one. Recently, a phase I/II prospective study of proton therapy was carried out by Chang et al. 2011b for inoperable stage IA (T1N0M0) NSCLC placed centrally or superiorly, any stage IB (T2N0M0) NSCLC, and selected stage II (T3N0M0) NSCLC. Chang et al. 2011b used a relatively mild hypofractionation to treat 18 patients with a total dose of 87.5 CGE delivered in 2.5 CGE fractions, in contrast to the aforementioned trials that utilised very large fraction sizes. Grade 4 or 5 toxicity had not been reported by any patient at the median follow-up time of 16.3 months. Side effects of grade 2 were most frequently reported by patients in the following percentages: dermatitis (67%), weariness (44%), pneumonitis (11%), esophagitis (6%), and chest wall pain (6%). Although 38.9% of patients experienced illness spread to distant organs or regional lymph nodes, 88.9% of patients were able to establish local control. In the case of big, centrally situated, or exceptionally

Practical Results of Proton Beam Therapy

The majority of peripheral tumours can typically be effectively and safely treated with photon-based SBRT. Patients whose tumours are situated superiorly near the brachial plexus or other sensitive central structures may benefit from hypofractionated proton treatment, which aims to improve the toxic-therapeutic ratio. Considerable morbidity and potentially fatal complications, including severe pneumonitis, tracheal or great vessel rupture, oesophageal ulceration, and spinal cord myelopathy, can occur in patients who are not adequately screened when photons are used to administer the ablative dose-fractionation schemes mentioned earlier (refer to the section on Toxicity and Challenges for more information) [60]. Using real-time fluoroscopy to confirm patient posture without taking any particular measures to account for breathing movements, Bush et al. (2004) administered 51-60 CGEs in 10 fractions to 68 patients. In this trial, the 3-year rates of local control and cause-specific survival were 74% and72%, respectively, despite the use of an older method and a BED below 100 CGE. Additionally, no patients had early or late oesophageal or cardiac toxicity, acute radiation pneumonitis, or any other side effects. A local control rate of 95% was reported at 24 months by Nihei et al. (2006), who treated 37 patients with 60 CGE administered in 6 portions. Their approaches included 3DCT modelling, respiratory gating, and real-time digital radiography for position verification. In 2007, Hata et al. administered 50 or 60 CGE in 10 fractions to 21 patients with stage I NSCLC; after 2 years, the overall survival rate was 74% and the cause-specific survival rate was 86%. The toxicity profile was encouraging, with no grade 3 or higher reactions, and the investigators reported that all irradiation tumours were controlled throughout follow-up, with the exception of one. Recently, a phase I/II prospective study of proton therapy was carried out by Chang et al. 2011b for inoperable stage IA (T1N0M0) NSCLC placed centrally or superiorly, any stage IB (T2N0M0) NSCLC, and selected stage II (T3N0M0) NSCLC. Chang et al. 2011b used a relatively mild hypofractionation to treat 18 patients with a total dose of 87.5 CGE delivered in 2.5 CGE fractions, in contrast to the aforementioned trials that utilised very large fraction sizes. Grade 4 or 5 toxicity had not been reported by any patient at the median follow-up time of 16.3 months. Side effects of grade 2 were most frequently reported by patients in the following percentages: dermatitis (67%), weariness (44%), pneumonitis (11%), esophagitis (6%), and chest wall pain (6%). Although 38.9% of patients

experienced illness spread to distant organs or regional lymph nodes, 88.9% of patients were able to establish local control. To achieve a high BED while letting normal tissues recover between fractions, slightly hypofractionated proton therapy is an attractive method for high-risk big, centrally positioned, or superiorly situated tumours.

Selecting Patients

All of the proton studies that were cited had excellent local control of the primary tumour and favourable toxicity profiles, even though they used different fractionation methods, dosages, placement, immobilisation, respiratory compensation, and geometric verification procedures. It is up to the individual patient and the doctor's discretion to decide whether proton therapy or photon-based treatments are more appropriate. There are three subsets of early-stage non-small cell lung cancer (NSCLC) patients who might benefit greatly from proton therapy rather than photon-based radiation. For example, patients whose photon plan poses an intolerably high risk of radiation pneumonitis, those whose tumours are too close to vital structures to undergo ablative photon irradiation, and those whose fields have seen recurring lesions. Researchers at MD Anderson Cancer Centre are currently working on a prospective randomised study that will compare ablative proton therapy with ablative photon-based radiotherapy in patients with early stage or recurrent non-small cell lung cancer (NSCLC). The study will use a dose of 50 Gy in 4 fractions to treat the patients.

Dutch SABR Approach

The standard of care for medically inoperable patients with stage I NSCLC in the Netherlands is SABR, which was started in 2003. Interestingly, previous studies in similar populations in the Netherlands have shown that the risk of finding benign lesions in these patients with new or growing lesions, which were FDG-PET positive and had CT-characteristics of malignancy, is less than 5%. Hence, the majority of the Dutch SABR trials found that 60% of patients were clinically diagnosed with stage I NSCLC using pictures alone, without pathological confirmation. Overall survival and local control were not significantly different between patients with and without pathologically confirmed illness following SABR. The tumour size and location dictated the number of fractions used to provide a 60 Gy SABR dose in the Dutch experience; these might be 3, 5, or 8. There were three fractions given to tumours classified as T1, five fractions given to tumours classified as T1 that had extensive contact with the mediastinum or thoracic wall, and eight fractions given to tumours classified as T2 that were located near important structures. Every dosage was intended for the 80% isodose region surrounding the PTV. The BED10 Gy is 105 Gy10 or greater for all recommended dosages. Longitudinal follow-up data from 676 patients showed overall survival rates of 27.3% after 5 years and 52.2% after 3 years. At the 3-year mark, actuarial local control was 91.4%. With a p-value of only 0.031, local control was 93.7% for T1 tumours and 88.5% for T2 tumours after 3 years. When comparing patients with lesions situated in the centre vs those with lesions located on the periphery, there was no discernible change in toxicity. The three fractionation systems did not differ much in terms of local control. Three years later, the actuarial far failure rate was 17.0% and the regional failure rate was 9.3%. A randomised phase III experiment called ROSEL was started in 2010 to compare radiosurgery with surgery for operable early stage NSCLC patients, but it was closed due to inadequate accrual. The trial was for operable patients with stage I NSCLC. Having said that, the research was crucial in helping the Dutch apply SABR. Other academic and non-academic centres have been able to apply SABR with the support of the produced quality assurance criteria. In some regions, the public health benefits of this SABR discovery are already visible. The percentage of older patients with early-stage lung cancer who did not receive treatment decreased and their median survival improved after SABR was implemented in the Netherlands, according to population-based cancer registries.

Results and Failure Patterns

Cancer Stage I Unresectable by Medical Means

Patients treated with SABR for early stage NSCLC might anticipate great treatment, recovery, local tumour control, and, in numerous instances, oncologic cure, provided the aforementioned dosimetric and technical factors are optimised in a controlled environment with strict quality assurance. High primary lesion control and encouraging overall survival have been shown in prospective SABR investigations. As a general rule, local control rates were 90% when a BED of 100 Gy was administered to the tumour volume, not merely the isocenter. Regional lymph node recurrence occurred in 3- 10% of cases, while distant metastasis accounted for 10-25% of failure sites. Most notably,

from 2004 to 2006, 59 patients were treated in RTOG Trial 0236, which used established SABR techniques with explicit quality assurance procedures. The tumours in their early stages were exposed to 60 Gy over three parts, with a total of 54 Gy after adjusting for heterogeneity. One local failure within two centimetres of the initial lesion has happened up to the time of publishing, leading to a three-year actuarial local control rate of 98.0% (Timmerman et al. 2010). Conventional radiation therapy and supportive care were once the gold standards for inoperable patients, but SABR has now replaced them.

Renal Cancer Recurrence and Other Metastatic Sites

Those who have undergone traditional fractionated radiation therapy for the chest and have now developed a new primary or experienced a local recurrence make up one category. The dangers of operating or treating in an already irradiated field restrict the use of traditional radiation treatment and surgery in this context. Palliative chemotherapy is usually used to treat them. Thankfully, in these circumstances, re-irradiation with SABR can provide in-field local control of more than 90% with acceptable toxicity. Another target that shows potential for SABR is pulmonary metastases. At 2 years, a 96% local control rate was achieved in a phase I/II research involving 38 patients treated with SABR for 1-3 pulmonary metastases from a variety of primary locations, including non-small cell lung cancer (NSCLC). Only 3% of individuals had symptomatic pneumonitis, and only 8% of patients had grade 3 toxicities.

Operable or Nearly Operable Stage I Non-Small Cell Carcinoma

Is SABR a better alternative to surgery for patients with early stage lung cancer who are eligible for lobectomy or wedge resection? This is the more contentious subject. Regrettably, for individuals who are surgical candidates, no published randomised data directly compare SABR to surgery. The ACOSOG Z4099/RTOG 1021 trial is a randomised phase III comparison of SABR with sublobar resection. Due to inadequate accrual, the ROSEL study in the Netherlands had to close early. The experiment randomised patients with stage IA NSCLC to either surgery or SABR. The international STARS trial, which is sponsored by Accuray Inc. and has a similar design, has started collecting patient data and is expected to finish and publish its findings in 2014. Meanwhile, for patients who are able to undergo surgery, preliminary evidence indicates that SABR could be a comparable alternative. For instance, a Japanese multi-institutional study that looked back at medically operable patients indicated that, for those treated to a BED higher than 100 Gy, the overall survival rate was 70.8% and the rate of local recurrence was 8.4% after 5 years. A more recent article by the same team corroborated these findings. This is in line with the results seen in the lobectomy group of the North American Lung Cancer Study Group (LCSG) 821 trial, which compared lobectomy with wedge resection; after 5 years, patients in that group had a 6 percent chance of local recurrence and a 70 percent chance of overall survival. William Beaumont Hospital offered a more direct comparison, but it was retrospective. Patients at that facility who were considered to be on the verge of becoming operable were given SABR or sublobar (wedge) resections between the years 2003 and 2008. While both SABR and sublobar resection resulted in the same rates of distant metastases and cause-specific survival, a nonsignificant trend towards a reduced risk of local and regional recurrence was noted in the SABR group, according to the center's retrospective study. Washington University in St. Louis conducted a separate single-center investigation that utilised propensity matched score analysis. They found that both SBRT and surgery had equal rates of local recurrence and disease-specific survival. This study's 70% lobectomy rate is very noteworthy. Researchers in Japan and the Netherlands have published the results of two single-arm studies that used SABR to treat operable patients. These studies provide prospective data. Nagata et al. (2010) just published the results of the JCOG 0403 study, which is in Japan. Patients with operable stage IA were given 48 Gy divided into four divisions in this phase II trial. Despite their advanced years, all sixty-five patients included in the study were in good health, with a performance status of 0-2, a PaO2 C of 60 torr, and a FEV1.0 C of 700 mL. The median age of the patients was 79 years. On top of that, thoracic surgeons thought they were operable. Over the course of three years, with a median follow-up of 45.4 months, 76.0% of patients survived the disease, and 68.5% of patients did not experience local progression. Pneumonitis (3.1%), hypoxia (1.5%), dyspnea (3.1%), and chest discomfort (1.5%), all of which were classified as grade 3 toxicity. Patients who were considered "potentially operable" were observed in the Dutch trial after they had SABR rather than surgery. With a median age of 76 years, this somewhat younger patient group had an overall survival rate of 84.7% and an actuarial 3-year local control rate of 93.0%. While evidence from randomised trials would be more compelling, it's difficult to believe that surgery would have improved outcomes for the potentially operable patients in these two trials. We are all waiting

impatiently for the findings of the RTOG's single-arm study of operable patients that is currently underway in the US. In conclusion, the current body of evidence indicates that SBRT and surgical approaches may have comparable efficacy in terms of results. We stress, however, that there is a paucity of level I data, and that lobectomy is still the gold standard at the moment. We are hopeful that the promising early results will encourage radiation doctors and patients to participate in the trials that will answer this crucial topic. To conclude, it should be mentioned that the problem of local therapy will be further complicated by the advent of novel systemic chemotherapies, molecularly targeted medicines, and biological markers that identify subtypes of lung cancer. The future of SBRT is uncertain since it is not known if new drugs will be more effective at sterilising the tumor's surrounding lobe or at preventing distant metastases; hence, decisive surgery to local and regional structures is becoming increasingly important. As systemic drugs become more widely used in radiotherapy, there are still unanswered problems about when to administer the treatment (sequentially vs. concurrently) and whether to focus on the tumour alone or on both the tumour and nearby structures. At the end of this promising age for multimodality lung cancer therapy, treatment guidance will need to come from empirical trials.

Dangers and Obstacles

While stereotactic body radiotherapy (SABR) has many positive effects on patients and helps them avoid surgery's perioperative and long-term risks, poorly designed treatments using ablative radiation dosages can cause significant harm to healthy tissues. Thus, for the benefits of SABR to be meaningful for each patient, it is essential to choose candidates based on their anatomy. Since the lung is an organ that runs parallel to the chest wall, it can usually withstand the loss of functioning alveolar units immediately surrounding a neoplasm, making SABR a more acceptable choice for lesions situated on the lung's periphery but distant from the chest wall. Grade 3-4 toxicity rates in patients with peripheral tumours are currently between 0% and 15% due to modern advancements in SABR technical execution and quality assurance. The most prevalent hazard in this category is radiation pneumonitis. To prevent this, studies have indicated that restricting the volume of the lungs receiving 20 Gy (V20) to 5-20% of the total volume is a good threshold. Injury to mediastinal structures can be severe if the lesion is located in the centre and surgical ablation is performed. Seventy patients with tumours situated either peripherally or centrally were studied in a phase II trial that administered 60-66 Gy in three fractions without heterogeneity correction. The results showed that 83% of patients with peripherally located tumours were free from severe toxicity after two years, while 54% of patients with centrally located tumours were free. A decrease in pulmonary function, pneumonitis, and pleural effusion were among these effects. All six deaths—four in individuals with central tumors—were probably treatment-related. Patients whose tumours are located within 2 centimetres of the central airways should not undergo the 60 Gy in 3 fraction treatment, according to the study's authors. Torsion of the trachea or major vessels, ulceration of the oesophagus, and myelopathy of the spinal cord are other extremely unusual but catastrophic toxicities of central structures. Preventing these toxicities requires meticulous treatment planning to avoid overdosing these tissues with IMRT conformal avoidance or forward-planned 3D therapy with blocking. When blocking reduces the amount of radiation that reaches the tumour, an additional tactic is to adjust the SABR regimen's total dose and fraction size. Researchers at MD Anderson Cancer Centre found that a more conservative regimen of 50 Gy divided into four divisions was effective in treating 27 individuals with tumours placed either centrally or superiorly. Considering the tumours' central placement, the complication rates were moderate. Out of the total number of patients, fourteen (16.8%) experienced grade 2 pneumonitis, and eleven (11.1%) developed skin toxicity and/or chest wall pain. Optimising the SABR plan utilising the dosimetric approaches outlined in Sect. Reduce the likelihood of toxicities and enhance dose distribution to important normal structures by using 3.4. For centrally situated lesions, another reported regimen employed 70 Gy in 10 fractions; it also preserved tumour control and had reassuring toxicity rates. As part of ongoing clinical research on the best SABR regimen, the RTOG is doing two trials (RTOG 0813 and RTOG 0915) to determine the best dose and fractionation for various SABR populations. Serious harm, including neuropathic consequences and rib fractures, can occur from tumours close to the brachial plexus and the chest wall. The rate of brachial plexopathy was 19.4% in a series of 36 patients with apex tumours who were treated with a three-fraction regimen to a median dosage of 57 Gy. Also recorded were cases of neuropathic pain, weak arms, and paralysis of the extremities in one individual. The highest risk of neuropathy (46%), which is now considered the maximum acceptable dose for this structure, was observed in patients who received more than 26 Gy to the brachial plexus. In a big institutional series of 265 patients, 17% of those with tumours within 2.5 cm of the chest wall experienced chronic

pain in that area, suggesting neuropathic chest wall pain. Obesity and diabetes were linked to the onset of chronic pain in this research. Two studies have looked at the frequency of rib fractures, which is another possible consequence. In the first trial, 42 individuals experienced nine fracture occurrences, while 60 patients had five in the second trial. It was discovered that the incidence of both chest wall discomfort and rib fracture begins to increase with a dose of 30 Gy. In order to decrease the frequency of toxicities to the chest wall, we restrict the volume of the chest wall to less than 50 cc at MDAnderson Cancer Centre. A total of 18.9% of patients with recurrent disease treated with SABR who had previously undergone chest radiation developed grade 3 radiation pneumonitis (RP), and 1.4% developed grade 5 RP. Factors such as ECOG performance status, FEV1 (B65%), previous PTV (bilateral mediastinum), and composite V20 (C30%) were found to be predictive of the incidence of pneumonitis in this particular clinical setting.

Imaging Variations Following SABR

Imaging follow-up following therapy presents a distinct issue specific to SABR. Parenchymal alterations, including fibrosis and chronic pneumonitis, can manifest in a variety of ways on surveillance CT scans. Some of the observed phenomena include ground-glass opacities, focal consolidation and scarring, and diffuse consolidation. The problem with using the RECIST criteria and other similar diagnostic techniques to assess local response is that the broad range of radiographic changes can be mistaken for tumour recurrence. Promising as a way to differentiate post-irradiation effects from live tumours, positron emission tomography (PET) isn't very sensitive in the near term, especially as areas treated with SABR can retain [18F] fluorodeoxyglucose avidity for as long as a year after treatment. In order to clarify this uncertainty, several centres employ certain PET results, like a high post-SABR standardised uptake volume ([5]) beyond 6 months following SABR, to improve the selection of patients for confirmatory biopsy. The absence of obvious tumour progression after treatment is generally reassuring, and a radiologist with experience and knowledge of post-SABR effects should be able to spot worrisome radiographic alterations that need pathologic examination, so the diagnostic hurdles aren't insurmountable. Some early research has shown that salvage surgery after SABR is possible, therefore this identification is crucial.

CONCLUSION

Treatment of advanced-stage, low-performance, or concomitant patients with early-stage lung cancer might be difficult. To ensure the safe, effective, and ethical application of this technology, it is necessary to apply proper procedure, which involves reliable immobilisation, accurate tumour targeting, and precise verification of dose delivery. Treatment planning provides a number of dosimetric options for optimising dose while minimising toxicity. A high rate of local control and overall survival can be achieved with SABR, making it the standard of therapy for patients who are medically inoperable. Lesions situated in the middle or on top of the body can also be treated with a different dosage and fractionation strategy, however the toxicity is much higher for tumours positioned on the periphery. Proton-based SABR may potentially.

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