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#### Chapter

### Spinal Stereotactic Body Radiotherapy (SBRT) Planning Techniques

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#### **Abstract**

Stereotactic body radiotherapy (SBRT) delivers a highly conformal and hypofractionated radiation dose to a small target with minimal radiation applied to the surrounding areas. The spine is an ideal site for SBRT owing to its relative immobility, the potential clinical benefits of high-dose delivery to this area, and the presence of adjacent critical structures such as the spinal cord, esophagus, and bowel. However, with the potential for radiation myelopathy if the dose is delivered inaccurately or if the spinal cord dose limit is set too high, proper treatment planning techniques for SBRT are important. Intensity modulation techniques are useful for spinal SBRT because of a rapid dose falloff and spinal cord avoidance. In this chapter, various planning techniques will be discussed and reviewed.

Keywords: SBRT, spine, IMRT, IMAT, tomotherapy, CyberKnife

#### 1. Introduction

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Stereotactic body radiotherapy (SBRT) was developed using the concepts of stereotactic radiosurgery (SRS). SRS was conceived by neurosurgeons and physicists in Sweden to allow the delivery of radiation to precise targets in the brain while minimizing injury to adjacent areas. The procedure delivers a high dose of radiation to the target accurately focused using multimodality imaging, such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography/CT (PET/CT). The total dose is divided into several smaller doses of radiation, administered on separate days of treatment, typically in a single fraction or a few fractions. SRS treats tumors by destroying and distorting the DNA of these cells, in the same way as other forms of radiotherapy. As a result, these cells lose their ability to reproduce and die. Applied to the treatment of body tumors, the technique is called SBRT [1–4].

SBRT is also known as stereotactic ablative radiotherapy (SABR). SBRT ablates tumors by delivering precise and intensive radiation, guaranteeing minimal normal tissue complications. The characteristics of SBRT are summarized as follows: (1) a limited number of high dose-per-fraction treatments with a biologically equivalent dose (BED) of at least 75–100 as a minimum or even higher; (2) fields only slightly larger than gross tumor volume (GTV) with high accuracy even for moving targets, including the entire target with margins of 0.5–1.0 cm (i.e., exact delivery to tumor targets, sparing normal tissue); (3) dosimetry constructed to be very conformal,

with sharp gradients from high- to low-dose areas; and (4) secure patient fixation during treatment and accurate duplication of patient position between simulation and treatment [2, 5–8].

Because of the high dose in a single fraction or fewer than five fractions, organs at risk (OARs) can be greatly affected by slight positional errors. Therefore, positional errors should be minimized. The margins of expansion can be reduced through the immobilization and control of respiratory motion of patients. Various commercial treatment delivery units in conjunction with the immobilization and respiratory motion control systems are available for the delivery of SBRT.

SBRT is currently both in use and being investigated for use in treating malignant or benign small- to medium-sized tumors in the body and at common disease sites, including the head and neck, lung, liver, abdomen, spine, and prostate. In particular, up to 70% of patients with malignancies are found to have skeletal involvement on postmortem examination, with the spine being the most common location [9]. For the treatment of spinal tumors, an extremely rapid dose falloff between the vertebral body and the spinal cord should be achieved [10, 11]. Implementation of correct beam-shaping and image-guided techniques has improved SBRT safety margins as well as accuracy and efficiency while accurately meeting 3D tumor contours. Spinal SBRT demands the highest accuracy in dose placement. In addition to patient fixation and multi-image guidance, a sophisticated treatment planning system that accurately models highly modulated small field beams is an indispensable factor in achieving high accuracy of radiation delivery.

To achieve this high accuracy, appropriate treatment planning technique should be used. Therefore, we will discuss various planning techniques for spinal SBRT in this chapter.

#### 2. Spinal stereotactic body radiotherapy

#### 2.1 Spine

The spine is a frequent site of metastases from primary cancer of the prostate, lung, breast, and kidney. After the lung and liver, the skeletal system is the most frequent site of metastases [12, 13], and 30% of all patients with cancer develop bone metastases [12, 14, 15]. In particular, bone metastasis occurs in 85% of patients with breast, prostate, and bronchial carcinoma [12, 16]. Approximately 50% of all bone metastases occur in the spinal cord. Of these, 60–80% are located in the thoracic spine, followed by 15–30% in the lumbar spine and less than 10% in the cervical spine [12, 13].

If left untreated, spinal metastases can cause axial pain, vertebral body fractures, radiculopathy, and the debilitating complications of metastatic epidural spinal cord compression (MESCC) [9]. The major complications of spinal metastases include neurologic dysfunction [12, 17, 18] and potential hypercalcemia, reduced activity, and bone fractures, resulting in a reduced quality of life [12, 16].

In general, primary spinal tumors are treated surgically, with the goal of maximal tumor removal. Numerous important blood vessels and adjacent organs surround the vertebrae. In particular, the spinal cord located in the vertebrae is a part of the central nervous system, which includes sensory and motor nerves. Complete resection of a tumor while preserving the nerve function of the spinal cord is difficult. In addition, vertebral instability due to tumor destruction or complete resection of the tumor must be considered, and fusion or fixation is often required for stability of the vertebrae. Depending on the malignancy of the tumor or the difficulty of complete resection, the patient may be treated with radiotherapy.

#### 2.2 Radiotherapy for spinal tumors

#### 2.2.1 Conventional method

Traditional radiotherapy methods of treating spinal tumors use large field radiation to treat the entire pathological vertebra and to treat one or two vertebral bodies, generally above and below the disease. This practice prevents missing the tumor owing to the limitations of diagnostic imaging and localization. In addition, the irradiation field of this technique is large but safe in the volume of the normal tissues irradiated because of the low biological effectiveness.

Large field radiation for spinal metastases has been the standard approach with outcomes of ~30% complete pain response and ~70% any response. The main limitation of the dose prescribed by traditional radiation techniques was the spinal cord. Overdosing radiation to the spinal cord has the devastating consequence of radiation-induced myelopathy that can leave the patient paralyzed. In addition to radiation myelopathy, possible toxicities include vertebral compression fractures and pain flares. Owing to the limitations of technology to prevent overdosing, clinical trials of high-dose effects on spinal metastasis have not been possible [19].

#### 2.2.2 Stereotactic body radiotherapy

To overcome the limitations of conventional radiotherapy for the spine, hypofractionated treatment has been proposed, to deliver a high dose per fraction (typically 10–20 Gy/fraction), in contrast to the conventional fractionated treatment (2 Gy/fraction). The cumulative BED is significantly higher than that received in conventional treatment. Accurate delivery is of utmost importance owing to the high fractional dose and a small number of fractions. The delivery of an ablative dose to the target and rapid falloff doses away from the target enables minimization of the treatment toxicity to a tolerable level [20, 21]. In addition, there are other characteristics that distinguish SBRT from conventional radiotherapy, such as the number of beams used for treatment, the frequent use of non-coplanar beam arrangements, small or no beam margins on the penumbra, and the use of inhomogeneous dose distributions and dose-painting techniques 'including IMRT'. All of these technology improvements result in the highly conformal dose distribution that characterizes the SBRT technique [2].

Hypofractionated spinal SBRT has been shown to effectively and rapidly alleviate pain and improve neurological function in patients with or without epidural cord compression. SBRT allows minimal radiation exposure outside the target; the most significant problem associated with this procedure is related to spinal cord dose tolerance. Depending on the vertebral level of spinal metastasis, adjacent organs should be considered OARs. The tolerance of OARs to radiation from conventional fractionated radiotherapy is based on the entire organ or on a considerably large irradiated volume. SBRT delivers a highly conformal, hypofractionated radiation dose to a small target with minimal exposure of the surrounding areas to radiation [22].

A new radiotherapy technology that allows for intensity-modulated radiotherapy (IMRT) has emerged with spinal SBRT. IMRT is a technique designed to deliver a high biologically effective dose only to tumors within the vertebra for the purpose of tumor regression through permanent local control. The technique allows radiation beams to avoid the spinal cord, and even though a high dose is delivered to tumors, the dose received by the spinal cord is below the toxic threshold dose [23]. More details will be discussed in Section 3.

**Table 1** lists maximum dose limits to a point or volume within several critical organs recommended for SBRT in one fraction (refer to TG-101 for

Serial tissue	Max critical volume	Max dose in critical volume (Gy)	End point (≥ Grade 3)
Spinal cord	<0.035 cc	14 Gy	Myelitis
	<0.35 cc	10 Gy	
	<1.2 cc (SBRT only)	7 Gy (SBRT only)	
Cauda equina	<0.035 cc	16 Gy	Neuritis
	<5 cc	14 Gy	
Sacral plexus	<0.035 cc	18 Gy	Neuropathy
	<5 cc	14.4 Gy	
Esophagus*	<0.035 cc	16 Gy	Stenosis/fistula
	<5 cc	11.9 Gy	
Ipsilateral brachial plexus	<0.035 cc	17.5 Gy	Neuropathy
	<3 cc	14 Gy	
Heart/pericardium	<0.035 cc	22 Gy	Pericarditis
	<15 cc	16 Gy	
Great vessels*	<0.035 cc	37 Gy	Aneurysm
	<10 cc	31 Gy	
Trachea* and larynx	<0.035 cc	20.2 Gy	Stenosis/fistula
	<4 cc	10.5 Gy	
Skin	<0.035 cc	26 Gy	Ulceration
	<10 cc	23 Gy	
Stomach	<0.035 cc	16 Gy	Ulceration/fistula
	<10 cc	11.2 Gy	
Duodenum*	<0.035 cc	16 Gy	Ulceration
	<5 cc	11.2 Gy	
Jejunum/ileum*	<0.035 cc	15.4 Gy	Enteritis/obstruction
	<5 cc	11.9 Gy	
Colon*	<0.035 cc	18.4 Gy	Colitis/fistula
	<20 cc	14.3 Gy	
Rectum*	<0.035 cc	18.4 Gy	Proctitis/fistula
	<20 cc	14.3 Gy	
Renal hilum/vascular trunk	<2/3 volume	10.6 Gy	Malignant hypertension
Parallel tissue	Critical volume (cc)	Max dose in critical volume (Gy)	End point (≥Grade 3)
Lung (right and left)	1000 сс	7.4 Gy	Pneumonitis
Renal cortex (right and left)	200 сс	8.4 Gy	Basic renal function

**Table 1.**One fraction dose constraints of several critical organs from RTOG 0613 [24].

multiple-fraction dose constraints [2]). The recommended dose constraints are shown in max critical volume and the maximum dose to the given volume for each organ. These limitations have been determined based on the widely accepted radio-surgery norms currently in practice. Regardless of these limitations, the participating centers are encouraged to adhere to the prudent treatment planning principle to avoid unnecessary radiation exposure to critical normal structures [24].



**Figure 1.**Commercial treatment delivery units. From left to right are versa HD (Elekta AB), Radixact (Accuray Inc.), and CyberKnife M6 (Accuray Inc.).

#### 2.2.3 SBRT delivery systems

Various commercial treatment delivery units can be used to deliver SBRT [1, 5, 7], as shown in **Figure 1**. They all have the capability of image-guided radiotherapy, enabling tumor or target localization prior to treatment delivery and allowing treatment setup uncertainty to be significantly reduced. All delivery units, with the exception of proton therapy, used as photon-based SBRT, are linear accelerators (LINACs). There are several types of image-guidance equipment: 2D imaging types, including room-mounted or gantry-mounted orthogonal kilovoltage (kV) radiographs and fluoroscopy, and 3D imaging types including kV or megavoltage (MV) cone-beam CT (CBCT) and CT-on-rails in room.

In addition to general LINACs, there are many types of treatment systems. The CyberKnife (CK, Accuray Inc., Sunnyvale, CA, USA) unit has a six-axis robotic manipulator that enables delivery of the beam to the target from many different directions in order to minimize radiation exposure to nearby organs. A pair of orthogonally positioned imaging systems enables monitoring of the target motion, with automatic correction. CK is a commonly used modality for SBRT owing to its highly conformal dose distributions, steep gradient, and near real-time imageguidance system. The helical tomotherapy (HT, Accuray) unit is a special device performing continuous 360° rotations using a binary multi-leaf collimator (MLC), with the treatment couch moving continuously during the treatment [1].

Each treatment delivery system has strengths and weaknesses. An appropriate treatment delivery system and corresponding optimal planning technique should be used for successful and safe treatment.

#### 3. SBRT planning techniques

SBRT is a high-precision radiotherapy technique that utilizes the high doses of radiation in a single fraction or a few fractions, as mentioned in the above sections. In principle, three-dimensional conformal radiotherapy (3D-CRT) planning can be applied to SBRT. When the beams at multiple angles are concentrated at the center of small lesions, a high-dose heterogeneity that contributes to a steep dose gradient

at the target edge appears and may be desirable in terms of normal tissue sparing and dose escalation to the GTV [1].

To treat a spinal tumor, conventionally fractionated 3D-CRT modifies the beam shape to match the projection of target volume at each gantry angle using an MLC. The accuracy of the shape of the beam projected onto the target depends on the width of leaves. MLC leaf widths of 2.5–10 mm have been reported for use in SBRT planning [25, 26].

However, delivery to the target is limited by tolerance of normal tissues, particularly the spinal cord, so it is necessary to irradiate the target with lower dose. In suboptimal cases, several side effects can occur, such as paraplegia, pain, increased steroid use, and reduced survival rate.

#### 3.1 Intensity-modulated radiation treatment

The development of IMRT was a major improvement over 3D-CRT for SBRT [27]. IMRT allows for the radiation dose to conform more precisely to the shape of the tumor by modulating the intensity of the radiation beam and allows higher radiation doses to be focused to regions within the tumor, sparing the surrounding normal critical structures. In particular, when treating spinal tumors, intensity modulation allows production of a concave-shaped dose distribution with the exception of the spinal cord.

The IMRT technique uses computerized inverse planning. Conformal radiotherapy is forward planning and depends on the skills of the treatment planner to determine the number, shape, and orientation of the beams. Inverse planning, in contrast, specifies the plan outcome in terms of the tumor dose and normal structure dose limits. The computer system then adjusts the beam intensities to identify a configuration best matched to the desired plan [28].

During the procedure, each beam is divided into several beam elements (beamlets) of a few millimeters, and the relative weight is optimized so that the desired dose distribution appears. The optimization process involves inverse planning in which beamlet weights or intensities are adjusted to satisfy predefined dose criteria for the composite plan. When optimization is complete, an optimized fluence map generates a sequence of MLC leaves for each beam. The field at one gantry angle is subdivided into a set of subfields irradiated at a uniform beam intensity level. The subfields are shaped by the MLC, and the intensity-modulated field is obtained by summing several subfields.

The two most common methods of IMRT delivery are segmental (step-and-shoot) and dynamic (sliding window). The difference between the two is the motion of MLC at a given gantry angle. In segmental MLC delivery, the beam is turned off while the leaves move until the next subfield is prepared. The advantage of the segmental MLC method is that it is easy to plan and no additional dose can occur while the MLC is moving to create the next subfield. On the other hand, the dose delivery is slow owing to the delay in turning the beam on and off, resulting in an increase in treatment time. In the dynamic MLC delivery, the MLC leaves are moving during irradiation. Each pair of leaves sweeps across target volumes under computer control. Dynamic MLC delivery offers better dose homogeneity for target volume and shorter treatment time in comparison to the segmental MLC; however, the larger total irradiated dose is a disadvantage.

Compared to 3D-CRT, the dose distribution can be made even more sophisticated because target coverage and avoidance of critical structures located adjacent to the target volume are better. The more sophisticated implementation of SBRT has become possible with the IMRT technique. The technique mentioned in this section (Section 3.1) was the IMRT technique with a fixed gantry, and IMRT with a rotating gantry will be discussed in the following section (Section 3.2).

#### 3.2 Intensity-modulated arc therapy

Intensity-modulated arc therapy (IMAT) is a combined technique of IMRT and rotational treatment. When performed for a C-shaped target with a sensitive structure in the concavity of the "C," like a spinal tumor, the rotational treatment has a dosimetric advantage. The result of simulation that supports this is that when all the planning parameters except the beam angle number are constant, the dose becomes more homogeneous in the tumor and decreased in the critical structures as the number of angles increased [29].

IMAT uses rotational cone beams of varying aperture shapes and varying dose weightings to achieve intensity modulation. However, the speed of rotation cannot have frequent and drastic variations owing to the weight of the LINAC gantry; therefore, the variations in dose weighting are primarily achieved through varying the machine dose weight. MLC moves dynamically to shape each subfield while the gantry is rotating and the beam is on continuously [30]. Arcs are approximated as multiple-shaped fields in a regular angular interval. One subfield is delivered at each arc. The next new arc is started to deliver the next subfield and so on until all the planned arcs and their subfields have been delivered. That is, overlapping arcs create intensity modulation.

To create more effective treatment plans, various techniques have been purposed within IMAT. Volumetric-modulated arc therapy (VMAT) and modulated arc therapy (mARC) are examples of such techniques. VMAT is a single or multi-arc form of IMRT technique that changes the dose rate and gantry speed while the gantry is rotating. Currently there are several VMAT systems available under various names (RapidArc, Varian Medical Systems, Palo Alto, CA, USA; SmartArc, Philips Radiation Oncology Systems, Fitchburg, WI, USA; and Elekta VMAT, Elekta, Stockholm, Sweden) [31]. The mARC technique as an alternative to VMAT is a rotational IMRT irradiation with burst mode delivery. Both the dose rate and gantry speed are modulated to allow for delivery of the correct dose per IMRT segment, and an MLC velocity servo is required to continuously adjust the leaf velocity to facilitate accurate, and timely, leaf positioning [32].

The technique is similar to HT, which is an IMRT technique that rotates in a helical form and will be discussed in Section 3.3. As compared with HT, IMAT has certain advantages: (1) IMAT eliminates the need for transferring the patient during treatment and avoids abutment issues as seen with serial HT, (2) IMAT retains the ability to use non-coplanar beams and arcs, and (3) IMAT uses a conventional LINAC; thus, complex rotational IMRT treatments and simple palliative treatments can be delivered with the same treatment unit [30].

The main advantages of rotational therapy compared to fixed-gantry IMRT are improved conformity of the dose distribution in the high-dose regions, as well as possible reduction of the treatment time. The short treatment time can lead to improved patient comfort and reduce the risk of movement. Moreover, shorter treatment times can be biologically beneficial. Radiation survival is not only a function of the total dose delivered but also depends on the duration of radiation delivery [33, 34]. IMAT offers the efficient use of monitor units (MUs). The number of MUs per treatment is correlated with the amount of scatter dose and leakage radiation, which could be important in view of the induction of secondary malignancies [35]. The decrease in MUs achieved with IMAT partly addresses this issue, which is one of the major concerns with IMRT [36].

However, the complex nature of IMAT planning has been one of the primary barriers to routine clinical implementation. From one angle to the next in each VMAT arc, leaf motion between adjacent angles is limited by leaf travel speed and gantry rotation speed. Therefore, the technique has disadvantages such as difficulty and complexity of planning.

#### 3.3 Helical tomotherapy

HT is a radiotherapy modality that combines helical CT scanning with an MV linear accelerator. A 6 MV LINAC rotates on a ring gantry at a source-axis distance (SAD) of 85 cm, and the beam passes through a primary collimator into a fan-beam shape. During treatment, the ring gantry continuously rotates, while the couch is continuously translated through the rotating beam plane. The dose is thus delivered in a helical fashion. The ring gantry also contains a detector system that is mounted opposite the accelerator and is used to collect data for megavoltage CT (MVCT) acquisition. A beam stopper is used to reduce room-shielding requirements [37].

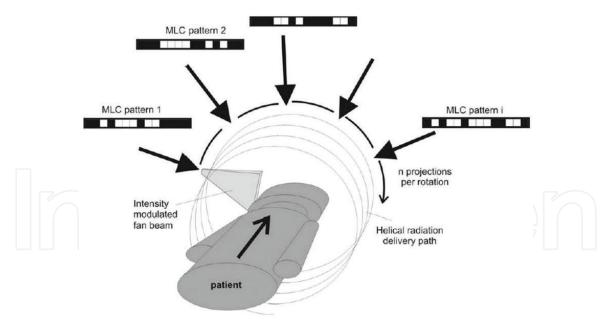
The MVCT in HT is used as a tool to enhance image-guided daily treatment setup and positioning of the patient. Because SBRT usually requires a longer treatment period owing to the use of high-dose hypofraction, the patient must be fixed in place to limit the patient's movement during treatment. However, patients with vertebral metastases, in particular, often move involuntarily during treatment owing to back pain that cannot be controlled. Therefore, it is important to ensure the accuracy of high-dose delivery and to avoid side effects of OARs on intrafractional movement. A daily MVCT image scan is generated prior to treatment to ensure accurate delivery of each treatment according to the patient's anatomy on a particular day. This MVCT is integrated with the kilovoltage CT (kVCT) imaging plan to provide a reference for patient setup and positioning [38].

The fan-beam has an extension of 40 cm in the lateral direction and smaller or equal to 5 cm (typically 1.0, 2.5, and 5.0 cm) in the longitudinal direction at the isocenter. With the use of a compressed air-driven multi-leaf (64 leaves) binary collimator (MLC), radiation beams are shaped, and their intensities are modulated. The leaves are mounted on two opposite blocks, and each individual leaf is driven from open to closed state. The intensity modulation is achieved by controlling the length of time each leaf is open. Each leaf has a width of 6.25 mm (40 cm divided by 64 leaves) and rapid transitioning (about 20 ms); thus it can produce a sufficiently accurate shape even within a short rotation period. Therefore, HT offers a very useful treatment modality of spinal SBRT by implementing image-guided radiation therapy (IGRT) and IMRT techniques.

For the treatment planning of each rotation, a rotation is divided into 51 projections (360°/7° = 51). For each projection, each MLC leaf has a unique opening time as shown in **Figure 2** [39]. Unlike the usual LINAC radiotherapy, there are additional parameters: slice width, pitch factor, and modulation factor. These parameters influence both treatment time and quality of the treatment plan.

Slice width (or field width) is the longitudinal extent (i.e., in the y-direction) of the treatment field. For planning purposes, a nominal 1.0, 2.5, or 5.0 cm is selected. Pitch is defined as distance traveled by the couch per gantry rotation, divided by the slice width. With a lower pitch value, there is greater overlap between spirals. This factor influences the treatment time. Modulation factor is defined as the maximum leaf opening time divided by the average opening time of all leaves. This value can range from 1.0 to 10 (typically using from 1.5 to 3.5). For a complex treatment requiring a lot of MLC motion, a high modulation factor is selected.

One of the most important differences between the HT system and other radiotherapy systems is that the HT system does not have a flattening filter. The main advantages of an absent flattening filter are an increased dose rate, reduced scatter, reduced leakage, and reduced out-of-field doses [40, 41]. The main reason for allowing the nonuniform profile is that HT is a dedicated IMRT system, without the need for a flat dose profile. If it is still desired, the MLC can be used to modulate the treatment field to produce a flat dose distribution [42].



**Figure 2.** *Illustration of the helical tomotherapy delivery. Copyright* © *Journal of Medical Physics.* 

In treating spinal tumors, the major requirement is minimization of the dose to the spinal cord. The dose gradient should be increased to improve the conformity while allowing increased heterogeneity in the tumor volume coverage. In addition, the slice width and pitch parameters are considered to increase cord avoidance and target coverage.

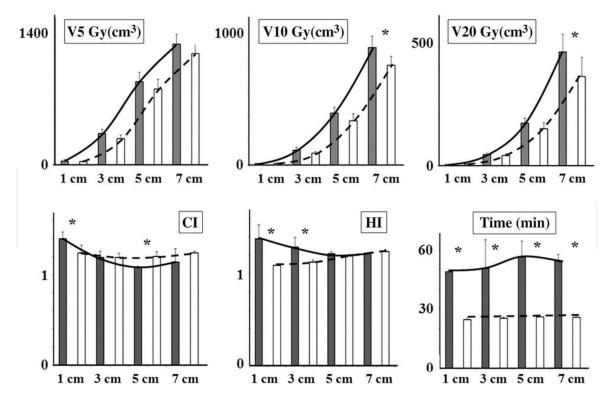
#### 3.4 CyberKnife

CK is one of the representative delivery units of SBRT. As mentioned briefly in the above section, CK has uniquely different features compared with the common medical LINACs. The compact LINAC mounted on a computer-controlled six-axis robotic manipulator delivers radiation beams anywhere in the body with submillimeter accuracy. The integrated orthogonally positioned kV X-ray imaging system is utilized to monitor the patient position throughout the course of radiotherapy. Patients are positioned automatically or manually by a therapist by matching fiducial markers or bony anatomy from X-ray images to digital reconstructed radiographs generated by CT simulation [43].

The robotic manipulator with six degrees of freedom can deliver the beam anywhere in space. Accordingly, the beam position and orientation can be adjusted by the robot to accommodate changes in target position and orientation during treatment without the need to move the patient.

The beam field size is controlled through various collimation types: 12 fixed cone collimators or an Iris variable collimator (Accuray) consisting of 12 tungsten leaves that produce beam diameters ranging from 5 to 60 mm (defined at 800 mm distance from the X-ray source) [44]. Furthermore, to compensate for the limit caused by the fixed field size, an MLC has recently been introduced for the CK [45]. The new MLC system consists of 41 leaf pairs, each with a width of 2.5 mm. The maximum field size is  $12 \times 10.25$  cm. This new system allows the fields to be shaped matching the tumor shape and allows reduction of treatment time. In particular, using the MLC offers a dosimetric advantage for targets near OARs, as shown in **Figure 3** [46].

The unit delivers multiple isocentric or non-isocentric photon beams to a desired target from many different angles through a robotic arm, as well as optic image guidance for motion management. The isocentric treatment planning is similar to



**Figure 3.**Dose-volume parameters in circular collimator and multi-leaf collimator (MLC) plans for 1–7 cm brain target volumes. (White bars indicate multi-leaf collimator (MLC) and gray indicate circular collimator.) Copyright © 2017, Oxford University Press.

that of the Gammaknife (Elekta) and conventional LINACs, which have a fixed mechanical center of the gantry and collimator. The location of the isocenter is not limited, providing a great advantage over many other delivery units. However, this advantage can be overcome by using inverse planning; the final target dose distributions can be manipulated to a certain level by modifying the order of the targets as well as the contours and dose limits assigned to the target and critical organs.

In non-isocentric treatment planning, radiation beams are delivered to a specific portion of the tumor without couch repositioning. This technique makes the high-dose isodose lines match the target shape and avoid nearby critical organs. Therefore, non-isocentric planning is very useful for treatment of irregularly shaped targets. CK, which is available with both plans, is advantageous for combining the rapid dose falloff of isocentric plans with the dose conformity of non-isocentric plans [1].

#### 3.5 Planning considerations

In spinal SBRT, the target volume includes the involved vertebral body and both left and right pedicles and the grossly visible tumor, if a paraspinal or epidural lesion is present. The target volume is generally delineated with no margin. However, depending on the treatment system, a beam aperture margin of 2–3 mm beyond the target volume is allowed to ensure adequate dose coverage of the target. This margin can be reduced to 0–1 mm in the area of the spinal cord to meet spinal cord dose constraints. The target volume may be selected at the discretion of the treating radiation oncologist based on the extent of tumor involvement. In any circumstance in which there is an epidural or paraspinal soft tissue tumor component, the visible epidural or paraspinal tumors are included in the target volume [24].

Normal tissue contouring is required starting at 10 cm above the target volume to 10 cm below the target. The treatment plan should be established according to the recommended maximum dose limit for several critical organs, as shown in **Table 1**.

Among the dose-limiting critical OARs, the spinal cord is a key concern. Because of the nature of radiosurgery with a rapid dose falloff, there is a radiation dose gradient within the diameter of the spinal cord. Therefore, a partial spinal cord volume defined as from 5 to 6 mm above to 5–6 mm below the target volume is used. The partial or absolute volume spinal cord constraints are applied to each treated spine level when the patient has multiple spine levels treated. Any spinal cord dose exceeding this constraint is not acceptable and is a major deviation [24].

Successful treatment planning requires 90% coverage of the target volume by the prescribed dose. Typically, the 80–90% isodose line is used as the prescription line, although the prescription isodose line may be different depending on the delivery system. Coverage of <90% of the target volume is an acceptable variation, and any coverage of <80% of the target volume is an unacceptable deviation. The treatment plan is acceptable as long as  $\geq$ 90% of the target volume receives the prescribed dose. It should be noted, however, that owing to the irregular shape of the target volume and the location of the spinal cord, hot spots may be created in the immediate vicinity outside of the target volume [24].

Because of the characteristics of the spinal SBRT, in the case of a beam with a small size, the higher the beam energy, the larger the beam penumbra as a result of lateral electron transport in the medium. The commonly available 5 mm MLC leaf width has been found to be adequate for most applications, with negligible improvements using the 3 mm leaf width MLC for all but the smallest lesions (<3 cm in diameter). A 6 MV photon beam, available on most modern treatment machines, provides a reasonable compromise between the beam penetration and penumbra characteristics. Additionally, beam arrays should be placed mostly in the posterior direction to avoid entrance of the radiation beam through the lungs. In the case of arc rotation techniques, every effort should be used to limit the passage of radiation through the lungs [2].

#### 4. Comparison of plan result

In Section 3, several spinal SBRT planning techniques were discussed. Because the planning technique should be selected depending on the patient's condition or situation, numerous studies have been performed to compare various planning techniques for treating spinal tumors. To evaluate the results of each plan for spinal SBRT, the following quantitative parameters were used [22, 47–50].

- Conformity index (CI): a measure of the dose coverage to the planned target volume (PTV).
- Dice similarity coefficient (DSC): a spatial overlap index and a reproducibility validation metric [51].
- Homogeneity index (HI): a measure of uniformity of the dose within the target volume.
- PTV coverage: 100% of the PTV receiving the prescribed dose [52].
- Spinal cord dose: maximum dose to the spinal cord.
- High-dose spillage: The cumulative volume of all tissue outside the PTV receiving a dose >105% of prescription dose should be no more than 15% of the PTV volume [53].

• Intermediate-dose spillage (R50% and D2cm): the falloff gradient located outside of the PTV.

R50%: volume that received 50% of the prescribed dose/PTV volume D2cm: maximum dose in terms of the percentage of the prescribed dose at 2 cm beyond the PTV in any direction

- Equivalent uniform dose (EUD): the absorbed dose that, if homogeneously delivered to a tumor, causes the same expected number of clonogens to survive as does the actual nonhomogeneous absorbed dose distribution.
- Biological effective dose (BED): the dose producing equivalent biological effect regardless of dose uniformity or fractionations.
- Gamma index: the standard method for planar dose verification in IMRT QA; calculates the quantity  $\gamma$  for each point of interest using preselected dose difference (DD) and distance to agreement (DTA) criteria and then uses the  $\gamma$  value to determine the outcome (pass-fail) of the IMRT QA [53].

In addition, plans were evaluated by the treatment delivery time (beam irradiated time) or the target point dose for the phantom measured in the ion chamber.

Zach et al. compared VMAT to static beam IMRT for spinal SBRT. The plans were compared for conformity, homogeneity, treatment delivery time, spinal cord dose, and  $D_{max}$  of the spinal cord and V 10 Gy, which is the volume of the spinal cord exposed to at least 10 Gy. The authors also compared the monitor units required in each plan to compute the net irradiated time.

All evaluated parameters were shown to favor the VMAT plans over the IMRT plans.  $D_{min}$  for PTV in the IMRT was significantly lower than that in the VMAT plan. The DSC and treatment time were found to be significantly better for the VMAT plans than for the IMRT plans. A reduction of almost 50% in the net treatment time was calculated. The authors reported that VMAT provides better conformity, homogeneity, and spinal cord dose. They also suggested that the shorter treatment time is a major advantage and not only provides convenience for patients experiencing pain but also contributes to the precision of this high-dose radiotherapy [47].

In another study, Choi et al. compared the treatment planning performance of RapidArc (i.e., VMAT) and CK for spinal SBRT. The optimized dose priorities for both plans were similar for all patients. The highest priority was to provide sufficient dose coverage to the PTV while limiting the maximum dose to the spinal cord. Plan quality was evaluated with respect to PTV coverage, CI, high-dose spillage, intermediate-dose spillage, and maximum dose to the spinal cord, which are criteria recommended by the RTOG 0631 spine and 0915 lung SBRT protocols.

The mean CI ± standard deviation (SD) values of the PTV were 1.11 ± 0.03 and 1.17 ± 0.10 for RapidArc and CK, respectively. On average, the maximum dose delivered to the spinal cord in CK plans was approximately 11.6% higher than that in RapidArc plans. High-dose spillages were 0.86 and 2.26% for RapidArc and CK, respectively. Intermediate-dose spillage characterized by D2cm was lower for RapidArc than for CK; however, R50% was not statistically different between the plans. Although both systems can create highly conformal volumetric dose distributions, the study of Choi et al. shows that RapidArc was associated with lower high- and intermediate-dose spillages than was CK. The authors also suggested that RapidArc plans for spinal SBRT may be superior to CK plans [48].

Sahgal et al. compared the treatment planning quality of the CK and Novalis (BrainLAB AG, Heimstetten, Germany) systems for vertebral body SBRT. Physical parameters and biological modeling parameters such as PTV dose coverage, dose conformity, EUD, integral BED, and a generalized BED were used to compare the treatment plans.

In the study, both the CK and Novalis treatment plans fulfilled the specified requirements with comparable PTV dose coverage and dose conformity. For the target volume, CK plans produced significantly higher values of all calculated parameters to the PTV. For OARs, CK plans produced a somewhat lower dose to small volumes (0.1–1 cm<sup>3</sup>) of the spinal cord and esophagus but exposed larger volumes of these structures to a low dose as compared to the Novalis plans.

The authors reported that restricting the dose to a small volume of the spinal cord and esophagus resulted in a modest decrease in the dose to 1 cm<sup>3</sup> volume of these structures for CK planning but at the expense of a larger volume of these structures exposed to low-dose levels [49].

In another study, Kim et al. compared the planning characteristics for hypo-fractionated spinal SBRT administered using three treatment techniques (IMRT, mARC, and HT). The factors evaluated for spinal SBRT planning were dose coverage, cord avoidance, target conformity, homogeneity, and dose spillage.

Target dose coverage was 82.74  $\pm$  3.35, 80.92  $\pm$  0.81, and 85.01  $\pm$  7.27% for IMRT, mARC, and HT, respectively. The authors reported that HT was therefore a powerful technique with respect to target coverage. The spinal cord dose for HT (mean, 1763.96 cGy; SD, 164.48) was significantly different from those for mARC (mean, 1991.75 cGy; SD, 248.00) and IMRT (mean, 2053.24 cGy; SD, 164.48). In addition, the partial spinal cord volume at 2000 cGy for HT (mean, 0.12 cc; SD, 0.01) was significantly different from those for IMRT and mARC (0.50  $\pm$  0.10 cc and 0.56  $\pm$  0.25 cc, respectively). The CIs were 1.30  $\pm$  0.12, 1.08  $\pm$  0.05, and 1.36  $\pm$  0.23 for IMRT, mARC, and HT planning, respectively. mARC showed the highest conformity. Regarding HI, HT (mean, 1763.96 cGy; SD, 164.48) differed statistically from both mARC (mean, 1991.75 cGy; SD, 248.00) and IMRT (mean, 2053.24 cGy; SD, 164.48) with respect to the spinal cord dose.

HT used a narrow field fan-beam and exhibited remarkable improvement of target coverage and cord dose, offering an important benefit to spinal SBRT. mARC had the highest target conformity and showed more favorable high- and intermediate-dose spillage than did HT and IMRT. These three planning techniques have different advantages. The authors suggested utilizing different planning techniques according to the cases. In the case of spinal SBRT, HT should be used for cord avoidance. In some cases, such as for a short treatment duration when the patient is considered to be in poor general condition, mARC can be used [22].

Gallo et al. performed end-to-end (E2E) testing for a set of representative spinal targets planned and delivered using four different treatment planning systems and delivery systems, specifically HT, Vero, TrueBeam with flattening filter free (FFF) and flattened, and CK, to evaluate the various capabilities of each. An anthropomorphic E2E SBRT phantom was simulated and treated on each system to evaluate agreement between measured and planned doses. The phantom accepted 0.007 cm<sup>3</sup> ion chambers in the thoracic region and radiochromic film in the lumbar region.

Ion chamber measurements in the thoracic targets resulted in an overall average difference of 1.5% with planned doses. Specifically, measurements agreed with the treatment planning system to within 2.2, 3.2, 1.4, 3.1, and 3.0% for all three measureable cases on HT, Vero, TrueBeam (FFF), TrueBeam (flattened), and CK, respectively. Film measurements for the lumbar targets resulted in average global gamma index passing rates of 100 at 3%/3 mm, 96.9 at 2%/2 mm, and 61.8 at 1%/1 mm, with a 10% minimum threshold for all plans on all platforms. Local

gamma analysis was also performed with similar results. While gamma passing rates were consistently accurate across all platforms through 2%/2 mm, treatment beam-on delivery times varied greatly among the platforms, with TrueBeam (FFF) the shortest, averaging 4.4 min, TrueBeam using flattened beam at 9.5 min, HT at 30.5 min, Vero at 19 min, and CK at 46.0 min.

In the study, despite the complexity of the representative targets and their proximity to the spinal cord, all treatment platforms were able to create plans that meet all RTOG 0631 dose constraints and produced exceptional agreement between calculated and measured doses. However, there were differences in the plan characteristics and significant differences in the beam-on delivery time between platforms. Thus, the authors stated that clinical judgment is required in each particular case to determine the most appropriate treatment planning/delivery platform [50].

#### 5. Conclusion

This chapter has described various planning techniques for spinal SBRT and summarized the studies comparing these techniques. The spine is a frequent site of tumor metastasis, but there are many important vessels and adjacent organs in the vicinity of the vertebrae. In particular, the spinal cord within the spine is part of the central nervous system. Radiotherapy is performed depending on the malignancy of the tumor or the difficulty of complete resection, considering potential spinal instability caused by the tumor destruction or complete resection. However, the major limitation of traditional radiotherapy is the tolerance dose of the spinal cord. If the spinal cord is irradiated with an overdose, toxicities such as radiation-induced myelopathy, vertebral compression fracture, or pain flare may occur. To overcome the limitation of conventional radiotherapy, SBRT has been proposed. The technique of SBRT delivers a higher BED, within the range of what is considered locally curative. A conformal high-dose beam in a few fractions should be used, and an intensity modulation technique is required for the sparing of normal organs surrounding the spinal lesion. Various planning technologies based on intensity modulation technology are available, including IMRT with fixed gantry, IMAT, HT, and CK. Different planning techniques have their distinct features and advantages. Therefore, it is important to use appropriate treatment planning depending on the patient's condition and situation.

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#### Conflict of interest

The authors report no conflicts of interest.

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