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REVIEW

Planning issues on linac-based stereotactic radiotherapy

Yang-Yang Huang, Jun Yang, Yi-Bao Liu

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Abstract

This work aims to summarize and evaluate the current planning progress based on the linear accelerator in stereotactic radiotherapy (SRT). The specific techniques include 3-dimensional conformal radiotherapy, dynamic conformal arc therapy, intensity-modulated radiotherapy, and volumetric-modulated arc therapy (VMAT). They are all designed to deliver higher doses to the target volume while reducing damage to normal tissues; among them, VMAT shows better prospects for application. This paper reviews and summarizes several issues on the planning of SRT to provide a reference for clinical application.

Key Words: Stereotactic radiotherapy; Treatment technology; Energy; Isocenters; Coplanar/noncoplanar fields; Calculation algorithm; Multileaf collimator leaf width; Flattening filter free mode; Small field dosimetry; Grid size

Core Tip: In recent years, stereotactic radiotherapy (SRT) has been moving towards large-scale applications with radiotherapy device hardware and software development. SRT has the advantages of a high single dose (6-30 Gy/fraction), low treatment frequency (1-5 fraction), a high biological effect dose ≥ 100, high target volume conformity index, and a hefty dose gradient index outside the target volume. This paper analyzes the SRT planning issues such as the treatment technology, energy, number of isocenters, number of fields, coplanar/noncoplanar issue, the dose calculation algorithm of treatment planning system, multileaf collimator leaf width, flattening filter free mode, auxiliary contours such as ring/shell, small field dosimetry, grid size and auto planning.

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INTRODUCTION

Stereotactic radiotherapy (SRT) is a technique that delivers high doses of radiation to tumors while preserving normal tissue function and has high requirements for planning. SRT includes stereotactic radiosurgery (SRS), fractioned SRT (FSRT), and stereotactic body radiotherapy (SBRT). Generally, SRS is a single fractional head treatment, FSRT is a multiple fractional head treatment, and SBRT is a multiple fractional body treatment[1,2]. Among SRS/FSRT/SBRT, SRS was the first to emerge and inspired the use of SBRT[3]. In recent years, SRT has been moving toward large-scale applications with radiotherapy device hardware and software development. SRT has the advantages of a high single dose (6-30 Gy/fraction), low treatment frequency (1-5 fraction), a high biological effect dose ≥ 100, high target volume conformity index (CI), and a high dose gradient index (GI) outside the target volume. However, there are also controversial points, such as the increased probability of organ damage, applicability to small tumors with a target volume diameter between 2-5 cm, and uneven dose distribution within the target volume[4-6].

SRT is generally part of the multidisciplinary treatment of cancer; however, in some cases, it can even replace surgery as the preferred treatment option, showing a bright future of application. Persson *et al*[7] suggested that SRS is superior to microsurgery when vestibular schwannoma < 3 cm requires intervention. Chang *et al*[8] showed that the estimated 3-year overall survival rate for inoperable stage I non-small cell lung cancer (NSCLC) was 95% in the SBRT group compared with 79% in the surgical group, and the 3-year recurrence-free survival rate was 86% in the SBRT group compared with 80% in the surgical group, making SBRT a possible alternative to surgery in the treatment of stage I NSCLC. Voglhuber *et al*[9] found that there appeared to be no high-grade toxicities > grade 2, and 79.4% of treated metastases were progression-free after SBRT for adrenal metastases. Tandberg *et al*[10] similarly concluded that SBRT should be considered an alternative to surgery or systemic therapy under certain conditions in patients with poor pulmonary reserve, advanced age, or other comorbidities who are considered at excessive risk for complications after surgery. Park *et al*[11] found that short-term outcomes after SBRT for stage I NSCLC were significantly better than resection, did not affect the quality of life, and mean lung function was not altered; however, a few patients may gradually develop late toxicity.

Initially, SRT was performed on specialized equipment, such as gamma knife (GK) and Cyber Knife [12-15]. A large number of studies in recent years have shown that SRT based on linear accelerators and multileaf collimators (MLCs) has gradually matured and been widely used[16-18]. Brezovich *et al*[19] suggested that SRS can be planned and delivered on a standard linear accelerator without a dedicated collimator system, with spatial accuracy better than 0.5 mm and dosimetric error less than 5%. Liu *et al* [20] compared the dosimetric parameters between linac-based volumetric-modulated arc radiotherapy (VMAT)-SRS and GK-SRS for multiple brain metastases and found that VMAT plans had a smaller CI (1.19 ± 0.14 *vs* 1.50 ± 0.16, $P < 0.001$) but an enormous GI (4.77 ± 1.49 *vs* 3.65 ± 0.98, $P < 0.01$). GK appeared better at reducing only very low-dose spread (< 3 Gy); however, the treatment time of VMAT-SRS was significantly reduced (3-5 times) compared to GK-SRS.

SRT planning faces several critical issues. Based on the search strategy of "stereotactic radiosurgery" OR "stereotactic body radiotherapy" OR "SABR" AND "planning" AND "linac", we studied 161 English articles on SRT planning issues based on a linear accelerator included in PubMed from 2017 to September 2022. Excluding nonlinac planning articles, 113 articles were included in the research. In addition, some articles on SRT planning were covered or overlapped by other representative articles, and therefore we finally selected 13 representative articles. The detailed data are listed in Table 1[5,21-32]. This paper analyzes SRT planning issues such as the treatment technology, energy, number of isocenters, number of fields, coplanar/noncoplanar issue, dose calculation algorithm of the treatment planning system (TPS), MLC leaf width, flattening filter free (FFF) mode, auxiliary contours such as ring/shell, small field dosimetry, grid size (GS) and autoplanning (AP). The purpose of this paper is to serve as a reference for the clinical application of SRT planning.

TREATMENT TECHNIQUES

Techniques that can be used for linac-based SRT include 3-dimensional conformal radiotherapy (3DCRT), dynamic conformal arc therapy (DCAT), intensity-modulated radiotherapy (IMRT), and VMAT[33-35]. Among them, 3DCRT and DCAT are forward designs with few control variables and

Table 1 The detailed data of 13 representative articles on stereotactic radiotherapy planning

Ref.	Planning issues	Conclusions
Podder *et al*[5], 2018	Treatment technology	In SBRT treatment of prostate cancer, IMRT/VMAT was superior to 3DCRT/DCAT in terms of target dose conformality and protection of organs at risk
Fernandez *et al*[21], 2020	Interplay effects	Interplay effects were most evident for large amplitude respirations, complex fields, and small field margins
Tahmasebi *et al*[22], 2019	Energy	Mixing different ratios of 6 MV and 18 MV X-rays in radiotherapy could fit PDD data equivalent to 6-18 MV energies, thus controlling the incidence of hot spots and better regulating the dose distribution in the target volume
Ruggieri *et al*[23], 2018	Number of isocenters	Using the novel VMAT technique to perform single-isocenter treatment of multiple intracranial metastases could achieve similar plan quality as multiple-isocenters while significantly reducing treatment time
Tajaldeen *et al*[24], 2019	Number of fields	In the 3DCRT plans, a minimum of nine beams were used to reduce the dose to the chest wall
Hanna *et al*[25], 2019	Coplanar/noncoplanar issue	The noncoplanar plans were superior to the coplanar plans in terms of CI of the target volume and protection of healthy brain tissues
Hoffmann *et al*[26], 2018	The dose calculation algorithm of treatment planning system	Both AcurosXB and MC algorithms had matured to a level where their differences were below the typical experimental detection thresholds for clinical treatment
Younge *et al*[27], 2017	MLC leaf width	In spinal SBRT, 2.5 mm MLC had limited improvement in planning quality yet increased planning complexity and decreased dose delivery accuracy compared with 5 mm MLC
Ma *et al*[28], 2019	FFF mode	The FFF mode was fully available for all sizes of clinical fields and had outstanding advantages in reducing treatment time, and predicted a trend of complete replacement of the FF mode by the FFF mode
Duan *et al*[29], 2020	Auxiliary contours such as ring/shell	When the numbers of peripheral lung cancer SBRT plans shells did not exceed 6, it could consistently improve CI and GI in the target volume and reduce the maximum dose in the spinal cord and V_{20} and V_{10} to the bilateral lung
Huq *et al*[30], 2018	Small field dosimetry	The beam model used to simulate the small field in TPS should pay special attention to the influence of the primary beam source and collimator in the calculation of energy fluence and dose
Snyder Karen *et al*[31], 2017	Grid size	The use of the 1.5 mm grid size balanced dose accuracy and calculation time
Visak *et al*[32], 2021	Auto planning	The KBP program reduced the maximum dose of OARs compared to the manual VMAT plans, and each of the planning time was less than 30 min

SRT: Stereotactic radiotherapy; SBRT: Stereotactic body radiotherapy; IMRT: Intensity-modulated radiotherapy; VMAT: Volumetric-modulated arc therapy; 3DCRT: Three-dimensional conformal radiotherapy; DCAT: Dynamic conformal arc therapy; PDD: Percentage depth dose; CI: Conformity index; MC: Monte carlo; MLC: Multi-leaf collimator; FFF: Flattening filter free; GI: Gradient index; V_{20}, V_{10}: Greater than or equal to 20 Gy/10 Gy dose wrap volume as a percentage of total volume; TPS: Treatment planning system; OAR: Organ at risk; KBP: Knowledge-based planning; OARs: Organs at risk.

thus have low geometric complexity, high tolerance, and no interplay effects. IMRT and VMAT are inverse designs that can set auxiliary contours such as rings and shells, with high modulation freedom, low tolerance, and the need to overcome interplay effects. The quality of the SRT plans includes the prescription dose coverage, the maximum dose in the target volume (D_{max}), the CI/GI of the target volume, and the dose of organs at risk (OARs)[36].

Soda *et al*[37] concluded that 3DCRT and DCAT had more significant advantages over IMRT and VMAT in terms of tolerances. Moon *et al*[38] found that for liver SBRT, DCAT was an effective alternative to VMAT to meet the plan goals proposed by the RTOG protocol for SBRT and increased the efficiency of plan execution. Stathakis *et al*[34] concluded that in lung and liver SBRT, DCAT demonstrated a plan validation passing rate consistent with VMAT and 2.5 times less monitor units (MUs) than VAMT, leading to the conclusion that DCAT could replace VMAT in lung and liver SBRT. However, some authors also proposed that the VMAT-based SRS plan was significantly better than DCAT in terms of CI in radiotherapy for solitary brain metastases[39]. SRT requires IGRT and a respiratory management system to correct patients' positional error and reduce the planned target volume (PTV) margin to manage and monitor patients' respiratory motion error, so the high tolerance of 3DCRT and DCAT has no prominent advantage[40]. Scaringi *et al*[41] concluded that SRS based on IMRT and VMAT can increase the dose to brain tumor target volume and reduce exposure to OARs

compared to 3DCRT; meanwhile, VMAT reduced the number of MUs and treatment time compared to IMRT. Podder *et al*[5] similarly concluded in their study of SBRT for prostate cancer that better dose conformality to target volume and to spare OARs were usually achievable using IMRT/VMAT compared to 3DCRT. Navarria *et al*[42] proposed that VMAT provided better lung protection than 3DCRT in NSCLC-SBRT. Dwivedi *et al*[43] also concluded that VMAT-SBRT-based lung cancer plans were of better quality, with a lower OAR dose and a 57.09% to 60.39% reduction in treatment time compared to 3DCRT. Rauschenbach *et al*[44] had similar conclusions; they found that IMRT- and VMAT-based plans were superior to DCAT- and 3DCRT-based plans in terms of CI and GI of the target volume and protection of OARs and therefore recommended that IMRT- and VMAT-based SBRT should be carried out in priority in radiotherapy where available; if only DCAT and 3DCRT were available, then DCAT was superior to 3DCRT.

In thoracic SBRT, interplay effects occur due to respiratory rates, respiratory amplitudes, fractions, dose rates, inaccurate calculation of small field boundary doses, and plan complexity, manifesting as potential consequences such as inaccurate dose delivery[21,45]. Moon *et al*[38] found that for liver SBRT, DCAT overcame the interplay effect compared to VMAT. Wu *et al*[46] studied liver metastatic cancer SBRT and found that the interplay effect was less pronounced with 3DCRT and DCAT than IMRT. The interplay effect of IMRT occurred mainly at the edge of the target volume, resulting in a maximum dose error of 20%. However, IMRT was still the best choice among the three techniques under respiratory motion control. The simulation of Edvardsson *et al*[47] showed a significant interplay effect for the single treatment modality. Ong *et al*[48] found that VMAT using two or more arcs and increasing the fraction of treatment to more than 2 reduced the interplay effect to a clinically negligible level. Some authors also concluded that the interplay effect was minimal with controlled motion amplitude (< 30 mm), reduced motion cycles (< 5 s), and a deviation of less than ± 2.5% from the D99% dose index in the target volume[49].

The interplay effect was minimal with the 3DCRT and DCAT techniques, and the interplay effect was significantly reduced with the IMRT technique by the respiratory management system. In contrast, using more than two arcs and a fraction of more than two arcs can reduce the interplay effect on VMAT to a clinically negligible level.

Based on the above four techniques, other authors have practiced a mixture of two of them. Zhao *et al*[50] designed IMRT and VMAT hybrid radiotherapy, IMRT alone and VMAT alone for nasopharyngeal carcinoma and found that IMRT and VMAT hybrid techniques could improve CI and HI in the target volume and reduce OAR endangerment and therefore concluded that IMRT and VMAT hybrid techniques may be feasible radiotherapy techniques. Huang *et al*[51] compared a hybrid technique of DCAT and IMRT with IMRT alone and VMAT alone for the implementation of spinal SBRT and found that all three plans could meet clinical needs, but quality efficiency and dose delivery accuracy were highest with VMAT alone. Raturi *et al*[52] found little difference in OAR protection between the hybrid IMRT and VMAT plans compared with IMRT alone and VMAT alone techniques in olfactory neuroblastoma radiotherapy and little clinical benefit in optic nerve protection with the hybrid IMRT and VMAT technique compared with the other two techniques. Current research shows that SRT can meet clinical needs using one technique alone, and there is not much practice in applying hybrid radiotherapy techniques. However, hybrid radiotherapy techniques may have unique advantages in certain diseases. Therefore, considering the planning quality, treatment efficiency, and dose delivery accuracy, SRT based on VMAT is the best under current techniques and qualified quality control levels. If technical conditions are insufficient, SRT based on DCAT and 3DCRT can be considered appropriate.

ENERGY

Most linear accelerators are equipped with 6 MV X-rays, whose proper energy has a small dose build-up depth and a strong penetration ability and is the energy commonly used in SRT. According to the laws of physics, the higher the X-ray energy is, the greater the penumbra and the greater the dose calculation error in areas of low tissue density; also, low-energy X-rays have more significant scattering, and high-energy X-rays have neutron contamination; medium-energy rays such as 10 MV X-ray may be a reasonable energy choice for SRT[53,54].

It has been suggested that electronic devices such as pacemakers are sensitive to high linear energy transfer radiation; therefore, low energy radiation has a unique advantage in treating such individuals [53]. Weiss *et al*[55] analyzed the effects of 6 MV and 18 MV X-rays on lung cancer patients using the IMRT technique and found that 6 MV X-ray was superior to 18 MV X-ray in protecting most OARs. In proximal gastric cancer (PGCC) radiotherapy, 10 MV-VMAT produced a higher dose gradient than 6 MV-VMAT and was more suitable for PGCC radiotherapy[56]. Ost *et al*[57] concluded that no difference was found between the 6- and 18-MV photon beams, except for a reduction in the number of MUs needed for 18 MV ($P < 0.05$). Tahmasebi Birgani *et al*[22] suggested that mixing different ratios of 6 MV and 18 MV X-rays in radiotherapy could fit percentage depth dose (PDD) data equivalent to 6-18 MV energies, thus controlling the incidence of hot spots and better regulating the dose distribution in the target volume. Park *et al*[58] investigated the characteristics of IMRT plans using mixed energies and

found no significant differences in target volume coverage, CI, and GI; however, mixed energies improved the overall plan quality for IMRT plans targeting deep tumors. In conclusion, 6 MV X-rays for SRT are appropriate, mixed energy photons have some dosimetric advantages, and 10 MV X-rays may be the most promising energy source.

NUMBER OF ISOCENTERS

The number of isocenters for multiple independent target volumes is also critical when conducting SRT. In general, using a single isocenter can improve treatment efficiency, and using multiple isocenters can improve plan quality and reduce the low-dose volume in OARs.

Huang *et al*[59] found that when conducting intracranial multiple metastases SRS, the number of treatment isocenters for 3DCRT and DCAT must be consistent with the number of independent target volumes and that VMAT using a single isocenter would ensure plan quality, with a 42% reduction in the number of MUs and 49% reduction in treatment time compared with 3DCRT. Algan *et al*[60] concluded that when conducting IMRT-SRS for multiple intracranial metastases (> 3), there was no significant difference between single- and multiple-isocenter plans for target volumes V_{95}, V_{99}, and D_{100} and similar doses for OARs such as the hippocampus and normal brain but a 35% reduction in beam-on time for single-isocenter plans. Zhang *et al*[61], Ballangrud *et al*[62] and Ruggieri *et al*[23] also concluded that using the novel VMAT-SRS technique to perform single-isocenter treatment of multiple intracranial metastases can achieve similar plan quality as multiple-isocenters while significantly reducing treatment time. Sanford *et al*[63] showed that in isocenter selection for SBRT treatment of lung cancer with an average isocenter distance of 6.7 ± 2.3 cm between two independent target volumes, both single- and multiple-isocenters could meet the requirements with no significant differences in CI, GI, and lung V_{20}; however, with increasing distance between target volumes, there was a slight increase in V_5, V_{10}, and mean lung dose (MLD) for single isocenter plans. Similarly, van Timmeren *et al*[64] designed single- and multi-isocenter SBRT plans based on the VMAT technique for multiple lung cancer targets and found an 11.6% increase in bilateral lung MLD and a 0.2% increase in bilateral lung V_{20} for the single-isocenter plans. Pokhrel *et al*[65] found that the low-dose volume of bilateral lung and other normal tissues increased when the VMAT-SBRT plans for double-lesion lung cancer used a single isocenter.

In conclusion, when performing multiple intracranial metastases SRS, single isocenter treatment based on VMAT or IMRT is a more reasonable choice considering the brain volume size, while VMAT is superior to IMRT; if 3DCRT or DCAT is used, multiple isocenters are a compromise of last resort. When performing SBRT with multiple independent targets in the lung, multiple isocenters are required based on 3DCRT and DCAT; when performing single isocenter therapy based on the VMAT technique, normal lung V_{20}, V_{10}, V_5, MLD, and the maximum dose of 1000 cc normal lung volume are increased with increasing distance between the target volume and the isocenter[65]. Considering the treatment efficiency, the complexity of technicians' positioning and the error caused by repeated positioning, when the target spacing is small, using a single isocenter can improve the treatment efficiency and reduce the cumulative error caused by multiple positioning. When the target spacing is large or the target volume is large, using multiple isocenters can reduce the low-dose volume of normal tissues while maximizing the advantage of thinner leaves in some MLC center regions.

NUMBER OF FIELDS AND COPLANAR/NONCOPLANAR ISSUE

In clinical practice, 3DCRT, DCAT, IMRT, and VMAT can be applied to SRT plans, depending on the equipment and patient conditions. In general, VMAT has the highest degree of freedom of modulation and the broadest range of applicability.

The 3DCRT and IMRT plans generally use multiple coplanar or noncoplanar fields to reduce the dose on the path[66,67], with some authors suggesting six[68], others seven[46], and still others nine[24] and ten[67], with the collimator angle of each field also adjusted to the shape of the target volume and the IMRT technique avoiding the mirror field. DCAT and VMAT can use 1-3 full arcs or partial arcs; the advantage of full arcs is that the CI of the target volume is good, and the dose falls evenly in all directions, which is more suitable for the central target volume; partial arcs have poorer CI than full arcs. Clark *et al*[69] found that both 3-arc coplanar VMAT and 3-arc noncoplanar VMAT could be designed for qualified intracranial multiple metastases SRS plans, and the 3-arc noncoplanar VMAT plans were superior to the coplanar plans in terms of CI and other dosimetric parameters when applied to multiple target volumes nearby; the 3-arc coplanar and noncoplanar VMAT plans did not show significant differences when applied to multiple target volumes at a greater distance. Hanna *et al*[25] found that the noncoplanar VMAT-SRS plans were superior to the coplanar plans in terms of CI of the target volume and protection of healthy brain tissues. Pursley *et al*[35] used DCAT for lung cancer. For peripheral tumors with chest wall interference, additional oblique fields were used to help pull the dose off of the chest wall; for tumors located in the central region or close to the spine, multiple arcs were used, and the PTV coverage of the 100% isodose line was ≥ 95% in all cases; the conformality index

ranged from 1.12-4.5, with an average of 2.5. Ishii *et al*[70] conducted VMAT-SBRT in central lung cancer with two coplanar partial arcs (CP-VMAT), two noncoplanar partial arcs (NCP-VMAT), and one full coplanar arc (Full-VMAT) and found that the prescription dose coverage in the target volume was almost the same for all plans, with the CP-VMAT plan having a significantly lower whole-lung $V_{10\,Gy}$ than the NCP-VMAT plan. At the same time, no significant differences were observed for MLD, $V_{5\,Gy}$, $V_{20\,Gy}$, or $V_{40\,Gy}$. Full-VMAT increases contralateral lung V_5 by 12.57% and 9.15% compared to NCP-VMAT and CP-VMAT, respectively, so from the perspective of protecting healthy lungs, CP-VMAT is optimal.

3DCRT and IMRT plans generally need many fields (6-10), and DCAT and VMAT plans require 1-3 full or partial arcs. The use of noncoplanar fields in 3DCRT and DCAT is necessary in many cases, while using noncoplanar fields or arcs in IMRT and VMAT can improve the quality of plans. The use of the VMAT technique in SRT increases OAR low-dose volume, but the reasonable use of multiple noncoplanar partial arcs can circumvent this problem. The choice of specific treatment techniques must consider device availability and expected patient outcomes.

THE DOSE CALCULATION ALGORITHM OF TPS

The TPS is a vital tool to simulate the distribution of doses in the human body. The accuracy of its dose calculation is closely related to its built-in algorithm, and the accuracy of the dose calculation algorithm directly affects the clinical treatment effect[71]. The accuracy of the dose calculation algorithm has a direct impact on clinical outcomes. The difficulties in dose calculation are dose accumulation in inhomogeneous media, small field dose, and dose accumulation at high- and low-density junctions[72-74]. SRT requires higher accuracy of the TPS algorithm due to the high fractional dose and low fraction of treatments.

Common TPS algorithms for calculating SRT plan dose in clinical practice are the collapsed cone convolution (CCC)[75], the anisotropic analytic algorithm (AAA)[76], the Monte Carlo (MC), and the AcurosXB, among which the computational accuracy of the CCC and AAA algorithms is lower than that of the MC and AcurosXB algorithms[77-79]. The latest commercial TPSs, such as Monaco and Eclipse, have built-in CCC and AAA algorithms, respectively, both of which are convolutional superposition algorithms. Saadatmand *et al*[80] found that the CCC algorithm for head and neck dose calculation resulted in a discrepancy of -19.77% to 27.49% between the dose calculation results and thermoluminescent dosimeter measurements due to the use of high-Z materials for dental repair, which was then analyzed as a result of the CCC algorithm's inaccurate calculation of attenuation and scattering-induced dose perturbations caused by high-Z materials. Fogliata *et al*[78] found that the AAA algorithm had a significant error in calculating dose accumulation at high- and low-density junctions, such as the lung. Chen *et al*[81] found that the AAA algorithm overestimated the tumor dose by 15% and underestimated the lung V_9 by approximately 5% when performing lung SBRT using a 15 MV X-ray compared to the MC algorithm.

Monaco and Eclipse also have built-in MC and AcurosXB algorithms, respectively, which are improved transport models for secondary electrons based on the CCC and AAA algorithms, resulting in more accurate results[77,82,83]. Tugrul[84] used the RANDO lung phantom to study the accuracy of radiotherapy dose calculation for esophageal cancer and found that the MC algorithm was the most accurate; therefore, they recommended using the MC algorithm when calculating dose accumulation in inhomogeneous tissues. Yan *et al*[85] found that the AcurosXB algorithm was more accurate in inhomogeneous media compared to the AAA algorithm. The findings of several authors all support the above statement[24,43,85,86]; that is, the AcurosXB algorithm is more accurate than the AAA algorithm in lung cancer SBRT dose calculation. Both MC and AcurosXB have been simplified to strike a balance between computational accuracy and computational time, although the overall accuracy level of both algorithms remains highly consistent. The high-precision dose algorithms represented by the AcurosXB and MC algorithms have matured to a level where their differences are below the typical experimental detection thresholds for clinical treatment[26]. Based on the above analysis, more accurate dose calculation results can be achieved by preferentially using the MC and AcurosXB algorithms when designing SRS/SBRT plans.

MLC LEAF WIDTH

In SRT planning, the choice of MLC leaf width affects parameters such as CI, GI, plan complexity, and dose delivery accuracy. In general, the smaller the leaf width is, the better the dose modification capability, but the leaves are not as small as possible. This is because the virtual source of the accelerator has a certain size, the X-ray and secondary electrons have a certain scattering, and the leaf width is small to a critical value that does not further improve the dose distribution.

Some studies concluded that a 5-mm MLC could meet clinical requirements when the target volume is larger than 3 cm in diameter[4]; when the target volume is smaller than 3 cm in diameter, an MLC smaller than 5 mm in width can be selected. Serna *et al*[39] found that 2.5 mm MLC provided better dose gradients in noncoplanar DCAT and VMAT plans for isolated brain metastases smaller than 10 cc compared to 5 mm MLC, and 2.5 mm MLC significantly improved the CI of DCAT plans. Yoganathan *et al*[87] found that for small target volumes (mean volume, 42.99 cc), 3 mm MLC had better CI than 5 mm and 10 mm MLC; for large target volumes (mean volume, 361.14 cc), no significant differences in CI and OARs protection were observed between 5 mm and 10 mm MLC. Abisheva *et al*[88] applied 2.5 mm MLC and 5 mm MLC to VMAT-SRS for intracranial metastases and found no significant difference in the target volume of CI. Monk *et al*[89] concluded that in the SRT plan, compared to 3 mm MLC, 5 mm MLC increased the wrapping volume of 50% and 70% isodose line by 5.7% and 4.9%, respectively, and 3 mm MLC improved the IC of PTV; however, these improvements were minor, so the choice of 3 mm MLC should be cautious. Younge *et al*[27] based on the SBRT spinal radiotherapy plan, compared a high-definition MLC (HD-MLC) with 32 pairs of 2.5 mm widths in the center and 28 pairs of 5 mm widths on the outer side with a standard Varian Millennium MLC (M120) with 40 pairs of 5 mm widths in the center and 20 pairs of 10 mm widths on the outside. They found that the HD-MLC had limited improvement in planning quality yet increased planning complexity and decreased dose delivery accuracy.

In conclusion, using 5 mm MLC for SRT plans is sufficient for most cases, especially for VMAT technology. An MLC width less than 5 mm has some advantages in the small target volume of SRS plans, and there is a trade-off between plan complexity and plan quality when using less than 5 mm MLC.

FFF MODE

The features of the FFF mode that distinguish it from the FF mode are the ultrahigh dose rate and the variable dose intensity of the field. The FFF mode has become the standard for accelerators in today's rapidly developing radiotherapy technology. FFF significantly reduces treatment time without compromising plan quality or dose delivery accuracy[90-92]. Stieler *et al*[93] found that the FFF mode reduced treatment time by 51.5% compared to the FF mode without altering the plan quality when performing the SRS to the brain based on IMRT and VMAT techniques. Prendergast *et al*[94] investigated the advantages of the FFF mode applied to SBRT and concluded that the FFF mode reduced the treatment time by more than 50%. Ma *et al*[28] studied all clinical treatment fields used for IMRT and VMAT techniques and found that the FFF mode was fully available for all sizes of clinical fields, had outstanding advantages in reducing treatment time, and predicted a trend of complete replacement of the FF mode by the FFF mode. Vassiliev *et al*[95] believed that compared with FFF mode, FF mode would increase the dose loss at the edge of the radiation field, resulting in insufficient dose in the spherical shell area approximately 5 mm thick at the edge of the field, which extended to 2-3 mm inside the radiation field; therefore, for smaller tumors and lower density lung tissues, FFF mode had higher dose coverage in the target volume. Pokhrel *et al*[91] similarly concluded in their study that 6X-FFF-VMAT-SBRT plans provided similar target volume coverage while improving dose coverage at the target-OAR junction, providing better OAR protection and significantly reducing treatment time compared to conventional 6X-FF-VMAT-SBRT plans. The AAPM TG158 has more detailed information on the advantages of the FFF mode[53]; in SRT, the FFF mode reduces the leakage of the accelerator collimator, which is more conducive to small field therapy and dramatically reduces the dose outside the target volume. Fiorentino *et al*[96] concluded that the FFF mode had acceptable acute and late toxicity with no severe events (no ≥ G2 adverse events recorded). Some studies have also concluded that the FFF mode leads to an earlier radiation response in NSCLC patients than the FF mode[42]. In conclusion, when applied to SRT, the FFF mode shows strong application prospects by better protecting OARs and significantly shortening the treatment time without changing the quality of plans.

AUXILIARY CONTOURS SUCH AS RING/SHELL

Appropriate setting of ring/shell auxiliary contours can significantly help improve the plan quality by improving the CI and GI of the target volume and protecting the OARs. Clark *et al*[97] used VMAT-SRS to treat multiple intracranial metastases. Three rings were set outside the target volume to reduce the dose of OARs, limiting 100% of the prescribed dose volume, 50% of the prescribed dose volume, and 40% of the prescribed dose volume in turn, and eventually achieved good results. Price *et al*[98] pointed out that setting different rings outside the target volume could increase the dose consistency and reduce the treatment time of IMRT plans, with a 15.7% reduction in the off-target volume of the prescription dose envelope and more than a 29% reduction in treatment time. While Desai *et al*[99] went one step further, they proposed a new optimized shell structure OptiForR50 based on RTOG 0813 and 0915 protocols; the structure was designed based on a series of mathematical formulas to extend the PTV in

VMAT-SBRT-based lung cancer plans, which made significant progress in improving the CI, off-target dose attenuation of the target volume, and reducing the dose to normal lung, heart, and aorta. Duan *et al* [29] found that when the numbers of peripheral lung cancer SBRT plan shells did not exceed 6, it could consistently improve CI and GI in the target volume and reduce the maximum dose in the spinal cord and V_{20} and V_{10} to the bilateral lung. Wang *et al*[100] found that the modified GI (mGI) and Paddick CI (PCI) of the VMAT-SRS plans for multiple intracranial metastases were limited by setting three and four shells in the target volume and outside the target volume, respectively.

The mGI of the target volume was significantly reduced, and the PCI was significantly improved. Hence, the authors concluded that this method was applied to intracranial VMAT-SRS planning and could increase the protection of OARs. However, Reese *et al*[101] concluded that shells, in reducing the IMRT plan site-specific dose, necessarily increased the dose at locations at a similar distance from the specific site, *i.e.*, shell only redistributed the dose within the tissue surrounding the target volume, not reduced it. After the above analysis, it can be seen that 3-6 rings/shells are more suitable for IMRT/VMAT plans, and these rings/shells can be set inside and outside the target volume, which is helpful to improve the CI and GI of the target volume and protect OARs.

SMALL FIELD DOSIMETRY AND GS

To achieve high CI and GI when treating smaller lesions, SRT plans extensively use small fields less than 10 mm in diameter. Small field dose calculations are subject to significant errors due to inadequate lateral electron balance, small average volume, cross-sectional detector artifacts, collimator action, *etc* [102]. Both the IAEA TRS 483[30] and the AAPM TG155[103] are specialized reports on small field dosimetry, which analyze small field dosimetry parameters such as percent depth dose, tissue model ratio/tissue maximum ratio, off-axis ratio, and field output factor (FOF), as well as the necessary perturbation corrections for various detectors, discuss errors and uncertainties in measurements and suggest that the beam model used to simulate the small field in TPS should pay special attention to the influence of the primary beam source and collimator in the calculation of energy fluence and dose. Mamesa *et al*[104] performed FOF correction for small fields less than 10 mm × 10 mm in an Eclipse TPS based on IAEA TRS 483 and found that the standard deviation of MU calculated based on IMRT-SRS decreased from 6.0% to 2.5%, and the standard deviation of MU calculated by the VMAT-SRS decreased to less than 2.0% after correction, indicating that the correction of FOFs can improve the dose calculation accuracy of small fields. Baek and Beachey[105] used an EBT3 film to collect small field data at different depths and sizes and found that as the small field size decreased, the field center fell within the penumbra of each MLC edge for megavoltage photon energies and suggested that careful characterization of small field dose and leaf end modeling within a TPS were crucial in both predicting accurate small field dosimetry and off-axis dosimetry.

The computational GS in the TPS also affects the dose calculation accuracy. Dempsey *et al*[106] found that the dose error of 2.5 mm GS was less than 1%. Bedford *et al*[107] found that the dose error of 4 mm GS was less than 5%. Chung *et al*[108] showed that the dose error of 2 mm and 4 mm GS for head and neck tumors was 2.3% and 5.6%, respectively, compared with 1.5 mm GS in the dose calculation of shallow target volume 0.5 cm below the skin, and 2.0% and 4.6%, respectively, compared with 1.5 mm GS in the dose calculation of deep target volume 6 cm below the skin; they also recommended that a 2 mm or less GS be used during SRS dose calculation, especially in the high dose gradient region, to ensure the accuracy of the dose calculation. Snyder Karen *et al*[31] set 1 mm, 1.5 mm, and 2.5 mm GS in the design of vertebral VMAT-SBRT plans and found that the distance-to-falloff between the 90% and 50% isodose levels in the axial plane for 2.5 mm, 1.5 mm and 1 mm GS plans were tightened sequentially, with the lowest spinal cord dose and highest gamma passing rates in the 1.5 mm GS plans and a 61% and 84% increase in plan calculation time for the 1 mm GS over the 1.5 and 2.5 mm GS, respectively, concluding that using 1.5 mm GS balanced dose accuracy and calculation time.

Therefore, the smaller the GS in the TPS, the smaller the dose error is in general and the longer the planning time is. Considering the dose calculation accuracy and planning time, 1.5 mm is a reasonable GS for SRT; 1 mm GS can be chosen for special scenarios such as high dose gradient areas or small field dose calculations.

AUTO PLANNING

Auto planning is a new field in radiation therapy. Auto planning dramatically improves planning efficiency and ensures the stability of plan quality, and it is being increasingly studied and applied. Gallio *et al*[109] compared the SBRT-VMAT plans for hepatocellular carcinoma designed by the AP module of Pinnacle TPS with the SBRT-VMAT plan designed by the manual planning (MP) module, comparing metrics including various dosimetric parameters of target volumes and OARs, MU, the number of segments, plan complexity metrics, and plan time-consumption, and found that AP plans were comparable to MP plans in terms of plan metrics, but AP had a significant advantage over MP in

plan time-consumption, thus suggesting that the use of AP in simple plans could save the time of designers to allow designers to devote more time to more complex plans. Ouyang *et al*[110] evaluated whether the Pinnacle AP module could design clinically acceptable pulmonary SBRT plans and assessed the effectiveness of the dose prediction model; they designed 20 AP plans based on 20 manual pulmonary SBRT plans and found that all manual and AP plans achieved clinically desired target volume dose coverage, that AP plans achieved equal or better OARs protection compared to the manual plans, most notably the AP plans had lower maximum doses to the spinal cord, ipsilateral brachial plexus, esophagus, and trachea. To study the robustness of the automatic planning software, Hito *et al*[111] designed 32 scenarios to simulate the changes in the anatomical position of patients with pancreatic cancer, including displacement, expansion, rotation, and a combination of three, and used the Manhattan map to evaluate the indicators of the plans, including the coverage of the target volume and the dose of gastrointestinal and other OARs; the results showed that the automatic planning software of the pancreatic SBRT plan had good robustness. Visak *et al*[32], Visak *et al*[112] and Ziemer *et al*[113] developed a knowledge-based planning (KBP) program using the commercial RapidPlan™ model, trained the program using existing SRT-VMAT plans, and validated it with independent clinical plans. The results showed that the KBP program reduced the maximum dose of OARs compared to the existing SRT-VMAT plans, and each of the planning times was less than 30 min.

Auto planning is a promising approach in SRT planning by improving plan quality and reducing the dose of OARs while increasing plan design efficiency and maintaining plan quality robustness. With the development of computer and software technologies, as well as the training of big data and a large number of excellent clinical treatment plans, the result is even revolutionary. In the future, physicists may be left with the functions of device QA and plan signature, as well as assuming the responsibility of the medical activity subject.

CONCLUSION

Linac-based SRT is becoming increasingly widely used, its therapeutic value is increasingly recognized, planning issues are widely discussed, and systematic organization and generalization have become necessary. This paper discusses the advantages and disadvantages of four techniques based on linear accelerators for SRT, 3DCRT, DCAT, IMRT, and VMAT, specifically, tolerance and ability to overcome the interplay effects, energy, single or multiple treatment isocenters, number of fields, and coplanar/noncoplanar issue, TPS algorithms, MLC leaf width, FFF mode, auxiliary contours such as ring/shell, small field dosimetry and GS, and auto planning.

Among the four technologies, SRT based on VMAT technology is increasingly used. With the help of modern IGRT devices and respiratory motion management equipment, the drawbacks of VMAT technology with smaller tolerances and more significant interplay effects are effectively overcome. At the same time, its advantages of high planning quality, short treatment time, and wide range of adapted diseases are carried forward.

The use of 6 MV X-rays for SRT is appropriate, mixed energy photons have some dosimetric advantages, and 10 MV X-rays are likely to be the most promising energy level. In terms of the number of isocenters for multiple independent targets, a reasonable choice for SRS is single-isocenter treatment using VMAT technology, while multi-isocenter is a compromise if SRS is performed using 3DCRT/DCAT technology. For SBRT, all four technologies require consideration of target spacing, and multi-isocenter is a compromise if the distance is greater than a certain value. Regarding the number of fields and coplanar/noncoplanar issues, 3DCRT/IMRT plans require 6-10 fields, and DCAT/VMAT require 1-3 full or partial arcs; 3DCRT/DCAT using noncoplanar fields is necessary in many cases, while IMRT/VMAT uses noncoplanar fields to improve plan quality. The algorithm is the soul of TPS; among the commonly used algorithms, AcurosXB and MC are superior to AAA and CCC, and the AcurosXB and MC algorithms are preferred in consideration of calculation time and plan accuracy. The SRT plans use 5 mm MLC to cope with most situations, especially when based on VMAT technology. In SRT planning based on the IMRT/VMAT technique, 3-6 rings/shells are more appropriate, and these rings/shells can be set inside and outside the target volume, which helps greatly improve the CI and GI and protect the OARs. For the specificity of small field dose calculation, a small field dose model needs to be established before SRT plans are carried out; for computational GS, considering the dose accuracy and calculation time, 1.5 mm GS is more reasonable to be applied to SRT. Auto planning is a new field in radiotherapy; it greatly improves the planning efficiency and ensures the stability of plan quality and may make revolutionary progress in the future.

The future of SRT is exciting, and we believe that there are three critical issues that need to be highlighted. First, linear accelerators used for SRT must be equipped with IGRT devices and respiratory management equipment, and dedicated positioning frames and treatment tables are also necessary. Second, VMAT technology has gained significant advantages in plan quality, treatment time, and accuracy of dose delivery; continuing to explore the potential applications of VMAT technology requires the continuous efforts of radiologists. Once again, auto planning is the future of plan design by providing significant savings in plan time while maintaining the stability of plan quality.

FOOTNOTES

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