Review Article

Volumetric intensity modulated arc therapy in lung cancer: Current literature review

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ABSTRACT

The volumetric intensity modulated arc therapy (VMAT) is a novel radiation technique that delivers a highly conformal radiation dose to the target by allowing the simultaneous variation of gantry rotation speed, dose rate and multiple-leaf collimators leaf positions. The aim of this study was to review the current literature on two VMAT systems, RapidArc and SmartArc with main focus on planning studies of lung cancer. A systematic review of available data was conducted using MEDLINE/PubMed with the keywords "lung" and "VMAT". The published data show that VMAT techniques have clear superiority over three-dimensional conformal radiation therapy with regard to improving dose conformity and sparing of organs at risks (OARs). The data indicates that for lung tumor VMAT and intensity modulated radiation therapy (IMRT) provide equivalent dose homogeneity, dose conformity and target volume coverage; however, contradictory results were obtained in terms of OARs sparing. The major advantages of VMAT over IMRT are the reduction in the number of monitor units and faster treatment delivery times without compromising the quality of the treatment plans. Moreover, faster delivery time is more patient-friendly and it minimizes intra-fractional patient motion allowing treatment volumes stay within their respective treatment margins. Current literature data shows that VMAT can be a good option to treat lung cancer; however, data on clinical trials are still lacking. The clinical trials are essential to confirm the safety and efficacy of VMAT techniques.

Key words: Lung cancer, RapidArc, SmartArc, volumetric intensity modulated arc therapy

INTRODUCTION

The main objective of external beam radiation therapy (EBRT) is to deliver a homogeneous radiation dose to the tumor target, while minimizing the dose to surrounding organs at risks (OARs).[1] Three-dimensional conformal radiotherapy (3DCRT) is an example of EBRT and it includes direction of multiple radiation beams conformed to the shape of the target.[2] The 3DCRT aims to escalate the radiation dose to the tumor target while sparing the normal tissues; however, complex target volume shapes may result in irradiation of large volume of OARs in 3DCRT plans.[2,3] The significant advances in EBRT such as development of more accurate treatment planning systems (TPS) and linear accelerator delivery capabilities, over the past few decades have improved the dose conformity and distributions.[4,5] For example, in the early 2000s, multiple-leaf collimators (MLCs) and inverse TPS were introduced. The MLCs are used as intensity modulators to divide the radiation beam into a set of smaller radiation beamlets. The individual MLC leaf moves separately in a computer control at desired speeds and the intensity of beamlets vary from 0% to 100%, thus resulting into intensity modulated radiation therapy (IMRT).[4,5] The IMRT is an advanced form of 3DCRT that combines intensity modulated beams leading to the construction of highly conformal dose distributions. Some of the benefits of IMRT over 3DCRT are the improved conformity for target volume that has complex shape, and better sparing of OARs.[6-8]

Despite the advantages of IMRT, this technique could affect the reproducibility of treatment setup and intra-fraction patient motion since IMRT plan requires multiple fixed angle beams that can increase the treatment delivery time.[8,9] Although image-guided radiation therapy has improved the patient positioning accuracy as an integration of image receptors to the linear accelerator, it often requires more time on the treatment couch with a possibility of delivering increased radiation to the patient as imaging of the patient

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is done before each treatment session.[10] Furthermore, a higher number of monitor units (MUs) in IMRT plans could potentially increase the exposure of patient's body to low dose radiation, and this has led to concerns of increased risk of secondary radiation-induced malignancies, especially for pediatric patients.[11,12]

In 2007, a novel radiation technique called volumetric intensity modulated arc therapy (VMAT) was introduced.[13] The VMAT system can deliver a highly conformal radiation dose to the target using one or two arcs, although complex shaped targets may require more arcs, and the delivery technique allows the simultaneous variation of gantry rotation speed, dose rate and MLC leaf positions.[13] The major advantages of VMAT systems over IMRT are the decrease in number of MUs and the reduction in treatment delivery time.[14,15] A shorter treatment delivery time per fraction is particularly important for moving target such as lung tumor since the degree of intra-fraction motion has been found to increase with time.[16] Furthermore, radiation therapy for lung cancer can be challenging since the target is surrounded by a healthy lung tissue, a radiosensitive organ that has a low radiation tolerance. The aim of this study was to review the current literature on two VMAT systems, RapidArc (Varian Medical Systems, Palo Alto, CA, USA) and SmartArc (Philips Radiation Oncology Systems Philips, Fitchburg, WI, USA) with main focus on planning studies of lung cancer. A systematic review of available data was conducted using MEDLINE/PubMed with the keywords ''lung'' and "VMAT". A total of 17 articles were identified of which 8 were relevant for the purpose of this review.

LUNG CANCER

Lung cancer is the leading cancer killer in both men and women in the United States, causing more deaths than the next three most common cancers combined (colon, breast and prostate).[17] According to the American Cancer Society's most recent statistics, an estimated 226,160 new cases of lung cancer were expected to be diagnosed in 2012, representing almost 14% of all cancer diagnoses.[17]

LITERATURE REVIEW

Several planning studies have evaluated VMAT techniques in lung cancer. Bree, *et al*.[18] conducted a planning study in 20 inoperable non-small cell lung cancer (NSCLC) patients comparing 3DCRT with dynamic IMRT (d-IMRT) (7-9 fields) and RapidArc. The results from that study showed that, in comparison to 3DCRT, both the d-IMRT and RapidArc techniques resulted in a better conformity of the dose.[18] Furthermore, d-IMRT and RapidArc allowed higher dose to the target volume, thus improving regional tumor control.[18] However, there were no significant differences in homogeneity of dose in the target volume.

For NSCLC patients who are not candidates for surgical therapy, stereotactic body radiotherapy (SBRT) can be an alternative method for the treatment of small lung tumors. SBRT is a highly conformal technique that delivers high radiation dose with few treatment fractions to the tumor while limiting the doses received by OARs. Ong, *et al*.[19] compared RapidArc SBRT with conventional 3DCRT, dynamic conformal arcs, and IMRT for 18 patients with Stage I NSCLC. Ong, *et al.* reported the highest dose conformity and shortest delivery times for RapidArc SBRT plans compared to all other techniques.[19] For chest wall, a lower V (45 Gy) value was achieved in RapidArc plans; however, a small increase in V (5 Gy) value to contralateral lung was obtained in RapidArc plans compared to 3DCRT plans.[19] A higher dose to contralateral lung in RapidArc plans might have been due to use of full arcs in that study.[19] A better RapidArc plan set up would have been the use of partial arcs avoiding direct beam entrance via contralateral lung, and such partial-arc technique could potentially lower contralateral lung dose [Figure 1].

Scorsetti, *et al.*[20] performed a planning study on 6 patients that had malignant pleural mesothelioma, and the IMRT plans (9 fields) were compared against RapidArc (2 arcs) plans. Scorsetti, *et al.* reported that RapidArc and IMRT provided equivalent coverage and homogeneity, and RapidArc demonstrated better dose sparing to the OARs.[20] Similar to the findings of Ong, *et al*.,[19] the treatment delivery time was much lower for RapidArc in that study too.[20] Verbakel, *et al.*[21] published a paper on a clinical application of a novel hybrid IMRT (h-IMRT) technique for large Stage III lung tumor. The study was performed by utilizing h-IMRT to treat 14 patients. In that study,[21] h-IMRT

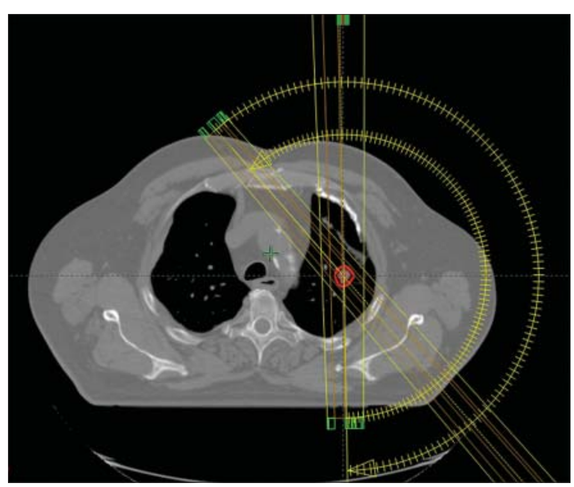

Figure 1: RapidArc plan set up in Eclipse treatment planning system for lung cancer using partial-arc technique (Figure courtesy of Department of Radiation Oncology, Arizona Center for Cancer Care, Peoria, Arizona, USA)

plans consisted of 2 components: (1) an anterior-posterior/posterior-anterior/posterior-anterior oblique, and (2) a 3-field IMRT. For the purpose of comparisons, all h-IMRT plans were retrospectively re-planned using RapidArc (2 full arcs), IMRT (6-fields), 3DCRT (5-9 fields), and a hybrid RapidArc (h-RapidArc) technique similar to the h-IMRT. Verbakel, *et al*.[21] reported that both h-IMRT and h-RapidArc permitted delivery of 66 Gy to large stage III lung tumors, and both were superior to either IMRT or RapidArc plans for reducing lung doses. Furthermore, the authors also showed that RapidArc plans achieved comparable V (20 Gy) values but led to slightly higher V (5 Gy) values.[21] It would be interesting to investigate the dosimetric impact of this hybrid technique on small lung tumors in the future.

Rao, *et al*.[22] compared SmartArc with IMRT for 6 cases of lung cancer. The results from that study[22] showed comparable planning target volime (PTV) coverage and OAR sparing. In comparisons to IMRT plans, the values of mean lung dose and V (20 Gy) were slightly higher in the SmartArc plans.[22] In another study, Holt, *et al*.[23] performed the comparison study between SmartArc (coplanar) and IMRT (coplanar and non-coplanar) for SBRT for 27 early-stage lung cancer patients. The results from that study showed that coplanar SmartArc achieved plan quality comparable to those using non coplanar IMRT and slightly better than those with coplanar IMRT.[23]

Zhang, *et al*.[24] performed a planning study on SmartArc planning for 15 SBRT lung patients and compared its dosimetric results with 3DCRT. In that study,[24] two types of SmartArc plans were created: (1) coplanar and non-coplanar SmartArc and (2) flattening filter free SmartArc (FFF-SmartArc). Each SmartArc plan utilized two dynamic arcs, whereas 3DCRT plan consisted of non-coplanar fields. The results from that study showed that SmartArc techniques demonstrated faster treatment delivery times, superior dose conformity to the target and sharper dose fall-off in normal tissues than the 3D plans.[24] Furthermore, the V (5 Gy) and V (20 Gy) values for lungs were lower with SmartArc techniques compared with 3D, and the dose to the target was more homogeneous in FFF-SmartArc plans; however, FFF-SmartArc plans required more MUs than non-coplanar SmartArc or 3D ones.[24]

Jiang, *et al*.[25] conducted the retrospective study of 12 locally advanced lung cancer patients and analyzed the differences between IMRT and single/partial-arc SmartArc (SA/PA-SmartArc) techniques in treatment planning. The SA-SmartArc plans showed the superior target dose coverage and comparable target dose (minimum, mean and maximum). For the total and contralateral lung, in comparison to IMRT plans, the V (5 Gy) and V (10 Gy) values were higher; whereas the V (20 Gy) and V (30 Gy) values as well as mean lung doses were lower in the SmartArc plans.[25] The SA/PA-SmartArc plans also reduced the treatment delivery time.[25]

DISCUSSION AND CONCLUSION

The published data in the current literature on VMAT (RapidArc and SmartArc) planning studies of lung cancer show that VMAT techniques have clear superiority over 3DCRT with regard to improving dose conformity and sparing of OARs. However, dosimetric differences between VMAT and IMRT planning studies are less distinct.[18-25] Specifically, the data indicates that for lung tumor VMAT and IMRT provide equivalent dose homogeneity, dose conformity and target volume coverage. Furthermore, planning studies[18-25] have reported contradictory results in terms of OARs sparing. For example, in the case of normal lung tissue, Verbakel, *et al*.[21] showed that RapidArc and IMRT plans achieved comparable V (20 Gy) values; whereas Rao, *et al*.[22] showed that the V (20 Gy) value was slightly higher in the SmartArc plans than in the IMRT plans.

One of the factors that might have contributed to the conflicting OAR results among different studies is the variability in treatment machines, and radiation techniques, such as the number of fields and arcs in the IMRT and VMAT plans, respectively. Several authors pointed out that adding an extra arc in the VMAT plan might be effective in reducing the OAR dose since VMAT plan with an additional arc consists of more control points and a higher degree of freedom for possible leaf positions, leading to a higher degree of modulation.[26,27] However, such strategy will make the optimization and dose calculation processes longer, and the dosimetrist will be required to make a compromise between the planning time and plan quality. Furthermore, the radiation dose to the OARs not in the proximity of the target volume arises largely from the secondary collimator transmission and scatter radiation from the treatment machine.[27,28] The amount of scatter radiation from secondary collimators depends on the configuration of the MLC and the treatment machine head. Thus, the OAR results from a RapidArc plan created based on the configuration of Varian linear accelerator may not be same as the OAR results from the SmartArc plan created based on the configuration of Phillips linear accelerator.

Another factor that affects the quality of treatment plans is the dose calculation algorithm employed within TPS, especially when there is an involvement of small fields and low-density medium such as air. The presence of air causes the electronic disequilibrium effect near the air/tissue interfaces as the lateral range of secondary electrons becomes longer than the width of the small field segments.[29,30] Thus, when a lung tissue is to be irradiated, dose calculation algorithms must have tissue heterogeneity corrections that will account accurately for the electron transport near air/tissue interface. Currently, collapsed cone convolution superposition algorithm (CCCS) and anisotropic analytic algorithm (AAA) are commonly used for SmartArc and RapidArc planning, respectively. Due to the differences in beam modeling approach within CCCS and AAA, discrepancies in their dose predictions exist. Several authors have documented the inadequacy of CCCS and AAA to calculate the dose accurately inside heterogeneous media.[31-42] It is clear that the discrepancies can occur between CCCS and AAA, and the dose prediction errors can be made when an insufficiently accurate dose calculation algorithm is used for the dose computations of clinical radiation treatment plans, especially for lung cases.

The major advantages of VMAT over IMRT are the reduction in the number of MUs and faster treatment delivery times without compromising the quality of the treatment plans. Moreover, faster delivery time is more patient-friendly and it minimizes intra-fractional patient motion allowing treatment volumes stay within their respective treatment margins.[16]

Current literature data shows that VMAT can be a good option to treat lung cancer; however, data on clinical trials are still lacking. The clinical trials are essential to confirm the safety and efficacy of VMAT techniques. The impact of different radiation treatment techniques on clinically important end points such as tumor control and side effects will be an interesting topic for future studies.

REFERENCES

1. Webb S. Developments and controversies in three-dimensional treatment planning: The physics of conformal radiotherapy: Advances in technology. Bristol: Institute of Physics Publishing; 1997, pp. 1-75.
2. Lawrence TS, Kessler ML, Robertson JM. 3-D conformal radiation therapy in upper gastrointestinal cancer. The University of Michigan experience. Front Radiat Ther Oncol 1996;29:221-8.
3. Zelefsky MJ, Fuks Z, Happersett L, Lee HJ, Ling CC, Burman CM, *et al*. Clinical experience with intensity modulated radiation therapy (IMRT) in prostate cancer. Radiother Oncol 2000;55:241-9.
4. Sternick ES. Commissioning and quality assurance of an IMRT system. The Theory and Practice of Intensity Modulated Radiation Therapy. Madison WI: Advanced Medical Publishing; 1997,121-26.
5. Webb S. IMRT: general considerations. Intensity-modulated radiation therapy. Bristol: Institute of Physics Publishing; 2000, pp. 1-30.
6. Veldeman L, Madani I, Hulstaert F, De Meerleer G, Mareel M, De Neve W. Evidence behind use of intensity-modulated radiotherapy: A systematic review of comparative clinical studies. Lancet Oncol 2008;9:367-75.
7. Guerrero Urbano MT, Nutting CM. Clinical use of intensity-modulated radiotherapy: Part I. Br J Radiol 2004;77:88-96.
8. Guerrero Urbano MT, Nutting CM. Clinical use of intensity-modulated radiotherapy: Part II. Br J Radiol 2004;77:177-82.
9. Wang JZ, Li XA, D'Souza WD, Stewart RD. Impact of prolonged fraction delivery times on tumor control: A note of caution for intensity-modulated radiation therapy (IMRT). Int J Radiat Oncol Biol Phys 2003;57:543-52.
10. Podgarsak EB. Special procedures and techniques in radiotherapy. Radiation Oncology Physics-A Handbook for Teachers and Student, First Edition. Vienna, Austria: IAEA Publications; 2008, 538-47.
11. Hall EJ, Wuu CS. Radiation-induced second cancers: The impact of 3D-CRT and IMRT. Int J Radiat Oncol Biol Phys 2003;56:83-8.
12. Ruben JD, Davis S, Evans C, Jones P, Gagliardi F, Haynes M, *et al*. The effect of intensity-modulated radiotherapy on radiation-induced second malignancies. Int J Radiat Oncol Biol Phys 2008;70:1530-6.
13. Otto K. Volumetric modulated arc therapy: IMRT in a single gantry arc. Med Phys 2008;35:310-7.
14. Yu CX, Li XA, Ma L, Chen D, Naqvi S, Shepard D, *et al*. Clinical implementation of intensity-modulated arc therapy. Int J Radiat Oncol Biol Phys 2002;53:453-63.
15. Palma DA, Verbakel WF, Otto K, Senan S. New developments in arc radiation therapy: A review. Cancer Treat Rev 2010;36:393-9.
16. Hoogeman MS, Nuyttens JJ, Levendag PC, Heijmen BJ. Time dependence of intrafraction patient motion assessed by repeat stereoscopic imaging. Int J Radiat Oncol Biol Phys 2008;70:609-18.
17. American Cancer Society, Cancer facts and figures 2012. Available from: http://www.cancer.org [Last accessed on November 20, 2012].
18. Bree Id, van Hinsberg MG, van Veelen LR. High-dose radiotherapy in inoperable nonsmall cell lung cancer: Comparison of volumetric modulated arc therapy, dynamic IMRT and 3D conformal radiotherapy. Med Dosim 2012;37:353-7.
19. Ong CL, Verbakel WF, Cuijpers JP, Slotman BJ, Lagerwaard FJ, Senan S. Stereotactic radiotherapy for peripheral lung tumors: A comparison of volumetric modulated arc therapy with 3 other delivery techniques. Radiother Oncol 2010;97:437-42.
20. Scorsetti M, Bignardi M, Clivio A, Cozzi L, Fogliata A, Lattuada P, *et al*. Volumetric modulation arc radiotherapy compared with static gantry intensity-modulated radiotherapy for malignant pleural mesothelioma tumor: A feasibility study. Int J Radiat Oncol Biol Phys 2010;77:942-9.
21. Verbakel WF, van Reij E, Ladenius-Lischer I, Cuijpers JP, Slotman BJ, Senan S. Clinical application of a novel hybrid intensity-modulated radiotherapy technique for stage III lung cancer and dosimetric comparison with four other techniques. Int J Radiat Oncol Biol Phys 2012;83:e297-303.
22. Rao M, Yang W, Chen F, Sheng K, Ye J, Mehta V, *et al*. Comparison of Elekta VMAT with helical tomotherapy and fixed field IMRT: Plan quality, delivery efficiency and accuracy. Med Phys 2010;37:1350-9.
23. Holt A, van Vliet-Vroegindeweij C, Mans A, Belderbos JS, Damen EM. Volumetric-modulated arc therapy for stereotactic body radiotherapy of lung tumors: A comparison with intensity-modulated radiotherapy techniques. Int J Radiat Oncol Biol Phys 2011;81:1560-7.
24. Zhang GG, Ku L, Dilling TJ, Stevens CW, Zhang RR, Li W, *et al*. Volumetric modulated arc planning for lung stereotactic body radiotherapy using conventional and unflattened photon beams: A dosimetric comparison with 3D technique. Radiat Oncol 2011;6:152.
25. Jiang X, Li T, Liu Y, Zhou L, Xu Y, Zhou X, *et al*. Planning analysis

for locally advanced lung cancer: Dosimetric and efficiency comparisons between intensity-modulated radiotherapy (IMRT), single-arc/partial-arc volumetric modulated arc therapy (SA/PA-VMAT). Radiat Oncol 2011;6:140.
26. Oliver M, Gagne I, Popescu C, Ansbacher W, Beckham WA. Analysis of RapidArc optimization strategies using objective function values and dose-volume histograms. J Appl Clin Med Phys 2009;11:3114.
27. Kan MW, Wong W, Leung LH, Yu PK, So RW, Cheng AC. A comprehensive dosimetric evaluation of using RapidArc volumetric-modulated arc therapy for the treatment of early-stage nasopharyngeal carcinoma. J Appl Clin Med Phys 2012;13:3887.
28. Verbakel WF, Cuijpers JP, Hoffmans D, Bieker M, Slotman BJ, Senan S. Volumetric intensity-modulated arc therapy vs. conventional IMRT in head-and-neck cancer: A comparative planning and dosimetric study. Int J Radiat Oncol Biol Phys 2009;74:252-9.
29. Chow JC, Seguin M, Alexander A. Dosimetric effect of collimating jaws for small multileaf collimated fields. Med Phys 2005;32:759-65.
30. Knöös T, Wieslander E, Cozzi L, Brink C, Fogliata A, Albers D, *et al*. Comparison of dose calculation algorithms for treatment planning in external photon beam therapy for clinical situations. Phys Med Biol 2006;51:5785-807.
31. Pasciuti K, Iaccarino G, Strigari L, Malatesta T, Benassi M, Di Nallo AM, *et al*. Tissue heterogeneity in IMRT dose calculation for lung cancer. Med Dosim 2011;36:219-27.
32. Han T, Mikell JK, Salehpour M, Mourtada F. Dosimetric comparison of Acuros XB deterministic radiation transport method with Monte Carlo and model-based convolution methods in heterogeneous media. Med Phys 2011;38:2651-64.
33. Fogliata A, Nicolini G, Vanetti E, Clivio A, Winkler P, Cozzi L. The impact of photon dose calculation algorithms on expected dose distributions in lungs under different respiratory phases. Phys Med Biol 2008;53:2375-90.
34. Calvo OI, Gutiérrez AN, Stathakis S, Esquivel C, Papanikolaou N. On the quantification of the dosimetric accuracy of collapsed cone convolution superposition (CCCS) algorithm for small lung volumes using IMRT. J Appl Clin Med Phys 2012;13:3751.
35. Hasenbalg F, Neuenschwander H, Mini R, Born EJ. Collapsed cone convolution and analytical anisotropic algorithm dose calculations compared to VMC++ Monte Carlo simulations in clinical cases. Phys Med Biol 2007;52:3679-91.
36. Francescon P, Cora S, Chiovati P. Dose verification of an IMRT treatment planning system with the BEAM EGS4-based Monte Carlo code. Med Phys 2003;30:144-57.
37. Azcona JD, Siochi RA, Azinovic I. Quality assurance in IMRT: Importance of the transmission through the jaws for an accurate calculation of absolute doses and relative distributions. Med Phys 2002;29:269-74.
38. Gray A, Oliver LD, Johnston PN. The accuracy of the pencil beam convolution and anisotropic analytical algorithms in predicting the dose effects due to attenuation from immobilization devices and large air gaps. Med Phys 2009;36:3181-91.
39. Robinson D. Inhomogeneity correction and the analytic anisotropic algorithm. J Appl Clin Med Phys 2008;9:2786.
40. Rana SB. Dose prediction accuracy of anisotropic analytical algorithm and pencil beam convolution algorithm beyond high density heterogeneity interface. South Asian J Cancer 2013;2:26-30.
41. Van Esch A, Tillikainen L, Pyykkonen J, Tenhunen M, Helminen H, Siljamäki S, *et al*. Testing of the analytical anisotropic algorithm for photon dose calculation. Med Phys 2006;33:4130-48.
42. Rana S, Rogers K. Dosimetric evaluation of Acuros XB dose calculation algorithm with measurements in predicting doses beyond different air gap thickness for smaller and larger field sizes. J Med Phys 2013;38:9-14.

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