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Automated VMAT treatment planning for stage III lung cancer: how does it compare with IMRT?

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Abstract

Purpose—To compare the quality of volumetric modulated arc therapy (VMAT) or intensity-modulated radiation therapy (IMRT) plans generated by an automated inverse planning system with that of dosimetrist-generated IMRT treatment plans for patients with stage III lung cancer.

Methods and Materials—Two groups of eight patients with stage III lung cancer were randomly selected. For group I, the dosimetrists spent their best effort in designing IMRT plans to compete with the automated inverse planning system (mdaccAutoPlan); for group II, the dosimetrists were not in competition and spent their regular effort. Five experienced radiation oncologists independently blind-reviewed and ranked the three plans for each patient, a rank of “1” being the best and “3” the worst. Dosimetric measures were also performed to quantitatively evaluate the three types of plans.

Results—Blind rankings from different oncologists were generally consistent. For group I, the auto-VMAT, auto-IMRT, and manual-IMRT plans received average ranks of 1.6, 2.13, and 2.18, respectively. The auto-VMAT plans in group I had 10% higher PTV conformity and 24% lower esophagus V70 than the manual-IMRT plans; they also resulted in over 20% higher complication-free tumor control probability (p+) than either type of IMRT plans. The auto- and manual-IMRT plans in this group yielded generally comparable dosimetric measures. For group II, the auto-VMAT, auto-IMRT, and manual-IMRT plans received average ranks of 1.55, 1.75, and 2.75, respectively. Compared to the manual-IMRT plans in this group, the auto-VMAT plans and the

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CONFLICTS OF INTEREST NOTIFICATION

There are no actual or potential conflicts of interest.

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auto-IMRT plans showed, respectively, 17% and 14% higher PTV dose conformity, 8% and 17% lower mean lung dose, 17% and 26% lower mean heart dose, and 36% and 23% higher p+.

Conclusions—mdaccAutoPlan is capable of generating high-quality VMAT and IMRT treatment plans for stage III lung cancer. Manual-IMRT plans could achieve quality similar to auto-IMRT plans if best effort were spent.

Keywords

VMAT; IMRT; Stage III lung cancer; Automated inverse planning

Introduction

Volumetric modulated arc therapy (VMAT) is attracting attention because of its improved delivery efficiency over fixed-field intensity-modulated radiotherapy (IMRT) (1). The shorter treatment time of VMAT can increase patient throughput, reduce the risk of intrafraction motion, and improve patient comfort during treatment. Although VMAT has been previously compared to IMRT for various types of cancer (1–12), it is still unclear whether VMAT also generates a better plan quality than IMRT for stage III lung cancer.

Our previous study showed that VMAT has significant advantage over 8-field IMRT for prostate cancer treatment (13). VMAT for stage I lung cancer, which usually is treated with stereotactic body radiation therapy, was studied by Matuszak *et al.* and promising results were observed (14). However, we have found few studies on VMAT plan quality for stage III lung cancer, which involves larger tumors than stage I cancer with less regular shapes. This has posed a challenge for the application of VMAT for stage III lung cancer. Another major challenge in designing VMAT treatment plans is that VMAT takes a much longer time to optimize than IMRT, which may introduce more variations in plan quality because of limits on planners' time and effort. Assurance of high-quality treatment plans is more difficult for VMAT than for IMRT.

Automated inverse treatment planning for IMRT has been proven to be possible in practice by our group's and other groups' work (15, 16). We previously reported development of an automatic inverse planning algorithm for IMRT, the "mdaccAutoPlan system" (16). The mdaccAutoPlan system automatically sets up IMRT beams, sets inverse planning initial conditions and initiates the optimization process, automatically adjusts inverse planning parameters based on objective cost functions, and finally generates a high-quality IMRT plan, an "auto-IMRT" plan.

For this study, we developed a version of the mdaccAutoPlan system for VMAT and stage III lung cancer to improve the efficiency of VMAT treatment planning and to assure high-quality VMAT plans for a variety of patients. We compared the quality of automatically generated VMAT plans to that of the IMRT plans generated by experienced dosimetrists and IMRT plans generated by the mdaccAutoPlan system, with the objective of identifying the superior modality for treating stage III lung cancer.

Methods

Study Design

Computed tomography datasets for a total of 16 patients with stage III lung cancer who were treated at the University of Texas MD Anderson Cancer Center (MDACC) between 2009 and 2010 were randomly selected. Fourteen of the patients were prescribed 74 Gy/37 fractions, one was prescribed 66 Gy/33 fractions, and one was prescribed 68 Gy/34 fractions. For each patient, we compared the quality of a VMAT plan generated by

mdaccAutoPlan to two IMRT plans generated independently. The patients were divided into two groups.

The eight patients in group I were randomly chosen from a stage III lung cancer treatment protocol at MDACC. For each of these patients, two IMRT plans were generated simultaneously, one by an experienced dosimetrist and one by mdaccAutoPlan; the attending radiation oncologist selected the superior plan to use in the treatment of each patient. In designing these plans, the dosimetrists were aware to compete with the mdaccAutoPlan system, and thus put in much more time and effort than usual to attain the best plan quality. The eight patients in group II were not involved in this protocol and were treated with an IMRT plan that was designed by an experienced dosimetrist in MDACC. Another IMRT plan was generated retrospectively for each patient in group II by the mdaccAutoPlan system. Therefore, each patient in the two groups had two IMRT plans, one generated by a dosimetrist and another by the mdaccAutoPlan system. A VMAT plan was generated by mdaccAutoPlan (auto-VMAT) for each of the 16 patients in groups I and II and was compared to the manual-IMRT and auto-IMRT plans.

To further validate the effectiveness of the mdaccAutoPlan system, a larger sample comprising another 48 patients with stage III lung cancer was randomly selected. The patients were treated with a dosimetrist-designed IMRT plan prior to this study. For each patient, an auto-IMRT plan was generated using the mdaccAutoPlan system. Dosimetric indices of the auto-IMRT plan were compared to those of the manual plan for these patients.

VMAT Version of mdaccAutoPlan

The VMAT plans were generated by a VMAT version of the mdaccAutoPlan system (21) for stage III lung cancer, which is based on the same framework as the IMRT version (13). The mdaccAutoPlan system is built upon the Pinnacle³ version 9.0 treatment planning system and makes use of its built-in dose calculation and the SmartArc module, which is based on the direct machine parameter optimization method (17).

A flowchart of the VMAT version of the mdaccAutoPlan algorithm for stage III lung cancer is shown in Figure 1. Two dynamic arcs, each with 360° rotations (one from 182° to 178° and the other from 178° to 182°), are automatically added and configured for the plan.

At the beginning of the inverse planning procedure, a set of initial objective functions are loaded into the Pinnacle³ treatment planning system. The initial objectives, which are shown in Table 1, put strong emphasis on the planning target volume (PTV) coverage and were defined on the basis of previous planning experience, as described in (16). Therefore, the initial optimization results in a plan that has optimal PTV coverage. Then, the weight of the lung constrain in the objective function is increased and the plan is re-optimized to generate improved lung sparing. The maximum doses to the spinal cord and esophagus are controlled to make sure that the dose tolerances of these organs are not exceeded. A similar procedure is followed to generate improved heart sparing. A final round of optimization is performed to eliminate hot spots after adding an objective of the automatically generated contours of hot spots.

Plan Evaluation

To obtain an unbiased evaluation of the three planning strategies (manual-IMRT, auto-IMRT, and auto-VMAT), plan quality underwent a “blind” review by five radiation oncologists from four different hospitals. Each oncologist independently reviewed all three plans for each patient. While reviewing each plan, each oncologist was given only the dose-volume histograms (DVHs) and the corresponding dose distributions; other information, including the treatment modality and designer of the plan, were hidden. For each patient, the

oncologist evaluated and ranked the three plans by their overall quality. A rank of “1” indicates the most preferred plan for treating the patient and “3” the least preferred; plans with similar quality could be given the same rank. An average rank for each type of plan was obtained for the two groups of patients.

To measure the variations in plan rankings among different oncologists (A, B, C, D, and E), we performed a two-sided paired *t*-test for the rankings of all 16 patients and calculated the *p*-values for rankings between pairs of oncologists (A–B, B–C, C–D, D–E, and E–A). A *p*-value of < 0.05 was considered statistically significant.

We also measured various dosimetric indices to which the radiation oncologists in our institution pay most attention while evaluating a plan. PTV coverage was measured using D_{95} , D_1 , the conformity index (CI) (defined in (18)), and the heterogeneity index (HI) ($= D_1/D_{95}$). Normal tissue sparing was measured by the 50% prescription dose conformity:

$$50\%Rx\ CI = \frac{V_{50\%D_p}}{TV},$$

where $V_{50\%D_p}$ is the volume enclosed by the isodose surface of 50% of prescription and TV is the target volume. OAR sparing was measured by mean lung dose (MLD), lung volume receiving 5 Gy (V5), lung V20, heart mean dose, cord D1, esophagus V70, and esophagus D1. The complication-free tumor control probability (p+) (19) was calculated for each plan. Calculated values were compared by the two-sided paired *t*-test. A *p*-value 0.05 was defined as statistically significant.

Results

The results of the blind ranking by five radiation oncologists are shown in Figure 2. The values shown are averaged over the eight patients in each group (left and middle) and over all 16 patients (right); the error bars indicate the standard deviations among the rankings of the five oncologists. A lower rank value indicates higher plan quality and vice versa. For group I, the difference between manual- and auto-IMRT plans was small and the auto-VMAT plans were ranked approximately 0.5 point lower (better quality) than the IMRT plans. For group II, the auto-VMAT plans were ranked significantly (44%) better than the manual-IMRT plans and were also ranked better than the auto-IMRT plans. Overall, auto-VMAT plans received the best ranking and the manual-IMRT plans received the worst. The *p*-values of the five oncologists' rankings (10 pairs of comparisons) were all larger than the 0.05 threshold (range 0.07 to 1), indicating that, for each patient, there was no significant difference in the rankings by different oncologists.

Figure 3 shows the average dosimetric indices measured for groups I and II, respectively. For group I, the auto-VMAT plans yielded values for most indices comparable to those of the two IMRT plans. The auto-VMAT plans had 0.8% lower PTV coverage but 10% better PTV dose conformity and 24% lower esophagus V70 than the manual-IMRT plans. The auto-VMAT plans also resulted in over 20% higher p+ values than either type of IMRT plans. Other indices were comparable among the plans. For group II, the auto-VMAT plans on average were better on several dosimetric indices than the manual-IMRT plans: the auto-VMAT plans had 17% better PTV dose conformity, 8% lower MLD, 17% lower mean heart dose, 19% lower esophagus V70, as well as 36% higher p+. Compared to the auto-IMRT plans, the auto-VMAT plans showed 11% higher MLD and 10% higher lung V20 but 3% more homogeneous PTV.

Figure 4 shows the DVHs and dose distributions of the three types of plan for a typical patient in group I. All three plans achieved prescribed target coverage and satisfied the OAR dose tolerances. The auto-VMAT plan resulted in levels of PTV coverage, lung sparing, and heart sparing similar to those of the two IMRT plans, and slightly better esophagus sparing.

Figure 5 compares the auto-IMRT plans with manual-IMRT plans for the larger sample of 56 patients. Although the auto-IMRT plans showed an average 1.8% increase in PTV D_1 , they showed, on average, 18.4% better target CI, 8.2% better 50%Rx CI, 9.3% lower MLD, 11.1% lower lung V20, 7.6% lower heart dose, 10.1% lower D_1 in the cord, and 14.0% higher p+. No statistically significant differences were observed on other dosimetric indices.

Discussion

VMAT treatment planning for stage III lung cancer is difficult, as can be surmised from the relatively few publications in the literature and the limited clinical applications. One possible reason is the underlying difficulty of sparing the large area of the lung that surrounds the target while giving a high dose to large target with radiation beams coming from directions all around the patient. This is the first work that develops and validates an automated VMAT treatment planning software for stage III lung cancer. The software's performance has been examined for 16 patients with a variety of tumor sizes (77 cm³ to 1,886 cm³) and locations (central, left, right, upper, or lower lung); plan quality acceptable for treatment was attained consistently for every patient.

The plan quality of manual-VMAT or IMRT treatment planning depends heavily on the amount of effort spent in the planning and the level of experience of the planner (20). To perform an unbiased comparison between the two modalities, special consideration had to be taken of the optimality of the VMAT and IMRT plans. In this work, we generated VMAT plans using the mdaccAutoPlan software, which represents a high level of quality we could achieve, and compared these plans to IMRT plans generated automatically or manually by different degrees of effort. For the same group of dosimetrists from our institution, when the usual amount of effort was spent in manually designing an IMRT plan, the plan quality was inferior to VMAT on several dosimetric indices, as seen in Figure 3(a); however, when greater effort was spent, only a few dosimetric indices were significantly different, and the IMRT plan quality was generally comparable to that of VMAT, as seen in Figure 3(c). Auto-IMRT plans, which were superior in quality to IMRT plans generated manually with usual effort (Figure 5) and similar in quality to IMRT plans generated with great effort, yielded dosimetric measures that were essentially comparable to those of the auto-VMAT plans.

An important finding of this work is that auto-VMAT plans stood out in the rankings of the blind plan review, which coincides with the complication-free tumor control probability measures (p+ values). Although the five participating radiation oncologists reviewed the plans and blind-ranked the plans independently from each other, their ranking results agreed fairly well. These results are probably due to the auto-VMAT plans' more conformal isodose lines, fewer hot spots in normal tissues, and more homogeneous dose coverage in the target areas. They indicate that radiation oncologists weight dose distribution heavily in plan evaluation and favor auto-VMAT plans more than IMRT plans designed by either method. On the other hand, the ranking by radiation oncologists was consistent with the p+ values, which represent an overall evaluation of plan quality from quantitative dosimetric indices. The auto-VMAT plans yielded significantly higher p+ values than the IMRT plans, especially those designed manually, as shown in Figure 3. One of the major contributions to the higher p+ values was the much better esophagus sparing achieved by VMAT as a result of its greater number of beam angles. This finding suggests the superiority of auto-VMAT plans over IMRT plans.

The delivery efficiencies of VMAT and IMRT have been extensively compared elsewhere (3–10). It has been widely accepted that VMAT has a significantly lower delivery time than IMRT. Although the focus of this work is on comparison of plan quality, we did record the estimated delivery time for each plan. The delivery times of VMAT plans were on average 2.2 minutes, 71% less than those of the IMRT plans (7.5 minutes average delivery time).

The greater treatment planning time of VMAT, as reported by others (2, 4, 8), may be a limiting factor in its clinical applications. In our current computation environment, each VMAT optimization cycle takes around 30 minutes to complete, and several such cycles are required to optimize objective function parameters to generate the final plan, adding up to hours of total planning time. With manual planning, the planners compromise the number of the trial-and-error cycles to shorten the total planning time so that usually unable to generate clinically acceptable plans in their available time, which is the reason why we do not have manual-VMAT plans to compare to in this study. The automated planning approach, i.e., the mdaccAutoPlan system, mitigates this problem to some extent because it frees the planner from the long manual trial-and-error planning process, and the final plan quality is not affected by limits on planner's available time. The mdaccAutoPlan system can be a powerful tool to bring the VMAT technique into routine clinical practice.

Besides, it was observed that V1 of the whole body from the VMAT plans was, on average, 9% larger than that from the manual-IMRT plans ($p = 0.002$) and 7% larger than that from the auto-IMRT plans ($p = 0.005$), which suggests that VMAT tends to create a larger volume of low dose irradiation to the whole body than IMRT.

Conclusions

mdaccAutoPlan system can generate high-quality VMAT treatment plans for stage III lung cancer. Quality of VMAT plans generated in this manner is superior to that of IMRT plans. However, VMAT quality is comparable to that of an IMRT plan if the latter are generated considerably greater trial-and-error using large amounts of dosimetrists' time and effort. Considering the significant advantage of VMAT in delivery efficiency, VMAT appears to be the superior treatment modality for stage III lung cancer.

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HIGHLIGHT

This work compares the quality of VMAT and IMRT plans generated by an automated inverse planning system with that of dosimetrist-generated IMRT treatment plans for patients with stage III lung cancer. Independent blind-review by 5 experienced radiation oncologists and dosimetric measures both show that mdaccAutoPlan is capable of generating high-quality VMAT and IMRT treatment plans for stage III lung cancer. Manual-IMRT plans could achieve quality similar to auto-IMRT plans if considerably greater efforts were expended.

Figure 1.

(a) Flowchart of the VMAT version of the mdaccAutoPlan algorithm and (b) details of the "control dose in the esophagus and the cord" box. "obj value" is the value of each objective function; $D_{threshold}^{cord}$ and $D_{threshold}^{esophagus}$ are, respectively, the dose threshold for the D_{max} of the cord and the esophagus. DMPO = direct machine parameter optimization.

Figure 2.
Results of blind ranking of three types of plans by five radiation oncologists.

Figure 3. Average dosimetric indices. (a) auto-VMAT plans compared with manual-IMRT plans by the dosimetrists for group I, (b) auto-VMAT plans compared with auto-IMRT plans for group I, (c) auto-VMAT plans compared with manual-IMRT plans by the dosimetrists for group II, and (d) auto-VMAT plans compared with auto-IMRT plans for group II. The p -values of each comparison are marked on the graph. The dosimetric values are scaled up or down if necessary to keep all values between 10 and 60.

Figure 4. Dose-volume histograms (a) and dose distributions (b) of a typical patient from the manual-IMRT plan generated by a dosimetrist, the auto-IMRT plan, and the auto-VMAT plan. The patient was prescribed 74 Gy/37 fractions. In (b): left two columns, transverse views; right two columns, sagittal views.

Figure 5. Average dosimetric indices of manual-IMRT plans designed by a dosimetrist and auto-IMRT plans for a large sample of patients. The *p*-values of each comparison are marked on the graph.

Table 1

Initial objectives of mdaccAutoPlan that are loaded into the Pinnacle inverse planning system for stage III lung cancer using VMAT.

ROI	Type	Target cGy	Volume (%)	Weight	a
FS-PlanPTV	Uniform Dose	7400		100	
FS-PlanPTV	Max Dose	7400		100	
FS-PlanPTV	Min Dose	7400		100	
FS-PTVRing	Max Dose	6600		50	
FS-NTAvoid	Max Dose	5000		10	
FS-LungAvoid	Max EUD	200		0.01	1
FS-LungAvoid	Max DVH	250	15	0.01	
FS-CLungAvoid	Max EUD	120		0.01	1
FS-ILungAvoid	Max EUD	800		0.005	1
FS-PrvCord	Max EUD	500		0.01	50
FS-PrvCordRing	Max Dose	1500		0.01	
FS-HeartAvoid	Max EUD	300		0.01	2
FS-PlanEsoph	Max EUD	900		0.01	5
FS-PlanEsoph	Max Dose	3500		0.01	

ROI = region of interest; EUD = equivalent uniform dose; DVH = dose volume histogram; a = EUD control parameter.