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Scientific Article

Dosimetric Advantage of Combined IMRT for Whole Lung and Abdomen Irradiation for Wilms Tumor

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Purpose: In patients with Wilms tumor with lung metastases, a cardiac-sparing intensity modulated radiation therapy (CS-IMRT) technique is increasingly being adopted for whole lung irradiation. However, the standard technique for flank and whole abdomen radiation remains 2-dimensional anterioposterior (AP), and overlap at the junction between the whole lung CS-IMRT and abdominal AP fields can result in overdose to normal organs. Here, we compared the dosimetry of patients who received whole lung irradiation and flank or abdominal radiation therapy with CS-IMRT with AP abdominal field (IMRT-AP) versus CS-IMRT with IMRT abdominal field (combined IMRT).

Methods and Materials: We retrospectively reviewed the radiation plans of 2 patients with Wilms tumor who received CS-IMRT and flank or whole abdomen irradiation with a combined IMRT approach. Comparison IMRT-AP plans were generated with equivalent target coverage of 95% receiving the prescribed dose. Maximum doses to normal organs were compared at the junctional overlap.

Results: Overlap at the junction between CS-IMRT and abdominal fields resulted in a significantly lower dose with combined IMRT plans compared with IMRT-AP plan. Differences in maximum doses (in cGy) to normal organs between combined IMRT versus IMRT-AP plans were most significant in the vertebral body (patient 1 = 1277 vs 2065; patient 2 = 1334 vs 2287), lungs (patient 1 = 1298 vs 2081; patient 2 = 1234 vs 1820), spinal cord (patient 1 = 1235 vs 1975; patient 2 = 1345 vs 2253), stomach (patient 1 = 1264 vs 1977; patient 2 = 1118 vs 2062), and liver (patient 1 = 1297 vs 1889; patient 2 = 1334 vs 2237).

Conclusions: The combined IMRT approach for Wilms patients who require whole lung and abdomen irradiation can provide more uniform dose distribution in the junction area and significantly lower doses to normal organs at the junctional overlap.

Introduction

Wilms' tumor is the most common pediatric renal malignancy and accounts for 6% of all childhood malignancies.[1] Incremental improvement in treatment technique and multimodality has led to an overall survival

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rate of 90%.[2] However, Wilms tumor survivors have been associated with late adverse effects such as secondary malignancy, gastrointestinal, cardiac, renal, pulmonary, and musculoskeletal side effects.[3-8] Emphasis is now on reducing toxicity and improving the quality of life of long-term survivors.

Whole lung irradiation (WLI) has traditionally been given to patients who have lung metastases. In the past, WLI has been delivered with an anteroposterior-posteroanterior (AP/PA) field approach. More recently, there has been a transition to using intensity modulated radiation therapy (IMRT) to reduce the long-term effect of radiation on cardiac functions.[9-11] Meanwhile, the standard technique for flank and whole abdomen irradiation remains the AP/PA approach.[12-14] For patients who require concurrent WLI and abdominal irradiation (either flank or whole abdomen irradiation), the overlap at the junction of the lung and abdomen fields can cause overdosing of normal structures.

Using combined IMRT for whole lung and abdominal irradiation may avoid the issue of overlap with cardiac-sparing whole lung irradiation and standard AP/PA flank or whole abdomen irradiation fields. This is supported by studies showing favorable dosimetry of the IMRT technique for flank irradiation alone.[15-17]

Methods and Materials

Case selection

We retrospectively reviewed 2 patients with Wilms tumor with lung metastases who received neoadjuvant chemotherapy and surgical resection of the primary tumors. One patient received concurrent WLI plus flank irradiation and the other patient received concurrent WLI plus whole abdomen irradiation. WLI was treated with a dose of 12 Gy in 8 fractions. Flank and whole abdomen irradiation were treated to 10.5 Gy in 7 fractions to have the same dose per fraction as WLI. For better visualization of dose overlap, comparison plans were generated after adjusting WLI dose to the same dose as flank or whole abdomen irradiation (10.5 Gy in 7 fractions). Our study was approved by VUMC institutional review board (IRB #230276)

Patient simulation and target volume and normal structure delineation

Patients were immobilized with a vac-lok in supine position with arms up. A 3-dimensional chest and abdomen computed tomography scan was performed with a 2-mm slice thickness. A separate 4-dimensional chest computed tomography was performed for WLI planning. WLI target delineation was performed based on published guidelines on cardiac-sparing whole lung IMRT.[11] Flank and whole abdomen irradiation targets and normal structure delineation were based on the most recently published Children's Oncology Group stage IV favorable histology Wilms Tumor protocol (AREN0533).[18]

Planning design

For combined IMRT for whole lung and flank or abdomen irradiation planning, we used a volumetric modulated arc therapy approach. Isocenters were set at the center of the diaphragm. Specifically for whole lung and flank irradiation, 3 6-MV full rotational arcs with a collimator offset of 15° were used. The Y jaws were opened to 34 cm to encompass both the lungs and left flank. For combined IMRT for whole lung and whole abdomen irradiation, 5 6-MV full rotational arcs with a combination of collimator offsets of 10°, 35°, and 45° were used for the initial plan. The Y jaws were opened to a maximum field size of 40 cm, to cover both targets in the initial plan.

Comparison AP/PA flank and AP/PA whole abdomen plans were retrospectively generated and matched with cardiac-sparing IMRT with a match line at the isocenter and 95% of the abdominal field receiving the prescribed dose. All the treatment plans in this study were conducted with Eclipse AAA version 13.6.23 and 15.6.05 (Varian). In terms of treatment delivery time, the patient set-up time was the same for the combined IMRT and IMRT-AP approaches. Monitoring units (MU) were also approximately the same. For the whole lung and flank irradiation case, combined IMRT required 558 versus 628 MU with IMRT-AP/PA. For the whole lung and whole abdomen case, combined IMRT required 640 versus 535 MU with IMRT-AP/PA. Delivery time was also approximately the same for both approaches, accounting for fewer isocenters with the combined IMRT approach.

Statistical analyses

Maximum doses of normal organs at risk (OAR) in the area of overlap between WLI and flank/whole abdomen irradiation fields were compared between combined-IMRT and IMRT-AP approaches. OARs included the liver, lungs, stomach, esophagus, contralateral kidney, vertebral body, spinal cord, pancreas, small bowel, and heart. A dose gradient profile was generated at 4 cm superior and inferior from the isocenter.

Results

For the patient who received WLI and flank irradiation (patient 1), the overall composite hotspot for the combined-IMRT plan was 12.98 Gy, located in the lungs. In comparison, the IMRT-AP plan for this patient generated

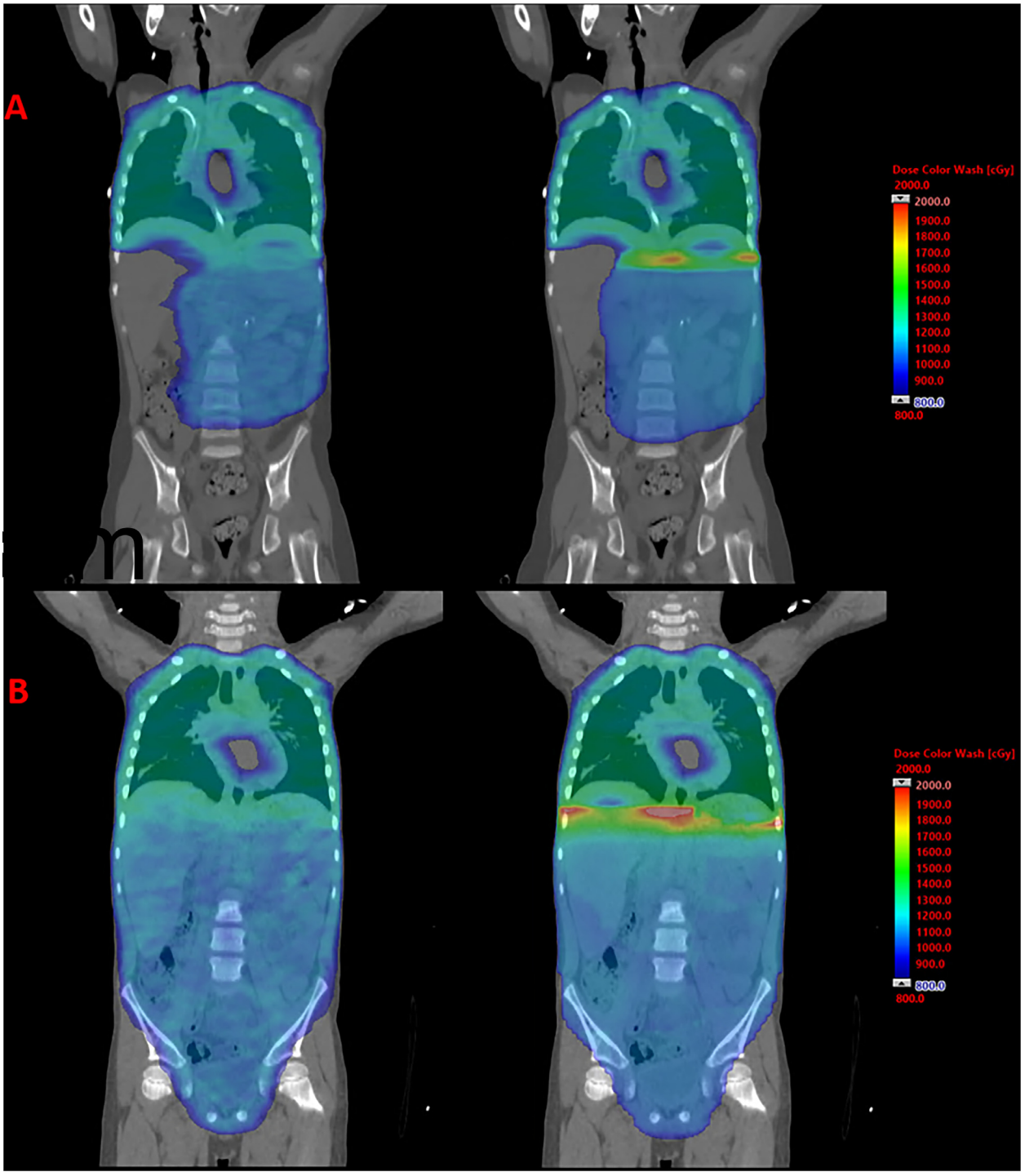

Figure 1 (A) Dose color wash of combined IMRT to whole lung and flank (left) versus cardiac sparing IMRT + anteroposterior-posteroanterior flank field (right). (B) Dose color wash of combined IMRT to whole lung and whole abdomen (left) versus cardiac sparing IMRT + anteroposterior-posteroanterior flank field (right). Isocenters are shown in green crosshair. For better visualization of dose overlap, comparison plans were generated with whole lung irradiation and abdomen receiving the same dose at 10.5 Gy in 7 fractions.
Abbreviation: IMRT = intensity modulated radiation therapy.

a hot spot of 20.81 Gy, located in the lungs. The dose color washes for comparison of patient 1's plans are illustrated in Fig. 1A.

For the patient who received WLI and whole abdomen irradiation (patient 2), the overall composite hotspot was 13.45 Gy in the spinal cord. The hotspot from the

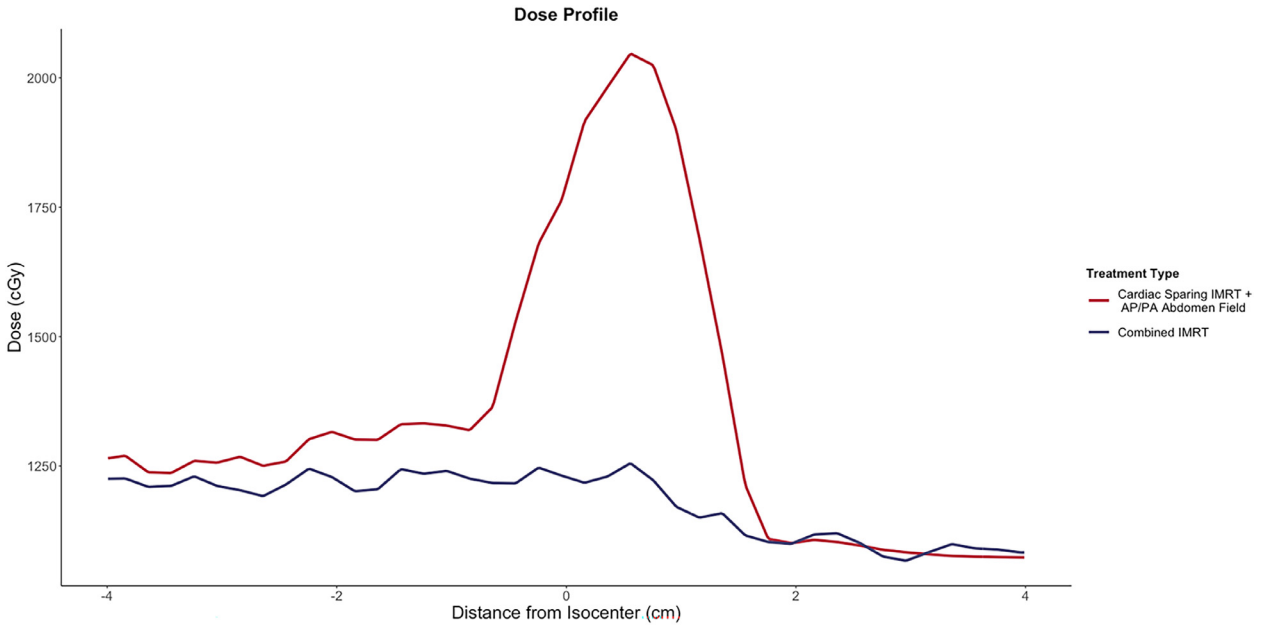

Figure 2 Dose gradient profiles of combined intensity modulated radiation therapy (blue) versus cardiac sparing intensity modulated radiation therapy + anteroposterior-posteroanterior flank field (red), 4-cm superior and inferior from the isocenter.

comparison IMRT-AP plan was 22.87 Gy in the thoracic vertebral body. The dose color washes for comparison of patient 2's plans are illustrated in Fig. 1B.

Dose gradient profiles were generated 4 cm superior and inferior from the isocenter for combined-IMRT and IMRT-AP plans. The dose gradient of IMRT-AP plans showed an approximately 1 cm segment receiving above 18 Gy because of overlap (Fig. 2).

Significant differences in maximum doses for multiple OARs were seen between combined-IMRT and IMRT-AP plans in each patient (Fig. 3). The following OAR doses in the WLI-flank patient (patient 1) had the most significant differences between plans (doses in cGy in combined-IMRT and IMRT-AP plans, respectively): vertebral body (1277 vs. 2065), lungs (1298 vs. 2081), spinal cord (1235 vs. 1975), stomach (1264 vs. 1977), and liver (1297 vs. 1889). The following OAR doses in the WLI-whole abdomen patient (patient 2) had the most significant dose differences (in cGy) in vertebral body (1334 vs. 2287), stomach (1118 vs. 2062), small bowel (1297 vs. 2219), spinal cord (1345 vs. 2253), liver (1334 vs. 2237), esophagus (1315 vs. 2060), lungs (1234 vs. 1820), and contralateral kidney (1157 vs. 1583).

Discussion

As the cardiac-sparing IMRT technique for WLI has been increasingly adopted as a new standard of care, the best approach for concurrent abdominal irradiation remains unclear. In our retrospectively generated AP/PA plan matched to IMRT-WLI, challenges exist to achieve good coverage with acceptable hot spots in the junction area.[11] This is understandable given that the IMRT WLI plan has a complicated gradient at the inferior border. Forward planning with manual contouring of beam fluence for AP and PA fields has been proposed as a possible solution; however, it is labor-intensive and does not completely eliminate the hotspots. The combined IMRT technique for both the lungs and the abdomen area, however, can eliminate these challenges because now both target volumes in the lungs and abdomen area can be optimized simultaneously with one IMRT plan. Our study has highlighted how a combined IMRT plan can decrease hot spots at the overlap between lung and abdominal plans, spare many OARs, and simplify treatment planning by necessitating only a single combined IMRT plan as opposed to both an IMRT and an AP/PA plan. In rare cases in which the target volumes in the lung and abdomen exceed the limits that a mono-isocenter plan can cover with a normal linear accelerator, separate isocenters can be used to cover the lungs and the abdomen, respectively, and the combined IMRT solution is still feasible for achieving a uniform dose distribution in the junction area because most modern inverse planning systems have an auto-feathering function.

The ability to decrease radiation to normal OARs is especially important in the pediatric population because the long-term effects of radiation in pediatrics have been well documented. In fact, a study by Paulino et al[5] showed that lower doses of radiation for Wilms tumor are related to a lower incidence of severe functional and physical deformities. The study specifically demonstrated that scoliosis development increases when radiation doses are

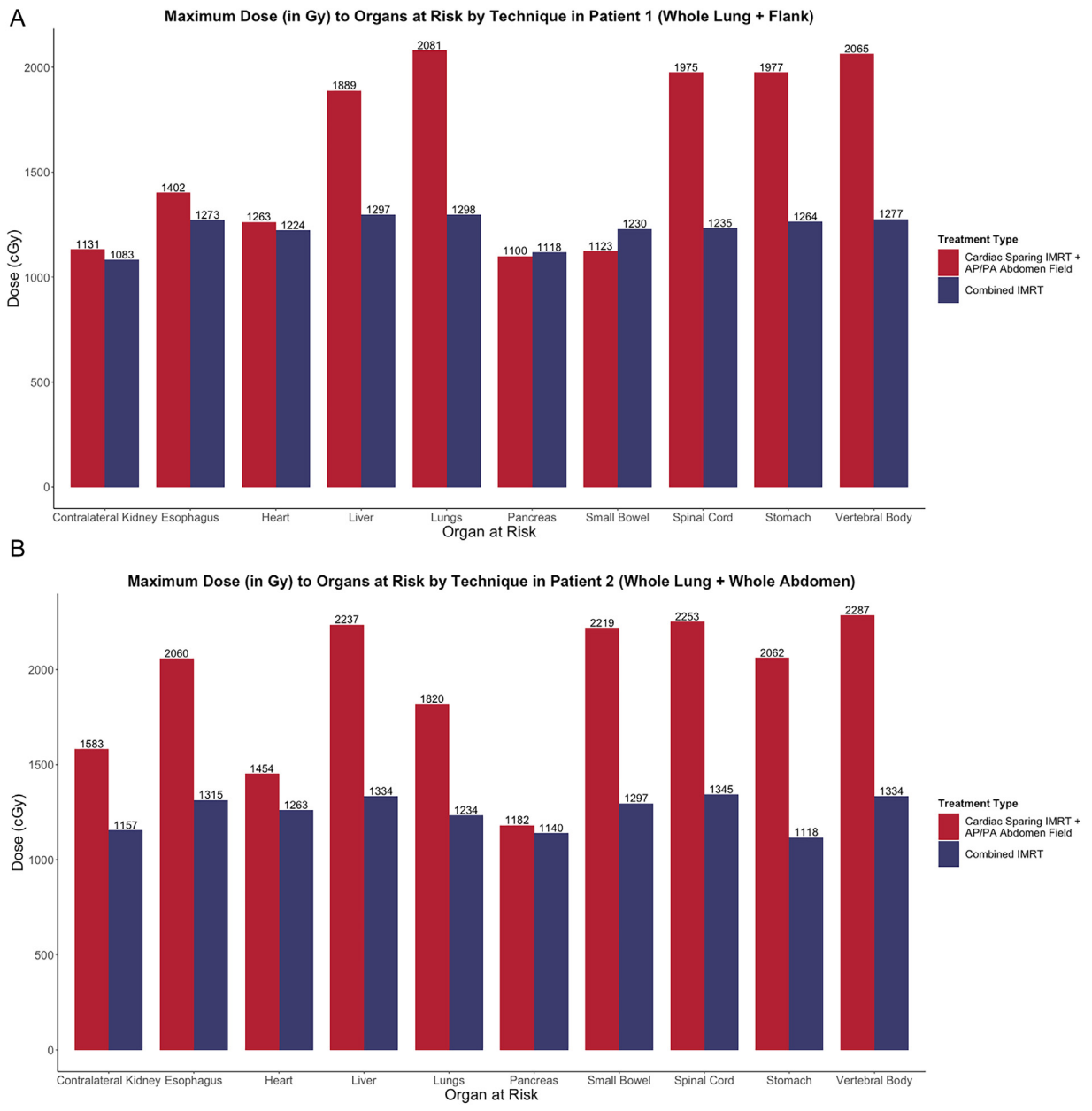

Figure 3 (A) Maximum doses (in cGy) to organs at risk by treatment technique in Wilms patient treated with whole lung and flank irradiation. (B) Maximum doses (in cGy) to organs at risk by treatment technique in Wilms patient treated with whole lung and whole abdomen irradiation.

above 2400 cGy and is significantly less when the doses are less than 1200 cGy.[5] A study by Baeza et al[19] demonstrated that a lung dose greater than 1500 cGy was associated with increased radiation pneumonitis after WLI. Other long-term effects of radiation include small bowl obstruction, ovarian failure, renal nephritis, and secondary neoplasms, among others. As shown by our patients, 5 organs in patient 1 and 6 organs in patient 2 received a dosage near that level at above 2000 cGy with the AP/PA approach, and no OAR received a dosage greater than 1350 cGy with the total IMRT approach (see Fig. 3). The total IMRT approach for both patients demonstrated significantly less dosage across all OARs than the AP/PA approach. Hence, our findings highlight that total IMRT does in fact significantly reduce radiation to OARs.

Although our results are promising, there are several limitations ofour study. The largest is that the sample size, consisting of only 2 patients treated at a single academic institution, reduced the generalizability of the study. Additionally, the combined IMRT approach is designed for a specific subset of Wilms tumor cases treated with neoadjuvant chemotherapy and surgery. This approach cannot be applied to cases in which patients receive upfront surgery and immediate postoperative abdominal

radiation is required. Despite this, we believe that the results of our study provide valuable dosimetric analyses on the advantages of the combined IMRT approach for stage IV Wilms tumor with lung metastases. We strongly recommend a prospective study with a larger cohort to collect dosimetric data and long-term clinical outcomes.

Conclusion

We describe methods for applying a combined IMRT approach to treating the whole lung and flank/abdomen in patients with Wilms tumor. The combined IMRT approach has dosimetric advantages, including a more uniform dose distribution in the junction area and ability to significantly reduce hot spots in critical OARs. Therefore, this combined IMRT approach merits further study and evaluation as an approach for treating patients with Wilms tumor.

Disclosures

LYL reports travel reimbursement from GT Medical Technologies, unrelated to this study. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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