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Scientific Article

Target Contour Consistency During Magnetic Resonance-Guided Online Adaptive Stereotactic Body Radiation Therapy

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Purpose: Adaptive magnetic resonance-guided stereotactic body radiation therapy (MRgSBRT) requires expeditious recontouring of target volumes based on daily anatomy. Contouring of the gross tumor volume (GTV) is frequently performed by covering radiation oncologists who may be less familiar with the case than the primary physician (PP). The objective of this study is to determine consistency in GTV contouring between PP and covering physician (CP) and to analyze the effect of resources to support accurate GTV delineation.

Methods and Materials: Between 2021 and 2023, 59 patients underwent 302 fractions of MRgSBRT at our institution. GTVs were analyzed for the effect of 3 different types of contouring support resources: (a) number of slices of the original GTV, (b) external software displaying original GTV contours, and (c) alerting if GTVs differed > 10% from the original. Differences between physicians and contouring support resources were analyzed for different tumor sites and fractions using 2-tailed *t* test and analysis of variance.

Results: One hundred nineteen out of 302 (39.4%) MRgSBRT treatments were supervised by a CP. The difference in the mean absolute percent volume change of GTV compared with original GTV for PPs (11.1%) versus CPs (4.6%) across all treatment fractions was statistically significant (P = .00006). Significant differences were observed for pancreas (12.8% vs 5.0%, P = .03), liver (13.0% vs 4.0%, P = .007), and lymph nodes (12.4% vs 2.1%, P = .004) with larger volume differences for PPs. No significant differences were observed for tumors of the prostate (3.7% vs 3.6%) and adrenal glands (9.7% vs 12.2%). No significant GTV differences between the 3 contouring support techniques were observed.

Conclusions: Our results show larger GTV changes by PPs for most tumor sites with little impact from contouring support resources. Observed differences might be related to higher contouring confidence of PPs who are more familiar with the case. Further investigation into enhancing contouring support methods is warranted.

Introduction

Online adaptive radiation therapy (ART) is a technique used in radiation oncology that allows the treatment team to evaluate daily changes in patient anatomy and target volumes, reoptimizing the dose plan accordingly before treatment delivery. These changes can range from patient-specific systematic (such as changes in tumor size or position) to random variations (such as organ motion and deformation).[1] The use of ART has been shown to provide benefits for multiple tumor sites, including reducing dose to the bowel and stomach in abdominopelvic regions and improving target coverage in pancreatic lesions.[2,3] The use of magnetic resonance

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imaging-guided stereotactic body radiation therapy (MRgSBRT) in particular further enhances the benefits of ART by allowing greater dose escalation and improved soft tissue visualization.[4,5] The latter is especially useful for accurately delineating the gross tumor volume (GTV) because it is adjusted for each daily treatment.

Ideally, the patient's primary physician (PP) would be present for each adapted fraction of their treatment course, because they are most familiar with the history of disease, the patient's pathoanatomic information, and other patient-specific considerations. However, the PP may not always be available because of the increased time and staffing demands of an ART program and conflicting clinical obligations. For many sites, this issue is addressed by assigning a covering physician (CP) to supervise the adaptive treatment in case of the PPs absence.[6] Although each site may develop their own methods, such as handoff procedures between physicians, this coverage model may lead to uncertainties in real-time decision making, including contouring variability during the delineation of the GTV as part of the ART process.[7]

Numerous studies on interobserver contour variation in the radiation oncology setting across various anatomic sites have demonstrated that manual delineation of target volumes may be affected by variabilities between physicians.[8-11] These discrepancies are especially prevalent in complex cases involving ambiguous anatomic boundaries.[12] In addition to contour variability, the differences in target volume contours over a treatment course may also be attributed to physiological fluctuations in tumor size and dimensions.[13,14] For example, adrenal gland metastases may exhibit a rebound pattern, enlarging and then shrinking after the start of radiation treatments.[15]

Although it has been well-demonstrated that target volumes are both difficult to delineate uniformly and prone to natural fluctuations, little data has been collected on the consistency of target volume contours between PPs and CPs supervising daily ART cases. Although some departments have shared their ART-specific handoff processes, there is limited discussion on the support methods used to assist CPs with contouring target volumes and organs at risk (OARs). The objective of this study is to evaluate the consistency of GTV contouring between physicians for patients treated with online adaptive MRgSBRT in our clinic and to analyze the effects of different resources to support accurate GTV delineation.

Methods and Materials

Patient selection

The inclusion criteria for this study were carefully selected to ensure the study population was representative of patients who would most benefit from MRgSBRT. The patients included in this institutional review board-approved study were part of the cohort treated using a magnetic resonance imaging-guided linear accelerator MR-Linac (MRIdian, ViewRay Systems, Inc) between February 2022 and October 2023 at our institution. The 59 patients included received at least one fraction of adaptive SBRT to one of the 5 most common treatment sites in our clinic: lymph nodes, liver, adrenal glands, pancreas, and prostate. The 5 tumor sites allow for a comprehensive evaluation of the adaptive process across different anatomic regions that face unique challenges in contouring and radiation delivery.

Treatment methods

At the time of simulation, 3-dimensional volumetric scans were acquired with the True Fast Imaging with steady-state precession sequence with an in-plane resolution of 1.5 and 3 mm slice thickness. MR images were reviewed by the treatment team and PP to evaluate the patients' candidacy for MRgSBRT, while determining the necessity for motion management techniques such as voluntary breath hold. Additionally, a computed tomography scan (Canon Medical Systems USA, Inc) with 2 mm slice thickness was acquired in the treatment position for dose calculation purposes. After simulation, the MR images were exported to the external contouring software MIM Maestro (MIM Software, Version 7.3.3), where the original contours including the GTV were delineated and intensity modulated step-and-shoot dose plans were created using 6 MV flattening filter free photons. Planning target volume (PTV) margins were generally 2 mm for prostate tumors and 3 mm for all other sites. Occasionally, 5 mm PTV margins were used to compensate for low target tracking certainty, for example in liver lesions that were more difficult to visualize on real-time MR imaging because of low contrast.

All treatment plans underwent a thorough peer review during departmental quality assurance rounds. This review included a detailed assessment of contours in MIM. In more complex cases, such as infrequently treated tumor sites or patients requiring special consideration, a pretreatment discussion was held between the PP and CPs, which included a review of diagnostic images.

Typical treatment start date was 2 weeks after simulation. During treatment, after setting the patient up in the treatment position, MR images were acquired and registered to the planning images by aligning to the GTV. The PP or CP was present to determine if the original plan could be used (nonadaptive) or if changes in patient anatomy or tumor characteristics required replanning (adaptive) (Fig. 1). The adaptive workflow was initiated by deforming and auto-contouring the original structures, with the exclusion of GTVs, which were rigidly copied. Contours for OARs were then adjusted by the radiation

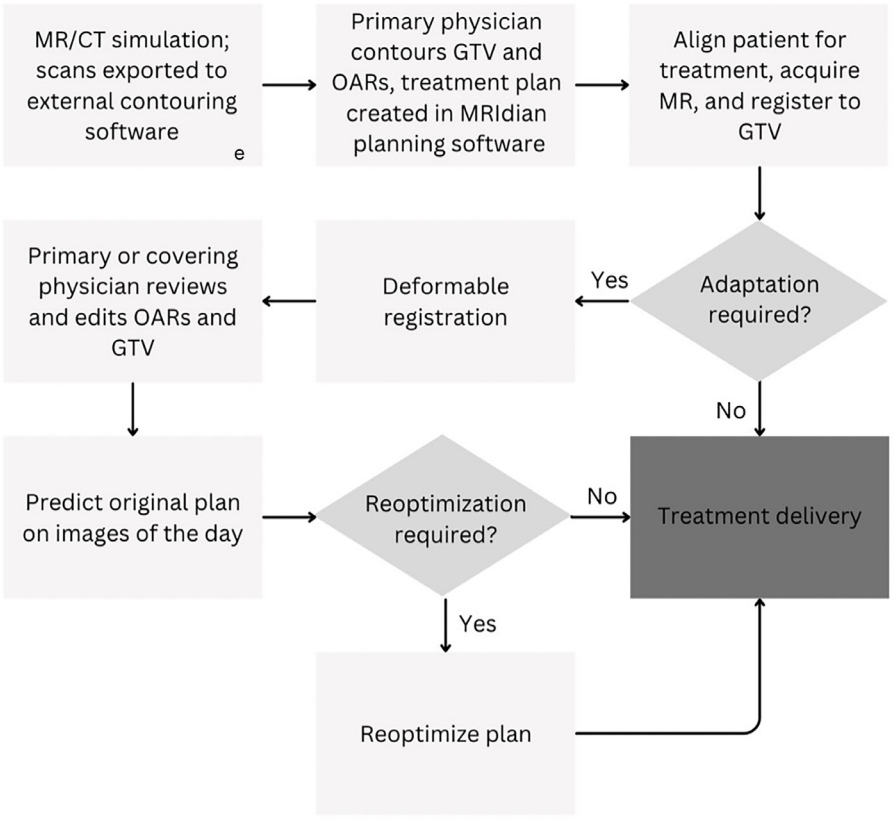

Figure 1 Example of an adaptive stereotactic body radiation therapy workflow using an MR-Linac.
Abbreviations: CT = computed tomography; GTV = gross tumor volume; MR = magnetic resonance; OAR = organ at risk.

therapist and reviewed by the covering radiation oncologist. Adjustments to the GTV were manually made by the physician, who had access to various contouring support methods. Preset rules were then applied to the set of new contours, including a PTV expansion and cropping of the PTV from adjacent critical structures in case of overlap.

In the MRIdian treatment planning software, the original plan was applied to the adapted contours and a predicted dose volume histogram was generated. If dose constraints were not met, the plan was reoptimized and normalized to dose-limiting OARs and target coverage. Once the radiation oncologist determined that an acceptable plan had been achieved based on determined dose volume histogram parameters, the plan was approved and evaluated with online quality assurance. Before treatment delivery, a tracking structure consisting of the GTV or an adjacent structure was delineated on the sagittal plane, and a 3 mm boundary was generated. Beam gating was used to ensure that treatment was delivered only when the tracking structure was contained within the boundary by at least 95%. Radiation prescription dose and fractionation were site-dependent, and treatments were generally delivered every other day. For upper abdomen sites, dose constraints were based on the stereotactic MR-guided online-ART trial for pancreas cancer.[16] Dose constraints for other sites were based on the Timmerman constraint table recommendations.[17] Although all patients included in this study received at least one fraction of ART, plan adaptation was not necessarily indicated for every fraction of the treatment course.

Contouring support methods

Ideally, the PP would be present for every treatment in a patient's course. However, this was not always feasible without delaying patient treatment. Our institution used a doctor of the day coverage system, in which a physician familiar with ART was designated as the CP for the day's treatments. Over the course of this study, 3 separate contouring support methods were used to improve contour consistency and assist PPs and CPs with more complex cases (Table 1). These methods were naturally introduced as our institution's adaptive program evolved:

1. *Number of slices:* After recontouring the GTV, the physician counted the number of slices of the new GTV (GTV_n, where n =1, 2, . . .5 represents each adapted fraction) and compared it to the number of slices in the original plan (GTV_o). This original number was recorded before initiation of the adaptive workflow, because the MRIdian software did not

Table 1 Contouring support phases

Phase 1 Initial 7 mo	Phase 2 Months 7 through 14	Phase 3 Month 15 and later
• Number of GTV slices	• Number of GTV slices • External contouring software	• Number of GTV slices • External contouring software • Alerting primary physician

Abbreviation: GTV = gross tumor volume.

display original GTV and OAR contours after deformation and auto-contouring.

2. *Referencing original target and OAR contours on external contouring software:* A separate monitor was installed adjacent to the treatment planning computer displaying the original contours on MIM. As the physician recontoured target volumes and OARs, they were able to systematically compare each slice of the adapted contours to the original contours. By using separate software to compare the 2 sets of contours, the adaptive workflow on the treatment planning computer did not have to be interrupted.
3. *Alerting PP:* After plan reoptimization, the volume of the new GTV could be determined. If this value differed from the original GTV by > 10%, the PP was alerted to review the adapted plan before the next treatment fraction.

Data collection

Patient information collected for this study included demographic data, dates of simulation and treatment, contour support phases, and treatment sites. Data were collected from treatment delivery reports, external contouring software, and electronic medical records. Details of radiation treatments were also collected and included prescription dose, dose per fraction, percent of fractions that were adapted, and whether the PP or CP was present for each treatment. Most relevant to this study were the data on target volumes: original GTV, original PTV, and GTVs and PTVs for each adapted plan.

Statistical analysis

All statistical analyses were conducted using a web-based statistical tool that incorporates standard statistical algorithms for hypothesis testing and data analysis (Statistics Kingdom, 2024). The baseline characteristics and demographics of the study population were summarized using descriptive statistics. Specifically, continuous variables were summarized using means, medians, and ranges, whereas categorical variables were summarized using percentages and frequencies. Boxplots were generated showing median values, interquartile range, minimum and maximum values defined as 1.5 × interquartile range represented by whiskers, and outliers. Inferential statistics were used to test the hypothesis of the study. A 2-tailed *t* test was performed to compare differences in GTV contouring across 5 fractions of SBRT, across the 5 different tumor sites, and across the 3 contouring support phases when comparing GTV contouring completed by PPs with those completed by CPs. One-way and 2-way analysis of variance tests were performed to examine the effect of different parameters, such as contouring support phases, tumor sites and fractions on GTV contours. A P value < .05 was considered significant in the data analysis.

Results

Patient and treatment demographics

Overall, the study consisted of 59 patients who collectively received treatment to 63 tumor sites with 65 GTVs. Of the 63 tumor sites treated, 11 were to the lymph nodes (20.3%), 16 to the liver (27.1%), 8 to the adrenal glands (13.6%), 19 to the pancreas (32.2%), and 9 to the prostate gland (15.3%). Two patients received treatment to > 1 site, and 4 patients had > 1 GTV. The age range of the study population was between 34 and 80 years, with a median age of 67 years. The fractionation and prescription dose to the PTV were site-dependent as outlined in Table 2. Out of a total of 302 MRgSBRT treatment fractions, 183 were supervised by the PP (60.6%) and 119 were supervised by a CP (39.4%). Of the PP-supervised fractions, GTVs were adapted in 153 (83.6%) fractions; of CP-supervised fractions, GTVs were adapted in 88 (73.9%) fractions. Twenty-three patients were treated during contouring support phase 1 (38.9%), 27 were treated during phase 2 (45.8%), and 10 were treated during phase 3 (16.9%).

Primary versus covering physician by tumor site

The mean absolute and relative changes in GTV contouring were compared between PP and CP across

Table 2 Treatment dose and fractionation by tumor site

Tumor site	Most common fractionation (range of fractionations)	GTV average in cc (interquartile range)
Lymph node	30 Gy/5 fractions (24-50 Gy/3-5 fractions)	13.06 (3.72-23.16)
Liver	50 Gy/5 fractions (35-54 Gy/3-5 fractions)	32.83 (7.65-40.48)
Adrenal gland	50 Gy/5 fractions (35-40 Gy/3-5 fractions)	37.74 (25.68-42.44)
Pancreas	50 Gy/5 fractions (20-33 Gy/3-5 fractions)	40.13 (20.23-44.21)
Prostate	36.25 Gy/5 fractions (24-36.25 Gy/3-5 fractions)	59.37 (27.70-78.58)

Abbreviation: GTV = gross tumor volume.

different tumor sites for all fractions. PPs made significantly larger mean absolute volume changes compared with GTV_o than CPs for lymph nodes (12.4% vs 2.1%, $P = .004$), liver (13.0% vs 4.0%, $P = .007$), pancreas (12.8% vs 5.0%, $P = .029$), and all sites combined (11.1% vs 4.6%, $P = .00006$) for all fractions, but not for adrenal gland (9.7% vs 12.2%, $P = .47$) or prostate (3.7% vs 3.6%, $P = .97$) sites. With regards to relative volume changes, PPs contoured on average significantly smaller lymph node volumes than CPs (−9.4% vs −1.11%, $P = .04$). No statistically significant changes were seen in the mean relative volume change in GTV contouring performed by PPs compared with CPs for liver (1.0% vs 0.3%, $P = .87$), adrenal glands (−5.8% vs 0.4%, $P = .22$), pancreas (4.4% vs 2.4%, $P = .62$), prostate (0.4% vs 1.8%, $P = .41$), and for all sites combined (−0.5% vs 1.0%, $P = .44$). Absolute and relative volume changes in PTV contouring compared between PP and CP across different tumor sites were found to be proportional to their respective absolute and relative GTV changes. Boxplots (Fig. 2) show a wide distribution of values. Median values were close to zero with the exception of adrenal glands, which displayed a negative median for both PPs and CPs indicating smaller volumes for adapted plans.

Primary versus covering physician by fraction

The mean absolute and relative volume changes in GTV contouring were compared between PPs and CPs across fractions over a treatment course for all tumor sites combined. On average, PPs made significantly larger absolute changes compared with GTV_o over a treatment course than CPs for all tumor sites. Absolute changes became larger with increasing fraction number for PP, but not for CP. There was a statistically significant difference in the mean absolute change between PPs and CPs for GTV_2 (10.1% vs 3.9%, $P = .03$), GTV_3 (11.4% vs 4.8%, $P = .02$), GTV_5 (16.6% vs 4.0%, $P = .02$), when compared with GTV_o, but not for GTV_1 (6.7% vs 6.0%, $P = .81$) or GTV_4 (13.3% vs 5.3%, $P = .08$). Mean relative changes for any $GTV_{1\text{-}5}$ or all fractions combined were < 5% and not significant between PP and CP. Of note, absolute and relative volume changes in PTV contouring compared between PP and CP across different fractions for all tumor sites were found to be proportional to their respective absolute and relative GTV changes. Boxplots show a wide distribution of values and median values close to zero (Fig. 3). No statistically significant interactions between fraction number and tumor site on absolute or relative percent changes in GTV contouring were noticed ($P = .53$ and .98, respectively), indicating that the effect of fraction number on percent change in GTV does not differ depending on tumor site.

Primary versus covering physician by contouring support phase

The mean absolute and relative volume changes in GTV contouring were compared between the PPs and CPs across the 3 contouring support phases for all fractions and tumor sites. Absolute and relative GTV changes were not statistically significant by contouring support phase except for absolute changes during phase 2 (11.8% for PPs vs 3.59% for CPs, $P = .00007$), see Fig. 4. No statistically significant interactions between contouring support phases and fraction number on absolute or relative percent change in GTV contouring were identified ($P = .99$ and .8, respectively).

Discussion

Although ART holds significant potential in improving treatment quality and advancing the field of radiation

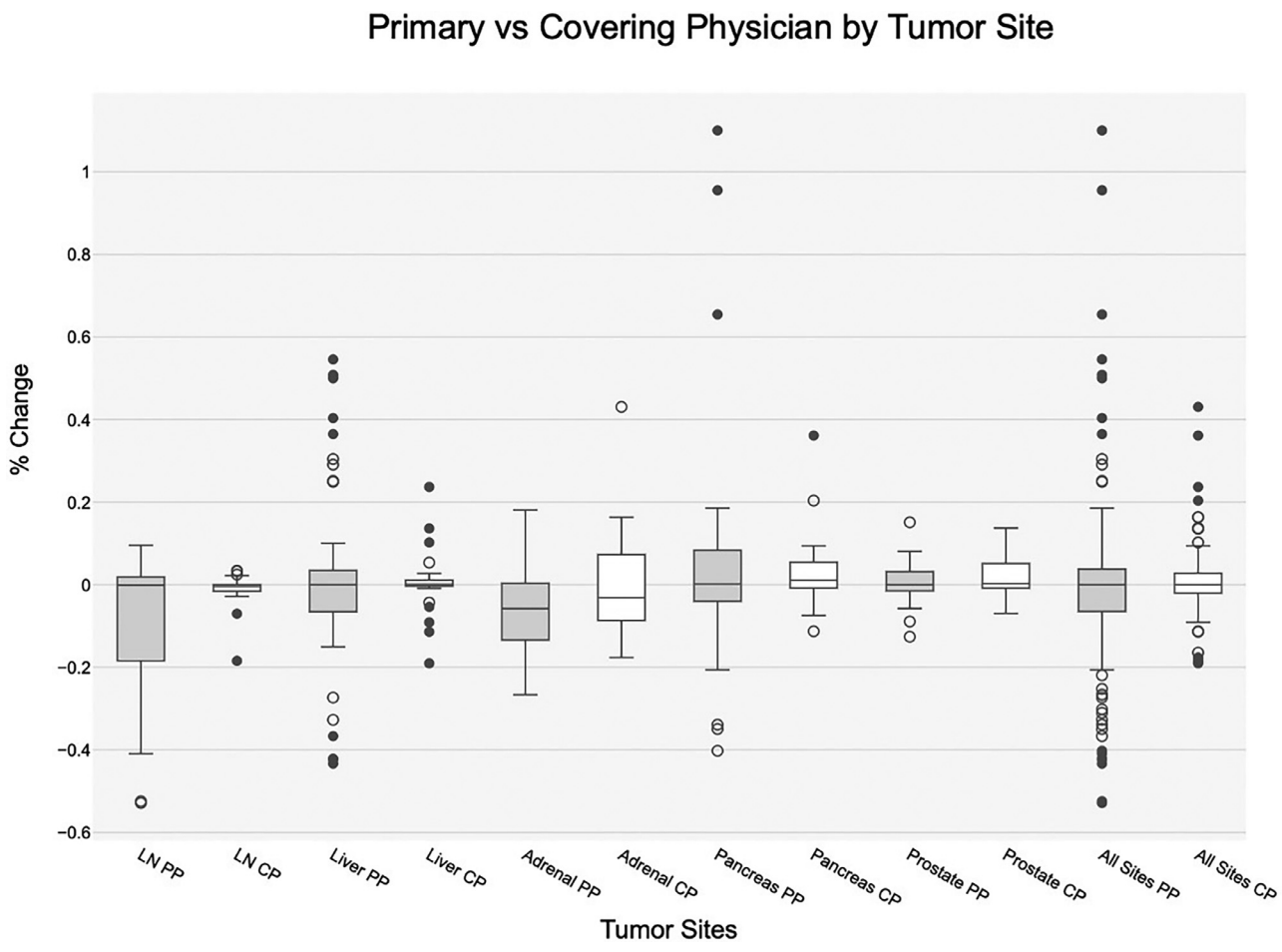

Figure 2 Boxplots showing percent change of gross tumor volumes by PPs versus CPs across tumor sites.
Abbreviations: CP = covering physician; LN = lymph nodes; PP = primary physician.

oncology, it presents considerable logistical challenges including the need for recontouring of target and OAR structures. Interobserver variability when contouring the same image set between physicians with identical background knowledge of the case has been described in detail and is likely one of the largest uncertainties during radiation treatment delivery.[11] Contour discrepancies can potentially lead to underdosages, compromised tumor control, exceeding safe treatment limits, and ultimately increase the risk of radiation-related damage to nearby organs.[7,12,14,18] Contour variability is multifactorial and is especially pronounced in tumors where soft tissue boundaries are difficult to identify either based on motion or lack of contrast relative to neighboring organs. For example, when reviewing GTV delineation variations for pancreatic lesions, Versteijne et al[19] noted large differences between observers with ratios of the largest to the smallest delineated GTV within the same patient of 6.8. Some measures that have been able to reduce contour variabilities are the inclusion of site-specific imaging modalities and techniques. MR imaging is known to improve soft tissue contrast and therefore offers advantages in target contouring of several tumor sites, such as for prostate cancer.[18] Nonetheless, the unique characteristics of each tumor and the individual anatomy of each patient makes consistent and accurate contouring heavily reliant on physician experience and knowledge of the patient-specific situation.[12,18]

Online adaptation is a valuable technique for detecting anatomic variations as they arise, offering advantages such as enabling dose escalation and improving sparing of OARs.[1] Compared with offline adaptation, online adaptation requires real-time contouring of targets and OARs, placing tight time constraints on physicians and other staff involved with contouring. Additionally, not all information and imaging available during initial planning may be accessible during the online adaptive process, creating an even more challenging situation. Interphysician variations in real-time contouring have not been extensively investigated. Our study, therefore, aimed to evaluate the consistency of real-time adaptive SBRT using an MR-Linac. The findings provide insight into the influence of various factors on variability in GTV contouring, suggesting potential areas for improvement in the adaptive MRgSBRT workflow.

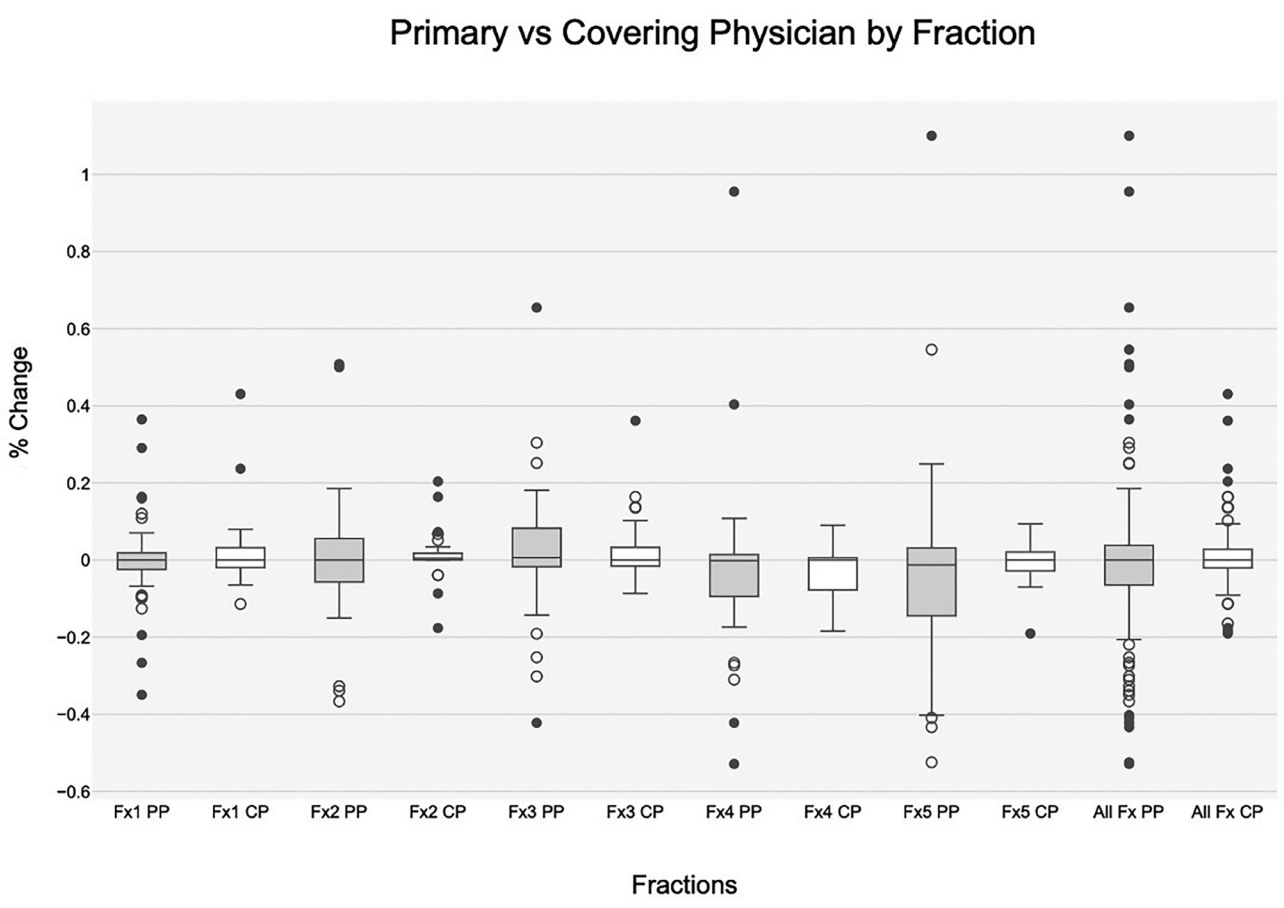

Figure 3 Boxplots showing percent change of gross tumor volumes by PPs versus CPs across treatment fractions.
Abbreviations: CP = covering physician; PP = primary physician.

Online adaptive treatment contouring variability and physician coverage

In our study, we observed significant contouring differences between PPs and CPs for lymph nodes, liver targets, and pancreas tumors. PPs made significantly larger absolute changes across all tumor sites, except for adrenal glands, where CPs exhibited larger GTV changes, and for prostate targets, where both PPs and CPs demonstrated only small GTV changes. Relative contour changes for prostate targets were also minimal for both groups, likely reflecting good target visibility on online MR images. For other tumor sites, relative contour changes were minimal for CPs but showed decreased GTVs for lymph nodes and adrenal glands among PPs. This, along with a negative median for relative adrenal gland GTV percent changes, may indicate true target shrinkage and possibly reflect hesitation among CPs to make more extensive changes without having full case details. A reduction of adrenal gland GTVs during MRgSBRT had previously been observed by Giraud et al,[15] who reported that 47% of adrenal gland GTVs decreased at the last fraction. In addition, the authors observed that GTV variations of ≥20% occurred in 59% adrenal gland treatments at some point between simulation and end of SBRT. Absolute variations of adrenal gland volumes in our cohort were smaller with on average about 10%. Relative liver GTV changes were minimal in our study but showed larger variability for PPs. Liver tumors and their boundaries may be difficult to identify on available MRs, particularly for physicians less familiar with the case at hand.[20] PPs may be more inclined to adjust contours because of their background knowledge of the individual case. The observed variations in interphysician contouring across different tumor sites with unique challenges highlight the need for further investigation into tumor-specific adaptation processes.

Regarding fraction number, PPs, on average, made increasingly larger absolute changes to subsequent GTVs compared with GTV_o than CPs across all tumor sites combined; these differences were significant for several fractions. Additionally, PPs were more likely to adapt any given fraction than CPs (83.6% vs 73.9%). These findings may be attributed to the PPs greater familiarity with the patients' clinical history, tumor characteristics, and progress thus far in the treatment process. In contrast, CPs may rely more heavily on the original plan, leading to smaller adjustments in subsequent GTVs. This

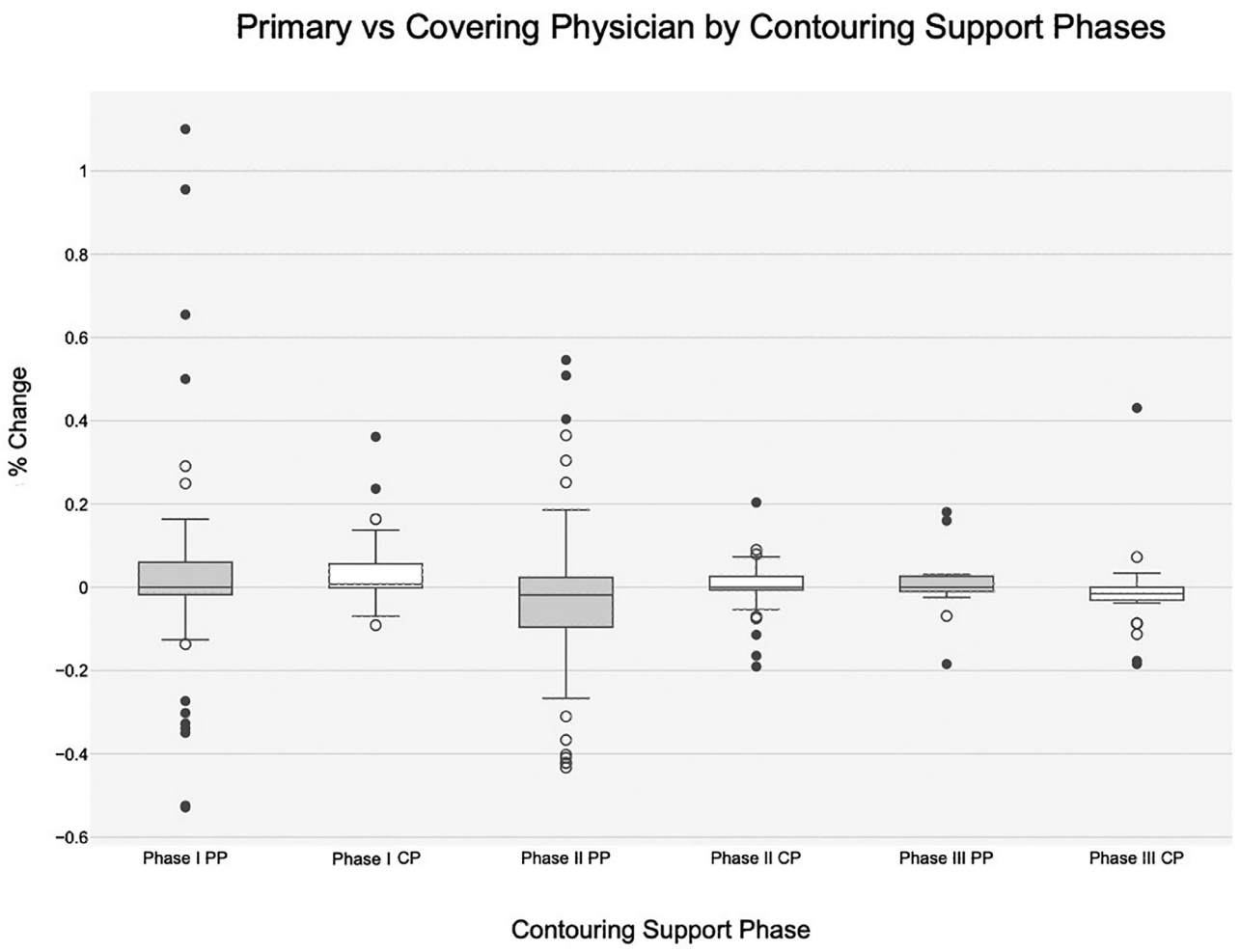

Figure 4 Box plot showing percent change of gross tumor volumes by PPs versus CPs across contour support phases.
Abbreviations: CP = covering physician; PP = primary physician.

observation aligns with Walker et al,[9] who highlighted how interphysician variability can influence isocenter placement and treatment volumes, with more experienced physicians making larger, and perhaps more appropriate, adaptations based on patient-specific factors. The observed variations underscore challenges faced in online adaptive MRgSBRT in maintaining contouring consistency, especially when PPs are not available for each fraction.

Utility of contouring support phase

The use of the 3 contouring support phases demonstrates the evolution of practices aimed at ensuring consistency and accuracy in treatment delivery in our clinic. The duration and methods of each phase were not predetermined, but a result of our gradual inclusion of additional safeguards to support accurate physician contouring as our ART program evolved. For example, once it was suggested to display external contouring software with the original contours during adaptation, the second monitor had to be purchased and installed while clinical operations were ongoing. Furthermore, the number of patients treated across the 3 phases is not balanced, with only a few patients treated in phase 3 because of a vendor-related shutdown of operations in October 2023.

Overall, there is no clear evidence that contour support methods helped to homogenize GTV contours between PPs and CPs. In fact, discrepancies increased during phase 2, when absolute GTV changes became significant between the 2 groups. PPs made larger changes for phases 1 and 2, whereas, interestingly, in phase 3 there was good agreement between PPs and CPs. This is primarily because of smaller absolute changes made by PPs, possibly reflecting greater experience with adaptive workflows. Segedin and Petric[11] emphasized that variability in contouring is often linked to the learning curve associated with novel technologies and workflows, suggesting that with increased experience, contouring support measures may be less impactful. The introduction of a "doctor of the day" coverage system and various contouring support

methods was aimed at mitigating contouring discrepancies. However, our findings suggest that these measures alone may not be sufficient to entirely standardize contouring practices across different physicians, leaving room for some residual interphysician variability. Onal et al[21] found that training programs significantly reduced contouring variability, especially among less experienced physicians, suggesting that standardized training may be crucial to achieving greater consistency in adaptive workflows. Further standardization through enhanced training and the development of more robust protocols may be necessary to minimize variability and ensure uniformity in treatment course even when the PP is unavailable for adaptations. Importantly, adhering to the Adaptive Radiation Therapy Physician Guidelines by Kim et al,[6] including how to address tumor growth, shrinkage, or deformation in a patient-specific handoff protocol, could help harmonize GTV contours between PPs and CPs.

The limitations of this study include small sample size and the exclusive use of volume as the metric for determining contour consistency, which may not fully capture the range of variability relevant to clinical practice. Furthermore, although the contour support methods evolved with time and ongoing experience with the challenges of the adaptive process, a more strategic approach, for example, focusing on high variability tumor sites and including more stringent contour guidelines, might have delivered higher contouring consistency. Despite these shortcomings, our study provides relevant information on contouring variability during online ART, highlighting the need for improved contouring consistency for tumors with boundaries that are difficult to identify.

Conclusions

This study underscores the challenges of reproducible target contouring and the importance of developing effective contouring support methods for online adaptive MRgSBRT. Although the online adaptive MR-Linac workflow offers significant advantages in treatment precision, continued standardization and refinement of adaptive workflows are needed to further minimize interphysician variability to the greatest extent possible.

Future research should focus on optimizing contouring support methods, standardizing real-time adaptive workflows, and developing tumor site-specific contouring guidelines, particularly for tumor sites with larger contouring variability as demonstrated in this work.

Disclosures

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