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Retroperitoneal Sarcoma (RPS) High Risk Gross Tumor Volume Boost (HR GTV Boost) Contour Delineation Agreement Among NRG Sarcoma Radiation and Surgical Oncologists

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Abstract

Purpose—Curative intent management of retroperitoneal sarcoma (RPS) requires gross total resection. Preoperative radiotherapy (RT) often is used as an adjuvant to surgery, but recurrence rates remain high. To enhance RT efficacy with acceptable tolerance, there is interest in delivering “boost doses” of RT to high-risk areas of gross tumor volume (HR GTV) judged to be at risk for

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positive resection margins. We sought to evaluate variability in HR GTV boost target volume delineation among collaborating sarcoma radiation and surgical oncologist teams.

Methods—Radiation planning CT scans for three cases of RPS were distributed to seven paired radiation and surgical oncologist teams at six institutions. Teams contoured HR GTV boost volumes for each case. Analysis of contour agreement was performed using the simultaneous truth and performance level estimation (STAPLE) algorithm and kappa statistics.

Results—HRGTV boost volume contour agreement between the seven teams was “substantial” or “moderate” for all cases. Agreement was best on the torso wall posteriorly (abutting posterior chest abdominal wall) and medially (abutting ipsilateral para-vertebral space and great vessels). Contours varied more significantly abutting visceral organs due to differing surgical opinions regarding planned partial organ resection.

Conclusions—Agreement of RPS HRGTV boost volumes between sarcoma radiation and surgical oncologist teams was substantial to moderate. Differences were most striking in regions abutting visceral organs, highlighting the importance of collaboration between the radiation and surgical oncologist for “individualized” target delineation on the basis of areas deemed at risk and planned resection.

Surgery is the only potentially curative treatment for localized retroperitoneal sarcoma (RPS). However, local recurrence rates following resection alone are very high, ranging from 50 to 80 %.¹ Randomized trials have clearly demonstrated that adjuvant radiation therapy (RT) is associated with improved local control for extremity soft-tissue sarcoma (STS).^{2–4} Extrapolating from these data, preoperative RT may be similarly beneficial for RPS. To date, retrospective studies assessing benefits of RT for RPS have shown mixed results.^{5–12} The ongoing European Organization for Research and Treatment of Cancer (EORTC) randomized, controlled trial assessing surgery alone compared with preoperative RT followed by surgery will hopefully provide robust data to address this important question.¹³

In the absence of conclusive data, many RPS multidisciplinary teams empirically utilize preoperative RT as part of initial treatment or at the time of resectable local recurrence. Because attaining negative surgical margins in the retroperitoneum is rarely feasible, there also is interest in the concept of delivering an additional “boost dose” of radiation to the part of the gross tumor judged to be at high risk to result in positive surgical margins. This additional dose can be delivered using an intensity modulated RT (IMRT) technique called “dose-painting” or “simultaneous integrated boost” (SIB) whereby the entire tumor receives one dose and the high-risk boost volume receives a concurrent higher dose during the same treatment delivery. The RT nomenclature for this volume is “high-risk gross tumor volume” (HR GTV) and the corresponding volume expansion to include potential adjacent microscopic disease is called “high-risk clinical target volume” (HR CTV). One series utilizing this IMRT-SIB approach reported acceptable efficacy and toxicity, but patient numbers were small and follow-up was short.¹⁴ Consequently, there is debate regarding whether higher doses (>50 Gy) to HR GTVs are effective and safe, and the IMRT-SIB technique is not currently considered “standard of care” for RPS.

An international panel recently developed consensus recommendations for preoperative RT for RPS, which include guidelines for RT target volume contouring.¹⁵ In a subsequent project, 12 sarcoma radiation oncologists contoured preoperative target volumes (gross tumor volume: GTV, clinical target volume: CTV, and HR CTV) for two RPS cases to assess levels of contouring agreement and determine whether the guidelines were practical, feasible, and reproducible.¹⁶ GTV and CTV were contoured with a high level of agreement. However, agreement for HR CTV was only moderate. Hence, to facilitate consistent implementation of SIB, further clarification of the “high-risk” volume is needed. Because collaboration with surgical oncologists is critical to determine tumor regions at high risk for positive margins, radiation oncologist and surgical oncologist teams were asked to contour HR GTVs together to serve as a basis for contour agreement analysis and further discussion of appropriate high-risk volumes.

METHODS

Project participants included eight radiation oncologists and six surgical oncologists from six institutions. All radiation oncologists and some of the surgeons are members of the Sarcoma Working Group of NRG Oncology. Participants were selected based on their active involvement in sarcoma clinical trials in NRG Oncology and other multi-centre groups. Anonymized radiation planning CT scans for three cases of RPS were distributed to seven radiation oncologist/surgical oncologist teams (one surgeon worked on a team with two radiation oncologists and one surgeon worked separately with two different radiation oncologists to form two teams). Planning images were acquired in the supine position with arms supported over the head. No patient histories, accompanying diagnostic scans, or formal radiology reports were provided. The first case (RPS1) was a patient with a de-differentiated (DD) liposarcoma (LPS) of the right upper quadrant. The second case (RPS2) was a leiomyosarcoma of the left upper quadrant. The third case (RPS3) was a DD LPS of the left lower quadrant with extension through the inguinal canal into upper scrotum. Participants downloaded data sets from the Image-Guided Therapy QA Center web server and imported them into their treatment planning workstations.

Contours of GTV and organs at risk were provided along with these instructions: “As a team, contour the HR GTV Boost using the following guidelines. The HR GTV is the area considered to be at high risk for positive margins following resection. It generally includes areas of tumor located along posterior retroperitoneal musculature, postero-lateral abdominal wall, ipsilateral para- and pre-vertebral space, major vessels, or organs that the surgeon would leave in situ. Contour GTV boost structures on every axial CT slice with a thickness of about 1.5 cm. An example of a high-risk GTV boost volume is provided.” (Figure 1).

Each team contoured HR GTV Boost structures using their institution’s planning system. Completed contours were sent to the Image-Guided Therapy QA Center as Digital Imaging Communications in Medicine (DICOM) datasets. Individual contours were imported to the Computational Environment for Radiotherapy Research for analysis.¹⁷ Apparent volume overlap was assessed by calculating the intersection and mean of volumes contoured by the participating teams. Contour data also were analyzed by the simultaneous truth and

performance level estimation (STAPLE) algorithm which uses an iterative approach to estimate the “true” contour structure.¹⁸ The STAPLE 95 contour, also called the consensus contour, is a probabilistic estimate of the “true” contour at a 95 % confidence level. Contour agreement sensitivity is an estimate of the true positive rate, (proportion of voxels within the “true” structure that are included in the consensus); agreement specificity is an estimate of the true negative rate, (proportion of voxels outside the “true” structure that are excluded from the consensus.)¹⁹ Kappa statistics were used to correct for agreements that could be derived by chance. Kappa values of -1 represent complete disagreement, 0 represents no agreement above chance, and $+1$ represents complete agreement. Descriptive categories for the strength of kappa agreement were used as defined by Landis and Koch as follows: <0 is poor, $0-0.20$ slight, $0.21-0.40$ fair, $0.41-0.60$ moderate, $0.61-0.80$ substantial, $0.81-1.00$ almost perfect.²⁰

RESULTS

All three cases were contoured by each of the seven radiation oncologist/surgical oncologist teams. Overall, HR GTV contour agreement was substantial for RPS1 ($\kappa 0.66$), substantial for RPS2 ($\kappa 0.61$), and moderate for RPS3 ($\kappa 0.52$). Additional quantitative measures of HR GTV contour agreement are shown in Table 1. Maximum, minimum, mean ($\pm$ standard deviation) and STAPLE95 consensus HR GTV volumes were 1399.2, 689.7, 947 (± 29 %), and 1100.8 cc for RPS1; 419.1, 173.2, 290.2 (± 27 %), and 316.5 cc for RPS2; and 921.7, 174.2, 414.4 (± 60 %), and 434.9 cc for RPS3. Median volume overlap for HR GTV contours is the intersection volume common to all teams as a percentage of the mean volume, and these values are 44 % for RPS1, 26 % for RPS2, and 60 % for RPS3. In all three cases, HR GTV agreement sensitivity was lower than specificity (Table 1).

Detailed examination of HR GTV contours with respect to retroperitoneal compartment and pelvic anatomy for each case showed very good qualitative contour agreement postero-laterally along chest and abdominal walls as well as medially along ipsilateral para- and pre-vertebral space and great vessels. An axial slice of the RPS2 planning CT scan depicting this significant contour agreement is shown in Fig. 2 where six of seven HR GTV contours are almost superimposable and one of seven does not extend as far laterally (see arrow). Conversely, there was marginal HR GTV contour agreement in areas where tumor abutted visceral organs (e.g., liver, bladder, duodenum, testicle) as well as the anterior abdominal wall and occasionally, the lateral abdominal wall. Figure 3 shows axial slices with HR GTV contours depicting marginal agreement (for case RPS1). Four of seven HR GTV contours extend to include the entire liver surface whereas three of the seven contours excluded liver (Fig. 3a). Figure 3b is a more inferior axial slice, which shows significant variation in how far anterior along the lateral abdominal wall HR GTV contours are drawn (arrows depict the various anterior-most extents of the boost volumes.) Another example of marginal HR GTV contour agreement is shown in Fig. 4. The axial slice for case RPS3 depicts significant variation of HR GTV contours with one of seven contours extending to include anterior abdominal wall and three of seven extending to include lateral border of bladder. More inferiorly, tumor extended through the inguinal canal into ipsilateral scrotum to abut the testicle (image not shown). Three of seven contours extended into the scrotum to the level of the testicle; four contours did not include the scrotum.

DISCUSSION

There are several controversies regarding optimal treatment for localized RPS. Due to retroperitoneal anatomy, resection with negative margins is rarely feasible. Although the primary role of surgery is uncontested, the appropriate extent of surgery is a subject of ongoing debate.^{7,21–28} Some have advocated for an aggressive “compartmental”-type en bloc resection of tumor with multiple adjacent organs to improve local control.^{7,21,22} Others have questioned the rationale for aggressive resection of selective organs or structures (those associated with less surgical morbidity) when other critical adjacent organs and structures (i.e., great vessels, vertebral bodies, rectus abdominus musculature) are left in situ.^{23,24} In essence, is there meaningful benefit to obtaining negative margins for some areas if there will be positive margins for others? Additional unsettled issues pertain to appropriate extent of surgery for low- versus high-grade tumors and LPS versus leiomyosarcoma and other histologies.^{23,25,26} Risk–benefit in terms of resection morbidity versus risk for recurrence is likely different for each of these scenarios and is not yet fully understood. In attempt to address many of these questions, a Transatlantic Retroperitoneal Sarcoma Working Group has been established.²⁹

For extremity STS, unambiguous data demonstrate improved local control with RT.^{2–4} It also is clear that local recurrence rates following surgery and RT are higher in the setting of positive margins.^{2,4,30–34} DeLaney et al. showed higher doses help mitigate the adverse effect of a positive margin.³⁵ Extrapolating from the extremity STS data, there is great interest in the potential role of preoperative RT for RPS. Further, delivery of additional “boost doses” to areas of RPS at risk for positive margins is appealing to further reduce recurrence risk.

Investigators from the University of Alabama (UAB) pioneered a simultaneous integrated boost (SIB) approach for RPS whereby the entire tumor was treated to 45 Gy and the high risk region received a boost dose to 57.5 Gy using an IMRT-SIB technique.¹⁴ Toxicity was acceptable, but efficacy was difficult to evaluate due to the small sample size (16 patients) and short follow up (median 28 months). Consequently, until more data are available, treatment with the IMRT-SIB technique to high risk regions is best confined to the setting of a clinical trial or experienced centers. More data are expected from an ongoing multicenter phase I/II dose escalation trial of preoperative RT for RPS using SIB to high-risk volumes (T. DeLaney, personal communication).

In the UAB study, the high-risk region was defined by radiation oncologists in consultation with surgeons.¹⁴ In our prior report, where only radiation oncologists contoured volumes, contour agreement for HR CTV Boost was only moderate.¹⁶ This prompted the current investigation to better define the high-risk boost volume. Interestingly, in this project where radiation oncologists contoured HR GTV Boost volumes together with surgeons, contour agreement between teams was similar to our prior study.

On first impression, it is somewhat disappointing the contour agreement for the radiation oncology/surgical oncology team approach was not higher. With further reflection, the areas of greatest discordance (adjacent organs and the lateral abdominal wall) highlight the

previously noted controversies regarding appropriate extents of resection, complexities of intra-abdominal/ retroperitoneal anatomy, and anticipated morbidity associated with en bloc visceral organ resection. Unlike extremity STS where tumor is typically surrounded by soft tissues, portions of RPS can project into the free intra-abdominal cavity. Therefore, although RPS may appear to be next to a critical structure on imaging, there may be intervening free space at the time of resection. Areas where such free space is more likely to exist include posterior aspect of inferior liver, spleen, stomach, small bowel, and transverse colon (all along intra-peritoneal surfaces, which are in a separate compartment from the retroperitoneum). In contrast, organs with a retroperitoneal component (posterior aspect of superior liver, pancreas, duodenum, ascending/descending colon, rectum, and major vessels) may be directly invaded by adjacent RPS. This also would explain the difficulty with HR GTV boost contouring along lateral abdominal wall; musculature posterior to peritoneal reflection/pericolic gutter would be in direct contact with RPS (high-risk margin), whereas abdominal wall anterior to the reflection would simply be adjacent to tumor, with an intervening free intra-abdominal cavity (low-risk margin). The precise location of this intra-abdominal/retroperitoneal interface adjacent to a large RPS is almost impossible to assess except at exploration. Hence, this anatomic ambiguity could explain the variability of the anterior-most extent of the contours along lateral abdominal wall (Fig. 3b).

Resectability is “in the eye of the beholder.” All anatomic structures are potentially resectable. However, removal is tempered by anticipated post-operative morbidity, both acute and long-term. In this regard, the overall construct of our project was somewhat artificial. Participants were only provided with radiographic images; there was no provided information on patients’ clinical histories, performance statuses, comorbidities, *et cetera*. This made it difficult for the surgical oncologist to anticipate potential morbidity of any planned contiguous organ resection and may have affected the concordance of the teams’ contours. Amongst our seven teams, three surgeons envisioned a partial liver resection for RPS1 and four envisioned a partial bladder resection for RPS3. Given the planned aggressive surgical approaches in these instances, the RT high-dose target volumes were correspondingly less aggressive in that those organ interfaces were appropriately excluded from the respective HR GTV boost volumes. On the other hand, there was near uniform inclusion of tumor interfaces along vertebral bodies, major vessels, and posterior trunk musculoskeletal tissues. Resection of these structures is possible, but there appeared to be general consensus amongst the surgeons that, in most cases, the anticipated morbidity was too great to justify such resections. Moreover, variability of planned surgical aggressiveness and corresponding RT target volumes may be related to anticipated biologic behavior and imaging characteristics of histologic subtype (DD or well-differentiated LPS vs. leiomyosarcoma vs. others) and specific anatomic locations (left or right retroperitoneum vs. pelvis). Further study is needed to better understand recurrence patterns for these different scenarios. Last, our sample size was small, limiting the robustness of the results.

CONCLUSIONS

Defining RPS HR GTV volumes is subjective and will vary based on planned resection. It is evident that these volumes should always be derived through direct collaboration between the treating radiation and surgical oncologists. Thoughtful, individualized discussion

regarding which organs/structures are likely to be resected is critical and highlights the importance of delivering both RT and surgery at the same institution so radiation target volumes can be planned and reviewed by the radiation oncologist/surgeon team. HR GTV boost volumes should typically include RPS interfaces with vertebral bodies, great vessels (aorta, inferior vena cava, portal vein), and abdominal wall musculature up to anticipated location of the free intra-abdominal cavity. In lieu of resection, HR GTV boost should be considered for visceral organs with a retroperitoneal component where potential morbidity of en bloc resection is considered significant or prohibitive. In each case, the surgeon and radiation oncologist should weigh the pros and cons of their respective modalities. Further study of appropriate HR GTV boost volumes is needed and should include careful examination of recurrence patterns as well as toxicities associated with dose escalation and extent of resection. Finally, to the extent possible, treatment should be at centers with multispecialty RPS expertise and enrollment in protocols is recommended to further our knowledge regarding optimal treatment of this rare disease.

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References

1. Swallow CJ, Catton CN. Improving outcomes for retroperitoneal sarcomas: a work in progress. *Surg Oncol Clin N Am.* 2012; 21(2):317–31. [PubMed: 22365522]
2. Rosenberg SA, Tepper J, Glatstein E, et al. The treatment of soft-tissue sarcomas of the extremities: prospective randomized evaluations of (1) limb-sparing surgery plus radiation therapy compared with amputation and (2) the role of adjuvant chemotherapy. *Ann Surg.* 1982; 196(3):305–15. [PubMed: 7114936]
3. Yang JC, Chang AE, Baker AR, et al. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. *J Clin Oncol.* 1998; 16(1):197–203. [PubMed: 9440743]
4. Pisters PW, Harrison LB, Leung DH, Woodruff JM, Casper ES, Brennan MF. Long-term results of a prospective randomized trial of adjuvant brachytherapy in soft tissue sarcoma. *J Clin Oncol.* 1996; 14(3):859–68. [PubMed: 8622034]
5. Stoeckle E, Coindre JM, Bonvalot S, et al. Prognostic factors in retroperitoneal sarcoma: a multivariate analysis of a series of 165 patients of the French Cancer Center Federation Sarcoma Group. *Cancer.* 2001; 92(2):359–68. [PubMed: 11466691]
6. Heslin MJ, Lewis JJ, Nadler E, et al. Prognostic factors associated with long-term survival for retroperitoneal sarcoma: implications for management. *J Clin Oncol.* 1997; 15(8):2832–9. [PubMed: 9256126]
7. Gronchi A, Miceli R, Colombo C, et al. Frontline extended surgery is associated with improved survival in retroperitoneal low-to intermediate-grade soft tissue sarcomas. *Ann Oncol.* 2012; 23(4): 1067–73. [PubMed: 21765179]
8. Sampath S, Hitchcock YJ, Shrieve DC, Randall RL, Schultheiss TE, Wong JY. Radiotherapy and extent of surgical resection in retroperitoneal soft-tissue sarcoma: multi-institutional analysis of 261 patients. *J Surg Oncol.* 2010; 101(5):345–50. [PubMed: 20119974]
9. Singer S, Corson JM, Demetri GD, Healey EA, Marcus K, Eberlein TJ. Prognostic factors predictive of survival for truncal and retroperitoneal soft-tissue sarcoma. *Ann Surg.* 1995; 221(2):185–95. [PubMed: 7857146]

10. Catton CN, O'Sullivan B, Kotwall C, Cummings B, Hao Y, Fornasier V. Outcome and prognosis in retroperitoneal soft tissue sarcoma. *Int J Radiat Oncol Biol Phys.* 1994; 29(5):1005–10. [PubMed: 8083069]
11. Le Pechoux C, Musat E, Baey C, et al. Should adjuvant radio-therapy be administered in addition to front-line aggressive surgery (FAS) in patients with primary retroperitoneal sarcoma? *Ann Oncol.* 2013; 24(3):832–7. [PubMed: 23123508]
12. Hassan I, Park SZ, Donohue JH, et al. Operative management of primary retroperitoneal sarcomas: a reappraisal of an institutional experience. *Ann Surg.* 2004; 239(2):244–50. [PubMed: 14745333]
13. EORTC Protocol 62092-22092. [Accessed 2 Aug 2014] A phase III randomized study of preoperative radiotherapy plus surgery versus surgery alone for patients with retroperitoneal sarcomas (RPS)—STRASS. 2012. <http://www.eortc.be/clinicaltrials/Details.asp?Protocol=62092&T>
14. Tzeng CW, Fiveash JB, Popple RA, et al. Preoperative radiation therapy with selective dose escalation to the margin at risk for retroperitoneal sarcoma. *Cancer.* 2006; 107(2):371–9. [PubMed: 16752414]
15. Baldini EH, Wang D, Haas RLM, et al. Treatment guidelines for preoperative radiation therapy (RT) for retroperitoneal sarcoma (RPS): preliminary consensus of an international expert panel. *Int J Radiat Oncol Biol Phys.* 2015 in press.
16. Baldini EH, Bosch W, Abrams RA, et al. Retroperitoneal sarcoma (RPS) target volume and organ at risk (OAR) contour delineation agreement among RTOG sarcoma radiation oncologists. *Int J Radiat Oncol Biol Phys.* 2015 in press.
17. Deasy JO, Blanco AI, Clark VH. CERR: a computational environment for radiotherapy research. *Med Phys.* 2003; 30(5):979–85. [PubMed: 12773007]
18. Warfield SK, Zou KH, Wells WM. Simultaneous truth and performance level estimation (STAPLE): an algorithm for the validation of image segmentation. *IEEE Trans Med Imaging.* 2004; 23(7):903–21. [PubMed: 15250643]
19. Allozi R, Li XA, White J, et al. Tools for consensus analysis of experts' contours for radiotherapy structure definitions. *Radiother Oncol.* 2010; 97(3):572–8. [PubMed: 20708285]
20. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics.* 1977; 33(1):159–74. [PubMed: 843571]
21. Bonvalot S, Miceli R, Berselli M, et al. Aggressive surgery in retroperitoneal soft tissue sarcoma carried out at high-volume centers is safe and is associated with improved local control. *Ann Surg Oncol.* 2010; 17(6):1507–14. [PubMed: 20393803]
22. Bonvalot S, Raut CP, Pollock RE, et al. Technical considerations in surgery for retroperitoneal sarcomas: position paper from E-Surge, a master class in sarcoma surgery, and EORTC-STBSG. *Ann Surg Oncol.* 2012; 19(9):2981–91. [PubMed: 22476756]
23. Pisters PW. Resection of some—but not all—clinically uninvolved adjacent viscera as part of surgery for retroperitoneal soft tissue sarcomas. *J Clin Oncol.* 2009; 27(1):6–8. [PubMed: 19047279]
24. Raut CP, Swallow CJ. Are radical compartmental resections for retroperitoneal sarcomas justified? *Ann Surg Oncol.* 2010; 17(6):1481–4. [PubMed: 20401636]
25. Tseng WW, Madewell JE, Wei W, et al. Locoregional disease patterns in well-differentiated and dedifferentiated retroperitoneal liposarcoma: implications for the extent of resection? *Ann Surg Oncol.* 2014; 21(7):2136–43. [PubMed: 24705628]
26. Crago AM. Extended surgical resection and histology in retroperitoneal sarcoma. *Ann Surg Oncol.* 2014; 21(10):1245–1245/s10434-014-4135-2
27. Gronchi A, Lo Vullo S, Fiore M, et al. Aggressive surgical policies in a retrospectively reviewed single-institution case series of retroperitoneal soft tissue sarcoma patients. *J Clin Oncol.* 2009; 27(1):24–30. [PubMed: 19047283]
28. Bonvalot S, Rivoire M, Castaing M, et al. Primary retroperitoneal sarcomas: a multivariate analysis of surgical factors associated with local control. *J Clin Oncol.* 2009; 27(1):31–7. [PubMed: 19047280]

29. Trans-Atlantic RPSWG. Management of primary retroperitoneal sarcoma (RPS) in the adult: a consensus approach from the TransAtlantic RPS Working Group. *Ann Surg Oncol*. 2014;10.1245/s10434-014-3965-2
30. Zagars GK, Ballo MT, Pisters PW, et al. Prognostic factors for patients with localized soft-tissue sarcoma treated with conservation surgery and radiation therapy: an analysis of 1225 patients. *Cancer*. 2003; 97(10):2530–43. [PubMed: 12733153]
31. Trovik CS, Bauer HC, Alvegard TA, et al. Surgical margins, local recurrence and metastasis in soft tissue sarcomas: 559 surgically-treated patients from the Scandinavian Sarcoma Group Register. *Eur J Cancer*. 2000; 36(6):710–6. [PubMed: 10762742]
32. Gronchi A, Casali PG, Mariani L, et al. Status of surgical margins and prognosis in adult soft tissue sarcomas of the extremities: a series of patients treated at a single institution. *J Clin Oncol*. 2005; 23(1):96–104. [PubMed: 15625364]
33. Gerrand CH, Wunder JS, Kandel RA, et al. Classification of positive margins after resection of soft-tissue sarcoma of the limb predicts the risk of local recurrence. *J Bone Joint Surg Br*. 2001; 83(8):1149–55. [PubMed: 11764430]
34. Singer S, Corson JM, Gonin R, Labow B, Eberlein TJ. Prognostic factors predictive of survival and local recurrence for extremity soft tissue sarcoma. *Ann Surg*. 1994; 219(2):165–73. [PubMed: 8129487]
35. Delaney TF, Kepka L, Goldberg SI, et al. Radiation therapy for control of soft-tissue sarcomas resected with positive margins. *Int J Radiat Oncol Biol Phys*. 2007; 67(5):1460–9. [PubMed: 17394945]

FIG. 1.

Example of a high-risk gross tumor boost volume (HR GTV boost) for a left upper quadrant retroperitoneal sarcoma (RPS). The gross tumor volume (GTV) is represented by the outline of the entire tumor (*red*). The HR GTV boost volume is the smaller volume that is 1.5-cm thick and along the postero-lateral abdominal wall, ipsilateral para-vertebral space, and aorta (*blue*)

FIG. 2.

Example of very good HR GTV contour agreement for the case of left upper quadrant leiomyosarcoma (RPS2). GTV for the entire tumor is shown in *red*, and the seven HR GTV volumes are shown in other *colors*. Note that six of seven HR GTV contours are almost superimposable and one of seven (*pale green*) does not extend as far laterally (see *arrow*), thus demonstrating very good contour agreement along the postero-lateral chest wall and medially along the ipsilateral para-vertebral space and aorta

FIG. 3.

First example of marginal HR GTV contour agreement. The seven HR GTV contours are shown in different *colors*. **a** Right upper quadrant (DD) liposarcoma (LPS) for case RPS1 showing that four of seven HR GTV contours include the entire liver surface and three of seven exclude the liver. **b** More inferior axial slice shows significant variation in how far anterior the lateral abdominal wall HR GTV contours are drawn. *Arrows* depict the various anterior-most extents of the contoured volumes

FIG. 4. Second example of marginal HR GTV contour agreement. Left lower quadrant DD LPS for case RPS3 depicting the significant variation of HR GTV contours with one of seven contours extending to include the anterior abdominal wall and three of seven extending to include the lateral border of the bladder

TABLE 1

Summary of high-risk gross tumor volume (HR GTV) agreement statistics for three retroperitoneal cases: RPS1, RPS2, and RPS3

	RPS1	RPS2	RPS 3
Maximum volume (cc)	1399.2	419.1	921.7
Minimum volume (cc)	689.7	173.2	174.2
Mean volume (cc)	947	290.2	414.4
Standard deviation (SD)	275.8	78.1	249.8
As a % of mean volume	(29 %)	(27 %)	(60 %)
STAPLE 95 consensus volume (cc)	1100.8	316.5	434.9
Intersection volume (cc)	420.8	74.3	93.0
As a % of mean volume	(44 %)	(26 %)	(22 %)
Union volume (cc) (largest volume assuming outermost contours)	1786.8	590.4	1105.8
Agreement sensitivity (mean $\pm$ SD)	0.72 $\pm$ 0.13	0.72 $\pm$ 0.14	0.67 $\pm$ 0.22
Agreement specificity (mean $\pm$ SD)	0.99 $\pm$ 0.024	0.98 $\pm$ 0.024	0.99 $\pm$ 0.024
Overall Kappa (<i>p</i> value)	0.66 (< 0.0001)	0.61 (<0.0001)	0.52 (< 0.0001)
	“Substantial”	“Substantial”	“Moderate”