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Retroperitoneal sarcoma

Spatial and volumetric changes of retroperitoneal sarcomas during pre-operative radiotherapy

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ABSTRACT

Purpose: To determine the positional and volumetric changes of retroperitoneal sarcomas (RPS) during pre-operative external beam radiotherapy (PreRT).

Material and methods: After excluding 2 patients who received chemotherapy prior to PreRT and 15 RPS that were larger than the field-of-view of cone-beam CT (CBCT), the positional and volumetric changes of RPS throughout PreRT were characterized in 19 patients treated with IMRT using CBCT image guidance. Analysis was performed on 118 CBCT images representing one image per week of those acquired daily during treatment. Intra-fraction breathing motions of the gross tumor volume (GTV) and kidneys were measured in 22 RPS patients simulated using 4D-CT. Fifteen other patients were excluded whose tumors were incompletely imaged on CBCT or who received pre-RT chemotherapy.

Results: A GTV volumetric increase (mean: 6.6%, $p = 0.035$) during the first 2 weeks (CBCT1 vs. CBCT2) of treatment was followed by GTV volumetric decrease (mean: 4%, $p = 0.009$) by completion of radiotherapy (CBCT1 vs. CBCT6). Internal margins of 8.6, 15 and 15 mm in the lateral, anterior/posterior and superior/inferior directions would be required to account for inter-fraction displacements. The extent of GTV respiratory motion was significantly ($p < 0.0001$) correlated with more superiorly positioned tumors.

Conclusion: Inter-fraction CBCT provides important volumetric and positional information of RPS which may improve PreRT quality and prompt re-planning. Planning target volume may be reduced using online soft-tissue matching to account for interfractional displacements of GTVs. Important breathing motion occurred in superiorly placed RPS supporting the utility of 4D-CT planning.

Retroperitoneal sarcomas (RPS) are rare cancers that comprise 10–15% of soft-tissue sarcomas (STS) [1]. Unlike STS from the extremities in which approximately 90% local control is achieved largely through wide excision ± adjuvant radiotherapy (RT), the 5-year local control rate in RPS from surgical series ranges from 30 to 50% [2] and locoregional abdominal failure is the principle cause of death [3–11]. Efforts to improve local control in RPS have included the use of pre-operative RT (PreRT) [12–14]. This strategy produced 5 and 10-year relapse free survival rates of 69% and 63% respectively, in a Princess Margaret Cancer Centre (PMH)/Mt-Sinai Hospital Phase I/II study and has been adopted as standard practice at the PMH [15]. The European Organization for Research and Treatment of Cancer (EORTC) is currently leading an ongoing phase III randomized control trial (RCT) (EORTC 66092-22092) that studies the addition of PreRT to surgery in the management of primary resectable RPS.

The advantages of delivering PreRT for RPS include displacement of normal tissues and organs outside the high-dose volume. Post-operatively, radiosensitive normal organs fill the surgical cavity and render RT difficult to tolerate. Moreover, delineating the clinical target volume (CTV) is more accurate in the presence of the gross tumor volume (GTV) in the pre-operative setting than post-operatively where lack of a GTV and surgical disruption add uncertainty. A potential criticism of PreRT is the risk that RPS continues to grow during PreRT, which may render the tumor unresectable. While prior studies have described the range of interfractional and intrafractional motions of abdominal organs and structures [16–18], there are no prior publications to describe RPS motions, which may differ from other abdominal tumors and structures due to RPS's large sizes and lack of organ confinement. Since 2007, PMH implemented the use of daily cone-beam CT (CBCT) to guide the delivery of intensity modulated radiotherapy (IMRT) for PreRT of RPS. Since 2010, 4D-CT simulation of RPS has

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been used to incorporate potential breathing motion of the target into the planning target volumes. The current study aims to characterize the volumetric and spatial changes of RPS during the course of radiotherapy by using the information gathered through CBCT imaging and 4D-CT simulations of RPS.

Materials and methods

Patients

Approval from the PMH Research Ethics Board was obtained. From 2007 to 2012, 56 patients with RPS were treated with PreRT using IMRT and daily CBCT (Elekta XVI, Stockholm, Sweden) soft-tissue image guided radiotherapy (IGRT). Patients with primary ($n = 52$) or recurrent ($n = 4$) RPS of any histology with no prior exposure to RT were included. Patients initially judged by the consulting surgical oncologists to have resectable, borderline resectable, or unresectable disease were included.

There were 2 cohorts of patients included in this study. From 2007 to 2010, 36 patients underwent PreRT and daily image guidance with CBCT. Seventeen patients were excluded from analysis due to chemotherapy prior to RT ($n = 2$) or tumor larger than CBCT field-of-view ($n = 15$) which represent a conical volume with a maximum diameter of 41 cm (axial direction) and 26 cm width (superior–inferior direction). The remaining 19 patients formed the "IGRT cohort" in which GTV expansion, contraction and inter-fractional motion during RT were characterized. Of these 19 patients, 3 had been deemed unresectable prior to RT, 15 resectable, and 1 borderline.

From 2010 to 2012, 26 patients were simulated using 4D-CT simulation (Philips Brilliance Large Bore, Amsterdam, Netherlands). Four patients had GTVs (maximum dimensions (sup-inf; right–left) and volumes): 23.5 × 13.3 cm (2883 cc), 27.9 × 21.0 cm (5484 cc), 31.0 × 15.7 cm (6809 cc), AND 33.7 × 26.0 cm (11,456 cc) that were incompletely encompassed by the field-of-view of the 4D-CTs, which required the imaging of the diaphragmatic dome, and were excluded from analysis; these were also excluded from the IGRT cohort. The remaining 22 patients formed the "4D-CT cohort" and were used to characterize the intra-fractional breathing motion of RPS and kidneys. Table 1 summarizes the characteristics of the patients.

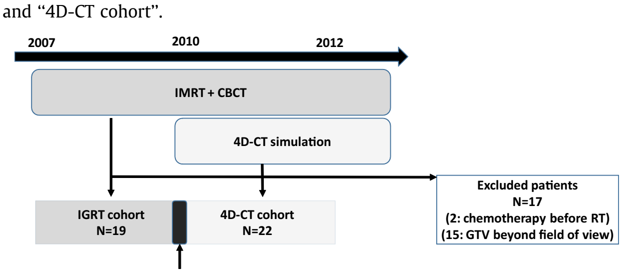
Patient positioning and simulation

Patients were positioned supine with their arms above the head and immobilized using an evacuated cushion and leg immobilizers. Helical CT scans were used for planning from 2007 to 2010. From 2010, CT simulation was acquired with 4D-bellows around the abdomen. Following the helical scan acquisition, 4D-CT free breathing acquisition was performed. The 4D-CT dataset at maximum inhale and exhale phases was used for planning. The estimated additional irradiation dose from the 4D-CT simulation is estimated to be 4 times that of a helical CT scan [19].

Planning and treatment

All patients treated for RPS pre-operatively were planned using Pinnacle[3] (Philips Healthcare, Amsterdam, Netherlands). Prior to 2010, planning was done using the following targets and structures contoured by radiation oncologists: GTV, CTV, individual kidneys, and specific organs at risk relative to the local anatomy. Since 2010, patients were simulated using 4D-CT scans in which targets and critical structures were contoured at maximum inspiration and expiration. The combined contours from inspiration and

Table 1
Characteristics of patients in the "IGRT cohort" and "4D-CT cohort".



Variables	IGRT cohort ($n = 19$)	4D-CT cohort ($n = 22$)	Included patients "IGRT" + "4D-CT" cohorts ($n = 39$) 2 overlaps	Excluded patients ($n = 17$)	All patients ($n = 56$)
Median age (range)	61 (31–88)	61 (38–88)	60 (31–88)	55 (34–81)	59 (31–88)
Gender					
F	14 (74%)	8 (36%)	21 (54%)	6 (35%)	27 (48%)
M	5 (16%)	14 (64%)	18 (46%)	11 (65%)	29 (52%)
Tumor grade					
Low	2 (10%)	4 (18%)	6 (15%)	10 (59%)	16 (28%)
High	14 (74%)	17 (77%)	29 (74%)	7 (41%)	36 (64%)
N/A	3(16%)	1 (4%)	4 (19%)	0	4 (7%)
Histology					
Liposarcoma	8 (42%)	7 (32%)	14 (36%)	14 (82%)	28 (50%)
Leiomyosarcoma	4 (21%)	6 (27%)	10 (26%)	3 (18%)	13 (23%)
Sarcoma NOS/UPS	5 (26%)	5 (23%)	9 (23%)	0	9 (16%)
Synovial sarcoma	0 (0%)	2 (9%)	2 (5%)	0	2 (4%)
Malignant solitary fibrous tumor	1 (5%)	1 (4%)	2 (5%)	0	2 (4%)
Malignant peripheral nerve sheath tumor	1 (5%)	1 (4%)	2 (5%)	0	2 (4%)
Median GTV (range) cc	417 (61–3516)	836 (57–7639)	506 (57–7639)	4828 (1088–11,456)	1196 (57–11,456)
Median RT dose (range)	50 Gy (14.4–50.4)	50.4 Gy (45–50.4)	50 Gy (14.4–50.4)	45 Gy (34.4–50)	50 Gy (14.4–50.4)