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**CLINICAL INVESTIGATION** **Metastasis**

# CLINICAL OUTCOME OF HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR ABDOMINAL LYMPH NODE METASTASES

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**Purpose: We report the medium-term clinical outcome of hypofractionated stereotactic body radiotherapy (SBRT) in a series of patients with either a solitary metastasis or oligometastases from different tumors to abdominal lymph nodes.**

**Methods and Materials: Between January 2006 and June 2009, 19 patients with unresectable nodal metastases in the abdominal retroperitoneal region were treated with SBRT. Of the patients, 11 had a solitary nodal metastasis and 8 had a dominant nodal lesion as part of oligometastatic disease, defined as up to five metastases. The dose prescription was 45 Gy to the clinical target volume in six fractions. The prescription had to be downscaled by 10% to 20% in 6 of 19 cases to keep within dose/volume constraints. The first 11 patients were treated with three-dimensional conformal techniques and the last 8 by volumetric intensity-modulated arc therapy. Median follow-up was 1 year.**

**Results: Of 19 patients, 2 had a local progression at the site of SBRT; both also showed concomitant tumor growth at distant sites. The actuarial rate of freedom from local progression was 77.8% ± 13.9% at both 12 and 24 months. Eleven patients showed progressive local and/or distant disease at follow-up. The 12- and 24-month progression-free survival rates were 29.5% ± 13.4% and 19.7% ± 12.0%, respectively. The number of metastases (solitary vs. nonsolitary oligometastases) emerged as the only significant variable affecting progression-free survival ($p < 0.0004$). Both acute and chronic toxicities were minimal.**

**Conclusions: Stereotactic body radiotherapy for metastases to abdominal lymph nodes was shown to be feasible with good clinical results in terms of medium-term local control and toxicity rates. Even if most patients eventually show progressive disease at other sites, local control achieved by SBRT may be potentially significant for preserving quality of life and delaying further chemotherapy.** © 2011 Elsevier Inc.

**SBRT, Lymph node metastases, IMRT, Volumetric modulated arc therapy, RapidArc.**

## INTRODUCTION

Stereotactic body radiotherapy (SBRT) has proved its efficacy in several patient populations with primary and metastatic limited tumors (1). In particular, SBRT may be appropriate for selected patients with oligometastatic disease, defined as fewer than five lesions (2). Abdominal SBRT has been reported with reference mainly to primary and secondary liver tumors, as well as pancreatic and renal tumors (1). Stereotactic body radiotherapy for metastases to abdominal lymph nodes has rarely been reported, with only three articles reporting on it as a specific topic (3–5) and with it most often comprising a few cases in mixed series (6–10). In one article reporting the outcome of SBRT for isolated lymph node recurrence from prostate cancer, the target lesion was within the pelvis in most cases, which poses different technical problems (11).

The rationale for administering SBRT with a curative intent to patients with limited nodal metastatic disease may be the same as that in selected patients with liver or lung metastases. Whereas most patients with metastases to abdominal nodes are unfit for surgery, it is known that in the setting of limited metastatic burden, SBRT leads to local control rates higher than 70% to 80% (1, 10), which may turn into increased survival and better quality of life. Conversely,

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conventionally fractionated non-stereotactic radiotherapy is generally believed to attain poorer results, because doses are limited by normal tissue tolerance. Actually, few published data do exist on local control rates of conventional radiotherapy in this context. Although several articles dealt with conventional radiotherapy of isolated para-aortic lymph node recurrence from cervix cancer, most of them reported only survival rates (12–15). A 33% to 50% rate of progressive disease in the para-aortic lymph node–treated area was reported in two studies (16, 17).

Between January 2006 and June 2009, 19 patients with unresectable nodal metastases in the abdominal region were treated with SBRT. We have previously reported early results in a series of 15 patients with abdominal nodal metastases, including 12 treated by SBRT alone with three-dimensional conformal radiotherapy (CRT) techniques (18). In that series no major toxicity was observed, and 6-month local control was achieved in 10 of 12 cases. Because in 6 of 12 cases our standard dose of 45 Gy in 6 fractions had to be downscaled by 10% to 20% to keep within dose/volume constraints for organs at risk (OARs), we also investigated the potential role of volumetric intensity-modulated arc therapy given by RapidArc (Varian Medical Systems, Palo Alto, CA) in this patient population (19). RapidArc has been investigated previously for some other clinical cases (20–25), showing significant improvements over other advanced techniques. Because we also found advantages in dose distribution in this setting, since November 2008, SBRT to abdominal nodes has been delivered by volumetric intensity-modulated radiotherapy.

This retrospective study is an update of our previous report. Our aim was to evaluate the clinical effectiveness of SBRT for patients with solitary or nonsolitary oligometastases to abdominal lymph nodes. Medium-term (12–24 months) local control and acute and late toxicity were considered as the main endpoints.

## METHODS AND MATERIALS

### *Patient selection*

From October 2005 to June 2009 at Istituto Clinico Humanitas, Rozzano, Italy, 80 patients were treated by linear accelerator–based hypofractionated SBRT to abdominal targets, including liver, pancreatic, and lymph nodal lesions. Since January 2006, 29 consecutive patients with unresectable nodal metastases in the abdominal region were treated. Six patients treated with a single-dose SBRT boost after external beam fractionated radiation over an extended volume are not the subject of this report. In addition, among the 23 patients treated by SBRT alone, we excluded 4 cases because the nodal site was at the hepatic hilum, which entails special issues in terms of organ motion. Thus, on the whole, this report regards 19 patients.

Disease extension was evaluated in all the cases by computed tomography (CT) with or without magnetic resonance imaging. The presence of metabolic active tumor in the nodal site was confirmed by fluorodeoxyglucose positron emission tomography (PET) performed in 17 of 19 patients. In all patients the target metastasis was in the abdominal retroperitoneal region, with either a solitary lesion (11 patients) or a dominant nodal lesion as part of oligometastatic disease (nonsolitary oligometastases) (8 patients). Among the latter 8 cases, nontarget metastases were either PET negative after previous chemotherapy (3 patients: 1 with a single lung metastasis, 1 with a single liver metastasis, and 1 with multiple abdominal lymph nodes) or after SBRT at other sites (3 patients: 1 with a single lung metastasis, 1 with a single liver metastasis, and 1 with a single adrenal metastasis) or PET positive and thereafter treated by chemotherapy (2 patients: 1 with a single liver metastasis and 1 with multiple mediastinal lymph nodes).

The anatomic site was defined according to the most involved nodal station: left para-aortic in 5 patients; right para-aortic in 7; posterior to inferior vena cava in 2; posterior to head of pancreas, or celiac, or near the origin of the superior mesenteric artery in 5. In 8 patients the clinical target volume (CTV) was in close proximity to some part of the duodenum, with a minimal distance of 8 mm or less. Computed tomography images of four representative cases are shown in Fig. 1.

All the patients had been considered unfit for surgery at the time of radiation. In 3 patients the lesion was a nodal recurrence after nonradical surgery at the same site. Chemotherapy was stopped at least 3 weeks before SBRT and withheld until disease progression. Other relevant patient, tumor, and treatment characteristics, stratified by radiation technique, are reported in Table 1.

### *CT simulation*

During CT simulation, the patients were positioned supine, with their arms above the head, and were immobilized by means of a vacuum bag combined with a thermoplastic body mask including a Styrofoam block for abdominal compression to minimize organ motion. Contrast-enhanced planning CT scans were acquired in free quiet breathing mode with a 3-mm slice thickness with a stereotactic body frame composed of a bridge-like removable cover coupled to a carbon fiber basement (Stereotactic Body Frame; Elekta [Milan, Italy]). Oral contrast was given 30 to 60 minutes before CT scan to visualize the duodenum and small bowel.

### *Contouring and dose prescription*

The gross tumor volume included macroscopic nodal disease apparent on CT as well as on PET if available. The CTV was kept equivalent to the gross tumor volume. The planning target volume (PTV) was defined by taking into account both the internal margin and the setup margin (26). The internal margin depends on intrafraction organ motion and interfraction organ motion, which are not expected to be substantial in a short course of radiation for retroperitoneal nodes adjacent to the spine and large vessels. Scarce data are available regarding organ motion of retroperitoneal nodes: in a similar setting regarding the celiac axis, Wysocka *et al.* (27) calculated a median intrafraction craniocaudal displacement of 3.8 mm and lower displacements in the other axes. The setup margin was estimated to be lowered close to 0, given the cone-beam computed tomography (CBCT) systematic verification of setup variations. This led us to cut down the CTV–PTV margin to 6 mm in the cranial–caudal axis and 3 mm in the anterior–posterior and lateral axes, allowing mainly for residual intrafraction organ motion, as well as for inaccuracies in CBCT image interpretation.

The main OARs considered were the spinal cord, kidneys, stomach, duodenum, small bowel, and liver. The stomach, duodenum, and small bowel were contoured when appropriate. Organ motion was taken into account for the small bowel by contouring the intestinal cavity (the volume containing bowel loops as defined in a specific comparison) (28), a method that seems both practical and robust (28, 29). For the duodenum, on the contrary, we decided to avoid either