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CLINICAL INVESTIGATION **Cervix**

HELICAL TOMOTHERAPY VERSUS CONVENTIONAL INTENSITY-MODULATED RADIATION THERAPY FOR PRIMARY CHEMORADIATION IN CERVICAL CANCER PATIENTS: AN INTRAINDIVIDUAL COMPARISON

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Purpose: To compare intensity-modulated radiotherapy (IMRT) delivered by helical tomotherapy (HT) with conventional IMRT for primary chemoradiation in cervical cancer patients.

Methods and Materials: Twenty cervical cancer patients undergoing primary chemoradiation received radiation with HT; 10 patients underwent pelvic irradiation (PEL) and 10 extended-field irradiation (EXT). For treatment planning, the simultaneously integrated boost (SIB) concept was applied. Tumor, pelvic, with or without paraaortic lymph nodes were defined as planning target volume A (PTV-A) with a prescribed dose of 1.8/50.4 Gy (28 fractions). The SIB dose for the parametrium (PTV-B), was 2.12/59.36 Gy. The lower target constraints were 95% of the prescribed dose in 95% of the target volume, and the upper dose constraint was 107%. The irradiated small-bowel volumes were kept as low as possible. For every HT plan, a conventional IMRT plan was calculated and compared with regard to dose–volume histogram, conformity index and conformity number, and homogeneity index.

Results: Both techniques allowed excellent target volume coverage and sufficient SB sparing. Conformity index and conformity number results for both PTV-A and PTV-B, homogeneity index for PTV-B, and SB sparing for V45, V50, Dmax, and D1% were significantly better with HT. SB sparing was significantly better for conventional IMRT at low doses (V10).

Conclusions: Both HT and conventional IMRT provide optimal treatment of cervical cancer patients. The HT technique was significantly favored with regard to target conformity, homogeneity, and SB sparing. Randomized trials are needed to assess the oncological outcome, toxicity, and clinical relevance of these differences. © **2011 Elsevier Inc.**

Cervical cancer, Small bowel irradiation, Helical tomotherapy, Intensity-modulated radiotherapy, Conformity, Homogeneity.

INTRODUCTION

Concomitant cisplatin-based chemoradiation is the therapy of choice in patients with locally advanced cervical cancer. However, there is considerable acute and late toxicity affecting the gastrointestinal (GI) and the genitourinary (GU) tracts (1, 2). Even with careful planning and conventional fractionation, severe Grade 3 and 4 acute GI toxicity is reported in approximately 8% of patients (3, 4). In the Radiation Therapy Oncology Group (RTOG) studies 90-01 and 92-10, 35% of all patients experienced Grade 3 and 4 GI toxicity (1, 5).

Intensity-modulated radiotherapy (IMRT) significantly reduces acute and late toxicity to the organs at risk (OAR) (6, 7). Reducing the small bowel (SB) volume that receives the prescribed dose by half with IMRT compared with three-dimensional (3D) techniques, Roeske *et al*. (7) demonstrated a reduction in Grade 2 GI toxicity from 91% with 3D techniques to 60% with IMRT and decreased the incidence of chronic GI toxicity from 50% to 11%. A growing body of evidence indicates a strong dose–volume relationship for the development of SB toxicity for pelvic tumors (8, 9). Using the constraints of <40% of the SB should receiving at least 35 Gy and <50% of the rectum receiving at least 45 Gy,

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only 1 of 54 patients developed Grade 3 GI toxicity during an adjuvant chemoradiation trial in cervical cancer (10). Nevertheless, even for primary chemoradiation in cervical cancer patients, no dose–volume histogram (DVH) parameter is defined to predict an elevated risk of high-grade GI toxicity.

Compared with ''conventional'' IMRT, helical tomotherapy (HT) delivers a highly conformal dose distribution with a greater number of independent beam directions. Analyzing HT and IMRT plans for extended field radiation in International Federation of Gynecologists and Obsetricians (FIGO) stage IIIC endometrial cancer patients, Lian *et al.* demonstrated the superiority of the HT with respect to PTV coverage, a reduced integral dose, and a decreased dose to most OAR (11). However, the potential benefit of HT over IMRT is still under investigation. The on-board megavoltage computed tomography (CT) allows daily setup verification, assuming that, by reducing the setup error, the margins of the planning target volume (PTV) may be reduced, leading to decreased doses to the SB (12). Although the role of conformity and homogeneity in predicting therapy-related toxiciy is not defined, we compared the conformity of the two plans using the conformity index (CI) (RTOG) (13), the homogeneity index (HI) (14), and the conformity number (CN) (15). To the best of our knowledge, there are no published data comparing the planning parameters of HT vs. IMRT in cervical cancer patients.

The aim of this study was to compare HT IMRT with conventional IMRT in regard to dosimetric parameters for target volumes (PTV) and the SB in an intraindividual comparison. The planning goal was to maintain high PTV coverage while keeping the dose to the SB as low as possible.

METHODS AND MATERIALS

Patient characteristics

Twenty patients with histologically confirmed cervical cancer (2xFIGO IB2; 2X FIGO IIA; 11x FIGO IIB, 1x FIGO IIIA; 3x FIGO IIIB, 1x FIGO IVA) undergoing primary chemoradiation received radiation with HT. Plans for HT were compared with conventional IMRT plans with regard to DVH parameters. The study was approved by the institutional ethical committee. Patient characteristics are shown in Table 1.

Table 1. Patient characteristics, including stage, grading, histology, radiation fields, and pelvic and para-aortic lymph node status

Patient	FIGO stage	Radiation field	Grading	Histology	pN	pM (LYM)
1	IIIB	PEL	2	SCC	pN0	pM0
2	IVA	PEL	2	SCC	pNX	pMX
3	IIB	PEL	2	ASC	pN1	pM0
4	IIB	PEL	2	Adeno	pNX	pMX
5	IIB	PEL	2	SCC	pN0	pM0
6	IIB	PEL	3	SCC	pN0	pM0
7	IB2	PEL	2	SCC	pNX	pMX
8	IIB	PEL	2	SCC	pN1	pM0
9	IIB	PEL	3	SCC	pN1	pM0
10	IIB	PEL	3	SCC	pNX	pMX
11	IIA	EXT	3	SCC	pN1	pM1
12	IIB	EXT	2	SCC	pN1	pM0
13	IIIB	EXT	2	SCC	pNX	pMX
14	IIA	EXT	2	SCC	pN1	pM1
15	IIB	EXT	2	SCC	pN0	pM1
16	IIIA	EXT	3	Adeno	pN1	pM1
17	IIB	EXT	3	SCC	pN1	pM1
18	IIB	EXT	2	Adeno	pN1	pM1
19	IB2	EXT	2	SCC	pN1	pM1
20	IIIB	EXT	2	SCC	pN1	pM1

Abbreviations: Adeno = adenocarcinoma; ASC = adenosquamous carcinoma; EXT = extended field irradiation; FIGO = International Federation of Gynecologists and Obstetricians; PEL = standard pelvic fields; pM(LYM) = para-aortic lymph node; pN = pelvic lymph node; SCC = squamous cell carcinoma.

Treatment planning

All patients received a planning CT scan (CT scanner LightSpeed, GE Healthcare) with intravenous contrast media (Xenetix 350) at a slice thickness of 3.75 mm. In case of para-aortic involvement, the CT scans were done from the diaphragm to the trochanter minor. In histologically proven negative para-aortic lymph nodes (LN), the CT scan was performed from the second lumbar vertebra to the trochanter minor. The planning CT was performed while the patient was in the supine position using a knee and foot positioning device, and patients were asked to have a full bladder.

Target volumes and OAR

Target volumes and OAR were delineated in all axial CT slices according to the recommendations of RTOG (16) and the International Commission on Radiation Units and Measurements Reports (ICRU) 50 (17), respectively. The target volumes were defined on the basis of the full-bladder CT scan. They were divided into PTV-A and PTV-B (boost) volumes, and the concept of simultaneously integrated boost (SIB) was applied. The clinical target volume (CTV-A) was defined as the macroscopic tumor, including the cervix and the corpus uteri and external, internal, common iliac, and pre-sacral LNs plus/minus the paraaortic LNs with a 5-mm margin. The volume (PTV-A) was outlined as the CTV-A with a 1-cm margin in all directions. In patients with negative para-aortic LNs, the upper field border was at the level of the L4/5 interspace (PEL). In patients with para-aortic LN metastases, the para-aortic region was included in the CTV-A up to the level of the renal vessels (extended field irradiation [EXT]). The caudal PTV slice was at the level of the obturator foramen.

For the SIB target volume defined as CTV-B, the high-risk volume (parametria and surrounding lymphatic tissue) was delineated by titanium clips that were positioned during laparoscopic staging. The cranial border of the CTV-B was clip-marked medial to the bifurcation of the internal and external iliac arteries. Caudally, a clip was placed below the obturator vena. The clip was placed at the crossover of the uterine artery and the ureter medially, and on the fascia of the iliopsoas muscle laterally. In patients who refused laparoscopic staging, standardized borders for boost definition were as follows: for the cranial border, the bifurcation of the common iliac artery; for the lateral border, the iliopsoas muscle; for the medial border, the lateral part of the uterus; and for the caudal border, the pubococcygeal muscle as part of the levator ani. For the SIB target volume PTV-B, 1 cm was added to the CTV-B.

The following OARs were delineated: spinal cord, femoral heads, kidneys, bladder, rectum up to the sigmoidal loop, and the SB as a whole peritoneal cavity except for LNs, muscles, and OAR other than the SB. The delineation of the SB exceeded the upper and lower border of the PTV-A by two slices.