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Original research article

Safety of adjuvant intensity-modulated postoperative radiation therapy in endometrial cancer: Clinical data and dosimetric parameters according to the International Commission on Radiation Units (ICRU) 83 report

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ABSTRACT

Aim: To report a single-institution experience using postoperative pelvic Intensity Modulation Radiation Therapy (IMRT) using tomotherapy accelerators (TA) in postoperative endometrial cancer (EC) regarding ICRU 83 recommendations.
Background: IMRT in gynecological malignancies provides excellent dosimetric data, lower rates of adverse events and clinical data similar to historical series.
Material and methods: Seventy-six patients with EC were postoperatively treated with adjuvant IMRT using TA. The IMRT dose was 45 Gy for patients without positive lymph nodes and Type I histology and 50.4 Gy for patients with positive lymph nodes and/or type II histology.
Results: With a median follow-up of 29 months, the 12- and 24-month Overall Survival (OS) and Disease-Free Survival (DFS) were 96%, 93%, 87%, and 74%, respectively. Age of less than 60 years was associated with better OS (HR: 8.9; CI: 1.1–68) and DFS (HR: 3.5; CI: 1.2–10.2). Patients with Type II and Type I Grade III histology had a worse OS (HR: 3.3; CI: 1.1–11). Five women (6.6%) presented in-field local vaginal recurrence, 2 (2.6%) presented non-in-field

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vaginal recurrence, 4 (5.2%) presented pelvic node and distant recurrence and 11 (14.4%) presented only distant metastases. One patient stopped radiation treatment due to Grade III acute diarrhea. No Grade III late toxicity was observed. Planning Target Volume (PTV) coverage showed mean D2, D50, D95, and D98 of 51.64–46.23 Gy, 49.49–44.97 Gy, 48.62–43.96 Gy, and 48.47–43.58 Gy for patients who received 45 and 50.4 Gy, respectively.

Conclusions: IMRT with TA in postoperative EC shows excellent conformity and homogeneity of PTV dose. Without Grade III late toxicity, data from this cohort demonstrated the utility of IMRT.

1. Background

Radiotherapy in the pelvic area is not without acute and chronic adverse effects. Intensity-Modulated Radiation Therapy (IMRT) provides excellent Planning Target Volume (PTV) coverage and conformational planning treatment in the pelvic postoperative area while sparing normal tissues. IMRT in postoperative endometrial cancer patients could provide promising loco-regional data with low rates of urinary and gastrointestinal secondary events.

2. Aim

Endometrial carcinoma is the most frequent gynecological (GYN) cancer in the western world, with an incidence of 15 to 25/100,000 women per year.[1,2] More than 75% of endometrial carcinoma patients are diagnosed at an early stage, resulting in a five-year overall survival rate of 80%.

Randomized trials[3–6] have established that pelvic radiotherapy (RT) as an adjuvant to surgery provides a significant improvement in the local control of tumor growth, primarily in terms of intermediate-risk prognoses. Unfortunately, no effects on survival have been observed. However, the conventional techniques for whole-pelvis RT include four static photon fields and expose most of the contents of the pelvis, including the small bowel, to the prescribed dose of 45 Gy–50 Gy. Several factors predispose patients to acute and late small bowel effects,[7,8] such as prior pelvic surgery, hypertension, diabetes mellitus, pelvic inflammatory disease, extended field radiation, and dose of irradiation. Consequently, the severe morbidity of the small bowel (published rates of 1–25%) significantly reduces the quality of life,[9,10] and these radiation treatments remain a subject of debate.

The development of radiation treatment techniques, such as IMRT, has produced similar control data with lower rates of secondary effects. The data resemble those of gastrointestinal therapies due to the highly conformal technique of IMRT, which improves the therapeutic ratio of postoperative radiation treatments while sparing more of the adjacent normal tissues.[11–13] Similarly, early published results have shown a 30–60% reduction in small bowel doses following GYN IMRT.[14–16] Likewise, these reductions in dose have been suggested to decrease the rates of both acute[11] and chronic gastrointestinal side effects[17,18] in only a small number of patients. Moreover, the results of the ongoing Phase III trials are not expected for another 4–5 years.

Therefore, we sought to report on the clinical data and the feasibility and safety of surgery-adjuvant IMRT in endometrial cancer patients and dosimetric parameters according to the ICRU83 criteria[19] of a prospective observational study performed in the Oscar Lambret Center from 2009 to 2012.

3. Materials and methods

From January 2009 to June 2012, 76 patients with locally advanced endometrial cancer were treated consecutively and prospectively in an observational study registered at the French National Commission for Informatics and Liberty by the Oscar Lambret Center Clinical Research Unit.

Initial tumor staging included a clinical pelvic examination, histological proof of endometrial cancer and pelvic magnetic resonance imaging (MRI). All patients underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomies. Pelvic lymph node dissections were performed in 62 (81.6%) patients based on the preoperative MRI data, the histopathology type and the initial medical condition of the patient. Additional para-aortic dissection surgeries were planned for 29 (38.2%) patients, primarily in cases of malignant infiltration of the pelvic nodes and/or Type II adenocarcinoma diagnosed by histology.

The Clinical Target Volume (CTV) included the upper third of the vagina with an expansion of 1 cm, which was limited to the external contours of the organs at risk (OAR). The CTV also included the pelvic nodes up to the L4–L5 junction and the para-aortic nodes in cases of histologically demonstrated malignant infiltration. The contour of the pelvic nodes was defined according to the RTOG recommendations.[20] The PTV was fixed as a 0.5-cm expansion from the CTV. The rectum was drawn from the ano-rectal junction to the recto-sigmoid junction and from the upper rectum limit to the sigmoid until in the last slide on which it could be observed. The small bowel was contoured as the peritoneal cavity (in all possible places in which it could be positioned).

A dose of 45 Gy was delivered to the PTV in 25 fractions at 5 fractions per week. However, in 17 patients, the PTVs received 50.4 Gy in 28 fractions when IIIc1 or IIIc2 Stage or Type II adenocarcinoma was present and the patient was aged 70 years or less. In one patient, the treatment ceased at 48.6 Gy due to acute severe toxicity. Six patients (7.8%) with IIIc2 stage received 50.4 Gy to the pelvis and para-aortic nodes. The pre-planning theoretical maximum doses to the OAR were as follows: for the small bowel, 50 Gy was the theoretically maximal tolerated dose, and V45 and V40 were required to