Int. J. Radiation Oncology Biol. Phys., Vol. 72, No. 3, pp. 665–670, 2008

0360-3016/08/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2008.01.030

CONTACT X-RAY THERAPY FOR RECTAL CANCER: EXPERIENCE IN CENTRE ANTOINE-LACASSAGNE, NICE, 2002–2006

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Purpose: To report the results of using contact X-ray (CXR), which has been used in the Centre-Lacassagne since 2002 for rectal cancer.

Methods and Materials: A total of 44 patients were treated between 2002 and 2006 using four distinct clinical approaches. Patients with Stage T1N0 tumors were treated with transanal local excision (TLE) and adjuvant CXR (45 Gy in three fractions) ($n = 7$). The 11 inoperable (or who had refused surgery) patients with Stage T2-T3 disease were treated with CXR plus external beam radiotherapy (EBRT). Those with Stage T3N0-N2 tumors were treated with preoperative CXR plus EBRT (with or without concurrent chemotherapy) followed by surgery ($n = 21$). Finally, the patients with Stage T2 disease were treated with CXR plus EBRT followed by TLE ($n = 5$).

Results: The median follow-up was 25 months. In the 7 patients who underwent TLE first, no local failure was observed, and their anorectal function was good. Of the 11 inoperable patients who underwent CXR plus EBRT alone, 10 achieved local control. In the third group (preoperative CXR plus EBRT), anterior resection was performed in 16 of 21 patients. Complete sterilization of the operative specimen was seen in 4 cases (19%). No local recurrence occurred. Finally, of the 5 patients treated with CXR plus EBRT followed by TLE, a complete or near complete clinical response was observed in all. TLE with a R0 resection margin was performed in all cases. The rectum was preserved with good function in all 5 patients.

Conclusion: These early results have confirmed that CXR combined with surgery (or alone with EBRT) can play a major role in the conservative and curative treatment of rectal cancer.

Rectal cancer, Contact X-ray therapy, Conservative treatment, Local excision, Endocavitary treatment.

INTRODUCTION

Since the pioneering work of Papillon in Lyon between 1960 and 1990, contact X-ray therapy (CXR) has been a validated treatment for rectal cancer in selected cases (1, 2). Such a technique has been used with reproducible results in many centers in France, the United Stages, Canada, and the United Kingdom (3–8). The Lyon R96-02 randomized trial (9) compared preoperative external beam radiotherapy (EBRT) alone with a CXR boost to treat distal T2-T3 rectal adenocarcinoma. The boost dose with CXR was able to significantly increase the complete clinical response rate (28% vs. 2%) and use of conservative rectal surgery (72% vs. 40%). This CXR technique was introduced for the first time in the Centre Antoine-Lacassagne in January 2002. This report has reviewed our early results achieved during a 5-year period in 44 patients treated with four distinct clinical approaches.

METHODS AND MATERIALS

A total of 56 patients underwent RT in the Centre Antoine-Lacassagne between January 2002 and December 2006, with CXR for a rectal adenocarcinoma located in the distal or middle rectum. Of these 56 patients, 12 were eliminated from this analysis for the following reasons: 5 were treated for an intrarectal local recurrence; 4 underwent RT for a symptomatic reason (bleeding, rectal discharge) in the presence of inoperable locally advanced or metastatic rectal cancer; 2, with Stage T3 disease, had previously undergone RT to the pelvis for prostate cancer and received CXR only without EBRT; and 1 had been treated with preoperative combined CXR plus EBRT but was lost to follow-up immediately after RT.

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Conflict of interest: J. P. Gerard is a clinical advisor to Ariane Medical Systems Limited.

Acknowledgments—We are very grateful to Mrs. J. Bof for collecting the data from the patient records and to Mrs. Y. Lautrette for typing the manuscript.

Received Nov 21, 2007, and in revised form Jan 23, 2008. Accepted for publication Jan 23, 2008.

Thus, 44 patients were included in this Phase IV study. All 44 had undergone staging with endorectal ultrasonography, careful digital rectal examination, and rigid rectoscopy. CXR was given using a RT 50 Philips unit delivering a 50-kV maximal energy X-ray beam. This beam was filtered by a 0.5-mm-thick aluminum window. The depth dose percentage with a localizer of 3 cm in diameter was 50% at 5 mm. The source–surface distance was 4 cm, and the dose rate was 20 Gy/min. The X-ray tube was handheld, and the precision was controlled through direct vision by the radiation oncologist using an applicator 3 cm in diameter (or 2 cm in the case of a very small lesion) (1). The dose was prescribed at the exit surface of the applicator. According to the tumor size, the dose delivered per fraction was 25–40 Gy (1–2 min) into the gross visible lesion and 10–20 Gy when irradiating the rectal mucosa with no demonstrable tumor. The interval between fraction was 1 week between the first and second treatment and 2–3 weeks subsequently. The radiobiologic equivalence of these doses (with heterogeneous distribution within the tumor or tissues) was difficult to determine precisely, although with 50 kV was much greater than the same dose given with a standard 2-Gy/fraction schedule.

The main endpoint of this study was local control. Regular follow-up examinations were performed in all cases. For patients with preservation of the anal sphincter or rectum, careful clinical examination by the radiation oncologist using digital rectal examination and rigid rectoscopy was the main method used to assess local control. It was completed by endoluminal biopsy or imaging studies depending on each clinical situation. Local control was defined as no evidence of locally evolutive disease within the rectum or pelvis. The secondary endpoints were distant recurrence and survival. Anorectal function was evaluated according to the Memorial Scoring System (10). Acute and late toxicity were scored using the standard Common Terminology Criteria for Adverse Events, version 3.0.

For 44 patients included in this analysis, four different clinical approaches were used according to the tumor stage and treatment strategy.

Group 1 patients (n = 7) had Stage T1N0 tumor and underwent transanal local excision (TLE), followed by adjuvant CXR. TLE was performed by a surgeon (5 patients) or gastroenterologist (2 patients). A careful analysis of the pathologic specimen was performed in all cases and showed in situ carcinoma in 1 patient and pT1 in 6. The resection margin was negative in 5 cases and was R1 in 2. The interval between TLE and CXR was usually 6–8 weeks to allow for good healing of the excision scar. The surface dose was 45 or 50 Gy in three fractions within 3 or 4 weeks. In 1 patient with R1 resection and judged to have a risk of subclinical perirectal lymphatic spread >10%, CXR delivered only 30 Gy in two fractions and was combined with EBRT of 45 Gy in 25 fractions within 5 weeks. Table 1 lists the characteristics and results for Group 1.

Group 2 patients (n = 11) had Stage T2-T3N0-N2M0 tumor treated with combined CXR plus EBRT (no surgery) with curative intent. These patients were medically inoperable or had refused permanent colostomy. Of these 11 patients, 8 were judged inoperable because of a severe comorbidity, mainly related to advanced age (≥80 years), and 3, much younger, patients had adamantly refused radical surgery of tumor of the distal rectum close to the anal canal. Treatment was initiated with CXR, with a total dose of 75–110 Gy in three to five fractions within 4–7 weeks. No CXR was given after 2 weeks of EBRT to avoid performing rectoscopy when the mucosal reaction to EBRT was at its greatest level. On Day 35 or 42, CXR was given on the same day as EBRT, with a 30–60-min interval. Usually, after the second CXR treatment on Day 28 or 35, EBRT was started and was given with the patient in the prone position using a conformal three-dimensional technique and three fields (one posterior and two lateral). The target volume encompassed the gross rectal tumor, mesorectum, and soft tissues of the posterior pelvis. The external iliac lymph nodes were not included, nor was the anal canal for tumor of the middle rectum (>6 cm from the anal verge).

The upper limit of the cephalad extent of the planning target volume (PTV) was always below the sacral promontory. The anterior extent of the PTV never reached the pubic symphysis. The dose was prescribed, delivered, and recorded at the International Commission on Radiation Units and Measurements point (middle of the PTV, usually at the intersection of the beam axes). The volume of the 95% isodose of the International Commission on Radiation Units and Measurements point encompassing the PTV was always <2 L. The total dose was 50 Gy in 25 fractions within 5 weeks or 45 Gy in 25 fractions within 5 weeks when EBRT was combined with concurrent chemotherapy (5-fluorouracil or capecitabine). In 3 patients with tumor close to the anal canal, an ultimate boost was given to the tumor bed with interstitial ^{192}Ir brachytherapy 3 weeks after EBRT. Four to five radioactive lines (5–6 cm long) were used with a single curved perineal implant and a spacing of 1 cm between lines. The dose delivered to 85% of the basal dose was 20–25 Gy in 1 day. Table 2 lists the characteristics and results for Group 2.

Group 3 patients had Stage T3 (or low T2) N0-N1M0 tumor treated with preoperative CXR and EBRT followed by radical surgery. This was the largest group and included 21 patients (Table 3).

Table 1. Patient characteristics and results for Group 1*

Pt. no.	Gender	Age (y)	uT	uN	Distance from anal verge (cm)	TLE date	pT	R	CXR dose (Gy)	EBRT dose (Gy)	Local recurrence	Distant recurrence†	Last follow-up date	Clinical result at follow-up (mo)
1	F	59	1	0	2	Feb 04	IS	1	45	0	No	No	June 07	NED (40)
2	F	61	1	0	2	Apr 04	1	0	60	0	No	No	Dec 06	NED (32)
3	F	63	1	0	2	May 04	1	0	55	0	No	No	June 07	NED (37)
4	M	47	1	0	5	July 04	1	0	45	0	No	No	Aug 07	NED (37)
5	M	66	1	0	4	June 05	1	0	45	0	No	No	Dec 06	NED (18)
6	M	77	1	0	6	Dec 05	1	0	45	0	No	No	Dec 07	NED (24)
7	M	87	1	0	3	July 06	1	1	30	44	No	No	May 07	NED (10)

Abbreviations: Pt. no. = patient number; uT = T stage on endorectal ultrasonography; uN = N stage on endorectal ultrasonography; TLE = transanal local excision; pT = pathologic T stage; R = resection margins on TLE specimen (0, free margin; 1, involved margin); CXR = contact X-ray; EBRT = external beam radiotherapy; F = female; NED = alive with no evidence of disease; M = male.

* TLE for T1 tumor, followed by CXR.

† Recurrence outside pelvis.