# Treatment of Rectal Cancer

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The treatment of rectal cancer has changed dramatically over the past two decades. Diagnostic techniques and surgical approaches, as well as adjuvant treatment have undergone major changes. Based on clinical trial data (1), the NCI recommended in 1990 that patients with rectal cancer and a high risk of recurrence, i.e. node positive, should receive postoperative adjuvant radiation in combination with chemotherapy. In many countries outside the US other adjuvant regimens have been recommended. Surgery has been, and still is, the cornerstone in the treatment of rectal cancer, but the use of adjuvant treatment in the form of radiation therapy and chemotherapy has increased (2).

In Sweden the activity in the field of rectal cancer has been intensive over the past 2 decades. The Stockholm I trial was initiated in 1980 to assess surgery alone compared with preoperative short-term radiation therapy with $5 \times 5$ Gy (3). This trial showed a significant reduction in pelvic recurrences in the preoperatively radiated group, but the price for this was a significantly increased postoperative mortality in the group that had undergone combination therapy. It was felt that this increased mortality was related to the large treatment fields used in the trial in combination with high age and other risk factors in many patients. In the second Stockholm trial as well as the National Swedish trial initiated in 1989, a more modern technique was used and patients over the age of 80 years were not included (4, 5). This led to no significant difference in postoperative mortality, but still a significant reduction in mortality as well as an improved overall survival. This reduction in local recurrences as well as improvement was seen regardless of tumor stage at surgery. Thus, most Swedish institutions today recommend preoperative radiation therapy in patients with operable rectal cancer. The main issue is whether any patients can be excluded from this preoperative treatment, due to limited disease, improved surgical technique or other improvements in the adjuvant therapy.

## SHOULD PATIENTS WITH RECTAL CANCER RECEIVE RADIATION THERAPY?

The Swedish trials have shown that short-term, preoperative radiation can be given safely. The treatment will significantly decrease local recurrences and improve survival. However, short-term treatment has yet to be compared with more conventional preoperative treatment with 1.8–2.0–3.0 Gy fractions, with respect to both side effects and long-term efficacy.

## SHOULD WE USE PRE- OR POSTOPERATIVE TREATMENT?

The Uppsala trial comparing pre- vs. postoperative treatment still holds the best information with respect to this question (6). In this trial the preoperative short-term treatment was conducive to both efficacy and tolerability. An ongoing US trial will probably give us a definite answer with respect to this matter.

## CAN WE WITH PROPER DIAGNOSTIC WORK-UP AND PROPER SURGICAL TECHNIQUE EXCLUDE SOME PATIENTS FROM ADJUVANT THERAPY?

The introduction of a more precise surgical technique by Heald et al. has changed the scene of rectal cancer treatment over the past decade (7). However, the role of radiation in combination with total mesorectal excision (TME) has yet to be defined. Ongoing trial activity will most probably give us guidelines on how to select the proper patients for combination therapy.

## CAN WE IMPROVE QUALITY OF LIFE IN PATIENTS AND, FOR EXAMPLE, AVOID AMPUTATION?

Has preoperative radiation the potential to downgrade tumor extension in such a way that patients can be saved from rectal amputation and instead have a sphincter-sav-

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ing procedure? Will this give the same local and distant control? Data from trials indicate that this is the case, but it is still an open question.

This paper in a previous issue in Acta Oncologica by Gerald et al. (8) addressed several of these questions. The Lyon group has a long and outstanding tradition in the treatment of rectal cancer following the pioneering work of Papillon. The experience of this group with different treatment approaches to rectal cancer, from local contact therapy to external beam and intraoperative radiation, illustrates what can be achieved when a critical body of dedicated surgeons, radiotherapists, physicists and radiologists devote themselves to a certain field in medicine. Still, how reproducible is their experience? What can be done outside of this unique institution?

If we first concentrate on the Lyon experience with endocavitary irradiation alone. In this group of 101 patients with T1 or T2 lesions, excellent local control was achieved with contact therapy with or without the addition of $^{192}$Ir implants. Thus, this technique gives excellent results, but one must remember that the proper selection of patients using ultrasound, and the proper endocavitary treatment requires the competence of a group like that in Lyon. Still, it should be possible to form such units. This technique can also be used in more advanced cases, then in combination with external beam therapy, as shown in the second series of patients reported by Gerard et al. In this group the initial response to therapy was excellent, but 10 out of 42 patients later developed a local relapse. Still, these results are impressive given the group of patients being treated.

The second group of patients in this report addresses the question of preoperative radiotherapy and timing of surgery. In the pilot study including 158 patients, a pathological complete response (pCR) was achieved in 6% of patients when they underwent surgery within 3 weeks after the end of irradiation and in 16% when surgery was performed after 4 weeks of rest. Furthermore, the rate of anterior resection was higher (65% vs. 41%) if there was a longer rest period before surgery. These results are in line with the early experience from a randomized trial reported here. This study will be fully reported later this year. Preliminary data from the first 170 patients showed 5% pCR in the patients with a short interval between radiation and surgery and a 15% pCR in patients with a longer interval.

Taken together, the experience from the Lyon group, as reported in their paper, adds valuable information to the field of rectal cancer. In skilled hands, the use of contact therapy, in selected patients, will offer an excellent alternative to external beam therapy and surgery. It is important to stress that these results have been achieved by a group with a long and dedicated tradition in this field of radiotherapy. To reproduce such results will be a major challenge. The second most important contribution from this report is the aspect of timing of surgery. The randomized trial will, when it is fully reported, give us important information about the optimal timing of surgery after preoperative radiation. Furthermore, the role of adjuvant and/or concomitant chemotherapy is under evaluation in ongoing trials.

The treatment of rectal cancer has undergone profound changes during the past 2 decades. From being a surgical domain only in many institutions, rectal cancer treatment is now a concern involving all modalities of cancer diagnostics/treatment (9). We are also rapidly increasing our basic knowledge of the disease. The true potential of a multidisciplinary approach to cancer therapy had yet to be reached, but dedicated groups such as the Lyon group continue to add excellent clinical data and set a good example to all of us.

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