



INTRAOPERATIVE RADIATION THERAPY IN THE TREATMENT OF COLORECTAL CANCER

[Spanish full text](#)

SUMMARY

Introduction: Radiotherapy is one of the pillars of cancer treatment, with growing interest in techniques that irradiate only the area at greatest risk of local recidivation. In recent decades, there have been important advances in intraoperative radiation techniques, both as part of combined treatment of different types of tumours, locally advanced and recurrent stages of colorectal tumours in particular, and in association with conventional radiotherapy. Such techniques include intraoperative radiotherapy (IORT), which seeks to enhance local control of the disease by administering a single dose of ionising radiation directly to the tumour in the surgical cavity, thereby enabling dosages to be raised without increasing related toxicity, and thus constituting a complement to current treatment.

Objectives: To assess the effectiveness of IORT as adjuvant treatment for the current standard treatment of colorectal cancer, in terms of recurrence, survival, cosmetic results and impact on quality of life; and to ascertain the safety of this procedure, in terms of acute and late toxicity.

Methods: A search of the scientific literature was made from January 2000 to August 2013 in the main biomedical databases, i.e., Centre for Reviews and Dissemination (Health Technology Assessment, Database of Abstracts of Reviews of Effectiveness, NHS Economic Evaluation Database), Cochrane Plus Library, Medline, Embase, ISI Web of Knowledge, CSIC-*Índice Médico Español*, Clinical Trials Registry, WHO International Clinical Trials Registry Platform and Current Controlled Trials. This process was completed by a general search of quality Internet web pages to locate grey literature. Two independent reviewers selected the papers in accordance with pre-established inclusion and exclusion criteria, excluding, among others, studies that assessed internal sources of radiation or brachytherapy (HDR-IORT) and studies with fewer than 100 patients, with any disagreements being resolved by consensus. A manual review was also performed of the bibliographic references cited in the papers selected. The data were then extracted and summarised in evidence tables. Study quality was assessed using the SIGN scale.

Results: Of the 43 studies selected for full-text appraisal, a total of 22 met the inclusion criteria, made up as follows: 2 systematic reviews; 3 randomised clinical trials; 1 combined analysis of international case series; and 16 case series. Indication for IORT was locally advanced colorectal cancer (66.5%) and recurrent cancer (33.5%), with a total of 3058 patients included. Tumours in the colon accounted for 1.9% of locally advanced tumours and 18% of recurrent tumours. In both cases, patients were recruited from the early 1990s until 2010-2011. In the treatment of locally advanced tumours, the clinical trials resulted in no significant improvement over controls in terms of efficacy of survival, with local control and overall survival at 5 years of 90%-92% and 64%-70% respectively. The systematic reviews indicated that associating IORT with multidisciplinary treatment reduced incidence of local recurrences and helped improve local control and survival, without increasing



complications. The remaining observational studies reported a low incidence of local recurrences (within the area treated with IORT) of 2%-19%, local control in excess of 90% and overall survival ranging from 52% to 82%. The studies that analysed the efficacy of combined treatment (radiochemotherapy+surgery+IORT) in recurrent disease were of an observational and descriptive nature, and indicated an incidence of recurrences at 5 years of 30%-46% and local control at 5 years of 44%-68%. Overall survival at 5 years did not exceed 43%, with results being broken down by resection margin status (R0:46%-60%, R1:26% and R2:0%-24%). No increase in safety was observed in either locally advanced or recurrent tumours. None of the clinical trials detected significant differences between the two types of treatment, though patients treated with IORT developed greater toxicity overall, with certain complications not observed in the controls raising concern. The most frequent complications were those linked to surgical wound (infection, abscess, anastomotic ruptures), gastrointestinal complications, urethral obstruction or strictures, and peripheral neuropathy.

Discussion: The main obstacle when it comes to assessing the impact of IORT on clinical results is the difficulty of undertaking clinical trials. In addition, most of the available data come from experiences at a single centre, and the comparison of treatments is limited by the selection of patients and retrospective analysis. Furthermore, as IORT is administered as a booster to neoadjuvant treatment of chemoradiation and standard radiotherapy is generally administered after IORT, the incremental value of IORT and its impact on clinical results is difficult to ascertain. Despite the fact that the clinical trials which evaluate the use of IORT in the treatment of locally advanced tumours show no significant improvement with respect to controls, some organisations and clinical practice guidelines consider the use of IORT in certain patients in those instances where the technique is available at the health centre, while others, in contrast, regard it as experimental. In the case of recurrent tumours, as all the studies retrieved were of an observational nature, lacked a comparison group and were thus liable to a greater number of biases, it is not known to what extent their results provide valid and applicable information. In general, the heterogeneity observed in patient characteristics, in aspects associated with the technique's performance that are considered relevant, and in the treatment protocol or follow-up time, coupled with the addition of treatments, are aspects that seriously limit the possibility of drawing definitive conclusions.

Conclusions: The results which evaluate IORT's association with combined treatment of locally advanced colorectal cancer indicate that, while this association achieves good results, it does not amount to an increase in effectiveness and overall survival, or to a significant reduction in safety vis-à-vis conventional treatment (surgery and radiochemotherapy). In terms of safety, IORT does not increase the complication rate, displaying comparable short- and long-term adverse effects. A matter for concern is the higher incidence of adverse effects related with the surgical incision and the appearance of complications that do not arise in controls. In the case of recurrent tumours, the available evidence is, not only of low quality, but is far less abundant.