Intraoperative Radiation Therapy in the treatment of colorectal cancer

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BACKGROUND AND AIMS

•Intraoperative Radiation Therapy **(IORT)** seeks to enhance local control by administering, during surgery, a high single dose directly to the tumour bed or on a non-resectabe tumour, while moving and protect the sensitive structures, thereby enabling dosages to be raised without increasing related toxicity.

•The **aims** of this systematic review were to assess the effectiveness of IORT boost for the conventionally treatment of **colorectal cancer**, in terms of recurrence, survival and impact on quality of life; and to ascertain the safety in terms of acute and late toxicity.

METHODS

Bibliographic search: from January 2000 to August 2013, in:

- Centre for Reviews and Dissemination
- Cochrane Plus Library
- Medline
- Embase
- ISI Web of Knowledge
- CSIC-Índice Médico Español,
- Clinical Trials Registry,
- WHO International Clinical Trials Registry Platform,
- Current Controled Trials
- a general search of quality internet web pages to locate grey literature

Selection papers: two independent reviewers in accordance with pre-established inclusion and exclusion criteria, with any disagreements being resolved by consensus. Manual review was performed of the bibliographic references cited in the papers selected.

Data extraction: were summarised in evidence tables. Study quality was assessed using the SIGN scale.

RESULTS

20 REPORTS:
- 2 RCT,
- 1 pooled analisis,
- 17 case series

LARC (64,4%): 2033 patients, 55-68 years, T3-4N0/+ rectal tumors
IORT dose: R0: 7,5-10Gy; R1: 10-12Gy; R2: 12,5-20Gy

LRRC (35,6%): 1122 patients, 56-62 years. Recurrent tumors
IORT dose: R0:12Gy; R1: 15Gy; R2: 20Gy

Neoadyvant treatment + IORT
Adyuvant treatment
Treatment modality:
Transport´s patient (from OR to RT)
Recruitment: 1990-2011

Locally Advanced Rectal Cancer (LARC)

•Clinical trials: didn´t show any significant improvement over controls in terms of efficacy and survival, with local control and overall survival rate of 90%-92% and 64%-70% at 5-year respectively.

•Observational studies: low local recurrences rate of 2%-19%, local control in excess of 90% and overall survival from 52% to 82%.

Study	N IORT	N Cont	LC (%) 5 years		LR(%) 5 years		DM (%) 5 years		OS (%) 5 years		Mortality	
RCT	72	68	91.8	92.8	8.5	5.8	31	30	70	74.8	33	21
	28	27	89.2	88.8	11	11	26	14	64	58	--	--
Pooled	605		88		12		29.2		67		--	
CASE SERIES	99	68	98	84	2	16	20	20	79	58	1	3
	125		94		5.6		18		82		16.8	
	338		--		6.1		--		80		2.3	
	146		86		19		47		52		59	
	243		92		7		5		69		--	
	115		94		6.1		21		74		4.5	
	100		94		2		12		65		23	

Locally Recurrent Rectal Cancer (LRRC)

Effectiveness

- 5-year recurrence rate: 30-46% and 5-years local control rate: 44-68%.
- Overall survival <43% at 5-year, with results being broken down by resection margin status (R0:46%-63%, R1:26% and R2:0%-24%).

Safety

No increase was obseved in either LARC or LRRC disease.

Toxicity:

- None of the RCT detected significant differences between the two types of treatment, though IORT patients developed greater overall toxicity, with certain complications not observed in the controls.
- Frequent complications: surgical wound (infection, abscess, anastomotic leakage), gastrointestinal, urethral obstruction and peripheral neuropathy.

N	LC (%) 5 year	R (%) 5 year	DM (%) 5 year	OS (%) 5 year	Mortality
607	Total: 68 R0:79 R1:68	42	53	Total: 30 R0: 46 R1: 27 R2: 16	<1
147	Total: 57 (5 y.) R0: 75 R1:50 R2:28	43 (3 y.)	---	Total: 43.8 (3 y.) R0: 59 R1: 26 R2: 24	8.2 (3 months)
107	44	Total: 30 R0: 50 R1: 65	---	Total: 30 R0: 63 R1-2: 11	0
65	Total: 68 R0: 78 R1:58 R2:29	29 (3 y.)	46 (3 y.)	39	27.7
60	44	46.6	47	43	66.7

CONCLUSIONS

Efficacy:

- ✓ IORT's association with combined treatment of LARC reporter 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 regard to conventional treatment.
- ✓ Depending on the status of the edges of resection, shown greater benefit in patients who undergo incomplete resection compared with complete resection.

Safety:

- ✓ IORT does not increase the complication rate, displaying comparable short- and long-term complications.
- ✓ 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 disease, the available evidence is, not only of low quality, but is far less abundant.

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