Review Article

Intraoperative Radiotherapy in Rectal Cancer: A Narrative Review

Radioterapia Intraoperatória no Cancro do Reto: Uma Revisão Narrativa

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ABSTRACT

Intraoperative radiotherapy (IORT) delivers an elevated radiation dose directly to the tumour bed or high-risk resection areas during rectal cancer surgery, enabling dose escalation beyond the limits of conventional external beam radiotherapy (EBRT). Despite decades of clinical use in specialized centres, its benefit over standard multimodal therapy remains in debate. This narrative review synthesises the available evidence on IORT in primary locally advanced rectal cancer (LARC) and locally recurrent rectal cancer (LRRC), drawing on randomized trials, prospective and retrospective series, population-based analyses, national cancer registry data, and current international guidelines. IORT consistently reduces local recurrence rates in R1 and close-margin resections and achieves pelvic control rates exceeding 85% in selected series when integrated with neoadjuvant chemoradiation and radical surgery. A meta-analysis of seven studies demonstrated a non-significant reduction in local recurrence (14.7% *vs* 21.4%; OR 0.55), with no demonstrated overall survival benefit. Patient selection, surgical radicality, and institutional experience remain the dominant determinants of outcome.

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IORT is an effective dose-escalation adjunct for carefully selected patients with LARC or LRRC at high risk of R1 resection, but its survival impact has not been proven. Standardization of technique, prospective multicentre data collection, and integration with novel systemic agents represent the most critical priorities for future research.

Keywords: Combined Modality Therapy; Intraoperative Care; Margins of Excision; Neoplasm Recurrence, Local; Rectal Neoplasms/radiotherapy; Rectal Neoplasms/surgery

RESUMO

A radioterapia intraoperatória (RIO) consiste na administração de uma dose alta de radiação direitamente sobre o leito tumoral ou nas áreas de ressecção de maior risco durante a cirurgia do cancro do reto, permitindo a escalada de dose para além dos limites da radioterapia externa (EBRT) convencional. Apesar de décadas de utilização em centros especializados, o seu benefício relativamente à terapêutica multimodal padrão permanece em debate. Esta revisão narrativa sintetiza a evidência disponível sobre a RIO no cancro do reto localmente avançado (CRLA) e na recidiva local do cancro do reto (RLCR), com base em ensaios randomizados, séries prospetivas e retrospetivas, análises populacionais, dados de registos nacionais de cancro e recomendações das normas de orientação clínica internacionais em vigor. A IORT reduz consistentemente as taxas de recidiva local em ressecções R1, atingindo taxas de controlo pélvico superiores a 85% em séries selecionadas quando integrada com quimiorradioterapia neoadjuvante e cirurgia radical. Uma meta-análise de sete estudos demonstrou uma redução não estatisticamente significativa da recidiva local (14,7% *vs* 21,4%; OR 0,55), sem benefício demonstrado na sobrevivência global. A seleção criteriosa dos doentes, a radicalidade cirúrgica e a experiência institucional permanecem os principais determinantes do prognóstico. A RIO é um adjuvante eficaz, permitindo escalar a dose de radioterapia em doentes cuidadosamente selecionados com CRLA ou RLCR com elevado risco de resseções R1, mas o seu impacto na sobrevivência não foi demonstrado. A padronização da técnica, a recolha prospetiva de dados multicêntricos e a integração com novos agentes sistémicos representam as prioridades mais críticas para a investigação futura nesta área.

Palavras-chave: Cuidados Intraoperatórios; Margens de Excisão; Neoplasias do Recto/cirurgia; Neoplasias do Recto/radioterapia; Recidiva Local de Neoplasia; Terapia Combinada

INTRODUCTION

Colorectal cancer is the third most common malignancy worldwide and the second leading cause of cancer-related mortality. In Portugal, rectal cancer represents a significant oncological challenge, accounting for approximately one-third of all colorectal cancers, with a substantial proportion of patients presenting with locally advanced disease (T3–T4 or node-positive tumours). Despite the routine adoption of multimodal strategies — including total mesorectal excision (TME), neoadjuvant chemoradiation, and systemic chemotherapy — local recurrence remains a clinically meaningful problem, particularly in patients with threatened or involved circumferential resection margins (CRM), those undergoing non-curative (R1) resections, and in the setting of locally recurrent rectal cancer (LRRC).

Intraoperative radiotherapy (IORT) is a technique that delivers a single high dose of radiation directly to the tumour bed intending to sterilize the resection margin and reduce local recurrence. IORT aims to treat high-risk areas for residual microscopic disease at the time of surgery, while the adjacent radiosensitive structures (small bowel, bladder, ureters, and neurovascular bundles) are physically displaced or shielded. By concentrating the biologically effective dose precisely where the risk of local failure is greatest, IORT circumvents the practical limits of external beam dose escalation imposed by surrounding organ tolerance.

Two principal IORT modalities are in clinical use: intraoperative electron beam radiotherapy (IOERT), which delivers megavoltage electron beams via a dedicated linear accelerator in a shielded operating theatre, and high-dose-rate intraoperative brachytherapy (HDR-IORT), which uses an afterloader device with an interstitial or surface applicator. Both modalities have been employed in LARC and LRRC, with institutional experience and infrastructure determining the choice of platform.

The present review critically examines the scientific evidence underpinning IORT in rectal cancer, with particular attention to novel technological developments, current evidence gaps, methodological limitations of the existing literature, and the

most pressing unanswered clinical questions. It is intended to inform the practice of surgeons and radiation oncologists in Portugal and to support appropriate patient selection for this resource-intensive intervention.

CLINICAL INDICATIONS AND PATIENT SELECTION

Given the logistic and clinical implications of IORT, this technique should be reserved for anatomically and oncologically high-risk scenarios in which conventional multimodal therapy is deemed insufficient to ensure durable locoregional control. Current international guidelines (ESTRO/ACROP) and expert consensus support its use in three principal clinical contexts:

Optimal patient selection integrates clinical, radiological, and pathological staging. In the setting of locally advanced disease, candidates are those with high risk of local recurrence even after total neoadjuvant treatment (TNT), namely those maintaining T4 tumors with threatened or involved CRM on high-resolution pelvic MRI or cases in which achieving an R0 resection is anatomically challenging (e.g., involvement of the sacrum, lateral pelvic sidewall, or iliac vessels), and the surgeon anticipates a high probability of R1 margins.

ANOTHER SCENARIO IS THAT OF LRRC IN WHOM SALVAGE SURGERY IS PLANNED

In all cases, patient performance status, prior radiation history, and surgical resectability are essential co-determinants of candidacy, since the benefit of this technique depends on a macroscopic complete resection.

ONCOLOGIC OUTCOMES

1. LOCAL CONTROL

The primary oncological justification for IORT is the improvement of locoregional control in patients at the highest risk of local failure. Large retrospective series from specialised centres consistently report pelvic control rates exceeding 85% when IORT is integrated into a multimodal treatment strategy including neoadjuvant chemoradiation and radical surgery.[5,6]

The most comprehensive systematic quantification of the local control benefit derives from a meta-analysis by Fahy *et al* (2021), encompassing seven studies published between 2000 and 2020.[9] Pooled data demonstrated a lower local recurrence rate in IORT-treated patients compared with those receiving surgery with or without EBRT alone (14.7% *vs* 21.4%; OR approximately 0.55). However, this difference did not reach conventional statistical significance, a limitation attributable to the substantial heterogeneity of the included studies, variability in IORT dose and modality, and differences in neoadjuvant regimens.

The main randomized trial in this setting is the multicenter French trial from Dubois *et al* (2011), which included 142 patients with T3-T4 and/or N+ tumours.[4] In this trial, there was no significant impact with the addition of 18Gy of IORT to neoadjuvant therapy in local control or survival. However, 90% of tumors were T3 and 66% N0, making this already a group with good prognosis, probably not benefiting from IORT. Besides, the majority of resections were R0, once again limiting the benefit. Nonetheless, this trial established the feasibility and safety of the technique in a randomized setting.

Table 1. Clinical indications for IORT in rectal cancer, with recommended dose ranges and supporting evidence.

Clinical Scenario	Role of IORT	Typical Dose (Gy)	Key References
Primary LARC (T4 / threatened CRM)	Boost after neoadjuvant CRT + radical surgery (R0 or R1)	10–12.5 Gy (R0); 12.5–15 Gy (R1)	Calvo *et al*, 2020[1]; Amarnath, 2023[2]; Haddock, 2017[3]; Dubois *et al*, 2011[4]
R1 resection (positive or close margins)	Local dose intensification to reduce locoregional recurrence risk	15–20 Gy	Calvo *et al*, 2020[1]; Amarnath, 2023[2]; Erkaya *et al*, 2025[5]; Khan *et al*, 2022[6]; Voogt *et al*, 2021[7];
Locally recurrent rectal cancer (LRRC)	Component of multimodal salvage strategy; often combined with re-irradiation	10–20 Gy	Calvo *et al*, 2020[8]; Fahy *et al*, 2021[9]; Haddock, 2017[3]; Roeder *et al*, 2023[10]

CRM: circumferential resection margin; CRT: chemoradiotherapy; EBRT: external beam radiotherapy; LARC: locally advanced rectal cancer; R0: microscopically clear margins; R1: microscopically positive margins.

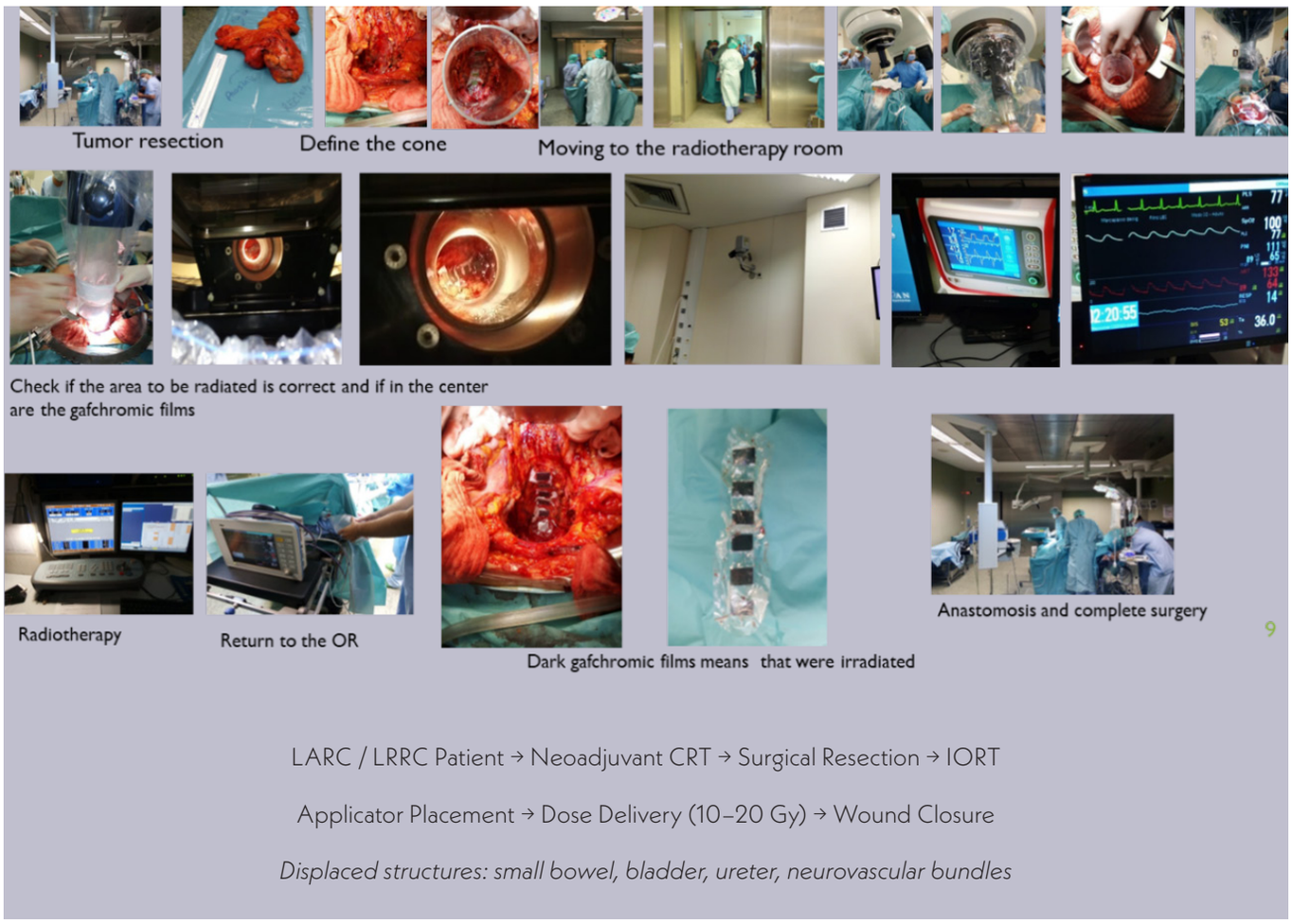

Figure 1. Stepwise integration of IORT into the multimodal treatment pathway for locally advanced or locally recurrent rectal cancer. IORT is applied after tumour resection, targeting the tumour bed and high-risk regions while radiosensitive structures are surgically displaced (IPO-PORTO).

In the recurrent disease setting, in patients in whom an R0 resection can be accomplished, IORT is associated with local control in 60%–80% of patients. When margins are microscopically positive, local control is in the range of 30%–60%.[3] A particularly challenging group of patients includes those who have received previous pelvic irradiation for their primary tumour. In this context, reirradiation is possible, although with some limitations regarding dose and volume.

2. OVERALL SURVIVAL

No level I evidence has demonstrated a statistically significant overall survival (OS) benefit attributable to IORT. More recently, a population-based propensity-matched analysis of the National Cancer Database (NCDB) examined patients with margin-positive T3–T4 M0 rectal adenocarcinoma.[5] Although a numerically higher five-year OS was observed in the IORT group (58.4% *vs* 54.9%), this difference did not achieve statistical significance (HR not reported as significant).

The consistent absence of a proven survival benefit is likely multifactorial: the dominant prognostic influence of achieving an R0 resection, the competing risk of distant metastasis, the rarity of the patient population limiting statistical power, and the absence of large randomised controlled trials specifically designed to test IORT in the modern era of total neoadjuvant therapy (TNT).

3. PROGNOSTIC DETERMINANTS

A consistent and critically important finding across the IORT literature is that the most powerful predictor of both locoregional control and survival is the achievement of a macroscopically clear margin resection. Multiple series and guideline documents emphasise that IORT functions as an adjunct to, and not a substitute for, radical surgical resection.[2,3,5] In patients in whom R0 resection is achieved, the incremental benefit of IORT is smallest; its greatest utility lies in scenarios where complete resection is anatomically or

Table 2. Summary of key studies evaluating oncologic outcomes with IORT in rectal cancer.

Study	Design	Population	Primary Outcome	Key Findings
Fahy *et al*, 2021[9]	Meta-analysis (7 studies)	LARC / LRRC	Local recurrence	LR 14.7% *vs* 21.4% (IORT *vs* no-IORT); OR ~0.55; NS. No OS benefit.
Dubois *et al*, 2011[4]	RCT (Phase III)	T3–T4/N+, preop RT 40 Gy	Local recurrence, OS	No significant benefit of adding 18 Gy IORT in mostly T3 disease.
Erkaya *et al*, 2025[5]	NCDB propensity-matched	R1, T3–T4 M0	Overall survival	5-yr OS: 58.4% (IORT) *vs* 54.9%; non-significant.
Voogt *et al*, 2021[7]	Retrospective comparative	R1, LARC / LRRC	OS, LRFS	HDR-IORT superior local recurrence-free survival *vs* IOERT; more major complications in LRRC.
Haddock, 2017[3]	Clinical review	Colon and rectal cancer	Multiple	Pelvic control ≥85% in locally advanced primary tumours with multimodal approach.

LR: local recurrence; LRFS: local recurrence-free survival; NCDB: National Cancer Database; NS: not statistically significant; OS: overall survival; RCT: randomised controlled trial.

technically challenging and an R1 margin is suspected and IORT is employed to sterilize microscopic residual disease.

TECHNICAL MODALITIES AND INNOVATIONS

1. INTRAOPERATIVE ELECTRON BEAM RADIOTHERAPY (IOERT)

IOERT remains the most widely deployed IORT modality in Europe and North America. It requires either a dedicated shielded operating theatre equipped with a linear accelerator or a mobile electron IORT (MOERT) device, enabling treatment delivery in a conventional surgical suite. Electron energies between 6 and 12 MeV are selected based on the depth of target tissue, and circular or customized applicators (diameters typically about 6 cm) are placed in direct contact with the target volume after surgical exposure. Dose prescription is typically defined at the 90% isodose surface. Advantages include precise energy selection, sharp lateral dose fall-off, and broad institutional experience.

2. HIGH-DOSE-RATE INTRAOPERATIVE BRACHYTHERAPY (HDR-IORT)

HDR-IORT employs an iridium-192 afterloading source delivered via flexible surface applicators, cylinders, or interstitial needles placed directly on the resection bed. It also requires a shielded operating theatre, however, if low-voltage X-rays are used (kV-IORT) only minimal protection is needed, affording logistical advantages in centers without dedicated intraoperative EBRT infrastructure. In the comparative analysis by Voogt *et al* (2021), HDR-IORT was associated with significantly better local recurrence-free survival compared with IOERT in R1 resections for LARC and LRRC ($p = 0.02$), although this benefit came at the cost of higher rates of major complications, specifically in the LRRC subgroup.[7]

3. NOVEL TECHNOLOGY: IMAGE-GUIDED IOERT

A significant recent technological advance is the development of image-guided IOERT (IG-IOERT) with real-time intraoperative cone-beam computed tomography (CBCT) and online dose calculation. Roeder *et al* (2023) reported the first clinical application of this approach in recurrent rectal cancer. Real-time CBCT imaging enables three-dimensional visualisation of the applicator position relative to the target and adjacent structures, facilitating adaptive dose prescription based on intraoperatively measured tissue geometry.[10] This innovation addresses a fundamental limitation of conventional IOERT — the dependence on pre-treatment imaging and surgeon estimation for applicator placement — and represents a meaningful step toward the precision IORT paradigm.

The early clinical experience confirms that IG-IOERT is technically feasible in rectal cancer surgery, with the intraoperative workflow adding approximately 20–30 minutes to the surgical time. Validation in larger cohorts with dosimetric and clinical outcome data is awaited.

4. MARGIN EVALUATION AND FROZEN SECTION

Frozen section has long been utilized in surgery to evaluate margins at risk during surgery. This becomes extremely important in IORT surgery, given that in most recent

Table 3. Comparison of IORT modalities and their principal characteristics.

Parameter	IOERT	HDR-IORT	IG-IOERT (Novel)
Radiation source	Electron beam (linac)	Ir-192 afterloader	Electron beam + CBCT guidance
Theatre requirement	Shielded OR or MOERT	Shielded OR or MOERT (unlesse low voltage is used)	Shielded OR with CBCT
Dose homogeneity	Moderate	High at surface	Adaptive / optimized
Real-time imaging	No	No	Yes (CBCT)
Evidence base	Extensive retrospective / prospective	Moderate retrospective	First clinical series (2023)
Main limitation	Infrastructure cost; no real-time imaging	Infrastructure cost; no real-time imaging More major complications in LRRC	Limited clinical data; longer workflow

CBCT: cone-beam computed tomography; HDR-IORT: high-dose-rate intraoperative brachytherapy; IG-IOERT: image-guided intraoperative electron radiotherapy; IOERT: intraoperative electron beam radiotherapy; LRRC: locally recurrent rectal cancer; MOERT: mobile electron IORT device; OR: operating room.

guidelines,[1,8] the dose of radiotherapy varies according to the margin status (R1 *vs* R0). This demands centralized evaluation by pathologists with extensive experience, especially given that the majority of these patients will have had neoadjuvant treatment, making the analysis more challenging.

SAFETY AND PERIOPERATIVE MORBIDITY

Overall, IORT in rectal cancer is feasible with acceptable perioperative morbidity in experienced centers.[2,3,6] The addition of IORT to the surgical procedure consistently results in increased operative time, but multiple series have not found statistically significant increases in anastomotic leak rates, hospital stay, or major systemic complications compared with surgery alone.

However, certain morbidity patterns merit attention:

- **Wound infection and pelvic abscess:** Several series report higher rates of surgical site infection and pelvic abscess in IORT-treated patients, frequently with rates ≥25%.[1,5,8] These are generally manageable with antibiotics and radiological drainage, but contribute to morbidity and length of stay.
- **Peripheral neuropathy:** The dose-limiting late toxicity of IOERT to the pelvic region is radiation-induced peripheral neuropathy, primarily affecting the sacral plexus. The risk escalates substantially at doses exceeding approximately 15 Gy,[3] mandating careful dose prescription and applicator positioning when neurovascular structures cannot be displaced from the high-dose zone.
- **Modality-dependent morbidity:** In the comparative study of HDR-IORT versus IOERT,[7] major complication rates were significantly higher with HDR-IORT in the LRRC subgroup despite superior local recurrence-free survival. This morbidity trade-off must be factored into treatment decisions, particularly in patients who have undergone prior pelvic surgery and irradiation.
- **Urological and vascular complications:** Ureteric injury, bladder dysfunction, and rarely vascular injury have been reported but are generally attributable to the extent of pelvic surgery rather than IORT per se.

INNOVATIONS AND RECENT DEVELOPMENTS

Several advances in the past decade have the potential to substantially refine the clinical application and outcomes of IORT in rectal cancer:

- **Image-guided IOERT (IG-IOERT):** As described above, the integration of intraoperative CBCT with real-time dose calculation represents the most technically significant recent advance.[10] Prospective validation in larger cohorts and comparison with conventional IOERT outcomes are ongoing.

- **Total neoadjuvant therapy (TNT):** The shift from sequential neoadjuvant chemorradiation towards induction/consolidation chemotherapy-inclusive TNT protocols — which achieve substantially higher rates of pathological complete response and organ preservation — is redefining the patient populations who will ultimately require IORT. The 2024 focused update of the ASTRO rectal cancer guideline[11] now strongly recommends TNT for patients at higher risk of locoregional recurrence and conditionally supports omission of radiotherapy in selected lower-risk patients, reflecting a rapidly evolving treatment landscape. Whether IORT retains its additive value in the context of TNT remains an open question requiring dedicated evaluation.

- **Integration with immunotherapy:** Early clinical trials are exploring the potential synergy between radiotherapy (including IORT) and immune checkpoint inhibitors (PD-1/PD-L1 blockade) in microsatellite-stable (MSS) rectal cancer, in which immunotherapy has thus far demonstrated limited single-agent activity. The immunogenic cell death and abscopal effects induced by high-dose focal radiation may enhance tumour immunogenicity. Notably, the 2024 ASTRO focused update[11] now formally recommends omission of neoadjuvant radiotherapy in patients with MMRd/MSI-H rectal cancer who achieve a clinical complete response to upfront checkpoint inhibitor therapy — a landmark paradigm shift that further narrows the population for whom conventional chemoradiation (and potentially IORT) will be required.

- **HDR-IORT applicator design:** Improvements in flexible surface applicator geometry and dosimetric planning software have expanded the anatomical sites and clinical scenarios amenable to HDR-IORT, particularly for curved or irregular target surfaces in the sacral hollow.

- **Proton and carbon ion IORT:** Theoretical dosimetric advantages of particle IORT — notably the Bragg peak and sharp lateral penumbra — are under exploration in experimental settings. Clinical application in rectal cancer remains under investigation but may be relevant for complex LRRC involving the sacrum or pelvic sidewall.

LIMITATIONS OF THE CURRENT EVIDENCE BASE

A dispassionate assessment of the IORT literature in rectal cancer reveals substantial methodological limitations that constrain the interpretation and wide applicability of existing data:

- **Absence of contemporary randomised controlled trials:** The only published RCT examining IORT in rectal cancer (Dubois *et al*, 2011)[4] was conducted in the pre-TME, pre-modern TNT era. Neither was powered to detect realistic effect sizes, and neither employed modern imaging staging, quality-assured surgery, or current neoadjuvant regimens. No adequately powered RCT has been conducted in the era of high-resolution pelvic magnetic resonance imaging (MRI) staging, TME, capecitabine-based concurrent chemoradiation, or TNT.

- **Retrospective, single-institution design predominance:** The large majority of IORT outcome data derives from retrospective series at high-volume, technically expert centers. Selection bias is present in the majority of the studies at specialized centres, namely patients with better performance status are selected, more thorough pre-treatment staging, and greater surgeon experience than the general population — factors that independently predict improved outcomes irrespective of IORT.

- **Heterogeneity of IORT modality, dose, and dose fraction:** Pooled analyses are confounded by the co-mingling of IOERT and HDR-IORT data, variable dose prescriptions (ranging from 10 to 25 Gy), differences in reference isodose, use or absence of concurrent EBRT, and widely varying neoadjuvant systemic therapy regimens.

- **Inconsistent outcome reporting:** Definitions of local recurrence, local recurrence-free survival, pelvic control, and R0/R1 resection vary markedly across studies, hampering meta-analytic synthesis. The absence of centralized pathological review and standardized MRI-based margin assessment is particularly problematic.

- **Short and variable follow-up:** Median follow-up in several published series is insufficient to capture the full incidence of late locorregional recurrence, late radiation toxicity, and long-term quality of life impairment.

- **Absence of quality-of-life data:** Despite the potential for IORT to cause peripheral neuropathy, bowel dysfunction, sexual dysfunction, and urinary morbidity, comprehensive patient-reported outcome (PRO) and health-related quality-of-life (HRQoL) data are almost entirely absent from the published literature.

UNANSWERED QUESTIONS AND RESEARCH PRIORITIES

Despite several decades of institutional experience, fundamental questions regarding IORT in rectal cancer treatment remain unresolved. The following represent the most clinically critical areas requiring prospective investigation:

From a research infrastructure perspective, the rarity of eligible patients and the concentration of IORT capability in a small number of highly specialized centers makes single-institution randomized trials impractical. Multicentre registries — ideally European or international in scope, coordinating under the ESTRO/ACROP framework — represent the most pragmatic mechanism for generating adequately powered prospective data on oncologic outcomes, morbidity, and quality of life.

CONCLUSION

Intraoperative radiotherapy is a technically advanced, resource-intensive, and evidence-supported dose-escalation strategy for a carefully selected minority of rectal cancer patients at the highest risk of locoregional failure. Its greatest clinical utility is in scenarios of R1 resection, threatened circumferential margins in T4 disease, and locally recurrent rectal cancer, precisely the situations in which conventional multimodal therapy is most likely to fail.

The available evidence consistently supports IORT's capacity to reduce local recurrence rates in these high-risk populations, though the magnitude of benefit is moderate, and a statistically significant overall survival advantage has not been demonstrated. The interpretation of available data is constrained by the limitations inherent to retrospective, single-centre series, the absence of modern RCT evidence, and substantial heterogeneity in treatment technique and patient selection.

Recent technological innovations — notably image-guided IOERT with real-time intraoperative CBCT and the comparative evidence from IOERT versus HDR-IORT series — are incrementally refining the precision and scope of IORT delivery. Integration with modern total neoadjuvant therapy regimens, immune checkpoint inhibitors, and proton therapy represents the frontier of future investigation.

For surgeons and radiation oncologists practising in Portugal and throughout Europe, IORT should be regarded as a critical component of the armamentarium at specialized pelvic oncology centers, reserved for patients in whom the risk-benefit calculation — weighing the potential for improved locoregional control against the added morbidity and resource requirements — favours its use. Achieving a complete macroscopic resection remains the single most important therapeutic goal, and IORT is always an adjunct to, and never a substitute for, radical surgical technique.

Table 4. Principal unanswered questions in IORT for rectal cancer.

Domain	Key Unanswered Question
Efficacy in modern treatment era	Does IORT improve local control or survival when integrated with TNT regimens?
Dose optimization	What is the optimal IORT dose for R0 vs R1 resections? Is dose escalation beyond 15 Gy in LRRC justified given the neuropathy risk?
Modality comparison	Is HDR-IORT superior to IOERT for locoregional control across all LARC/LRRC subgroups, or only in specific anatomical scenarios?
Image-guided IORT validation	Does IG-IOERT with real-time dose calculation reduce marginal misses and improve pelvic control compared with conventional IOERT?
Systemic therapy integration	Can IORT potentiate the activity of immune checkpoint inhibitors in MSS rectal cancer via immunogenic cell death?
Patient-reported outcomes	What is the impact of IORT on long-term HRQoL, bowel function, sexual function, and peripheral neuropathy compared with surgery alone?
Health economics	Is IORT cost-effective in the context of modern rectal cancer care, given infrastructure investment and the incremental clinical benefit?
Biomarker-guided selection	Can genomic, radiomic, or pathological biomarkers identify which patients will derive the greatest local control benefit from IORT?

HRQoL: health-related quality of life; IG-IOERT: image-guided intraoperative electron radiotherapy; LARC: locally advanced rectal cancer; LRRC: locally recurrent rectal cancer; MSS: microsatellite stable; TNT: total neoadjuvant therapy.

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CONTRIBUTORSHIP STATEMENT

All authors contributed to the design, analysis, and writing of the manuscript, contributed to the final manuscript, and approved the final version.

DECLARAÇÃO DE CONTRIBUIÇÃO

Todos os autores contribuíram para a conceção, análise, redação do manuscrito e contribuíram para o manuscrito final e aprovaram a versão final.

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