

Blue Cross Blue Shield of Massachusetts is an Independent Licenses of the Blue Cross and Blue Shield Association

Medical Policy Intraoperative Radiotherapy

Table of Contents

- Policy: Commercial
- Policy: Medicare
- Authorization Information
- <u>Coding Information</u>

Description

Policy History

- Information Pertaining to All Policies
- References

Policy Number: 278

BCBSA Reference Number: 8.01.08 NCD/LCD: N/A

Related Policies

Accelerated Breast Irradiation after Breast-Conserving Surgery for Early Stage Breast Cancer and Breast Brachytherapy, #<u>326</u>

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Use of intraoperative radiotherapy may be considered <u>MEDICALLY NECESSARY</u> in the following situation:

• Rectal cancer with positive or close margins with T4 lesions or recurrent disease.

Use of intraoperative radiotherapy is considered **INVESTIGATIONAL** for all other oncologic applications.

Prior Authorization Information

Inpatient

 For services described in this policy, precertification/preauthorization <u>IS REQUIRED</u> for all products if the procedure is performed <u>inpatient</u>.

Outpatient

 For services described in this policy, see below for products where prior authorization <u>might be</u> <u>required</u> if the procedure is performed <u>outpatient</u>.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is not required .
Commercial PPO and Indemnity	Prior authorization is not required .
Medicare HMO Blue sm	Prior authorization is not required .
Medicare PPO Blue SM	Prior authorization is not required .

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The above <u>medical necessity criteria MUST</u> be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
77424	Intraoperative radiation treatment delivery, x-ray, single treatment session
77425	Intraoperative radiation treatment delivery, electrons, single treatment session

ICD-10 Procedure Codes

ICD-10-PCS- procedure codes	Code Description
DDY7CZZ	Intraoperative Radiation Therapy (IORT) of Rectum

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT codes above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM diagnosis codes:	Code Description
C20	Malignant Neoplasm Of Rectum
D01.2	Carcinoma In Situ Of Rectum

Description

Intraoperative radiotherapy (IORT) increases the intensity of radiation delivered directly to tumors. The tumor and associated tissues at risk for micrometastatic spread are directly visualized during surgery. IORT is delivered directly to the tumor, and normal or uninvolved tissues are not exposed to radiation because they are removed or shielded from the treatment field.

Summary

Intraoperative radiotherapy (IORT) is delivered directly to exposed tissues during surgery and may allow higher radiation doses by excluding nearby radiation dose-sensitive tissues. Different IORT modalities are available that impact both the dose distribution and method of application. IORT techniques include electron beam IORT, high-dose rate brachytherapy based IORT, and low-energy x-ray IORT.

For individuals who have rectal cancer who receive adjunctive IORT, the evidence includes randomized controlled trials (RCTs), nonrandomized comparative studies, and systematic reviews of these studies. Relevant outcomes are overall survival (OS), disease-specific survival, change in disease status, and treatment-related morbidity. Adjunctive use of IORT as part of a multimodal treatment could permit an increase in radiation dose without increasing complications. However, a phase 3 RCT and meta-analysis of IORT for locally advanced rectal cancer did not find improved outcomes with IORT in combination with external-beam radiotherapy (EBRT) and surgery. One systematic review evaluating locally advanced and recurrent rectal cancers together, has shown a significant benefit with addition of IORT on local control, disease-free survival and OS. Additional data are needed to determine the effect of adjunctive IORT for

locally advanced rectal tumors with greater certainty. National Comprehensive Cancer Network guidelines suggest use of IORT in patients with T4 or recurrent cancers as an additional boost. Outside of those parameters, the evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have gastric cancer who receive adjunctive IORT, the evidence includes RCTs and a systematic review of RCTs. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. A meta-analysis of 8 RCTs found a benefit of IORT in locoregional control (but not OS) when used with EBRT. When IORT was administered without adjuvant EBRT in patients with stage III disease, OS improved. Thus, IORT might be considered an alternative to EBRT in patients undergoing surgery for stage III gastric cancer. Randomized studies comparing the benefits and harms of the 2 treatments are needed to determine the efficacy of IORT with greater certainty. It cannot be determined whether IORT provides any benefit for OS in this patient population (gastric cancer patients) when used with EBRT. Further study is needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have soft tissue sarcomas who receive adjunctive IORT, the evidence includes a systematic review, a small RCT, and several nonrandomized comparative studies. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. Overall, the study quality is low. The limited data suggest that IORT might improve local control and OS but adverse events might outweigh any treatment benefit. RCTs are needed to determine the risks and benefits of IORT for soft tissue sarcomas with greater certainty. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have gynecologic cancers who receive adjunctive IORT, the evidence includes a nonrandomized trial and case series. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. The contribution of adjuvant IORT cannot be determined from the available literature. There is no evidence that IORT improves survival rates, and there may be severe complications related to the therapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have head and neck cancers who receive adjunctive IORT, the evidence includes case series. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. The strongest evidence is from a retrospective analysis of patients who had recurrent salivary gland carcinomas and were at risk of radiation toxicity due to prior treatment with EBRT. Some patients received IORT plus salvage surgery, and multivariate analysis found that the use of IORT was a significant predictor of improved outcomes. Although these findings suggested an improvement in health outcomes for head and neck cancers that cannot be treated with EBRT due to toxicity, there was a high-risk of selection bias in this study. Comparative trials are needed to determine the efficacy of IORT with greater certainty. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have pancreatic cancer who receive adjunctive IORT, the evidence includes large case series, cohort studies, and systematic reviews of these studies. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. The systematic review found that in patients with resectable pancreatic cancer the addition of IORT to standard therapy was associated with improved median survival and reduced local recurrence; the evidence was limited by mostly smaller retrospective designs contributing to the review. However, the vast majority of patients present at diagnosis with more advanced disease, such as borderline resectable, locally advanced, or with distant metastases, where comparative evidence is limited to case series. More data are needed to determine the effect of adjunctive IORT for resectable, locally advanced and metastatic pancreatic cancer with greater certainty. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have renal cell carcinoma who receive adjunctive IORT, the evidence includes case series. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. No controlled trials were identified to determine whether adjunctive IORT improves

health outcomes when added to multimodal therapy with surgical resection and EBRT. Grade 3 or higher toxicity after IORT has been reported in a substantial percentage of patients. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have glioblastoma or neuroblastoma or fibromatosis who receive adjunctive IORT, the evidence includes case series. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. Compared with other therapies, it is unclear whether IORT improves OS. However, compared with historical controls, IORT for patients with previously untreated malignant gliomas had no survival benefit when given in conjunction with multimodal therapy. In addition, complication rates may be high. Comparative trials are needed to evaluate the safety and efficacy of this treatment modality. The evidence is insufficient to determine the effects of the technology on health outcomes.

Date	Áction
9/2020	BCBSA National medical policy review. Description, summary and references updated.
	Policy statements unchanged.
9/2019	BCBSA National medical policy review. Description, summary and references updated.
	Policy statements unchanged.
9/2018	BCBSA National medical policy review. No changes to policy statements. New
	references added. Background and summary clarified.
3/2018	New references added from BCBSA National medical policy.
1/2017	New references added from BCBSA National medical policy.
11/2015	New references added from BCBSA National medical policy.
9/2015	Clarified coding information.
10/2014	New references added from BCBSA National medical policy.
8/2014	Coding information clarified.
12/2013	New references from BCBSA National medical policy.
11/2011-	Medical policy ICD 10 remediation: Formatting, editing and coding updates.
4/2012	No changes to policy statements.
7/2011	Reviewed - Medical Policy Group - Hematology and Oncology.
	No changes to policy statements.
9/2010	Reviewed - Medical Policy Group - Hematology and Oncology.
	No changes to policy statements.
9/2009	Reviewed - Medical Policy Group - Hematology and Oncology.
	No changes to policy statements.
5/2009	BCBSA National medical policy review.
	No changes to policy statements.
10/2008	Reviewed - Medical Policy Group - Hematology and Oncology.
	No changes to policy statements.
8/2008	BCBSA National medical policy review.
	No changes to policy statements.
1/2008	Reviewed - Medical Policy Group - Neurology and Neurosurgery.
	No changes to policy statements.
9/2007	Reviewed - Medical Policy Group - Hematology and Oncology.
	No changes to policy statements.
7/2007	BCBSA National medical policy review.
	No changes to policy statements.
1/2007	Reviewed - Medical Policy Group - Neurology and Neurosurgery.
	No changes to policy statements.

Policy History

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information: <u>Medical Policy Terms of Use</u> Managed Care Guidelines Indemnity/PPO Guidelines Clinical Exception Process Medical Technology Assessment Guidelines

References

- Dubois JB, Bussieres E, Richaud P, et al. Intra-operative radiotherapy of rectal cancer: results of the French multi-institutional randomized study. Radiother Oncol. Mar 2011; 98(3): 298-303. PMID 21339010
- Masaki T, Matsuoka H, Kishiki T, et al. Intraoperative radiotherapy for resectable advanced lower rectal cancer-final results of a randomized controlled trial (UMIN000021353). Langenbecks Arch Surg. May 2020; 405(3): 247-254. PMID 32347365
- 3. Wiig JN, Giercksky KE, Tveit KM. Intraoperative radiotherapy for locally advanced or locally recurrent rectal cancer: Does it work at all?. Acta Oncol. Jul 2014; 53(7): 865-76. PMID 24678823
- Mirnezami R, Chang GJ, Das P, et al. Intraoperative radiotherapy in colorectal cancer: systematic review and meta-analysis of techniques, long-term outcomes, and complications. Surg Oncol. Mar 2013; 22(1): 22-35. PMID 23270946
- 5. Yu WW, Guo YM, Zhang Q, et al. Benefits from adjuvant intraoperative radiotherapy treatment for gastric cancer: A meta-analysis. Mol Clin Oncol. Jan 2015; 3(1): 185-189. PMID 25469292
- 6. Skandarajah AR, Lynch AC, Mackay JR, et al. The role of intraoperative radiotherapy in solid tumors. Ann Surg Oncol. Mar 2009; 16(3): 735-44. PMID 19142683
- Sindelar WF, Kinsella TJ, Chen PW, et al. Intraoperative radiotherapy in retroperitoneal sarcomas. Final results of a prospective, randomized, clinical trial. Arch Surg. Apr 1993; 128(4): 402-10. PMID 8457152
- Lehnert T, Schwarzbach M, Willeke F, et al. Intraoperative radiotherapy for primary and locally recurrent soft tissue sarcoma: morbidity and long-term prognosis. Eur J Surg Oncol. Nov 2000; 26 Suppl A: S21-4. PMID 11130875
- Calvo FA, Sole CV, Polo A, et al. Limb-sparing management with surgical resection, external-beam and intraoperative electron-beam radiation therapy boost for patients with primary soft tissue sarcoma of the extremity: a multicentric pooled analysis of long-term outcomes. Strahlenther Onkol. Oct 2014; 190(10): 891-8. PMID 24715241
- Stucky CC, Wasif N, Ashman JB, et al. Excellent local control with preoperative radiation therapy, surgical resection, and intra-operative electron radiation therapy for retroperitoneal sarcoma. J Surg Oncol. Jun 2014; 109(8): 798-803. PMID 24862926
- 11. Giorda G, Boz G, Gadducci A, et al. Multimodality approach in extra cervical locally advanced cervical cancer: chemoradiation, surgery and intra-operative radiation therapy. A phase II trial. Eur J Surg Oncol. May 2011; 37(5): 442-7. PMID 21492777
- Martinez-Monge R, Jurado M, Aristu JJ, et al. Intraoperative electron beam radiotherapy during radical surgery for locally advanced and recurrent cervical cancer. Gynecol Oncol. Sep 2001; 82(3): 538-43. PMID 11520152
- Gao Y, Liu Z, Chen X, et al. Intraoperative radiotherapy electron boost in advanced and recurrent epithelial ovarian carcinoma: a retrospective study. BMC Cancer. Oct 11 2011; 11: 439. PMID 21989202
- 14. Zeidan YH, Yeh A, Weed D, et al. Intraoperative radiation therapy for advanced cervical metastasis: a single institution experience. Radiat Oncol. Jun 15 2011; 6: 72. PMID 21676211
- 15. Zeidan YH, Shiue K, Weed D, et al. Intraoperative radiotherapy for parotid cancer: a single-institution experience. Int J Radiat Oncol Biol Phys. Apr 01 2012; 82(5): 1831-6. PMID 21514074
- 16. Perry DJ, Chan K, Wolden S, et al. High-dose-rate intraoperative radiation therapy for recurrent headand-neck cancer. Int J Radiat Oncol Biol Phys. Mar 15 2010; 76(4): 1140-6. PMID 19560882
- 17. Chen AM, Garcia J, Bucci MK, et al. Recurrent salivary gland carcinomas treated by surgery with or without intraoperative radiation therapy. Head Neck. Jan 2008; 30(1): 2-9. PMID 17828788
- Chen AM, Bucci MK, Singer MI, et al. Intraoperative radiation therapy for recurrent head-and-neck cancer: the UCSF experience. Int J Radiat Oncol Biol Phys. Jan 01 2007; 67(1): 122-9. PMID 17084543

- Jin L, Shi N, Ruan S, et al. The role of intraoperative radiation therapy in resectable pancreatic cancer: a systematic review and meta-analysis. Radiat Oncol. Apr 09 2020; 15(1): 76. PMID 32272945
- Chen Y, Che X, Zhang J, et al. Long-term results of intraoperative electron beam radiation therapy for nonmetastatic locally advanced pancreatic cancer: Retrospective cohort study, 7-year experience with 247 patients at the National Cancer Center in China. Medicine (Baltimore). Sep 2016; 95(38): e4861. PMID 27661028
- Cai S, Hong TS, Goldberg SI, et al. Updated long-term outcomes and prognostic factors for patients with unresectable locally advanced pancreatic cancer treated with intraoperative radiotherapy at the Massachusetts General Hospital, 1978 to 2010. Cancer. Dec 01 2013; 119(23): 4196-204. PMID 24006012
- Harrison JM, Wo JY, Ferrone CR, et al. Intraoperative Radiation Therapy (IORT) for Borderline Resectable and Locally Advanced Pancreatic Ductal Adenocarcinoma (BR/LA PDAC) in the Era of Modern Neoadjuvant Treatment: Short-Term and Long-Term Outcomes. Ann Surg Oncol. May 2020; 27(5): 1400-1406. PMID 31758284
- 23. Paly JJ, Hallemeier CL, Biggs PJ, et al. Outcomes in a multi-institutional cohort of patients treated with intraoperative radiation therapy for advanced or recurrent renal cell carcinoma. Int J Radiat Oncol Biol Phys. Mar 01 2014; 88(3): 618-23. PMID 24411190
- 24. Calvo FA, Sole CV, Martinez-Monge R, et al. Intraoperative EBRT and resection for renal cell carcinoma : twenty-year outcomes. Strahlenther Onkol. Feb 2013; 189(2): 129-36. PMID 23223810
- 25. Hallemeier CL, Choo R, Davis BJ, et al. Long-term outcomes after maximal surgical resection and intraoperative electron radiotherapy for locoregionally recurrent or locoregionally advanced primary renal cell carcinoma. Int J Radiat Oncol Biol Phys. Apr 01 2012; 82(5): 1938-43. PMID 21514065
- 26. Nemoto K, Ogawa Y, Matsushita H, et al. Intraoperative radiation therapy (IORT) for previously untreated malignant gliomas. BMC Cancer. 2002; 2: 1. PMID 11818027
- 27. Sarria GR, Sperk E, Han X, et al. Intraoperative radiotherapy for glioblastoma: an international pooled analysis. Radiother Oncol. Jan 2020; 142: 162-167. PMID 31629553
- 28. Rich BS, McEvoy MP, LaQuaglia MP, et al. Local control, survival, and operative morbidity and mortality after re-resection, and intraoperative radiation therapy for recurrent or persistent primary high-risk neuroblastoma. J Pediatr Surg. Jan 2011; 46(1): 97-102. PMID 21238648
- 29. Roeder F, Timke C, Oertel S, et al. Intraoperative electron radiotherapy for the management of aggressive fibromatosis. Int J Radiat Oncol Biol Phys. Mar 15 2010; 76(4): 1154-60. PMID 19647952
- 30. Tom MC, Joshi N, Vicini F, et al. The American Brachytherapy Society consensus statement on intraoperative radiation therapy. Brachytherapy. May 2019; 18(3): 242-257. PMID 31084904
- 31. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Cervical cancer. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed May 22, 2020.
- 32. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Colon cancer. Version 3.2020. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed May 20, 2020.
- National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Gastric cancer. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed May 22, 2020.
- 34. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Head and neck cancers. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/headand-neck.pdf. Accessed May 20, 2020.
- 35. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Ovarian cancer. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed May 20, 2020.
- 36. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Pancreatic adenocarcinoma. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed May 21, 2020.
- National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Rectal cancer. Version 3.2020 http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed May 20, 2020.

- National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Kidney cancer. Version 2.2020. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed May 20, 2020.
- 39. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology: Soft tissue sarcoma. Version 1.2020.
- https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed May 20, 2020. 40. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology:
- Uterine neoplasms. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed May 20, 2020.
- 41. Bosset JF, Collette L, Calais G, et al. Chemotherapy with preoperative radiotherapy in rectal cancer. N Engl J Med. Sep 14 2006; 355(11): 1114-23. PMID 16971718
- 42. Diaz-Gonzalez JA, Calvo FA, Cortes J, et al. Prognostic factors for disease-free survival in patients with T3-4 or N+ rectal cancer treated with preoperative chemoradiation therapy, surgery, and intraoperative irradiation. Int J Radiat Oncol Biol Phys. Mar 15 2006; 64(4): 1122-8. PMID 16406393
- 43. Ferenschild FT, Vermaas M, Nuyttens JJ, et al. Value of intraoperative radiotherapy in locally advanced rectal cancer. Dis Colon Rectum. Sep 2006; 49(9): 1257-65. PMID 16912909
- Gerard JP, Conroy T, Bonnetain F, et al. Preoperative radiotherapy with or without concurrent fluorouracil and leucovorin in T3-4 rectal cancers: results of FFCD 9203. J Clin Oncol. Oct 01 2006; 24(28): 4620-5. PMID 17008704
- 45. Harris GJ, Senagore AJ, Lavery IC, et al. Factors affecting survival after palliative resection of colorectal carcinoma. Colorectal Dis. Jan 2002; 4(1): 31-35. PMID 12780652
- 46. Huber FT, Stepan R, Zimmermann F, et al. Locally advanced rectal cancer: resection and intraoperative radiotherapy using the flab method combined with preoperative or postoperative radiochemotherapy. Dis Colon Rectum. Jul 1996; 39(7): 774-9. PMID 8674370
- Krempien R, Roeder F, Oertel S, et al. Long-term results of intraoperative presacral electron boost radiotherapy (IOERT) in combination with total mesorectal excision (TME) and chemoradiation in patients with locally advanced rectal cancer. Int J Radiat Oncol Biol Phys. Nov 15 2006; 66(4): 1143-51. PMID 16979835
- 48. Kusters M, Valentini V, Calvo FA, et al. Results of European pooled analysis of IORT-containing multimodality treatment for locally advanced rectal cancer: adjuvant chemotherapy prevents local recurrence rather than distant metastases. Ann Oncol. Jun 2010; 21(6): 1279-84. PMID 19889621
- Kusters M, Holman FA, Martijn H, et al. Patterns of local recurrence in locally advanced rectal cancer after intra-operative radiotherapy containing multimodality treatment. Radiother Oncol. Aug 2009; 92(2): 221-5. PMID 19339070
- 50. Larsen SG, Wiig JN, Dueland S, et al. Prognostic factors after preoperative irradiation and surgery for locally advanced rectal cancer. Eur J Surg Oncol. Apr 2008; 34(4): 410-7. PMID 17614249
- Lim SB, Yu CS, Hong YS, et al. Long-term outcomes in patients with locally advanced rectal cancer treated with preoperative chemoradiation followed by curative surgical resection. J Surg Oncol. Nov 2012; 106(6): 659-66. PMID 22674581
- Mannaerts GH, Martijn H, Crommelin MA, et al. Feasibility and first results of multimodality treatment, combining EBRT, extensive surgery, and IOERT in locally advanced primary rectal cancer. Int J Radiat Oncol Biol Phys. May 01 2000; 47(2): 425-33. PMID 10802370
- Masaki T, Takayama M, Matsuoka H, et al. Intraoperative radiotherapy for oncological and functionpreserving surgery in patients with advanced lower rectal cancer. Langenbecks Arch Surg. Mar 2008; 393(2): 173-80. PMID 18172677
- 54. Mathis KL, Larson DW, Dozois EJ, et al. Outcomes following surgery without radiotherapy for rectal cancer. Br J Surg. Jan 2012; 99(1): 137-43. PMID 22052336
- 55. Nakfoor BM, Willett CG, Shellito PC, et al. The impact of 5-fluorouracil and intraoperative electron beam radiation therapy on the outcome of patients with locally advanced primary rectal and rectosigmoid cancer. Ann Surg. Aug 1998; 228(2): 194-200. PMID 9712564
- 56. Nuyttens JJ, Kolkman-Deurloo IK, Vermaas M, et al. High-dose-rate intraoperative radiotherapy for close or positive margins in patients with locally advanced or recurrent rectal cancer. Int J Radiat Oncol Biol Phys. Jan 01 2004; 58(1): 106-12. PMID 14697427
- Pacelli F, Di Giorgio A, Papa V, et al. Preoperative radiotherapy combined with intraoperative radiotherapy improve results of total mesorectal excision in patients with T3 rectal cancer. Dis Colon Rectum. Feb 2004; 47(2): 170-9. PMID 15043286

- Palmer G, Martling A, Cedermark B, et al. A population-based study on the management and outcome in patients with locally recurrent rectal cancer. Ann Surg Oncol. Feb 2007; 14(2): 447-54. PMID 17139457
- Park JH, Yoon SM, Yu CS, et al. Randomized phase 3 trial comparing preoperative and postoperative chemoradiotherapy with capecitabine for locally advanced rectal cancer. Cancer. Aug 15 2011; 117(16): 3703-12. PMID 21328328
- 60. Ratto C, Valentini V, Morganti AG, et al. Combined-modality therapy in locally advanced primary rectal cancer. Dis Colon Rectum. Jan 2003; 46(1): 59-67. PMID 12544523
- Roeder F, Treiber M, Oertel S, et al. Patterns of failure and local control after intraoperative electron boost radiotherapy to the presacral space in combination with total mesorectal excision in patients with locally advanced rectal cancer. Int J Radiat Oncol Biol Phys. Apr 01 2007; 67(5): 1381-8. PMID 17275208
- Sadahiro S, Suzuki T, Ishikawa K, et al. Preoperative radio/chemo-radiotherapy in combination with intraoperative radiotherapy for T3-4Nx rectal cancer. Eur J Surg Oncol. Sep 2004; 30(7): 750-8. PMID 15296989
- 63. Sanfilippo NJ, Crane CH, Skibber J, et al. T4 rectal cancer treated with preoperative chemoradiation to the posterior pelvis followed by multivisceral resection: patterns of failure and limitations of treatment. Int J Radiat Oncol Biol Phys. Sep 01 2001; 51(1): 176-83. PMID 11516868
- 64. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med. Oct 21 2004; 351(17): 1731-40. PMID 15496622
- 65. Valentini V, Coco C, Rizzo G, et al. Outcomes of clinical T4M0 extra-peritoneal rectal cancer treated with preoperative radiochemotherapy and surgery: a prospective evaluation of a single institutional experience. Surgery. May 2009; 145(5): 486-94. PMID 19375606
- 66. Willett CG, Shellito PC, Tepper JE, et al. Intraoperative electron beam radiation therapy for recurrent locally advanced rectal or rectosigmoid carcinoma. Cancer. Mar 15 1991; 67(6): 1504-8. PMID 2001537
- 67. Abuchaibe O, Calvo FA, Azinovic I, et al. Intraoperative radiotherapy in locally advanced recurrent colorectal cancer. Int J Radiat Oncol Biol Phys. Aug 01 1993; 26(5): 859-67. PMID 8344855
- 68. Bedrosian I, Giacco G, Pederson L, et al. Outcome after curative resection for locally recurrent rectal cancer. Dis Colon Rectum. Feb 2006; 49(2): 175-82. PMID 16392024
- 69. Dresen RC, Gosens MJ, Martijn H, et al. Radical resection after IORT-containing multimodality treatment is the most important determinant for outcome in patients treated for locally recurrent rectal cancer. Ann Surg Oncol. Jul 2008; 15(7): 1937-47. PMID 18389321
- 70. Eble MJ, Lehnert T, Treiber M, et al. Moderate dose intraoperative and external beam radiotherapy for locally recurrent rectal carcinoma. Radiother Oncol. Nov 1998; 49(2): 169-74. PMID 10052883
- Haddock MG, Miller RC, Nelson H, et al. Combined modality therapy including intraoperative electron irradiation for locally recurrent colorectal cancer. Int J Radiat Oncol Biol Phys. Jan 01 2011; 79(1): 143-50. PMID 20395067
- 72. Hansen MH, Balteskard L, Dorum LM, et al. Locally recurrent rectal cancer in Norway. Br J Surg. Oct 2009; 96(10): 1176-82. PMID 19787766
- 73. Hashiguchi Y, Sekine T, Sakamoto H, et al. Intraoperative irradiation after surgery for locally recurrent rectal cancer. Dis Colon Rectum. Jul 1999; 42(7): 886-93; discussion 893-5. PMID 10411435
- Hashiguchi Y, Sekine T, Kato S, et al. Indicators for surgical resection and intraoperative radiation therapy for pelvic recurrence of colorectal cancer. Dis Colon Rectum. Jan 2003; 46(1): 31-9. PMID 12544519
- Kanemitsu Y, Hirai T, Komori K, et al. Prediction of residual disease or distant metastasis after resection of locally recurrent rectal cancer. Dis Colon Rectum. May 2010; 53(5): 779-89. PMID 20389212
- 76. Lee JH, Kim DY, Kim SY, et al. Clinical outcomes of chemoradiotherapy for locally recurrent rectal cancer. Radiat Oncol. May 20 2011; 6: 51. PMID 21595980
- 77. Lindel K, Willett CG, Shellito PC, et al. Intraoperative radiation therapy for locally advanced recurrent rectal or rectosigmoid cancer. Radiother Oncol. Jan 2001; 58(1): 83-7. PMID 11165686
- Mannaerts GH, Rutten HJ, Martijn H, et al. Comparison of intraoperative radiation therapy-containing multimodality treatment with historical treatment modalities for locally recurrent rectal cancer. Dis Colon Rectum. Dec 2001; 44(12): 1749-58. PMID 11742155

- Martinez-Monge R, Nag S, Martin EW. Three different intraoperative radiation modalities (electron beam, high-dose-rate brachytherapy, and iodine-125 brachytherapy) in the adjuvant treatment of patients with recurrent colorectal adenocarcinoma. Cancer. Jul 15 1999; 86(2): 236-47. PMID 10421259
- 80. Mohiuddin M, Lingareddy V, Rakinic J, et al. Reirradiation for rectal cancer and surgical resection after ultra high doses. Int J Radiat Oncol Biol Phys. Dec 01 1993; 27(5): 1159-63. PMID 8262842
- Park JK, Kim YW, Hur H, et al. Prognostic factors affecting oncologic outcomes in patients with locally recurrent rectal cancer: impact of patterns of pelvic recurrence on curative resection. Langenbecks Arch Surg. Jan 2009; 394(1): 71-7. PMID 18663464
- Pezner RD, Chu DZ, Ellenhorn JD. Intraoperative radiation therapy for patients with recurrent rectal and sigmoid colon cancer in previously irradiated fields. Radiother Oncol. Jul 2002; 64(1): 47-52. PMID 12208575
- Rahbari NN, Ulrich AB, Bruckner T, et al. Surgery for locally recurrent rectal cancer in the era of total mesorectal excision: is there still a chance for cure?. Ann Surg. Mar 2011; 253(3): 522-33. PMID 21209587
- 84. Salo JC, Paty PB, Guillem J, et al. Surgical salvage of recurrent rectal carcinoma after curative resection: a 10-year experience. Ann Surg Oncol. Mar 1999; 6(2): 171-7. PMID 10082043
- Shoup M, Guillem JG, Alektiar KM, et al. Predictors of survival in recurrent rectal cancer after resection and intraoperative radiotherapy. Dis Colon Rectum. May 2002; 45(5): 585-92. PMID 12004205
- 86. Suzuki K, Gunderson LL, Devine RM, et al. Intraoperative irradiation after palliative surgery for locally recurrent rectal cancer. Cancer. Feb 15 1995; 75(4): 939-52. PMID 7531113
- 87. Valentini V, Morganti AG, De Franco A, et al. Chemoradiation with or without intraoperative radiation therapy in patients with locally recurrent rectal carcinoma: prognostic factors and long term outcome. Cancer. Dec 15 1999; 86(12): 2612-24. PMID 10594856
- 88. Vermaas M, Nuyttens JJ, Ferenschild FT, et al. Reirradiation, surgery and IORT for recurrent rectal cancer in previously irradiated patients. Radiother Oncol. Jun 2008; 87(3): 357-60. PMID 18353474
- 89. Wells BJ, Stotland P, Ko MA, et al. Results of an aggressive approach to resection of locally recurrent rectal cancer. Ann Surg Oncol. Feb 2007; 14(2): 390-5. PMID 17063304
- Wiig JN, Larsen SG, Dueland S, et al. Preoperative irradiation and surgery for local recurrence of rectal and rectosigmoid cancer. Prognostic factors with regard to survival and further local recurrence. Colorectal Dis. Jan 2008; 10(1): 48-57. PMID 18028472