BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 09/19/22**
SECTION: MEDICINE	**LAST REVIEW DATE: 09/03/24**
	CURRENT EFFECTIVE DATE: 09/03/24
	LAST CRITERIA REVISION DATE: 09/21/23
NEXT ANNUAL REVIEW DATE: 3RD QTR 2025	**ARCHIVE DATE:**

INTRAOPERATIVE RADIOTHERAPY

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 09/19/22**
SECTION: MEDICINE	**LAST REVIEW DATE: 09/03/24**
	CURRENT EFFECTIVE DATE: 09/03/24
	LAST CRITERIA REVISION DATE: 09/21/23
NEXT ANNUAL REVIEW DATE: 3RD QTR 2025	**ARCHIVE DATE:**

INTRAOPERATIVE RADIOTHERAPY

Description:

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.

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.

The INTRABEAM® system was first approved for use by the U.S. Food and Drug Administration (FDA) for intracranial tumors in 1999 and was subsequently approved for whole body use in 2005. INTRABEAM spherical applicators are indicated for use with the INTRABEAM system to deliver a prescribed dose of radiation to the treatment margin or tumor bed during intracavity radiotherapy or IORT treatments. In 1998, the Mobetron® mobile electron beam accelerator, designed for use during surgery, was cleared for marketing by the FDA through the 510(k) process. Xoft® Axxent® electronic brachytherapy system is also available and was approved to deliver high dose rate X-ray radiation for brachytherapy in 2008.

Criteria:

- Use of intraoperative radiotherapy for the treatment of rectal cancer with positive or close margins with T4 lesions or recurrent disease is considered ***medically necessary***.

- Use of intraoperative radiotherapy for all other oncologic applications not previously listed or if above criteria not met is considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

INTRAOPERATIVE RADIOTHERAPY

Resources:

Literature reviewed 09/03/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. Abuchaibe O, Calvo FA, Azinovic I, Aristu J, Pardo F, Alvarez-Cienfuegos J. Intraoperative radiotherapy in locally advanced recurrent colorectal cancer. *Int J Radiat Oncol Biol Phys*. Aug 1 1993;26(5):859-67. doi:10.1016/0360-3016(93)90502-m

2. Alberda WJ, Verhoef C, Nuyttens JJ, et al. Intraoperative radiation therapy reduces local recurrence rates in patients with microscopically involved circumferential resection margins after resection of locally advanced rectal cancer. *Int J Radiat Oncol Biol Phys*. Apr 1 2014;88(5):1032-40. doi:10.1016/j.ijrobp.2014.01.014

3. 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. doi:10.1007/s10350-005-0276-5

4. 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. doi:10.1056/NEJMoa060829

5. 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 1 2013;119(23):4196-204. doi:10.1002/cncr.28329

6. 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. doi:10.1007/s00066-012-0272-3

7. 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. doi:10.1007/s00066-014-0640-2

8. 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 1 2007;67(1):122-9. doi:10.1016/j.ijrobp.2006.08.038

9. 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. doi:10.1002/hed.20651

10. Chen HH, Hou PY, Ting WH, Shueng PW, Hsiao SM. Feasibility and Safety of Intraoperative Radiotherapy with Low Energy X-ray Photon Therapy for Recurrent Gynecological Cancer: A Case Series. *Life (Basel)*. May 5 2022;12(5)doi:10.3390/life12050685

INTRAOPERATIVE RADIOTHERAPY

11. 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. doi:10.1097/MD.0000000000004861

12. Cho Y, Kim JW, Kim HS, Park JS, Lee IJ. Intraoperative Radiotherapy for Resectable Pancreatic Cancer Using a Low-Energy X-Ray Source: Postoperative Complications and Early Outcomes. *Yonsei Med J*. May 2022;63(5):405-412. doi:10.3349/ymj.2022.63.5.405

13. 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. doi:10.1016/j.ijrobp.2005.09.020

14. 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. doi:10.1245/s10434-008-9896-z

15. 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. doi:10.1016/j.radonc.2011.01.017

16. Eble MJ, Lehnert T, Treiber M, Latz D, Herfarth C, Wannenmacher M. Moderate dose intraoperative and external beam radiotherapy for locally recurrent rectal carcinoma. *Radiother Oncol*. Nov 1998;49(2):169-74. doi:10.1016/s0167-8140(98)00124-8

17. Fahy MR, Kelly ME, Power Foley M, Nugent TS, Shields CJ, Winter DC. The role of intraoperative radiotherapy in advanced rectal cancer: a meta-analysis. *Colorectal Dis*. Aug 2021;23(8):1998-2006. doi:10.1111/codi.15698

18. 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. doi:10.1007/s10350-006-0651-x

19. Gao Y, Liu Z, Chen X, Luo W, Zhang L, Wang J. Intraoperative radiotherapy electron boost in advanced and recurrent epithelial ovarian carcinoma: a retrospective study. *BMC Cancer*. Oct 11 2011;11:439. doi:10.1186/1471-2407-11-439

20. 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 1 2006;24(28):4620-5. doi:10.1200/JCO.2006.06.7629

21. 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. doi:10.1016/j.ejso.2011.02.011

22. 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 1 2011;79(1):143-50. doi:10.1016/j.ijrobp.2009.10.046

23. 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 1 2012;82(5):1938-43. doi:10.1016/j.ijrobp.2011.02.026

24. Hansen MH, Balteskard L, Dorum LM, Eriksen MT, Vonen B, Norwegian Colorectal Cancer G. Locally recurrent rectal cancer in Norway. *Br J Surg*. Oct 2009;96(10):1176-82. doi:10.1002/bjs.6699

25. Harris GJ, Senagore AJ, Lavery IC, Church JM, Fazio VW. Factors affecting survival after palliative resection of colorectal carcinoma. *Colorectal Dis*. Jan 2002;4(1):31-35. doi:10.1046/j.1463-1318.2002.00304.x

26. 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. doi:10.1245/s10434-019-08084-2

27. 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. doi:10.1007/s10350-004-6493-5

28. 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. doi:10.1007/BF02237096

29. Huber FT, Stepan R, Zimmermann F, Fink U, Molls M, Siewert JR. 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. doi:10.1007/BF02054443

30. 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 9 2020;15(1):76. doi:10.1186/s13014-020-01511-9

31. Kanemitsu Y, Hirai T, Komori K, Kato T. Prediction of residual disease or distant metastasis after resection of locally recurrent rectal cancer. *Dis Colon Rectum*. May 2010;53(5):779-89. doi:10.1007/DCR.0b013e3181cf7609

32. Klink CD, Binnebosel M, Holy R, Neumann UP, Junge K. Influence of intraoperative radiotherapy (IORT) on perioperative outcome after surgical resection of rectal cancer. *World J Surg*. Apr 2014;38(4):992-6. doi:10.1007/s00268-013-2313-1

INTRAOPERATIVE RADIOTHERAPY

33. 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. doi:10.1016/j.ijrobp.2006.06.008

34. 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. doi:10.1016/j.radonc.2009.03.002

35. 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):1279-1284. doi:10.1093/annonc/mdp501

36. Larsen SG, Wiig JN, Dueland S, Giercksky KE. Prognostic factors after preoperative irradiation and surgery for locally advanced rectal cancer. *Eur J Surg Oncol*. Apr 2008;34(4):410-7. doi:10.1016/j.ejso.2007.05.012

37. Lee JH, Kim DY, Kim SY, et al. Clinical outcomes of chemoradiotherapy for locally recurrent rectal cancer. *Radiat Oncol*. May 20 2011;6:51. doi:10.1186/1748-717X-6-51

38. 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.

39. Lim SB, Yu CS, Hong YS, Kim TW, Kim JH, Kim JC. 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. doi:10.1002/jso.23181

40. 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. doi:10.1016/s0167-8140(00)00309-1

41. Liu B, Ge L, Wang J, et al. Efficacy and safety of intraoperative radiotherapy in rectal cancer: A systematic review and meta-analysis. *World J Gastrointest Oncol*. Jan 15 2021;13(1):69-86. doi:10.4251/wjgo.v13.i1.69

42. Mannaerts GH, Martijn H, Crommelin MA, Dries W, Repelaer van Driel OJ, Rutten HJ. 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 1 2000;47(2):425-33. doi:10.1016/s0360-3016(99)00492-7

43. Mannaerts GH, Rutten HJ, Martijn H, Hanssens PE, Wiggers T. 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. doi:10.1007/BF02234450

INTRAOPERATIVE RADIOTHERAPY

44. 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. doi:10.1006/gyno.2001.6329

45. 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. doi:10.1002/(sici)1097-0142(19990715)86:2<236::aid-cncr7>3.0.co;2-9

46. 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. doi:10.1007/s00423-020-01875-2

47. Masaki T, Takayama M, Matsuoka H, et al. Intraoperative radiotherapy for oncological and function-preserving surgery in patients with advanced lower rectal cancer. *Langenbecks Arch Surg*. Mar 2008;393(2):173-80. doi:10.1007/s00423-007-0260-8

48. 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. doi:10.1002/bjs.7739

49. 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. doi:10.1016/j.suronc.2012.11.001

50. Mohiuddin M, Lingareddy V, Rakinic J, Marks G. Reirradiation for rectal cancer and surgical resection after ultra high doses. *Int J Radiat Oncol Biol Phys*. Dec 1 1993;27(5):1159-63. doi:10.1016/0360-3016(93)90538-7

51. Nakfoor BM, Willett CG, Shellito PC, Kaufman DS, Daly WJ. 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. doi:10.1097/00000658-199808000-00008

52. National Comprehensive Cancer Network. Central nervous system cancers. Version 1.2024. Updated May 31, 2024. Accessed June 3, 2024. https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf

53. National Comprehensive Cancer Network. Cervical cancer. Version 3.2024. Updated May 6, 2024. Accessed June 2, 2024. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf

54. National Comprehensive Cancer Network. Colon cancer. Version 3.2024. Updated May 24, 2024. Accessed June 1, 2024. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf

55. National Comprehensive Cancer Network. Gastric cancer. Version 2.2024. Updated May 29, 2024. Accessed May 31, 2024. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf

INTRAOPERATIVE RADIOTHERAPY

56. National Comprehensive Cancer Network. Head and neck cancers. Version 4.2024. Updated May 1, 2024. Accessed May 30, 2024. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf

57. National Comprehensive Cancer Network. Kidney cancer. Version 4.2024. Updated May 30, 2024. Accessed May 29, 2024. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf

58. National Comprehensive Cancer Network. Ovarian cancer. Version 2.2024. Updated May 13, 2024. Accessed May 28, 2024. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf

59. National Comprehensive Cancer Network. Pancreatic adenocarcinoma. Version 2.2024. Updated April 30, 2024. Accessed May 27, 2024. https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf

60. National Comprehensive Cancer Network. Rectal cancer. Version 2.2024. Updated April 30, 2024. Accessed May 26, 2024. https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf

61. National Comprehensive Cancer Network. Soft tissue sarcoma. Version 1.2024. Updated April 26, 2024. Accessed May 25, 2024. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf

62. National Comprehensive Cancer Network. Uterine neoplasms. Version 2.2024. Updated March 6, 2024. Accessed May 24, 2024. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf

63. Nemoto K, Ogawa Y, Matsushita H, et al. Intraoperative radiation therapy (IORT) for previously untreated malignant gliomas. *BMC Cancer*. 2002;2:1. doi:10.1186/1471-2407-2-1

64. 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 1 2004;58(1):106-12. doi:10.1016/s0360-3016(03)01494-9

65. 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. doi:10.1007/s10350-003-0028-3

66. Palmer G, Martling A, Cedermark B, Holm T. 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. doi:10.1245/s10434-006-9256-9

67. 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 1 2014;88(3):618-23. doi:10.1016/j.ijrobp.2013.11.207

68. Park JH, Yoon SM, Yu CS, Kim JH, Kim TW, Kim JC. Randomized phase 3 trial comparing preoperative and postoperative chemoradiotherapy with capecitabine for locally advanced rectal cancer. *Cancer*. Aug 15 2011;117(16):3703-12. doi:10.1002/cncr.25943

INTRAOPERATIVE RADIOTHERAPY

69. 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. doi:10.1007/s00423-008-0391-6

70. Perry DJ, Chan K, Wolden S, et al. High-dose-rate intraoperative radiation therapy for recurrent head-and-neck cancer. *Int J Radiat Oncol Biol Phys*. Mar 15 2010;76(4):1140-6. doi:10.1016/j.ijrobp.2009.03.025

71. 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. doi:10.1016/s0167-8140(02)00139-1

72. 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. doi:10.1097/SLA.0b013e3182096d4f

73. 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. doi:10.1007/s10350-004-6497-1

74. Rich BS, McEvoy MP, LaQuaglia MP, Wolden SL. 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. doi:10.1016/j.jpedsurg.2010.09.068

75. 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. doi:10.1016/j.ijrobp.2009.03.067

76. 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 1 2007;67(5):1381-8. doi:10.1016/j.ijrobp.2006.11.039

77. 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. doi:10.1016/j.ejso.2004.04.012

78. Salo JC, Paty PB, Guillem J, Minsky BD, Harrison LB, Cohen AM. Surgical salvage of recurrent rectal carcinoma after curative resection: a 10-year experience. *Ann Surg Oncol*. Mar 1999;6(2):171-7. doi:10.1007/s10434-999-0171-8

79. 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 1 2001;51(1):176-83. doi:10.1016/s0360-3016(01)01610-8

INTRAOPERATIVE RADIOTHERAPY

80. Sarria GR, Sperk E, Han X, et al. Intraoperative radiotherapy for glioblastoma: an international pooled analysis. *Radiother Oncol*. Jan 2020;142:162-167. doi:10.1016/j.radonc.2019.09.023

81. 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. doi:10.1056/NEJMoa040694

82. Sekigami Y, Michelakos T, Fernandez-Del Castillo C, et al. Intraoperative Radiation Mitigates the Effect of Microscopically Positive Tumor Margins on Survival Among Pancreatic Adenocarcinoma Patients Treated with Neoadjuvant FOLFIRINOX and Chemoradiation. *Ann Surg Oncol*. Aug 2021;28(8):4592-4601. doi:10.1245/s10434-020-09444-z

83. 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. doi:10.1007/s10350-004-6250-9

84. 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. doi:10.1001/archsurg.1993.01420160040005

85. Skandarajah AR, Lynch AC, Mackay JR, Ngan S, Heriot AG. The role of intraoperative radiotherapy in solid tumors. *Ann Surg Oncol*. Mar 2009;16(3):735-44. doi:10.1245/s10434-008-0287-2

86. Stucky CC, Wasif N, Ashman JB, Pockaj BA, Gunderson LL, Gray RJ. 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. doi:10.1002/jso.23576

87. 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. doi:10.1002/1097-0142(19950215)75:4<939::aid-cncr2820750408>3.0.co;2-e

88. Tom MC, Joshi N, Vicini F, et al. The American Brachytherapy Society consensus statement on intraoperative radiation therapy. *Brachytherapy*. May - Jun 2019;18(3):242-257. doi:10.1016/j.brachy.2019.01.015

89. 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. doi:10.1016/j.surg.2009.01.007

90. 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. doi:10.1002/(sici)1097-0142(19991215)86:12<2612::aid-cncr5>3.0.co;2-m

INTRAOPERATIVE RADIOTHERAPY

91. Vermaas M, Nuyttens JJ, Ferenschild FT, Verhoef C, Eggermont AM, de Wilt JH. Reirradiation, surgery and IORT for recurrent rectal cancer in previously irradiated patients. *Radiother Oncol*. Jun 2008;87(3):357-60. doi:10.1016/j.radonc.2008.02.021

92. 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. doi:10.1245/s10434-006-9119-4

93. 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. doi:10.3109/0284186X.2014.895037

94. Wiig JN, Larsen SG, Dueland S, Giercksky KE. 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. doi:10.1111/j.1463-1318.2007.01398.x

95. Wiig JN, Poulsen JP, Tveit KM, Olsen DR, Giercksky KE. Intra-operative irradiation (IORT) for primary advanced and recurrent rectal cancer. a need for randomised studies. *Eur J Cancer*. May 2000;36(7):868-74. doi:10.1016/s0959-8049(00)00015-0

96. Willett CG, Shellito PC, Tepper JE, Eliseo R, Convery K, Wood WC. Intraoperative electron beam radiation therapy for recurrent locally advanced rectal or rectosigmoid carcinoma. *Cancer*. Mar 15 1991;67(6):1504-8. doi:10.1002/1097-0142(19910315)67:6<1504::aid-cncr2820670607>3.0.co;2

97. Yu WW, Guo YM, Zhang Q, Fu S. Benefits from adjuvant intraoperative radiotherapy treatment for gastric cancer: A meta-analysis. *Mol Clin Oncol*. Jan 2015;3(1):185-189. doi:10.3892/mco.2014.444

98. Zeidan YH, Shiue K, Weed D, et al. Intraoperative radiotherapy for parotid cancer: a single-institution experience. *Int J Radiat Oncol Biol Phys*. Apr 1 2012;82(5):1831-6. doi:10.1016/j.ijrobp.2011.02.033

99. 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. doi:10.1186/1748-717X-6-72

100. Zhang Q, Tey J, Yang Z, et al. Adjuvant chemoradiation plus intraoperative radiotherapy versus adjuvant chemoradiation alone in patients with locally advanced rectal cancer. *Am J Clin Oncol*. Feb 2015;38(1):11-6. doi:10.1097/COC.0b013e318287bb8d

101. Zhang Q, Tey J, Yang Z, et al. Intraoperative radiotherapy in the combination of adjuvant chemotherapy for the treatment of pT3N0M0 rectal cancer after radical surgery. *Am J Clin Oncol*. Feb 2014;37(1):8-12. doi:10.1097/COC.0b013e31825eb75c

EVIDENCE-BASED CRITERIA
SECTION: MEDICINE

NEXT ANNUAL REVIEW DATE: 3RD QTR 2025

ORIGINAL EFFECTIVE DATE: 09/19/22
LAST REVIEW DATE: 09/03/24
CURRENT EFFECTIVE DATE: 09/03/24
LAST CRITERIA REVISION DATE: 09/21/23
ARCHIVE DATE:

INTRAOPERATIVE RADIOTHERAPY

Coding:

CPT: 0735T, 77424, 77425, 77469

History:	Date:	Activity:
Medical Policy Panel	09/03/24	Review with revisions
Medical Director (Dr. Raja)	08/08/24	Review with no revisions
Medical Policy Panel	09/21/23	Review with revisions
Medical Policy Panel	08/01/23	Review with no revisions
Medical Policy Panel	08/16/22	Approved guideline (Effective 09/19/22)

Policy Revisions:

09/03/24	Updated:	Resource section
09/21/23	Added:	“Insufficient evidence to support improvement of the net health outcome; or”, and “Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, or” to experimental or investigational criteria.
09/21/23	Revised:	“Insufficient evidence to support improvement outside the investigational setting” from #3 to #5 in experimental or investigational criteria.
09/21/23	Updated:	Description, Resources, and Coding sections.

BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 09/19/22**
SECTION: MEDICINE	**LAST REVIEW DATE: 09/03/24**
	CURRENT EFFECTIVE DATE: 09/03/24
	LAST CRITERIA REVISION DATE: 09/21/23
NEXT ANNUAL REVIEW DATE: 3RD QTR 2025	**ARCHIVE DATE:**

INTRAOPERATIVE RADIOTHERAPY

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nílínigíí Blue Cross Blue Shield of Arizona haada yit'éego bína'ídíłkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yína'ídíłkidgo beehaz'áanii hóló díí t'áá hazaadk'ehjí háká a'doowołgo bee haz'ą doo bąąh íłínígóó. Ata' halne'ígíí kojį' bich'į' hodíilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون اية تكلفة. للتحدث مع مترجم اتصل ب 877-475-4799.

BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA		**ORIGINAL EFFECTIVE DATE:**	**09/19/22**
SECTION:	**MEDICINE**	**LAST REVIEW DATE:**	**09/03/24**
		CURRENT EFFECTIVE DATE:	**09/03/24**
		LAST CRITERIA REVISION DATE:	**09/21/23**
NEXT ANNUAL REVIEW DATE: 3RD QTR 2025		**ARCHIVE DATE:**	

INTRAOPERATIVE RADIOTHERAPY

Multi-Language Interpreter Services:

Tagalog: Kung ikaw, o ang iyong tinutulangan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799 로 전화하십시오.

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d'obtenir de l'aide et l'information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizona についてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:

اگر شما، یا کسی که شما به او کمک میکنید ، سوال در مورد Blue Cross Blue Shield of Arizona ، داشته باشید حق این را دارید که کمک و
اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799
تماس حاصل نمایید.]

Assyrian:

[illegible] Blue Cross Blue Shield of Arizona [illegible]
[illegible] 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคณ หรอคนทคณกาลงชวยเหลอมคาถามเกยวกบ Blue Cross Blue Shield of Arizona
คณมสทธทจะไดรบความชวยเหลอและขอมลในภาษา ของคณไดโดยไมมคาใชจาย พดคยกบลาม โทร 877-475-4799