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. IORT can be delivered by electron beams produced by linear accelerators or high-dose rate brachytherapy.

OBJECTIVE

The objectives of this evidence review are two-fold: (1) to determine whether intraoperative radiotherapy improves the net health outcome when used in conjunction with surgery and external-beam radiotherapy (EBRT); and (2) to determine whether the use of intraoperative radiotherapy improves the net health outcome in patients who cannot be treated with external-beam radiotherapy due to radiation toxicity.
POLICY STATEMENT

Use of intraoperative radiotherapy may be considered medically necessary 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.

POLICY GUIDELINES

There are specific CPT codes for intraoperative radiotherapy.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

The INTRABEAM system was first was cleared for marketing by the Food and Drug Administration through the 510(k) process 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 Food and Drug Administration through the 510(k) process. Food and Drug Administration product codes: JAD, LHN.

This evidence review does not address the use of IORT for breast cancer.

RATIONALE

Summary of Evidence

For individuals who have rectal cancer who receive adjunctive IORT, the evidence includes a randomized controlled trial (RCT), nonrandomized comparative studies, and systematic reviews of these studies. The 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 EBRT and surgery. Nonrandomized comparative studies and a meta-analysis of these studies have shown some benefit in health outcomes with adjunctive IORT for recurrent rectal cancer, but these studies are limited by a high-risk of selection bias, heterogeneous patient populations, and heterogeneous delivery of other treatments. Large RCTs are needed to determine the effect of IORT with greater certainty. 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. The relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. A meta-analysis of eight 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 two 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. The 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. The 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. The 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 renal cell carcinoma (RCC) who receive adjunctive IORT, the evidence includes case series. The 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. The 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.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

Table 1 lists the National Comprehensive Cancer Network guidelines on the use of intraoperative radiotherapy for the treatment of various cancers relevant to this evidence review.

The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.
## Table 1. Recommendations for the Use of IORT

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Version</th>
<th>Recommendation</th>
<th>COR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>v.4.2019</td>
<td>IORT “is particularly useful in patients with recurrent disease within a previously radiated volume. During IORT, overlying normal tissue (such as bowel or other viscera) can be manually displaced from the region at risk.”</td>
<td>3</td>
</tr>
<tr>
<td>Colon</td>
<td>v.2.2019</td>
<td>IORT “may be considered for patients with T4 or recurrent cancers as an additional boost.”</td>
<td>2A</td>
</tr>
<tr>
<td>Gastric</td>
<td>v.2.2019</td>
<td>IORT is currently not recommended</td>
<td>NA</td>
</tr>
<tr>
<td>Head/neck</td>
<td>v.1.2019</td>
<td>IORT is not addressed</td>
<td>NA</td>
</tr>
<tr>
<td>Ovarian</td>
<td>v.1.2019</td>
<td>IORT is not addressed</td>
<td>NA</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>v.2.2019</td>
<td>&quot;Overall, there is no clear established role for IORT in patients with pancreatic cancer, and the panel believes it should only be performed at specialized centers.&quot;</td>
<td>NA</td>
</tr>
<tr>
<td>Rectal</td>
<td>v.2.2019</td>
<td>IORT &quot;if available, may be considered for very close or positive margins after resection, as an additional boost, especially for patients with T4 or recurrent cancers.”</td>
<td>2A</td>
</tr>
<tr>
<td>Renal</td>
<td>v.1.2020</td>
<td>IORT is not addressed</td>
<td>NA</td>
</tr>
<tr>
<td>Soft tissue sarcoma</td>
<td>v.2.2019</td>
<td>For patients with resectable disease, consider boost with IORT for positive margins &quot;10-12.5 Gy for microscopic residual disease&quot; and &quot;15 Gy for gross residual disease&quot;.</td>
<td>2A</td>
</tr>
</tbody>
</table>
| Uterine          | v.2.2018  | • For patients with "locoregional recurrence ... [and] prior RT to site of recurrence ... surgical exploration + resection IORT" may be considered.  
• For patients with "radiologically isolated vaginal/pelvic recurrence ... surgical exploration + resection IORT systemic therapy" may be considered. | 3   |

COR: category of recommendation; Gy: gray; IORT: intraoperative radiotherapy; NA: not applicable; RT: radiotherapy.

## U.S. Preventive Services Task Force Recommendations

Not applicable.
Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


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