Introduction

The goal of breast-conserving surgery in treating localized breast cancer is to obtain tumor-free margins around the surgical resection site. Surgical margins that are not clear will often require additional surgery to remove additional breast tissue. Currently the only method to completely determine whether clear margins have been achieved is histologic examination of the surgically removed tissue. Intraoperative methods of assessing surgical margins, including specimen imaging, frozen section pathology, and touch print cytology, are either not highly accurate, not commonly available, or require considerable time and resources.

The MarginProbe is an intraoperative device that uses radiofrequency spectroscopy to analyze benign and malignant areas of the lumpectomy specimen. Use of the MarginProbe is intended to increase the likelihood that the surgeon will achieve clear margin and avoid the need for another procedure to remove more breast tissue.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
Policy Coverage Criteria

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Handheld radiofrequency spectroscopy (eg, MarginProbe)</td>
<td>Handheld radiofrequency spectroscopy for intraoperative assessment of surgical margins during breast-conserving surgery is considered investigational.</td>
</tr>
</tbody>
</table>

Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>CPT 0546T</td>
<td>Radiofrequency spectroscopy, real time, intraoperative margin assessment, at the time of partial mastectomy, with report (code effective 7/1/19)</td>
</tr>
</tbody>
</table>

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Related Information

N/A

Evidence Review

Description

As part of the treatment of localized breast cancer, breast-conserving surgery is optimally achieved by attaining tumor-free margins around the surgical resection site. Handheld radiofrequency spectroscopy for intraoperative assessment of surgical margins (eg, MarginProbe) is intended to increase the probability that the surgeon will achieve clear margins.
in the initial procedure, thus avoiding the need for a second surgery to excise more breast tissue.

**Background**

As part of the treatment of localized breast cancer, breast-conserving surgery is optimally achieved by attaining tumor-free margins around the surgical resection site. Failure to achieve clear margins will often require additional surgery to re-excise breast tissue. Currently, histologic examination of excised tissues after completion of surgery is the only method to determine definitively whether clear margins were achieved. Intraoperative methods of assessing surgical margins, such as specimen imaging, frozen section pathology, and touch print cytology, are either not highly accurate, not commonly available, or require considerable time and resources.

A device to detect positive margins should have a high sensitivity, indicating the ability to accurately detect any tumor found in the margins, ideally above 95%. While specificity is less important, excess false positive margin detection would lead to additional unnecessary tissue removal. A new device should have a specificity at least matching current standard best practices, estimated at 85%.¹

The MarginProbe is an intraoperative device which uses radiofrequency spectroscopy to measure the dielectric properties of tissue into which it comes in contact. Cancer cells and normal breast tissues produce different signals. A handheld probe is applied to a small area of the lumpectomy specimen and analyzes whether the tissue is likely malignant or benign. The device gives a positive or negative reading for each touch. If any touch on a particular margin gives a positive reading, the margin is considered to be positive and more tissue should be re-excised if possible. The device can only be used on the main lumpectomy specimen; it cannot be used on shavings or in the lumpectomy cavity of the patient’s breast. Use of MarginProbe is intended to increase the probability that the surgeon will achieve clear margins in the initial surgery, thus avoiding the need for a second procedure to excise more breast tissue.

**Summary of Evidence**

For individuals who have localized breast cancer or DCIS undergoing breast-conserving surgery (lumpectomy) who receive handheld radiofrequency spectroscopy for intraoperative assessment of surgical margins (eg, MarginProbe), the evidence includes a randomized trial, several historical control studies, and a systematic review. Relevant outcomes are change in disease status and morbid events. In the randomized trial, histologic examination of surgical margins
was not used in the control arm; the outcome measure (complete surgical resection) was not directly clinically relevant and was biased against the control arm; and patient follow-up was insufficient to assess local recurrence rates. The difference in re-excision rates between the 2 trial arms was not statistically significant. Diagnostic characteristics of the device showed only moderate sensitivity and poor specificity; thus, the device will miss some cancers and provide frequent false-positive results. Although several historical control studies have shown lower re-excision rates among patients in whom MarginProbe was used, the studies lacked adequate rigor to demonstrate whether the outcomes are attributable to MarginProbe. The studies did not report recurrence outcomes, which is important for assessing adequacy of resection. A randomized trial that assesses recurrence rates is required to evaluate whether the net health outcome improves with handheld radiofrequency spectroscopy compared with standard intraoperative surgical margin evaluation, including histologic techniques. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might impact this review are listed in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02774785</td>
<td>Reducing Re-excisions After Breast Conserving Surgery: A Randomized Controlled Trial Comparing the MarginProbe Device in Addition to Standard Operating Procedure Versus Standard Operating Procedure Alone in Preventing Re-excision</td>
<td>460</td>
<td>Dec 2018 (recruiting)</td>
</tr>
<tr>
<td>NCT02406599a</td>
<td>MarginProbe® System U.S. Post-Approval Study Protocol CP-07-001</td>
<td>440</td>
<td>March 2020</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.
Practice Guidelines and Position Statements

**National Comprehensive Cancer Network**

Current National Comprehensive Cancer Network guidelines for breast cancer (v.3.2018) do not include recommendations for intraoperative assessment of surgical margins using radiofrequency spectroscopy for ductal carcinoma in situ or invasive breast cancer.\(^{16}\)

**American Society of Breast Surgeons**

The most current version of the American Society of Breast Surgeons’ performance and practice guidelines for breast-conserving surgery (2015) mention that specimens should be submitted for margin assessment either intraoperatively or post-surgery, depending on each institution’s protocol. A recommendation for one margin assessment method over another was not made.\(^{17}\)

**Medicare National Coverage**

There is no national coverage determination.

**Regulatory Status**

In January 2013, MarginProbe® (Dune Medical Devices, Caesarea, Israel) was approved by the U.S. Food and Drug Administration through the premarket approval process as an adjunctive diagnostic tool for identification of cancerous tissue at the margins (≤1 mm) of the main ex vivo lumpectomy specimen after primary excision. It is indicated for intraoperative use in conjunction with standard methods (eg, intraoperative imaging and palpation) for patients undergoing lumpectomy for previously diagnosed breast cancer. Food and Drug Administration product code: OEE.

**References**


<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>08/01/19</td>
<td>New policy, approved July 9, 2019. Add to Surgery section. This policy was previously archived but is now being reinstated. Policy created with literature review through</td>
</tr>
</tbody>
</table>

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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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