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

#### Service

<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>
</thead>
<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>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

### 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 ductal carcinoma in situ (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. The 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.3.2019) do not include recommendations for intraoperative assessment of surgical margins using radiofrequency spectroscopy for ductal carcinoma in situ or invasive breast cancer.\(^{17}\)


(ii) NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

American Society of Breast Surgeons

In 2015, the most current version of the American Society of Breast Surgeons performance and practice guidelines for breast-conserving surgery mention that specimens should be submitted for margin assessment either intraoperatively or post-surgically, depending on each institution's protocol. A recommendation for 1 margin assessment method over another was not made.\(^{18}\)

In 2017, the American Society of Breast Surgeons issued a consensus guideline for breast cancer lumpectomy margins, providing an algorithm for re-excision surgery after lumpectomy or breast conservation for invasive or in-situ breast cancer. Margin definitions and treatment recommendations are based on inked specimen edges and do not include recommendations for the intraoperative assessment of surgical margins via radiofrequency spectroscopy.\(^{19}\)

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


### History

<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 January 2019. Handheld radiofrequency spectroscopy for intraoperative assessment of surgical margins during breast-conserving surgery is considered investigational.</td>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2020 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination Is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
• Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  • Qualified sign language interpreters
  • Written information in other formats (large print, audio, accessible electronic formats, other formats)
• Provides free language services to people whose primary language is not English, such as:
  • Qualified interpreters
  • Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera 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:
Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the 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, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

Email AppealsDepartmentInquiries@Premera.com

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.

Call 800-722-1471 (TTY: 800-842-5357).

Arabic (Arabic):
يحيى هذا الإشعار معلومات هامة. قد يحتوي هذا الإشعار معلومات مهمة تتعلق بطلبي أو طلبك. قد تكون هناك تأثيرات على صحتك أو صحة شخص آخر من عائلتك أو أي شخص آخر. 

Premera Blue Cross

Italian (Italian):
Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente.

Chinese (Chinese):
本通知有重要的讯息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知可能有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357).

Oromo (Cushite):

French (French):

German (German):

Hmoob (Hmong):
Tsab ntawv tshaj xo no muaj cov ntsiib lus tsem ceeb. Tey zaum tsab ntawv tshaj xo no muaj cov ntsiib lus tsem ceeb txog kog daim ntawv thov kv pow los yoy kog kvv pow cbu pow los ntsawm Premera Blue Cross. Tey zaum muaj cov hnhv tsem ceeb lus cov pow rau hauv daim ntawv no. Tey zaum kog jyu pow tau ua qee yam pow kog pow cib hauv daim ntawv no. Tey zaum kog jyu pow tau ua qee yam pow kog pow cib hauv daim ntawv no. Tey zaum kog jyu pow tau ua qee yam pow kog pow cib hauv daim ntawv no.

Kreyòl Ayisyen (Creole):
Avi sila a gen Enfòmasyon Enpòtan Ilayand. Avi sila a kapab genyên enfòmasyon enpòtan konsënan aplikasyon w lan oswa konvèti asirans lan atravé Premera Blue Cross. Kapab genyên dat ki enpòtan nan avi sila a. Ou ka gen pou pran kék aksyon avan sèten dat limit pou ka kwele kouvètì asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou yonè enfòmasyon sa a ak asisants nan lang ou pale a, san ou pa gen pou pè yeu pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Kushite (Oromo):
Daytoy a Pakdaar ket naglaan iti Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket naglaan iti napateg nga impormasion maijanggeppi iti aplikasyonny weno coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petsa iti daytoy a pakdaar. Mabalin nga adda rumbeg na aramideno nga addang sakbay dagiti particular a naituding nga aldaw tapno mapagtalaidooy ni coverage ti salun-atyo weno tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagasao nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Ilocano (Ilocano):
Daytoy a Pakdaar ket naglaan iti Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket naglaan iti napateg nga impormasion maijanggeppi iti aplikasyonny weno coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petsa iti daytoy a pakdaar. Mabalin nga adda rumbeg na aramideno nga addang sakbay dagiti particular a naituding nga aldaw tapno mapagtalaidooy ni coverage ti salun-atyo weno tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagasao nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).
This notice contains important information. You may need to take action within a certain time frame to keep your health coverage. This notification may contain important dates.

800-722-1471 (TTY: 800-842-5357)