Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

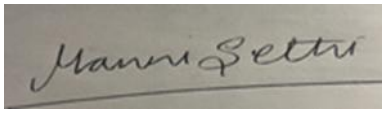
Plan: AmeriHealth Caritas Pennsylvania & Keystone First	Submission Date:11/1/2025
Policy Number: CCP.1430	Effective Date:12/1/2019 Revision Date:10/1/2025
Policy Name: MarginProbe®	

Type of Submission:

☐ New Policy	☒ Prior Authorization Policy
☒ Revised Policy*	☐ Base Policy
☐ Annual Review- no revisions	☒ Experimental/Investigational Policy
	☐ Statewide PDL
	☐ Other:

*All revisions to the policy must be highlighted using track changes throughout the document.

Please provide any clarifying information for the policy below:

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	Signature of Authorized Individual: 

Keystone First
Family of Health Plans

MarginProbe®

Clinical Policy ID: CCP.1430

Recent review date: 10/2025

Next review date: 2/2027

Policy contains: Breast cancer, lumpectomy, MarginProbe; radiofrequency spectroscopy; tumor margin.

Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First's clinical policies are not guarantees of payment.

Coverage policy

MarginProbe® (Dune Medical Devices Inc., Framingham, Massachusetts, now distributed by Dilon Technologies, Inc., Newport News, Virginia) is investigational/not clinically proven and, therefore, not medically necessary for increasing the efficacy of a breast cancer lumpectomy procedure.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Standard tissue histopathology assessment.

Background

Early-stage breast cancer is defined as having a tumor size of 4 cm or less, with three or fewer positive nodes. In women with early breast cancer, 70% elect lumpectomy, a type of breast-conserving surgery (Agarwal, 2014). Lumpectomy, combined with subsequent radiation, is as effective or more effective in the treatment of early-stage breast cancer as mastectomy alone or mastectomy with radiation and is associated with reduced mortality compared with these other procedures (Agarwal, 2014; Kurian, 2014).

The efficacy of lumpectomy is achieved by attaining tumor-free margins around the surgical resection site. When tumor-free margins are not obtained, additional surgery to re-excise breast tissue is often necessary. Histologic examination of excised tissues after completion of surgery is the sole method of ascertaining whether clear margins were achieved. The evaluation of surgical margins during surgery through methods such as specimen imaging, frozen section pathology, or touch print cytology is either not sufficiently accurate or not feasible due to

unavailability or the length of time needed for testing. Thus, intraoperatively determining whether surgical margins are clear would enhance the efficacy of the primary lumpectomy procedure.

The MarginProbe System is a handheld radiofrequency spectroscopy diagnostic device designed to intraoperatively identify cancerous tissue at the margins of excision specimens, along with standard methods (such as intraoperative imaging and palpation), in patients undergoing breast lumpectomy for previously diagnosed breast cancer. It is not intended to replace standard tissue histopathology assessment (Dilon Technologies, 2022).

MarginProbe uses radiofrequency spectroscopy to measure the dielectric properties of tissue with which it comes in contact. The handheld probe is applied to a small area of the excised lumpectomy specimen within 20 minutes of removal. It analyzes whether the margins are likely malignant or benign based on the different signals produced by cancer cells as compared to normal breast tissues. 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. MarginProbe was granted expedited review status as the first device of its kind, and received premarket approval from the U.S. Food and Drug Administration in 2012 (U.S. Food and Drug Administration, 2022).

Findings

Across guidelines, systematic reviews, and meta-analyses, the evidence base converges on 3 points relevant to intraoperative use of bioimpedance-type devices that measure tissue dielectric properties, such as radiofrequency spectroscopy with MarginProbe. First, guideline bodies prioritize margin definitions and established intraoperative methods, and they do not endorse bioimpedance devices for routine use. Second, quantitative syntheses consistently show that adjunctive intraoperative strategies can lower positive-margin and re-excision rates, but diagnostic accuracy varies by modality; frozen section analysis and cytology are most accurate, while radiofrequency spectroscopy shows only moderate sensitivity with comparatively low specificity and a higher false-positive burden that can prompt additional tissue removal. Third, reductions in re-excision have not translated into demonstrated improvements in local recurrence or survival, and study heterogeneity, modest sample sizes, and variable protocols limit causal inference about long-term oncologic benefit.

Guidelines

Current guidelines emphasize pathology-defined margin thresholds and rely on individualized surgical judgment rather than recommending specific intraoperative technologies. For invasive breast cancer, a negative margin is defined as "no ink on tumor," meaning no cancer cells are present at the inked surface on microscopic examination (National Comprehensive Cancer Network, 2025). For ductal carcinoma in situ treated with whole-breast radiation, the standard is a margin of at least 2 mm, which is associated with lower ipsilateral breast tumor recurrence compared with positive margins (Morrow, 2016).

Guideline bodies have not endorsed intraoperative margin assessment devices such as those based on bioimpedance or radiofrequency spectroscopy. Both the National Comprehensive Cancer Network (2025) and

the consensus guideline from the Society of Surgical Oncology, American Society for Radiation Oncology, and American Society of Clinical Oncology (Morrow, 2016) base their recommendations on final pathological evaluation, without reference to devices like MarginProbe.

The approach to emerging technologies has remained consistent. In 2015, the American Society of Breast Surgeons acknowledged randomized trial evidence showing fewer reoperations with MarginProbe but excluded such devices from its consensus toolbox pending further study (Landercasper, 2015; Schnabel, 2014). Their 2024 margin resource guide reaffirmed “no ink on tumor” for invasive disease and a 2 mm margin for ductal carcinoma in situ with radiation, listing bioimpedance among investigational technologies rather than accepted standards (American Society of Breast Surgeons, 2024). Across all guidelines, surgical judgment remains central when margins are negative but under 2 mm in ductal carcinoma in situ (Morrow, 2016; American Society of Breast Surgeons, 2024).

Systematic reviews

Earlier systematic reviews focused on technique performance and general intraoperative approaches. Butler-Henderson, 2014 reviewed intraoperative margin techniques and concluded that while several methods can reduce second operations, more large, rigorous studies were required before firm conclusions could be drawn (Butler-Henderson, 2014). Gray, 2018 synthesized contemporary intraoperative strategies and graded recommendations; the authors highlighted that techniques differ in accuracy, logistics, and downstream effects on positive margins and tissue volume, and they cautioned about relatively high false-positive rates with radiofrequency spectroscopy that can increase excised volume (Gray, 2018). St. John, 2017 conducted a meta-analysis of 35 studies and reported that only 1 study evaluated MarginProbe, with sensitivity and specificity of 71.4% and 67.7%; participant totals were not aggregated because most studies reported margin- or specimen-level data rather than patient-level counts (St. John, 2017).

A 2024 systematic review of 12 studies (N = 2,680) centered on MarginProbe reported a mean relative reduction in re-excision of 54.68% with use of radiofrequency spectroscopy, with typical device sensitivity near 69% and specificity near 63%, and no consistent increase in total tissue volume excised or decrement in cosmesis. The review also noted the heterogeneity of designs, frequent single-center experiences, and the likelihood that false positives drive additional cavity shaves in some settings (Rossou, 2024).

A 2024 diagnostic-accuracy systematic review and meta-analysis of 61 studies reported that cytology and frozen section analysis had the highest pooled accuracy; optical spectroscopy performed well; and MarginProbe—represented by 3 small studies—showed pooled sensitivity of 0.73 and pooled specificity of 0.53. The MarginProbe subset comprised 3 studies (N = 165) within the 61-study corpus (Dowling, 2024).

Meta-analyses

A 2023 meta-analysis of 10 studies (N = 2,335) comparing MarginProbe to historical controls reported an overall relative reduction in re-excision of 0.49, with a 95% confidence interval of 0.38 to 0.64. Local recurrence was not evaluated. Small sizes and heterogeneity of surgical techniques, tumor types, and margin protocols limited firm conclusions about care management or patient outcomes (Wang, 2023).

A 2025 meta-analysis of randomized and prospective trials across 6 randomized comparisons (N = 4,968) found that intraoperative margin optimization strategies, including MarginProbe-assisted assessment, reduced re-excisions (odds ratio 0.54, 95% confidence interval 0.32 to 0.90) and positive margins (odds ratio 0.40, 95% confidence interval 0.22 to 0.73), without differences in local recurrence or overall survival. This pattern indicates a consistent surgical benefit, with uncertain impact on oncologic endpoints (Mirza, 2025).

The 2024 diagnostic-accuracy meta-analysis further contextualizes these findings: while several modalities can reduce re-excisions, radiofrequency spectroscopy's moderate sensitivity and lower specificity mean more false positives than frozen section analysis or cytology, which may increase cavity shaving, even as re-excisions decline (Dowling, 2024).

Other evidence

Randomized evidence and prospective cohorts converge on margin clearance trade-offs. In a randomized trial with 596 participants comparing standard lumpectomy to standard lumpectomy plus MarginProbe, the device arm had lower false-negative rates but higher false-positive rates. Positive margins on the main specimen were resected more often with the device, and re-excision occurred in 19.8% versus 25.8% in controls, with no long-term recurrence data (Schnabel, 2014; ClinicalTrials.gov, 2014). Observational series generally show lower re-excisions after device adoption: 9.9% versus 25.8% in historical controls in a cohort of 165 patients (Sebastian, 2015); a 14.6% absolute reduction across 150 patients in a prospective clinical study with larger effects in intraductal and invasive lobular histologies (Blohmer, 2016); 6.6% versus 15.1% in a 137 versus 199 comparison that also reported a 32% reduction in overall tissue volume removed (Coble, 2017); and a single-center pre–post cohort of 240 consecutive cases with a 10-point decrease in re-lumpectomy (5.8% versus 15.8%) without an increase in total tissue volume (Kupstas, 2018).

One prospective single-surgeon study with 60 cases reported sensitivity and specificity near 67% and 60% and no significant change in re-excision (LeeVan, 2020). Evidence specific to neoadjuvant settings is mixed but suggests potential benefit: a cohort of patients receiving neoadjuvant chemotherapy and breast-conserving surgery reported re-excisions of 6% with device use versus 31% with gross assessment (Cen, 2021); another series of 66 patients concluded that combining radiofrequency spectroscopy with intraoperative pathology reduced positive margins more than pathology alone (Qafiti, 2022). A prospective analysis of 48 patients found that device readings would have prevented only 2 re-excisions among 12 patients who required re-excision, highlighting modest incremental value over standard assessment in that practice (Hoffman, 2022).

In 2025 we reorganized the findings section and incorporated five new evidence sources: an American Society of Breast Surgeons resource guide (ASBrS, 2024), a systematic review (Rossou, 2024), a meta-analysis (Mirza, 2025), the updated National Comprehensive Cancer Network guideline (NCCN, 2025). No policy changes were warranted.

References

On September 10, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "breast cancer," "lumpectomy," "margin assessment," "breast neoplasms (MeSH)," "MarginProbe," and "radiofrequency spectroscopy." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

10/2019: initial review date and clinical policy effective date: 12/2019

11/2020: Policy references updated.

11/2021: Policy references updated.

11/2022: Policy references updated.

10/2023: Policy references updated.

10/2024: Policy references updated.

10/2024: Policy references updated.