Radiofrequency Ablation of Tumors Outside the Liver

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INSTRUCTIONS FOR USE: Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

SCOPE: Providence Health Plan, Providence Health Assurance, and Providence Plan Partners as applicable (referred to individually as "Company" and collectively as "Companies").

PLAN PRODUCT AND BENEFIT APPLICATION

☒ **Commercial** ☒ **Medicaid/OHP*** ☐ **Medicare****

*Medicaid/OHP Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

**Medicare Members

This *Company* policy may be applied to Medicare Plan members only when directed by a separate *Medicare* policy. Note that investigational services are considered **"not medically necessary"** for Medicare members.

COVERAGE CRITERIA

Note:

- This policy does not address liver tumors (primary or metastatic). Please refer to the Medical Policy "Liver Tumor Treatment (All Lines of Business Except Medicare)" for further information.
- This policy is specific to radiofrequency ablation only. All other ablative procedures not addressed by this policy may be considered medically necessary unless otherwise stated by a separate medical policy.

Medically Necessary

I. Radiofrequency ablation may be considered **medically necessary** to treat tumors when one or more of the following criteria are met (A.-F.):

A. Thyroid carcinoma with any of the following subtypes (1.-7.):
1. Papillary; **or**
2. Medullary; **or**
3. Hurthle Cell; **or**
4. Follicular carcinoma with locoregional recurrence; **or**
5. Structurally persistent/recurrent locoregional or distant metastatic disease in papillary, Hurthle Cell or follicular carcinoma when not amenable to radioactive iodine (RAI) therapy; **or**
6. Bone metastases if symptomatic; **or**
7. Bone metastases if asymptomatic in weight-bearing sites; **or**

B. Kidney cancer in patients with either of the following (1.-2.):
1. Clinical stage T1 lesions; **or**

2. Relapsed or Stage IV cancer; **or**

C. Non-small cell lung cancer for patients with both of the following (1.-2.)
   1. Patient has any of the following (a.-c.):
      a. Stage 1A NCSLC; **or**
      b. Multiple lung cancers; **or**
      c. Locoregional recurrence of symptomatic local thoracic disease; **and**
   2. Both of the following are met (a.-b.):
      a. Tumor is no bigger than 3cm in size; **and**
      b. Patient is not receiving stereotactic ablative radiotherapy or definitive radiotherapy; **or**

D. Pain palliation in patients with osteolytic bone metastases who has failed or is a poor candidate for standard treatments (e.g. radiation or opioids); **or**

E. Osteoid osteomas that cannot be managed successfully with medical treatment (e.g. non-steroidal anti-inflammatory drugs); **or**

F. Colon cancer when either of the following criteria are met (1.-2.):
   1. Disease is metastatic to the lung; **or**
   2. Patient is not a candidate for resection.

Note: This policy does not address colon cancer tumors metastatic to the liver. Please refer to the Medical Policy "Liver Tumor Treatment (All Lines of Business Except Medicare)" for further information.

Not Medically Necessary

II. Radiofrequency ablation is considered **not medically necessary and not covered** for the treatment of tumors other than liver tumors that do not meet the criterion I. above including but not limited to breast tumors (e.g. malignant breast cancer and breast fibroadenomas).

III. Ultrasound-guided radiofrequency ablation (e.g., Acessa™, Sonata®) is considered **not medically necessary and not covered** for the treatment of symptomatic uterine fibroids.

Link to Evidence Summary

POLICY CROSS REFERENCES

Liver Tumor Treatment, MP151

The full Company portfolio of current Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

BACKGROUND

Radiofrequency Ablation (RFA)

Radiofrequency ablation (RFA) of breast tumors is currently being investigated either as an alternative to excision, or as a pre- or post-operative adjunct to surgery. RFA is based on the local production of heat through the application of electric alternating current flowing from the tip of an uninsulated electrode. The tissue heats resistively in the area that is in contact with the electrode tip, and the heat is transferred conductively to more distant tissues.[1]

One limitation of RFA is that as soon as the treatment is initiated, the region surrounding the target lesion becomes highly echogenic, completely obscuring the tumor, making it difficult to monitor and control the ablation procedure. More importantly, the amount of pain associated with high temperatures elicited during RFA is not trivial, requiring carefully designed and applied anesthesia if general anesthesia has been avoided.[1] Furthermore, RFA can cause burning of the skin or damage to muscle, possibly limiting use in patients with tumors near the skin or chest wall.

REGULATORY STATUS

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Approval or clearance by the Food and Drug Administration (FDA) does not in itself establish medical necessity or serve as a basis for coverage. Therefore, this section is provided for informational purposes only.

WOMEN'S HEALTH AND CANCER RIGHTS ACT (WHCRA) OF 1998 STATEMENT

The Women's Health and Cancer Rights Act (WHCRA) of 1998 provides protections to individuals who have opted to undergo breast reconstruction in connection with a mastectomy. Under the WHCRA, coverage is provided for all stages of breast reconstruction for both the affected breast (the breast undergoing the mastectomy procedure) and the contralateral breast (for symmetry) and breast prostheses, as well as treatment of complications caused by the mastectomy, such as lymphedema. While the criteria in this policy are primarily based on Medicare guidance, in accordance with the WHCRA, Company coverage may exceed Medicare coverage for items or services required to treat conditions that are the direct result of a mastectomy.

CLINICAL EVIDENCE AND LITERATURE REVIEW

EVIDENCE REVIEW

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of radiofrequency ablation for tumors outside the liver. Below is a summary of the available evidence identified through December 2022.

Thyroid Cancer

- In 2021, Cho and colleagues conducted a systematic review and meta-analysis of five-year outcomes of thermal ablation for papillary thyroid microcarcinoma.[2] In total, 3 studies (n=207) were included for review. No local tumor recurrence, lymph node metastasis, distant metastasis or delayed surgery were reported during a mean pooled 67.8-month follow-up. The pooled mean major complication rate was 1.2%, with no reported life-threatening or delayed complications. New tumors in the remaining thyroid gland were successfully treated by repeat thermal ablation in four patients.

- In 2020, Choi and colleagues conducted a systematic review of thermal ablation techniques for the treatment of primary papillary thyroid microcarcinoma.[3] A total of 11 studies of radiofrequency-, laser-, and microwave-ablation were included for review (n=715). There was significant between-study heterogeneity for complete disappearance, mean volume reduction, and volume reduction rate. A subgroup analysis showed heterogeneity of the complete disappearance proportion among the treatment modality. The pooled estimates of complete disappearance, mean volume reduction, and volume reduction rate were 57.6%, 73.5mm^3, and 98.1%, respectively. RFA showed the highest mean volume reduction rate (99.3%), followed by MWA (95.3%) and LA (88.6%). The pooled proportions of overall and major complications were 3.2% and 0.7%, respectively.

Benign Thyroid Tumors (Nodules)

- In 2021, Monpeyssen and colleagues published a systematic review of RFA for the treatment of benign thyroid nodules.[4] Seventeen included studies addressed RFA for the treatment of benign solid (nonfunctioning or autonomous) thyroid nodules with at least 18 months of follow-up. At 12- 15 months post-procedure, the volume reduction rate was 67% to 75% from a single procedure and 93.6% for nodules that received multiple ablations. The 12-month regrowth rate was reported between 0% and 34%.

- In 2020, Cho and colleagues reported a systematic review of the efficacy of thermal ablation (RFA and laser ablation) for the treatment of benign thyroid nodules.[5] The analysis demonstrated long-term maintenance (up to 36 months) of volume reduction. Further, RFA was found to be superior to laser ablation. The volume reduction rate for RFA at last follow up was 92.2%, whereas in the laser ablation group, the volume reduction rate peaked at 12 months (52.3%) and was at 43.3% at last follow up.

- In 2019, Trimboli and colleagues conducted a systematic review and meta-analysis on the efficacy of thermal ablation for benign non-functioning solid thyroid nodules.[6] Twelve studies per therapy were identified addressing RFA and laser ablation, with three RCTs on RFA and four

on laser ablation. The remainder were prospective and retrospective cohort studies. Overall there was high heterogeneity. Only studies with six months or longer follow-up were included and median follow-up was 12 months. The primary outcome was the volume reduction rate at 6, 12, 24, and 36 months. The volume reduction rate for the RFA group was 68%, 75%, and 87%, respectively, with insufficient 36-month reporting for analysis. The volume reduction rate for the laser ablation group was 48%, 52%, 45%, and 44%, respectively.

- In 2014, Fuller and colleagues conducted a systematic review and meta-analysis of studies on RFA for benign thyroid tumors.[7] Nine studies comprising 306 treatments were included for review. After RFA, statistically significant improvements were reported in nodule size reduction (29.77 mL), combined symptom improvement and cosmetic scores on the 0 to 6 scale (mean, -2.96) and withdrawal from methimazole. Twelve adverse events were reported, two of which were considered significant but did not require hospitalization

Kidney Cancer

- In 2019, Uhlig and colleagues conducted a systematic review and meta-analysis, comparing oncologic, perioperative, and functional outcomes for partial nephrectomy (PN) with outcomes for various ablative techniques, including RFA and others, for small renal masses (mean diameter=2.53 to 2.84 cm).[8] They identified 47 moderate-quality studies, mostly retrospective, published from 2005 to 2017, including one RCT. A total of 24,077 patients were included, of whom 15,238 received PN and 1,877 received RFA. The network meta-analysis used PN as the reference point. Cancer-specific mortality and local recurrence were calculated as incidence rate ratio. According to the meta-analysis, for RFA and PN, respectively, cancer-specific mortality was 2.03 and 1.00 (95% CI 0.81 to 5.08), local recurrence was 1.79 and 1.00 (95% CI 1.16 to 2.76), complications OR was 0.89 and 1.00 (95% CI 0.59 to 1.33), and renal function decline (mean difference in glomerular filtration rate) was 6.49 and 0.00 (95% CI 2.87 to 10.10). The overall results indicated that PN had better overall survival (OS) and local control over ablative techniques, but it was not significantly better for cancer-related mortality. In addition, ablation had fewer complications and better renal function outcomes. Across the studies included, patients treated by PN tended to be younger with less comorbidity compared with patients receiving thermal ablation—a consideration when assessing the outcomes for survival and local control.

- In 2019, Favi and colleagues conducted a systematic review, including a descriptive summary of ablative therapy for renal allograft tumors.[9] The 28 studies that met inclusion criteria assessed RFA (n=78), cryoablation (n=15), MWA (n=3), HIFU (n=3), and irreversible electroporation (n=1) for mainly papillary renal cell carcinoma (RCC) and clear cell RCC. All but two neoplasms were stage T1a N0 M0. In this population, three cases of primary treatment failure, a single case of recurrence, and no cancer-related deaths were reported. Complication rate was mostly below 10% and graft function remained stable in the majority of patients. No meta-analyses were performed and due to the limited sample size the authors were not able to determine a clear benefit of one procedure over the others.

- In 2014, Wang and colleagues published a meta-analysis of 145 studies published through July 2013 comparing effectiveness and complications of radiofrequency ablation and partial nephrectomy (PN) for treatment of stage T1 renal tumors.[10] The rate of local progression was greater with RFA than laparoscopic/robotic or open partial nephrectomy (4.6%, 1.2%, 1.9%, respectively; p<0.001.) RFA had more frequent minor complications than laparoscopic/robotic or open partial nephrectomy (13.8%, 7.5%, 9.5%, respectively; p<0.001). However, the rate of major complications was greater with open partial nephrectomy than laparoscopic/robotic partial nephrectomy or RFA (7.9%, 7.9%, 3.1%, respectively, p<0.001). Several limitations to this meta-analysis were discussed in the article. These included the limited follow-up duration of the included studies and the unavailability of the original study data. Despite the limitations, the data was sufficient for the authors to conclude that both RFA and PN were viable in terms of short-term outcomes and low complication rates. RFA showed a higher risk of local tumor progression but lower complication rates.

Non-Small Cell Lung Cancer

- In 2021, Chan and colleagues published a systematic review and meta-analysis of CT-guided percutaneous ablation for stage 1 NSCLC.[11] A total of eight studies with 792 patients met inclusion criteria. Statistically significant differences were identified for one- and two-year disease-free survival, favoring surgery OR 2.22, 95% CI 1.14 to 4.34; OR 2.60, 95% CI 1.21 to 5.57 respectively). No statistically significant differences between groups were identified for one- to five-year OS or cancer-specific survival or three- to five-year disease-free survival. According to the subgroup analysis, there was no statistically significant difference in OS between lobectomy and microwave ablation but patients treated with sublobar resection (wedge resection or segmentectomy) had significantly longer one- and two-year OS versus RFA.

- In a 2012 review of evidence from 16 studies, Bilal compared RFA to stereotactic ablative radiotherapy (SABR) in patients with inoperable early stage non-small cell lung cancer (NSCLC).[12] Authors found overall survival rates for RFA and SABR were similar in patients at one year (68.2 to 95% vs. 81 to 85.7%) and three years (36 to 87.5% vs. 42.7 to 56%). However, survival rates at five years were lower with RFA (20.1 to 27%) than with SABR (47%). Caution must be used in interpreting these findings drawn from comparisons of results from uncontrolled, case series and retrospective reviews.

- In 2011, Chan and colleagues conducted a systematic review that reported low quality evidence consisting of nonrandomized observational case series with no control group. The review included 46 studies with a total of 2,905 ablations in 1,584 patients.[11,13] The mean tumor size of 2.8 ± 1.0 cm. Local recurrence occurred in 282 cases (12.2%) and ranged from 0% to 64% as reported in 24 studies. Overall survival rates ranged from 25% to 100% with a mean of 59.4% as reported in 21 studies with a mean of 17.7 ± 12.4 months follow-up. The mean cancer-specific survival rate was 82.6% as reported in 24 studies with a range of 55% to 100% with a mean of 17.4 ± 14.1 months followup. Mean overall morbidity was 24.6% and most commonly included pneumothorax, pleural effusion and pain. Mortality related to the RFA procedure was 0.21% overall. The authors concluded RFA for the treatment of lung tumors demonstrated promise but

that higher quality studies comparing RFA to other local treatment options "are urgently needed."

Osteoid Osteomas

In 2020, Lindquester and colleagues published a systematic review of various thermal ablation techniques for the treatment of osteoid osteomas.[14] Of the total of 36 studies that met inclusion criteria (n=1798), 32 evaluated RFA, three evaluated cryoablation, and one evaluated microwave ablation. The overall success rate, defined as all ablations minus technical failures, clinical failures, and recurrences, was 91.9% (95% CI 91 to 93%). The rates of technical failure, clinical failure, and recurrence were 0.3%, 2.1%, and 5.6%, respectively. Complications occurred in 2.5% (95% CI 1.9 to 3.3%) of patients.

Palliation of Pain from Bone Metastases

- In 2020, Mehta and colleagues published a systematic review and meta-analysis of RFA for painful osseous metastases.[15] A total of 14 studies with 426 patients met inclusion criteria. The median pain reduction at a median follow-up of 24 weeks post-RFA was 67% (R2=-0.66, 95% CI -0.76 to - 0.55, I2=71.24%). Pain scores were not significantly affected by primary tumor type or tumor size.

- In 2019, Gennaro and colleagues published a systematic review reported by assessed four percutaneous thermal ablation techniques for pain reduction in patients with bone metastases.[16] A total of eleven studies addressing RFA (n=3), MWA (n=1), cryoablation (n=2), and MRgFUS (n=5) were included (total n=364 patients). Mean pain reduction for all techniques combined ranged from 25 to 91% at four weeks and from 16 to 95% at 12 weeks. There were no complications in the MWA group while the MRgFUS group had the highest complication rate. Overall, the number of minor complications reported ranged from 0 to 59 and the number of significant adverse events ranged from 0 to 4.

Colon Cancer

No recent, high-quality clinical trials addressing RFA for the treatment of colon cancer (excluding liver metastases) were identified.

Breast Cancer

<u>Systematic Reviews</u>

In 2010, Zhao and Wu published the results of a systematic review of minimally invasive ablation techniques for the treatment of early-stage breast cancer, including nine small case series (n=5-34 patients) on RFA for small breast tumors (0.5-7.0cm diameter).[17] In most studies, tumor resection was performed immediately after RFA or up to four weeks post-RFA. Complete ablation rates of 76% to 100% were reported. Complication rates typically ranged from 0-7%, but one study reported muscle burns in 23% of patients. The reviewers conceded that the included studies were almost all feasibility or

pilot studies using different energy sources, patients, tumor characteristics and ablation settings; and they were conducted in research settings and not in clinical practice. The reviewers concluded that RFA for breast tumors was feasible but further studies with longer follow-up on survival rates and tumor recurrence were needed.

In 2010 Soukup et al., published the results of a systematic review that included 17 studies that evaluated RFA of breast lesions.[18] The reviewers concluded that RFA is emerging as a promising treatment, but comparison between studies was challenging due to the heterogeneity of treatment protocols between groups. Although minimal adverse effects and complications have been reported, the reviewers noted that incomplete tumor ablation remained a concern. In addition, the reviewers indicated that further studies are required to delineate suitable patients populations for successful RFA intervention (e.g., tumors <2 cm in diameter and at least 1 cm away from skin and chest wall). Regarding the use of RFA for benign breast tumors, the reviewers concluded that further research was required, since they were unable to identify any studies that evaluated the potential role of RFA in benign breast disease.

In 2016, Chen et al. reported results from a meta-analysis of clinical trials assessing the safety and efficacy of RFA for breast cancer, including 15 nonrandomized trials.[19] Of the 15 trials, eight studies reported that the tumor size was <2 cm in diameter, five studies reported <3 cm, and the remaining two studies reported <5 cm tumor diameter. Pooled analyses from 11 studies indicated a complete ablation rate of 89% (95% CI: 85-93%). Pooled analyses from five studies reported no local recurrence at a maximum follow-up of 76 months, however, one case of relapse and three cases of recurrence outside the ablation zone were observed in various studies. Pooled estimates from seven studies showed an incidence of skin burn was 4%. The reviewers concluded that large-scale, well-performed trials were needed, since included studies were limited by small sample size, lack of randomization and heterogeneity in patient selection.

In 2016, Peek et al. published the results of a systematic review that assessed clinical outcomes of minimally invasive ablative techniques for breast cancer, including RFA, high intensity focused ultrasound (HIFU), cryoablation, laser ablation, or microwave ablation.[20] RFA was used in 27 studies in a total of 657 patients (26 case series with 14-52 patients and one nonrandomized comparative study). Mean follow-up period of RFA was 28.1 ± 15.6 months. Of all the techniques reviewed, the highest rate of complete ablation was achieved with RFA (87.1 %, 491/564 patients. Short-term complication rate was 10.5% (58/555), the most frequent of which were skin burns (23), muscle burns (12) and blistering (5). RFA recurrence rate of 3.1% (9 patients out of 291) was reported at a mean follow-up time of 30.8 ± 16.9 months. The reviewers concluded that RFA demonstrated the most promise of any minimally invasive technique for the non-surgical treatment of breast cancer, but there are no RCTs that have evaluated this technique. The reviewers conceded that more RCTs comparing ablative techniques with surgical excision or with each other are needed with larger sample sizes to accurately evaluate differences between the techniques.

In 2017, Mauri et al. published the results of a systematic review that evaluated the technical success, technique efficacy, and complications of minimally invasive percutaneous ablation procedures of breast cancer, including 23 studies on RFA (N=577 lesions).[21] Only one comparative study was identified for

RFA, and this study is described in detailed below.[22] Other techniques evaluated in the review included microwaves, laser, cryoablation and high-intensity focused ultrasound (HIFU). Of all the techniques assessed, RFA had the highest technical success rate at 96% (95%CI 93-97%) and the second highest technique efficacy at 82% (95%CI 74-88%). Major and minor complication rates for RFA were lower than those of HIFU at 6% (95% CI 4–9%) and 8% (95% CI 5-13%), respectively. The reviewers concluded that while minimally invasive techniques may offer several advantages, that large, multicenter, RCTs comparing these approaches breast-conserving surgery are needed.

Randomized Controlled Trials (RCTs)

In 2018, Garcia-Tejedor and colleagues published results from a randomized phase 2 clinical trial evaluating RFA followed by surgical excision versus lumpectomy for the treatment of early stage breast cancer.[23] In total, 40 women with invasive ductal carcinoma of the breast were randomly assigned to review RFA or lumpectomy alone (control group). Outcomes of interest included margin status at surgery, tumor cell viability after RFA (with NADH and CK18 staining), cosmetic results, adverse advents, and local recurrences. Median follow-up was 25 months (range, 1-83 months). Investigators reported that NADH and CK18 staining demonstrated absence of tumor cell viability after RFA with at least of one the two staining techniques. Surgical margins were positive in 4 of the 20 RFA patients (p = 0.02). Limitations included the comparably higher rates of adverse events among RFA patients (8 of 20 vs. 1 of 20) and local infection (3 of 20 participants). Moreover, staining technique interpretations are subjective measures. The study was also under-powered as the target sample size for the main outcome was not reached. Larger RCTs with longer follow-up periods measuring clinical endpoints are needed to validate the authors' conclusion that RFA is effective for local tumor control.

Uterine Fibroids

- In 2022, Hayes conducted a systematic review assessing the safety and efficacy of the Acessa System for the treatment of uterine fibroids.[24] The literature search identified 6 clinical studies reported in 11 publications that evaluated the efficacy and safety of RFVTA with the Acessa System for treatment of symptomatic UF. The only comparator evaluated in the eligible studies was laparoscopic myomectomy (LM) (2 studies). Follow-up periods ranged from 3 months to 3 years.

  Evidence suggests that RFVTA generally resulted in statistically significant improvements from baseline in symptomatology. RFVTA did not result in any statistically significant differences in UF-related symptom severity or quality of life (QOL) compared with LM; however, comparative analyses were limited to 2 studies and were not always conducted statistically. Comparatively, 1 study performed a between-group analysis at 12 months and found no statistically significant differences between scores of the SF-36 Health Survey (SF-36) (RAND Corp.) among patients who received RFVTA or LM. Other evaluations demonstrated statistically significant improvements from baseline at 3 months (1 study) and 36 months (1 study). A third study found changes from baseline were statistically significant on the mental component of the SF-36 at 6 weeks but not 12 weeks; changes from baseline were statistically significantly improved on the physical component at both 6 and 12 weeks.

Time to return to normal activity ranged from 3.4 to 20.5 days for those treated with RFVTA. Differences were not assessed statistically in the only comparison of RFVTA and LM at the 3-month follow-up. Missed work varied among studies, ranging from 4.1 to 11 days. Compared with LM, treatment with RFVTA resulted in statistically significantly less days missed from work at 3 months according to 1 study (11.1 versus 18.5; P=0.0193). A second comparative study did not assess statistical differences between RFVTA (10 days) and myomectomy (17 days). Reductions in mean uterine volume were statistically significant in 2 studies, ranging from 24.3% to 41.8% at 12 months follow-up (P<0.05). Of these studies, 1 study also noted significant uterine reduction at 3 months (15.7%; P<0.001). A third study evaluated uterine volume reduction at 12 months and found no statistically significant difference from baseline (21% change from baseline; P=0.192).

Authors ultimately assigned a "C" rating (potential but unproven benefit.) In general, a low-quality body of evidence derived from 6 studies (published in 11 articles) suggests that RFVTA may result in improved symptoms and some improvements in general QOL assessments from baseline. Comparative effectiveness evidence comparing RFVTA with alternative uterine-sparing fibroid treatments is insufficient to draw conclusions. In general, statistically significant differences were not noted in most outcomes; however, comparative analyses were limited to 1 to 2 randomized controlled trials and were not always conducted statistically. No studies evaluated success in achieving pregnancy among women attempting to conceive after RFVTA. Three studies limited the eligible patient populations to women who had no desire to maintain fertility. Furthermore, the efficacy of RFVTA for fibroids of varying International Federation of Gynecology and Obstetrics classification was evaluated by only 1 study. Large, well-controlled trials comparing RFVTA with other minimally invasive, uterine-sparing procedures are needed especially evaluating the safety and effectiveness of RFVTA among women wishing to maintain fertility.

- In 2022, ECRI conducted a systematic review assessing the safety and efficacy of the Acessa System for the treatment of uterine fibroids.[25] In total, 1 SR with meta-analyses of comparative and observational studies (45 studies; n = 521,683) compared hysterectomy, uterine artery embolization, Acessa, and magnetic resonance-guided focused ultrasound (MRg-FUS) and reported on estimated blood loss, health-related QOL, symptom severity, reintervention, hospital readmission, and adverse events (AEs) in patients treated for symptomatic uterine fibroids. Three RCTs were also included for review. The systematic review is limited by its included studies' heterogeneity, but meta-analysis provides sufficient precision to support some conclusions. Also, of the 521,683 patients assessed in the systematic review, only 269 were treated with Acessa. The other studies are at risk of bias because of one or more of the following: small size, single-center focus, retrospective design, and lack of control groups. Large, multicenter RCTs comparing the Acessa RFA System with other RFA systems and uterine fibroid treatments and reporting on long-term outcomes (i.e., beyond two years) would be useful to support stronger conclusions and guide physician and patient choices. Evidence was determined to be "somewhat favorable" but that additional studies were necessary to confirm the safety of pregnancy after fibroid ablation with Acessa.

- In 2022, Hayes conducted a systematic review assessing the safety and efficacy of the Sonata System for the treatment of uterine fibroids.[26] The evidence base for this report includes 3 studies reported

in 7 articles. Of the eligible studies, 2 were prospective pretest/posttest studies and 1 was a case series. Follow-up ranged from 6 weeks to 5 years. All patients received transcervical RFA with the Sonata system. No study performed comparisons with clinical alternatives. Authors concluded that a very-low-quality body of evidence is insufficient to draw conclusions regarding the efficacy and safety of transcervical RFA for symptomatic UF. Compared with pretreatment status, the Sonata procedure was associated with statistically significant improvements in symptoms, quality of life, and fibroid volume. Due to the limited number of studies, consistency of results cannot be determined. Additional studies comparing the Sonata procedure with established treatments for UF are needed to determine whether the Sonata procedure provides meaningful clinical benefits relative to currently available options. All 3 studies excluded women with an intent for future fertility; however, 2 studies reported that 1 woman in each study conceived, carried to term, and delivered infants. A "D2" rating (insufficient evidence) was assigned.

- In 2022, ECRI conducted a systematic review assessing the safety and efficacy of the Sonata System for the treatment of uterine fibroids.[27] Despite evidence available from 2 systematic reviews and 1 pre-/post study, the studies assessed too few patients treated with Sonata to permit conclusions. Available studies, all at high risk of bias, suggest TFA with Sonata is safe and works as intended; it may work as well as other RFA procedures for fibroid ablation, reduce symptoms, and improve quality of life (QOL) up to 5-year follow-up in most women with symptomatic uterine fibroids. However, results need validation in controlled studies comparing Sonata with other uterine fibroid treatments. Studies are also needed that compare Sonata with other uterine-sparing treatments (e.g., laparoscopic or robotic myomectomy, laser ablation) and report on patient-centered outcomes (e.g., pain, symptom reduction, fibroid regrowth, sexual function, pregnancy). Studies were determined to be at high risk of bias due to 3 or more of the following: small sample size, retrospective design, single-center focus, high attrition, and lack of blinding, randomization, and control groups. Furthermore, studies in the systematic reviews included patients with different characteristics (e.g., age, symptoms; fibroid size, type, and number; symptom severity), and findings may not fully generalize across all patients. Authors concluded that evidence was inconclusive to support the efficacy of the Sonata procedure.

CLINICAL PRACTICE GUIDELINES

Thyroid Cancer

National Comprehensive Cancer Network (NCCN)

In 2022, the NCCN published guidelines addressing thyroid carcinoma (v.3.2022).[28] Authors stated that for papillary, Hurthle Cell, or follicular carcinoma with locoregional recurrence, surgery is preferred if resectable, and/or local therapies when available, including RFA. For the same subtypes of thyroid carcinoma, RFA may also be considered for structurally persistent/recurrent locoregional or distant metastatic disease when not amenable to RAI therapy. In addition, consideration of local therapies, including RFA, is recommended for bone metastases if symptomatic or asymptomatic in weight-bearing sites.

American Thyroid Association

The 2021 American Thyroid Association (ATA) Guidelines for Management Of Patients With Anaplastic Thyroid Cancer state that local therapy (including RFA) is a reasonable option for oligo-progressive metastases "to postpone the need to change otherwise beneficial systemic therapy."[29]

Kidney Cancers

National Comprehensive Cancer Network (NCCN)

In 2022, NCCN guidelines for kidney cancer (v.4.2022) indicate RFA is an ablative option for the treatment of kidney cancer in select patients with clinical stage T1 lesions, though ablative techniques have shown higher local recurrence rates than surgery and may require more treatments.[30] RFA is also an option for relapse or Stage IV and in select patients (e.g., elderly patients, others) with competing health risks.

American Urological Association (AUA)

In 2017, the AUA stated that "physicians should consider TA [thermal ablation] as an alternate approach for the management of cT1a renal masses <3 cm in size."[31] Authors also noted that "both radiofrequency ablation and cryoablation are options for patients who elect thermal ablation." Both are rated as "Conditional Recommendation; Evidence Level Grade C."

Non-Small Cell Lung Cancer

National Comprehensive Cancer Network (NCCN)

In 2022, the NCCN published guidelines addressing the treatment of non-small cell lung cancer (version 6.2022).[32] Authors stated that for medically operable disease, resection is the preferred local treatment modality (other modalities include SABR, thermal ablation such as radiofrequency ablation and cryotherapy. IGTA is listed as an option for the management of NSCLC lesions <3cm, and on patients with Stage 1A NSCLC, those who present with multiple lung cancers, or those with locoregional recurrence of symptomatic local thoracic disease.

Colon Cancer

National Comprehensive Cancer Network (NCCN)

In 2022, the NCCN published guidelines addressing the treatment of colon cancer (version 2.2022).[33] Addressing metastases, authors stated that "ablative techniques may be considered alone or in conjunction with resection. All original sites of disease need to be amenable to ablation or resection."[182] The guidelines also state that "ablative techniques can also be considered [in patients whose primary colon tumor was resected for cure when metastatic lung tumors are] unresectable and amenable to complete ablation" (category 2A). "

Breast Cancer

<u>American Society of Breast Surgeons (ASBS)</u>

The 2018 ASBS published a consensus guideline on the use of transcutaneous and percutaneous ablation for the treatment of benign and malignant tumors of the breast.[34] This guideline was evidence-based, but was not based on a systematic review of the evidence. The committee recommended the following for percutaneous treatment of benign and malignant breast tumors:

"Indications for percutaneous or transcutaneous ablative treatment of malignant tumors of the breast: At this time, there are no FDA approved percutaneous or transcutaneous ablative treatments for breast cancer. At the present time, cryoablation is approved for treatment of soft tissue malignancies. However, there is emerging data from clinical trials utilizing percutaneous ablative therapies for patients with early stage breast cancer without surgical excision. Techniques being evaluated include ablation by focused ultrasound, laser, cryotherapy, microwave, and radiofrequency. Percutaneous excision by vacuum-assistance is also being
Investigated."

Neither the National Comprehensive Cancer Network (NCCN) nor the American Society of Clinical Oncology guidelines address radiofrequency ablation (RFA) as a treatment option for breast cancer.

Uterine Fibroids

American College of Obstetrics and Gynecology

In 2021, the ACOG published guidelines addressing the management of symptomatic uterine Leiomyomas.[35] On the basis of level B evidence ("limited or inconsistent evidence"), authors wrote that laparoscopic radiofrequency ablation can be considered as a minimally invasive treatment option for the management of symptomatic leiomyomas in patients who desire uterine preservation and are counseled about the limited available data on reproductive outcomes.

Other Indications

Neither the National Comprehensive Cancer Network (NCCN) nor the American Society of Clinical Oncology guidelines address radiofrequency ablation (RFA) as a treatment option for osteoid osteomas or pain palliation for bone metastases.

EVIDENCE SUMMARY

Low-quality, but consistent evidence supports the use of radiofrequency ablation for the treatment of select patients with renal cell carcinoma, colon cancer, lung tumors, osteoid osteomas and thyroid tumors, as well as for use in pain palliation for bone metastases. Radiofrequency ablation is recommended for these indications by the latest National Comprehensive Cancer Network guidelines.

Evidence is insufficient, however, to support the use of RFA as a safe or effective treatment for other tumors not addressed above, including uterine fibroids, benign thyroid tumors and malignant breast tumors, whether used as an alternative or an adjunct to standard breast conserving surgery. One clinical

practice guideline endorsing the selective use of RFA for the treatment of uterine fibroids was identified, however, this recommendation was made on the basis on low-quality studies with inconsistent findings.

Long-term improvements in health outcomes have not been demonstrated and studies comparing RFA to other minimally invasive therapy techniques or to breast conserving surgery are lacking. Comparative studies, with long-term follow-up and adequately sized patient populations, should focus on whether RFA can provide local control and survival rates comparable with conventional breast conserving treatment. In addition, there is a paucity of evidence on the safety and effectiveness of RFA as a treatment for benign breast tumors such as fibroadenomas. Furthermore, current clinical practice guidelines recommend against the use of RFA for malignant breast tumors, but recommend RFA for fibroadenomas, despite the lack of evidence.

BILLING GUIDELINES AND CODING

CODES*		
CPT	0404T	Transcervical uterine fibroid(s) ablation with ultrasound guidance, radiofrequency
	19499	Unlisted procedure, breast
	20982	Ablation therapy for reduction or eradication of 1 or more bone tumors (eg, metastasis) including adjacent soft tissue when involved by tumor extension, percutaneous, including imaging guidance when performed; radiofrequency
	31641	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with destruction of tumor or relief of stenosis by any method other than excision (eg, laser therapy, cryotherapy)
	32998	Ablation therapy for reduction or eradication of 1 or more pulmonary tumor(s) including pleura or chest wall when involved by tumor extension, percutaneous, including imaging guidance when performed, unilateral; radiofrequency
	32999	Unlisted procedure, lungs and pleura
	45399	Unlisted procedure, colon
	50549	Unlisted laparoscopy procedure, renal
	50542	Laparoscopy, surgical; ablation of renal mass lesion(s), including intraoperative ultrasound guidance and monitoring, when performed
	50592	Ablation, one or more renal tumor(s), percutaneous, unilateral, radiofrequency
	58674	Laparoscopy, surgical, ablation of uterine fibroid(s) including intraoperative ultrasound guidance and monitoring, radiofrequency
	60699	Unlisted procedure, endocrine system
HCPCS	None	

***Coding Notes:**

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted

code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.

- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. Fornage BD, Hwang RF. Current status of imaging-guided percutaneous ablation of breast cancer. *AJR American journal of roentgenology.* 2014;203(2):442-448
2. Cho SJ, Baek SM, Na DG, Lee KD, Shong YK, Baek JH. Five-year follow-up results of thermal ablation for low-risk papillary thyroid microcarcinomas: systematic review and meta-analysis. *European radiology.* 2021;31(9):6446-6456
3. Choi Y, Jung S-L. Efficacy and safety of thermal ablation techniques for the treatment of primary papillary thyroid microcarcinoma: a systematic review and meta-analysis. *Thyroid.* 2020;30(5):720-731
4. Monpeyssen H, Alamri A, Ben Hamou A. Long-term results of ultrasound-guided radiofrequency ablation of benign thyroid nodules: state of the art and future perspectives—a systematic review. *Frontiers in endocrinology.* 2021:530
5. Cho SJ, Baek JH, Chung SR, Choi YJ, Lee JH. Long-term results of thermal ablation of benign thyroid nodules: a systematic review and meta-analysis. *Endocrinology and Metabolism.* 2020;35(2):339-350
6. Trimboli P, Castellana M, Sconfienza LM, et al. Efficacy of thermal ablation in benign non-functioning solid thyroid nodule: a systematic review and meta-analysis. *Endocrine.* 2020;67(1):35-43
7. Fuller CW, Nguyen SA, Lohia S, Gillespie MB. Radiofrequency ablation for treatment of benign thyroid nodules: systematic review. *The Laryngoscope.* 2014;124(1):346-353
8. Uhlig J, Strauss A, Rücker G, et al. Partial nephrectomy versus ablative techniques for small renal masses: a systematic review and network meta-analysis. *European radiology.* 2019;29(3):1293-1307
9. Favi E, Raison N, Ambrogi F, et al. Systematic review of ablative therapy for the treatment of renal allograft neoplasms. *World journal of clinical cases.* 2019;7(17):2487
10. Wang S, Qin C, Peng Z, et al. Radiofrequency ablation versus partial nephrectomy for the treatment of clinical stage 1 renal masses: a systematic review and meta-analysis. *Chinese Medical Journal.* 2014;127(13):2497-2503
11. Chan MV, Huo YR, Cao C, Ridley L. Survival outcomes for surgical resection versus CT-guided percutaneous ablation for stage I non-small cell lung cancer (NSCLC): A systematic review and meta-analysis. *European radiology.* 2021;31(7):5421-5433
12. Bilal H, Mahmood S, Rajashanker B, Shah R. Is radiofrequency ablation more effective than stereotactic ablative radiotherapy in patients with early stage medically inoperable non-small cell lung cancer? *Interactive cardiovascular and thoracic surgery.* 2012;15(2):258-265
13. Chan VO, McDermott S, Malone DE, Dodd JD. Percutaneous radiofrequency ablation of lung tumors: evaluation of the literature using evidence-based techniques. *Journal of thoracic imaging.* 2011;26(1):18-26

14. Lindquester WS, Crowley J, Hawkins CM. Percutaneous thermal ablation for treatment of osteoid osteoma: a systematic review and analysis. *Skeletal Radiology.* 2020;49(9):1403-1411
15. Mehta TI, Heiberger C, Kazi S, et al. Effectiveness of radiofrequency ablation in the treatment of painful osseous metastases: a correlation meta-analysis with machine learning cluster identification. *Journal of Vascular and Interventional Radiology.* 2020;31(11):1753-1762
16. Gennaro N, Sconfienza LM, Ambrogi F, Boveri S, Lanza E. Thermal ablation to relieve pain from metastatic bone disease: a systematic review. *Skeletal Radiology.* 2019;48(8):1161-1169
17. Zhao Z, Wu F. Minimally-invasive thermal ablation of early-stage breast cancer: a systemic review. *Eur J Surg Oncol.* 2010;36(12):1149-1155.https://www.ncbi.nlm.nih.gov/pubmed/20889281.
18. Soukup B, Bismohun S, Reefy S, Mokbel K. The evolving role of radiofrequency ablation therapy of breast lesions. *Anticancer Res.* 2010;30(9):3693-3697.https://www.ncbi.nlm.nih.gov/pubmed/20944155.
19. Chen J, Zhang C, Li F, et al. A meta-analysis of clinical trials assessing the effect of radiofrequency ablation for breast cancer. *Onco Targets Ther.* 2016;9:1759-1766.https://www.ncbi.nlm.nih.gov/pubmed/27042126.
20. Peek MC, Ahmed M, Napoli A, Usiskin S, Baker R, Douek M. Minimally invasive ablative techniques in the treatment of breast cancer: a systematic review and meta-analysis. *International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group.* 2016:1-12
21. Mauri G, Sconfienza LM, Pescatori LC, et al. Technical success, technique efficacy and complications of minimally-invasive imaging-guided percutaneous ablation procedures of breast cancer: A systematic review and meta-analysis. *European radiology.* 2017;27(8):3199-3210
22. Manenti G, Scarano AL, Pistolese CA, et al. Subclinical Breast Cancer: Minimally Invasive Approaches. Our Experience with Percutaneous Radiofrequency Ablation vs. Cryotherapy. *Breast care (Basel, Switzerland).* 2013;8(5):356-360
23. Garcia-Tejedor A, Guma A, Soler T, et al. Radiofrequency Ablation Followed by Surgical Excision versus Lumpectomy for Early Stage Breast Cancer: A Randomized Phase II Clinical Trial. *Radiology.* 2018;289(2):317-324
24. Hayes Inc. Laparoscopic Radiofrequency Volumetric Thermal Ablation (Acessa System; Halt Medical Inc.) for Treatment of Uterine Fibroids. https://evidence.hayesinc.com/report/htb.laparoscopic2839. Published 2022. Accessed 12/18/2022.
25. ECRI Institute. Acessa Radiofrequency Ablation System (Hologic, Inc.) for Treating Uterine Fibroids. https://www.ecri.org/components/ProductBriefs/Pages/13785.aspx. Published 2022. Accessed 12/17/2022.
26. Hayes Inc. Transcervical Radiofrequency Ablation with the Sonata System for Symptomatic Uterine Fibroids. https://evidence.hayesinc.com/report/htb.sonatafibroid4941. Published 2022. Accessed 12/18/2022.
27. ECRI Institute. Sonata Transcervical Ablation System (Gynesonics, Inc.) for Treating Uterine Fibroids. https://www.ecri.org/components/ProductBriefs/Pages/28216.aspx. Published 2022. Accessed 12/17/2022.
28. National Comprehensive Cancer Network. Thyroid Carcinoma - Version 3.2022 — November 1, 2022. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Published 2022. Accessed 12/14/2022.
29. Bible KC, Kebebew E, Brierley J, et al. 2021 American Thyroid Association Guidelines for Management of Patients with Anaplastic Thyroid Cancer. *Thyroid.* 2021;31(3):337-386

30. National Comprehensive Cancer Network. Kidney Cancer - Version 3.2023 — November 1, 2022. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Published 2022. Accessed 12/14/2022.
31. Campbell S, Uzzo RG, Allaf ME, et al. Renal Mass and Localized Renal Cancer: AUA Guideline. *J Urol.* 2017;198(3):520-529
32. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer - Version 6.2022 - December 2, 2022. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Published 2022. Accessed 12/14/2022.
33. National Comprehensive Cancer Network. Colon Cancer - Version 2.2022 — October 27, 2022. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Published 2022. Accessed 12/14/2022.
34. American Society of Breast Surgeons (ASBS). Consensus Guideline on the Use of Transcutaneous and Percutaneous Ablation for the Treatment of Benign and Malignant Tumors of the Breast. Approved 10/16/2018. https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-the-Use-of-Transcutaneous-and-Percutaneous-Methods-for-the-Treatment-of-Benign-and-Malignant-Tumors-of-the-Breast.pdf. Accessed 12/18/2020.
35. American College of Obstetrics and Gynecology. Management of Symptomatic Uterine Leiomyomas: ACOG Practice Bulletin, Number 228. *Obstetrics & Gynecology.* 2021;137(6):e100-e115.https://journals.lww.com/greenjournal/Fulltext/2021/06000/Management_of_Symptomatic_Uterine_Leiomyomas__ACOG.36.aspx.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
2/2023	Converted to new policy template.
4/2023	Expanded scope of policy to include other tumors outside the liver other than breast tumors. Added medical necessity criteria for certain indications.
8/2023	Interim update; added relevant unlisted code and resorted code table