

Radiofrequency Ablation (RFA) of Tumors Other than Liver

Effective: January 1, 2024

Next Review: November 2024

Last Review: December 2023

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Radiofrequency ablation kills cells using the heat produced by radiofrequency energy delivered into the tumor via a probe.

MEDICAL POLICY CRITERIA

Note: This policy does not address liver tumors (primary or metastatic). See Cross References.

- I. Radiofrequency ablation may be considered **medically necessary** to treat tumors when one or more of the following criteria are met:
 - A. Localized renal cell carcinoma that is no more than 4 cm in size when one or both of the following criteria are met:
 1. Preservation of kidney function is necessary (i.e., the patient has one kidney or renal insufficiency defined by a glomerular filtration rate (GFR) of less than 60 mL/min per m²) and standard surgical approach (i.e., resection of renal tissue) is likely to substantially worsen kidney function; or
 2. Patient is not considered a surgical candidate.

- B. Osteoid osteomas that are unresponsive to initial medical treatment.
 - C. To palliate pain in patients with osteolytic bone metastases who have failed or are poor candidates for standard treatments (e.g., radiation).
 - D. Isolated peripheral non-small cell lung cancer (NSCLC) lesion that is no more than 3 cm in size when both of the following criteria are met:
 - 1. Surgical resection or radiation treatment with curative intent is considered appropriate based on stage of disease, however, medical co-morbidity renders the individual unfit for those interventions; and
 - 2. Tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.
 - E. Malignant non-pulmonary tumor(s) metastatic to the lung that are no more than 3 cm in size when all of the following criteria (1. – 3.) are met:
 - 1. In order to preserve lung function when surgical resection or radiation treatment is likely to substantially worsen pulmonary status, or the patient is not considered a surgical candidate; and
 - 2. There is no evidence of extrapulmonary metastases; and
 - 3. The tumor is located at least 1 cm from the trachea, main bronchi, esophagus, aorta, aortic arch branches, pulmonary artery and the heart.
 - F. Renal angiomyolipomas when one or more of the following criteria are met:
 - 1. Symptomatic lesion (e.g., hemorrhage), or
 - 2. Asymptomatic lesion larger than 4 cm.
 - G. Benign thyroid nodules when the following criteria are met (1. – 2.):
 - 1. Nodule is symptomatic; and
 - 2. Nodule is confirmed as benign using fine needle aspiration (FNA)
- II. Ultrasound-guided radiofrequency ablation (e.g., Acessa™, Sonata®) may be considered **medically necessary** for the treatment of symptomatic uterine fibroids when there are significant clinical manifestations or findings attributable to fibroids, including one or more of the following:
- A. Abnormal uterine bleeding
 - B. Iron-deficiency anemia
 - C. Dyspareunia
 - D. Pelvic pain or pressure
 - E. Urinary or bowel dysfunction
- III. Radiofrequency ablation is considered **investigational** as a technique for ablating all other benign or malignant tumors other than liver tumors that do not meet the policy criteria above including but not limited to breast tumors, initial treatment of osteoid osteomas and painful bony metastases, and all primary or metastatic lung (pulmonary) tumors that do not meet medical necessity.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

LIST OF INFORMATION NEEDED FOR REVIEW

REQUIRED DOCUMENTATION

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

1. Specific description of the tumor(s) targeted for treatment including the following:
 - Tumor type (primary vs. metastatic; primary tumor type)
 - The location of tumor(s)
 - The number and size(s) of lesion(s) being treated
2. For requests for ultrasound-guided radiofrequency ablation for the treatment of symptomatic uterine fibroids, documentation of significant clinical manifestations or findings attributable to fibroids
3. Rationale for the determination that the patient is not a surgical candidate or the tumor is unresectable
4. Whether the goal of treatment is curative or palliative
5. Comorbidities and any contraindicated treatments (e.g., surgery; radiation therapy)
6. Prior treatments, if any, and tumor response
7. Documentation of whether this treatment is to preserve organ function

CROSS REFERENCES

1. [Radioembolization, Transarterial Embolization \(TAE\), and Transarterial Chemoembolization \(TACE\)](#), Medicine, Policy No. 140
2. [Cryosurgical Ablation of Miscellaneous Solid Tumors](#), Surgery, Policy No. 132
3. [Magnetic Resonance \(MR\) Guided Focused Ultrasound \(MRgFUS\) and High Intensity Focused Ultrasound \(HIFU\) Ablation](#), Surgery, Policy No. 139
4. [Microwave Tumor Ablation](#), Surgery, Policy No. 189
5. [Ablation of Primary and Metastatic Liver Tumors](#), Surgery, Policy No. 204

BACKGROUND

Radiofrequency ablation (RFA) was initially developed to treat inoperable tumors of the liver (see Cross References). Recently, studies have reported on the use of RFA to treat other tumors. For some of these, RFA is being investigated as an alternative to surgery for operable tumors. Well-established local or systemic treatment alternatives are available for each of these malignancies. The hypothesized advantages of RFA for these cancers include improved local control and those common to any minimally invasive procedure (eg, preserving normal organ tissue, decreasing morbidity, decreasing length of hospitalization).

Goals of RFA may include 1) controlling local tumor growth and preventing recurrence; 2) palliating symptoms; and 3) extending survival duration for patients with certain cancerous tumors. The effective volume of RFA depends on the frequency and duration of applied current, local tissue characteristics, and probe configuration (eg, single vs multiple tips). RFA can be performed as an open surgical procedure, laparoscopically or percutaneously, with ultrasound or computed tomography guidance.

Potential complications associated with RFA include those caused by heat damage to normal tissue adjacent to the tumor (e.g., intestinal damage during RFA of kidney), structural damage along the probe track (e.g., pneumothorax as a consequence of procedures on the lung), and secondary tumors (if cells seed during probe removal).

REGULATORY ISSUES

The U.S. Food and Drug Administration (FDA) issued the following statement September 24, 2008 concerning the regulatory status of radiofrequency ablation.^[1] “The FDA has cleared RF ablation devices for the general indication of soft tissue cutting, coagulation, and ablation by thermal coagulation necrosis. Some RF ablation devices have been cleared for additional specific treatment indications, including partial or complete ablation of nonresectable liver lesions and palliation of pain associated with metastatic lesions involving bone. The FDA has not cleared any RF ablation devices for the specific treatment indication of partial or complete ablation of lung tumors, citing lack of sufficient clinical data to establish safety and effectiveness for this purpose. The FDA has received reports of death and serious injuries associated with the use of RF ablation devices in the treatment of lung tumors.”

In 2012, the Acessa™ System (Acessa Health, formerly Halt Medical) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for percutaneous laparoscopic coagulation and ablation of soft tissue and treatment of symptomatic uterine fibroids under laparoscopic ultrasound guidance (K121858). The technology was previously approved in 2010, at which time it was called the Halt 2000GI™ Electrosurgical Radiofrequency Ablation System. In 2014, the ultrasound guidance system received marketing clearance from the FDA (K132744). FDA product code: GEI. In 2018, the third-generation Acessa™ ProVu System® was cleared for marketing by the FDA through the 510(k) process for use in percutaneous, laparoscopic coagulation and ablation of soft tissue, including treatment of symptomatic uterine fibroids under laparoscopic ultrasound guidance. (K181124). FDA product code: HFG.

In 2018, the Sonata® Sonography-Guided Transcervical Fibroid Ablation System (Gynsonics) was cleared for marketing by the FDA through the 510(k) process for diagnostic intrauterine imaging and transcervical treatment of symptomatic uterine fibroids (K173703). The Sonata system was previously known as Vizablate. FDA product codes: KNF, ITX, and IYO.

EVIDENCE SUMMARY

RENAL CELL CARCINOMA

BACKGROUND

Radical nephrectomy, partial nephrectomy, or nephron-sparing surgery remains the principal treatments of renal cell carcinoma (RCC).

RFA may be considered a treatment option when surgical excision is not an option such as the following:

- When preservation of renal function is necessary (e.g., in patients with marginal renal function, a solitary kidney, bilateral tumors)
- In patients with comorbidities that would render them unfit for surgery.

- In patients at high risk of developing additional renal cancers (as in von Hippel-Lindau disease).

SYSTEMATIC REVIEWS

Green (2023) published a systematic review that evaluated metastasis-directed ablative therapies in extracranial metastatic renal cell carcinoma.^[2] 18 prospective and matched-pair case control studies of RFA, cryotherapy, microwave ablation, and stereotactic body radiotherapy (SBRT) in metastatic renal cell carcinoma were included. Most were single-arm studies (n=17), and one study was an RCT. Overall, 570 patients were treated across studies: 56 were treated with cryotherapy (n=2 studies), 90 were treated with RFA (n=2 studies), and 424 (n=14 studies) were treated with SBRT. Study sample sizes ranged from 12 to 69 participants, and mean follow-up occurred at 17.3 months. A median overall survival of 22.7 months was reported in eight studies (five SBRT, two cryotherapy, and one RFA). Median progression-free survival was reported in seven studies (five SBRT, one cryotherapy, and one RFA); the median was 9.3 months (range 3.0 to 22.7 months). The toxicity grade greater than or equal to three ranged from 1.7% to 10%. Due to low sample size, direct comparison of SBRT to ablative studies was not feasible.

Li (2022) conducted a systematic review and meta-analysis to compare the long-term outcomes of RFA to partial nephrectomy for cT1 renal cancer.^[3] Seven studies (n=1,635 patients) were included; reviews and case reports were excluded from the review and meta-analysis. Treatment efficacy of RFA was not different than partial nephrectomy in terms of cancer recurrence (OR=1.22, 95% CI, 0.45 to 3.28), progression-free survival (HR=1.26, 95% CI, 0.75 to 2.11), and cancer-specific survival (HR=1.27, 95% CI, 0.41 to 3.95) as well as major complications (OR=1.31, 95% CI, 0.55 to 3.14) (p>0.05 for all). RFA was a potential significant risk factor for overall survival (HR=1.76, 95% CI, 1.32 to 2.34, p<0.001). The authors did not identify significant heterogeneity or publication bias and concluded that RFA has comparable therapeutic efficacy to partial nephrectomy.

Yanagisawa (2022) published a systematic review (SR) with meta-analysis comparing differential clinical outcomes of partial nephrectomy (PN) versus ablation techniques, including RFA, cryoablation, and microwave ablation, for cT1b and cT1a renal tumors.^[4] The review included 27 studies with 13,996 total patients who received either PN or ablation for treatment of their tumors. There were no differences in the percent decline of estimated glomerular filtration rates (eGFR) or in the overall complication rates between PN and ablation therapy for either tumor type. There was no difference in cancer mortality rates between PN and ablation in patients with either cT1a or cT1b tumors. However, compared to ablation, PN was associated with a lower risk of local recurrence in patients with either tumor type (cT1a: pooled risk ratio [RR]; 0.43, 95% confidence intervals [CI]; 0.28-0.66, cT1b: pooled RR; 0.41, 95%CI; 0.23-0.75). A majority of the included studies were retrospective with a significant heterogeneity in methodology.

In their systematic review and meta-analysis, Uhlig (2019) compared oncologic, perioperative, and functional outcomes for PN with outcomes for various ablative techniques, including RFA and others, for small renal masses (mean diameter=2.53 to 2.84 cm).^[5] 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.

A 2019 systematic review reported by Favi included a descriptive summary of ablative therapy for renal allograft tumors.^[6] 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.

An AHRQ Evidence Report, most recently amended in 2016, included thermal ablation (RFA or cryoablation; surgical or image-guided) as an available management strategies for stage I or II RCC.^[7] The report noted that better oncologic outcomes were believed to be achieved with partial or radical nephrectomy; however, these procedures were associated with significantly higher complication rates than thermal ablation or active surveillance.

In 2014 Wang 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.^[8] 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.

RANDOMIZED CONTROLLED TRIALS

Since the systematic reviews reported above, no additional randomized controlled trials evaluating RFA as a treatment for renal cell carcinoma were identified.

NONRANDOMIZED STUDIES

Published studies have consistently reported fairly high success rates at up to six years follow-up; two to five re-ablation sessions were often necessary to achieve 95% tumor necrosis.^[9-32] Numerous case series, while unreliable, consistently suggest that the benefits of RFA outweigh the risks in patients for whom nephrectomy is not possible. Current studies suggest

that physician specialty (i.e., interventional radiology, urology) and experience, and procedure approach (i.e., percutaneous, open, laparoscopic) may impact tumor recurrence and patient survival outcomes, and authors have recommended further study on these variables.

ADVERSE EVENTS

Reported complication rates have been low.^[9-31, 33] Complications reported in the literature to date have included the following:

- Perinephric hematomas
- Hemorrhage
- Ureteral strictures
- Percutaneous urinary fistula
- Appendiceal perforation

BREAST TUMORS

BACKGROUND

The standard treatment for breast cancer is surgical excision by lumpectomy or mastectomy. Adjuvant radiation therapy, chemotherapy, and/or hormone therapy may also be used. If treated, fibroadenomas, benign tumors of the breast, are typically surgically excised.

SYSTEMATIC REVIEWS

Xia (2021) conducted a SR and meta-analysis of studies assessing RFA in patients with breast cancer and tumors that were 2 cm or smaller.^[34] The primary endpoints of interest were technical success rate, complete ablation rate, and rate of complications. A total of 17 studies were identified, which accounted for 399 patients (401 lesions). Technical success rate ranged from 86.67% to 100% in the included studies; the pooled technical success rate was 99% (95% CI 98% to 100%). After RFA, the majority of patients underwent surgical tumor excision (65.74%, 261/397). The pooled complete ablation rate was 98% (95% CI 97% to 100%). The complication rate in the entire cohort was 6.8%; the most common complications were skin burn (2%), breast inflammation (1.5%), and infections (1%). The pooled complications rate was 2% (95% CI 1% to 4%). Local recurrence was reported in 10 studies (232 cases); there was no local recurrence reported after a median follow-up of 27 months in these patients. The authors noted that prospective studies evaluating the use of RFA alone are needed to validate the place in therapy.

In 2016, Chen reported results from a meta-analysis of clinical trials assessing the effect of RFA for breast cancer.^[35] The authors pooled data from fifteen nonrandomized studies that were published between 2001 and 2012. Of the 15 studies, eight studies reported that the tumor size was <2 cm, five studies reported <3 cm, and the remaining two studies reported <5 cm; eleven studies reported complete ablation rate, from which pooled estimates were 89% (95% CI 85 to 93%) of patients receiving RFA achieved a complete ablation. Five studies reported recurrence rate, from which pooled data suggest no local recurrence at a maximum follow-up of 76 months. A statistical test of publication bias showed no potential publication bias ($Z=0.78$, $p=0.436$). The analyses were limited by small sample size of the included studies, and heterogeneity in patient selection; the authors conclude large, well-designed studies are necessary.

In 2010, Zhao conducted a systematic review of 38 studies on ablation techniques for breast cancer treatment published from 1994 to 2009.^[36] Nine of the studies reviewed focused on RFA for small breast tumors ranging in size from 0.5 – 7 cm. Tumor resection was performed immediately after ablation or up to four weeks after RFA. Complete coagulation necrosis rates of 76% to 100% were reported. These studies were limited to feasibility or pilot studies that were difficult to compare due to heterogeneous patient and tumor characteristics and energy sources. In addition, the studies were conducted in the research setting rather than in clinical practice. The authors concluded that RFA for breast cancer tumors was feasible but further studies with longer follow-up on survival, tumor recurrence and cosmetic outcomes are needed.

Similarly, another 2010 review of 17 studies by Soukup reported that RFA for the treatment of breast tumors was feasible and promising.^[37] However, while minimal adverse effects and complications occurred with breast RFA, the authors noted that incomplete tumor ablation remained a concern. Additional studies of health outcomes and refinement of the procedure were recommended.

RANDOMIZED CONTROLLED TRIALS

No randomized controlled trials of RFA as a treatment for breast tumors were identified.

NONRANDOMIZED STUDIES

Ito (2018) retrospectively studied the safety and efficacy of percutaneous RFA of breast carcinomas in 386 patients from 10 institutions treated with RFA between 2003 and 2009.^[38] Patients were followed for a median of 50 months and ipsilateral breast tumor recurrence was more frequent in patients with initial tumor sizes of 2 cm or more (10% [3/30]) than those with initial tumors 2 cm or less (2.3% [8/355]; $p=0.015$). Ipsilateral breast tumor recurrence rates five years after RFA were 97%, 94%, and 87% in patients with initial tumor sizes of 1 cm or less, 1.1 to 2.0 cm, and greater than 2 cm, respectively. The authors concluded that RFA was safe for tumors of 2 cm or less. The retrospective design and lack of data on ipsilateral breast tumor recurrence for different types of chemotherapy and endocrine therapy and analyses to ascertain whether adjuvant chemotherapy or endocrine therapy influenced outcomes are the limitations of this study.

The efficacy and safety of using ultrasound-guided RFA for multiple breast fibroadenoma as an alternative to surgical resection were retrospectively analyzed by Li (2016).^[39] From 2014 to 2016, 65 patients with 256 nodules were treated with ultrasound-guided RFA and complete ablation was achieved for 251 nodules (98.04%) after the first month of treatment; after the first and third months, tumor volume overall was reduced by 39.06% and 75.99%, respectively. The study reported minimal to no complications such as skin burns, hematoma, or nipple discharge. The retrospective design and short follow-up time limited the conclusions drawn from this study.

The remainder of the published evidence is primarily limited to nonrandomized studies with small numbers of patients.^[40-51] These studies preclude conclusions due to methodologic limitations such as non-random allocation of treatment and a lack of appropriate comparison groups.

Systematic reviews, retrospective studies, and observational studies have reported varied and incomplete ablation rates as well as concerns about postablation tumor cell viability. Long-term

improvements in health outcomes have not been demonstrated. Additionally, available studies have not compared RFA with conventional breast-conserving procedures. For small breast tumors, further prospective study, with long-term follow-up, is needed to determine whether RFA can provide local control and survival rates compared with conventional breast-conserving treatment.

LUNG (PULMONARY) TUMORS

BACKGROUND

Surgery is the preferred treatment for primary non-small cell lung carcinoma (NSCLC). Patients with early-stage NSCLC who are not surgical candidates may be candidates for radiation treatment with curative intent. RFA is being investigated as a treatment of small primary lung cancers or lung metastases in patients who are not surgical candidates.

SYSTEMATIC REVIEWS

Laeseke (2023) conducted a systematic review and meta-analysis that compared the efficacy of image guided thermal ablation, including RFA, to SBRT in patients with stage IA NSCLC among studies with at least 40 patients.^[52] Comparative and single-arm studies, as well as single treatments from comparative studies were included in the meta-analysis. Studies that enrolled patients with recurrent NSCLC, or that used interventions as salvage treatments, were excluded. Key outcomes of interest were local tumor progression, overall survival, and disease-free survival. 40 image-guided thermal ablation study-arms (n=2,691 patients) and 215 SBRT study-arms (n=54,789 patients) were identified. Local tumor progression was lowest after SBRT at years one and two in single-arm pooled analyses (4% and 9% versus 11% and 18%) and at one year in meta-regressions when compared to ablative therapies (odds ratio [OR]=0.2, 95% CI = 0.07 to 0.63). Microwave ablation patients had the highest disease-free survival of all treatments in single-arm pooled analyses. In meta-regressions at two and three years, disease-free survival was significantly lower for RFA compared to microwave ablation (OR=0.26, 95% CI = 0.12 to 0.58; OR=0.33, 95% CI = 0.16 to 0.66, respectively). Overall survival was similar across treatment types and time points. Older age, male patients, larger tumors, retrospective studies, and non-Asian study region were predictors of worse clinical outcomes. Among high quality studies, stage IA microwave ablation patients had lower local tumor progression, higher overall survival, and generally lower disease-free survival, compared to the main analysis of all NSCLC patients.

Sultan (2023) published a systematic review conducted by the Department of Veterans Affairs to compare the effectiveness of surgery to SBRT, stereotactic ablative radiotherapy (SABR), RFA, cryoablation, microwave ablation, laser ablation, and brachytherapy in patients with early-stage lung cancer.^[53] The review authors did not identify any RCTs that examined ablation therapies for stage I lung cancer. RFA, cryoablation, microwave ablation, and laser ablation were assessed in non-randomized comparative studies. RFA was most often studied (k=11). Three retrospective studies compared any type of ablation with SBRT/SABR, and three retrospective studies compared RFA to SBRT/SABR. Ten retrospective studies reported on ablation compared to surgery (n=4 microwave ablation, n=4 RFA, n=2 combined ablation of any type, n=2 SBRT/SABR versus RFA versus surgery). Most of these studies (n=12) had 300 or fewer participants, except for six studies of the National Cancer Database and the Surveillance, Epidemiology and End-Results Database datasets which included 2,000-30,000 participants. All studies included older adults, and most studies did not report on whether participants were medically operable or inoperable. Two studies reported on only medically operable individuals. Due to heterogeneity of patient populations, interventions, and study designs, review authors did not pool data across studies to compare ablative therapies to surgery.

Chan (2021) published a SR and meta-analysis of CT-guided percutaneous ablation for stage I NSCLC.^[54] 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 (OR 2.85, 95% CI 1.33 to 6.10; OR 4.54, 95% CI 2.51 to 8.21, respectively).

In a 2013 Agency for Healthcare Research and Quality (AHRQ) Comparative Effectiveness Review on local nonsurgical therapies for stage I non–small-cell lung cancer (NSCLC), no comparative RFA studies were identified.^[55] The AHRQ report found available evidence is insufficient to draw conclusions on the comparative effectiveness of local nonsurgical therapies for NSCLC including RFA.

In a 2013 SR of RFA, surgical excision and stereotactic radiotherapy (SBRT) for colorectal cancer lung metastases, no randomized trials were identified and evidence was also insufficient to draw conclusions on the comparative effectiveness of these therapies.^[56]

A 2011 SR also 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.^[57] 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 follow-up. 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.”

In a 2012 review of evidence from 16 studies, Bilal compared RFA to SABR in patients with inoperable early stage non-small cell lung cancer (NSCLC).^[58] The 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.

RANDOMIZED CONTROLLED TRIALS

No randomized controlled trials of RFA as a treatment for pulmonary tumors were identified.

NONRANDOMIZED STUDIES

Current studies consist of small case series, retrospective reviews, or uncontrolled cohort studies which focused primarily on technical feasibility and initial tumor response.^[59-91]

One larger nonrandomized case series was published in 2011. Huang prospectively followed 329 consecutive patients treated with RFA for lung tumors.^[92] Complications were experienced

by 34.3% (113) patients and was most commonly pneumothorax (19.1%). Overall survival at two and five years was 35.3% and 20.1%, respectively. The risk of local progression was not significantly different in tumors < 4 cm but became significant in tumors > 4 cm.

In 2015 de Baere review of a database from two cancer centers that included all consecutive patients (n=566) with lung metastases treated with RFA.^[93] Median follow-up was 35.5 months (range 20 to 53 months) with 235 patients followed for more than two years. During follow-up, 176 patients died, of which 112 had progression of their lung tumor disease. Disease progression was also found in 227 of the 390 patients who were alive at last follow-up. Four-year local efficacy was 89% and lung disease control was 44.1%. Median overall survival was 62 months. Limitations of this study included the lack of a control group, and the lack of consideration of the impact of adjuvant chemotherapy.

Study quality concerns include lack of long-term follow-up, significant interstudy heterogeneity in terms of study design, patient populations and RFA methods used, and non-uniformity of reporting and efficacy scoring criteria. Prospective comparison in an RCT would permit greater certainty for this finding but the studies are consistent with some effect of RFA on lung tumors.

ADVERSE EVENTS

Acute, delayed or recurrent pneumothorax is the most commonly reported complication of lung RFA for primary or metastatic tumors (30 to 56% of treatment sessions).^[84, 92, 94-97] Most cases resolved without chest tube placement. Other complications reported in the literature to date are considered uncommon and include, but are not limited to:^[96-101] pleural effusion, intrathoracic hemorrhage with or without hemothorax, hemoptysis, pneumonia, pneumonitis, stellate ganglion injury, and brachial plexus injury.

OSTEIOD OSTEOMAS

BACKGROUND

Osteiod osteomas (OO) usually heal spontaneously in three to four years and standard initial treatment includes medical management with NSAIDs. Invasive procedures including open surgery, laser photocoagulation, radiofrequency ablation, or core drill excision may be necessary if symptoms cannot be managed with NSAIDs.

SYSTEMATIC REVIEWS

Sangiorgio (2022) published a SR with meta-analysis to evaluate the safety and efficacy of radiofrequency ablation (RFA) versus surgical excision (SE) for the treatment of spinal OO. A total of 31 studies (n=749 patients) were included.^[102] The main outcomes were pain before and after intervention, treatments success rate (complete pain relief with no recurrence until the last follow-up) and the number and type of complications. The reported mean treatment success rate was 85.6% (19 studies) for the SE group and 88.6% for the RFA group (18 studies). At last follow-up, the pooled mean difference in pain scores from baseline on a 0–10 scale was 5.8 points in the SE group and 6.7 points in the RFA group. Recurrences were observed in 5.6% of the patients who underwent SE and in 6.7% of the patients treated with RFA. The complication rate was 7.8% in the SE group and 4.4% in the RFA group. The authors conclude that the complication rate was low for both treatments and that RFA is a less invasive procedure which is as a safe and effective option for the treatment of spinal OO.

Lindquister (2020) reported a SR of various thermal ablation techniques for the treatment of OOs.^[103] Of the total of 36 studies that met inclusion criteria (n=1798 patients), 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.

RANDOMIZED CONTROLLED TRIALS

No randomized controlled trials of RFA as a treatment for osteoid osteomas were identified.

NONRANDOMIZED STUDIES

Numerous nonrandomized uncontrolled case series have consistently suggested that the benefits of RFA outweigh the risks in patients who require treatment due to failed response to nonsurgical treatments.^[104-111]

SECTION SUMMARY

Despite the weaknesses in the published clinical evidence, RFA of osteomas has become a standard of care for osteomas that have failed standard treatments. This was based on the lower morbidity and quicker recovery time associated with the procedure compared with open surgery. The risk of osteoma recurrence with RFA is 5 to 10%; recurrent tumors can be retreated with RFA. There are minimal clinical trial data on the risks and benefits of RFA as initial treatment of osteoid tumors. Since most of these tumors heal spontaneously with medical treatment, the necessity of surgical intervention as initial treatment is unclear.

PALLIATION OF PAIN FROM BONE METASTASES

BACKGROUND

External beam irradiation is often the initial palliative therapy for osteolytic bone metastases. However, pain from bone metastases is refractory to radiation therapy in 20% to 30% of patients, while recurrent pain at previously irradiated sites may be ineligible for additional radiation due to risks of normal tissue damage. Other alternatives include hormonal therapy, radiopharmaceuticals such as strontium-89, and bisphosphonates. Less often, surgery or chemotherapy may be used for palliation and intractable pain may require opioid medications. RFA may be considered another alternative for palliating pain from bone metastases.

SYSTEMATIC REVIEWS

Mehta (2020) published a systematic review and meta-analysis of RFA for painful osseous metastases.^[112] 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% ($R^2=-0.66$, 95% CI -0.76 to -0.55, $I^2=71.24\%$). Pain scores were not significantly affected by primary tumor type or tumor size.

A systematic review reported by Gennaro (2019) assessed four percutaneous thermal ablation techniques for pain reduction in patients with bone metastases.^[113] 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.

RANDOMIZED CONTROLLED TRIALS

No randomized controlled trials of RFA as a treatment for palliation of pain from bone metastases were identified.

NONRANDOMIZED STUDIES

Levy (2020) conducted a global, multicenter, nonrandomized, prospective postmarketing study to evaluate the effectiveness of RFA in patients with painful osteolytic bone metastases.^[114] Between October 2017 and March 2019, 134 ablations were performed in 100 patients (68% vs. 32% of the cohort had a single vs. multiple sites treated, respectively). The most common tumor location was thoracic (44%) followed by lumbar (33%). Patient outcomes including pain, pain interference, and quality of life were collected. Forty percent of the cohort did not participate through the six-month follow-up, with two additional discontinuations after six months. The most common reason for discontinuation was death (30 patients), which were all classified as related to the underlying malignancy. The primary endpoint evaluated was pain improvement, from baseline to three months. At baseline, the mean score for worst pain (measured by Brief Pain Inventory) for the entire cohort was 8.2. After RFA, worst pain significantly improved, with mean scores decreasing to 5.6, 4.7, 3.9, 3.7, and 3.5 at three days, one week, one month, three months, and six months, respectively ($p < 0.0001$ for all visits). Immediate improvement in pain (≥ 2 -point change in worst pain at the treatment site(s) three days after RFA) was achieved by 59% of patients. Four adverse events were reported, of which two resulted in hospitalization for pneumonia and respiratory failure, respectively.

Additional nonrandomized evidence is limited to data from small, poorly designed case series.^[115-119] However, though small and uncontrolled, available studies consistently reported significant improvement in pain following RFA in patients who failed or were poor candidates for standard treatments. Clinical trial data is lacking for use of RFA as an alternative to conventional techniques for initial treatment of painful bony metastases.

ANGIOMYOLIPOMA

BACKGROUND

Angiomyolipomas (AMLs) or angiomyolipomata are rare benign tumors that contain blood vessels, smooth muscle, and fat. They are usually associated with the kidneys but may also be in the liver or other locations. They are more frequently seen in patients with tuberous sclerosis complex (TSC). These lesions are usually asymptomatic but may hemorrhage, particularly if large (4 cm or larger). Treatment consists of surveillance as long as the lesion remains small and asymptomatic. Treatment or prevention of hemorrhage may include surgical resection, arterial embolization, or laparoscopic or percutaneous ablation.

PUBLISHED STUDIES

Due to the rare nature of these tumors, there is limited published evidence on the tumor management.^[120-125] The current studies have significant methodological limitations including retrospective records review, small size ($n=4$ to 32), heterogeneity of patients and treatment

modalities, and short-term follow-up. However, the available studies consistently reported low rates of complications and high rates of successful ablation, generally without recurrence at mean follow-up ranging between 9 and 45 months. Some larger tumors (>3.5 cm) required two RFA sessions. Minor complications included transient perinephric hematoma, intercostal nerve transection. A patient in one early study developed a small skin metastasis at the electrode insertion site which was resected and did not recur.

SECTION SUMMARY

Because this is a rare tumor that is often identified incidentally and may not require treatment, it is unlikely that large randomized controlled trials or comparative studies will become available. Due to the risk of potentially life-threatening hemorrhage in large (≥ 4 cm) AMLs and the low rate of adverse effects, treatment of symptomatic or large lesions may be warranted.

HEAD AND NECK TUMORS

BACKGROUND

Tumors of the head and neck arise in the lip, oral cavity, pharynx, larynx, paranasal sinuses and salivary glands. Treatment depends on the location and extent of the disease.^[126] Standard treatment for patients with early-stage disease (stage I or II) is single-modality with surgery or radiation therapy. The two modalities result in similar survival. Combined modality therapy is required for locally advanced disease. In patients with recurrent head and neck cancer, surgical salvage attempts are poor in terms of local control, survival and quality of life, and these recurrent tumors are often untreatable with standard salvage therapies. Palliative chemotherapy or comfort measures may be offered.

SYSTEMATIC REVIEWS RANDOMIZED CONTROLLED TRIALS

No systematic reviews or randomized trials evaluating the safety and effectiveness of RFA for treatment of head and neck tumors were identified.

NONRANDOMIZED STUDIES

Current published evidence is limited to poorly designed case series, feasibility, and retrospective studies that are considered unreliable due to lack of a control group for comparison and lack of randomization to control for bias.^[127-131]

In addition to these methodological limitations, prospective case series included small numbers of patients. Small study populations limit the ability to rule out the role of chance as an explanation of study findings.

ADVERSE EVENTS

Complications and adverse events are reported to be uncommon, but are often severe. They are generally related to burning of local soft tissue (e.g., fistula formation).^[127-130]

THYROID CANCER

BACKGROUND

Thyroid carcinoma is uncommon, with a lifetime risk of being diagnosed with thyroid carcinoma less than 1%. Thyroid carcinoma occurs two to three times more often in women than men.

The main histological types of thyroid carcinoma include: 1) differentiated (including papillary, follicular, and Hürthle); 2) medullary; 3) anaplastic (aggressive undifferentiated tumor). All anaplastic thyroid carcinomas are considered stage IV and are almost uniformly lethal, however most deaths are from papillary, follicular, and Hürthle cell carcinomas, which account for nearly 95% of thyroid carcinoma cases. The treatment of choice for differentiated thyroid carcinoma is surgery followed by radioiodine in selected patients and thyroxine therapy in most patients. There is no effective therapy for anaplastic thyroid carcinoma; most are unresectable, but EBRT may improve local control and provide palliation. Surgical resection is the primary treatment choice for medically unresponsive, symptomatic benign thyroid tumors and thyroid carcinomas. However, techniques for ablation of thyroid tumors (eg, RFA, microwave ablation) are being investigated.

SYSTEMATIC REVIEW

Sun (2022) published a SR to evaluate tumor progression and complications between RFA and thyroidectomy for patients with Papillary thyroid cancer (PTC) or papillary thyroid microcarcinoma (PTMC).^[132] Six retrospective, single-center non randomized studies (1708 patients) were included in their analysis (two for PTC and 4 for PTMC). The tumor progression of the RFA group was similar to the surgical groups [odds ratio, 1.31; 95% CI, 0.52-3.29; heterogeneity (I² statistic), 0%, $p = 0.85$]. The risk of complication rates was significantly lower in the RFA group than that in the surgical group [odds ratio, 0.18; 95% CI, 0.09-0.35; heterogeneity (I² statistic), 40%, $p = 0.14$]. The authors conclude that RFA can achieve a good efficacy and has a lower risk of major complications. The authors indicate that multi-center, large-scale studies with sufficient follow-up (minimum 5 years) analysis are needed.

Cho (2021) reported a systematic review and meta-analysis of five-year outcomes of thermal ablation for papillary thyroid microcarcinoma.^[133] A total of three studies (including 207 patients) met inclusion criteria. 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.

Choi (2020) reported a systematic review of thermal ablation techniques for the treatment of primary papillary thyroid microcarcinoma.^[134] A total of 11 studies of radiofrequency-, laser-, and microwave-ablation met inclusion criteria. The included 715 patients were pooled for analysis. There was significant between-study heterogeneity for complete disappearance ($p < 0.001$, I² 99%), mean volume reduction ($p < 0.001$, I² 93%), and volume reduction rate ($p < 0.001$, I² 86%). A subgroup analysis showed heterogeneity of the complete disappearance proportion among the treatment modality (I² range 95 to 100%). The pooled estimates of complete disappearance, mean volume reduction, and volume reduction rate were 57.6% (95% CI 35.4 to 79.8), 73.5 mm³ (52.4 to 94.6 mm³), and 98.1% (95% CI 96.7 to 99.5), respectively. RFA showed the highest mean volume reduction rate (99.3%), followed by MWA (95.3%) and LA (88.6%; $p < 0.001$). The pooled proportions of overall and major complications were 3.2% (95% CI 1.1 to 5.2) and 0.7% (95% CI 0 to 1.5), respectively.

RANDOMIZED CONTROLLED TRIALS

No new RCTs were published since those included in the systematic reviews summarized above.

NONRANDOMIZED STUDIES

Xiao (2021) published a retrospective study of RFA for solitary T1aN0M0 and T1bN0M0 papillary thyroid carcinoma.^[135] The overall local tumor progression (LTP) rate was 3.82%. LTP and LTP-free survival rates were not significantly different between those with T1a and T1b disease. One patient with T1b disease developed transient recurrent laryngeal nerve injury. There was an 81.7% rate tumor disappearance in those with T1a disease and 52.7% in those with T1b disease ($p<0.001$).

Cao (2021) reported a multicenter retrospective study of thermal ablation for the treatment of solitary T1N0M0 papillary thyroid carcinoma.^[136] A total of 847 patients were included, of whom 645 underwent MWA and 202 underwent RFA. Statistically significant reductions in tumor size were reported at six, nine, and twelve months ($p<0.001$). There was complete disappearance of tumors in 68% of T1a patients and 64% of T1b patients ($p<0.001$). Postablation disease progression occurred in 1.1% of T1a patients and 1.7% of T1b patients ($p=0.54$). The overall complication rate was 3.4%.

In 2016, Kim reported on a comparative review of 73 patients with recurrent thyroid cancer smaller than 2 cm who had been treated with RFA ($n=27$) or repeat surgery ($n=46$).^[137] RFA was performed in cases of patient refusal to undergo surgery or poor medical condition. Data were weighted to minimize potential confounders. The three-year recurrence-free survival rates were similar for RFA (92.6%) and surgery (92.2%, $p=0.681$). Posttreatment hoarseness rate did not differ between the RFA (7.3%) and surgery (9.0%) groups. Posttreatment hypocalcemia occurred only in the surgery group (11.6%).

ADVERSE EVENTS

In 2017, Chung reported results of a systematic review and meta-analysis evaluating the safety of RFA for benign thyroid nodules and recurrent thyroid cancers.^[138] Twenty-four studies were included, totalling 2,421 participants and 2,786 thyroid nodules. Overall, 41 major complications and 48 minor complications (as defined by the Society of Interventional Radiology) of RFA were reported, giving a pooled proportion of 2.38% for overall RFA complications (95% CI 1.42% to 3.34%) and 1.35% for major RFA complications (95% CI 0.89% to 1.81%). Subgroup analysis found major complication rates were significantly higher for malignant thyroid nodules than for benign. Major complications included voice change, nodule rupture, permanent hypothyroidism, and brachial plexus injury. Minor complications included pain, hematoma, vomiting, skin burns, and transient thyroiditis.

BENIGN THYROID TUMORS (NODULES)

Thyroid nodules (including multinodal goiter) that have been verified as benign using fine needle aspiration (FNA) may require treatment when they cause symptoms, such as obstruction or compression.

SYSTEMATIC REVIEWS

In 2021, Monpeyssen published a systematic review of RFA for the treatment of benign thyroid nodules.^[139] The 17 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-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%.

Cho (2020) reported a systematic review of the efficacy of thermal ablation (RFA and laser ablation) for the treatment of benign thyroid nodules.^[140] 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.

A 2019 systematic review and meta-analysis was reported by Trimboli on the efficacy of thermal ablation for benign non-functioning solid thyroid nodules.^[141] 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 reported on a systematic review and meta-analysis of studies on RFA for benign thyroid tumors.^[142] Included in the review were nine studies (five observational studies^[143-147], four randomized studies^[148-151]) totaling 306 treatments. After RFA, statistically significant improvements were reported in nodule size reduction (29.77 mL; 95% CI -13.83 to -5.72), combined symptom improvement and cosmetic scores on the 0 to 6 scale (mean, -2.96; 95% CI -2.66 to -3.25) and withdrawal from methimazole (odds ratio, 40.34; 95% CI 7.78 to 209.09). Twelve adverse events were reported, two of which were considered significant but did not require hospitalization.

RANDOMIZED CONTROLLED TRIALS

No new RCTs were published since those included in the systematic reviews summarized above.

NONRANDOMIZED STUDIES

Kandil (2022) published a prospective, cohort study of benign thyroid nodules (n=233) treated with RFA at two institutions.^[152] The median and interquartile range of volume reduction rate (VRR) at 1, 3, 6, and 12 months were 54% [interquartile range (IQR): 36%-73%], 58% (IQR: 37%-80%), 73% (IQR: 51%-90%), and 76% (IQR: 52%-90%), respectively (p<0.001). Four patients presented with toxic adenomas and two patients developed temporary hoarseness of voice, but no hematoma or nodular rupture occurred postprocedure. All patients were confirmed euthyroid at 3-month postprocedure follow-up. The authors also report that VRR was significantly related with elastography with stiff and mixed elasticity more likely to have lower VRR than soft nodules. The authors conclude that RFA is a safe and effect treatment option that allows preservation of thyroid function with minimal risk of procedural complications.

ADVERSE EVENTS

See the systematic review above by Chung (2017) that addressed the safety of RFA for benign thyroid nodules and recurrent thyroid cancers and reported significantly higher major complication rates for malignant thyroid nodules than for benign nodules.

CHOLANGIOMAS

BACKGROUND

Cholangiocarcinomas are tumors that originate in the bile duct epithelium; 90% are adenocarcinomas. Intrahepatic cholangiocarcinomas (ICC) are located within the hepatic parenchyma and are reviewed under Ablation of Primary and Metastatic Liver Tumors, Surgery, Policy No. 204 (see Cross References for a link to the policy). They may also be referred to as peripheral cholangiocarcinomas. Extrahepatic cholangiocarcinomas (ECC) are more common than intrahepatic cholangiocarcinoma and are located within the extrahepatic bile duct. Complete resection with negative margin is potential curative, though recurrence is common and most cases are unresectable due to advanced disease when diagnosed. For unresectable or metastatic cholangiocarcinomas at any location, the primary treatment may include chemotherapy, treatment within a clinical trial, or best supportive care. RFA and other locoregional therapies may be an option. Biliary drainage with biliary stenting may be warranted for unresectable or metastatic extrahepatic disease. Liver transplantation is potentially curative in carefully selected patients with lymph node negative, nondisseminated locally advanced hilar cholangiocarcinomas and otherwise normal biliary and hepatic function or underlying liver disease precluding surgery.

SYSTEMATIC REVIEWS AND RANDOMIZED CONTROLLED TRIALS

No systematic reviews or randomized controlled trials regarding radiofrequency ablation for the treatment of extrahepatic cholangiocarcinomas were identified.

NONRANDOMIZED STUDIES

The evidence for ECC consists of a single short-term case series.^[153] This study included 11 patients with hilar ECC. At one-month follow-up after RFA, the reduction in tumor size was 30% in six tumors, 20% in two tumors, and size was unchanged in three tumors. At six months following RFA, the overall size reduction was 35%, with the largest reduction 60%. Overall survival ranged from 10-30 months.

UTERINE FIBROIDS (LEIOMYOMAS OR MYOMAS)

BACKGROUND

Uterine fibroids, also known as leiomyomas or myomas, are benign smooth muscle tumors of the uterus occurring in women during their reproductive years. They frequently occur in multiples, and the tumor location within the uterus is often used to describe the fibroids (intramural, submucosal, subserosal, or cervical myomas). Surgery, including hysterectomy and various myomectomy procedures, is considered the criterion standard treatment for symptom resolution. There has been long-standing research interest in developing minimally invasive alternatives for treating uterine fibroids, including procedures that retain the uterus and allow for future childbearing. Various techniques to induce myolysis have also been studied including Nd:YAG lasers, bipolar electrodes, cryomyolysis, and radiofrequency

ablation. With these techniques, an energy source is used to create areas of necrosis within uterine fibroids, reducing their volume and thus relieving symptoms.

SYSTEMATIC REVIEWS

Polin (2022) published a SR of pregnancy outcomes after radiofrequency ablation (RFA) of uterine myomas.^[154] Ten publications were included in the review. There were 50 pregnancies reported among 923 RFA patients: 40 pregnancies after 559 laparoscopic RFAs and 10 pregnancies after 364 transcervical RFAs. Most patients had between 1 and 3 myomas ablated, and myomas size ranged from <2 cm to 12.5 cm. The authors reported two complications of the 44 deliveries (placenta previa and delayed postpartum hemorrhage). There were no cases of uterine rupture, uterine window, or invasive placentation and no fetal complications. The spontaneous abortion rate (12%) was comparable with the general obstetric population. The authors conclude that hat radiofrequency myoma ablation may offer a safe and effective alternative to existing treatments for women who desire future fertility.

Morris (2022) completed a SR evaluating the associations between minimally invasive approaches to fibroid treatment and quality of life (QoL) or fibroid-associated symptoms.^[155] A total of 37 studies were included (26 evaluating individual approaches and 11 comparative studies of minimally invasive approaches and surgical interventions). Radiofrequency ablation and ultrasound-guided sclerotherapy (USGS) significantly improved overall QoL. The authors conclude that outcomes among minimally invasive approaches were similar, presenting patients with numerous non-surgical options for fibroid treatment.

Zhang (2022) published a SR evaluating the efficacy of uterine-preserving, minimally invasive treatment modalities in reducing fibroid-related bleeding.^[156] Eighty-four studies were included in the review (10 RCTs and 74 observational studies). Fifteen studies demonstrated significantly reduced bleeding severity after radiofrequency ablation (RFA). The authors conclude that additional research is needed to determine best practices and that long-term evidence is limited in current literature.

Arnreiter and Oppelt reported on the safety and efficacy of transcervical ultrasound-guided RFA using the Sonata system in a 2021 systematic review.^[157] A total of 10 studies met inclusion criteria, all of which were rated as fair quality on the Newcastle Ottawa Scale (NOS). The reported reduction in total and perfused myoma volume was 63.2% and 64.5%. Clinically meaningful reduction in menstrual blood loss after 12 months was achieved in 87.2% of patients. Symptom Severity Scores dropped by 28.8 ± 19.3 , 23.3 ± 23.7 , and 23.7 ± 19.4 points at three, six, and twelve months and Health-Related Quality of Life Scores increased to 77.5 ± 22.0 , 82.8 ± 19.0 , and 83.3 ± 20.5 points. The reintervention rate at an average of 64 months post-ablation was 11.8%. Time to return to activities of daily life was 2.9 ± 2.5 days. There were three reported pregnancies following ablation, all of which were without complications.

Berman (2020) conducted a retrospective review of pregnancy delivery and safety after laparoscopic RFA of uterine fibroids.^[158] The review included results from two RCTs, six cohort studies, and commercial cases (total N=28) that evaluated rates of spontaneous abortion, preterm delivery, postpartum hemorrhage, placental abnormalities, intrauterine growth restriction, and rates of cesarean delivery. Thirty pregnancies resulted in 26 full-term births (86.7%), with an equal distribution of vaginal and cesarean deliveries, and the spontaneous abortion rate (13.3%) was within the range for the general population. There were no cases of preterm delivery, uterine rupture, placental abruption, placenta accreta, or intrauterine growth

restriction. One patient experienced severe postpartum hemorrhage. More rigorous prospective studies evaluating pregnancy outcomes after laparoscopic RFA are needed.

Bradley (2019) published a systematic review and meta-analysis of RFA for the treatment of uterine fibroids.^[159] A total of 32 articles representing 20 studies of percutaneous laparoscopic (19 articles; Accessa device; n=461 patients), transvaginal (8 articles; n=579 patients), and transcervical RFA (5 articles; Sonata device; n=214 patients) met inclusion criteria. The number of patients ranged from 11 to 153 and the mean follow-up ranged from in-hospital to 64 months. Study quality was rated as good or fair for 19 of 20 studies. A meta-analysis was conducted of 1,283 patients at the 12-month follow-up. The weighted mean time to discharge was 8.2 hours (95% CI 6.3 to 10.0 hours) and the weighted mean time to normal activities was 5.2 days (95% CI 3.3 to 7.1 days). There was a decrease in fibroid volume of 66%, an increase in health-related quality of life by 39 points, and a decrease in symptom severity score of 42 points (all $p < 0.001$ versus baseline). The annual cumulative rates of reintervention due to fibroid-related symptoms were 4.2%, 8.2%, and 11.5% at one, two, and three years, respectively. Complication reporting within the included studies was highly inconsistent and inadequate and therefore was not reported in this systematic review. However, the authors noted that no serious procedural complications such as death or iatrogenic injury to the bowel, bladder, or ureter were reported in any study. There were no statistically significant differences across RFA approaches for reintervention rates or fibroid volume reduction, but procedure time was significantly different (all pairwise comparisons $p \leq 0.002$), with laparoscopic being longest (73 minutes) followed by transcervical (44 minutes) and transvaginal (24 minutes).

A systematic review and meta-analysis by Sandberg (2018) evaluated the risk of reintervention for hysterectomy and QOL after uterine-sparing interventions for fibroids.^[160] Risk of reintervention at 12 months was 0.3% for radiofrequency volumetric thermal ablation (RFVTA) compared with 3.6% for UAE and 1.1% for myomectomy. Symptom severity and QOL scores were similar for the three treatments. Only one RFVTA study was identified on reintervention risk at 36 months; none was identified on reintervention risk at 60 months.

A systematic review by Havryliuk (2017) that did not separate outcomes by the length of follow-up found a reintervention rate of 5.2% after RFVTA (four studies, 12- to 36-month follow-up) compared to 4.2% after myomectomy (six studies, 12- to 52-month follow-up).^[161] There was no significant difference in complication rates between RFVTA (6.3%) and myomectomy (7.9%). The length of stay after myomectomy was two days (range 0.5 to 6.0). No data were provided on length of stay after RFVTA.

Lin (2018) conducted a meta-analysis of improvement in symptom severity, QOL, and reintervention after laparoscopic radiofrequency ablation.^[162] The review included one RCT and seven non-comparative trials. The recurrence risk at a weighted mean follow-up of 24.65 months (range, 3 to 36 months) was 4.4%. Improvements in symptoms and QOL were maintained out to 24 months in three studies and out to 36 months in one study. No studies were identified that had follow-up longer than 36 months.

RANDOMIZED CONTROLLED TRIALS

Ratray (2018) and Yu (2022) published three- and 12-month outcomes of a RCT comparing laparoscopic radiofrequency ablation (Lap-RFA) and myomectomy for patients with symptomatic uterine leiomyomas (ULs).^[163, 164] Patients (n=57) were randomized to either laparoscopic RFA (n=30) or myomectomy (n=27). There was a significant improvement in UL symptoms at 3 and 12 months after the procedure within each treatment group, and these

improvements were similar between treatment groups. At 3 and 12 months after the procedure, the percentages of patients who were hospitalized in the LAP-RFA group were 74% and 49% lower than those of patients in the laparoscopic myomectomy group, respectively, with the 3-month difference being statistically significant. The authors conclude that LAP-RFA has lower healthcare resource use overall, including lower postprocedure hospitalization rate and shorter length of stay. Both studies reported 1 (<1%) serious adverse event within 30 days of the procedure. No efficacy outcomes were reported. The authors conclude that the results suggest that LAP-RFA is a safe, effective, uterine-sparing alternative to laparoscopic myomectomy in the treatment of ULs.

In Germany in 2014, Brucker published a single-center manufacturer-sponsored randomized controlled trial (RCT) comparing radiofrequency volumetric thermal ablation (RFVTA) with the Acessa system to laparoscopic myomectomy.^[165] The trial included 51 premenopausal women at least 18 years old with symptomatic uterine fibroids less than 10 cm in any diameter and a uterine size of less than 17 weeks of gestation. Pregnancy and lactation were exclusion criteria. Prior to randomization, all women underwent laparoscopic ultrasound mapping. Data on 50 of the 51 women were analyzed. The primary study outcome, mean (SD) time to hospital discharge, was 10.0 (5.5) hours in the RFVTA group and 29.9 (14.2) hours in the myomectomy group. The criterion for noninferiority (no more than 10% longer hospital stay with RFVTA than laparoscopic myomectomy) was met at a significance level of $p < 0.001$. All patients in the myomectomy group were hospitalized overnight; although not explicitly stated, this appeared to be the standard procedure at the study hospital. In the Acessa group, there was one unplanned hospitalization due to unexplained vertigo and four hospitalizations as standard procedure because the patients also underwent adhesiolysis.

Secondary outcomes of the RCT were reported in a 2015 publication by Hahn^[166] (12-month outcomes) and a 2016 publication by Kramer^[167] (24-month outcomes). Analysis was per protocol and 43 (84%) of 51 randomized participants were available for both the 12- and 24-month analyses. Each publication reported on 12 symptoms: heavy menstrual bleeding, increased abdominal gait, dyspareunia, pelvic discomfort/pain, dysmenorrhea, urinary frequency, urinary retention, sleep disturbance, backache, localized pain, and “other symptoms” (not specified). At 12 months, no participants reported four of the symptoms (dyspareunia, urinary retention, sleep disturbance, uterine pain) and there were no statistically significant between-group differences in the frequency of any of the remaining eight symptoms (at the $p < 0.05$ level). The most commonly reported symptom at 12 months (heavy menstrual bleeding) occurred in seven (33%) of women in the RFVTA group and two (9%) of women in the laparoscopic myomectomy group ($p = 0.069$) after controlling for baseline bleeding. At 24 months, no participants reported urinary retention or “other” symptoms, and there were no statistically significant between-group differences in any of the 10 reported symptoms. The most commonly reported symptom at 24 months (dysmenorrhea) occurred in eight (38%) in the RFVTA group and in seven (32%) in the laparoscopic myomectomy group ($p = 0.67$). Patients were also assessed using several validated questionnaires (eg, the Uterine Fibroid Symptom and Quality of Life). There were no statistically significant between-group differences at 12 or 24 months on these validated questionnaires. In addition, the authors described pregnancy outcomes. Three patients in the RFVTA group conceived and all delivered a healthy neonate; the number of women who desired to become pregnant was not reported. Limitations of the 12- and 24-month analyses included lack of intention-to-treat analysis and failure to describe secondary study hypotheses and statistical analyses clearly. The RCT was relatively small in size and thus may have been underpowered to detect clinically meaningful

differences in secondary outcomes, so these results do not rule out potential differences between treatments.

NONRANDOMIZED STUDIES

Shifrin (2021) conducted a subgroup analysis of patients with submucous (type 1, 2, or 2-5) or large fibroids (> 5 cm) from patients in the FAST-EU and SONATA clinical trials.^[168] In total, 72.5% of the 534 treated fibroids were not amenable to hysteroscopic resection because they were intramural, transmural, or subserous. At 3 month follow-up, 86% of women with only submucous fibroids and 81% of women with large fibroids experienced bleeding reduction. At 12 month follow-up, a reduction in menstrual bleeding was found in 92% to 96% of women with submucous fibroids and 86% to 100% of women with large fibroids (although fibroids >5 cm was an exclusion in SONATA, 2.5% (n=11) of patients were in this category). Improvement in the SSS, HR-QoL, and EQ-5D were also noted in these subgroups. Rates of surgical reintervention for women with submucous fibroids was less than 3.7%.

Yüce (2020) reported on 35 patients treated with percutaneous RFA.^[169] The fibroid volume was reduced significantly compared to baseline at 3, 6, and 12 months ($p < 0.001$), and Visual Analogue Scores were significantly reduced at 6 and 12 months ($p < 0.01$).

A prospective observational study by Rey (2019) assessed the effectiveness of transvaginal ultrasound-guided RFA of myomas (TRFAM) in reducing tumor volume and eliminating metrorrhagia associated with myomas.^[170] The study included 205 women with symptomatic type II/III uterine submucosal or intramural cavity-distorting myomas undergoing RFA. The preoperative mean standard deviation (SD) volume of the myomas was 122.4 (182.5) cm³ (95% CI 82.1 to 162.8). Mean myoma volume decreased significantly at one (85.2 [147.9] cm³; $p = 0.001$), three (67.3 [138.0] cm³; $p = 0.001$), six (59.3 [135.3] cm³; $p = 0.001$), and 12 months (49.6 [121.4] cm³; $p = 0.001$). At 12 months, the mean volume reduction was 60% compared with preoperative volume. All patients returned to normal menstruation at a mean follow-up of three months and 12 months. Of the 205 patients, 201 (98.04%) were satisfied with the procedure. The investigators conceded that a larger population with a longer follow-up is needed, but their study suggests that transvaginal ultrasound-guided RFA of myomas TRFAM is effective and safe for treating select patients with metrorrhagia secondary to myomas.

A large retrospective case series was published by Yin in 2015.^[171] The study was conducted in China and used Chinese gynecologic radiofrequency ablation devices. It included 1216 consecutive patients treated at a single hospital over a 10-year period. All fibroids were less than 6 cm in size and mean diameter was 4.5 cm (range, 3.1 to 6.0 cm). Mean follow-up time was 36.5 months. Among the 476 premenopausal women, the mean reduction in myoma diameter was 2.7 cm at six months, 2.4 cm at 12 months, and 2.2 cm at 24 months. Among the 740 peri- or postmenopausal women, mean reduction was 3.3 cm at six months, 2.3 cm at 12 months, and 2.3 cm at 24 months. Myoma diameter was significantly lower at each of these time-points posttreatment compared with pretreatment. In the premenopausal subgroup, the proportion of women with dysmenorrhea decreased from 43.7% at baseline to 7.6% at 12 months and to 6.7% at 24 months; rates were significantly lower after treatment.

In 2013, Chudnoff published a prospective industry-funded multicenter study.^[172] It included 135 premenopausal women at least 25 years old with symptomatic uterine fibroids, a uterine size of 14 weeks of gestation or less, and six or fewer treatable fibroids, with no single fibroid larger than 7 cm. In addition, women desired to preserve their uteri but not to have children in the future. RFVTA was conducted using the Acessa system. According to the study protocol,

most fibroids less than 1 cm in diameter were not treated. The primary efficacy outcomes were change in the volume of menstrual bleeding and the surgical reintervention rate after 12 months. A total of 127 (94%) of 135 women completed the study. From baseline to 12 months, 53 (42%) of 127 women (95% confidence interval, 32% to 49%) experienced at least a 50% reduction in the volume of menstrual bleeding. Most women (104/127 [82%]) experienced a decrease in menstrual bleeding at 12 months. Only one woman underwent a surgical reintervention through 12 months (this woman had been lost to follow-up and was not included in the other efficacy analyses). Three-year outcomes were reported by Berman in 2014.^[173] A total of 104 (77%) of the 135 women who participated in the study were evaluable at three years. Fourteen underwent reintervention over the three years to treat uterine fibroid symptoms. Eleven women had hysterectomies, two had myomectomies, and one had uterine artery embolization. Bleeding outcomes were not reported at three years, but the authors stated that quality-of-life variables improved from baseline to 36 months and that most of the improvement in quality of life occurred within three months of the procedure.

MISCELLANEOUS TUMORS

BACKGROUND

The standard treatment of miscellaneous tumors depends on the type, location, and extent of the cancer. A large number of phase II or III clinical trials involving the use of RFA in the treatment of primary or metastatic cancers are underway.^[174]

SYSTEMATIC REVIEWS

Tang (2022) published a SR evaluating the safety and efficacy of RFA, microwave ablation (MWA), and laser ablation (LA) for the treatment of cervical metastatic lymph nodes (CMLNs) of papillary thyroid carcinoma (PTC). A total of 17 studies were included (312 patients and 559 CMLNs).^[175] The pooled proportions of VRR, complete disappearance and recurrence of CMLNs were 91.28% [95% confidence interval (CI): 86.60-95.97%], 67.9% [95% CI: 53.1-81.1%] and 7.8% [95%CI: 3.0-14.1%], respectively. The pooled proportions of overall and major complications were 2.9% [95%CI: 0.3-7.1%] and 0.3% [95%CI: 0-1.9%], respectively. The VRR of MWA was the highest (97.97%), followed by RFA (95.57%) and LA (84.46%) ($p < 0.001$). The authors conclude that thermal ablations were safe and effective for the treatment of CMLNs of PTC. Each treatment had significant heterogeneity in VRR.

Nadeem (2021) published a SR of RFA for adrenal tumors. A total of 15 studies including 292 patients were included. No comparative results were reported. Overall, cumulative technical success, primary technique efficacy, and secondary technique efficacy rates were 99%, 95.1% and 100%, respectively. Local progression rates at three, six, and 12 months were 20.3%, 26.3%, and 29.3%, respectively, and overall survival rates at six, 12, and 18 months were 81.8%, 59.6%, and 62.9%. The intraprocedural complication rate was 30.2%.

Imperatore (2020) and Dhaliwal (2020) performed SR of RFA of pancreatic neuroendocrine tumors and unresectable pancreatic ductal adenocarcinoma (PDAC), respectively.^[176, 177] Zhang (2020) published a systematic review of various ultrasound-guided ablation techniques for the treatment of solid pancreatic tumors.^[178] Additionally, a systematic review by Rombouts (2015) examined studies of ablative therapies, including RFA, in patients with locally advanced pancreatic cancer.^[179] No RCTs were identified in any of these systematic reviews, and conclusions are limited by the sparse evidence available on RFA in this setting.

Thomson (2019) published a SR on non-surgical treatments for Morton's neuroma.^[180] A total of 22 studies, addressing nine non-operative treatment modalities, met inclusion criteria. In addition to RFA, treatment modalities included corticosteroid injection, alcohol injection, extracorporeal shockwave therapy (ESWT), cryoablation, capsaicin injection, Botulinum toxin, orthosis and YAG laser therapy. All showed statistically significant improvements, but the pain-relieving results for alcohol injection were only short-term and orthotics, capsaicin injections, cryoablation, Botulinum toxin, RFA and ESWT had limitations to their application.

The remainder of the current published evidence on RFA for other tumors is limited to unreliable data from small case series and retrospective reviews. Evidence from these studies is considered unreliable due to methodological limitations such as non-random allocation of treatment and a lack of appropriate comparison groups.^[127, 143, 144, 181-196]

PRACTICE GUIDELINE SUMMARY

NATIONAL COMPREHENSIVE CANCER NETWORK

The National Comprehensive Cancer Network (NCCN) guidelines for thyroid carcinoma (v.2023) indicate that local therapies such as RFA may be considered for locoregional recurrence of thyroid carcinoma-papillary carcinoma in select individuals with limited burden nodal disease. Additionally, local therapies, including RFA, can be considered in those with metastatic disease.^[197]

NCCN guidelines for colon cancer (v.3.2023) indicate that for metastases, “ablative techniques may be considered alone or in conjunction with resection. All original sites of disease need to be amenable to ablation or resection.”^[198] 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).“

NCCN guidelines for kidney cancer (v.1.2024) indicate “thermal ablation (e.g., cryosurgery, radiofrequency ablation) is an option for the management of individuals with clinical stage T1 renal lesions.” Thermal ablation is an option for masses <3 cm, but it may also be an option for larger masses in select individuals. Ablation in masses >3 cm is associated with higher rates of local recurrence/persistence and complications.^[199] RFA is also an option for relapse or Stage IV and in select patients (e.g., elderly patients, others) with competing health risks.

NCCN guidelines for the treatment of non-small cell lung cancer (v.4.2023) state: “For medically operable disease, resection is the preferred local treatment modality (other modalities include SABR, thermal ablation such as radiofrequency ablation and cryotherapy. Image-guided thermal ablation (cryotherapy, microwave, radiofrequency) may be an option for selected patients who will not be receiving SABR or definitive RT”^[200]

AMERICAN COLLEGE OF RADIOLOGY

The American College of Radiology (ACR) Appropriateness Criteria® (updated in 2021) consider RFA to be an alternative to partial nephrectomy for small (<4 cm) RCC tumors.^[201]

The 2014 ACR Appropriateness Criteria on early-stage NSCLC that current evidence from a number of retrospective series involving varied patient populations reported a wide range of responses to RFA, ranging from 38% to 93%.^[202] Primary tumor relapse rate after RFA ranged from 8% to 43% and two-year cancer-specific survival after RFA ranged from 57% to 93%,

with three-year OS of 15% to 46%. Predictors of complete response included smaller tumor size metastases, and ablation zone four times the tumor diameter. The document quoted the 2012 ACCP/STS guidelines^[203] summarized below.

AMERICAN COLLEGE OF CHEST PHYSICIANS

The American College of Chest Physicians (ACCP) guidelines on the treatment of stage I and II NSCLC indicate RFA has been used effectively in clinical stage 1 NSCLC. Therefore, in medically inoperable patients, peripheral NSCLC tumors less than 3 cm may be treated with RFA.^[204]

The ACCP also joined with the Society of Thoracic Surgeons (STS) to develop consensus guidelines on the treatment of high-risk patients with stage I NSCLC.^[203] These consensus guidelines indicate RFA is an alternative treatment option in patients who are not surgical candidates due to severe medical comorbidity.

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.”^[205]

AMERICAN UROLOGICAL ASSOCIATION

The 2017 American Urological Association (AUA) Guidelines state that “Physicians should consider TA [thermal ablation] as an alternate approach for the management of cT1a renal masses <3 cm in size.” and “Both radiofrequency ablation and cryoablation are options for patients who elect thermal ablation.” Both are rated as “Conditional Recommendation; Evidence Level Grade C.”^[206] The guidelines were updated in 2021 and recommendations are generally consistent with the 2017 guideline.^[207] The 2021 AUA guideline explicitly states that RFA and cryoablation may be offered as options to patients who elect thermal ablation.

AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS

The American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin #96 (now #228), *Management of Symptomatic Uterine Leiomyomas* states “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.”^[208]

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS

The American Association of Clinical Endocrinologists, American College of Endocrinology, and Associazione Medici Endocrinologi Medical published clinical practice guidelines (updated in 2016) for the diagnosis and management of thyroid nodules provides the following recommendations:^[209] “Consider laser or radiofrequency ablation for the treatment of solid or complex thyroid nodules that progressively enlarge, are symptomatic or cause cosmetic concern [BEL 2, GRADE C]. Repeat FNA for cytologic confirmation before thermal ablation treatment [BEL 3, GRADE B].” BEL2 indicates a level of evidence that includes RCTs with limited body of data and well-conducted prospective cohort studies and meta-analyses of

cohort studies and BEL3 indicates a level of evidence that includes methodologically flawed clinical trials and observational studies.

SOCIETY OF INTERVENTIONAL RADIOLOGY

The Society of Interventional Radiology (2020) published a position statement on the role of percutaneous ablation in renal cell carcinoma.^[210] The relevant recommendations are as follows: In patients with small renal tumors (stage T1a), percutaneous thermal ablation is a safe and effective treatment with fewer complications than nephrectomy and acceptable long-term oncological and survival outcomes. In selected patients with suspected T1a renal cell carcinoma, percutaneous thermal ablation should be offered over active surveillance. (Level of Evidence: C; Strength of Recommendation: Moderate)"

In high-risk patients with T1b renal cell carcinoma who are not surgical candidates, percutaneous thermal ablation may be an appropriate treatment option; however, further research in this area is required. (Level of Evidence: D; Strength of Recommendation: Weak)"

Radiofrequency ablation, cryoablation, and microwave ablation are all appropriate modalities for thermal ablation, and method of ablation should be left to the discretion of the operating physician. (Level of Evidence: D; Strength of Recommendation: Weak)"

SUMMARY

RENAL CELL CARCINOMA

Although there are currently no high-quality studies of radiofrequency ablation (RFA) of renal cell carcinoma (RCC), the overall body of published evidence suggests RFA may be beneficial in the short- to mid-term for small (4 cm or smaller), localized RCCs in patients who are not considered candidates for partial or complete surgical removal of the kidney. Therefore, RFA may be medically necessary for small RCCs in patients who are not surgical candidates or when preservation of kidney function is necessary, such as in patients with only one kidney.

Surgical excision is the preferred treatment for renal cell carcinoma (RCC) in patients who are considered to be healthy enough for surgery. There is insufficient evidence to determine whether radiofrequency ablation (RFA) is effective as surgical excision for treatment of RCC tumors. Therefore, RFA is considered investigational for treatment of RCC tumors for which surgical resection is an option.

BREAST TUMORS

There is insufficient evidence to determine the effectiveness of radiofrequency ablation for treatment of benign or malignant breast masses. Therefore, this treatment is considered investigational for the treatment of these tumors.

LUNG TUMORS

Surgical resection is the treatment of choice for primary non-small cell lung cancer (NSCLC) or metastatic tumors in the lung. For those patients who are unable to tolerate surgery, radiofrequency ablation (RFA) may be a treatment option in certain cases. While available studies are limited by study design, accumulating evidence suggests that RFA may be

similar to surgery in survival rates, and rates of procedure-related complications and mortality. Therefore, in patients with NSCLC or metastatic tumors in the lung who are ineligible for surgical treatment, RFA may be medically necessary when the policy criteria are met. There is not enough evidence to show that radiofrequency ablation (RFA) is effective as alternative treatments when criteria are not met. Therefore, RFA is considered investigational when the policy criteria are not met.

OSTEOID OSTEOMAS

Although the published evidence is limited to studies of lower methodological quality, radiofrequency ablation (RFA) of osteomas has become a standard of care based on expert opinion that the potential benefits of RFA outweigh risks in patients with osteoid tumors who have failed nonsurgical treatments. Therefore, RFA may be medically necessary for select patients when policy criteria are met.

The current preferred treatment of osteoid osteomas is non-surgical medical treatment. There is insufficient evidence to determine the effectiveness of radiofrequency ablation (RFA) for initial (first-line) treatment of osteoid tumors. RFA is, therefore, considered investigational as initial treatment of these tumors in patients who have not undergone standard medical management.

ANGIOMYOLIPOMAS

The current published evidence on radiofrequency ablation (RFA) of angiomyolipomas (AMLs) is limited to studies of lower methodological quality. However, because these tumors are rare, it is unlikely that evidence from large comparative studies will become available. Given the potential for life-threatening hemorrhage from large AMLs (4 cm or larger), and the consistent reports that the potential benefits of treatment outweigh any risks, RFA may be medical necessary to treat symptomatic or large asymptomatic AMLs. There is not enough evidence to show that radiofrequency ablation (RFA) is effective as alternative treatments when criteria are not met. Therefore, RFA of asymptomatic AMLs smaller than 4 cm is considered investigational.

PALLIATION OF PAIN FOR BONE METASTASES

The current evidence for radiofrequency ablation (RFA) for treatment of painful metastatic tumors in the bone is limited to studies of lower methodological quality; however, these studies have consistently reported significant improvement in pain following RFA in patients who have failed or are poor candidates for standard treatments. In light of this evidence, the unlikelihood of randomized controlled trials in these patients, and the lack of treatment options, the potential benefits of RFA appear to outweigh risks. Therefore, RFA may be medically necessary in patients with painful metastatic bone lesions who have failed or are poor candidates for standard treatments.

Because of the lack of data on the effectiveness of radiofrequency ablation (RFA) for initial (first-line) treatment of painful bony metastases, this indication is considered investigational.

HEAD AND NECK CANCERS

There is insufficient evidence to determine whether radiofrequency ablation (RFA) is effective for treatment of tumors of the head and neck. Therefore, RFA is considered investigational for the treatment of head and neck cancers.

THYROID TUMORS

Radiofrequency ablation (RFA) appears to be a safe alternative to more invasive surgical treatment for benign thyroid tumors. In addition, clinical guidelines based on evidence recommend this treatment. Therefore, RFA may be considered medically necessary for the treatment of benign thyroid tumors (nodules) when criteria are met.

There is not enough evidence to show that radiofrequency ablation (RFA) is safe and effective for benign thyroid tumors that do not meet the criteria. Therefore, RFA is considered investigational for the treatment of benign thyroid tumors (nodules) when criteria are not met.

While radiofrequency ablation (RFA) has been shown to reduce the size of malignant thyroid tumors and improve clinical symptoms, complications can be common. The available evidence is insufficient to determine whether any beneficial effects of RFA outweigh the risks. Therefore, RFA for the treatment of malignant thyroid tumors is considered investigational.

UTERINE FIBROIDS

There is enough research to show that radiofrequency ablation (RFA) may improve health outcomes for people with uterine fibroids. Additionally, clinical guidelines based on evidence from the American College of Obstetricians and Gynecologists (ACOG) recommend this treatment option. Therefore, RFA may be considered medically necessary for treating uterine fibroids when criteria are met.

There is not enough research to show that radiofrequency ablation (RFA) improves health outcomes for people with uterine fibroids when policy criteria are not met. Therefore, RFA is considered investigational for the treatment of uterine fibroids when policy criteria are not met.

MISCELLANEOUS TUMORS

There is insufficient evidence to determine whether radiofrequency ablation (RFA) is effective for treatment of other tumors. Therefore, RFA is considered investigational for all other tumors.

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CODES

Codes	Number	Description
CPT	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
	50542	Laparoscopy, surgical; ablation of renal mass lesion(s), including intraoperative ultrasound guidance and monitoring, when performed

Codes	Number	Description
	58580	Transcervical ablation of uterine fibroid(s), including intraoperative ultrasound guidance and monitoring, radiofrequency
	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
	0404T	Transcervical uterine fibroid(s) ablation with ultrasound guidance, radiofrequency (Deleted 01/01/2024)
HCPCS	None	

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