



**Kaiser Foundation Health Plan  
of Washington**

**Clinical Review Criteria  
Radiofrequency Ablation**

- Barrett’s Esophagus
- Lung Cancer
- Renal Tumors
- Primary HCC and Metastatic Liver Cancer
- Uterine Fibroids

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**Criteria**

**For Medicare Members**

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	None
Local Coverage Article	None
KPWA Policy	Due to the absence of a NCD, LCD, or other coverage guidance, KPWA has chosen to use their own Clinical Review Criteria, “Radiofrequency Ablation” for medical necessity determinations. Use the Non-Medicare criteria below.

**For Non-Medicare Members**

Service	Criteria Used
Barrett’s Esophagus	Radiofrequency ablation is considered medically necessary for the treatment of members with Barrett’s esophagus (BE) who have histological confirmation of low-grade dysplasia by two or more endoscopies three or more months apart.
Lung Cancer	There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.
Renal Tumors Primary HCC and Metastatic Liver Cancer	Medical necessity review is no longer required for this service.
Transcervical Ablation of Uterine Leiomyomas	MCG* A-1039 This is not covered per MCG* For access to the MCG Clinical Guidelines criteria, please see the MCG Guideline Index through the provider portal under Quick Access.

**\*MCG are proprietary and cannot be published and/or distributed.** However, on an individual member basis, Kaiser Permanente can share a copy of the specific criteria document used to make a utilization management decision. If one of your patients is being reviewed using these criteria, you may request a copy of the criteria by calling the Kaiser Permanente Clinical Review staff at 1-800-289-1363 or access the MCG Guideline Index using the link provided above.

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage

## Evidence and Source Documents

[Radiofrequency Ablation for the Treatment of Barrett's Esophagus](#)

[Radiofrequency Ablation in the Treatment of Lung Cancer](#)

[Radiofrequency Ablation of Renal Tumors](#)

[Radiofrequency Ablation of Primary HCC and Metastatic Liver Cancer](#)

[Radiofrequency Volumetric Thermal Ablation \(RFVTA\) of Uterine Fibroids Using the Acessa™ System](#)

## Medical Technology Assessment Committee (MTAC)

### *Radiofrequency Ablation for the Treatment of Barrett's Esophagus*

#### **BACKGROUND**

Barrett's esophagus is a disease wherein the stratified squamous epithelium lining the esophagus gets replaced by metaplastic columnar epithelium. The disease affects more Caucasians than Blacks and is diagnosed around 55 years (Spechler & Goyal, 1996) and its prevalence varied widely from 0.4% to 20% (Gerson, Shetler, & Triadafilopoulos, 2002; Ormsby et al., 2000; Ward et al., 2006). Barrett's esophagus is caused by chronic gastro esophageal reflux disease (GERD). While Body mass index (BMI), is believed to be associated with increased risk of Barrett's esophagus (Kamat, Wen, Morris, & Anandasabapathy, 2009), studies have found that abdominal obesity is a risk factor for Barrett's esophagus (Corley et al., 2007; Edelstein, Farrow, Bronner, Rosen, & Vaughan, 2007; Kramer et al., 2013). It is not well known if germline mutations are associated with the disease.

Initially, Barrett's esophagus manifests with no symptoms or patients show signs of GERD. The most common symptoms of GERD are pyrosis (heart burn), regurgitation and dysphagia. Other manifestations of GERD are chronic cough, bronchospasm and laryngitis, chest pain resembling angina pectoris. GERD is complicated by erosive esophagitis, esophageal ulceration, stricture and hemorrhage (Spechler & Goyal, 1996), and Barrett's esophagus. The annual cancer incidence varied from 0.1 to 0.4% (Desai et al., 2012; Hvid-Jensen, Pedersen, Drewes, Sørensen, & Funch-Jensen, 2011; Rugge, Fassan, Cavallin, & Zaninotto, 2012; Shakhathreh et al., 2014). Studies have shown that the risk of developing cancer is proportional to dysplasia status and length of Barrett's esophagus (Pohl et al., 2016; Sikkema et al., 2011; Thota et al., 2015; Van der Veen, Dees, Blankensteijn, & Van Blankenstein, 1989). Patients with high-grade dysplasia have higher risk (4-8%) of progression to adenocarcinoma while patients with Barrett's esophagus, low-grade dysplasia and indefinite for dysplasia have a risk ranging from 0.2 to 1.2% (Singh et al., 2014; Verbeek et al., 2012). However, mortality due to esophageal adenocarcinoma is lower than that of other causes (Sikkema, De Jonge, Steyerberg, & Kuipers, 2010). Diagnostic is based on endoscopy and biopsy showing columnar epithelium and intestinal metaplasia respectively. Histology classification has described four types of Barrett's esophagus (BE); these include non-dysplastic (ND), low-grade for dysplasia (LGD), indefinite for dysplasia (ID), high-grade dysplastic (HGD).

General management includes proton pump inhibitor (PPI). Fundoplication may be an alternative for PPI resistance. Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) that inhibit cyclooxygenase (COX) have been described; however, these drugs have potential side effects. Surveillance has been promoted by many guidelines (Association, 2011; Fitzgerald et al., 2014; Shaheen, Falk, Iyer, & Gerson, 2016) but its benefit is not well documented. In addition, surveillance modality depends on the type of dysplasia. Treatment of dysplasia is of greatest importance. Several approaches have been described and include endoscopic ablative therapies, endoscopic resection or the combination of both, and esophagectomy. Endoscopic resection encompasses removal of both mucosa and submucosa (Pech, May, Gossner, Rabenstein, & Eil, 2004) and can lead to stricture. Endoscopic ablative therapies consist of radiofrequency ablation (RFA), photodynamic therapy, and endoscopic spray cryotherapy.

RFA uses radiofrequency energy and produces thermal injury to destroy the mucosa. Energy used comes from a balloon equipped with a series of electrodes to ablate the mucosa (Sharma et al., 2007). The radiofrequency energy can either be delivered circumferentially or focally. There are two different devices and accessories, both manufactured by BARRX. The balloon based HALO360 device is used to treat circumferential areas of BE. The system includes a high-power energy generator, a sizing balloon catheter and several balloon-based ablation catheters. There are 60 tightly spaced, bipolar independent electrodes encircling the balloon through which the energy is delivered. A preselected amount of energy is delivered in less than a second at 350 W. This allows for full thickness ablation of the epithelium without damage to the submucosa. The HALO [90] ablation system is used to treat more focal areas and uses a radiofrequency generator and an endoscope mounted electrode. Both procedures can be done on an outpatient basis. Barrx90 ULTRA, Barrx60, and Channel RFA device are alternative options for focal ablations.

## **02/01/2010: MTAC REVIEW**

### **Radiofrequency ablation for the treatment of Barrett's Esophagus**

**Evidence Conclusion:** The literature search revealed only one published randomized controlled trial (Shaheen et al, 2009) that compared radiofrequency ablation of Barrett's esophagus to a sham endoscopic procedure. The trial had valid design and analysis; it was multicenter, appropriately randomized, controlled, blinded, had sufficient statistical power, and with low dropout rate. However, radiofrequency ablation was compared to a sham procedure and not to another established alternative procedure with a curative intent for BE with dysplasia e.g. endoscopic resection, esophagectomy, or photodynamic therapy. Moreover, the trial had only one year of follow-up which is insufficient to determine the long-term efficacy, and safety of the procedure. Due to the short follow-up duration, the authors used neoplastic progression and eradication of dysplasia and metaplasia as surrogates for death from cancer. The trial randomized 127 patients (in a 2:1 ratio) with low- or high-grade dysplasia to undergo either radiofrequency ablation or sham endoscopic therapy. Randomization was stratified according to grade of dysplasia (LGD or HGD) and length of BE lesion (<4 or 4-8cm). Those in the ablation group underwent step-wise circumferential and focal ablation using HALO 360 and HALO 90 systems (BARRX Medical Inc, Sunnyvale, CA). Patients in the two groups underwent endoscopic surveillance for the study period; biopsies were obtained throughout the BE length every 3 months in patients with HGD or 6 months among those with LGD. After 12 months of follow-up, the results of the trial showed that more than three fourths of patients treated with radiofrequency ablation had complete eradication of intestinal metaplasia and dysplasia (77 % of all BE was completely reversed into normal epithelium among those who received RFA, vs. 2% in the control; 90% of patients with LGD, and 81.5% with HGD had complete eradication of the dysplasia vs. 23% and 19% of the controls respectively). The ablation therapy was also associated with a significant decrease in the risk of cancer but, as acknowledged by the authors this should be interpreted with caution due to the small number of cases. RFA therapy was not without risk as 5 (6%) cases developed esophageal stricture that required endoscopic dilatation, and 3 (3.5%) had other serious events as bleeding and chest pain.

Conclusion:

- There is fair evidence from one RCT with short-term follow-up that radiofrequency ablation using the HALO systems is superior to sham therapy (no therapy) in the treatment of BE with dysplasia.
- There is insufficient evidence to determine that RFA has better outcomes and less harms than alternative therapies with curative intent for BE with dysplasia.
- There is insufficient evidence to determine the long-term efficacy, and safety of radiofrequency ablation therapy in the management of patients with Barrett's esophagus with dysplasia, and whether the risk of ablation is less than the risk of progression of BE.
- There is insufficient evidence to determine that radiofrequency ablation therapy eliminates the necessity for of further endoscopic surveillance of patients with Barrett's esophagus with dysplasia.
- There is insufficient evidence to determine that radiofrequency ablation therapy reduces or eliminates cancer risk in patients with Barrett's esophagus with dysplasia.

**Articles:** The search yielded around forty articles. Many were reviews, letters, and editorials. There was one randomized controlled trial and number of case series and reports. The RCT and the majority of the case series were conducted by the same group of investigators. The RCT with the following citation was critically appraised. Shaheen NJ, Sharma P, Overholt B, et al. Radiofrequency ablation in Barrett's esophagus with dysplasia. N Engl J Med 2009; 360:2277-2288. See [Evidence Table](#)

The use of Radiofrequency ablation for the treatment of Barrett's esophagus with dysplasia does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

#### **09/19/2016: MTAC REVIEW**

##### **Radiofrequency ablation for the treatment of Barrett's Esophagus**

**Evidence Conclusion: RFA vs alternative treatment Systematic review comparing radiofrequency ablation and complete endoscopic resection in treating dysplastic Barrett's esophagus: a critical assessment of histologic outcomes and adverse events (Chadwick et al, 2014)** (evidence table 1) The first study is a systematic review aiming to compare the efficacy and safety of complete endoscopic mucosal resection (EMR) and radiofrequency ablation (RFA) in the treatment of dysplastic BE. It was reported that dysplasia was eradicated in 95% and 92% of patients treated with EMR and RFA respectively. Intestinal metaplasia (IM) eradication was similar between both groups. After (23 and 21 months for EMR and RFA respectively) months of follow-up for patients, who were treated with EMR, dysplasia eradication was achieved in 85% of patients versus 79% among RFA group. In EMR group, additional treatments were reported in 7 studies. In EMR group, overall short-term adverse events were 12.5% and most frequently acute bleeding. In RFA group, overall short-term adverse events were 2.5% and most frequently acute bleeding (1%). In EMR group, overall long-term adverse events were 38% and most frequently stricture compared to 4% in RFA group. Buried BE was 3.8% in EMR group vs. 0% in RFA group (not reported in table).

Progression to cancer appeared to be low in both groups. This indicates that both treatments are effective in the management of HGD BE but more events that are adverse are observed with EMR. However, the review is mostly based on observational studies. Ten studies were directly or indirectly industry funded; only 3 RCTs were represented in the review. Individual studies were small. Follow-ups periods were short (<1 year) and varied greatly limiting accurate assessment of cancer progression and incidence of recurrence. Fair evidence shows that both treatments are effective in managing HGD BE but RFA has less adverse events.

**Radiofrequency ablation vs endoscopic surveillance for patients with Barrett's esophagus and low-grade dysplasia a randomized clinical trial (Phoa et al 2014)** (evidence table 2) This RCT investigated whether endoscopic radiofrequency ablation could decrease the rate of neoplastic progression. Compared to control group, patients who were treated with RFA, were less likely to progress to high grade dysplasia or cancer. At the end of endoscopic treatment, (After RFA), 92.6% and 88.2% of complete eradication of dysplasia and IM were observed respectively. During follow-up, patients who were treated with RFA were more likely to obtain complete eradication of dysplasia; the risk of complete eradication of dysplasia was increased by 70.5%. Complete eradication of intestinal metaplasia was maintained in 54 of 60 patients (90.0%) receiving ablation compared with 0 of 68 patients receiving control (risk difference, 90% [95% CI, 82.4%-97.6%]; P < .001). Adverse events are represented by abdominal pain, bleeding, stricture, laceration, retrosternal pain while no adverse events were reported for endoscopic surveillance. The results indicate that in patients with low-grade dysplasia, RFA reduced the risk of progression to high-grade dysplasia or adenocarcinoma by 25% corresponding to an NNT of 4.0. Study had a valid methodology in general.

However, it had some limitations: external validity is compromised (referral centers), study was underpowered for cancer-related death outcome which is the primary end point. Endoscopic rescue therapy was performed to decrease residual Barrett tissue. Based on the Cochrane collaboration's tool for bias assessment, the overall risk of bias is low with unclear information on blinding. Fair evidence supports efficacy of RFA over endoscopic surveillance for low grade dysplasia. **Endotherapy versus surgery for early neoplasia in Barrett's esophagus: a meta-analysis (Wu et al., 2014)** (evidence table 5) This meta-analysis aimed to compare the efficacy and safety of endotherapy and surgery for early neoplasia in BE. A systematic literature search was performed up to December 2012 and included 870 patients. No significant difference between endotherapy and esophagectomy in the outcomes presented in the table below. However, endotherapy was associated with a higher neoplasia recurrence rate and fewer major adverse events.

Limitations include: a small number of studies including retrospective studies; patients were not comparable in some studies leading to bias of the results. Different endotherapies including EMR, PDT, RFA and argon plasma coagulation were used. The type of surgery and the experiences of surgeons were different.

Publication bias might also exist. Low evidence supports similar efficacy between endotherapy and surgery in the treatment of early Barrett's neoplasia with fewer adverse events. Efficacy of RFA (non-comparative studies).

**Efficacy and durability of radiofrequency ablation for Barrett's esophagus: systematic review and meta-analysis** (Orman et al, 2013) (evidence table 3) This systematic review aimed to determine the efficacy and durability of RFA for patients with dysplastic and nondysplastic BE. The authors found 91% of patients achieved CE-IM while 78% achieved CE-D and that in 13% of cases, IM recurred after successful

treatment. Most common adverse events were stricture (5%) and pain (3%). Although the study has valid methodology, limitations included the poor quality of included studies and external validity. Settings include referral centers with capability in RFA. Heterogeneity was high. Adverse events may have been underestimated due to the retrospective design of a number of studies. Individual studies were small in size. Follow-up periods were short. RFA was not compared to alternative treatment limiting accurate assessment. The results indicate that CE-IM and CE-D were achieved in most of the patients undergoing RFA with low IM recurrence and low adverse events.

Several prospective studies have assessed the efficacy of RFA. Their findings can be found in the following table. However, none of these studies compare RFA to alternative treatment.

Author, year	N	Intervention	Protocol	BE baseline	Median Follow-up (mos)	Findings	Adverse events
(Phoa et al., 2014)	132	ER combined with RFA	Visible lesions were removed with ER followed by serial RFA every 3 months. Follow-up endoscopy was scheduled at 6 months after the first negative post-treatment endoscopic control and annually thereafter	BE≤12 cm with HGD and/or EC	27	CE-neo:92% CE-IM: 87% Recurrence: neo and IM 4% & 8% respectively	Mucosal lacerations (8%) and stenosis (6%).
(He et al., 2015)	96	RFA	RFA was used at baseline to treat all unstained lesions (USL), and then biopsy (and focal RFA if USL persisted) was performed every 3 months until all biopsies were negative for MGIN, HGIN, and ESCC	moderate/high grade intraepithelial neoplasia [MGIN/HGIN] and early flat-type esophageal squamous cell carcinoma [ESCC]	12	73% & 84% of complete response at 3 and 12 months respectively. Progression in 2%	Stricture (21%)
(Haidry et al., 2014)	508	RFA/EMR	Visible lesions were removed by EMR. Thereafter, patients had RFA 3-monthly until all BE was ablated or cancer developed	HGD or IMC	6 years	CE-D: 77% to 92% CE-IM:56% to 83% (p<0.0001) Progression to OAC at 12 months (3.6% vs. 2.1%, p=0.51) Risk of IM recurrence at 5 years: 32%	
(Small et al., 2015)	246	EMR and/or ablation therapy		HGD/IMC		83.7% with HGD 75.7% with IMC	

BE, Barrett's esophagus; ER, endoscopic resection; EMR, endoscopic mucosal resection

**Low grade dysplasia Meta-analysis of endoscopic therapy for low-grade dysplasia in Barrett's oesophagus (Almond et al 2014)** (evidence table 4) This systematic review aimed to identify systematically all reports of endoscopic treatment of LGD, and to assess outcomes in terms of disease progression, eradication of dysplasia and intestinal metaplasia, and complication rates. The search was performed from January 1988 to January 2013. 37 studies reporting outcomes of endoscopic therapy for 521 patients with LGD. Study quality was assessed using Jadad scale for controlled trials and the Newcastle–Ottawa scale for uncontrolled trials. The results indicated that 67.8% and 88.9% achieved CE-IM and CE-D respectively. The overall incidence of progression to cancer is 3.90. The authors concluded that RFA does not eradicate the risk of progression to cancer, but it appears to be safe and effective at eliminating LGD. Fair evidence supports the efficacy and safety of RFA in the treatment of low-grade dysplastic BE. However, studies with longer follow-up are needed.

**Conclusion:**

- Fair evidence shows that Radio frequency ablation (RFA) and endoscopic mucosal resection are both effective in managing HGD BE but RFA has less adverse events.

- Fair evidence supports efficacy of RFA over endoscopic surveillance for low grade dysplasia.
- Low evidence supports similar efficacy between endotherapy and surgery in the treatment of early Barrett's neoplasia
- There is fair evidence that RFA is effective and safe for the treatment of low-grade dysplasia; however, studies with long follow-up are needed.
- There is sufficient evidence to determine whether RFA is effective and safe for the treatment of high-grade dysplastic Barrett's esophagus.

**Articles:** The literature revealed a number of articles, but the following articles were selected for critical appraisal: Systematic review comparing radiofrequency ablation and complete endoscopic resection in treating dysplastic Barrett's esophagus: a critical assessment of histologic outcomes and adverse events (Chadwick et al, 2014) [See Evidence Table 1](#). Radiofrequency ablation vs endoscopic surveillance for patients with Barrett's esophagus and low-grade dysplasia a randomized clinical trial (Phoa et al 2014) [See Evidence Table 2](#). Efficacy and durability of radiofrequency ablation for Barrett's esophagus: systematic review and meta-analysis (Orman et al, 2013) [See Evidence Table 3](#). Meta-analysis of endoscopic therapy for low-grade dysplasia in Barrett's oesophagus (Almond et al 2014) [See Evidence Table 4](#). Endotherapy versus surgery for early neoplasia in Barrett's esophagus: a meta-analysis (Wu, Pan, Wang, Gao, & Hu, 2014) [See Evidence Table 5](#).

The use of Radiofrequency ablation for the treatment of Barrett's esophagus with dysplasia does meet the Kaiser Permanente Medical Technology Assessment Criteria.

### **Radiofrequency Ablation in the Treatment of Lung Cancer**

#### **BACKGROUND**

Lung cancer is the leading cause of cancer related mortality in the United States. It has two main types; the non-small cell lung cancer (NSCLC) which accounts for approximately 80-85% of cases, and the small cell lung cancer (SCLC). After the initial diagnosis of the disease is made, it is essential to have an accurate TNM staging in order to determine the appropriate therapy. The standard treatment of patients with stage I or II NSCLC is surgical resection, and in order to achieve a potential cure from the disease, the cancer must be completely resectable through pneumonectomy or lobectomy, and the patient should be able to tolerate the surgery and have adequate pulmonary function. Patients with more advanced or metastatic lung disease, or who cannot tolerate surgery, due to age or the presence of other co-morbidities, are poor surgical candidates. They are traditionally offered treatment with conventional external beam radiotherapy which is considered the most reasonable alternative. However, its results have not been satisfactory, and it has lower overall long-term survival than complete surgical resection. This radiation therapy may also be associated with regional complications as radiation pneumonitis, fibrosis, and esophagitis, and is not indicated for pulmonary metastases. Chemotherapy was found to have only a modest therapeutic effect and is usually used as palliative therapy. This has led the researchers to develop minimally invasive techniques as stereotactic radiotherapy, brachytherapy, photodynamic therapy, bronchial artery infusion of chemotherapy, cryotherapy and radiofrequency ablation (RFA) (D'Amico 2003, Qiao 2003, Pennathur 2007). Radiofrequency ablation is a relatively new minimally invasive therapy that potentially leads to localized tissue destruction. It works by transferring radiofrequency (RF) energy from a generator through an electrode, to the target tissues. The waves are converted into heat, resulting in thermal damage, and coagulative necrosis of the tissues. For solid organ tumor ablation, thin RF electrodes are introduced laparoscopically or percutaneously to the target lesion under ultrasound, CT, or MRI guidance. A power of 5-120W is delivered to the electrodes, and an alternating current of 450-1,200 kHz passes from the tip to the surrounding tissue. When the temperature of the tumor cells is raised above 70°C cell destruction occurs. Several radiofrequency ablation devices were cleared by the FDA as tools for general ablation of soft tissue by thermal necrosis. The devices were also cleared for ablation of liver lesions, and bone metastases. According to the FDA, they have not been cleared for lung tumor ablation as their safety and effectiveness have not been fully established. In December 2007, the FDA issued a public health notification to alert the health practitioners of the deaths associated with lung tumor ablation using the radiofrequency devices (FDA Web site).

#### **06/04/2008: MTAC REVIEW**

#### **Radiofrequency Ablation in the Treatment of Lung Cancer**

**Evidence Conclusion:** There is limited evidence on the efficacy and safety of radiofrequency ablation for the treatment of lung cancer in patients who are not candidates for surgical resection. The body of evidence

consists of small observational case series with no control or comparison groups that compare the RF ablation with conventional or other noninvasive techniques used for the treatments of patients with non-operable lung cancer, or those who cannot tolerate surgery. The published studies were heterogeneous; there were differences in the eligibility criteria of the studies, patient characteristics, stage of the disease, cancer type, number and sizes of the lesions, as well as other tumor characteristics. There were also variations in the ablation approaches, types of devices used to deliver the therapy, follow-up, endpoints, and outcome measures. Moreover, the follow-up duration in the majority of the studies was too short to determine the long-term safety and effectiveness of the therapy. Overall, the results of the published studies indicate that the median survival of patients receiving the therapy ranged from 8.6 months to 33 months. The one-year survival rate ranged from 63-85%, the two-year survival was 55-65% and the three-year survival rate was 15-46%. Complete tumor necrosis ranged from 38% to 95%, and local disease recurrence varied from 3% to 38.1%. The studies indicate the RF ablation has better outcomes with tumors smaller than 3 cm in diameter vs. those >3cm in diameter, as this would allow oversizing of the ablation areas. The adverse effects associated with RF ablation included pneumothorax that often-needed aspiration, pleural effusion, hemoptysis, pain, as well as other complications some of which required hospitalization of the patients. The authors of the published studies presented the results for all patients combined, with no adjustments for confounding factors as age of the patients, presence of other co-morbidities and/or malignancies, or the use of other adjuvant therapy. Moreover, in the absence of comparison groups, it is hard to determine whether radiofrequency ablation leads to better local control or improved survival outcomes than external beam radiation therapy or any other noninvasive treatment. In conclusion there is insufficient published evidence to determine the efficacy and safety of radiofrequency ablation for the treatment of lung cancer.

**Articles:** The search yielded over 300 articles. Many were review articles or publications not related to the current review. No meta-analyses of empirical studies randomized, or non-randomized controlled studies were identified. The majority were observational prospective case series with population sizes ranging from <10 to 60 patients. There was a larger (N=153) retrospective observational study that evaluated the long-term efficacy and safety of the therapy. Prospective series with at least 50 patients, and/or with longer-term follow-up, as well as the larger retrospective series were selected for critical appraisal. *The following studies were critically appraised:* DE Baire T, Palussiere J, Auperin A, et al. Midterm local efficacy and survival after radiofrequency ablation of lung tumors with minimum follow-up of 1 year. Prospective evaluation. *Radiology* 2006.240:587-596. See [Evidence Table](#). Ambrogi MC, Lucchi M, Dini P, et al. Percutaneous radiofrequency ablation of lung tumors: results in mid-term. *Eur J Cardiothorac Surg*. 2006. 30:177-183. See [Evidence Table](#). Gadaleta C, Catino A, Mattioli V. Radiofrequency thermal ablation in the treatment of lung metastases. *In Vivo*. 2006; 20:765-768. See [Evidence Table](#). Simon CJ, Dupuy DE, DiPetrillo TA, et al. Pulmonary radiofrequency ablation: Long-term safety and efficacy. *Radiology* 2007.243:268-275. See [Evidence Table](#).

The use of Radiofrequency ablation in the treatment of lung cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

### **Radiofrequency Ablation of Renal Tumors**

#### **BACKGROUND**

With the widespread use of body imaging techniques as magnetic resonance imaging (MRI), computed tomography (CT), there is an increasing number of pre-symptomatic, incidentally detected small renal masses or lesions with unclear clinical significance. The standard treatment for renal masses is radical nephrectomy. Other available treatment options for these small, incidentally discovered masses include watchful waiting or partial nephrectomy. Recently, with the current trend of minimally invasive surgery, nephron-sparing approaches have gained more acceptance. Among these are radiofrequency (RF) ablation, cryoablation, microwaves, and high intensity focused ultrasonography (HIFU). These techniques are still under development and only target selected, small renal tumors with a diameter of 4 cm or less. RF ablation works by transferring RF energy from a generator through an electrode, to the target tissues. The waves are converted into heat, resulting in thermal damage, and coagulative necrosis of the tissues. For solid organ tumor ablation, thin RF electrodes are introduced laparoscopically, or percutaneously to the target lesion under ultrasound, CT, or MRI guidance. A power of 5-120W is delivered to the electrodes, and an alternating current of 450-1,200 kHz passes from the tip to the surrounding tissue. When the temperature of the tumor cells is raised above 70°C cell destruction occurs. The size of the lesion depends on the thermal properties of the tissue, the time, and the amount of the energy delivered. Radiofrequency ablation has been used for selected liver and bone tumors. It is approved by the FDA for ablation of aberrant atrioventricular conduction

pathways in patients with Wolf-Parkinson-White syndrome, and for treating soft-tissue lesions in the liver. Its use for human renal tumors is still under investigation, and its efficacy and safety as well as its dosimetry have not been fully established.

#### **12/11/2002: MTAC REVIEW**

##### **Radiofrequency Ablation of Renal Tumors**

**Evidence Conclusion:** There is insufficient published evidence to determine the efficacy and safety of radiofrequency ablation for the treatment of renal tumors.

**Articles:** The search yielded one review article, two case reports and three case series with 10-15 patients each. There were no meta-analyses or randomized controlled studies.

The use of radiofrequency ablation in the treatment of renal tumors does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

##### **Radiofrequency Ablation of Primary HCC and Metastatic Liver Cancer**

###### **BACKGROUND**

The liver is a common site for primary and secondary malignancies. Hepatocellular carcinoma (HCC), the most common primary tumor is the fifth most common cancer in the world, and the third most common cause of cancer-related mortality. It is responsible for more than half a million deaths across the globe each year. Treatment options for patients diagnosed with primary and secondary malignancies are limited. Less than 15% are candidates for surgical resection at presentation because of inadequate liver functional reserve, extrahepatic disease, anatomic constraints of the tumor, or medical comorbidities. The use of external beam radiation is limited due to the intolerance of normal liver parenchyma to tumoricidal radiation doses (the dose required to destroy solid tumors (>70 Gy) is much higher than the liver tolerance dose of 35 Gy). In addition, systematic chemotherapy was found to have little impact on survival, and negative impact on the health-related quality of life due to the toxicity to other organs and systems. These limitations have led to the emergence of other therapies, such as radiofrequency ablation (RFA), cryosurgical ablation (CSA), percutaneous ethanol injections (PEI), hepatic arterial infusion chemotherapy, transarterial chemo-embolization (TACE), and selective intrarterial radioembolization therapy (Steel 2003, Salem 2005, Ibrahim 2008, Bult 2009, Riaz 2009, Bhardwaj 2010). Ablative techniques improve the ability to treat patients with unresectable hepatic tumors. Thermal ablative techniques, such as RFA, destroy tumors via a source that changes temperature to levels that are associated with cell death while causing minimal damage to adjacent, normal tissue. Chemical ablative techniques, such as PEI, involve the injection of cancer killing chemicals such as pure alcohol (ethanol) or acetic acid directly into the tumor. The choice of technique depends on equipment availability and physician preference. PEI is a chemical ablative technique where absolute or 95% ethanol is injected into tumor tissue resulting in coagulative necrosis through cytoplasmic dehydration, denaturation of cellular proteins, and small vessel thrombosis. When the consistency of the tumor is 'soft' within a 'hard' cirrhotic liver (most HCCs), the distribution of ethanol is relatively uniform; however, when the tumor is 'hard' within a 'soft' normal liver (most metastases), the distribution is not as uniform. For this reason, PEI works better for HCC than for metastases. Complications of PEI include: hyperthermia, pain, elevated serum liver function tests, needle-tract seeding, pleural effusion, biliary stricture, portal vein thrombosis, and bleeding in the biliary tract (Clark 2007, Yamane 2009). The most commonly used ablative technique in the United States is RFA. RFA causes tumor destruction through the use of alternating high-frequency electric current in the radiofrequency range (460-500 kHz). This current is delivered through an electrode placed in the center of a lesion. Ions within the cell follow the alternating current creating frictional heat producing local tissue temperatures that can exceed 100°C. This ionic agitation leads to tissue destruction via tissue boiling and creation of water vapors. Once temperatures greater than 60°C are reached, protein denaturation, tissue coagulation, and vascular thrombosis result in a zone of complete ablation. Partial tissue destruction can occur up to 8 mm in diameter from the zone of complete ablation. RFA can be delivered either percutaneously, laparoscopically, or through open approaches (laparotomy). Complications from RFA include pleural effusion, hepatic abscess, biliary injury, liver failure, intra-abdominal hemorrhage, pneumothorax, and hypoxemia. The most troubling complications arise when a probe is placed too close to the diaphragm or intra-abdominal organ, resulting in ablation of the surrounding viscera with the accompanying complications of perforation, diaphragmatic injury, or pulmonary damage. Limitations of RFA include: treating lesions in perihilar areas or near large vascular structures, and real time monitoring of the ablative zone is difficult due



to air released during heating (Yamane 2009, Arciero 2006). RFA has received FDA approval for generic tissue ablation and the ablation of unresectable colorectal cancer metastases.

#### **08/11/1999: MTAC REVIEW**

##### **Radiofrequency Ablation of Primary HCC and Metastatic Liver Cancer**

**Evidence Conclusion:** The best published scientific evidence evaluating percutaneous radiofrequency (RF) ablation of liver cancer consists of one case series of 39 patients with primary hepatocellular carcinoma and 11 patients with other primary tumors who had liver metastases. The majority of patients had 3-4 treatments with one or more nodules being ablated at each session. Five patients experienced mild pain during the procedure; no other complications were reported. The 5-year survival rate among those with primary hepatocellular carcinoma was 40%; the period of follow-up for persons with liver metastases was too short for the calculation of a 5-year survival rate. Because the survival rate of patients treated with RF ablation was not directly compared to that of a control group, it is not possible to determine whether this treatment improves survival among patients with liver cancer.

**Articles:** Rossi S, DiStasi M, Buscarini E, Quartetti P, Garbagnati F, Squassante L, Paties CT, Silverman DE, Buscarini L. Percutaneous RF interstitial thermal ablation in the treatment of hepatic cancer. *AJR Am J Roentgenol* 1996; 167: 759-68. See [Evidence Table](#).

The use of radiofrequency ablation in the treatment of primary HCC does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

#### **08/08/2001: MTAC REVIEW**

##### **Radiofrequency Ablation of Primary HCC and Metastatic Liver Cancer**

**Evidence Conclusion:** Only one study on radiofrequency ablation was a controlled trial. The remainder were case series. The trial reported on a clinically intermediate outcome, liver necrosis, not survival. The case series reports had survival information, but this was not presented in a standardized format (e.g. 1-year survival, 3-year survival). Instead, they reported on survival after a certain mean or median follow-up time (patients had different amounts of follow-up time) which is more difficult to interpret. For primary HCC, in the one trial comparing RF ablation to an alternative technique, PEI, both techniques resulted in high rates of complete necrosis and the difference in rates was not statistically significant (Livraghi). PEI required more sessions and RF ablation had more adverse effects (there was 1 major and 4 minor complications with RF ablation, none with PEI). In the case series reviewed (Curley), there was a 72% survival rate after a median of 19 months of follow-up (all patients had at least 12 months follow-up). Livraghi (2001) (not critically appraised for this review) reported on a case series of patients with HCC treated with PEI. The 1-year survival rate for patients with a single HCC 5 cm or smaller was 98, 93 and 64%, respectively for Child's A, B and C cirrhosis. For metastatic hepatic cancer, de Barre found that 81% patients survived after a mean follow-up of 14 months; 62% of these who survived had hepatic disease or distant metastases. 2-year or longer follow-up data were not available. This does not appear to be a dramatic increase in survival compared to untreated metastatic liver cancer (mean survival 6 to 21 months), but there is not strong evidence to support this claim. No studies compared RF ablation treatment to another treatment for metastatic liver cancer such as cryosurgery. In a case series on cryosurgery for hepatic colorectal metastases (Ruers, 2001) (not critically appraised for this review), the 1-year survival was 76% and the 2-year survival was 61%. The effectiveness of RF ablation may differ depending on the type of metastatic tumor.

**Articles:** The search yielded 85 articles, many of which were review articles, opinion pieces, dealt with technical aspects of the procedures or addressed other, similar treatments. There were no randomized controlled trials or meta-analysis. There was one non-randomized controlled trial and the rest of the empirical articles were case series. Articles on HCC and metastatic liver cancer were analyzed separately. Two studies on primary hepatocellular carcinoma were reviewed (the non-randomized trial and a recent case series with a moderate sample size by a different research group): Livraghi T, Goldberg SN, Lazzaroni S, Meloni F, Solbiati L, Gazelle GS. Small hepatocellular carcinoma: Treatment with radiofrequency ablation versus ethanol injection. *Radiology* 1999; 210: 655-661. See [Evidence Table](#). Curley SA, Izzo F, Ellis LM, Vauthey JN, Vallone P. Radiofrequency ablation of hepatocellular cancer in 110 patients with cirrhosis. *Ann Surg* 2000; 232: 381-91. *One study on metastatic liver cancer was reviewed (the largest case series with the longest follow-up):* de Barre T, Ellas D, Dromain C, El Din MG, Kuocho V, Ducreux M. et al. Radiofrequency ablation of 100 hepatic metastases with a mean follow-up of more than 1 year. *AJR* 2000; 175: 1619-25. See [Evidence Table](#).

The use of radiofrequency ablation in the treatment of primary HCC does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

**06/21/2010: MTAC REVIEW**

**Radiofrequency Ablation of Primary HCC and Metastatic Liver Cancer**

**Evidence Conclusion:** While there are many studies comparing RFA with resection and other ablative techniques, such as PEI, for the treatment of liver cancer, the data are difficult to compare since the studies are heterogeneous in study design, patient selection, data collection, tumor characteristics, primary cause of liver disease, route of access, electrode types used, and periinterventional systemic treatment. **Primary Liver Cancer RFA vs. Resection** The study selected for critical appraisal was a randomized controlled trial that compared the results of RFA with resection for the treatment of solitary and small HCC. Overall and disease-free survival rates were not statistically different for patients with solitary HCC < 5 cm in diameter treated with either RFA or resection. Additionally, patients treated with RFA had fewer major complications than patients treated with resection (0.04% vs. 56%,  $p < 0.05$ ). Treatment groups were comparable at baseline for all characteristic measured with the exception of serum alanine aminotransferase (ALT). Patients in the RFA group had higher serum ALT concentrations compared to patients in the resection group. Factors that limit the validity of the study include: uneven dropout rates, use of additional techniques, and lack of generalizability (Chen 2006). Another nonrandomized study comparing RFA with resection demonstrated similar survival outcomes between RFA and resection for tumors <5 cm (Montorsi 2005). One recent retrospective study suggested that overall and disease-free survival was higher for patients treated with resection compared to patients treated with RFA. However, in a subgroup analysis by tumor size, there was no significant difference in survival between RFA and resection for patients with tumors  $\leq 3$  cm. Results from this study should be interpreted with caution as this study contained significant selection bias; most patients who underwent RFA had more advanced tumors and worse liver function than those who received resection (Guglielmi 2008). **RFA vs. PEI** There are several published randomized controlled trials and meta-analyses comparing the efficacy of RFA versus PEI. Two of the most recent meta-analyses were selected for appraisal (Germani 2010, Bouza 2009). Results were consistent across the two analyses. Compared to patients treated with PEI, patients treated with RFA had higher three-year overall survival rates (73% RFA vs. 58% PEI,  $p < 0.001$ ) and lower rates of local recurrence (7% RFA vs. 22% PEI,  $p < 0.001$ ). Patients treated with RFA experienced more complications (19% RFA vs. 11% PEI,  $p < 0.001$ ) than those treated with PEI; however, there was no difference in the rate of major complications (4% RFA vs. 3% PEI,  $p = 0.22$ ). The most frequent complication reported in both groups was severe pain. All studies included in the analysis were classified to be trials with high-risk of bias. **RFA + PEI vs. RFA alone** There have been several published studies comparing PEI + RFA versus RFA alone. A randomized controlled trial was selected for review (Zhang 2007). Results from this trial suggest that overall survival is higher for patients with HCC treated with PEI + RFA versus RFA only ( $p = 0.04$ ). In a subgroup analysis by tumor size, survival was significantly better for those treated with PEI + RFA who had tumors between 3.1 and 5.0 cm compared to those treated with RFA only ( $p = 0.03$ ). There was no significant difference in survival for patients with tumors  $\leq 3$  cm or tumors 5.1-7.0 cm. The local recurrence rate was higher for those treated with RFA alone compared to those treated with PEI + RFA ( $p = 0.01$ ). There was no significant difference in overall, intrahepatic, or extrahepatic recurrence rates. There were no procedure related mortalities or major complications. Pain and fever were the most commonly seen minor complications. Data after 2-years should be interpreted with caution as less than 45% of patients were followed for 3-years. Results are not generalizable to women as less than 15% of the patients enrolled in the study were women. Additionally, the predominant cause of HCC in the study was hepatitis B while the predominant cause of HCC in Japan, Europe, and the United States is hepatitis C and alcohol abuse. **Secondary Liver Cancer RFA vs. Resection** No randomized controlled trials evaluating RFA compared to resection for unresectable liver metastases from colorectal cancer were identified. Results from a retrospective cohort study indicate that patients treated with resection had the highest overall and disease-free survival rates and the lowest rates of recurrence compared to patients treated with RFA alone or RFA + resection. Results from this study should be interpreted with caution as this study contained significant selection bias. Patients who were treated with RFA were not eligible for resection (Abdalla 2004). The majority of other studies (Park 2007, Aloia 2006, Hur 2009) comparing RFA and resection reached similar conclusions regarding survival and recurrence rates; however, a few studies have found that survival rates were comparable (Oshowo 2003). It is hard to compare results across studies as the primary cause of the disease differs, techniques differ, and disease characteristics differ. Additionally, none of the treatment groups

were comparable at baseline. Patients treated with RFA were not eligible for resection. *Conclusion:* There is fair evidence that overall and disease-free survival rates were not statistically different for patient with solitary HCC <5 cm in diameter treated with either RFA or surgical resection. There is fair evidence that patients with HCC treated with RFA have better survival and lower recurrence rates than patients treated with PEI. There is fair evidence that for patients with HCC and tumors between 3.1 and 5.0 cm in diameter the combined treatment of PEI plus RFA versus RFA alone increases survival; however, long term follow-up is needed. There is insufficient evidence to determine the efficacy of RFA compared to surgical resection for patients with liver metastases. **Articles:** The literature search yielded around 250 articles pertaining to the use of RFA. The majority of these articles were case series and cohort studies. Only one randomized controlled trial (Chen 2006) was identified that compared RFA with resection for small HCC. There were several RCTs and meta-analyses comparing RFA with PEI. The two most recent meta-analyses (Bouza 2009, Germani 2010) were selected for review. There were several studies comparing the combined use of PEI and RFA. Many of these studies did not have a control group or did not assess survival as an outcome. An RCT that compared PEI + RFA with RFA alone was selected for review (Zhang 2007). No randomized controlled trials or meta-analyses were found pertaining to the use of RFA for metastatic liver cancer. The literature consisted mainly of case series and cohort studies. A retrospective cohort study (Abdalla 2004) that compared resection to RFA was selected for review. The following studies were critically appraised. Chen MS, Li JQ, Zheng Y et al. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. *Ann Surg* 2006; 243:321-328. See [Evidence Table](#). Bhardwaj N, Strickland AD, Ahmad F et al. Liver ablation techniques: a review. *Surg Endosc* 2010; 24:254-265. Bouza C, López-Cuadrado T, Alcázar R et al. Meta-analysis of percutaneous radiofrequency ablation versus ethanol injection in hepatocellular carcinoma. *BMC Gastroenterol* 2009; 9:31-39. See [Evidence Table](#). Germani G, Pleguezuelo M, Gurusamy K et al. Clinical outcomes of radiofrequency ablation, percutaneous alcohol ablation and acetic acid injection for hepatocellular carcinoma: A meta-analysis. *J Hepatol* 2010; 52:380-388. See [Evidence Table](#). Zhang YJ, Liang HH, Chen MS et al. Hepatocellular carcinoma treated with radiofrequency ablation with or without ethanol injection: A prospective randomized controlled trial. *Radiology* 2007; 244:599-607. See [Evidence Table](#). Abdalla EK, Vauthey JN, Ellis LM et al. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. *Ann Surg* 2004; 239:818-827. See [Evidence Table](#).

The use of radiofrequency ablation in the treatment of primary HCC does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

### **Laparoscopic Radiofrequency Volumetric Thermal Ablation (RFVTA) of Uterine Fibroids Using the Acessa™ System**

#### **BACKGROUND**

Uterine fibroids, also known as uterine myomas or leiomyomas, are non-cancerous tumors that grow within the wall of the uterus. They are the most common pelvic neoplasms in women, occurring among 20-40% of those in the reproductive age and 70%-80% by the age of 50. Uterine myomas are commonly classified into 3 subgroups according to their location: subserosal (projecting outside the uterus), intramural (within the myometrium) and submucosal (projecting into the cavity of the uterus). (A more recent classification was developed by International Federation of Gynecology and Obstetrics [FIGO]). Uterine fibroids also vary in size and number ranging from one tiny seedling to multiple bulky masses that can significantly enlarge the uterus. The majority of uterine leiomyomas are asymptomatic and can go unnoticed or are incidentally detected on clinical examination or imaging. However, 20-50% are symptomatic causing abnormal uterine bleeding (AUB) including menorrhagia, dysmenorrhea, pelvic pressure, back pain, and fertility issues (Brucker 2014, Chittawar 2015, Vilos 2015, Lee 2016).

Uterine fibroids are currently the leading indication of hysterectomy worldwide. Hysterectomy is the most effective and definitive treatment for symptomatic fibroids, however, many women desire to preserve their fertility and/or conserve their uterus. Myomectomy is the alternative procedure for these women; it can be performed by conventional laparotomy or by minimal access techniques such as laparoscopy, robotic-assisted laparoscopy, hysteroscopy, or other modified techniques depending on the number, size, and location of the fibroids. Each technique has its benefits and associated harms, but myomectomy in general carries the risk of fibroid recurrence and potential need for future hysterectomy. The recurrence rate ranges from 10-50% depending on age, number of fibroids, uterine size, and childbirth after myomectomy.

Conventional laparotomy has been the approach of choice for many surgeons, but it is associated with intra- and post-operative blood loss requiring blood transfusion in approximately 20% of cases. Laparoscopic myomectomy performed by a highly skilled laparoscopic surgeon is associated with less blood loss, diminished postoperative pain, faster recovery, and shorter hospital stay compared to abdominal myomectomy. However, the multilayer suturing may be challenging, and the procedure takes longer to perform and requires surgical expertise and specialized equipment. In addition, there may be a limit to the size and number of lesions removed laparoscopically. There is also a concern about the risk of uterine rupture occurring in the second or third trimester of pregnancy after laparoscopic myomectomy. A recently raised concern is the risk of power morcellation in cases of undiagnosed uterine malignancy while removing the fibroids laparoscopically as this may result in disruption and wide dissemination of an unrecognized sarcoma (Brucker 2014, Chittawar 2015, Vilos 2015 Kramer 2016).

Alternative non-surgical or minimally invasive management options for uterine fibroids include medical treatment (hormonal and non-hormonal); magnetic resonance guided focused ultrasound surgery (MRgFUS), uterine artery embolization (UAE), laparoscopic occlusion of uterine arteries, and radiofrequency (RF) myolysis or ablation of the myomas (Chittawar 2015, Vilos 2015).

Myolysis was introduced in the 1980s as a conservative option for treating myomas. It uses a focused energy to cause tissue destruction. Energy sources include laser, bipolar, monopolar, cryoprobe, or thermal radiofrequency ablation (RFA). In general, a radiofrequency system consists of a generator, an electrode, electrode return pads, and cables connecting these elements. The generator produces high frequency, low voltage, alternating current that is transmitted via an electrode with an insulated shaft. Placing the electrode into the target tissue results in transmission of the current through the tissue. The current then travels to the electrode return pads and back to the generator completing the circuit. The heat produced by ionic movement within the cells adjacent to the exposed portion of the electrode, spreads and produces volumetric ablation through coagulative necrosis (Lee 2016)

In 2002 Lee BB, first reported on the use of RF ablation under laparoscopic intraabdominal ultrasound guidance to treat patients with symptomatic myomas. A number of observational small feasibility studies using different systems were published along the years (Chudnoff 2013, Chittawar 2015, Kramer 2016, and FDA website accessed April 2017). The Acessa™ System (Halt Medical, Inc., Brentwood, CA) is an ultrasound guided system for performing radiofrequency volumetric thermal ablation (RFVTA) of fibroids in the outpatient setting. The system consists of several components including a dual function RF generator, a disposable 3.4 mm diameter hand piece with a deployable 7-needle electrode array, a handpiece cable, two disposable dispersive electrode pads, pad cable, power cord, and a foot pedal. It is designed to deliver up to 200W of RF power in 3 operational modes: Temperature Control, Manual Control, and Coagulation Mode. Additional equipment needed for the RFA procedure using the Acessa™ system include a standard laparoscopic tower (insufflator, camera box, light source and printer), laparoscope 5 or 10 mm, ultrasound machine with laparoscopic transducer, and two video monitors one for the laparoscopic image and one for the ultrasound image ( Chudnoff 2013, lee 2016 and Acessa website accessed April 2017).

The procedure is performed under general anesthesia and laparoscopic intra-abdominal ultrasound guidance. The laparoscopic ultrasound probe is used to determine the location and size of all fibroids present. The RFA handpiece tip is then inserted percutaneously through a 2-mm skin incision and directed into each myoma with laparoscopic and ultrasound guidance to verify the appropriate placement of the device within each myoma. The electrode array is then deployed, the appropriate duration of ablation is determined, and the treatment applied. Once the ablation is completed, the generator is switched to coagulation mode to seal the tract during withdrawal of the handpiece and provide hemostasis. Irregular myomas and those  $\geq 4$  cm in diameter require multiple overlapping ablations to ensure adequate ablation of the myoma periphery. After ablation, the myomas are not replaced by fibrous tissue, but are gradually reabsorbed by the surrounding myometrium. Complete reabsorption depends on the completeness of ablation, location of the myoma and weal as its size (Vilos 2015, Lee 2016).

More recently a transvaginal approach was introduced for delivering the energy without the need for general anesthesia. The procedure was examined in an observational study in China and used a different radiofrequency generator (Jiang 2014).

**06/21/2017: MTAC REVIEW**

**Evidence Conclusion: Comparative studies** the only randomized controlled trial identified by the literature search was a single center study that compared the laparoscopic ultrasound guided radiofrequency volumetric thermal ablation (RFVTA) of uterine fibroids versus laparoscopic myomectomy (LM). It is an industry sponsored ongoing post-market RCT trial with a 5-year follow-up plan. The perioperative results of the trial as well as follow-up data at 12 and 24 months were reported in three publications (Brucker 2014, Hahn 2015, and Kramer 2016) ([Evidence Table 1](#)). The trial compared RFVTA to LM which is more invasive treatment, rather than to a minimally invasive procedure such as uterine artery embolization (UAE). The primary outcome was the mean time to hospital discharge which may not be the ideal primary outcome as patients undergoing LM may require one day stay in the hospital. In this trial all 25 patients in the LM group were hospitalized overnight to monitor for potential post-procedure bleeding. Patient symptoms and safety of the procedure were secondary outcomes based on subjective responses to validated questionnaire. The study was not blinded, which is a potential source of bias, and it was only powered to detect significant differences between the two treatments for the primary outcome and not for the patient outcomes that matter. The perioperative results show significantly less time spent in hospital and less bleeding with RFVTA compared to LM (Brucker 2014 [Evidence Table 1](#)).

*Outcomes in the two intervention groups (Brucker 2014)*

Outcomes	LM group* N=25	RFVTA N=25	P value
Time to hospital discharge in hours, Mean	29.9 ± 14.2	10.0 ± 5.5	<0.001
Median	22.6	7.8	
Range	16.1-68.1	4.2-25.5	
Intraoperative blood loss in ml, Mean	51 ± 57	16 ± 9	Not provided
Median	35	20	
Range	10-300	0-30	

Patients were kept overnight in the hospital for observation

At 12-months women in the two treatment groups reported significant reduction in their symptom severity and improvement health related quality of life (HR-QoL) compared to baseline. The reported improvements were better with LM compared to RFVTA, but the differences between the two groups were not statistically significant. The only statistically significant difference between the two groups was the degree of patient satisfaction (very vs. moderately satisfied) favoring the myomectomy group. Two women in the ablation group underwent hysterectomy and one underwent myomectomy (Hahn 2015). The interim analysis at 24 months also showed significant improvement in the patient-reported symptom severity for both interventions compared to baseline. However, the improvement reported in health-related quality of life reached a statistically significant level only among patients in the LM group (Kramer 2016). The authors concluded that both interventions have similar clinical benefits, and that 12-and 24-months data suggest equivalence in safety and patient-reported efficacy of RFVTA and LM. However, the study was not designed nor powered as an equivalent trial and the numbers were too small to provide sufficient statistical power to detect significant differences. A lack of significant statistical difference does not necessarily indicate equivalence. The trial was randomized and controlled, but not without limitations. It was a single-center, relatively small, and unblinded trial. 14% of the study population was not included in the 12- and 24-months analysis which was based on per-protocol rather than on intention to treat (ITT) analysis, and on patient-reported outcomes. The study was conducted in Germany among 100% white women, with symptomatic fibroids <10 cm diameter, and other strict inclusion/exclusion criteria, that may limit generalization of the results. In addition, there were some baseline differences between the two study groups as regard age, number, size, and location of fibroids. The authors indicated that randomization occurred intraoperatively after laparoscopic ultrasound mapping of the uterus to classify the fibroid and define its size and location, and did not indicate whether any patient was excluded from randomization based on the ultrasound results, which may be a potential source of selection bias. **Non-comparative studies** the literature search identified two small low-quality feasibility studies and a one non-comparative observational study (Halt trial), the pivotal study that led to the FDA clearance of the

Acessa System in 2012. [Halt trial \(Chudnoff 2013, Guido 2013, Berman 2014\)](#). (See Evidence Table 2) was a prospective multicenter study that examined the efficacy and safety of laparoscopic ultrasound-guided RFVTA of uterine myomas in symptomatic women. The study enrolled 137 women with documented fibroids and menstrual blood loss between 150 and 500mL from 11 centers in the US and Latin America (additional inclusion /exclusion criteria are provided in the evidence table). The primary outcomes were the volume of menstrual bleeding compared to baseline, surgical re-intervention and device related adverse events at 12 months, Secondary outcomes included uterine volume measurements, patient-reported Uterine Fibroid Symptom and Health Related Quality of Life (QoL) scores and general health outcome scores at 3-6 and 12 months. Guido, 2013 and Berman, 2014 reported on the effect of the RFVTA on symptom severity qualitative clinical outcomes at 2- and 3 years after the intervention based on the patients' responses to validated questionnaires.

*Rate of reduction in menstrual blood from baseline to 12 months*

<b>Outcome</b>	
<b>Decrease of menstrual blood from baseline to 12 months</b>	n/N 104/127    81.9%
% women with ≥ 50% reduction in menstrual flow from baseline to 12 m	42% (95% CI, 31.6-48.7%)
% women with ≥ 40% reduction in menstrual flow from baseline to 12 m.	48.8% (95% CI, 40.1-57.5%)
% women with ≥ 30% reduction in menstrual flow from baseline to 12m.	59.1% (95% CI, 50.5-67.6%)
% women with ≥ 22% reduction in menstrual flow from baseline to 12 m.	67.7% (95% CI, 59.6-75.8%)

The results suggest that menstrual blood loss was significantly reduced from baseline to 12 months post-procedure. By the end of 12 months after the procedure there was one surgical intervention for persistent bleeding and one serious adverse event. Between 12 and 24 months 6 more women underwent surgical intervention for fibroid-related bleeding and one experienced severe adverse event during and after a Cesarean section delivery. By 36 months a total of 14 women (11.0%) had repeat surgical re-interventions for fibroid symptoms (11 hysterectomies, 2 myomectomies, and 1 uterine artery embolization). The results also show significant improvement in patient-reported symptom severity and health related QoL at 3 months compared to baseline, and that all quality of life and health state scores remained stable over 12, 24, and 36 months of follow-up. 5 patients (4%) experienced treatment-related adverse events including pelvic abscess, laceration in sigmoid colon, vaginal bleeding, severe lower abdominal pain and superficial uterine serosal burn. One woman got pregnant and delivered a healthy full-term baby by C-section, but experienced severe bleeding during the surgery and 48 hours later. Halt trial was sponsored by Halt Medical, the manufacturer of Acessa™ System. It was not a comparative trial and only aimed at examining the safety and efficacy of the procedure. The study was multicenter and included a diverse population, but had strict inclusion /exclusion criteria as regards the size of the leiomyomas, size of the uterus, minimum preoperative hemoglobin and other variables including limiting the procedure to women who did not desire future childbearing, all of which may limit generalization of the results.

### **Conclusion**

- There is insufficient published evidence to determine that laparoscopic ultrasound guided radiofrequency volumetric thermal ablation (RFVTA) of symptomatic uterine myoma has superior or equivalent results as other therapies/interventions used among women with symptomatic fibroids who desire to conserve their uterus. The only comparative study published to date, was small, unblinded, and only powered to detect significant difference in the length of post procedural hospital stay with RFVTA versus laparoscopic myomectomy. It was not powered to detect differences in the clinical outcomes or quality of life. A lack of significant differences does not necessarily indicate equivalence.
- There is insufficient evidence to determine the safety of the laparoscopic ultrasound RFVTA or the durability of the observed benefit over the years. The comparative study was too small and with insufficient follow-up period. The other studies examining the safety of the procedure were all observational; the largest and longest of which was the pivotal Halt trial which reported significant benefit and durability of the effect of the intervention for up to three years. However, similar to the other published

observational studies on this technology, it had its limitations; had no control or comparison group, and the majority of outcomes were subjective. The three-year follow-up of Halt trial shows an increasing rate of repeat surgeries along the years. By the end of the third year, 14 (12%) of the women who entered the 3-year follow-up had repeat surgeries 11 (79%) of which were hysterectomies

**Articles:** The literature search for studies on laparoscopic radiofrequency volumetric thermal ablation of uterine fibroids identified 4 studies with population sizes ranging from 31 to 135, reported in 9 publications. Only one study was randomized and controlled with its results were published in three articles (Brucker 2014, Hahn 2015, and Kramer 2016). The others were observational, non-comparative studies including a very small short feasibility study (Garza 2011), a small study (N=35) with 12 months follow-up (Robles 2013) and the pivotal Halt trial (published in 4 articles (Chudnoff 2013, Guido 2013, Galen 2013, and Berman 2014). The RCT and the HALT trial were selected for critical appraisal. Berman JM, Guido RS, Garza Leal JG, et al. Three-year outcome of the Halt trial: a prospective analysis of radiofrequency volumetric thermal ablation of myomas. *J Minim Invasive Gynecol.* 2014 Sep-Oct; 21(5):767-774. Brucker SY, Hahn M, Kraemer D, et al. Laparoscopic radiofrequency volumetric thermal ablation of fibroids versus laparoscopic myomectomy. *Int J Gynaecol Obstet.* 2014 Jun; 125(3):261-265. Chudnoff SG, Berman JM, Levine DJ, et al. Outpatient procedure for the treatment and relief of symptomatic uterine myomas. *Obstet Gynecol.* 2013 May; 121(5):1075-1082. Galen DI, Isaacson KB, Lee BB. Does menstrual bleeding decrease after ablation of intramural myomas? A retrospective study. *J Minim Invasive Gynecol.* 2013 Nov-Dec; 20(6):830-835. Guido RS, Macer JA, Abbott K, et al. Radiofrequency volumetric thermal ablation of fibroids: a prospective, clinical analysis of two years' outcome from the Halt trial. *Health Qual Life Outcomes.* 2013 Aug 13; 11:139. Hahn M, Brucker S, Kraemer D, et al. Radiofrequency Volumetric Thermal Ablation of Fibroids and Laparoscopic Myomectomy: Long-Term Follow-up from a Randomized Trial. *Geburtshilfe Frauenheilkd.* 2015 May; 75(5):442-449. Krämer B, Hahn M, Taran FA, et al. Interim analysis of a randomized controlled trial comparing laparoscopic radiofrequency volumetric thermal ablation of uterine fibroids with laparoscopic myomectomy. *Int J Gynaecol Obstet.* 2016 May; 133(2):206-211.

The use of Laparoscopic Radiofrequency Volumetric Thermal Ablation (RFVTA) of Uterine Fibroids Using the Acessa™ System does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

## Applicable Codes

**Barrett's Esophagus- Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

CPT® or HCPC Codes	Description
43229	Esophagoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
43270	Esophagogastroduodenoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
<b>With Diagnosis Codes</b>	
K22.70	Barrett's esophagus without dysplasia
K22.710	Barrett's esophagus with low grade dysplasia
K22.711	Barrett's esophagus with high grade dysplasia
K22.719	Barrett's esophagus with dysplasia, unspecified

**Lung Cancer - Considered Not Medically Necessary:**

CPT® or HCPC Codes	Description
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

**Transcervical Uterine Ablation of Leiomyomas - Considered Not Medically Necessary:**

CPT® or HCPC Codes	Description
58674	Laparoscopy, surgical, ablation of uterine fibroid(s) including intraoperative ultrasound guidance and monitoring, radiofrequency
0404T	Transcervical uterine fibroid(s) ablation with ultrasound guidance, radiofrequency

**\*Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

\*\*To verify authorization requirements for a specific code by plan type, please use the [Pre-authorization Code Check](#).

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Date Created	Dates Reviewed	Date Last Revised
07/17/2008	Added to annual review on 04/04/2011 <sup>MDCRPC</sup> , 02/07/2012 <sup>MDCRPC</sup> , 12/04/2012 <sup>MDCRPC</sup> , 10/01/2013 <sup>MPC</sup> , 08/05/2014 <sup>MPC</sup> , 06/02/2015 <sup>MPC</sup> , 04/05/2016 <sup>MPC</sup> , 02/07/2017 <sup>MPC</sup> , 12/05/2017 <sup>MPC</sup> , 11/06/2018 <sup>MPC</sup> , 11/05/2019 <sup>MPC</sup> , 11/03/2020 <sup>MPC</sup> , 11/02/2021 <sup>MPC</sup> , 11/01/2022 <sup>MPC</sup> , 11/07/2023 <sup>MPC</sup>	04/05/2022

<sup>MDCRPC</sup> Medical Director Clinical Review and Policy Committee

<sup>MPC</sup> Medical Policy Committee

Revision History	Description
09/08/2015	Revised LCD L34886 and L35008 Non-Covered Services.
05/03/2016	Combined RFA Barrett's Esophagus and Lung Cancer into one policy
10/04/2016	Added MTAC Review
11/01/2016	MPC approved criteria of medical necessity for Barrett's Esophagus
08/01/2017	Added MTAC Review for RFVTA
12/05/2017	Adopted KPWA Policy for Barrett's Esophagus and Uterine Fibroids for Medicare
08/28/2018	Removed non-covered LCD for lung cancer
11/17/2020	Removed references to vertebral augmentation for painful spinal metastases as there is already separate criteria for vertebroplasty
04/05/2022	MPC approved to adopt MCG* A-1039 Transcervical Uterine Ablation of Leiomyomas. This service continues to be considered not medically necessary.