Radiofrequency Tumor Ablation

Aetna considers radiofrequency ablation (RFA) medically necessary for the following indications:

- Adrenocortical carcinoma not amenable to complete surgical resection
- Cancer bone pain, management of refractory bone pain in persons with cancer
- Gastro-intestinal stromal tumors (GIST), treatment of tumors with limited progression
- Malignant lung masses, in persons who are not candidates for surgical intervention
- Medullary thyroid carcinoma, treatment of distant metastases
- Osteoid osteoma, treatment of individuals that remain symptomatic despite treatment with nonsteroidal non-inflammatory drugs (NSAIDs), as a less invasive alternative to surgical resection of the tumor
- Renal cell carcinoma, up to 4-cm in size, in persons who meet the following criteria:
  - High-risk surgical candidates; or
  - Persons with renal insufficiency, as defined by a glomerular filtration rate of less than or equal to 60 ml/min/m²; or

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*
• Persons with a solitary kidney.

- Removal of other primary or metastatic malignant neoplasms, when removal of the neoplasm may be curative, and the member is unable to tolerate surgical resection
- Soft tissue sarcoma of the trunk or extremities, treatment of symptomatic persons with disseminated metastases
- Tumor debulking, as an alternative to surgical (cold knife) resection for debulking of primary and metastatic malignant neoplasms

Aetna considers RFA experimental and investigational for all other indications including the following (not an all-inclusive list) because its effectiveness for indications other than the ones listed above has not been established:

- Curative treatment of primary or metastatic malignant neoplasms (e.g., adrenal metastases from any primary tumor, breast cancer, cartilaginous tumors in the long bones, chondroblastoma, desmoid tumors, esophageal cancer, gallbladder cancer, kidney cancer including renal angiomyolipoma, lung cancer, pancreatic cancer, spinal metastases, and thymoma; not an all-inclusive list) in persons who are able to tolerate surgical resection
- Treatment of benign thyroid nodules
- Treatment of biliary obstructions / strictures
- Treatment of Brunner’s gland hyperplasia
- Treatment of large renal angiomyolipomas
- Treatment of malignant bile duct obstruction
- Treatment of renal cysts
- Unresectable localized recurrent thyroid cancers without distant metastases.

For Aetna's policy on RFA for the treatment of Barrett's esophagus, see [CPB 0728 - Barrett's Esophagus](../700_799/0728.html).

For Aetna's policy on RFA of hepatic tumors, see [CPB 0274 - Ablation of Hepatic Lesions](../200_299/0274.html).
For Aetna’s policy on RFA of benign prostatic hypertrophy (transurethral needle ablation or TUNA), see CPB 0079 - Benign Prostatic Hypertrophy (BPH) Treatments (/1_99/0079.html).

For Aetna’s policy on RFA of treatment of uterine fibroids, see CPB 0304 - Fibroid Treatment (/300_399/0304.html).

**Background**

Radiofrequency ablation (RFA) of tumor is a procedure in which a needle electrode is inserted (via image guidance) into a lesion (tumor) and electrical energy generates heat to destroy cancer cells. This can either be performed percutaneously or through an intraoperative approach. The procedure is typically used for those patients whose tumors are inoperable or for those who are ineligible for surgery due to age, presence of comorbidities or overall poor general health.

RF tumor ablation is performed by inserting electrodes directly into the affected area where alternating high frequency current is then emitted. The current moves from the tip of the electrode into the surrounding tissue. The movement of ions results in frictional heating of the tissue and as the temperature becomes elevated beyond 60 degrees Celsius, cells around the electrode begin to die (coagulative necrosis).

Osteoid osteoma is a benign neoplasm most often seen in young males. Most osteoid osteomas are found in the first 3 decades of life, but an occasional lesion in an older patient has been reported. Almost any bone can be involved. The typical patient has pain that is worse at night and relieved by aspirin. When the growth is near a joint, swelling, stiffness, and contracture may occur. When in a vertebra, scoliosis may occur. In children, over-growth and angular deformities may occur. Routine roentgenograms are often diagnostic, but bone scans or computed tomographies commonly are required to accurately localize the lesion. To effect a cure the entire nidus must be removed. The standard method of removal is surgical resection. Recurrence after apparently complete excision has been reported but is rare.
Percutaneous RF thermal ablation has been used as a less invasive alternative to surgical resection of osteoid osteoma. The primary advantage of percutaneous RF thermal ablation is a reduction in the need for post-operative hospitalization and a reduced duration of convalescence.

Several studies have been published reporting successful removal of osteoid osteoma using percutaneous RFA. Rosenthal et al (1998) compared percutaneous RFA with standard resection in 87 patients who were treated with operative excision and 38 patients who were treated with percutaneous RFA. The former group did not require post-operative hospitalization (average of 0.2 days), whereas the latter group required an average of about 5 days of post-operative hospitalization. The rates of recurrence between the 2 treatments were approximately the same. The rate of pain relief, as measured by questionnaire, was also similar between the 2 groups. An assessment conducted for the National Institute for Clinical Excellence (2004) concluded that the evidence supporting percutaneous RFA of osteoid osteoma appears adequate to support its use, provided that the normal arrangements are in place for consent, audit and clinical governance.

Radiofrequency ablation has been advocated as an alternative to resection in persons with lung nodules who can not be treated surgically because of medical problems, multiple tumors, or poor surgical risk. Satisfactory clinical results have been reported using this method for liver tumors, and several reports have been published regarding RFA therapy for human lung neoplasms. There are, however, no adequate prospective clinical studies that demonstrate that RFA of lung metastases is as effective as surgical (cold knife) resection in curative resection of malignant neoplasms. An important concern is that RFA does not allow for examination of surgical margins to ensure that cancer is completely resected. Le and Petrik (2005) considered RFA as a promising technique for the treatment of early stages (stage I and stage II) non-small cell lung cancer. Stamatis (2005) stated that for the treatment of lung metastases, RFA in particular is currently being investigated. An assessment by the National Institute for Health and Clinical Excellence (NICE, 2006) concluded: "Current evidence on the safety and efficacy of percutaneous radiofrequency ablation for primary and secondary lung cancers shows that there are no major safety concerns with this procedure. There is evidence that the treatment can reduce tumour bulk; however, this evidence is
limited and is based on heterogeneous indications for treatment. The procedure should therefore be used only with special arrangements for consent, audit and clinical governance.

Radiofrequency ablation has been used as a treatment of pancreatic cancer for a number of years in Japan. Current evidence of effectiveness of RFA for pancreatic cancer consists of case reports and a phase II (safety) study; the latter concluded that RFA was a relatively safe treatment for pancreatic cancer. However, this evidence is insufficient to draw conclusions about the effectiveness of RFA for this indication.

Girelli et al (2010) examined the feasibility and safety of RFA as a treatment option for locally advanced pancreatic cancer. A total of 50 patients with locally advanced pancreatic cancer were studied prospectively. Ultrasound-guided RFA was performed during laparotomy. The main outcome measures were short-term morbidity and mortality. The tumor was located in the pancreatic head or uncinate process in 34 patients and in the body or tail in 16; median diameter was 40 (inter-quartile range [IQR] of 30 to 50) mm. Radiofrequency ablation was the only treatment in 19 patients; it was combined with biliary and gastric bypass in 19 patients, gastric bypass alone in 8, biliary bypass alone in 3 and pancreatico-jejunostomy in 1. The 30-day mortality rate was 2 %. Abdominal complications occurred in 24 % of patients; in half they were directly associated with RFA and treated conservatively. Three patients with surgery-related complications needed re-operation. Reduction of RFA temperature from 105 degrees C to 90 degrees C resulted in a significant reduction in complications (10 versus 2 of 25 patients; p = 0.028). Median post-operative hospital stay was 10 (range of 7 to 31) days. The authors concluded that RFA of locally advanced pancreatic cancer is feasible and relatively well-tolerated, with a 24 % complication rate. This was a feasibility and safety study; it did not provide any data on the effectiveness of RFA in treating pancreatic cancer.

Several authorities have noted that RFA of renal tumors is a promising investigational alternative to partial or total nephrectomy (Janzen et al, 2002; Russo, 2001; Wood et al, 2002). Studies performed to date have focused on the technical feasibility of RFA of renal tumors. Prospective clinical studies are needed to determine if RFA of renal cell carcinomas improve survival and are as effective as total or partial nephrectomy.
An assessment conducted by the NICE (2004) reached the following conclusions about RFA of renal tumors: "Limited evidence suggests that percutaneous radiofrequency ablation (RFA) of renal cancer brings about reduction of tumor bulk as assessed by computed tomography, and that the procedure is adequately safe. However, the procedure has not been shown to improve symptoms or survival .... Patient selection is important and the procedure should normally be limited to patients who are unsuitable for surgery."

An assessment of the evidence for RFA of kidney cancer prepared by the Canadian Coordinating Office for Health Technology Assessment (Hailey, 2006) reached the following conclusions: "RFA is emerging as a useful alternative to nephrectomy in the management of some types of kidney cancer. It appears to be useful for smaller, non-central tumours, and for cases where surgery is contraindicated. A disadvantage is the possibility of residual cancer that cannot be detected by diagnostic imaging during follow-up. There are no results from randomized trials, and the period of follow-up for patients who have had the procedure is short. Only with longer follow-up evaluations (5 years to 10 years) will relevant comparison with radical and partial nephrectomy be possible."

Furthermore, Hinshaw and Lee (2004) stated that RFA, cryoablation, microwave ablation, and laser ablation have all shown promise for the treatment of renal cell carcinomas (RCC), with high local control and low complication rates for RFA and cryoablation. However, the clinical trial data remain early, and survival data are not yet available for a definitive comparison with conventional surgical techniques for removal of RCC (Hinshaw and Lee, 2004). Mahnken et al (2004) noted that the increasing number of clinical reports on RFA of the kidney show the promising potential of renal RFA for minimally invasive tumor treatment. Due to its technical benefits, RFA seems to be advantageous when compared to cryoablation or laser ablation. However, there are no long-term follow-up or comparative data proving an equal effectiveness to surgery (Mahnken et al, 2004).

In a systematic review on focal therapy for kidney cancer, Kutikov and colleagues (2009) stated that most cryoablations are performed using a laparoscopic approach, whereas RFA of the localized small renal masses (SRM) is more commonly administered percutaneously. Pre-treatment biopsy is performed more often for lesions treated by cryoablation than RFA with a significantly higher rate of indeterminate or unknown pathology for SRMs undergoing RFA versus cryoablation (p < 0.0001). Currently available data suggest that cryoablation results in lower re-
treatments \( (p < 0.0001) \), less local tumor progressions \( (p < 0.0001) \) and may be associated with a decreased risk of metastatic progression compared with RFA. It is unclear if these differences are a function of the technologies or their application. The extent to which focal ablation alters the natural history of SRMs has not yet been established. The authors concluded that currently, data on the ability of interventions for SRMs to affect the natural history of these masses are lacking. They stated that prospective randomized evaluations of available clinical approaches to SRMs are needed. This is in agreement with the observations of Carraway et al (2009) who noted that continued studies on renal RFA are needed, especially in regards to oncological outcomes.

A Cochrane systematic evidence review (Nabi et al, 2010) of surgical management of localized RCC found that the main source of evidence for the current practice of laparoscopic excision of renal cancer is drawn from case series, small retrospective studies and very few small randomized controlled trials. "The results and conclusions of these studies must therefore be interpreted with caution." The authors of the systematic evidence review did not identify any randomized trials meeting the inclusion criteria reporting on the comparison between open radical nephrectomy with laparoscopic approach or new modalities of treatment such as RFA or cryoablation. Three randomized controlled trials compared the different laparoscopic approaches to nephrectomy (trans peritoneal versus retroperitoneal) and found no statistical difference in operative or peri-operative outcomes between the 2 treatment groups. There were several non-randomized and retrospective case series reporting various advantages of laparoscopic renal cancer surgery such as less blood loss, early recovery and shorter hospital stay.

Sooriakumaran and co-workers (2010) examined the presentation, management and outcomes of patients with renal angiomyolipoma (AML) over a period of 10 years. These investigators evaluated retrospectively 102 patients (median follow-up of 4 years); 70 had tuberous sclerosis complex (TSC; median tumor size of 3.5 cm) and the other 32 were sporadic (median tumor size of 1.2 cm). Data were gathered from several sources, including radiology and clinical genetics databases. The 77 patients with stable disease were followed-up with surveillance imaging, and 25 received interventions, some more than one. Indications for intervention included spontaneous life-threatening hemorrhage, large AML (10 to 20 cm), pain and visceral compressive symptoms. Selective arterial embolization (SAE) was performed in 19 patients; 10 received operative management and 4 had a RFA. Selective arterial embolization was effective in controlling hemorrhage from AMLs...
in the acute setting (n = 6) but some patients required further intervention (n = 4) and there was a significant complication rate. The reduction in tumor volume was only modest (28%). No complications occurred after surgery (median follow-up of 5.5 years) or RFA (median follow-up of 9 months). One patient was entered into a trial and treated with sirolimus (rapamycin). The authors concluded that the management of AML is both complex and challenging, especially in those with TSC, where tumors are usually larger and multiple. Although SAE was effective at controlling hemorrhage in the acute setting it was deemed to be of limited value in the longer term management of these tumors. Thus, novel techniques such as focused ablation and pharmacotherapies including the use of anti-angiogenic molecules and mammalian target of rapamycin inhibitors, which might prove to be safer and equally effective, should be further explored.

Radiofrequency ablation has also been used to treat bone metastases. However, there are no adequate clinical studies reported in the literature on the use of RFA of metastatic lesions to bone.

In a review of the evidence on RFA of tumors, Wood et al (2002) concluded that “[m]ore rigorous scientific review, long-term follow-up, and randomized prospective trials are needed to help define the role of RFA [radiofrequency ablation] in oncology.” Rhim (2004) noted that although RFA represents a paradigm shift in local therapy for many commonly seen tumors, more sophisticated strategies to enhance the therapeutic effectiveness are needed and more randomized, controlled trials to estimate its clinical benefit are warranted. de Baere (2005) stated that RFA, although very efficient in local tumor control, has neither proven to prolong survival or to be equivalent to surgery in randomized trial, even if some retrospective studies have done so. Further studies are needed to evaluate the exact benefit of this promising technique.

Barrett's esophagus (BE) is defined as the presence of specialized intestinal metaplasia within the tubular esophagus, and is the pre-malignant precursor of esophageal adenocarcinoma. Esophageal cancer is one of the most deadly gastrointestinal cancers with a mortality rate over 90%. The principal risk factors for esophageal adenocarcinoma are gastro-esophageal reflux disease (GERD) and its sequela, BE. Gastro-esophageal reflux disease usually leads to esophagitis. However, in a minority of patients, ongoing GERD leads to replacement of
esophageal squamous mucosa with metaplastic, intestinal-type Barrett's mucosa. In the setting of continued peptic injury, Barrett's mucosa can give rise to esophageal adenocarcinoma (Feagins and Souza, 2005).

A new method of endoscopic ablation of BE is balloon-based, bipolar RFA (Stellartech Research Coagulation System; BARRx, Inc, Sunnyvale, CA), also known as Barrett's endoscopy. This technique requires the use of sizing balloons to determine the inner diameter of the targeted portion of the esophagus (Johnson, 2005). This is followed by placement of a balloon-based electrode with a 3-cm long treatment area that incorporates tightly spaced, bipolar electrodes that alternate in polarity. The electrode is then attached to a RF generator and a pre-selected amount of energy is delivered in less than 1 second at 350 W.

In a review of evidence on ablative techniques for BE, Johnston (2005) stated that it is not clear which of the numerous endoscopic ablative techniques available -- photodynamic therapy, laser therapy, multi-polar electrocoagulation, argon plasma coagulation, endoscopic mucosal resection, RFA or cryotherapy -- will emerge as superior for treatment of BE. In addition, it has yet to be determined whether the risks associated with ablation therapy are less than the risk of BE progressing to cancer. Whether ablation therapy eliminates or significantly reduces the risk of cancer, eliminates the need for surveillance endoscopy, or is cost-effective, also remains to be seen. Comparative trials that are now underway should help to answer these questions.

Hubbard and Velanovich (2007) stated that endoscopic endoluminal RFA using the Barrx device (Barrx Medical, Sunnyvale, CA) is a new technique to treat BE. This procedure has been used in patients who have not had anti-reflux surgery. This report presented an early experience of the effects of endoluminal ablation on the reflux symptoms and completeness of ablation in post-fundoplication patients. A total of 7 patients who have had either a laparoscopic or open Nissen fundoplication and BE underwent endoscopic endoluminal ablation of the Barrett's metaplasia using the Barrx device. Pre-procedure, none of the patients had significant symptoms related to GERD. One to 2 weeks after the ablation, patients were questioned as to the presence of symptoms. Pre-procedure and post-procedure, they completed the GERD-HRQL symptom severity questionnaire (best possible score, 0; worst possible score, 50). Patients had follow-up endoscopy to assess completeness of ablation 3 months after the original treatment. All patients completed the ablation without complications. No patients reported recurrence of
their GERD symptoms. The median pre-procedure total GERD-HRQL score was 2, compared to a median post-procedure score of 1. One patient had residual Barrett's metaplasia at 3 months follow-up, requiring re-ablation. The authors concluded that this preliminary report of a small number of patients demonstrated that endoscopic endoluminal ablation of Barrett's metaplasia using the Barrx device is safe and effective in patients who have already undergone anti-reflux surgery. There appears to be no disruption in the fundoplication or recurrence of GERD-related symptoms. Nevertheless, they stated that studies with longer-term follow-up and with more patients are needed.

Ganz et al (2008) evaluated the safety and effectiveness of endoscopic circumferential balloon-based ablation by using RF energy for treating BE that contains high-grade dysplasia (HGD). Patients with histologic evidence of intestinal metaplasia (IM) that contained HGD confirmed by at least 2 expert pathologists were included in this study. A prior endoscopic mucosal resection (EMR) was permitted, provided that residual HGD remained in the BE region for ablation. Histologic complete response (CR) end points: (i) all biopsy specimen fragments obtained at the last biopsy session were negative for HGD (CR-HGD), (ii) all biopsy specimens were negative for any dysplasia (CR-D), and (iii) all biopsy specimens were negative for IM (CR-IM). A total of 142 patients (median age of 66 years, IQR 59 to 75 years) who had BE HGD (median length of 6 cm, IQR 3 to 8 cm) underwent circumferential ablation (median of 1 session, IQR 1 to 2 sessions). No serious adverse events were reported. There was 1 asymptomatic stricture and no buried glands. Ninety-two patients had at least 1 follow-up biopsy session (median follow-up of 12 months, IQR 8 to 15 months). A CR-HGD was achieved in 90.2 % of patients, CR-D in 80.4 %, and CR-IM in 54.3 %. The authors concluded that endoscopic circumferential ablation is a promising modality for the treatment of BE that contains HGD. In this multi-center registry, the intervention safely achieved a CR for HGD in 90.2 % of patients at a median of 12 months of follow-up. Major drawbacks of this study were a non-randomized study design, absence of a control arm, a lack of centralized pathology review, ablation and biopsy technique not standardized, and a relatively short-term follow-up.

Shaheen and colleagues (2009) examined if endoscopic RFA could eradicate dysplastic BE and decrease the rate of neoplastic progression. In a multi-center, sham-controlled trial, these researchers randomly assigned 127 patients with dysplastic BE in a 2:1 ratio to receive either RFA (ablation group) or a sham procedure (control group). Randomization was stratified according to the grade of
dysplasia and the length of BE. Primary outcomes at 12 months included the complete eradication of dysplasia and intestinal metaplasia. In the intention-to-treat analyses, among patients with low-grade dysplasia, complete eradication of dysplasia occurred in 90.5% of those in the ablation group, as compared with 22.7% of those in the control group (p < 0.001). Among patients with high-grade dysplasia, complete eradication occurred in 81.0% of those in the ablation group, as compared with 19.0% of those in the control group (p < 0.001). Overall, 77.4% of patients in the ablation group had complete eradication of intestinal metaplasia, as compared with 2.3% of those in the control group (p < 0.001). Patients in the ablation group had less disease progression (3.6% versus 16.3%, p = 0.03) and fewer cancers (1.2% versus 9.3%, p = 0.045). Patients reported having more chest pain after the ablation procedure than after the sham procedure. In the ablation group, 1 patient had upper gastrointestinal hemorrhage, and 5 patients (6.0%) had esophageal stricture. The authors concluded that in patients with dysplastic BE, RFA was associated with a high rate of complete eradication of both dysplasia and intestinal metaplasia and a reduced risk of disease progression.

As stated by the authors, this study has several limitations: (i) these investigators used eradication of intestinal metaplasia and dysplasia, along with neoplastic progression, as surrogate markers for death from cancer, even though long-term data demonstrating an association between eradication of intestinal metaplasia and a decreased risk of cancer are sparse, (ii) the study duration was 1 year. Although other data suggest that reversion to neosquamous epithelium after RFA is durable, it is unclear if the results of the study will persist, (iii) because of stratified randomization according to the degree of dysplasia and the 2:1 ratio for assignment of patients to the ablation group and the control group, the number of patients in some groups was small, (iv) since this study did not compare RFA with other interventions, such as photodynamic therapy and esophagectomy, these researchers can not determine which of these interventions is superior, and (v) whether these findings can be generalized to community-practice settings is unknown.

Furthermore, the risk of subsquamous intestinal metaplasia following ablative therapy is a concern for all ablative techniques. However, the malignant potential of subsquamous intestinal metaplasia is unknown. In this study, subsquamous intestinal metaplasia was quite common in patients (25.2%) before enrollment and,
similar to previous reports, was low after RF ablation (5.1%). Although the biopsy regimen in this study was aggressive, it is possible that some patients had undetected subsquamous intestinal metaplasia.

Finally, because these investigators sought to define the efficacy of RFA for the spectrum of dysplasia, they enrolled patients with both low-grade dysplasia and high-grade dysplasia. However, the implications of these 2 diagnoses are markedly different. Low-grade dysplasia implies a risk of progression to cancer of less than 1% per patient-year, whereas the risk associated with high-grade dysplasia may be higher by a factor of 10. In making decisions about the management of pre-cancerous conditions, clinicians, patients, and policy-makers consider possible benefits and risks of competing strategies. Because high-grade dysplasia has a more ominous natural history than low-grade dysplasia (or non-dysplastic intestinal metaplasia), greater risks and costs are tolerable. For less severe disease, the safety profile and associated costs become increasingly important. Detailed consideration of these trade-offs is beyond the scope of this study. Regardless, both of the dysplasia subgroups showed high rates of reversion to squamous epithelium after RFA and reduced rates of disease progression with few serious adverse effects, suggesting that the application of ablative therapy in patients with low-grade dysplasia is worth further investigation and consideration.

In the accompanying editorial, Bergman (2009) stated that it is still too early to promote RFA for patients with non-dysplastic BE. Dr. Bergman also asked the following questions: (i) is complete response after ablation maintained over time, thus reducing the risk of progression to high-grade dysplasia or cancer?, (ii) will ablation improve patients' quality of life and decrease costs, as compared with the surveillance strategy?, and (iii) can we define a stratification index predicting disease progression or response to therapy? The author noted that "[w]e run the risk of losing the momentum to enroll patients in a trial that is required at this stage: a randomized comparison of endoscopic surveillance and radiofrequency ablation for non-dysplastic Barrett's esophagus. Such a study might truly revolutionize the management of this condition and answer the question as to whether radiofrequency ablation is great just for some or justified for many".

Furthermore, the American College of Gastroenterology's updated guidelines for the diagnosis, surveillance and therapy of BE (Wang and Sampliner, 2008) states that "further evaluation of the most recent technology, radiofrequency ablation is awaited. Cryotherapy is beginning clinical trials and older technologies are
becoming more refined (e.g., photodynamic therapy with the development of new agents). Documentation of the frequency and duration of the surveillance protocol after endoscopic ablation therapy requires careful study."

Yeh and Triadafilopoulos (2005) noted that a wide variety of endoscopic mucosal ablative techniques have been developed for early esophageal neoplasia. However, long-term control of neoplastic risk has not been demonstrated. The authors explained that most studies show that specialized intestinal metaplasia may persist underneath neo-squamous mucosa, posing a risk for subsequent neoplastic progression.

Shaheen (2005) noted that the pathogenesis of BE is poorly understood. Given that some patients will have repeated bouts of severe erosive esophagitis and never develop BE, host factors must play an important role. The author stated that the utility of neoadjuvant radiation and chemotherapy in those with adenocarcinoma, although they are widely practiced, is not of clear benefit, and some authorities recommend against it. Ablative therapies, as well as endoscopic mucosal resection, hold promise for those with superficial cancer or high-grade dysplasia. The author noted that most series using these modalities feature relatively short follow-up; longer-term studies are needed to better ascertain the effectiveness of these treatments.

Pedrazzani et al (2005) evaluated the effectiveness of 90 W argon plasma coagulation (APC) for the ablation of BE that is considered to be the main risk factor for the development of esophageal adenocarcinoma. They found that high-power setting APC showed to be safe. The effects persist at a mean follow-up period of 2 years with a comparable cost in term of complications with respect to standard power settings. The authors stated, however, that further studies with greater number of patients are required to confirm these results and to assess if ablation reduces the incidence of malignant progression.

Hage et al (2005) stated that although endoscopic removal of BE by ablative therapies is possible in the majority of patients, histologically complete elimination can not be achieved in all cases. Persistent BE may still harbor molecular aberrations and must therefore be considered still to be at risk of progression to adenocarcinoma.
Guidelines on thyroid cancer from the National Comprehensive Cancer Network (NCCN, 2010) state that distant metastases from recurrent or persistent medullary thyroid carcinoma that are causing symptoms (e.g., those in bone) could be considered for palliative resection, RFA, or other regional treatment. The guidelines state that these interventions may also be considered for asymptomatic distant metastases (especially for progressive disease) but observation is acceptable, given the lack of data regarding alteration in outcome.

Monchik and colleagues (2006) evaluated the long-term effectiveness of RFA and percutaneous ethanol (EtOH) injection treatment of patients with local recurrence or focal distant metastases of well-differentiated thyroid cancer (WTC). A total of 20 patients underwent treatment of biopsy-proven recurrent WTC in the neck. Sixteen of these patients had lesions treated by ultrasound-guided RFA (mean size of 17.0 mm; range of 8 to 40 mm), while 6 had ultrasound-guided EtOH injection treatment (mean size of 11.4 mm; range of 6 to 15 mm). Four patients underwent RFA treatment of focal distant metastases from WTC; 3 of these patients had CT-guided RFA of bone metastases (mean size of 40.0 mm; range of 30 to 60 mm), and 1 patient underwent RFA for a solitary lung metastasis (size, 27 mm). Patients were then followed with routine ultrasound, whole body scan, and/or serum thyroglobulin levels for recurrence at the treatment site. No recurrent disease was detected at the treatment site in 14 of the 16 patients treated with RFA and in all 6 patients treated with EtOH injection at a mean follow-up of 40.7 and 18.7 months, respectively. Two of the 3 patients treated for bone metastases were disease-free at the treatment site at 44 and 53 months of follow-up, respectively. The patient who underwent RFA for a solitary lung metastasis was disease-free at the treatment site at 10 months of follow-up. No complications were experienced in the group treated by EtOH injection, while 1 minor skin burn and 1 permanent vocal cord paralysis occurred in the RFA treatment group. The authors concluded that RFA and EtOH ablation show promise as alternatives to surgical treatment of recurrent WTC in patients with difficult reoperations. They stated that further long-term follow-up studies are needed to ascertain the precise role these therapies should play in the treatment of recurrent WTC.

The Food and Drug Administration (FDA) has issued a Public Health Notification as clarification for healthcare providers that no RFA devices are specifically approved for use in partial or full ablation of lung tumors (2008). This notification was sent in follow-up to an earlier notice in December 2007, which indicated that a number of deaths have been associated with the use of RFA for lung tumors. Radiofrequency
Ablation devices are minimally invasive tools used for general removal of soft tissue, such as those that contain cancer cells. It is an image-guided technique that heats and destroys cancer cells. Imaging techniques such as ultrasound and computed tomography (CT) are used to help guide a needle electrode into a cancerous tumor. High-frequency electrical currents are then passed through the electrode, creating heat that destroys the abnormal cells.

Radiofrequency ablation devices have been cleared by the FDA for the general indication of soft tissue cutting, coagulation, and ablation by thermal coagulation necrosis. This clearance was based only on bench testing or animal testing performance data. Under this general indication, RFA can be used as a tool to ablate tumors, including lung tumors. In addition, some RFA devices have been cleared for additional specific treatment indications, including partial or complete ablation of non-resectable liver lesions, and palliation of pain associated with metastatic lesions involving bone. Clearance for specific treatment indications requires the submission of clinical data to justify the indications by showing that the device, when used on a well-defined target population, consistently achieves the desired treatment effect.

As sufficient clinical data has not been submitted, the FDA emphasizes that it has not cleared any RFA devices for the specific treatment indication of partial or complete ablation of lung tumors. Therefore, FDA regulations prevent manufacturers from marketing or promoting the devices for this treatment, which would also include specific training programs; this does not apply to training available from sources other than the manufacturer. The FDA has received reports of death and serious injuries associated with the use of RFA devices in treatment of lung tumors. The actual rate of these adverse events is unknown because no pre-market clinical data have been obtained. It is unclear if these deaths or injuries occur more frequently with RFA devices than with other forms of treatment for lung tumors. These adverse events could be related to a number of factors, including patient selection and management, technical use of the RFA device, post-procedural treatments, and management of complications.

The FDA urges all clinicians to use MedWatch, the FDA’s voluntary reporting program, to report any adverse events related to this or any other device at: FDA MedWatch (http://www.fda.gov/medwatch/report.htm).
Guidelines from the National Comprehensive Cancer Network (NCCN, 2010) include recommendations for RFA of the trunk and extremities in metastatic soft tissue sarcoma. The guidelines include metastasectomy with RFA as an alternative method for control of metastatic lesions in limited metastases. The guidelines also include RFA as options for symptomatic patients with disseminated metastases. “The guidelines are intentionally nonspecific about this group of options, because many different issues are factored into this decision (e.g., patient performance status, patient preferences, specific clinical problems from the metastases, treatment availability).”

The guidelines (NCCN, 2010) also recommend the use of RFA for the treatment of gastrointestinal stromal tumors with limited progression. Progression is defined as a new lesion or increase in tumor size. The NCCN guidelines state that, for limited progressive disease that is potentially easily resectable, surgical resection should be considered. Other treatment options include RFA or embolization.

In an open-label, pilot study, Steel et al (2011) examined the safety of endobiliary bipolar RFA in patients with malignant biliary obstruction and reported the 90-day biliary patency of this novel procedure. Main outcome measures were immediate and 30-day complications as well as 90-day stent patency. A total of 22 patients (16 pancreatic, 6 cholangiocarcinoma) were included in this study. Deployment of an RFA catheter was successful in 21 patients. Self-expandable metal stents (SEMSs) placement was achieved in all cases of successful RFA catheter deployment. One patient failed to demonstrate successful biliary decompression after SEMS placement and died within 90 days. All other patients maintained stent patency at 30 days. One patient had asymptomatic biochemical pancreatitis, 2 patients required percutaneous gallbladder drainage, and 1 patient developed rigors. At 90-day follow-up, 1 additional patient had died with a patent stent, and 3 patients had occluded biliary stents. The authors concluded that endobiliary RFA treatment appears to be safe. They stated that randomized studies with prolonged follow-up are needed.

Lee and colleagues (2008) noted that Brunner's gland hyperplasia is a benign tumor of the duodenum and it is rarely associated with clinical symptoms. These investigators reported on the case of a 64-yr old man with Brunner's gland hyperplasia who had undergone a duodenocephalo-pancreatectomy. The reason was that he presented upper gastro-intestinal obstructive symptoms and the esophago-gastro-duodenoscopic finding revealed the lesion to be an infiltrating type.
mass on the second portion of the duodenum with luminal narrowing. An abdominal computed tomography showed a 2.5 cm-sized mass in the duodenal second portion with a suspicious pancreatic invasion and 7 mm-sized lymph node around the duodenum. Duodenocephalo-pancreatectomy was successfully performed. Histological examination revealed a Brunner’s gland hyperplasia. The final diagnosis was the coexistence of Brunner’s gland hyperplasia and pancreatic heterotopia with a pancreatic head invasion. These researchers (2008) stated that there is no consensus on the treatment of Brunner’s gland hyperplasia because follow-up study is insufficient. The medical treatment is to control gastric hyperacidity, which is one cause of Brunner’s gland hyperplasia. However, the regression of Brunner’s gland hyperplasia is rare. Thus, excision appears to be the treatment of choice. Lee and associates (2008) recommended complete removal of the lesion by endoscopic resection or surgical resection when Brunner’s gland hyperplasia results in symptoms and complications or when definite diagnosis is necessary. There is a lack of evidence on RFA as a treatment for Brunner’s gland hyperplasia.

Stewart et al (2009) stated that Brunner’s gland hamartomas (BGHs) are uncommon benign tumors of the duodenum forming mature Brunner’s glands. These researchers reported an unusual case of a giant BGH that was not amenable to endoscopic or surgical local resection; thus requiring a pancreaticoduodenectomy for extirpation.

Euanorasetr and Sommayura (2010) noted that BGHs are uncommon benign tumor of the duodenum. Most lesions are small and asymptomatic. Occasionally, those lesions may be large and manifest as a rare cause of upper gastro-intestinal hemorrhage or duodenal obstruction. The authors reported 2 cases of BGHs presenting with upper gastro-intestinal hemorrhage that were not amenable to endoscopic polypectomy; thus requiring surgical resection.

Kroon et al (2011) summarized the consensus developed by a group of Australasian subspecialists in reproductive endocrinology and infertility (the ACCEPT group) on the evidence concerning the impact and management of fibroids in infertility. The location of a fibroid within the uterus influences its effect on fertility. Subserosal fibroids do not appear to impact on fertility outcomes. Intra-mural (IM) fibroids may be associated with reduced fertility and an increased miscarriage rate (MR); however, there is insufficient evidence to inform whether myomectomy for IM fibroids improves fertility outcomes. Submucosal fibroids are
associated with reduced fertility and an increased MR, and myomectomy for submucosal fibroids appears likely to improve fertility outcomes. The relative effect of multiple or different sized fibroids on fertility outcomes is uncertain, as is the relative usefulness of myomectomy in these situations. It is recommended that fibroids with suspected cavity involvement are defined by magnetic resonance imaging, sonohysterography or hysteroscopy because modalities such as transvaginal ultrasound and hysterosalpingography lack appropriate sensitivity and specificity. Medical management of fibroids delays efforts to conceive and is not recommended for the management of infertility associated with fibroids. Newer treatments such as uterine artery embolization, RFA, bilateral uterine artery ligation, magnetic resonance-guided focussed ultrasound surgery and fibroid myolysis require further investigation prior to their establishment in the routine management of fibroid-associated infertility.

Fegrachi et al (2014) noted that median survival in patients with unresectable locally advanced pancreatic cancer lies in the range of 9 to 15 months. Radiofrequency ablation may prolong survival, but data on its safety and effectiveness are scarce. These investigators performed a systematic literature search in PubMed, EMBASE, and the Cochrane Library with the syntax ‘(radiofrequency OR RFA) AND (pancreas OR pancreatic)’ for studies published until January 1, 2012. In addition, a search of the proceedings of conferences on pancreatic disease that took place during 2009 to 2011 was performed. Studies with fewer than 5 patients were excluded as they were considered to be case-reports. The primary endpoint was survival; secondary endpoints included morbidity and mortality. A total of 5 studies involving a total of 158 patients with pancreatic cancer treated with RFA fulfilled the eligibility criteria. These studies reported median survival after RFA of 3 to 33 months, morbidity related to RFA of 4 to 37%, mortality of 0 to 19% and overall morbidity of 10 to 43%. Pooling of data was not appropriate as the study populations and reported outcomes were heterogeneous. Crucial safety aspects included ensuring a maximum RFA tip temperature of less than 90°C and ensuring minimum distances between the RFA probe and surrounding structures. The authors concluded that RFA seems to be feasible and safe when it is used with the correct temperature and at an appropriate distance from vital structures. It appears to have a positive impact on survival. Moreover, they stated that multi-center randomized trials are needed to determine the true effect size of RFA and to minimize the impacts of selection and publication biases.
In a phase II clinical trial, Takaki et al (2013) evaluated the safety and effectiveness of RFA with a multiple-electrode switching system for the treatment of RCC. From November 2009 to December 2010, a total of 33 patients (mean age of 70.7 years; range of 44 to 86 years) with histologically proved RCCs -- including 24 men (mean age of 69.5 years [range of 44 to 86 years]) and 9 women (mean age of 74.1 years [range of 64 to 83 years]) -- were enrolled in this study. The institutional review board approved the study after patients provided written informed consent. The mean maximum tumor diameter was 2.9 cm ± 1.0 (standard deviation) (range of 1.5 to 5.0 cm). Radiofrequency ablation was conducted with a multiple-electrode switching system. The primary end-point was evaluated with the Common Terminology Criteria for Adverse Events. Secondary end-points were changes in renal function, technique effectiveness, local tumor progression, and survival.

Changes in renal function were evaluated by using the Mann-Whitney U test. No severe adverse events occurred, but 3 of 33 patients (9 %) had grade-2 adverse events. Although the mean glomerular filtration rate at 1 year after RFA was similar to the baseline value in 26 patients with bilateral kidneys (p = 0.14), it was decreased significantly in 6 patients with a single kidney (p = 0.03). Tumor enhancement disappeared after a single RFA session in 31 patients and after 2 RFA sessions in the other 2 patients (rates of primary and secondary technique effectiveness, 94 % [31 of 33] and 100 % [33 of 33], respectively). No local tumor progression was found during the mean follow-up of 20.0 months (range of 11.6 to 27.6 months). The respective 1-year overall and RCC-related survival rates were 97 % (95 % confidence intervals [CI]: 91 % to 100 %) and 100 %. The authors concluded that RFA with a multiple-electrode switching system is safe and effective for treatment of RCCs. Moreover, they stated that further study is needed to examine if this technology is superior to other previously described methods.

Gunjur et al (2014) systematically reviewed the literature on the use of surgery, stereotactic ablative body radiotherapy (SABR) and percutaneous catheter ablation (PCA) techniques for the treatment of adrenal metastases to develop evidence-based recommendations. A systematic review of the MEDLINE database was performed using structured search terms following PRISMA guidelines. Eligible publications were those published from 1990 to 2012, written in English, had at least 5 patients treated for adrenal metastasis and reported on patient clinical outcomes (local control, survival and treatment related complications/toxicity). Where possible, these researchers analyzed pooled 2-year local control and overall survival outcomes. Their search strategy produced a total of 45 papers addressing the 3 modalities - 30 adrenalectomy, 9 SABR and 6 PCA (818, 178 and 51 patients,
respectively). There was marked heterogeneity in outcome reporting, patient selection and follow-up periods between studies. The weighted 2-year local control and overall survival for adrenalectomy were 84 % and 46 %, respectively, compared with 63 % and 19 %, respectively for the SABR cohort. Only 1 study of PCA with 5 patients analyzed clinical outcomes, reporting an actuarial local control of 80 % at 1 year. Treatment related complications/toxicities were inconsistently reported. The authors concluded that there is insufficient evidence to determine the best local treatment modality for isolated or limited adrenal metastases from any primary tumor. Published data suggested adrenalectomy to be a reasonable treatment approach for isolated adrenal metastasis in suitable patients; SABR is a valid alternative in cases when surgery is not feasible or the operative risk is unacceptable. They stated that PCA (including RFA) cannot be recommended until there are more robust studies that include long-term oncological outcomes.

Paliogiannis et al (2014) described a case of successful RFA of an unresectable stage III-type B3 thymoma, and discussed the role of this novel approach in the management of patients with advanced stage thymoma. The patient, a 59-year old Caucasian male underwent neoadjuvant chemotherapy with only a slight reduction of the mass. Subsequently, an explorative sternotomy and debulking were performed; before closing the thorax, RFA of the residual tumor was carried out and a partial necrosis of the mass was achieved. A further percutaneous RFA was performed subsequently, obtaining complete necrosis of the lesion. Successively, the patient underwent adjuvant radiotherapy. As a result of this multi-disciplinary treatment, complete and stable response was obtained. It is hard to say which of the single treatments had the major impact on cure; nevertheless, the results obtained suggest that RFA must be taken into account for the treatment of advanced stage thymomas, and its effectiveness must be further assessed in future studies.

Dierselhuis et al (2014) stated that atypical cartilaginous tumors are usually treated by curettage. In a proof-of-principle study, these researchers showed that RFA was an effective alternative treatment. They enrolled 20 patients (2 males, 18 females, mean age of 56 years (36 to 72). After inclusion, biopsy and RFA were performed, followed 3 months later by curettage and adjuvant phenolization. The primary end-point was the proportional necrosis in the retrieved material. Secondary end-points were correlation with the findings on gadolinium enhanced MRI, functional outcome and complications. The results showed that 95 % to 100 % necrosis was obtained in 14 of the 20 patients; MRI had a 91 % sensitivity and 67 % specificity for
detecting residual tumor after curettage. The mean functional outcome (MSTS) score 6 weeks after RFA was 27.1 (23 to 30) compared with 18.1 (12 to 25) after curettage (p < 0.001). No complications occurred after ablation, while 2 patients developed a pathological fracture after curettage. These researchers showed that RFA is capable of completely eradicating cartilaginous tumor cells in selective cases; MRI has a 91 % sensitivity for detecting any residual tumor. The authors concluded that RFA can be performed on an out-patient basis allowing a rapid return to normal activities. If it can be made more effective, it has the potential to provide better local control, while improving functional outcome.

Cobianchi et al (2014) noted that desmoid tumors are benign, myofibroblastic stromal neoplasms common in Gardner’s syndrome, which is a subtype of familial adenomatous polyposis characterized by colonic polyps, osteomas, thyroid cancer, epidermoid cysts, fibromas and sebaceous cysts. The primary treatment is surgery, followed by adjuvant radiotherapy, but the local recurrence rate is high, and wide resection can result in debilitating loss of function. These investigators reported the case of a 39-year old man with Gardner’s syndrome who had already undergone a total prophylactic colectomy. He developed desmoid tumors localized in the mesenteric root, abdominal wall and dorsal region, which were treated from 2003 through 2013 with several surgical procedures and percutaneous RFA. In 2008 and 2013, RFA was applied under ultrasonographic guidance to 2 desmoid tumors localized in the dorsal thoracic wall. The outcomes were low-grade pain and 1 case of superficial skin necrosis, but so far there has been no recurrence of desmoid tumors in these locations. The authors concluded that surgical resection remains the first-line therapy for patients with desmoid tumors, but wide resection may lead to a poor quality of life. They stated that RFA is less invasive and expensive and is a possible therapeutic option for desmoid tumors in patients with Gardner’s syndrome. Well-designed studies are needed to ascertain the effectiveness of RFA in the treatment of desmoid tumors.

Furthermore, an UpToDate review on “Desmoid tumors: Epidemiology, risk factors, molecular pathogenesis, clinical presentation, diagnosis, and local therapy” (Ravi et al, 2015) does not mention RFA as a therapeutic option.
The American Society for Gastrointestinal Endoscopy's guideline on "The role of endoscopy in the assessment and treatment of esophageal cancer" (Evans et al, 2013) stated that "APC [argon plasma coagulation], heater probe, cryotherapy, or radiofrequency ablation as monotherapy with curative intent for mucosal esophageal cancer was considered but not recommended".

Also, an UpToDate review on "Management of superficial esophageal cancer" (Wright and Saltzman, 2015) states that "Radiofrequency ablation -- A specialized circumferential device for delivering radiofrequency energy to ablate Barrett's esophagus is available and has promising initial results in patients with dysplastic Barrett's epithelium (the Halo system). A potential role for RFA in conjunction with ER for the treatment of early intramucosal esophageal cancer arising in the setting of Barrett's esophagus has been suggested but experience is limited".

Furthermore, National Comprehensive Cancer Network's clinical practice guideline on "Esophageal and esophagogastric junction cancers" (Version 3.2015) only mentions the use of RFA as an option for the treatment of Barrett's esophagus with high-grade dysplasia. It does not mention the use of RFA as a therapeutic option for esophageal and esophagogastric junction cancers.

Guidelines on adult cancer pain from the National Comprehensive Cancer Network (NCCN, 2015) state that radiofrequency ablation may be used to reduce bone pain and prevent skeletal related events. "Radiofrequency ablation of bone lesions has proven successful in pain management, especially for those failing to achieve adequate analgesia without intolerable side effects."

Unresectable Localized Recurrence of Thyroid Cancers

In a retrospective study, Kim and associates (2015) evaluate the safety and effectiveness of RFA for localized small recurrent thyroid cancers less than 2 cm by comparing them with those at repeat surgery. From December 2008 to December 2011, this study evaluated 73 patients (17 men and 56 women; age of 50.3 years ± 13.6) with recurrent thyroid cancer who had been treated with RFA (n = 27) or repeat surgery (n = 46) who met the following criteria: (i) 3 or fewer recurrences or lesions with high probability of recurrence at ultrasonography; (ii) no tumor other than the target tumors; and (iii) at least 1 year of follow-up. Radiofrequency ablation was recommended and performed in cases of surgical
ineligibility, such as patient refusal and poor medical condition. Recurrence-free survival rates and post-treatment complication rates (e.g., hoarseness and hypocalcemia) were compared between RFA and re-operation groups after adjustment with weighted analysis by using inverse probability of treatment weights. After this adjustment, the 1- and 3-year recurrence-free survival rates were comparable (p = 0.681) for RFA (96.0% and 92.6%, respectively) and re-operation (92.2% and 92.2%, respectively) groups. The post-treatment hoarseness rate did not differ between the RFA (7.3% [1.8 of 24]) and re-operation (9.0% [3.6 of 39.5]) groups (p = 0.812), and post-treatment hypocalcemia occurred exclusively in the re-operation group (11.6% [4.6 of 39.5]) but not in the RFA group (0% [0 of 24]) (p = 0.083). The authors concluded that RFA may be a safe and effective alternative to repeat surgery in patients with locally recurrent small thyroid cancers.

Zhao and colleagues (2016) evaluated the effectiveness of ultrasound (US)-guided RFA for localized recurrent thyroid cancers. These investigators performed a systematic review and meta-analysis of the scientific literature by searching the PubMed, Embase, Web of Science, Scopus and the Cochrane Library up to November 26, 2015. They assessed the pooled standard mean difference (SMD) of nodule volume, largest diameter and serum thyroglobulin (Tg) level by comparing pre-RFA with post-RFA using fixed or random-effects model. The Newcastle-Ottawa Scale was used to evaluate the methodological quality of the included studies, risk of bias in the selective populations, comparability of groups and exposure. These researchers identified 9 articles including 189 patients (54 males and 135 females) with 255 tumor lesions, who underwent US-guided RFA beyond the mean 6 months of follow-up. The results showed that tumor volume (SWD: 0.77, 95% CI: 0.57 to 0.97, I² = 25.9%, p = 0.231), largest diameter (SWD: 1.56, 95% CI: 0.94 to 2.17, I² = 82.6%, p < 0.001) and Tg level (SWD: 0.52, 95% CI: 0.30 to 0.73, I² = 0%, p = 0.493) were decreased and no significant publication bias was detectable. The authors concluded that the pooled data indicated that the prognosis improved for patients with localized recurrent thyroid cancers and RFA is a promising treatment for these patients with infeasible surgery.

National Comprehensive Cancer Network’s clinical practice guideline on “Thyroid carcinoma” (Version 2.2015) stated that “When locoregional disease is identified in the absence of distant metastases, surgical resection is recommended with (or without) post-operative EBRT or IMRT. For unresectable locoregional disease that
is symptomatic or structurally progressive, the following options can be considered:
(i) EBRT or IMRT; (ii) vandetanib; or (iii) cabozantinib°.

Breast Cancer

Agnese and Burak (2005) stated that ablative therapies, including RFA have been shown promise in the treatment of small cancers of the breast. However, more research is needed to ascertain the effectiveness of these techniques when they are used as the sole therapy and to determine the long-term local recurrence rates and survival associated with these treatment strategies. van der Ploeg et al (2007) reviewed the literature on the use of RFA for the treatment of small breast carcinoma. The authors concluded that RFA is a promising new tool for minimally invasive ablation of small carcinomas of the breast. They noted that a large randomized control study is needed to ascertain the long-term advantages of RFA compared to the current breast conserving therapies.

Grotenhuis et al (2013) summarized the reported treatment outcomes of ultrasound-guided RFA for early-stage breast cancer and high-lighted practical considerations with regard to this treatment. A search of the English-language literature concerning RFA for breast cancer treatment was performed. Radiofrequency ablation is a technique that can be safely applied in patients with early-stage breast cancer, which is restricted to cT1-T2N0 ductal carcinoma with radiologically defined borders without any signs of multi-focality or multi-centricity. However, before RFA can be adopted as local therapy for early-stage breast cancer, more research is needed to assess the post-treatment pathological complete response and margin status, the long-term oncologic outcome in comparison to current standard breast conserving therapy and the potential cosmetic superiority of percutaneous RFA. The authors concluded that RFA appeared to be a feasible technique for the treatment of early-stage breast cancer, but considerable practical considerations form an obstacle to introduce RFA as a standard of care.

Li and co-workers (2016) evaluated the safety and effectiveness of US-guided percutaneous RFA for multiple breast fibro-adenoma as an alternative to surgical resection. A total of 65 patients with multiple breast fibro-adenoma accepted general anesthesia and US-guided percutaneous RFA in the authors’ hospital from September 2014 to January 2016 were included in this study. Contrast-enhanced US (CEUS) was used immediately after operation to examine if the tumor was
ablated completely. The complete ablation rate (CAR) and the change of focal volume were evaluated by CEUS at the 1st month and the 3rd month after operation. All the patients were diagnosed by needle biopsy. Among all the patients, 256 nodules were found; 46 nodules (17.96 %) were located less than 5 mm from epidermis; 26 nodules (10.15 %) were located below areola. Complete ablation was achieved for 251 nodules (98.04 %) after the 1st month of operation. The volume reduce rate was 39.06 % and 75.99 % at the 1st and the 3rd month after operation, respectively, of which 45 nodules were completely absorbed (17.58 %). There was a statistically significant difference of the volume reduction rate (VRR) after operation (p < 0.01) compared with pre-operative breast nodules volume. There were no complications such as skin burn, hemorrhage, and hematoma, nipple discharge in the process during and after RFA. The authors concluded that given advantages of high CAR, mild injury, rapid recovery, and cosmetic outcome desired by the patients, RFA has the potential to become the preferred method in the treatment of breast fibro-adenoma.

Peek and colleagues (2017) performed a systematic review and meta-analysis to evaluate the current evidence for clinical outcomes with minimally invasive ablative techniques in the non-surgical treatment of breast cancer. A systematic search of the literature was performed using PubMed and Medline library databases to identify all studies published between 1994 and May 2016. Studies were considered eligible for inclusion if they evaluated the role of ablative techniques in the treatment of breast cancer and included ten patients or more. Studies that failed to fulfill the inclusion criteria were excluded. These researchers identified 63 studies including 1,608 patients whose breast tumors were treated with RFA, high intensity focused ultrasound (HIFU), cryoablation, laser ablation, or microwave ablation. A total of 50 studies reported on the number of patients with complete ablation as found on histopathology and the highest rate of complete ablation was achieved with RFA (87.1 %, 491/564) and microwave ablation (83.2 %, 89/107). Short-term complications were most often reported with microwave ablation (14.6 %, 21/144). Recurrence was reported in 24 patients (4.2 %, 24/570) and most often with laser ablation (10.7 %, 11/103). The shortest treatment times were observed with RFA (15.6 ± 5.6 mins) and the longest with HIFU (101.5 ± 46.6 mins). The authors concluded that minimally invasive ablative techniques are able to successfully induce coagulative necrosis in breast cancer with a low side effect profile. Moreover, they stated that adequately powered and prospectively conducted cohort trials are needed to confirm complete pathological ablation in all patients.
Fleming and associates (2017) examined the potential techniques for percutaneous ablation of breast cancer, discussed the advantages and disadvantages of each technique, and provided results from recent studies on these technologies. The techniques discussed are cryotherapy, laser irradiation, microwave irradiation, RFA, HIFU ablation, and irreversible electroporation. The authors concluded that although percutaneous ablation techniques have some promising potential for less-invasive treatment of breast cancer, larger multi-center trials are needed to confirm their effectiveness, especially in comparison with the reference standard of lumpectomy. The use of these techniques also led to other remaining unanswered questions, including how to manage the axilla and which patients are the best candidates for these treatments.

In a prospective, randomized, open-label, phase-II clinical trial, García-Tejedor and colleagues (2018) compared the safety and efficacy of US-guided percutaneous RFA as a local treatment for breast cancer with that of lumpectomy. This trial was conducted in a single institution from 2013 to 2017. Women with invasive ductal carcinoma of the breast measuring 2 cm or smaller were randomly assigned to receive RFA or lumpectomy alone (control group). Margin status at surgery, tumor cell viability after RFA (with nicotinamide adenine dinucleotide [NADH] and cytokeratin 18 [CK18] staining), cosmetic results, adverse events (AEs), and local recurrences were evaluated with uni-variable and multi-variable analyses. A total of 40 subjects (20 in the RFA group and 20 in the lumpectomy group) were evaluated. The mean age of subjects was 64 years (range of 46 to 86 years). NADH and CK18 staining demonstrated absence of tumor cell viability following RFA with at least one of the two techniques. The surgical margins were positive in 11 of the 20 subjects in the lumpectomy group (55 %) and 4 of the 20 in the RFA group (20 %) (p = 0.02). Median follow-up was 25 months (range of 1 to 83 months). Local breast inflammation after surgery was higher in the RFA group than in the lumpectomy group (40 % [8 of 20 participants] versus 5 % [1 of 20 participants], respectively; p = 0.01). Local infection occurred in 3 subjects who underwent RFA (2 of whom had undergone partial irradiation of the breast). None of the subjects in the control group developed local infection. No subjects had recurrence or the need for a 2nd surgery during the study period. The authors concluded that the findings of this preliminary study showed that RFA was effective for local tumor control and that tumor-free margins were obtained more often with RFA than with lumpectomy; surgical excision following RFA was infrequently associated with local infection.
In a retrospective study, Ito and co-workers (2018) examined the safety and efficacy of percutaneous RFA of breast carcinomas. This study was conducted by the Breast Cancer Society for Minimally Invasive Therapy following approval from institutional review boards (IRBs), and with the written informed consent of patients. A total of 386 patients with breast cancer treated with RFA at 10 institutions between July 2003 and June 2009 were identified and included in the analysis. Patients underwent a standard RFA procedure with US guidance and were followed-up every 6 to 12 months. In this study, feasibility of RFA procedure and related safety and ipsilateral breast tumor recurrence (IBTR) were examined. Fisher exact or χ2 test evaluated associations between clinicopathological factors and IBTR, and local recurrence-free survival was estimated using the Kaplan-Meier method. RFA-related AEs included local pain in 9 patients, skin burns in 15, and nipple retraction in 7. Patients were followed for a median of 50 months; IBTR was more frequently observed in patients with initial tumor sizes of greater than 2 cm (3 of 30, 10 %) than in those with initial tumors of less than or equal to 2 cm (8 of 355, 2.3 %; p = 0.015). IBTR-free rates 5 years after RFA were 97 %, 94 %, and 87 % in patients with initial tumor sizes of less than or equal to 1.0 cm, 1.1 to 2.0 cm, and greater than 2.0 cm, respectively. The authors concluded that RFA in breast cancer was a safe and promising minimally invasive treatment for tumors of less than or equal to 2 cm in diameter. These researchers stated that further studies are needed to optimize the technique and evaluate its future role as local therapy.

Kinoshita (2019) noted that early-stage breast cancer is increasingly detected by screening mammography, and these researchers aimed to establish RFA as a minimally invasive, cost-efficient, and cosmetically acceptable local treatment. Although there were many studies on resection after RFA, none of them provided sufficient evidence to support RFA as a standard therapy for breast cancer. In a phase-I clinical trial, localized tumors with a maximum diameter of 2 cm, pre-operatively diagnosed by imaging and histopathology, were treated with RFA. A 90 % complete ablation rate was confirmed histopathologically. A phase-II multi-center clinical trial of RFA without resection for early breast cancer will evaluate the long-term safety and efficacy of RFA as well as its cosmetic results, which are a perceived advantage of this technique. These investigators started a phase-III, multi-center clinical trial to demonstrate the non-inferiority of RFA compared with standard treatment (breast-conserving surgery [BCS]) in terms of IBTR rate, which is the best index of local control. The authors concluded that to standardize RFA
for breast cancer, the results of their multi-center clinical trial, “Radiofrequency Ablation Therapy for Early Breast Cancer as Local Therapy (the RAFAELO study)” that commenced in 2013, are eagerly awaited.

Large Renal Angiomyolipoma

Stamatiou and colleagues (2016) reported on the case of a 78-year old male patient with multiple angiomyolipomas of a solitary right kidney. The largest of these tumors (maximum diameter: 13.4 cm) caused significant extrinsic compression of the inferior vena cava complicated by thrombosis of this vessel. Treatment of thrombosis with anti-coagulants had been ineffective and the patient had experienced a bleeding episode from the largest right renal angiomyolipoma, which had been treated by trans-arterial embolization in another institution, 4 months prior to the authors’ intervention. Their approach included superselective transarterial embolization (SAE) of the dominant, right kidney angiomyolipoma with hydrogel microspheres, which was combined, 20 days later, with US-guided RFA; both interventions were uneventful. Computed tomography 2 months after ablation showed a 53 % reduction in tumor volume, reduced space-occupying effect on inferior vena cava, and resolution of caval thrombus; 9 months after intervention the patient has had no recurrence of thrombosis or hemorrhage and no tumor regrowth has been observed. The authors concluded that the combination of SAE and RFA may be a safe and effective option for the treatment of large renal angiomyolipomas. They stated that this combination is worth being assessed in the context of a large study with adequate follow-up.

Renal Cysts

Menezes and colleagues (2016) reported their initial experience with RFA of Bosniak IV renal cysts. From 2010 to 2014, a total of 154 renal tumor cases were treated with percutaneous thermal ablation, of which 10 cases (6.4 %) from 9 patients were complex renal cysts and were treated with RFA. All complex cysts were classified as Bosniak IV (4 women and 5 men; mean age of 63.6 years, range of 33 to 83 years); 1 patient had a single kidney. Lesion size ranged from 1.5 to 4.1 cm (mean of 2.5 cm) and biopsy was performed on 4 cysts immediately before the procedure, all of which were malignant (2 clear cell and 2 papillary carcinoma). Mean volume reduction of complex cysts was 25 % (range of 10 to 40 %). No patients required re-treatment with RFA and no immediate or late complications were observed. The follow-up of Bosniak IV cysts had a median of 27 months.
(IQR, 23 to 38) and no recurrence or significant loss of renal function were observed. The authors concluded that mid-term follow-up of the cases in their database suggested that image-guided percutaneous RFA can treat Bosniak IV cysts with very low complication rates and satisfactorily maintain renal function.

This study had several major drawbacks: (i) relatively small sample size (10 cases from 9 patients), (ii) intermediate follow-up time (mean of 27 months), and (iii) selection biases due to the retrospective series. The authors noted that more comprehensive studies are needed to support the effectiveness of RFA for the treatment of Bosniak IV renal lesions. These researchers also stated that another limitation of the study was the percentage of lesions submitted to biopsy prior to the RFA (40%). However, the technical difficulties of performing percutaneous biopsies of predominantly cystic lesions should be considered, because some lesions have a small solid component where the needle should be positioned for collecting material for pathological analysis. Moreover, even if no malignant cells were found in the biopsy, Bosniak IV renal cysts still can be excised based on the presumed risk of malignancy based on the Bosniak classification, and based on the fact that there are still few studies that demonstrate the negative predictive value of the biopsy of Bosniak IV renal cysts. Furthermore, if the lesion was not excised after biopsy, follow-up was compromised because of parenchymal distortion and changes in cyst density and signal on CT and MRI, respectively. The other Bosniak IV cysts were not biopsied and therapeutic indication was supported by presumed malignancy based on the Bosniak classification.

**Spinal Metastases**

Greenwood and associates (2015) noted that radiation therapy (RT) is the current gold standard for palliation of painful vertebral metastases; and combined RT and ablation may be more effective than either therapy alone in palliating painful metastatic disease to the spine. In a retrospective, single-center study, these researchers evaluated the safety and effectiveness of combined ablation, either RFA or cryoablation, and RT in the treatment of spinal metastases. Medical records of all patients who underwent ablation of spine lesions at a single institution between March 2012 and June 2014 were reviewed; patients treated with both RT and either RFA or cryoablation concurrently were identified. Pain scores before and after RFA were measured with the numerical rating scale (NRS) (0 to 10 point scale) and compared. Procedural complications, changes in general activity level, and pain medication usage after ablation were also recorded. When available,
follow-up imaging was evaluated for evidence of residual or recurrent disease. A total of 21 patients with 36 spine metastases were treated with RT and percutaneous ablation concurrently, either RFA (21/22) or cryoablation (1/22); 1 patient received 2 separate RFA treatments. Overall, mean worst pain score (8.0, SD = 2.3) significantly decreased at both 1 week (4.3, SD = 3.1; p < 0.02) and 4 weeks (2.9, SD = 3.3; p < 0.0003). Temporary post-procedural radicular pain occurred after 1 RFA treatment (4.5%; 1/22); 7 patients had radiation resistant tumors (renal cell, melanoma, or sarcoma). Post-procedural imaging (median of 6 months; range of 2 to 27 months) showed stable treated disease in 12/13 treatments at 3 months and 10/10 at 6 months. The authors concluded that percutaneous ablation and concurrent RT is safe and effective in palliating painful spinal metastases and can be effective in those who have radiation resistant tumor histology.

This study had 2 major drawbacks: (i) the therapeutic effect of vertebral augmentation versus percutaneous ablation cannot be separated in this retrospective study, and (ii) RT protocols were variable and included both stereotactic body and conventional RT which may have different safety and efficacy profiles. The authors stated that future prospective, multi-armed studies should be designed to determine the palliative and local tumor control benefit of combined RT and percutaneous ablation, particularly for radiation resistant tumors and metastases involving the posterior vertebral body, pedicles, neural foramina, and/or epidural space that cannot be adequately treated with either modality alone.

Madaelil and colleagues (2016) examined the safety and effectiveness of RFA to treat sacral metastases for pain palliation and local tumor control (LTC). An institutional tumor ablation registry was retrospectively reviewed for sacral RFA procedures performed between January 2012 and December 2015. Clinical history, pre-procedural imaging, and procedural details were reviewed to document indication for treatment, primary tumor histology, tumor volumes, presence of concurrent cementoplasty after RFA, and the occurrence of peri-procedural complications. Pain scores before and 4 weeks after the procedure were recorded. Post-procedure imaging was reviewed for imaging evidence of tumor progression. Long-term complications and duration of clinical follow-up were recorded. During the study period, a total of 11 RFA procedures were performed to treat 16 sacral metastases. All procedures were for pain palliation; 4 procedures (36%; 4 out of 11) were also performed with the intention of achieving LTC in patients with oligometastatic disease. Concurrent cementoplasty was performed in 63% of
cases (7 out of 11). The median pain score decreased from 8 (IQR, 6 to 9.25) at baseline to 3 (IQR, 1.75 to 6.3) 1 month following RFA (p = 0.004). In the 4 patients with oligometastatic disease, LTC was achieved in 3 patients (75%; 3 out of 4) after a median follow-up of 7.6 months (range of 3.6 to 11.9 months). No acute or long-term complications were documented during the overall median clinical follow-up of 4.7 months (range of 0.9 to 28.7 months). The authors concluded that RFA maybe a safe and potentially effective treatment for patients with painful sacral metastases and can achieve LTC in selected patients. These preliminary findings need to be validated by well-designed studies with larger sample size and longer follow-up.

Rosian and colleagues (2018) stated that metastatic spinal lesions are difficult-to-treat entities that are most commonly associated with pain and severely reduced health-related quality of life (HRQoL). Within the last 5 to 10 years, RFA has emerged as an option in the palliative treatment of vertebral metastases. In a systematic review, these researchers evaluated the safety and effectiveness of RFA, mostly in combination with vertebroplasty, in patients with painful vertebral metastases. These investigators conducted a systematic literature search and a manual search of 5 databases in December 2016. The review applied a methodological framework based on the HTA Core Model. Data on each selected outcome category were synthesized according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) scheme. Risk of bias was assessed using the Institute of Health Economics (IHE) Risk of Bias checklist for case series. These researchers identified 299 citations. After applying the inclusion criteria, a total of 9 studies (4 prospective and 5 retrospective studies) were determined to be eligible. These studies included a total of 583 patients with vertebral metastases who were treated with RFA and, in most cases, received an additional vertebroplasty treatment (n = 437). The studies were categorized as having a moderate-to-high risk of bias. The strength of evidence was found to be "very low" for safety outcomes and could not be assessed for efficacy outcomes. Current evidence suggested that RFA led to significant pain reduction. Furthermore, no major complications occurred when using RFA. The authors concluded that in patients with vertebral metastases who were unresponsive or have contraindications for conventional treatments such as radiation or chemotherapy, RFA was a safe therapy that could be effective to palliate pain. However, there is a substantial lack of evidence to evaluate the applicability of RFA. These researchers stated that further studies are need to determine the exact patient group that would benefit most from the intervention and
to compare individual operation techniques (e.g., differences in RFA techniques, vertebroplasty following RFA, etc.). These investigators stated that study registries may serve this purpose well; further evaluations of RFA (in combination with vertebroplasty) for longer-term clinical efficacy and complication rates, in particular evaluations comparing RFA with traditional therapies, e.g., radiation, are desirable.

The authors stated that the major drawback of this review was the low number of included patients and heterogeneity of study characteristics in most of the studies. The low number of patients also hampered comparison of the effectiveness of RFA alone to RFA in combination with vertebroplasty.

**Benign Thyroid Nodules**

Li and co-workers (2016) evaluated the safety and efficacy of US-guided percutaneous bipolar RFA (BRFA) of benign thyroid nodules (BTNs) by comparison with a matched untreated control group. A total of 35 patients who were subjected to a single session of US-guided percutaneous BRFA (Group A) for BTNs were compared with those in 35 untreated patients (Group B) with benign nodules. The benign nature of all the nodules was confirmed by US-guided fine-needle aspiration biopsy (FNAB), and all the patients had normal thyroid functions. BRFA was performed with a bipolar electrode (CelonProSurge 150-T20) with an output power of 20 W. Nodule volume, thyroid function and clinical symptoms of all the patients were compared before treatment and during follow-up. In Group A, the BRFA procedures were completed with a mean time of $10.02 \pm 3.30$ minutes (range of 5.47 to 16.03) and with a mean total energy deposition of $10,747 \pm 3,704$ J (range of 5,510 to 17,770). The procedures were well-tolerated in all the patients without causing any major complications. At the 6-month follow-up, all of the nodule volume decreased significantly (from $8.81 \pm 8.66$ to $1.59 \pm 1.55$ ml, $p < 0.001$) in Group A, whereas the nodule volume increased from $6.90 \pm 3.77$ to $7.87 \pm 3.95$ ml in Group B ($p < 0.001$). All (100 %) the 35 nodules in Group A had volume reduction ratios (VRRs) of greater than 50 %, among which 3 (8.57 %) had VRRs greater than 90 %. In Group A, the clinical symptoms of the patients who had symptoms before BRFA disappeared, whereas in Group B, the patients had no resolution of clinical symptoms at the 6-month follow-up. The authors concluded that US-guided percutaneous BRFA appeared to be a safe and effective method for the treatment of BTNs; it may gain a wide use in clinical practice. Moreover, they stated that a prospective, multi-center trial with larger sample size and longer follow-up is needed to confirm these findings.
The authors stated that this study had several drawbacks. First, only 35 patients were included in both groups, thus future studies with more patient numbers is needed. Second, no nodule disappeared after BRFA at the 6-month follow-up in this study. The follow-up was relatively short, and long-term results were not available at the current stage. Lastly, the technique of BRFA was not compared directly with laser ablation, microwave ablation or surgery.

In a retrospective, single-center study, Cesareo and associates (2017) evaluated the clinical outcomes and safety of RFA for BTNs over a 1-year follow-up. A total of 48 patients with solid, non-functioning BTNs were treated by RFA using a 17-G internally cooled electrode. These investigators categorized thyroid nodules as small (less than or equal to 12 ml), medium (12 to 30 ml), or large (over 30 ml); BTN volume reduction, thyroid function, cosmetic and compressive score changes and side effect evaluation at 6 and 12 months were evaluated. BTN volume decreased significantly from baseline to 6 (mean percentage decrease of BTN volume was 66.8 ± 13.6 %, p < 0.001). At 12 months, the mean percentage reduction of BTN volume compared to 6 months was 13.7 ± 17.1 % (p < 0.001). At 6-month, symptom score had improved significantly (p < 0.001) while it did not change significantly between 6 and 12 months. In particular, symptom score improved significantly in the medium (p < 0.001) and large (p < 0.01) subgroups. Cosmetic score improved significantly between baseline and 6 months (p < 0.001) and between 6 and 12 months (p < 0.01). In all the subgroups, cosmetic score improved significantly between baseline and 6 months, while between 6 and 12 months it improved significantly only in the large group (p < 0.05); RFA was well-tolerated; only 1 patient experienced permanent right para-median vocal cord palsy. The authors concluded that the findings of this study showed that a single RFA treatment was effective in reducing BTN volume. Moreover, larger BTNs appeared to be less responsive and perhaps in these cases a further RFA treatment should be used to get all the desired clinical and radiological outcomes. Cosmetic score improved in all treated BTNs, while symptom score got better only in medium and large BTN. They stated that RF ablation can be a valuable and generally safe tool for the non-surgical management of BTNs; other large and prospective studies are needed to confirm these findings. Moreover, these researchers noted that this study had several drawbacks; in particular, this was a retrospective study and the follow-up period was quite short (12 months).
In a systematic review, Wang and colleagues (2017) examined if RFA is a safe treatment modality for BTNs. PubMed, Embase, and the Cochrane Library database were searched for articles that targeted human beings and had a study population with BTNs that were confirmed by FNA cytology and/or core needle biopsy. A total of 32 studies relating to 3,409 patients were included in this systematic review. Based on literatures, no deaths were associated with the procedure, serious complications were rare, and RFA appeared to be a safe and well-tolerated treatment modality. However, a broad spectrum of complications offered insights into some undesirable complications, such as track needle seeding and Horner syndrome. The authors concluded that RFA appeared to be a safe and well-tolerated treatment modality for BTNs; more research is needed to characterize the complications of RFA for thyroid nodules.

The authors stated that this study had several drawbacks. First, the criteria used to define complications and the time sequences were different as the patients came from different centers with their own criteria. Only 1 retrospective study defined these terms according to the standardized terminology for image-guided tumor ablation from the Society of Interventional Radiology. Second, post-RFA thyroid complications were rarely recorded systematically. Even in large thyroid RFA series, complications were either not reported or were mentioned to be limited. Such results could reflect the inconsistent definitions of complications, and teams who performed RFA with undesirable consequences may be unwilling to publish their results. Moreover, case reports or case series of minor or previously reported complications were not typically accepted by journals. Third, the absence of randomized controlled trials (RCTs) and the availability of only 2 retrospective studies designed to record thyroid RFA complications as the primary aim prevented a meta-analysis from being performed. Moreover, a majority of the articles had an observational design, which precluded the ability to comment on the precise risks and causes of complications.

Furthermore, an UpToDate review on “Diagnostic approach to and treatment of thyroid nodules” (Ross, 2018) states that “Ablation techniques -- Benign, autonomous, and cystic thyroid nodules can be treated by ultrasound-guided injection of ethanol or sclerosing agents and by ultrasound-directed physical energy. These approaches have not gained widespread acceptance in the United States, because of potential complications, including occasional reports of prolonged pain after the procedure”.

http://www.aetna.com/cpb/medica l/data/400_499/0492.html
Adrenocortical Carcinoma

Fassnacht and colleagues (2018) noted that adrenocortical carcinoma (ACC) is a rare and in most cases steroid hormone-producing tumor with variable prognosis. The objective of these guidelines was to provide clinicians with best possible evidence-based recommendations for clinical management of patients with ACC based on the GRADE system. These investigators pre-defined 4 main clinical questions, which they judged as particularly important for the management of ACC patients and performed systematic literature searches: What is needed to diagnose an ACC by histopathology? Which are the best prognostic markers in ACC? Is adjuvant therapy able to prevent recurrent disease or reduce mortality after radical resection? What is the best treatment option for macroscopically incompletely resected, recurrent or metastatic disease? Other relevant questions were discussed within the group. Selected recommendations were:

- Every patient with (suspected) ACC should undergo careful clinical assessment, detailed endocrine work-up to identify autonomous hormone excess and adrenal-focused imaging
- Adrenal surgery for (suspected) ACC should be performed only by surgeons experienced in adrenal and oncological surgery aiming at a complete en bloc resection (including resection of oligo-metastatic disease)
- All suspected ACC should be reviewed by an expert adrenal pathologist using the Weiss score and providing Ki67 index
- Adjuvant mitotane treatment in patients after radical surgery that have a perceived high risk of recurrence (ENSAT stage III, or R1 resection, or Ki67 of greater than 10 %
- For advanced ACC not amenable to complete surgical resection, local therapeutic measures (e.g., radiation therapy, RFA, chemoembolization) are of particular value. However, the authors suggested against the routine use of adrenal surgery in case of widespread metastatic disease. In these patients, they recommended either mitotane monotherapy or mitotane, etoposide, doxorubicin and cisplatin depending on prognostic parameters. In selected patients with a good response, surgery may be subsequently considered.
- In patients with recurrent disease and a disease-free interval of at least 12 months, in whom a complete resection/ablation seems feasible, the authors recommended surgery or alternatively other local therapies.
Biliary Obstructions / Strictures

Acu and Kurtulus Ozturk (2018) examined the feasibility and safety of percutaneous trans-hepatic endo-biliary RFA combined with biliary stenting in palliative treatment of malignant biliary obstructions. A total of 21 patients who had undergone percutaneous trans-hepatic endo-biliary RFA as an adjunct to biliary stenting were included. There were 12 men and 9 women with a mean age of 67 ± 13.6 (SD) years (range of 34 to 86 years). Demographic data, procedure details and follow-up data including complications, survival time and stent patency time were documented. The median stent patency time and survival time, as well as the 30-day and 180-day cumulative survival and stent patency rates were estimated using the Kaplan-Meier method. A total of 24 percutaneous trans-hepatic endo-biliary RFA procedures were performed. There were no procedure-related major complications or death; 3 patients who had developed stent re-occlusion underwent a 2nd endo-biliary RFA, without insertion of a new stent. The most common complications were post-procedural pain and cholangitis. Overall survival (OS) and stent patency times ranged between 5 to 542 days and 5 to 251 days, respectively. The median survival time was 76 days (95% CI: 0 to 233 days) and stent patency time was 133 days (95% CI: 25 to 240 days). The 30- and 180-day cumulative stent patency rates were 75% and 34%, respectively. The authors concluded that percutaneous trans-hepatic endo-biliary RFA was a feasible, safe and cost-effective method in restoration of biliary drainage in patients with malignant biliary obstruction. Moreover, these researchers stated that the efficacy of percutaneous RFA in short- and long-term of survival and stent patency rates remains to be proven in future with randomized, controlled prospective clinical trials, enrolling homogenous, large group of patients and controls.

The authors stated that although this retrospective study was not designed to analyze the clinical efficacy of percutaneous endo-biliary RFA, these findings supported the previous observations that endo-biliary RFA may have more impact on stent patency and quality of life (QOL) but not on survival. The relatively small number of the patients with heterogeneous clinical and tumor characteristics was a limitation of the present study. A short follow-up period with high early mortality rate could have been prevented these investigators from identifying true stent patency rate. Furthermore, the type of the stent that was used may alone have played an important role on patency rate.
In a meta-analysis, Sofi and associates (2018) examined the safety and efficacy of biliary stent placement with RFA compared with stent placement alone in patients with malignant biliary strictures. These researchers performed a comprehensive search of electronic databases for all studies comparing RFA with biliary stent placement versus stent placement only. Measured outcomes included patient survival, stent patency, and procedure-related AEs. An inverse variance method was used to pool data on stent patency into a random-effects model. Cox-regression analysis was used to calculate hazard ratio (HR) for survival analysis. They used the GRADE framework to interpret these findings. A total of 9 studies (including 2 abstracts) with a total of 505 patients were included in the meta-analysis. The pooled weighted mean difference (WMD) in stent patency was 50.6 days (95% CI: 32.83 to 68.48), favoring patients receiving RFA. Pooled survival analysis of the reconstructed Kaplan-Meier data showed improved survival in patients treated with RFA (HR, 1.395; 95% CI: 1.145 to 1.7; p < 0.001). However, RFA was associated with a higher risk of post-procedural abdominal pain (31% versus 20%, p = 0.003). The findings of this meta-analysis did not show significant difference between the RFA and stent placement-only groups with regard to the risk of cholangitis, acute cholecystitis, pancreatitis, and hemobilia. The authors concluded that in the light of this limited data based on observational studies, RFA was found to be safe and was associated with improved stent patency in patients with malignant biliary strictures. In addition, RFA may be associated with improved survival in these patients.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CPT codes covered if selection criteria are met:</td>
</tr>
<tr>
<td></td>
<td>Radiofrequency ablation (RFA) for adrenal gland-no specific code:</td>
</tr>
<tr>
<td>20982</td>
<td>Ablation therapy for reduction or eradication of 1 or more bone tumors (e.g., metastasis) including adjacent soft tissue when involved by tumor extension, percutaneous, including imaging guidance when performed; radiofrequency</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
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<tr>
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<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>32998</td>
<td>Ablation therapy for reduction or eradication of one or more pulmonary tumor(s) including pleura or chest wall when involved by tumor extension, percutaneous, radiofrequency, unilateral</td>
</tr>
<tr>
<td>43270</td>
<td>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)</td>
</tr>
<tr>
<td>44369</td>
<td>Small intestinal endoscopy, enteroscopy, beyond second portion of duodenum, not including ileum; with ablation of tumor(s), polyp(s) or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique</td>
</tr>
<tr>
<td>47380</td>
<td>Ablation, open, of one or more liver tumor(s); radiofrequency</td>
</tr>
<tr>
<td>47381</td>
<td>cryosurgical</td>
</tr>
<tr>
<td>47382</td>
<td>Ablation, one or more liver tumor(s), percutaneous, radiofrequency</td>
</tr>
<tr>
<td>50592</td>
<td>Ablation, 1 or more renal tumor(s), percutaneous, unilateral, radiofrequency</td>
</tr>
<tr>
<td>53850</td>
<td>Transurethral destruction of the prostate tissue; by microwave thermotherapy</td>
</tr>
<tr>
<td>53852</td>
<td>by radiofrequency thermotherapy</td>
</tr>
</tbody>
</table>

CPT codes not covered for indications listed in the CPB:

Radiofrequency ablation of thyroid, Radiofrequency ablation of Biliary obstructions/ strictures, - no specific code:

Other HCPCS codes related to the CPB:

C1886     | Catheter, extravascular tissue ablation, any modality (insertable)               |

ICD-10 codes covered if selection criteria are met:

C16.0 - C18.9 | Malignant neoplasm of stomach, small intestine, and colon [metastatic gastrointestinal stromal tumors (GIST) with limited progression] |
C34.00 - C34.92 | Malignant neoplasm of bronchus and lung |
C49.0 - C49.9 | Malignant neoplasm of other connective and soft tissue of upper limb, including shoulder, lower limb, including hip, and trunk unspecified [in symptomatic persons with disseminated metastases] |
C64.1 - C64.9 | Malignant neoplasm of kidney, except renal pelvis |
C74.00-C74.92 | Malignant neoplasm of adrenal gland |
C78.00 - C78.02 | Secondary malignant neoplasm of lung

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D02.20 - D02.22</td>
<td>Carcinoma in situ bronchus and lung</td>
</tr>
<tr>
<td>D16.00 - D16.9</td>
<td>Benign neoplasm of bone and articular cartilage [osteoid osteoma] [not covered for chondroblastoma]</td>
</tr>
<tr>
<td>N18.3</td>
<td>Chronic kidney disease, stage 3 (moderate)</td>
</tr>
<tr>
<td>N18.4</td>
<td>Chronic kidney disease, stage 4 (severe)</td>
</tr>
<tr>
<td>N18.5</td>
<td>Chronic kidney disease, stage 5</td>
</tr>
<tr>
<td>Q60.0</td>
<td>Renal agenesis, unilateral</td>
</tr>
<tr>
<td>Z90.5</td>
<td>Acquired absence of kidney</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB [for radiofrequency ablation]:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C73</td>
<td>Malignant neoplasm of thyroid gland [distant metastases of medullary thyroid carcinoma]</td>
</tr>
<tr>
<td>D13.2</td>
<td>Benign neoplasm of duodenum [Brunner's gland hyperplasia]</td>
</tr>
<tr>
<td>D30.00 - D30.12</td>
<td>Benign neoplasm of kidney and renal pelvis [large renal angiomyolipomas]</td>
</tr>
<tr>
<td>E04.0 - E04.9</td>
<td>Other nontoxic goiter</td>
</tr>
<tr>
<td>E05.10 - E05.11</td>
<td>Thyrotoxicosis with toxic single thyroid nodule w ith/w ithout thyrotoxic crisis or storm</td>
</tr>
<tr>
<td>E05.2 - E05.21</td>
<td>Thyrotoxicosis with toxic multinodular goiter w ith/w ithout thyrotoxic crisis or storm</td>
</tr>
<tr>
<td>K83.1</td>
<td>Obstruction of bile duct</td>
</tr>
<tr>
<td>N28.1</td>
<td>Cyst of kidney, acquired</td>
</tr>
<tr>
<td>N28.84</td>
<td>Pyelitis cystica</td>
</tr>
<tr>
<td>Q61.00 - Q61.9</td>
<td>Cystic kidney disease, unspecified</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB [for curative treatment in persons who are able to tolerate surgical resection]:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C15.3 - C15.9</td>
<td>Malignant neoplasm of esophagus</td>
</tr>
<tr>
<td>C23 - C24.9</td>
<td>Malignant neoplasm of gallbladder and extrahepatic bile ducts</td>
</tr>
<tr>
<td>C25.0 - C25.9</td>
<td>Malignant neoplasm of pancreas</td>
</tr>
<tr>
<td>C37</td>
<td>Malignant neoplasm of thymus</td>
</tr>
<tr>
<td>C41.0 - C41.9</td>
<td>Malignant neoplasm of bone and articular cartilage [chondroblastoma]</td>
</tr>
</tbody>
</table>
The above policy is based on the following references:


149. Wright CD, Saltzman JR. Management of superficial esophageal cancer. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed March 2015.


173. Ross DS. Diagnostic approach to and treatment of thyroid nodules. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2018.


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0492 Radiofrequency Tumor Ablation

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania

revised 07/12/2019