Recent Advances in Lesion Formation for Catheter Ablation of Atrial Fibrillation

Adam S. Barnett, MD; Tristram D. Bahnson, MD; Jonathan P. Piccini, MD, MHS

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despite advances in ablation technology, many patients experience recurrent atrial fibrillation (AF) after radiofrequency ablation. Although estimates vary, the overall 1-year drug-free success for AF ablation is estimated at 40% to 60% for a single procedure and 70% for multiple procedures. The cornerstone of conventional AF ablation is pulmonary vein isolation (PVI), and in clinical practice, the most common PVI technique involves creating circular radiofrequency lesions in a point-by-point fashion around the PV ostia/annula. However, conventional radiofrequency ablation can be difficult and time-consuming, has less than outstanding efficacy, and can be associated with potentially serious complications, such as steam pops, perforation, tamponade, and thrombus formation, which can lead to thromboembolic events. Given the limitations of conventional radiofrequency ablation, there has been ongoing development of new technologies to facilitate the safety and efficacy of lesion formation and durability. This review will summarize several recent advancements in catheter technology for AF ablation aimed at improving lesion formation (Figure 1).

Contact Force Sensing Catheters

In radiofrequency ablation, the contact force (CF) between the ablation electrode and the atrial wall is a major determinant of lesion size and durability. Insufficient CF can result in inadequate lesion formation and higher rates of PV reconnection. However, excessive CF can result in complications, such as perforation. Therefore, monitoring CF would be expected to maximize ablation efficacy and improve safety. Until recent years, CF has been monitored indirectly using a combination of visual observation of catheter tip motion, tactile feedback, local electrogram attenuation, impedance monitoring, and in some laboratories, intracardiac echocardiography. Although widely used, these methods are a poor surrogate for CF.

Recently, ablation catheters that can directly measure CF have become available in the United States. A spring-coupled catheter (SmartTouch) was approved by the Food and Drug Administration in February, 2014. The catheter tip is mounted on a precision spring that deflects both axially and laterally (Figure 2). The deflection can then be converted to CF using the known spring characteristics and Hooke Law (F=kX; k=constant factor/stiffness and X=deformation distance), allowing the mean CF and force vector to be displayed to the operator. A fiberoptic CF catheter (TactiCath), which utilizes a Fabry-Perot interferometer (Figure 2), was also approved by the Food and Drug Administration in October, 2014.

The efficacy of CF sensing has been found to be comparable with standard radiofrequency ablation in several randomized and nonrandomized studies (Table I in the Data Supplement). Spring-coupled CF sensing was evaluated in the SMART-AF trial, a single-arm study of 160 patients with paroxysmal AF. Overall, the success rate at 12 months was 73%, similar to conventional radiofrequency ablation. Fiberoptic-mediated CF sensing was evaluated in the TOCCASTAR pivotal investigational device exemption study, which randomized 300 patients with paroxysmal AF to CF ablation or standard irrigated radiofrequency ablation. Success rates at 12 months off antiarrhythmic drugs were similar between the 2 groups (67.8% versus 69.4%, respectively).

Further analysis of data from these trials showed that operators who maintained CF above certain levels achieved better results. In the SMART-AF trial, when CF was maintained in the operator-specified reference range ≥80% of the time, 12-month success rates were improved (81% versus 66%, P=0.040). In the TOCCASTAR study, patients treated with more optimal CF (>10 g of force in ≥90% of lesions) also had higher success rates (75.9% versus 58.1%, P=0.018). In addition, a smaller study of patients with paroxysmal AF using a spring-coupled catheter (n=100), those treated with an average CF >22 g had a much higher rate of freedom from AF at 19 months compared with those treated with a CF<22 g (96% versus 80%, P=0.04). Taken together, these data suggest that CF-guided ablation may improve maintenance of sinus rhythm if minimum CF levels are achieved. Achieving these levels of performance, however, may not be easy. Optimal CF was achieved in only 57% of cases in TOCCASTAR and 47% in SMART-AF.

There are limited data directly comparing spring-coupled CF-sensing ablation catheters to conventional radiofrequency catheters. In 1 small study (n=60 patients), the success rate at 12 months was significantly higher in patients treated with a spring-coupled CF catheter (goal CF 10 g) compared with those treated with standard irrigated radiofrequency (89% versus 64%, P=0.04). A second, randomized trial (CF goal 5–50 g; n=75 patients) yielded similar results: freedom from AF off...
antiarrhythmic drugs at 12 months was 88% with CF guidance versus 66% with standard radiofrequency.\textsuperscript{13}

The optimal method of utilizing CF data to predict lesion formation remains unclear. The force-time integral (FTI), defined as the total CF integrated during the time of radiofrequency delivery, has been proposed as a method to predict lesion size and durability using CF. In 1 study, an FTI >392 gs was associated with transmural lesion formation with a positive predictive value of 0.98.\textsuperscript{14} In a subsequent study, patients treated with an FTI >400 gs had a much lower rate of PV reconnection compared with those treated with an FTI <400 gs (5\% versus 21\%, \textit{P}=0.0004).\textsuperscript{4} Other algorithms, such as the lesion size index (LSI=FTI\times power in Watts) aim to incorporate other variables into a prediction algorithm. Recent work suggests that CF >20 g, FTI >400 gs, and an LSI >5.0 are associated with more durable PVI.\textsuperscript{15} Further investigation is needed to determine the optimal combination of power, time, temperature, and CF to predict durable lesion formation.

No major safety concerns have been reported with CF-guided ablation in published studies to date. However, caution should be exercised in applying CF in excess of the manufacturer’s recommendation until more is known about optimal CF. One meta-analysis suggests that CF is associated with shorter procedure and fluoroscopic times, lower recurrence rates (odds ratio, 0.62; 95\% confidence interval, 0.45–0.86), and similar major complication rates (1.3\% versus 1.9\%, \textit{P}=0.45).\textsuperscript{16} Although the data, thus far, are encouraging, pragmatic clinical trials are needed to help clarify if there are better long-term results with CF-guided ablation.

**Multielectrode Ablation Catheters**

Because of the potential for point-to-point radiofrequency to leave gaps and PV reconnection, multipolar ablation catheters have been developed to create ostial or antral isolation with only a few energy applications. One such device is the phased radiofrequency pulmonary vein ablation catheter (PV AC). Introduced in Europe in 2006, the PV AC is a 9-French, decapolar mapping and ablation catheter with 10 platinum electrodes distributed over a circular catheter tip.\textsuperscript{17} PV AC applies current in a unipolar fashion between the electrodes and a dispersive electrode on the patient’s back or in a bipolar mode with current flowing between adjacent pairs of electrodes (Figure 3). PV AC is not irrigated; instead it utilizes duty-cycled radiofrequency technology to maintain acceptable electrode temperatures without irrigation.

Several studies have demonstrated similar success rates using the PV AC compared with conventional irrigated radiofrequency ablation. In a study of 161 patients, the 3-year single-procedure success rate was 65\% with PV AC compared with 55\% with irrigated radiofrequency ablation (\textit{P}=NS).\textsuperscript{18} Two smaller studies yielded success rates of 72\% to 76\% in 6- to 12-month follow-up.\textsuperscript{19,20} In the Tailored Treatment of Permanent Atrial Fibrillation (TTOP-AF) trial, 210 patients with persistent AF refractory to antiarrhythmic drug therapy were randomized to either ablation with PV AC or medical management.\textsuperscript{21} At 6 months, 56\% of ablated patients were free from AF, compared with 26\% of those treated medically. The data from TTOP-AF and other early studies suggest that the PV AC is at least as effective as standard ablation techniques.

Despite these promising data, safety concerns have prevented the device from becoming approved in the United States. In TTOP-AF trial, 4 of 138 (2.9\%) of patients experienced a stroke, and other studies have reported higher rates (38\% to 39\%) of asymptomatic cerebral embolism compared with other ablation technologies.\textsuperscript{22,23} Some of these events may have been because of suboptimal preprocedural and intraprocedural anticoagulation. Further investigation in animal models and humans revealed that most asymptomatic cerebral embolism could be prevented by avoiding overlap of the proximal and distal electrodes (electrodes 1 and 10).\textsuperscript{24} The PV AC catheter was redesigned with 9 gold electrodes, thereby eliminating the potential for electrode 1 to 10 overlap while enabling better temperature assessment. The safety of phased radiofrequency ablation is currently being evaluated in the single-arm VICTORY-AF trial, which will enroll 300 patients with persistent AF.\textsuperscript{25} The primary safety end point is the incidence of procedure-related strokes. Registry data from Europe (where the device is currently approved) involving 2748 ablation patients from 20 centers found that the efficacy and safety of duty-cycled/phased radiofrequency was similar to conventional radiofrequency with a procedural stroke and transient ischemic attack rate of 1.1\%.\textsuperscript{26}

A second investigational multielectrode catheter is the nMARQ, which is an 8.4-French decapolar mapping and ablation catheter with an adjustable circular array of 10 platinum electrodes.\textsuperscript{27} Unlike the PV AC, the nMARQ is irrigated at each electrode. The catheter is capable of both bipolar and unipolar ablation, and the diameter and shape of the catheter can be adjusted manually.
In the multicenter REVOLUTION trial, (n=167 patients), the success rate at 8 months with nMARQ was 71% with a repeat ablation rate of 24%. Some safety concerns exist. Asymptomatic cerebral emboli occur in ≤33% of patients treated with the nMARQ. Postablation discordance of pulmonary vein potential recordings from Lasso catheters and the nMARQ has also been reported. Finally, endoscopy identified esophageal lesions in 14 of 43 (33%) patients treated with the nMARQ. The nMARQ catheter was recalled in June 2015 because of technical issues with the thermocouple and 3 reported deaths, 2 of which were because of atrial-esophageal fistula formation. The safety and efficacy of the nMARQ ablation system were evaluated in the pivotal reMARQable trial, which randomized patients with PAF to nMARQ versus point-by-point ablation. Although enrollment was stopped early, the follow-up is ongoing.

Figure 2. Comparison of fiberoptic and spring-based contact force sensors for radiofrequency ablation. Two different technologies are currently used to measure contact force. One catheter uses a sensor based on a Fabry Pérot interferometer (left). Force on the distal catheter tip changes the length of an air cavity, altering the reflection pattern of light shining through 2 adjacent semireflective mirrors. This changes the interference pattern of the light, and this pattern is transmitted back to the operating system to calculate the contact force. A second catheter uses a spring-based sensor (right). Force on the distal tip of the catheter compresses a precision spring. Deflection (x) of the spring is determined by measuring micromovements of a transmitter coil distal to the spring, and the contact force is calculated using the known spring characteristics (k).

Other Energy Sources

Electroporation

Radiofrequency is the most common energy source used for AF ablation. Although radiofrequency ablation is effective, excessive tissue heating can lead to serious complications, such as steam pops, perforation, and thromboembolism. Other energy sources have been investigated for AF ablation in an effort to reduce complications and improve efficacy. Direct current (DC) ablation was investigated in the 1980s but was quickly abandoned because of a high rate of serious complications caused by high pressure shock waves and arcing. Additional limitations of DC ablation included heterogeneous lesion formation and the potential for proarrhythmia. However, recent innovation has led to the development of an improved method of DC ablation called electroporation. Electroporation uses large electrodes to reduce overall current density, thereby eliminating the arcing seen with previous DC ablation techniques. Irreversible and well-demarcated electroporation lesions are created by the application of an external electric field that disrupts cellular membranes, increases cell membrane permeability, and induces subsequent cellular apoptosis. In contrast to radiofrequency ablation, the effects of DC electroporation are nonthermal. Significant tissue heating does not occur. Electroporation has been used successfully as a therapeutic intervention in solid tumor oncology, but it...
remains unknown if it can be used successfully in cardiac ablation.

A recent study investigated epicardial electroporation in a swine model. In this study, a custom octapolar catheter was used to create ventricular ablation lesions over the left anterior descending and left circumflex coronary arteries. After 3 months, histological analysis demonstrated effective transmural lesion formation without significant stenosis of the coronary arteries. Moreover, a separate study using the same catheter showed that application of electroporation in the pulmonary veins did not lead to pulmonary vein stenosis. Further studies are needed to determine if this technique can be adapted to endocardial ablation of AF.

Cryothermal Ablation

Cryothermal ablation has also undergone extensive development during the past 10 years. Although radiofrequency ablation produces lesions by tissue heating, cryothermal technology aims to cool tissues to −20 to −40°C, thereby causing intracellular ice formation and irreversible disruption of organelles and cell membranes. Cryothermal ablation has several theoretical advantages to radiofrequency ablation, including lower incidence of thrombus formation. Cryothermy has been incorporated into a balloon-based catheter (cryoballoon) for efficient PVI. The first-generation cryoballoon catheter (Artic Front, Medtronic, Inc) featured an inflatable 23- or 28-mm balloon cooled by injection of liquid nitrous oxide, producing inner-balloon temperatures as low as −80°C and outer-balloon temperatures of −40 to −50°C in a ring-like zone at the balloon equator. During ablation, circumferential lesions are created with 2 to 3 applications of coolant for 240 to 360 seconds each. The safety and efficacy of the first-generation cryoballoon were evaluated in the Sustained Treatment of Paroxysmal Atrial Fibrillation (STOP-AF) trial, which demonstrated an acute isolation rate of 97% to 100% and a relatively low rate of complications. However, the long-term single-procedure success rate was only 62% with a single procedure and 77% after multiple procedures.

One limitation of the first-generation device was the relatively narrow zone of cooling around the equator of the balloon. The second-generation cryoballoon features an extended zone of cooling from the equator of the balloon to the tip, thereby producing more uniform lesions independent of balloon positioning. Several studies of the second-generation cryoballoon have demonstrated promising efficacy results in paroxysmal or early-persistent AF with maintenance of SR >80% at 1 year. A meta-analysis of 15 studies on the second-generation, cryoballoon found a 1-year success rate of 82% in patients with paroxysmal AF and 70% in patients with persistent AF. A meta-analysis of 10 studies comparing the first- and second-generation devices found improved efficacy (odds ratio, 0.34; P<0.00001), shorter procedure time (mean difference=−0.8, P<0.00001), and shorter fluoroscopy time (mean difference=−1.0, P<0.00001) with the second-generation device. Although longer-term data with the second-generation cryoballoon are limited, 1 study found a 2-year success rate of 73% after a single procedure and 88% with multiple procedures. Studies directly comparing radiofrequency and the second-generation cryoballoon are limited. A 2014 meta-analysis of 14 smaller studies using the first-generation cryoballoon found a higher success rate with cryoballoon ablation, although this did not reach statistical significance (odds ratio, 1.34; P=0.538). However, cryoballoon ablation was found to result in shorter fluoroscopy time.
by 13 minutes ($P=0.014$) and overall procedure time by 30
minutes ($P=0.006$). A multicenter, nonrandomized study with
the second-generation cryoballoon with 1196 patients found
higher success rates with cryoballoon ablation compared with
conventional radiofrequency ablation (76.6% versus 60.4%,$^5$ $P<0.001$). The cryoballoon and radiofrequency ablation will
be compared in the prospective randomized FIRE AND ICE
trial,$^6$ with results expected in 2016. Cryoballoon ablation is
also being investigated as first-line therapy in patients with
paroxysmal AF in the Cryo-FIRST Trial (NCT01803438). A
third-generation cryoballoon with a 40% shorter distal tip was
approved by the Food and Drug Administration in May 2015.

The potential for phrenic nerve injury remains a concern
with the cryoballoon. Initial studies with the second-
generation cryoballoon found a 19.5% incidence of phrenic
nerve palsy.$^5$ However, subsequent studies have found rates of
phrenic nerve palsy ranging from 3.5% to 10%, with most
cases being transient and resolving by the end of the proce-
dure.$^2$ As many as two thirds of patients recover phrenic nerve
function before discharge.$^2$ Several techniques can be used to
limit PN injury, including PN pacing with visual observation
of diaphragmatic excursion or electromyography.$^5$!

**Endoscopic Ablation Using Light Amplification by
Stimulated Emission of Radiation**

Another ablation technology currently being evaluated is
diagnostic laser ablation (EAS; CardioFocus, Inc, Marlbor-
ough, MA). The EAS system features a 980-nm diode laser and
a multifrequency catheter with a compliant, inflatable balloon
at the tip. Before ablation, the deflated balloon is advanced
into the left atrium, inflated with radiopaque deuterium oxide,
and wedged against the ostium of a PV. An endoscope is intro-
duced into the left atrium and live images are used to guide
ablation. The infrared laser can be aimed radially or at vari-
able angles toward the catheter tip to create point-by-point
circumferential lesions with a green aiming beam. The energy
does not react with the deuterium in the balloon but causes
heating of water molecules and coagulation necrosis of atrial
tissue.

The first-in-man study demonstrated acute PVI in 91% of
patients with a 12-month success rate of 60%.$^5$ The device
was subsequently redesigned with a compliant balloon that
can be adjusted through 9 different sizes, a reduced laser
arc, and a softer catheter tip. The second-generation device
was first studied in 27 patients with paroxysmal AF, where
it achieved acute PVI in 100% of cases with a 3-month PVI
rate of 83%.$^5$ Since then, several studies have been published
about the efficacy and safety of the second-generation EAS
(Table II in the Data Supplement). Adequate occlusion of the
PV and energy delivery (>8.5 W) are 2 important factors in
delivering effective ablation with the EAS.$^5,6$ In general, most
studies have found success rates similar to that of conven-
tional radiofrequency ablation.$^5,8-10$ In the randomized pivotal
IDE (investigational device exemption) Heartlight trial, the
EAS was noninferior to conventional irrigated RFA for both
efficacy (freedom from treatment failure at 12 months: 61.1% versus
61.7%, $P$-noninferiority$=0.003$) and safety (adverse
event rate 11.8% versus 14.5%, $P$-noninferiority$=0.002$).$^6$

In a smaller randomized trial of 140 patients, the EAS had a
similar success rate at 12 months compared with the cryobal-
loon (73% versus 63%, $P=0.18$).$^6$

Complication rates have generally been low with the EAS.
Phrenic nerve palsy has been reported in 2% to 4% of patients
(Table II in the Data Supplement) and phrenic nerve moni-
toring with superior vena cava pacing is recommended when
isolating the right-sided veins. Other rare complications have
included thermal esophageal lesions, cardiac tamponade, and
asymptomatic cerebral embolism.$^53-66$

**Acoustic Radiation Force Impulse Imaging**

Although most innovation aimed at lesion formation has
focused on catheter design and alternative energy sources,
these technologies cannot directly determine whether an abla-
tion lesion, though intended, has actually formed. In clinical
practice, ablation lesions are typically assessed indirectly by
identifying conduction block via changes in cardiac activation
sequence or arrhythmia noninducibility. Unfortunately, these
indirect measures cannot always distinguish between transient
conduction block because of tissue edema or stunning, and
long-lasting durable lesions.$^57$ Magnetic resonance imaging as
an experimental tool can identify and characterize radiofre-
quency lesions in situ;$^58$ however, widespread clinical applica-
bility has been limited by the need for nonmetallic catheters,
long image acquisition times, limited spatial resolution, and
the size and expense of magnetic resonance imaging scanner
hardware.

Acoustic radiation force impulse (ARFI) imaging is a
novel ultrasound technique that measures tissue elasticity with
high spatial (submillimeter) and temporal (subsecond) reso-
lution using standard clinical ultrasound imaging systems.$^69$
This method has recently been adapted to an integrated intra-
cardiac mapping and ultrasound imaging system.$^70$ An ARFI
image is created by delivering a series of ultrasound pulses to
mechanically displace tissue, measuring the displacement of
each image pixel in response to the push pulse using standard
ultrasound techniques, and then displaying high-resolution
displacement information superimposed on the ultrasound
image. Regions of tissue within the imaged field that are stiff
demonstrate smaller displacements than more elastic tissue.
Because radiofrequency energy ablates tissue through heat-
ing-induced coagulation necrosis, radiofrequency lesions in
myocardium are revealed as discrete stiff regions within the
ultrasound image.

In vitro studies show that myocardial ARFI images cor-
correlate with histological characterization of radiofrequency
lesions$^7$ and ARFI imaging can visualize formation of a
radiofrequency lesion in near real-time.$^72$ Furthermore, ARFI
imaging can distinguish between an incomplete atrial ablation
line with a gap and a complete ablation line.$^70$ The presence
of a lesion in the ARFI image is predictive of a conduction
disturbance at that location (positive predictive value=$96.4%$
and negative predictive value=$90.0%$), and the finding of
a gap in the ablation line by ARFI imaging predicts lack of
conduction block (negative predictive value=$71.2%$). Finally,
ARFI imaging has been successfully adapted to clinical ultra-
sound and mapping systems during routine clinical catheter
ablation procedures with demonstrated feasibility of acquir-
ing ARFI images of radiofrequency lesions from clinically
relevant ablation target regions in both the right and the left atria (Figure 4). 

Although ARFI imaging shows promise as a tool to evaluate cardiac ablation lesions in situ, and has potential to offer a new and complimentary procedure end point for therapeutic ablation by providing direct information about whether a radiofrequency lesion set is complete (contiguous and transmural lesions without gaps), further development of imaging catheters to enhance imaging depth and studies to establish the role of this technology in clinical practice are needed.

Conclusions

Despite advances during the past decade, recurrence of AF after ablation is common. Recent technological innovations are likely to increase the safety, efficiency, and durability of lesion formation. Contact-force (CF) sensing catheters could allow the delivery of more durable lesions and prevent complications caused by excessive CF. Alternative energy sources such as direct-current electroporation, laser energy, and cryothermal technology may lead to improvements in lesion formation and reductions in complication rates. PVI-specific catheters have shown promise in shortening procedure times by forming circumferential lesions with only a few energy applications but continue to face challenges. Finally, novel imaging technologies may also improve ablation by allowing real-time tissue-level assessment of myocardial injury and tissue death.

Disclosures

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registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APQRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. Heart Rhythm. 2012;9:632–696.e21. doi: 10.1016/j.hrrth.2011.12.016.


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Supplement Material

**Supplemental Table 1:** Published studies of the spring-based and fiberoptic-based contact-force sensing ablation catheters.

<table>
<thead>
<tr>
<th>Type of AF</th>
<th>Follow Up</th>
<th>CF Goal</th>
<th>N</th>
<th>Success</th>
<th>P value</th>
<th>Comments</th>
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<td><strong>Fiberoptic Sensor</strong></td>
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<tr>
<td>Reddy 2015¹ (TOCCASTAR)</td>
<td>PAF</td>
<td>12 mos</td>
<td>None</td>
<td>146</td>
<td>67.8%</td>
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<td></td>
<td></td>
<td></td>
<td>134</td>
<td>69.4%</td>
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</tr>
<tr>
<td>Wakili et al. 2014²</td>
<td>PAF+PERS AF</td>
<td>12 mos</td>
<td>10g</td>
<td>32</td>
<td>59.4%</td>
<td>P=0.78</td>
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<td></td>
<td></td>
<td></td>
<td>35</td>
<td>62.9%</td>
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<tr>
<td>Wutzler et al. 2014³</td>
<td>PAF+PERS AF</td>
<td>12 mos</td>
<td>None</td>
<td>31</td>
<td>84%</td>
<td>P=0.031</td>
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<td></td>
<td>112</td>
<td>63%</td>
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<tr>
<td>Reddy et al. 2012⁴ (TOCCATA)</td>
<td>PAF</td>
<td>12 mos</td>
<td>None</td>
<td>32</td>
<td>47%</td>
<td>N/A</td>
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<tr>
<td><strong>Spring-Based Sensor</strong></td>
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<tr>
<td>Andrade et al. 2014⁵</td>
<td>PAF</td>
<td>12 mos</td>
<td>5-50g</td>
<td>25</td>
<td>88%</td>
<td>P=0.047</td>
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<td></td>
<td></td>
<td></td>
<td>50</td>
<td>66%</td>
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<tr>
<td>Jourda et al. 2014⁶</td>
<td>PAF</td>
<td>12 mos</td>
<td></td>
<td>75</td>
<td>88%*</td>
<td>P=0.682</td>
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<td></td>
<td>75</td>
<td>85.3%</td>
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<tr>
<td>Natale et al. 2014⁷ (SMART-AF)</td>
<td>PAF</td>
<td>12 mos</td>
<td>None</td>
<td>160</td>
<td>72.5%</td>
<td>N/A</td>
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<tr>
<td>Providencia et al. 2014⁸</td>
<td>PAF</td>
<td>19 mos</td>
<td>&gt;22g</td>
<td>50</td>
<td>96%</td>
<td>P=0.04</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;22g</td>
<td>50</td>
<td>80%</td>
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<tr>
<td>Marijon et al. 2013⁹</td>
<td>PAF</td>
<td>12 mos</td>
<td>10g</td>
<td>30</td>
<td>89%*</td>
<td>P=0.04</td>
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<td></td>
<td></td>
<td></td>
<td>30</td>
<td>64%</td>
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Abbreviations: PAF = paroxysmal AF, PERS AF = persistent AF, CF = contact force.
### Table 2: Published studies of the CardioFocus Endoscopic Ablation System.

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Acute PVI</th>
<th>FU</th>
<th>Success</th>
<th>Safety</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dukkipati et al. 2015</td>
<td>178 PAF</td>
<td>97.7%</td>
<td>12 mos</td>
<td>61.1% (EAS)</td>
<td>2 stroke (1.2%)</td>
<td>EAS ablation was noninferior to RF ablation</td>
</tr>
<tr>
<td></td>
<td>175 PAF</td>
<td>99.1%</td>
<td></td>
<td>61.7% (RF)</td>
<td>6 PNP (3.5%)</td>
<td></td>
</tr>
<tr>
<td>Gal et al. 2014</td>
<td>50 (41 PAF)</td>
<td>99.5%</td>
<td>17 mos</td>
<td>58%</td>
<td>1 PNP (2%)</td>
<td></td>
</tr>
<tr>
<td>Perrotta et al. 2014</td>
<td>150 (111 PAF)</td>
<td>95%</td>
<td>12 mos</td>
<td>77%</td>
<td>3 PNP (2%)</td>
<td>Procedure time and PVI rate improved with operator experience.</td>
</tr>
<tr>
<td>Sediva et al. 2014</td>
<td>158 PAF</td>
<td>99.2%</td>
<td>12 mos</td>
<td>82.3%</td>
<td>4 PNP (2.3%), 1 tamponade, 1 TIA, 6 vasc injury</td>
<td>Showed significant reductions in procedure time with operator experience.</td>
</tr>
<tr>
<td>Bordignon et al. 2013</td>
<td>70 PAF</td>
<td>98.9%</td>
<td>12 mos</td>
<td>73% (EAS)</td>
<td>3 PNP (4.3%)</td>
<td>P=0.18.</td>
</tr>
<tr>
<td></td>
<td>70 PAF</td>
<td>99.6%</td>
<td></td>
<td>63% (Cryoballoon)</td>
<td>4 PNP (5.7%)</td>
<td></td>
</tr>
<tr>
<td>Dukkipati et al. 2013</td>
<td>200 PAF</td>
<td>98.8%</td>
<td>12 mos</td>
<td>60.2%</td>
<td>2% tamponade, 2.5% PNP.</td>
<td></td>
</tr>
<tr>
<td>Bordignon et al. 2013</td>
<td>30 PAF</td>
<td>89%</td>
<td>311 days</td>
<td>83% (HD)</td>
<td>2 PNP (3.3%)</td>
<td>P=0.04. Patients assigned to high energy (HD, &gt;8.5W) or lower energy group (LD, 5.5-8.5W).</td>
</tr>
<tr>
<td></td>
<td>30 PAF</td>
<td>69%</td>
<td></td>
<td>60% (LD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metzner et al. 2012</td>
<td>30 PAF</td>
<td>69-90%</td>
<td>186 days</td>
<td>60-80%</td>
<td>1 groin hematoma</td>
<td>Patients divided into three energy levels. Higher energy level was associated with higher PVI rate.</td>
</tr>
<tr>
<td>Dukkipati et al. 2012</td>
<td>56 PAF</td>
<td>98%</td>
<td>12 mos</td>
<td>71.2%</td>
<td>1 PNP (1.8%), 1 tamponade, 1 groin hematoma</td>
<td>Reported success rate is for two procedures.</td>
</tr>
<tr>
<td>Schmidt et al. 2012</td>
<td>35 (31 PAF)</td>
<td>98%</td>
<td>266 days</td>
<td>77%</td>
<td>1 PNP (2.9%), 1 tamponade</td>
<td></td>
</tr>
<tr>
<td>Metzner et al. 2011</td>
<td>40 PAF</td>
<td>99%</td>
<td>402 days</td>
<td>60%</td>
<td>1 PNP (2.5%), 2 tamponade</td>
<td></td>
</tr>
<tr>
<td>Schmidt et al. 2010</td>
<td>30 PAF</td>
<td>98%</td>
<td>168 days</td>
<td>80%</td>
<td>1 tamponade, 1 PNP (2.5%)</td>
<td></td>
</tr>
<tr>
<td>Dukkipati et al. 2010</td>
<td>27 PAF</td>
<td>100%</td>
<td>3 mos</td>
<td>83%</td>
<td>No major adverse events</td>
<td>First study with second generation device.</td>
</tr>
<tr>
<td>Reddy et al. 2009</td>
<td>30 PAF</td>
<td>91%</td>
<td>12 mos</td>
<td>60%</td>
<td>1 stroke, 1 tamponade, 1 PNP (3.3%)</td>
<td>First in-human study.</td>
</tr>
</tbody>
</table>

Abbreviations: PAF=paroxysmal AF. EAS=Endoscopic Ablation System. PNP=phrenic nerve palsy.
References:


