I. Policy

The maze or modified maze procedures, performed on a non-beating heart during cardiopulmonary bypass with concomitant cardiac surgery is considered medically necessary for treatment of symptomatic, drug-resistant atrial fibrillation or flutter.

Minimally invasive, off-pump maze procedures (i.e., modified maze procedures), including those done via mini-thoracotomy, are considered investigational for treatment of atrial fibrillation or flutter.

Hybrid ablation (defined as a combined percutaneous and thoracoscopic approach) is considered investigational for the treatment of atrial fibrillation or flutter.

There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with the above investigational procedures.

The use of an open maze or modified maze procedure performed on a non–beating heart during cardiopulmonary bypass without concomitant cardiac surgery is considered not medically necessary for treatment of symptomatic, drug-resistant atrial fibrillation or flutter.

Policy Guidelines

Given the availability of less-invasive alternative approaches in the treatment of atrial fibrillation performing the maze procedure without concomitant cardiac surgery should rarely be needed.

Published studies on the maze procedure describe patients with drug-resistant AF and atrial flutter as having experienced their arrhythmias for an average of 7 or more years and having unsuccessful results with an average of 5 or more antiarrhythmic medications.
**II. PRODUCT VARIATIONS**

This policy is applicable to all programs and products administered by Capital BlueCross unless otherwise indicated below.

FEP PPO*

*Refer to FEP Medical Policy Manual MP-7.01.14 Open and Thoracoscopic Approaches to Treat Atrial Fibrillation. The FEP Medical Policy manual can be found at: [www.fepblue.org](http://www.fepblue.org).

**III. DESCRIPTION/BACKGROUND**

There are a variety of surgical approaches to treat atrial fibrillation that work by interrupting abnormal electrical activity in the atria. Open surgical procedures, such as the Cox-Maze procedure were first developed for this purpose, and are now generally performed in conjunction with valvular or coronary artery bypass graft (CABG) surgery. Surgical techniques have evolved to include minimally invasive approaches that use epicardial radiofrequency ablation (RFA) a thoracoscopic or mediastinal approach and hybrid catheter ablations/open procedures.

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by disorganized atrial activation with ineffective atrial ejection. The underlying mechanism of AF involves interplay between electrical triggering events that initiate AF and the myocardial substrate that permits propagation and maintenance of the aberrant electrical circuit. The most common focal trigger of AF appears to be located within the cardiac muscle that extends into the pulmonary veins. The atria are frequently abnormal in patients with AF and demonstrate enlargement or increased conduction time. Atrial flutter is a variant of atrial fibrillation.

The first-line treatment for AF usually includes medications to maintain sinus rhythm and/or control the ventricular rate. Antiarrhythmic medications are only partially effective; therefore, medical treatment is not sufficient for many patients. Percutaneous catheter ablation, using
endocardial ablation, is an accepted second-line treatment for patients who are not adequately controlled on medications. Catheter ablation is successful in maintaining sinus rhythm for a majority of patients, but long-term recurrences are common and increase over time. Surgical ablation, performed either by open surgical techniques or thoracoscopy, is an alternative approach to percutaneous catheter ablation.

Open surgical techniques. The classic Cox-Maze III procedure is a complex surgical procedure that involves sequential atriotomy incisions that interrupt the aberrant atrial conduction pathways in the heart for patients with AF. The procedure is also intended to preserve atrial pumping function. It is indicated for patients who do not respond to medical or other surgical antiarrhythmic therapies and is often performed in conjunction with correction of structural cardiac conditions such as valve repair or replacement. This procedure is considered the gold standard for surgical treatment of drug-resistant AF with an approximately 90% success rate.

The maze procedure entails making incisions in the heart that:
- direct an impulse from the sinoatrial (SA) node to the atroventricular (AV) node;
- preserve activation of the entire atrium; and
- block re-entrant impulses that are responsible for AF or atrial flutter.

The classic Cox-Maze procedure is performed on a non-beating heart during cardiopulmonary bypass. Simplification of the maze procedure has evolved with the use of different ablation tools such as microwave, cryotherapy, ultrasound, and radiofrequency (RF) energy sources to create the atrial lesions instead of employing the incisional technique used in the classic maze procedure.

Minimally invasive (thoracoscopic) techniques. In addition, less invasive, transthoracic, endoscopic, off-pump procedures to treat drug-resistant AF have been developed. The evolution of these procedures involves both different surgical approaches and different lesion sets. Alternative surgical approaches include mini-thoracotomy, and total thoracoscopy with video assistance. Open thoracotomy and mini-thoracotomy employ cardiopulmonary bypass and open heart surgery, while thoracoscopic approaches are performed on the beating heart. Thoracoscopic approaches do not enter the heart and use epicardial ablation lesion sets, whereas the open approaches use either the classic “cut and sew” approach or endocardial ablation. Lesion sets may vary independent of the surgical approach, with a tendency toward less extensive lesion sets targeted to areas that are most likely to be triggers of AF. The most limited lesion sets involve pulmonary vein isolation and exclusion of the left atrial appendage. More extensive lesion sets include linear ablations of the left and/or right atrium and ablation of ganglionic plexi. Some surgeons perform left-atrial reduction in cases of left-atrial enlargement.

The type of energy used for ablation also varies; RF energy is most commonly applied. Other types of energy sources such as cryoablation and high-intensity ultrasound have also been used.
For the purposes of this policy statement, the variations on surgical procedures for AF will be combined under the heading of “modified maze” procedures.

Hybrid techniques. “Hybrid” ablation refers to a procedure that utilizes both thoracoscopic and percutaneous approaches in the same patient. Ablation is performed on the outer surface of the heart (epicardial) via the thoracoscopic approach, and on the inner surface of the heart (endocardial) via the percutaneous approach. The rationale for doing a hybrid procedure is that a combination of both techniques may result in more complete ablation. Thoracoscopic epicardial ablation is limited by the inability to perform all possible ablation lines, since the posterior portions of the heart are not accessible via thoracoscopy. Percutaneous, endoscopic ablation is limited by incomplete ablation lines that often require repeat procedures. By combining both procedures, a full set of ablation lines can be performed, and incomplete ablation lines can be minimized.

The hybrid approach first involves thoracoscopy with epicardial ablation. Following this procedure, an electrophysiologic study is performed percutaneously followed by endocardial ablation as directed by the results of electrophysiology. Most commonly, the electrophysiology study and endocardial ablation are done immediately after the thoracoscopy as part of a single procedure. However, some hybrid approaches perform the electrophysiology study and endocardial ablation, as directed by the electrophysiology study, on a separate day.

**Regulatory Status**

Several RFA systems that are used for cardiac tissue ablation have been cleared for marketing by FDA based on substantial equivalence to predicate devices. These include

- The Medtronic Cardioblate® System (Medtronic, Minneapolis, MN; cleared for marketing in January 2002);
- The Cardima Ablation System (Cardima, San Carlos, CA; cleared for marketing in January 2003);
- The Epicor™ Medical Ablation System (Epicor Medical, Sunnyvale, CA; cleared for marketing in February 2004);
- The Isolator™ Transpolar™ Pen (AtriCure, West Chester, OH; cleared for marketing in June 2005);
- The Estech COBRA® Cardiac Electrosurgical Unit (Endoscopic Technologies, Danville, CA; cleared for marketing in December 2005);
- The Coolrail™ Linear Pen (AtriCure, West Chester, OH; cleared for marketing in March 2008).
- The Numeris® Guided Coagulation System with VisiTrax® (nContact Surgical, Morrisville, NC; cleared for marketing in February 2009).
IV. RATIONALE

Traditional Maze Versus “Modified Maze” Procedures

Khargi et al analyzed 48 studies comprising 3832 patients who received surgical treatment of atrial fibrillation (AF) using the classic “cut-and-sew” Cox maze III technique or an alternative source of energy. They concluded that they could not identify any significant differences in the postoperative sinus rhythm conversion rates between the classic approach and alternative sources of energy. While prospective randomized studies are lacking, the data involve a wide range of ablative patterns and their effects on atrial tissue. Topkara et al reported comparable postoperative rhythm success in use of either radiofrequency (RF; 121 patients) or microwave (85 patients) energy in surgical ablation of AF.

Several observational studies compared the Cox maze III procedure with other procedures (radiofrequency ablation [RFA], pulmonary vein isolation) performed at single institutions, with procedure selection guided by the surgeon. Two studies attempted to address the selection bias inherent in these studies by matching. In the first, from the Washington University School of Medicine, wherein the maze procedure was developed, the 242 patients who underwent the Cox maze procedure (154 with the classic cut-and-sew [CMIII] procedure, and 88 in whom RFA replaced the incisions of the classic procedure [CMIV]) were matched on their propensity for treatment assignment (a logistic regression in which the outcome is treatment assignment and the predictors are covariates that might influence which procedure is chosen by the surgeon). Fifty-eight matched pairs were studied. At 1 year, survival was 94% and 89%, respectively (p=0.19), and freedom from AF recurrence was 96% and 93% (p=0.52) for the CMIII and CMIV groups, respectively. The authors note that the CMIV procedure was offered to higher risk patients than
the CMIII procedure, which is partly why only 58 of 88 CMIV patients were able to be matched in their analysis. The matched propensity analysis is able to remove measureable selection biases, but if unmeasured factors lead surgeons to choose 1 surgery over the other, these factors are not accounted for in the analysis.

In a second matched analysis, 56 patients who underwent a CMIV RFA procedure at Mayo Clinic were matched (historical controls) to 56 patients who underwent the CMIII procedure. Matching factors were age, sex, New York Heart Association (NYHA) class, AF type, and concomitant mitral valve surgery. Here the CMIV group had greater postoperative AF (43% vs 24%), more pacemaker requirements (25% vs 5%), greater use of antiarrhythmic drugs (75% vs 25%), and fewer patients with freedom from AF at late follow-up (mean 8.4 months; 62% vs 92%). Again, the CMIV patients had greater underlying disease (more concomitant procedures were performed).

In a second article reporting results from the Mayo Clinic, Stulak et al reported results from an unmatched retrospective comparison of CMIII and CMIV among 1540 patients who underwent surgical ablation for AF at a single institution from 1993 to 2011. Energy sources used to create lesions included cut and sew in 521 (44%), cryothermy in 267 (22%), RF in 262 (22%), and a combination of these sources in 139 patients (12%). On multivariate analysis, CMIII was independently associated with less risk of recurrent AF at a follow-up period of 1 to 5 years (hazard ratio [HR], 0.4; 95% confidence interval [CI], 0.24 to 0.69; p<0.001) and more than 5 years (HR=0.23; 95% CI, 0.12 to 0.42; p<0.001) for all patients. This study is limited by its retrospective design and lack of propensity score matching.

Section Summary: Traditional Maze Versus “Modified Maze” Procedures
There are numerous modifications on the original maze procedure, with variations in the surgical approach, the lesion set used, and the methods for creating lesions (eg, cut-and-sew, RFA). The evidence on comparative effectiveness of the different approaches is not of high quality and is incomplete in terms of addressing all of the possible comparisons. The limited available evidence from matched case series does not indicate that there are large differences in efficacy among the different approaches.

Maze and Related Procedures as an Adjunct to Open Heart Surgery
The evidence on this question consists of several randomized controlled trials (RCTs) evaluating AF ablation when performed as an add-on for patients undergoing open mitral valve surgery, and systematic reviews of these trials.

Systematic Reviews
In 2014, Phan et al reported results of a systematic review and meta-analysis of RCTs comparing surgical ablation with no ablation among patients with AF undergoing mitral valve surgery. Nine studies were included in the analysis: 5 that evaluated RFA, 2 that evaluated Cox maze cut-and-sew, 1 that evaluated cryoablation, and 1 that evaluated pulmonary vein isolation and Cox
maze cut-and-sew. In pooled analysis, the risk of 30-day all-cause mortality did not differ significantly between the ablation and nonablation groups (4.4% vs 2.7%, respectively; odds ratio [OR], 1.45; 95% CI, 0.55 to 3.83; p=0.46). The number of patients in sinus rhythm at discharge was significantly higher in the group receiving mitral valve repair plus surgical ablation compared with the group receiving mitral valve repair only (67.9% vs 17.0%; OR=13.96; 95% CI, 6.29 to 30.99; p<0.001); similarly, at 3-, 6-, 12-, and greater than 12-month follow-ups, a greater proportion of the surgical ablation group was in sinus rhythm.

In an earlier systematic review, Reston and Shuhaiber reviewed 4 RCTs and 6 comparative studies to determine whether a simultaneous maze procedure reduces the risk of stroke or death in patients with chronic or paroxysmal AF who receive mitral valve surgery. They concluded that the studies examined suggest a reduction in stroke rates and a small increased risk in the need for pacemakers among patients receiving simultaneous maze procedures. In addition, they noted that alternative energy sources, such as RF, may reduce the risk of postoperative bleeding associated with classic maze incisions.

**Randomized Controlled Trials**
Several RCTs evaluating atrial fibrillation ablation in conjunction with open surgery that were not included in the systematic reviews have also been published. In 2015, Gillinov et al published results of a large RCT that randomized 260 patients with persistent or long-standing AF who required mitral valve surgery to either ablation (either pulmonary vein isolation or ablation with a maze lesion set) during surgery (n=133) or no ablation (n=127). Compared with controls, significantly more patients in the ablation group were free from AF at both 6 and 12 months (63.2% vs 29.4%, p<0.001). The relative success ratio (ablation group: control group) was 2.15 (95% CI, 1.54 to 3.00) on the basis of observed data. At 1 year, mortality did not differ significantly between the ablation group and the control group (6.8% vs 8.7%, respectively, p=0.57). A composite safety endpoint did not differ significantly between groups at 30 days, and serious adverse event rates did not differ significantly between groups at 1 year.

Budera et al published an RCT in 2012, which randomized 224 patients from 3 clinical centers to cardiac surgery plus ablation versus cardiac surgery alone. Patients were eligible for inclusion if they had at least 2 episodes of documented AF in the last 6 months, as well as appropriate indications for cardiac surgery. Cardiac surgery procedures included coronary artery bypass graft (CABG), valve replacement/repair, or combined CABG and valve procedures. The primary efficacy outcome was sinus rhythm at 1 year following surgery, and the primary safety outcome was a composite outcome of death, myocardial infarction, stroke, or new-onset renal failure requiring hemodialysis at 30 days following surgery. Sinus rhythm at 1 year was documented in 60.2% (56/93) of patients in the surgery plus ablation group compared with 35.5% (27/76) of patients in the surgery-alone group. Adverse events were similar in both groups at 30 days and at 1-year follow-up. Secondary clinical outcomes, including mortality and NYHA functional class, did not differ between groups at 1 year.
The SAFIR study was a multicenter, double-blind, RCT conducted at 4 university hospitals. This trial randomly assigned 43 patients with mitral valve disease and long-standing persistent AF to mitral valve surgery alone (n=22) versus surgery plus RFA of the left atrium (n=21). At 12 months, 95.2% of patients in the RFA group were in sinus rhythm compared with 33.3% of patients in the surgery-alone group (p<0.005). The primary end point of sinus rhythm at 12 months without recurrence of any atrial arrhythmias was reached by a significantly greater percentage of patients in the RFA group (57% vs 4%, respectively; p=0.004). Rates of postoperative complications and stroke were similar between groups.

Von Oppell et al randomly assigned 49 patients with AF of greater than 6 months in duration who were scheduled for mitral valve surgery to a modified RF maze procedure versus mitral valve surgery alone. At 12-month follow-up, more patients in the maze group (75%) remained in sinus rhythm compared with the surgery-only group (39%; P=0.03). There was also a significant decrease in amiodarone use for the maze group and no difference in the use of warfarin.

Liu et al compared mitral valve surgery plus a modified maze procedure with mitral valve surgery alone followed by RF catheter ablation 6 months later in 99 patients with rheumatic heart disease. After a mean follow-up of 15 to 20 months, patients in the maze group (82%) had a higher rate of freedom from atrial arrhythmias compared with the RFA group (55.2%; p<0.001). Repeat procedures were required for 15/50 patients in the RFA group. Percutaneous catheter ablation was performed in 6 of 49 patients in the maze group for recurrent arrhythmias.

Van Breugel et al evaluated changes in quality of life (QOL) in a related patient population. One hundred fifty patients with AF who were scheduled to undergo either valve surgery or CABG surgery were randomly assigned to surgery alone or surgery plus a modified maze procedure. The primary end point was QOL, as measured by the 36-Item Short-Form Health Survey, the EuroQoL (EQ-5D), and the Multidimensional Fatigue Inventory. A total of 132 patients had usable survey results. Both groups improved on all QOL measures, but in general, there were no significant differences between groups. The only exception was on the Pain/Discomfort subscale of the EQ-5D, which showed a greater degree of worsening in the control group compared with the maze group.

In another evaluation of QOL, Chernyavskiy et al reported that randomized to CABG with a modified maze procedure (n=30) or with pulmonary vein isolation by radiofrequency ablation (n=31) had improved QOL scores compared with those randomized to CABG alone (n=34).

**Nonrandomized Comparative Studies**

Saint et al attempted to quantify the incremental risk conferred by adding a Cox maze IV procedure to open mitral valve repair in a comparison of 213 patients with mitral valve disease and preoperative AF who underwent mitral valve surgery only (n=109) or mitral valve surgery with a Cox maze IV procedure (n=104). The operative mortality for the mitral valve procedure alone was predicted for each group based on Society of Thoracic Surgeons (STS) perioperative
risk calculator; the risk attributed to the addition of the Cox maze IV procedure was calculated by comparing the predicted mortality from the isolated mitral valve procedure with the actual mortality rate. At baseline, patients who had an isolated mitral valve procedure differed significantly from those who underwent the mitral valve procedure plus a Cox maze IV procedure in terms of medical comorbidities and etiology of the mitral valve disease. The observed 30-day mortality for patients not offered a Cox maze IV procedure was 4.6% (expected 5.5%), yielding an observed: expected 30-day mortality ratio of 0.84 (95% CI, 0.13 to 1.54). The observed 30-day mortality for patients who underwent a concomitant Cox maze IV procedure with mitral valve surgery was 2.9%. The STS predicted score for isolated mitral valve surgery in this group was 2.5%, yielding an observed: expected 30-day mortality ratio of 1.16 (95% CI, 0.13 to 2.44). This study is limited by the fact that patients who received concomitant Cox maze IV procedures with mitral valve surgery were a selected low-risk population; however, it suggests that in the appropriate patient population, the Cox maze IV procedure can be added to mitral valve surgery with limited additional short-term mortality risk.

**Noncomparative Studies**

Since the publication of the RCTs previously described, several noncomparative studies have reported outcomes from surgical (cut-and-sew) maze and modified RF maze procedures as an adjunct to planned cardiac surgery. While single-arm studies can offer useful data on some parameters, such as durability of treatment effect and adverse events, they do not offer relevant evidence on the comparative efficacy of the procedure. For example, a study of long-term outcomes after 127 Cox maze cut-and-sew procedures in conjunction with mitral valve replacement was identified. Patient disposition was well-documented in the analysis. Thirty percent of patients experienced late AF recurrence at a mean of 44±27 months. Freedom from AF was 93%, 82%, 71%, and 63% at 1, 3, 5, and 7 years, respectively, and pacemakers were implanted in 4.7% of patients. Other case series have reported success rates of the procedure in different populations, with rates of freedom from AF ranging from 53% to 79% at latest follow-up.

**Section Summary: Maze and Related Procedures as an Adjunct to Open Heart Surgery**

Surgical treatment of AF can be performed in conjunction with valvular surgery or CABG surgery with little additional risk. Evidence from RCTs of open heart surgery plus surgical treatment of AF versus surgery alone establishes that there is a high rate of success in maintaining sinus rhythm and avoiding the need for antiarrhythmic medications. Evidence for a benefit in other health outcomes, such as stroke rate or quality of life, is currently insufficient to form conclusions.

**Maze and Related Procedures as a Stand-Alone Treatment for AF**

The evidence related to the use of maze and related procedures as stand-alone treatments for AF includes evaluations of open surgical ablation, minimally invasive surgical ablation, and “hybrid” approaches. The stand-alone procedures fall on a continuum of invasiveness, ranging...
from open repair with sternotomy to minimally invasive procedures done with video-assisted thoracoscopy. Hybrid approaches include concomitant epicardial/endocardial procedures and are discussed separately. The optimal study design for evaluating the effectiveness of these procedures is an RCT that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies can sometimes provide useful information on health outcomes, but may be affected by biases due to multiple confounding factors. Uncontrolled studies may provide useful information on procedure-related harms, but do not, by themselves, provide relevant information on the comparative efficacy of treatments. For maze and related procedures as stand-alone therapy, the appropriate comparison group is endocardial catheter ablation. Although freedom from AF is an important outcome following AF treatment procedures, the evaluation of stand-alone maze and related procedures requires assessment of surgery-related complications.

**Surgical Ablation as a Stand-Alone Treatment**

**Randomized Controlled Trials**

One RCT has been completed that compares stand-alone surgical ablation versus percutaneous ablation. The FAST trial enrolled 124 patients from 2 clinical centers in Europe, who had symptomatic AF for at least 1 year and had failed at least 1 antiarrhythmic medication. Patients were randomized to surgical ablation using video-assisted thoracoscopy under general anesthesia, or to percutaneous catheter ablation. Both techniques used RF energy. All patients in the surgical ablation group also had removal of the left atrial appendage. The primary outcome was freedom from AF off all antiarrhythmic medications during 12 months of follow-up. Secondary outcomes were freedom from AF including patients still on medications and adverse events. Prior unsuccessful catheter ablation had been performed in 67% of patients.

At 1 year, freedom from AF off all antiarrhythmic drugs was achieved by 65.6% (40/61) of the surgical ablation group compared with 36.5% (23/63) of the catheter ablation group (p=0.002). Freedom from AF, on or off medications, was achieved by 78.7% (48/61) of the surgical ablation group compared with 42.9% (27/63) of the catheter ablation group (p<0.001). Serious adverse events were more common in the surgical group, occurring in 23.0% (14/61) of patients compared with 3.2% (2/63) in the catheter ablation group (p=0.001). In both groups, there was 1 episode each of tamponade and stroke. Additional complications in the surgical group were 6 patients who had pneumothorax, 2 patients who required pacemaker insertion, and 1 patient each who had hemothorax, rib fracture, pneumonia, or required sternotomy for bleeding. In the catheter ablation group, 6.3% (4/63) of patients had a groin hematoma, which was considered a minor complication.

In a subsequent smaller RCT, Pokushalov et al randomized patients with a prior failed first catheter ablation procedure for AF to receive either repeat catheter ablation (n=32) or surgical ablation with video-assisted thoracoscopy (n=32). After 12 months, a higher proportion of
patients who underwent surgical ablation were free of AF or atrial tachycardia without antiarrhythmic drugs (81% vs 47%, p=0.004). Although the total number of adverse events did not differ significantly between groups, the number of serious adverse events was higher in the surgical ablation group (7 vs 1, p=0.02).

**Systematic Reviews**

A number of systematic reviews that have used different inclusion criteria have summarized the evidence on stand-alone surgical ablation. These studies have varied in their inclusion criteria. In 2016, Phan et al reported results of a systematic review and meta-analysis of studies comparing thoracoscopic surgical ablation with catheter ablation, including the FAST trial. Eight comparative studies, with a total of 321 video-assisted thoracoscopic surgical ablation patients and 378 catheter ablation patients, met the inclusion criteria. For the study’s primary efficacy end point of freedom from AF off antiarrhythmic drugs, the treatment success was significantly higher in the surgical ablation group compared with the catheter ablation group at 6 months post procedure (81% vs 64.3%; risk ratio [RR], 1.23; 95% CI, 1.02 to 1.49; p=0.03). This difference was maintained at 12 months post procedure. Patients treated with surgical ablation had significantly higher rates of major complications (including death, stroke, transient ischemic attack, major bleeding, pericardial effusion, cardiac tamponade, pulmonary vein stenosis, pneumothorax, hemothorax, pneumonia, myocardial infarction, conversion to complete thoracotomy), compared with catheter ablation-treated patients (28.2% vs 7.8%; RR=3.30; 95% CI, 1.73 to 6.29; p<0.001).

A systematic review of 28 single-arm studies reporting on 1051 patients who received minimally invasive surgical treatment for AF was published in 2013 by La Meir et al. This review noted substantial differences in patient populations, surgical techniques, and definitions of outcome across studies. At 1 year, the range of success, as defined by freedom from AF and off all medications, was 51% to 86%. Outcomes for RFA appeared superior to those using ultrasound or microwave energy sources. The authors also noted that success was higher for the population of patients who had paroxysmal AF compared with those having persistent and permanent AF. The early complication rate ranged from 0% to 39%, and the most common major complications were conversion to sternotomy, bleeding, port access problems, cardiac events, cerebrovascular accidents, and pulmonary complications.

A similar systematic review of 23 case series using minimally invasive surgical treatment for AF was published in 2013 by Krul et al. Surgical techniques varied considerably among the included studies. At 1-year follow-up, the combined estimate for single-procedure success rates off all antiarrhythmic drugs was 69% (95% CI, 58% to 78%), and for patients still taking antiarrhythmic drugs, the rate was 79% (95% CI, 71% to 85%). Mortality occurred in 0.4% of patients, and complications were reported in 12.8% of patients.
Nonrandomized Comparative Studies

There are several observational studies that include a matched comparison group of patients who received alternate treatments. These case series with matched control groups offer stronger evidence for comparative efficacy than do single-arm case series.

Stulak et al compared outcomes among patients with AF who underwent an isolated cut-and-sew Cox maze procedure or catheter ablation. Ninety-seven Cox maze patients were matched on a 1:2 basis by age, sex, and AF type with 194 patients undergoing catheter ablation. At last follow-up, 82% of patients who underwent the Cox maze procedure were free of AF and off all medications, compared with 55% of patients who underwent catheter ablation (p<0.001). Freedom from AF at 5 years was estimated to be 87% following Cox maze compared with 28% following catheter ablation (p<0.001).

Wang et al performed a retrospective matched comparison of 83 patients who underwent minimally invasive surgical ablation with 83 patients who underwent catheter ablation. All patients had long-standing persistent AF, were treated between 2006 and 2009, and were followed from 1 to 3.6 years. At last follow-up, 74.7% of patients who underwent surgical ablation were free of AF compared with 59% of patients treated with catheter ablation (p<0.05). Freedom from AF off all medications was 61.4% in the surgical group compared with 44.6% in the catheter ablation group (p<0.05).

Other observational studies report outcomes for stand-alone AF treatment. Representative studies are described next. Lawrance et al conducted a retrospective cohort study comparing patients who underwent a Cox maze IV procedure either by right minithoracotomy (n=104) or sternotomy (n=252) at a single center from 2002 to 2014. Patients included in the series could also have undergone a concomitant mitral valve procedure, if indicated. Freedom from atrial tachyarrhythmias off antiarrhythmic drugs was not significantly different between groups. The overall complication rate was lower in the minithoracotomy group (6%) than in the sternotomy group (13%; p=0.044).

De Maat et al published results of a retrospective observational study of minimally invasive surgical treatment for AF in 86 patients with symptomatic, drug-refractory paroxysmal or permanent AF. Patients were treated at 3 centers, via bilateral video-assisted mini-thoracotomy from 2005 to 2007 (n=13 patients) and subsequently via a totally thoracoscopic approach from 2007 to 2011 (n=73 patients). Fifteen (17%) patients had previous transcatheter ablation performed. The percentage of patients free from atrial arrhythmias without the use of antiarrhythmic drugs was 71% at 12 months, 72% at 24 months, and 69% at 36 months. Half of the 24 treatment failures underwent an additional transcatheter ablation. Major periprocedural adverse events occurred in 8%, which included 3 requirements for sternotomy or mini-thoracotomy due to complications, 2 cases of late pericardial tamponade, 1 pericardial effusion requiring video-assisted thoracoscopic surgery, and 1 stroke.
Massimiano et al reported outcomes for 292 consecutive patients from a single institution who underwent minimally invasive mitral valve surgery (n=177), surgical ablation for AF (n=81), or both (n=34). Among the 115 patients who underwent AF ablation, the percentage of patients in sinus rhythm at 6, 12, and 24 months was 93%, 93%, and 88%, respectively; the percentage of patients in sinus rhythm and not taking class I and III antiarrhythmic medications at 6, 12, and 24 months was 85%, 85%, and 77%, respectively.

**Single-Arm Studies**
Numerous single-arm case series report high success rates following one of these surgical procedures; however, these case series offer limited evidence regarding the efficacy of the procedure itself. Most of the case series are limited by a lack of control group, generally only report short-term outcomes, and do not consistently report adverse events.

Several single-arm case series of minimally invasive epicardial ablation report on the population of patients who had failed catheter ablation. These case series offer evidence that is more clinically relevant than studies of unselected patients, because this population has more limited treatment options and is more likely to benefit from surgical procedures. However, these studies only offer very limited evidence about comparative efficacy with alternatives such as catheter ablation. Ad et al reported on 40 patients who had failed catheter ablation, with a mean of 2.3 prior ablations per patient. Maintenance of sinus rhythm at 6, 12, and 24 months was 76% (29/38), 89% (23/26), and 93% (13/14), respectively. Castella et al enrolled 34 patients who had failed a mean of 2.0 prior catheter ablations; 17 with paroxysmal AF, 12 with persistent AF, and 5 with long-standing persistent AF. At 1-year follow-up sinus rhythm was maintained in 82% of patients with paroxysmal AF, 60% with persistent AF, and 20% with long-standing persistent AF.

**Hybrid Procedures as Stand-Alone Treatment**
The evidence on hybrid ablation consists of a number of case series, 1 of which included a matched comparison group of patients undergoing percutaneous ablation. The study with a comparison group enrolled 35 patients who underwent a hybrid procedure and 28 patients who underwent a standard percutaneous procedure. Approxiately two-thirds (42/63) of the patients had undergone a previous percutaneous ablation procedure. At 1 year, there were more patients in the hybrid group who were free of AF, but this difference was not statistically significant (91.4% vs 82.1%, p=0.07). On subgroup analysis, the success rate was higher for the hybrid group in patients with long-standing persistent AF (81.8% vs 44.4%; p=0.001). Significantly more patients in the hybrid group were on warfarin at 1 year (29% vs 13.4%, p<0.001). There was no difference between groups on the frequency of adverse events.

Other single-arm case series have been published that include populations of 19 to 104 patients. These series consistently report high success rates in maintaining sinus rhythm at 1-year follow-up, ranging from 71% to 91%. Some of these series report individual adverse events,
but reporting on adverse events is variable and not systematic in these case series, resulting in an inability to accurately estimate rates of adverse events.

Je et al reported results of a systematic review of 37 studies designed to compare minimally invasive AF ablation procedures, including minimally invasive endocardial Cox maze procedure with cardiopulmonary bypass support, epicardial surgical ablation, and hybrid surgical ablation.\(^\text{54}\) The studies included were 2 studies on minimally invasive endocardial Cox maze procedure (total sample size, 145 patients), 26 on epicardial surgical ablation (1382 patients), and 9 on hybrid surgical ablation (350 patients). No statistical analyses or meta-analyses were possible due to the heterogeneity in methodology and data reporting. However, the authors do report that treatment success (sinus rhythm without antiarrhythmic medications) at 12 months was 87% for the endocardial Cox maze procedure, 72% for epicardial surgical ablation, and 71% for hybrid surgical ablation.

**Section Summary: Maze and Related Procedures as a Stand-Alone Treatment for AF**

The evidence on the role of maze and related procedures as stand-alone procedures consists of 2 RCTs (FAST study) and many case series, some with matched control groups. The RCTs report higher success at maintaining sinus rhythm at 1-year follow-up with thoracoscopic ablation, but also report higher adverse event rates than catheter ablation. This evidence does not clearly support the superiority of 1 technique over the other, but suggests that other factors such as type of AF, prior treatments, inability to take anticoagulation, and patient preference may influence the decision for type of procedure. Case series with matched control groups also report higher success rates in maintaining sinus rhythm compared with catheter ablation. The single-arm case series corroborate the high success rates following surgical treatment, but do not provide sufficient evidence to form conclusions on the comparative efficacy of surgical treatment versus other treatments.

Some case series and one of the RCTs include only patients who have failed previous catheter ablation. These studies also report high success rates following thoracoscopic ablation, suggesting that patients who fail catheter ablation may still benefit from thoracoscopic ablation. However, the RCT demonstrated higher adverse event rates compared with catheter ablation, and the risk-benefit ratio is not well-defined.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.
Summary of Evidence

For individuals who have symptomatic, drug-resistant atrial fibrillation (AF) or flutter who are undergoing cardiac surgery with bypass who received a Cox maze procedure or modified maze procedure, the evidence includes several randomized controlled trials (RCTs) and nonrandomized comparative studies, along with systematic reviews of these studies. Relevant outcomes are overall survival, medication use, and treatment-related morbidity. The most direct evidence comes from several small RCTs confirming the benefit of a modified maze procedure for patients with AF who are undergoing mitral valve surgery. These trials establish that the addition of a modified maze procedure results in a lower incidence of atrial arrhythmias following surgery, with minimal additional risks. Observational studies support the RCT findings. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have symptomatic, drug-resistant AF or flutter who are not undergoing cardiac surgery with bypass who receive minimally invasive, off-pump thoracoscopic maze procedures, the evidence includes RCTs and observational studies, some of which identify control groups. Relevant outcomes are overall survival, medication use, and treatment-related morbidity. The most direct evidence comes from 1 RCT comparing surgical AF ablation with video-assisted thoracoscopy with percutaneous catheter ablation, which reported higher success at maintaining sinus rhythm at 1 year of follow-up with thoracoscopic ablation, but also reported higher adverse event rates compared with catheter ablation. The case series generally report high success rates, and the few case series with matched comparison groups report higher success rates with surgical treatment compared with catheter ablation. However, this evidence does not permit definitive conclusions whether 1 approach is superior to the other. Factors such as...
previous treatment, the probability of maintaining sinus rhythm, the risk of complications, contraindications to anticoagulation, and patient preference may all affect the risk-benefit ratio for each procedure. At present, it is not possible to define a subgroup of patients who will benefit more from thoracoscopic (or other minimally invasive) surgical ablation compared with percutaneous ablation, so the risks and benefits of surgical ablation compared with catheter ablation are not well-defined. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have symptomatic, drug-resistant AF or flutter who are not undergoing cardiac surgery with bypass who receive hybrid thoracoscopic/endocardial ablation procedures, the evidence includes 1 nonrandomized comparative study and single-arm case series. Relevant outcomes are overall survival, medication use, and treatment-related morbidity. The studies suggest that hybrid ablation procedures are associated with high rates of freedom from AF, but direct comparisons with catheter ablation are lacking. Comparative studies are needed allow direct comparisons of the benefits and harms of hybrid ablation procedures compared with alternatives. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Clinical Input Received From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

**2013 Input**

In response to requests, input was received from 6 academic medical centers (4 reviewers) and 2 physician specialty societies for review of this policy in 2013. There was consensus agreement on the medically necessary statements. For subgroups of populations, such as those who have failed percutaneous catheter ablation, there was mixed support without a clear consensus. There was also mixed support for the use of hybrid ablation.

**2010 Input**

In response to requests, input was received from 3 academic medical centers (4 reviewers) and 1 physician specialty society for review of this policy in 2010. There was unanimous support for the policy statement regarding on-bypass maze procedure. There was mixed support for the policy statement regarding off-bypass (off-pump) maze procedure; some of those providing input indicated off-pump procedures may be useful in selected patients (such as those who cannot tolerate anticoagulation). Several of those providing input also commented on the limited long-term data for off-pump procedures.
Practice Guidelines and Position Statements

American Heart Association, American College of Cardiologists, and Heart Rhythm Society
In 2014, the American Heart Association, American College of Cardiologists, and Heart Rhythm Society (HRS) issued guidelines on the management of patients with atrial fibrillation (AF). The guideline provides the following recommendations related to the use of surgical ablation to maintain sinus rhythm:

Class IIa recommendations: “An AF surgical ablation procedure is reasonable for selected patients with AF undergoing cardiac surgery for other indications. (Level of Evidence: C)”

Class IIb recommendations: “A stand-alone AF surgical ablation procedure may be reasonable for selected patients with highly symptomatic AF not well managed with other approaches. (Level of Evidence: B)”

HRS, European Heart Rhythm Association, and European Cardiac Arrhythmia Society
A 2012 expert consensus statement was developed by the HRS, European Heart Rhythm Association, and European Cardiac Arrhythmia Society. The document was also endorsed by the American College of Cardiology, American Heart Association, Asia Pacific Heart Rhythm Society, and Society of Thoracic Surgeons.

The following recommendations were made regarding concomitant surgical ablation in patients undergoing cardiac surgery for other purposes and who have symptomatic AF:

“Paroxysmal: Surgical ablation is reasonable for patients undergoing surgery for other indications (Class IIa; Level C)

Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications (Class IIa, Level C)

Longstanding Persistent: Surgical ablation is reasonable for patients undergoing surgery for other indications (Class IIa; Level C)”

The following recommendations were made regarding stand-alone surgical ablation in patients with symptomatic AF refractory or intolerant to at least one class 1 or 3 antiarrhythmic medication:

“Paroxysmal: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach (Class IIb, Level C)

Paroxysmal: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation (Class IIb, Level C)

Persistent: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach (Class IIb, Level C)
Persistent: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation (Class IIb, Level C)

Longstanding Persistent: Stand alone surgical ablation may be considered for patients who have not failed catheter ablation but prefer a surgical approach (Class IIb, Level C)

Longstanding Persistent: Stand alone surgical ablation may be considered for patients who have failed one or more attempts at catheter ablation (Class IIb, Level C)"

The following recommendations were made regarding stand-alone surgical ablation in patients with symptomatic AF prior to initiation of antiarrhythmic drug therapy with a class 1 or 3 antiarrhythmic agent:

“Paroxysmal: Stand alone surgical ablation is not recommended (Class III, Level C)

Persistent: Stand alone surgical ablation is not recommended (Class III, Level C)

Longstanding Persistent: Stand alone surgical ablation is not recommended (Class III, Level C)”

**Canadian Cardiovascular Society**

The Canadian Cardiovascular Society (CVS) published guidelines in 2011 on surgical therapy for AF. These guidelines state that there is a high rate of freedom from AF following surgical treatment, 70% to 85% at 1 year, but that surgical ablation of AF has not been shown to alter mortality. The following recommendations were made:

“We recommend that a surgical AF ablation procedure be undertaken in association with mitral valve surgery in patients with AF when there is a strong desire to maintain sinus rhythm, the likelihood of success of the procedure is deemed to be high, and the additional risk is low (Strong Recommendation, Moderate-Quality Evidence).

We recommend that patients with asymptomatic lone AF, in whom AF is not expected to affect cardiac outcome, should not be considered for surgical therapy for AF (Strong Recommendation, Low-Quality Evidence).

In patients with AF who are undergoing aortic valve surgery or coronary artery bypass surgery, we suggest that a surgical AF ablation procedure be undertaken when there is a strong desire to maintain sinus rhythm, the success of the procedure is deemed to be high, and the additional risk low (Conditional Recommendation, Low-Quality Evidence)…. This recommendation recognizes that left atrial endocardial access is not routinely required for aortic or coronary surgery.

We recommend that oral anticoagulant therapy be continued following surgical AF ablation in patients with a CHADS2 score ≥2 (Strong Recommendation, Moderate-Quality Evidence).”
Although not a formal recommendation, this guideline stated that stand-alone surgical ablation should be considered after failure of prior attempts at catheter ablation and antiarrhythmic drugs.

CVS published a 2012 focused update to their comprehensive 2010 guidelines on AF. The 2012 focused guidelines discuss the use of anticoagulants in the treatment of AF.

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

There is no national coverage determination (NCD).

**V. DEFINITIONS**

**Atrial Flutter** is a cardiac arrhythmia marked by rapid (about three hundred beats per minute) regular atrial beating, and, usually, a regular ventricular response.

**Atrioventricular (AV) Node** is an area of specialized cardiac muscle that receives the cardiac impulse from the sinoatrial (SA) node and conducts it to the AV bundle and then to the Purkinje fibers and the walls of the ventricles. The AV node is located in the septal wall between the left and right atria.

**Atrium** is the upper chamber of each half of the heart. Atria is the plural of atrium.

**Myocardium** is the middle layer of the walls of the heart, composed of cardiac muscle.

**Sinoatrial (SA) Node** is a specialized group of cardiac muscle cells in the wall of the right atrium at the entrance to the superior vena cava. These cells depolarize spontaneously and rhythmically to initiate normal heartbeats.

**Supraventricular Tachycardia (SVT)** is any cardiac rhythm with a rate exceeding one hundred (100) beats per minute that originates above the branching part of the atrioventricular bundle, that is, in the sinus node, atria, or AV junction.

**Tachycardia** is an abnormally rapid heart rate, greater than one hundred (100) beats per minute.
VI. BENEFIT VARIATIONS

The existence of this medical policy does not mean that this service is a covered benefit under the member’s contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member’s individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member’s benefit information or contact Capital for benefit information.

VII. DISCLAIMER

Capital’s medical policies are developed to assist in administering a member’s benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member’s benefit information, the benefit information will govern. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

**Investigational; therefore not covered:**

| CPT Codes® | 33255 | 33258 | 33265 | 33266 |


**Covered when medically necessary:**

| CPT Codes® | 33254 | 33256 | 33257 | 33259 |


<table>
<thead>
<tr>
<th>ICD-10-CM Diagnosis Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I48.1</td>
<td>Persistent atrial fibrillation</td>
</tr>
</tbody>
</table>
Medical Policy

<table>
<thead>
<tr>
<th>Policy Title</th>
<th>Open and Thoracoscopic Approaches to Treat Atrial Fibrillation and Atrial Flutter. (Maze and Related Procedures)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy Number</td>
<td>MP-2.083</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10-CM Diagnosis Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I48.3</td>
<td>Typical atrial flutter</td>
</tr>
<tr>
<td>I48.4</td>
<td>Atypical atrial flutter</td>
</tr>
</tbody>
</table>

*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.

IX. References


<table>
<thead>
<tr>
<th>POLICY TITLE</th>
<th>OPEN AND THORACOSCOPIC APPROACHES TO TREAT ATRIAL FIBRILLATION AND ATRIAL FLUTTER. (MAZE AND RELATED PROCEDURES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>POLICY NUMBER</td>
<td>MP-2.083</td>
</tr>
</tbody>
</table>

and/or valvular heart disease plus atrial fibrillation: final results of the PRAGUE-12 randomized multicentre study. Eur Heart J. Nov 2012;33(21):2644-2652. PMID 22930458


<table>
<thead>
<tr>
<th>POLICY TITLE</th>
<th>OPEN AND THORACOSCOPIC APPROACHES TO TREAT ATRIAL FIBRILLATION AND ATRIAL FLUTTER. (MAZE AND RELATED PROCEDURES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>POLICY NUMBER</td>
<td>MP-2.083</td>
</tr>
</tbody>
</table>


X. Policy History

<table>
<thead>
<tr>
<th>MP-2.083</th>
<th>CAC 4/26/11 Adopted BCBSA. Information regarding open and thoracoscopic approaches to treat atrial fibrillation (Maze and related procedures) removed from MP-2.067 and created in this separate policy. Maze procedure was previously considered on a “case-by-case” basis. Now considered “medically necessary”. Minimally invasive, off-pump procedures remain “investigational”.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAC 4/24/12 Consensus. Background/Description revised per BCBSA. No change to policy statement.</td>
<td></td>
</tr>
<tr>
<td>7/23/13 Admin coding review complete</td>
<td></td>
</tr>
<tr>
<td>CAC 9/24/13 Consensus review. References updated but no changes to the policy statements. Rationale added. FEP variation revised to refer to the FEP medical policy manual.</td>
<td></td>
</tr>
<tr>
<td>CAC 9/30/14 Consensus review. References and rationale updated. No changes to the policy statements. Policy coded.</td>
<td></td>
</tr>
<tr>
<td>CAC 9/29/15 Minor review. The phrase “without concomitant cardiac surgery” was removed from the medical necessary policy statement for maze or modified maze during cardiopulmonary bypass. Added statement indicating Maze procedure completed without concurrent cardiac surgery is not medically necessary. Added “Atrial Flutter” to title. Coding reviewed and un-ranged.</td>
<td></td>
</tr>
<tr>
<td><strong>Policy Title</strong></td>
<td><strong>Open and Thoracoscopic Approaches to Treat Atrial Fibrillation and Atrial Flutter. (Maze and Related Procedures)</strong></td>
</tr>
<tr>
<td>------------------</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Policy Number</strong></td>
<td><strong>MP-2.083</strong></td>
</tr>
</tbody>
</table>

*Health care benefit programs issued or administered by Capital BlueCross and/or its subsidiaries, Capital Advantage Insurance Company®, Capital Advantage Assurance Company® and Keystone Health Plan® Central. Independent licensees of the BlueCross BlueShield Association. Communications issued by Capital BlueCross in its capacity as administrator of programs and provider relations for all companies.*