Ontario Health Technology Assessment Series 2006; Vol. 6, No. 8

Advanced Electrophysiologic Mapping Systems

An Evidence-Based Analysis

March 2006

Ontario

Medical Advisory Secretariat
Ministry of Health and Long-Term Care

Suggested Citation

This report should be cited as follows:

Medical Advisory Secretariat. Advanced electrophysiologic mapping sstems: an evidence-based analysis. *Ontario Heath Technology Assessment Series* 2006;6(8)

Permission Requests

All inquiries regarding permission to reproduce any content in the *Ontario Health Technology Assessment Series* should be directed to MASinfo@moh.gov.on.ca.

How to Obtain Issues in the Ontario Health Technology Assessment Series

All reports in the *Ontario Health Technology Assessment Series* are freely available in PDF format at the following URL: www.health.gov.on.ca/ohtas .

Print copies can be obtained by contacting MASinfo@moh.gov.on.ca**.**

Conflict of Interest Statement

All analyses in the Ontario Health Technology Assessment Series are impartial and subject to a systematic evidence-based assessment process. There are no competing interests or conflicts of interest to declare.

Peer Review

All Medical Advisory Secretariat analyses are subject to external expert peer review. Additionally, the public consultation process is also available to individuals wishing to comment on an analysis prior to finalization. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Contact Information

The Medical Advisory Secretariat
Ministry of Health and Long-Term Care
20 Dundas Street West, 10th floor
Toronto, Ontario
CANADA
M5G 2N6
Email: MASinfo@moh.gov.on.ca
Telephone: 416-314-1092

ISSN 1915-7398 (Online)
ISBN 1-4249-1486-8 (PDF)

About the Medical Advisory Secretariat

The Medical Advisory Secretariat is part of the Ontario Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

The Medical Advisory Secretariat conducts systematic reviews of scientific evidence and consultations with experts in the health care services community to produce the *Ontario Health Technology Assessment Series.*

About the Ontario Health Technology Assessment Series

To conduct its comprehensive analyses, the Medical Advisory Secretariat systematically reviews available scientific literature, collaborates with partners across relevant government branches, and consults with clinical and other external experts and manufacturers, and solicits any necessary advice to gather information. The Medical Advisory Secretariat makes every effort to ensure that all relevant research, nationally and internationally, is included in the systematic literature reviews conducted.

The information gathered is the foundation of the evidence to determine if a technology is effective and safe for use in a particular clinical population or setting. Information is collected to understand how a new technology fits within current practice and treatment alternatives. Details of the technology's diffusion into current practice and information from practicing medical experts and industry, adds important information to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist policy makers to make timely and relevant decisions to maximize patient outcomes.

If you are aware of any current additional evidence to inform an existing Evidence-Based Analysis, please contact the Medical Advisory Secretariat: MASInfo@moh.gov.on.ca. The public consultation process is also available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Table of Contents

Executive Summary

Objective

To assess the effectiveness, cost-effectiveness, and demand in Ontario for catheter ablation of complex arrhythmias guided by advanced nonfluoroscopy mapping systems. Particular attention was paid to ablation for atrial fibrillation (AF).

Clinical Need

Tachycardia

Tachycardia refers to a diverse group of arrhythmias characterized by heart rates that are greater than 100 beats per minute. It results from abnormal firing of electrical impulses from heart tissues or abnormal electrical pathways in the heart because of scars. Tachycardia may be asymptomatic, or it may adversely affect quality of life owing to symptoms such as palpitations, headaches, shortness of breath, weakness, dizziness, and syncope. Atrial fibrillation, the most common sustained arrhythmia, affects about 99,000 people in Ontario. It is associated with higher morbidity and mortality because of increased risk of stroke, embolism, and congestive heart failure. In atrial fibrillation, most of the abnormal arrhythmogenic foci are located inside the pulmonary veins, although the atrium may also be responsible for triggering or perpetuating atrial fibrillation. Ventricular tachycardia, often found in patients with ischemic heart disease and a history of myocardial infarction, is often life-threatening; it accounts for about 50% of sudden deaths.

Treatment of Tachycardia

The first line of treatment for tachycardia is antiarrhythmic drugs; for atrial fibrillation, anticoagulation drugs are also used to prevent stroke. For patients refractory to or unable to tolerate antiarrhythmic drugs, ablation of the arrhythmogenic heart tissues is the only option. Surgical ablation such as the Cox-Maze procedure is more invasive. Catheter ablation, involving the delivery of energy (most commonly radiofrequency) via a percutaneous catheter system guided by X-ray fluoroscopy, has been used in place of surgical ablation for many patients. However, this conventional approach in catheter ablation has not been found to be effective for the treatment of complex arrhythmias such as chronic atrial fibrillation or ventricular tachycardia. Advanced nonfluoroscopic mapping systems have been developed for guiding the ablation of these complex arrhythmias.

The Technology

Four nonfluoroscopic advanced mapping systems have been licensed by Health Canada:

CARTO EP mapping System (manufactured by Biosense Webster, CA) uses weak magnetic fields and a special mapping/ablation catheter with a magnetic sensor to locate the catheter and reconstruct a 3-dimensional geometry of the heart superimposed with colour-coded electric potential maps to guide ablation.

EnSite System (manufactured by Endocardial Solutions Inc., MN) includes a multi-electrode non-contact catheter that conducts simultaneous mapping. A processing unit uses the electrical data to computes more than 3,000 isopotential electrograms that are displayed on a reconstructed 3-dimensional geometry of the

heart chamber. The navigational system, EnSite NavX, can be used separately with most mapping catheters.

The LocaLisa Intracardiac System (manufactured by Medtronics Inc, MN) is a navigational system that uses an electrical field to locate the mapping catheter. It reconstructs the location of the electrodes on the mapping catheter in 3-dimensional virtual space, thereby enabling an ablation catheter to be directed to the electrode that identifies abnormal electric potential.

Polar Constellation Advanced Mapping Catheter System (manufactured by Boston Scientific, MA) is a multielectrode basket catheter with 64 electrodes on 8 splines. Once deployed, each electrode is automatically traced. The information enables a 3-dimensional model of the basket catheter to be computed. Colour-coded activation maps are reconstructed online and displayed on a monitor. By using this catheter, a precise electrical map of the atrium can be obtained in several heartbeats.

Review Strategy

A systematic search of Cochrane, MEDLINE and EMBASE was conducted to identify studies that compared ablation guided by any of the advanced systems to fluoroscopy-guided ablation of tachycardia. English-language studies with sample sizes greater than or equal to 20 that were published between 2000 and 2005 were included. Observational studies on safety of advanced mapping systems and fluoroscopy were also included. Outcomes of interest were acute success, defined as termination of arrhythmia immediately following ablation; long-term success, defined as being arrhythmia free at follow-up; total procedure time; fluoroscopy time; radiation dose; number of radiofrequency pulses; complications; cost; and the cost-effectiveness ratio.

Quality of the individual studies was assessed using established criteria. Quality of the overall evidence was determined by applying the GRADE evaluation system. (3) Qualitative synthesis of the data was performed. Quantitative analysis using Revman 4.2 was performed when appropriate.

Quality of the Studies

Thirty-four studies met the inclusion criteria. These comprised 18 studies on CARTO (4 randomized controlled trials [RCTs] and 14 non-RCTs), 3 RCTs on EnSite NavX, 4 studies on LocaLisa Navigational System (1 RCT and 3 non-RCTs), 2 studies on EnSite and CARTO, 1 on Polar Constellation basket catheter, and 7 studies on radiation safety.

The quality of the studies ranged from moderate to low. Most of the studies had small sample sizes with selection bias, and there was no blinding of patients or care providers in any of the studies. Duration of follow-up ranged from 6 weeks to 29 months, with most having at least 6 months of follow-up. There was heterogeneity with respect to the approach to ablation, definition of success, and drug management before and after the ablation procedure.

Summary of Findings

- Evidence is based on a small number of small RCTS and non-RCTS with methodological flaws.
- Advanced nonfluoroscopy mapping/navigation systems provided real time 3-dimensional images with integration of anatomic and electrical potential information that enable better visualization of areas of interest for ablation
- Advanced nonfluoroscopy mapping/navigation systems appear to be safe; they consistently shortened the fluoroscopy duration and radiation exposure.

- Evidence suggests that nonfluoroscopy mapping and navigation systems may be used as adjuncts to rather than replacements for fluoroscopy in guiding the ablation of complex arrhythmias.
- Most studies showed a nonsignificant trend toward lower overall failure rate for advanced mapping-guided ablation compared with fluoroscopy-guided mapping.
- Pooled analyses of small RCTs and non-RCTs that compared fluoroscopy- with nonfluoroscopy-guided ablation of atrial fibrillation and atrial flutter showed that advanced nonfluoroscopy mapping and navigational systems:

    - Yielded acute success rates of 69% to 100%, not significantly different from fluoroscopy ablation.
    - Had overall failure rates at 3 months to 19 months of 1% to 40% (median 25%).
    - Resulted in a 10% relative reduction in overall failure rate for advanced mapping guided-ablation compared to fluoroscopy guided ablation for the treatment of atrial fibrillation.
    - Yielded added benefit over fluoroscopy in guiding the ablation of complex arrhythmia. The advanced systems were shown to reduce the arrhythmia burden and the need for antiarrhythmic drugs in patients with complex arrhythmia who had failed fluoroscopy-guided ablation

- Based on predominantly observational studies, circumferential PV ablation guided by a nonfluoroscopy system was shown to do the following:
    - Result in freedom from atrial fibrillation (with or without antiarrhythmic drug) in 75% to 95% of patients (median 79%). This effect was maintained up to 28 months.
    - Result in freedom from atrial fibrillation without antiarrhythmic drugs in 47% to 95% of patients (median 63%).
    - Improve patient survival at 28 months after the procedure as compared with drug therapy.
    - Require special skills; patient outcomes are operator dependent, and there is a significant learning curve effect.

- Complication rates of pulmonary vein ablation guided by an advanced mapping/navigation system ranged from 0% to 10% with a median of 6% during a follow-up period of 6 months to 29 months.
- The complication rate of the study with the longest follow-up was 8%.
- The most common complications of advanced catheter-guided ablation were stroke, transient ischemic attack, cardiac tamponade, myocardial infarction, atrial flutter, congestive heart failure, and pulmonary vein stenosis. A small number of cases with fatal atrial-esophageal fistula had been reported and were attributed to the high radiofrequency energy used rather than to the advanced mapping systems.

Economic Analysis

An Ontario-based economic analysis suggests that the cumulative incremental upfront costs of catheter ablation of atrial fibrillation guided by advanced nonfluoroscopy mapping could be recouped in 4.7 years through cost avoidance arising from less need for antiarrhythmic drugs and fewer hospitalization for stroke and heart failure.

Expert Opinion

Expert consultants to the Medical Advisory Secretariat noted the following:

- Nonfluoroscopy mapping is not necessary for simple ablation procedures (e.g., typical flutter). However, it is essential in the ablation of complex arrhythmias including these:
    - Symptomatic, drug-refractory atrial fibrillation

- Arrhythmias in people who have had surgery for congenital heart disease (e.g., macro re-entrant tachycardia in people who have had surgery for congenital heart disease).
- Ventricular tachycardia due to myocardial infarction
- Atypical atrial flutter

- Advanced mapping systems represent an enabling technology in the ablation of complex arrhythmias. The ablation of these complex cases would not have been feasible or advisable with fluoroscopy-guided ablation and, therefore, comparative studies would not be feasible or ethical in such cases.

- Many of the studies included patients with relatively simple arrhythmias (e.g., typical atrial flutter and atrial ventricular nodal re-entrant tachycardia), for which the success rates using the fluoroscopy approach were extremely high and unlikely to be improved upon using nonfluoroscopic mapping.
- By age 50, almost 100% of people who have had surgery for congenital heart disease will develop arrhythmia.
- Some centres are under greater pressure because of expertise in complex ablation procedures for subsets of patients.
- The use of advanced mapping systems requires the support of additional electrophysiologic laboratory time and nursing time.

Conclusions

- For patients suffering from symptomatic, drug-refractory atrial fibrillation and are otherwise healthy, catheter ablation offers a treatment option that is less invasive than is open surgical ablation.
- Small RCTs that may have been limited by type 2 errors showed significant reductions in fluoroscopy exposure in nonfluoroscopy-guided ablation and a trend toward lower overall failure rate that did not reach statistical significance.
- Pooled analysis suggests that advanced mapping systems may reduce the overall failure rate in the ablation of atrial fibrillation.
- Observational studies suggest that ablation guided by complex mapping/navigation systems is a promising treatment for complex arrhythmias such as highly symptomatic, drug-refractory atrial fibrillation for which rate control is not an option
- In people with atrial fibrillation, ablation guided by advanced nonfluoroscopy mapping resulted in arrhythmia free rates of 80% or higher, reduced mortality, and better quality of life at experienced centres.
- Although generally safe, serious complications such as stroke, atrial-esophageal, and pulmonary vein stenosis had been reported following ablation procedures.
- Experts advised that advanced mapping systems are also required for catheter ablation of:
  - Hemodynamically unstable ventricular tachycardia from ischemic heart disease
  - Macro re-entrant atrial tachycardia after surgical correction of congenital heart disease
  - Atypical atrial flutter
- Catheter ablation of atrial fibrillation is still evolving, and it appears that different ablative techniques may be appropriate depending on the characteristics of the patient and the atrial fibrillation.
- Data from centres that perform electrophysiological mapping suggest that patients with drug-refractory atrial fibrillation may be the largest group with unmet need for advanced mapping-guided catheter ablation in Ontario.
- Nonfluoroscopy mapping-guided pulmonary vein ablation for the treatment of atrial fibrillation has a significant learning effect; therefore, it is advisable for the province to establish centres of excellence to ensure a critical volume, to gain efficiency and to minimize the need for antiarrhythmic drugs after ablation and the need for future repeat ablation procedures.

Abbreviations

AF	Atrial fibrillation
AFL	Atrial flutter
AT	Atrial tachycardia
AV	Atrioventricular
AVNRT	Atrial ventricular nodal re-entrant tachycardia
AVRT	Atrioventricular re-entrant tachycardia
ECG	Electrocardiogram
EPS	Electrophysiological study
GY	Gray
ICD	Implantable cardioverter defibrillator
KHZ	Kilo Herz
LA	Left atrium
LVOT	Left ventricular outflow tract tachycardia
MEA	Multi-electrode array
MI	Myocardial infarction
PAF	Paroxysmal atrial fibrillation
PSD	Peak skin dose
PV	Pulmonary vein
QALY	Quality adjusted life years
RA	Right atrium
RAD	Radiation dose
RF	Radiofrequency
RVOT	Right ventricular outflow tract tachycardia
RCT	Randomized controlled trial
REM	Roentgen Equivalent Man
SV	Sievert
SVT	Supraventricular tachycardia
VT	Ventricular tachycardia
WPW Syndrome	Wolff-Parkinson-White Syndrome

Objective

To assess the effectiveness, cost-effectiveness, and demand in Ontario for catheter ablation of complex arrhythmias guided by advanced nonfluoroscopy mapping systems. Particular attention was paid to ablation for atrial fibrillation (AF).

Background

Clinical Need and Target Population

Tachycardia

Tachycardia refers to a diverse group of arrhythmias characterized by heart rates that are greater than 100 beats per minute. Tachycardia is a normal response to exercise or other physiologic causes. However, in most cases, tachycardia is a manifestation of heart disease or problems with the intrinsic electrical system of the heart, because of abnormal triggers of electrical impulses and/or abnormal electrical pathways. A brief description of the main categories of tachycardia is provided below.

There are two main categories of tachycardia:

- Supraventricular tachycardia (SVT)
- Ventricular tachyarrhythmia

Supraventricular tachycardia

These arrhythmias originate above the ventricles in the atria, the atrial ventricular node or both. Supraventricular tachycardias include sinus tachycardia, pre-excitation syndrome, atrial tachycardia, AF, atrial flutter (AFL), atrioventricular (AV) nodal re-entrant tachycardia, and AV re-entrant tachycardia using an accessory bypass connection.

- Of the SVT, AF is the most common sustained tachycardia. It is characterized by uncoordinated and rapid atrial activation at a rate of 350 to greater than 500 beats per minute with an irregular rhythm that varies continuously. Instead of contracting and relaxing in a rhythmic fashion, the whole atrium quivers in a chaotic manner. The ventricles also contract rapidly, resulting in impaired diastolic filling of the ventricles and decreased cardiac output. The pooling of blood in the ventricles and formation of blood clots increase morbidity and mortality, particularly from embolism and stroke. (4) It was estimated that one-third of patients undergoing coronary artery bypass graft surgery will develop AF. Atrial fibrillation is usually classified as paroxysmal, persistent, or permanent (Table 1). (5)

Table 1: Classification of Types of Atrial Fibrillation*

Terminology	Clinical Features	Arrhythmic Pattern
Initial event (1st episode)	- Symptomatic - Asymptomatic, onset unknown	May or may nor recur
Paroxysmal	- Spontaneous termination < 7 days - And most often < 48 hours	Recurrent
Persistent	- Not self-terminating - Lasting > 7 days or prior cardioversion	Recurrent
Permanent	- Not terminated - Terminated but relapsed - No cardioversion attempt	Established

**Source: Levy S, Camm AJ, Saksena S, Aliot E, Breithardt G, Crijns HJ et al. International consensus on nomenclature and classification of atrial fibrillation: A collaborative project of the Working Group on Arrhythmias and the Working Group of Cardiac Pacing of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. J Cardiovasc Electrophysiol 2003; 14(4): 443-445*

A study (6) of the Canadian Registry of Atrial Fibrillation involving 757 patients with paroxysmal AF showed that the probability of progression from paroxysmal to chronic AF by 1 year was 8.6%. This increased steadily to 24.7% by 5 years. The study also found that AF may be associated with significant underlying heart disease, such as heart failure, valvular disease, and hypertension, but it can also occur in the absence of any demonstrable disease. Lone AF refers to AF in people younger than 60 year of age with no evidence of underlying cardiopulmonary disease and no other identifiable underlying cause.

Evidence suggests that rapid firing ectopic foci originating in the pulmonary veins (PVs) are dominant regions for triggering and maintaining AF. (7) Atrial fibrosis resulting from congestive heart failure, inflammation, and ischemia can cause heterogeneous electrical conduction in the atria, promoting this substrate for AF perpetuation. (8)

- Atrial flutter is a condition of cardiac arrhythmia in which the atrial contractions are rapid (250–350 beats per minute), but regular. The ventricles are unable to respond to each atrial impulse so that at least a partial atrioventricular block must develop. Common AFL results from a counter-clockwise macro re-entrant circuit in the cavo-tricuspid isthmus of the right atrium. (9) Presence of AF, elevated blood pressure, ventricular dysfunction, prior atrial fibrillation, or diabetes has been associated with increased risk of stroke in patients with atrial flutter. (10)

- There are 2 forms of junctional re-entrant tachycardia: The permanent form of junctional re-entrant tachycardia is one in which an accessory pathway lies very close to the AV node. The other form is automatic junctional tachycardia of the AV node. It may be caused by drug toxicity, or it may be idiopathic.

- Pre-excitation syndromes (e.g., Wolfe-Parkinson-White syndrome) are congenital disorders caused by the presence of one or more alternative accessory electrical pathways between the atrium and ventricles.

Ventricular Tachyarrhythmia

These tachycardias arise from within the ventricles. The most common cause of ventricular tachyarrhythmia is ischemic coronary artery disease. Both ischemia and the scarred tissue can contribute to ventricular tachyarrhythmia. Ventricular tachyarrhythmia associated with acute myocardial infarction (MI) can appear years after the infarct has healed. Ventricular fibrillation can originate from many different locations in the ventricle. (11) Ventricular tachyarrhythmia may be monomorphic with a regular

rate, rhythm, and shape; or it may be polymorphic, characterized by irregular rate and rhythm, and with varying shapes on the electrocardiogram (ECG). Ventricular tachyarrhythmia is a potentially life-threatening disorder that may precipitate hypotension, syncope, and sudden death. It accounts for about 50% of all cardiac-related deaths. (11)

Prevalence and Burden of Illness

Atrial fibrillation, the most common tachycardia, affects about 200,000 Canadians and more than 5% of the population aged over 65 years. (4) Based on the data from the Anticoagulation And Risk Factors in Atrial Fibrillation (ATRIA) study, (1) it was estimated that about 99,000 Ontarians have AF. Patients with AF have a fourfold to fivefold increase in stroke compared to people without AF. Moreover, 15% of strokes occur in people with AF. (4;12)

Atrial fibrillation can adversely impact the quality of life of affected patients, owing to palpitations, headaches, shortness of breath, weakness, dizziness and syncope that tend to accompany the disorder. Moreover, AF and ventricular tachyarrhythmia significantly increase the rates and likelihood of morbidity and mortality.

Between 1997 and 2000, the mean annual number of admissions to Ontario hospitals of people with a diagnosis of AF or AFL was 43,680. (Humphries 2004) This increased to 50,340 by 2004. Of these people, about 9,374 (19%) had AF/AFL as the most responsible diagnosis (Personal communication, September 6, 2005). The most common comorbid conditions were congestive heart failure (1 in 3), diabetes (1 in 5), and stroke (1 in 10). The in-hospital mortality rate was about 9%, and 2.9% of people discharged were readmitted to hospital with stroke within 1 year. Southern Ontario had one of the highest stroke readmission rates in Canada. (13) In 2004, 14% of the people admitted to hospital had stroke as the most responsible diagnosis. Furthermore, 25% of people admitted with heart failure as the most responsible diagnosis also had AF.

The rate of AF increases markedly with age; the rate of hospital admission with AF/AFL in Ontario in males increased from 524 per 100,000 people for those aged 20–49 years to 7,144 per 100,000 people for those aged 80 years or older. (13) The same trend was observed in females.

Existing Treatments

There are 3 main types of treatment. The preferred choice varies according to the type of tachycardia.

- Drug therapy remains the first-line treatment for many types of tachycardia. For AF, there are 2 approaches for medical management: one is to maintain sinus rhythm using antiarrhythmic drugs and cardioversion (rhythm control); the other is to control the ventricular rate using rate-control drugs such as β blockers, calcium channel blockers, or digoxin while allowing AF to persist. Anticoagulation is used in both strategies. One of the most common and serious adverse cardiac effects of antiarrhythmic drugs is proarrhythmia, a new or worsened rhythmic disturbance paradoxically precipitated by antiarrhythmic therapy. About 36% to 62% of patients do not respond to or cannot tolerate antiarrhythmic drugs.

  The multicentre AFFIRM study (14) showed no significant differences in the primary outcomes of death and stroke between the rhythm control strategy and the rate-control strategy in patients aged over 65 years with paroxysmal or persistent AF. It did find that rhythm control is necessary to reduce symptoms in symptomatic AF patients. The AFFIRM study also confirmed the importance of ongoing anticoagulation in patients with AF even after attainment of successful rhythm control.

- Ventricular tachycardia may be treated by the surgical insertion of an implantable cardioverter defibrillator (ICD) in the patient's chest. The ICD monitors and, if necessary, corrects an abnormally fast heartbeat by delivering a low energy shock.

- For symptomatic patients who are unresponsive or intolerant to antiarrhythmic medications, or who are interested in curative measures, an ablation of the diseased tissues is an alternative treatment for achieving sinus rhythm. The Cox-Maze procedure is a surgical ablation (cut and sew) procedure that creates multiple linear scars in the atrium to compartmentalize the atrial chamber into smaller regions. Though effective, the use of this procedure has been limited by the need for general anesthesia and open heart surgery, and significant bleeding complications. (15) Catheter ablation is the more frequently used form of ablation.(16)

Catheter Ablation

Catheter ablation is a percutaneous procedure that delivers energy via a thin flexible wire (catheter) to destroy abnormal heart tissues responsible for the arrhythmia. The ablation catheter, along with a mapping catheter and pacing catheter, is inserted into a vein near the groin and threaded into the heart. Energy delivered through the catheter heats up the cardiac tissue at the tip of the catheter to destroy tissues that are capable of triggering or sustaining arrhythmia. Radiofrequency energy is the most common type of energy used in catheter ablation. Other energy sources under investigation include microwave and ultrasound.

As noted, the most common sustained arrhythmia is AF. Several approaches for catheter ablation of AF have been studied.

Atrial ventricular node ablation: Catheter ablation of the atrioventricular node to produce complete heart block followed by permanent pacemaker implantation has been shown to be effective in alleviating symptoms of the tachycardias and palpitation. However, it commits the patient to complete heart block and pacemaker dependency for life. A meta-analysis of 5 small randomized controlled trials (RCTs) reported a 1-year rate of total mortality of 6.3% and sudden death rate of 2%. (17) The use of this procedure is reserved as a palliative approach for patients with highly symptomatic, permanent AF. (18)

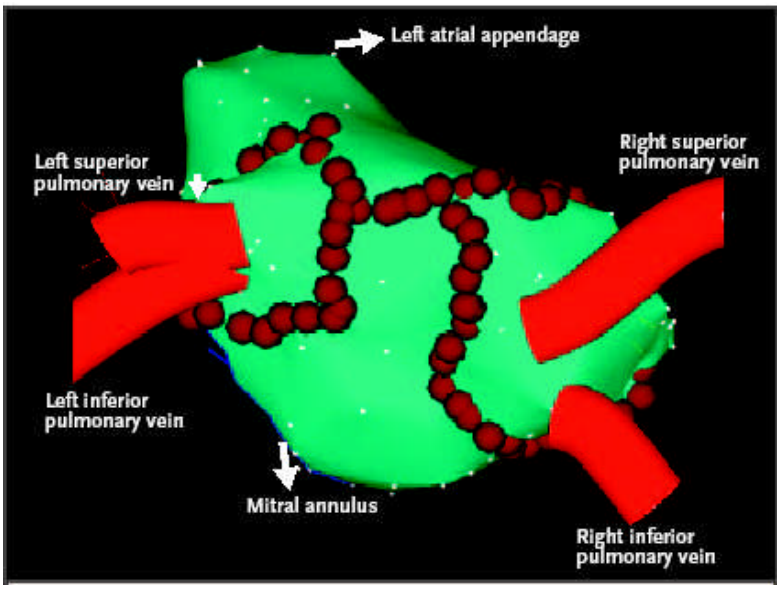
Focal AF ablation: This approach involves the identification and ablation of foci within PVs responsible for triggering AF. It necessitates the localization and ablation of earliest point of activation of ectopic beats, which may be difficult to achieve in patients with persistent AF. A potential adverse effect that limits the use of focal AF ablation is PV stenosis, reported to be as high as 42% in one study. (19)

Pulmonary vein (PV) isolation: In the last 5 years, catheter ablation of AF has focussed on removing or isolating electrical signals from within PVs, and on creating lesions in the atrium to reduce the tissue mass required to sustain fibrillation. Different approaches are used to ablate PVs. One of the most common is left atrial circumferential catheter ablation with continuous left atrial lesions that completely encircle the left- and right-sided PVs 1 to 5 cm from the PV ostia. This is an anatomic approach that does not require mapping of the earliest activation. Additional lines may be created in the posterior left atrium between the 2 encircling lesions and along the mitral isthmus from the inferior aspect of the left inferior PV to the mitral annulus (Figure 1). This anatomic approach necessitates the reconstruction of 3-D left ventricular maps and PV profiles through a transeptal route using an advanced nonfluoroscopic mapping system. (20) Another approach is segmental PV isolation. Instead of ablating completely around the ostium of the PV, this approach involves recording electrograms at the ostia of the PVs with a circular catheter, often in conjunction with a non-fluoroscopic navigation system, and ablating the ostial sites at which the earliest PV potentials are recorded to achieve PV isolation. (21) Transesophageal echocardiography is performed before catheter ablation of PVs to exclude the presence of thrombi in the

atrium. (Please see the Medical Advisory Secretariat's systematic review on catheter ablation for a detailed description of ablation procedures.)

For the treatment of typical (common) AFL, radiofrequency energy is usually applied to create a linear lesion in the cavo-tricuspid isthmus, a narrow strip of tissue between the tricuspid valve and the inferior vena cava. This creates a bidirectional conduction block in the tricuspid-inferior vena cava isthmus and eliminates the re-entrant circuit.

Figure 1: Circumferential Pulmonary Vein Ablation To Treat Atrial Fibrillation*



A 3-dimensional Electroanatomical depiction of the left atrium and the pulmonary veins shown in a right posterior oblique projection with cranial angulation. The two encircling lesions (red dots) were connected with an ablation line in the roof. Another ablation line was created along the mitral isthmus between the left inferior pulmonary vein and the lateral mitral annulus.

 Oral H, Pappone C, Chugh A, Good E, Bogun F, Pelosi F Jr, Bates ER, Lehmann MH, Vicedomini G, Augello G, Agricola E, Sala S, Santinelli V, Morady F. Circumferential pulmonary-vein ablation for chronic atrial fibrillation. New England Journal of Medicine. 2006 Mar 2;354(9):934-41.

Electrophysiologic Studies, Intracardiac Mapping, and Ablation

An electrophysiologic study (EPS) is the process of recording the electrical activity of the heart to verify that the rhythm abnormality is the cause of the patient's symptoms, and to characterize and locate the abnormal structure(s) responsible for the rhythm disturbances. The abnormal structure(s) can be removed by surgical resection or catheter ablation.

Electrophysiological study is usually performed on patients with moderate to severe left ventricular dysfunction, when other diagnostic methods for treating cardiac arrhythmia fail, or when ablation or ICD implantation is being considered. Electrophysiological study is generally performed on an outpatient basis or requires a brief (1-day) hospitalization.

Conventional Fluoroscopy-Guided Catheter Mapping

Conventionally, mapping in EPS is achieved by sequentially positioning catheters with a limited number

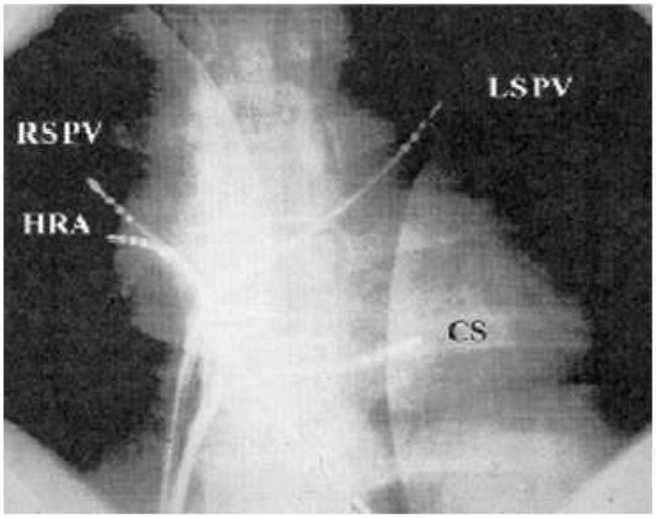
of electrodes at multiple endocardial sites guided by x-ray fluoroscopy during an induced arrhythmic episode. The fluoroscopy shows the location of the catheters (Figure 2). Ablation guided by conventional fluoroscopic mapping is successful in terminating stable arrhythmias with predictable anatomic locations such as idiopathic VT, atrial ventricular nodal re-entrant tachycardia, accessory pathways, and atrioventricular junction ablation for rate control in AF. For these types of arrhythmias, success rates have approached 90%. (22)

Conventional fluoroscopy has been shown to be less successful in mapping complex arrhythmias such as AF and most VTs that are devoid of fluoroscopic landmarks and lack characteristic electrogram patterns. For these types of arrhythmias, the use of fluoroscopy may be problematic because of the following:

- The inability to associate intracardiac electrograms accurately with their precise anatomical locations within the heart.
- The inability to visualize the endocardial surface using fluoroscopy, and target sites can only be approximated based on their relationship with nearby structures.
- The 2-dimensional nature of fluoroscopic images makes navigation inexact and time consuming.
- The inability to return the ablation catheter accurately to a previously mapped site.
- The absence of a global view of chamber activation.
- Prolonged exposure of the patient and medical team to ionizing radiation. (23)

Advanced mapping systems are developed to increase the precision of delivery of ablation to the complex substrate.

Figure 2: Fluoroscopy Image of Catheter Positions During Radiofrequency Ablation of Focal Foci in Pulmonary Veins*



* RSPV indicates right superior pulmonary vein; LSPV, left superior pulmonary vein.

Reproduced from Basu Ray I. Atrial fibrillation: present treatment protocols by drugs and interventions. Journal, Indian Academy of Clinical Medicine 4(3): 213-227. 2003.

New Technology Being Reviewed

Nonfluoroscopic computer-assisted advanced catheter mapping systems have been developed for the detection and ablation of complex arrhythmias. These are described after the section on regulatory status.

Regulatory Status

Advanced catheter mapping systems licensed by Health Canada are summarized in Table 2.

Table 2: Advanced Nonfluoroscopic Mapping Systems Licensed by Health Canada

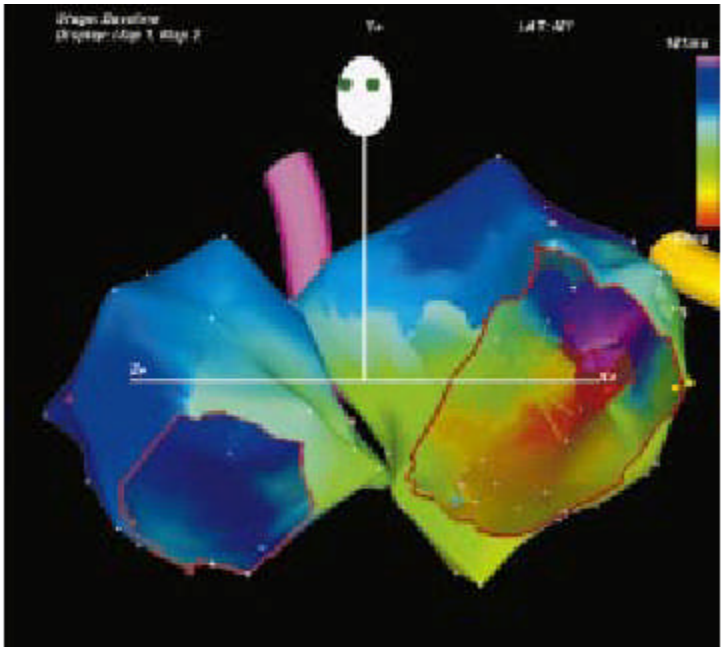
Name	Manufacturer and Location	Licence Number	Medical Device Class
CARTO EP Mapping Unit	Biosense Webster	9959	4
CARTO XP Navigation system	Johnson & Johnson, CA	60688	
EnSite FC1000 Multielectrode Diagnostic Catheter	Endocardial Solutions Inc, MN	12012	4
EnSite 3000 EP Workstation		12012	4
Polar Constellation Advanced Mapping Catheters & Accessories	Boston Scientific, MA	9808	4
LocaLisa Intracardiac Navigation system	Medtronics Inc, MN	37435	3

Lasso, a circular advanced catheter, is often used under fluoroscopy guidance or in conjunction with a nonfluoroscopy navigational system in PV ablation.

Electroanatomic Mapping System

The CARTO EP System (Biosense Webster) is a nonfluoroscopic system that combines anatomic and different types of electrophysiologic information. It consists of a miniature passive magnetic field sensor incorporated into a standard electrophysiological catheter (the location catheter), a magnetic field emitter (location pad) with 3 coils, and a processing unit. The location pad is placed under the catheterization table and generates 3 ultralow magnetic fields.

The magnetic fields are used to acquire anatomic information and location of the catheters to reconstruct the 3-dimensional geometry of the cardiac chamber(s) of interest. (24) Conventional bipolar and unipolar electrograms are recorded from the CARTO EP catheter. The catheter location and electrograms recorded continuously are reconstructed in real time and presented as a 3-dimensional geometrical map, colour-coded with activation times (Figure 3). Dynamic propagation maps can be displayed as movies of sequential activation. Moreover, the collected data can be displayed as voltage maps that can help define scar areas and electrically diseased tissues. Anatomical landmarks and regions of interest can be tagged. (25) One advantage of the CARTO EP system is that it can acquire voltage maps during sinus rhythm, thereby enabling scars to be identified. Pace mapping or entrainment mapping can then provide details of the key sites where arrhythmias originate. (24)



Reproduced with permission from the BMJ Publishing Group Limited; Friedman PA. Novel mapping techniques for cardiac electrophysiology. Heart 2002; 87(6):575-582. Figure 2., page 580

Figure 3: Three Dimensional Activation Maps Generated by CARTO*
Activation map from a patient with a figure of eight re-entrant tachycardia. The two atria are shown in the left anterior oblique view, with tricuspid valve and mitral valve cut out. The colour at each anatomic point shows local activation time relative to the reference catheter (scale at top right)

Non-Contact Endocardial Mapping System

The EnSite non-contact mapping system (EnSite 3000, Endocardial Solutions, Inc., St. Paul, Minnesota, United States) consists of an EnSite array catheter, a custom-designed amplifier system, and a computer workstation.

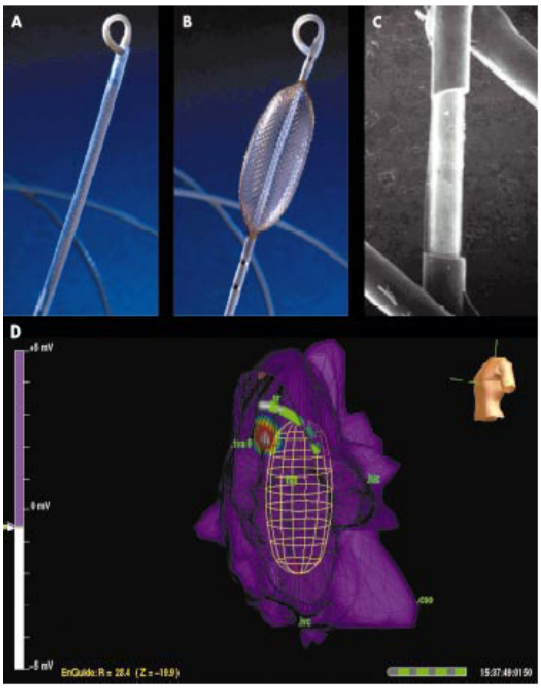
The EnSite catheter is a number 9 French double lumen polyurethane catheter with 64 unipolar electrodes mounted on the surface of an inflatable balloon (multielectrode array [MEA]) filled with a mixture of saline and contrast medium. The EnSite catheter and a roving catheter are inserted intravascularly over a guide wire into a selected chamber of the heart. When positioned, the wire braid of the MEA is expanded and the balloon under the array is inflated so that each electrode of the array is separated by 4 to 7 mm. (22)

The MEA does not require direct contact with the endocardium. Once deployed, the array senses electrical activities generated from the endocardial wall while floating in the cavity (Figure 4, A–C). Electrical potentials acquired simultaneously at the 64 electrodes of the MEA are recorded on the workstation and used to compute more than 3,000 virtual electrograms. These electrograms and colour-coded isopotential maps are displayed over a 3-dimensional geometric model of the endocardial chamber (Figure 4D).

To reconstruct the 3-dimensional endocardial chamber, the locator system of EnSite locates the conventional roving catheter in space with respect to the MEA and thus with respect to the cardiac chamber being mapped. The tip of this catheter emits a low-amplitude current (5.68 kHz) that enables its 3-dimensional localization. The roving catheter is steered over the endocardial contour via its tip. From the sampled location points, the most distant values are taken into account to determine a contour model

that is used to reconstruct the smoothed endocardial geometry. Over the constructed geometry, specific landmarks like the ostium of the coronary sinus, the tricuspid annulus, the anterior and posterior vena cava, and the His bundle position are annotated. (26)

Figure 4: Non-Contact Catheter



Reproduced with permission from the BMJ Publishing Group Limited; Friedman PA. Novel mapping techniques for cardiac electrophysiology. Heart 2002; 87(6):575-582. Figure 2., page 580

*A: Before deployment; B: Deployed; C: One of the 64 electrodes; D: Right atrial map of a patient with ectopic tachycardia.

EnSite Navigational System – EnSite NavX

The EnSite NavX (Endocardial Solutions Inc., St. Paul, MN) navigational system uses 3 pairs of nominally orthogonal patches on the patient to create an electric field that allows exact localization of the catheter electrodes within the cardiac chamber. The system allows the real-time visualization of the positions of up to 64 electrodes on standard EP catheters and can be used with any type of mapping catheters. Interrupted fluoroscopy is still required when an obstacle to catheter advancement is encountered. (27)

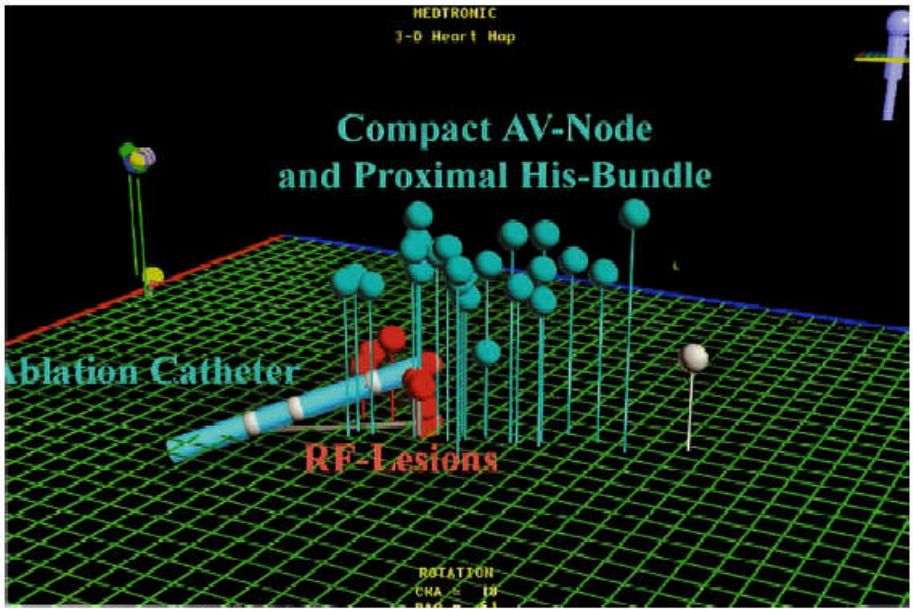
The system also enables the creation of a 3-dimensional geometry of the chamber of interest and automatically acquires points from a nominated electrode at a rate of 96 points per second. After creation of the 3-dimensional geometry, anatomic landmarks such as the PVs or mitral annulus and sites critical for the arrhythmia are identified and tagged for guidance. The ablation catheter is navigated to these critical sites for RF energy delivery.

LocaLisa Navigational System

The LocaLisa Navigational System (Medtronic EP Systems, Minneapolis, MN) uses weak electrical fields to locate mapping/ablation catheters within a cardiac chamber. LocaLisa has been used with a circular mapping catheter in the electrophysiologic approach to PV ablation. The position of the catheters relative

to a reference electrode positioned in the heart is determined by measuring the voltages on the electrodes of the mapping catheter resulting from high-frequency electric fields generated by electrodes on the patient's chest. After positioning the mapping catheter at the desired location, the LocaLisa system is used to store the position of the catheters and reconstructs the geometry of up to 10 electrodes on multiple catheters in 3-dimensional virtual space. Labelled landmarks are displayed by colour-coded dots in a Cartesian coordinate system and used to guide ablation (Figure 5). LocaLisa does not reconstruct a 3-dimensional geometry of the cardiac chamber. (26)

Figure 5: LocaLisa-Guided Right Atrial Flutter Ablation



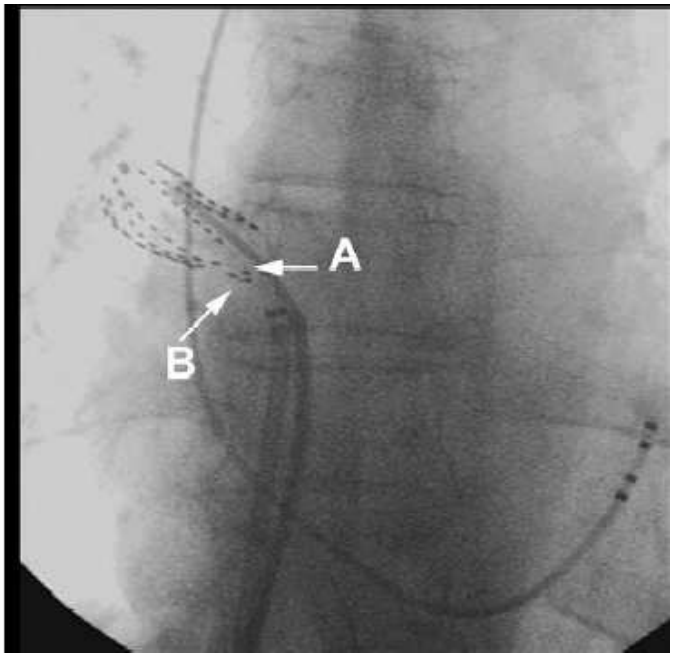
Reproduced from Kammeraad J, ten Cate FU, Simmers T, Emmel M, Wittkampf FHM, Sreeram N. Radiofrequency catheter ablation of atrioventricular nodal reentrant tachycardia in children aided by the LocaLisa mapping system. Europace 2004; 6(3):209-214, by permission of the European Society of Cardiology and the authors.

Localisa map in right anterior oblique projection demonstrating the location of the compact AV Node and proximal HIS bundle. Blue dots: sites @ which HIS bundle electrograms were recorded. Red dots: RF lesion. Yellow & green dots: coronary sinus. The ablation catheter with red electrode tip was also depicted.

Multipolar Basket Catheter

The basket catheter (Constellation, Boston Scientific) functions through direct contact with the tissue inside the heart. This mapping catheter is composed of 64 electrodes mounted on 8 flexible, self-expanding nitinol splines that encircle the cardiac contour (Figure 6). (28) The catheter is inserted percutaneously via the femoral vein and positioned in a cardiac chamber. Once deployed, each spline and electrode is automatically traced. The information enables a 3-dimensional model of the basket catheter to be computed. Colour-coded activation maps are reconstructed on-line and displayed on a monitor. By using this catheter, a precise electrical map of the atrium can be obtained in several beats of the heart.

Figure 6: Multielectrode Basket Catheter



Reproduced from *De Ponti R, Tritto M, Lanzotti ME, Spadacini G, Marazzi R, Moretti P et al. Computerized high-density mapping of the pulmonary veins: new insights into their electrical activation in patients with atrial fibrillation Europace 2004; 6(2):97-108, by permission of the European Society of Cardiology and the authors.*

Fluoroscopic image of the basket catheter positioned in a right superior pulmonary vein in anteroposterior view. The basket catheter & angiographic catheter are both positioned in the vein through transseptal catheterization. The arrow indicate the radiopaque markers (electrodes) which identify spline "A" and "B".

A comparison of the characteristics of the mapping systems is shown in Table 3.

Table 3: Comparison of Mapping Systems

Characteristics	Fluoroscopy	CARTO	EnSite NavX	LocaLisa	Constellation
Location of ablation catheter by	X-ray fluoroscopy	Magnetic field	Electrical field	Electrical field	Electrical field
Reconstructs 3-D geometry of heart cavity	No	Yes	Yes	No	No
Has computer-assisted navigation	No	Yes	Yes	Yes	Yes
Integrates electrical & anatomical information	No	Yes	Yes	Yes	Yes
Can be used with any mapping catheters	Yes	No	Yes	Yes	No
Needs X-ray fluoroscopy for catheter placement	Yes	Yes	Yes	Yes	Yes
Needs X-ray fluoroscopy for mapping & ablation	Yes	No	No	No	No
Allows activation mapping	No	Yes	No		Yes

Literature Review on Effectiveness

Objective

The objective of this review was to determine the effectiveness and cost-effectiveness of advanced nonfluoroscopic mapping/navigational systems compared with X-ray fluoroscopy in guiding radiofrequency catheter ablation of complex arrhythmias.

Questions Asked

- How effective is advanced nonfluoroscopic mapping/navigational-guided radiofrequency ablation in terminating arrhythmia in the short term and long term compared with fluoroscopy-guided ablation?
- What is the impact of nonfluoroscopic mapping/navigational systems on the total procedure time and fluoroscopy time of the ablation compared to fluoroscopy-guided mapping?
- How does advanced nonfluoroscopy-guided ablation compare with fluoroscopy-guided ablation on procedure-related complication rates and types of complications?
- Which types of arrhythmias require an advanced nonfluoroscopic mapping/navigational system?

Methods

During the first stage of this review, the Medical Advisory Secretariat scanned the leading international health technology assessment organizations for previous assessments of the technology. Scanned were the Canadian Coordinating Office of Health Technology (CCOHTA), International Network of Agencies for Health Technology Assessment (INAHTA), National Institutes of Clinical Excellence (NICE), and Database of Abstracts of Reviews of Effectiveness (DARE). The Cochrane Library Database and the Cochrane Incontinence Group Database were also scanned.

The peer-reviewed literature was searched from 1996 to the second week of August 2005. Searched were the following databases: MEDLINE, EMBASE, PREMEDLINE / MEDLINE In-Process & Other Non-Indexed Citations and the Cochrane Library Database. Case studies, review articles, editorials, and letters were not included. The search was limited to studies on humans.

Key words for the initial search included electrophysiologic mapping, ablation, arrhythmia, AFL, AF, noncontact, electroanatomic, CARTO, LocaLisa, EnSite, and Constellation. The detailed search strategy is shown in Appendix 1.

A separate search was conducted for reports on radiation safety relating to catheter ablation.

Other Web-based information, such as clinical position papers and guidelines for clinical management of electrophysiology studies, was taken from clinical societies or patient care Web sites.

Inclusion Criteria

This review included English-language journal articles that reported primary data on the effectiveness or cost-effectiveness of nonfluoroscopic mapping systems in the ablation of drug-refractory tachycardia, obtained in a clinical setting, or analyses of primary data maintained in registers or institutional databases. Studies had to meet the following criteria:

- The design and method are clearly described.
- Not superseded by a publication with the same purpose, by the same group, or a later publication that included the data from the same study (unless the article addressed different outcomes)
- English-language articles (published February 1, 2000 to August, 2005)
- Belong to one of the following 3 classifications:

Systematic reviews, prospective randomized controlled trials (RCTs) or non-RCTs with greater than or equal to 20 subjects that meet the following requirements:

- Population: people with drug-refractory AF, AFL, ventricular tachycardia, and macrore-entrant incisional tachycardia
- Intervention: ablation guided by a nonfluoroscopic mapping/navigational system
- Comparators: ablation guided by X-ray fluoroscopy
- Outcome measures: acute success rates, freedom from arrhythmia (or overall treatment failure), total procedure time, total fluoroscopy time, radiation dose, number of RF pulses, procedure- related complications including stroke

Observational studies of circumferential PV ablation that meet the following description:

- Population: people with drug-refractory AF (sample size $\geq$ 30)
- Intervention: circumferential PV catheter ablation guided by an advanced mapping/navigational system
- Outcome measures: acute success rates, freedom from arrhythmia (or overall treatment failure), total length of procedure time, total length of fluoroscopy time, radiation dose, number of RF pulses, and/or procedure- related complications

Studies pertaining to risks of radiation in catheter ablation of arrhythmias

Exclusion Criteria

- Non-systematic reviews, technical papers, editorials, and letters
- Studies that focus on comparison of different ablation techniques rather than on comparison of mapping techniques
- Foreign-language reports
- Studies with sample size less than stipulated

Results of Literature Review

No systematic reviews on nonfluoroscopic mapping were found. The search yielded 697 citations. One researcher and a medical information specialist reviewed the titles and abstracts and selected reports based on the inclusion and exclusion criteria. Thirty-four studies met the criteria, including 7 reports on the risk of radiation exposure related to catheter ablation (Table 4).

Reasons for exclusion were as follows:

- Nonsystematic reviews, editorials, technical papers, and letters
- Foreign-language reports
- Case series and case reports
- Insufficient sample size
- Technical papers

Although no published systematic reviews were found in the search, the hospital that applies to OHTAC for the review submitted a November 2004 systematic review of research evidence on CARTO, conducted by Covance on behalf of Biosense Webster (manufacturer of CARTO).

Table 4: Number of Studies Included in the MAS Review by Design*

Comparison	Type of Arrhythmia	Randomized Controlled Trials, No.	Non-Randomized Controlled Trials, No.	Case Series, No.
CARTO vs. fluoroscopy	Atrial fibrillation	0	2	
CARTO vs. fluoroscopy	Atrial flutter	3	3	
EnSite NavX vs. fluoroscopy	Atrial fibrillation	2		
EnSite NavX vs. fluoroscopy	Atrial flutter	1		
LocaLisa vs. fluoroscopy	Atrial fibrillation		2	
LocaLisa vs. fluoroscopy	Atrial flutter	1		
CARTO & EnSite in failed fluoroscopy	Mixed		1	
CARTO vs. EnSite	Atrial fibrillation	1		
Basket catheter vs. fluoroscopy	Atrial fibrillation	1		
Circumferential pulmonary vein ablation	Atrial fibrillation	1	2	7
Radiation exposure				7
Total		10	10	14

*Randomized controlled trials have level 2 evidence, nonrandomized controlled trials, level 3; case series, level 4b.

Quality Assessment and Data Extraction

One person assessed the quality of the individual reports using established criteria (Appendices 2–8). The same person extracted data using a data template. The studies were assigned a level of evidence according to the Medical Advisory Secretariat classification (Table 5).

Table 5: Level of Evidence of Included Studies*

Study Design	Level of Evidence	No. of Eligible Studies
Large RCTs, systematic reviews of RCTs	1	
Large RCT unpublished but reported to an international scientific meeting	1(g)	
Small RCT	2	10
Small RCT unpublished but reported to an international cientific meeting	2(g)	
Non-RCT with contemporaneous controls	3a	9
Non-RCT with historical controls	3b	1
Non-RCT presented at international conference	3(g)	
Surveillance (database or register)	4a	
Case series (multisite)	4b	14
Case series (single site)	4c	
Retrospective review, modelling	4d	
Case series presented at international conference	4(g)	
Total		34

*RCT represents randomized controlled trial; g, grey literature.

Data Analysis and Synthesis

Because ablation or AF involves PV ablation, which is quite different from the ablation procedure for AFL, studies on the 2 types of arrhythmia were analyzed separately and together.

The acute success rate, overall failure rate, mean length of total procedure time, and mean length of total fluoroscopy time were analyzed to provide a range and a median. Revman 4.2 (The Cochrane meta-analysis software) was used to test for heterogeneity of acute success rates, overall failure rates (relative difference), mean procedure time, and mean radiation time (difference). A point estimate with the 95% confidence interval was generated when appropriate using a random effects model. A descriptive synthesis was provided when statistical analysis was not appropriate.

Summary of Overall Quality of Evidence

The GRADE system (3) was used to summarize the overall quality of evidence supporting the findings relating to each key outcome measure. This system rates the overall quality based on the assessment of 4 key elements:

- Study design - (type of evidence), broadly categorized as RCTs and observational studies.
- Study quality - refers to whether there are limitations relating to the methods and execution that may result in biases. The assessment is based on appropriate criteria such as adequacy of allocation concealment, blinding, and follow-up.
- Consistency - refers to the similarity of estimates of effect across studies. Important unexplained inconsistency in the results decreases the confidence in the estimate of effects for the outcome.
- Directness - refers to the extent to which the people, interventions, and outcome measures are similar to those of interest.

Quality grades were assigned as follows:

Type of evidence

- RCT = high
- Observational study = low
- Any other evidence = very low

Decrease grade if:

- Serious (-1, reduce GRADE level by 1 so a high grading will become moderate) or very serious (-2, reduce GRADE level by 2 so a high grading will become low) limitation to study quality
- Important inconsistency (-1)
- Some (-1) or major (-2) uncertainty about directness
- Imprecise or sparse data (-1)
- High probability of reporting bias (-1)

Increase grade if:

- Strong evidence of association-significant relative risk of greater than 2 (< 0.5) based on consistent evidence from 2 or more observation studies, with no plausible confounders (+1, increase GRADE level by 1, so a moderate grade will become high. However a high grade will remain high)
- Very strong evidence of association-significant relative risk of greater than 5 (< 0.2) based on direct evidence with no major threats to validity (+2)
- Evidence of a dose response gradient (+1)
- All plausible confounders would have reduced the effect (+1).

High: ⊕⊕⊕⊕ Further research is very unlikely to change our confidence in the estimate of effect.

Moderate: ⊕⊕⊕◯ Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low: ⊕⊕◯◯ Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low: ⊕◯◯◯ Any estimate of effect is very uncertain.

Summary of Findings on Effectiveness

CARTO Electroanatomic Mapping System Versus Fluoroscopy: Atrial Fibrillation

Three comparative studies on the use of CARTO versus fluoroscopy in the ablation of AF were found. One RCT (29) was excluded because the focus of the study was to compare 2 different ablation procedures (segmental PV ostial ablation and atrial ablation); therefore, differences in outcomes could not be attributed solely to the use of CARTO. Sporton et al., (30) who conducted a comparison of CARTO-guided and fluoroscopy-guided ablation of a nonselected population with refractory arrhythmia stated that randomization for patients with AF for PV isolation was terminated after 8 patients because of a perceived advantage of CARTO imaging for pulmonary isolation.

The 2 studies that were included in the review were non-RCTS on patients with symptomatic, drug-refractory AF, with sample sizes of 35 and 196, respectively. Characteristics of the studies are summarized in Table 6. One of the studies had consecutive enrolment and indicated that both arms were similar at baseline. End points and success were clearly defined in both studies, and there was no loss to follow-up. However, there was no blinding in either study. Detailed quality assessment of the studies is shown in Appendix 2. Outcomes of the 2 studies are summarized in Table 7.

Table 6: Characteristics of Comparative Studies on Pulmonary Vein Ablation for the Treatment of Atrial Fibrillation

	Tse et al., 2002 (31)		**Ernst et al 2003 (32)**	
Type of arrhythmia	Paroxysmal atrial fibrillation		Atrial fibrillation: pulmonary vein ectopy	
Study design	Non-randomized Comparative		Non-randomized Comparative	
Quality	Moderate to low		Low	
Antiarrhythmic drugs	D/C 5 half-lives before procedure			
Mapping technique	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**
Sample size	10	25	39	157
Mean (SD) age, years	46 (9)	49 (7)	58.5 (8)	56 (10.1)
Males, %	80	73	85	77
Chronic AF: intermittent AF			8:31	32:125
Duration of AF**:** Mean (SD)	25 (14) months	30 (12) months	9.8 (6.7) years	7.9 (6.6) years
Number of failed antiarrhythmic drugs mean (SD)	3 (2)	4 (2)	n/r	n/r
Underlying heart disease, mean %	2	4	3.8 (1.4)	3.8 (1.5)
Mean (SD) LVEF, %	66 (8)	64 (7)	n/r	n/r

n/r not reported

Table 7: Outcomes of Comparative Studies on Pulmonary Vein Ablation for the Treatment of Atrial Fibrillation*

	Tse et al 2002 (31)		**Ernst et al 2003** (32)	
Type of arrhythmia	Paroxysmal atrial fibrillation		Atrial fibrillation: pulmonary vein ectopy	
Study design	Not randomized Comparative		Non-randomized Comparative	
Definition of successful ablation	Acute: elimination of the local pulmonary vein potential and ectopy Long-term: no recurrence in absence of antiarrhythmic drugs		Elimination of spike potentials on pulmonary vein angiography in pulmonary veins	
Mean (SD) follow-up, months	12 (9)		530 (228) days	
Mapping technique	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**
Sample size, n	10	25	39	157
Acute success rate (%)	90	84 *P* = NS	Achieved in both groups without significant difference	Achieved in both groups without significant difference
Cross over, %	0	0	0	0
Rate of recurrence during follow-up, % (with and without AAD) - overall failure	30 (3/10)	32 (8/25) *P* = NS	31 (12/39)	40 (63/157)
Mean (SD) total procedure time, minutes	199 (52)	221 (82) *P* > .05	8 (1.7) hrs	5.0 (1.6) hrs *P* < .005
Mean (SD) total fluoroscopy time, minutes	25 (6)	52 (12) *P* = .01	28.3 (8.6)	43.6 (27.6) *P* < .005
Mean (SD) number of radiofrequency pulses	5 (3)	12 (9) *P* = .02	27.1 (13)	22.6 (10.9) *P* = .028
Complications	0	1/25 (4%) developed 60% of narrowing at the PV ostium	- 18 acute PV stenosis, 2 were > 70% stenosed During follow-up: - 1 stroke and 2 transient ischemic attacks - 1/39 total PV occlusion in CARTO group - 1/157 severe PV stenosis in fluoroscopy group	
Comments	No significant differences in acute or long-term success. Procedure time, fluoroscopy time and number of RF lower with CARTO		Repeat procedures CARTO: 8% Fluoroscopy: 22% 3-D reconstruction to ID PV ostium is still time-consuming.	

* AAD indicates antiarrhythmic drug; PV, pulmonary vein.

Both studies compared CARTO-guided and fluoroscopy-guided radiofrequency ablation of PV foci. Success in both studies was defined as the elimination of high-frequency potentials in the PVs. Tse et al. (31) enrolled consecutive patients; the first 25 patients' procedures were guided by fluoroscopy, and the last 10 patients' procedures were guided by CARTO. The study by Ernst et al. (32) did not provide information on how patients were enrolled and allocated to the 2 groups. Because of the lack of randomization, patient selection bias exists in both studies, particularly in the study without consecutive enrolment.

In the study by Ernst et al., (32) PV isolation was achieved by interruption of all conductive myocardial fibres at the PV to left atrial junction using a circular catheter approach (ostial PV isolation). In the study

by Tse et al., (31) elimination of PV potential was achieved by focal ablation. Radiofrequency ablation was used in both studies.

There was no statistically significant difference in acute success (90% vs. 84% in Tse 2002, and 80%–90% for both groups in Ernst 2003) and recurrence rates between the 2 arms in both studies. Total procedure time was similar in atrial ablation but significantly longer in the CARTO group than the fluoroscopy group in ostial ablation (8 hours vs. 5 hours, $P < .005$). (32)

Pooled analyses of the 2 studies are shown in Figures 7 to 9 (next page).

The analyses showed that based on the 2 nonrandomized comparative studies, the use of CARTO in guiding PV ablation appears to have the following effects:

- Make no difference in short-term or long-term success rates (60%–70% free from AF; forest plot, Figure 8).
- Generate no consistent difference in total procedure time (Forest plot, Figure 9).
- Significantly shorten the fluoroscopy time for focal PV ablation and ostial ablation (by 36% to 52%). A forest plot showed significant difference in favour of CARTO (Forest plot Figure 10).
- Reduce the number of RF applications in focal ablation but increase the number of RF applications in ostial ablation.

Pulmonary vein stenosis was the main complication reported. Tse et al. (31) reported PV stenosis in 1 patient in the fluoroscopy group, whereas Ernst et al. (32) reported 18 cases of acute PV stenosis in the 2 groups. Stenosis was not severe in most cases. However, 1 patient in the fluoroscopy group had total PV occlusion, and 1 patient in the fluoroscopy group had severe PV stenosis. One case of stroke and 2 cases of transient ischemic attach were also reported. In this study, 8% of patients in the CARTO group and 22% of those in the fluoroscopy group required reablation procedures due to recurrence of AF, despite the elimination of PV potential.

Figure 7: Forest Plot of Overall Treatment Failure: CARTO- Versus Fluoroscopy-Guided Pulmonary Vein Ablation for Atrial Fibrillation

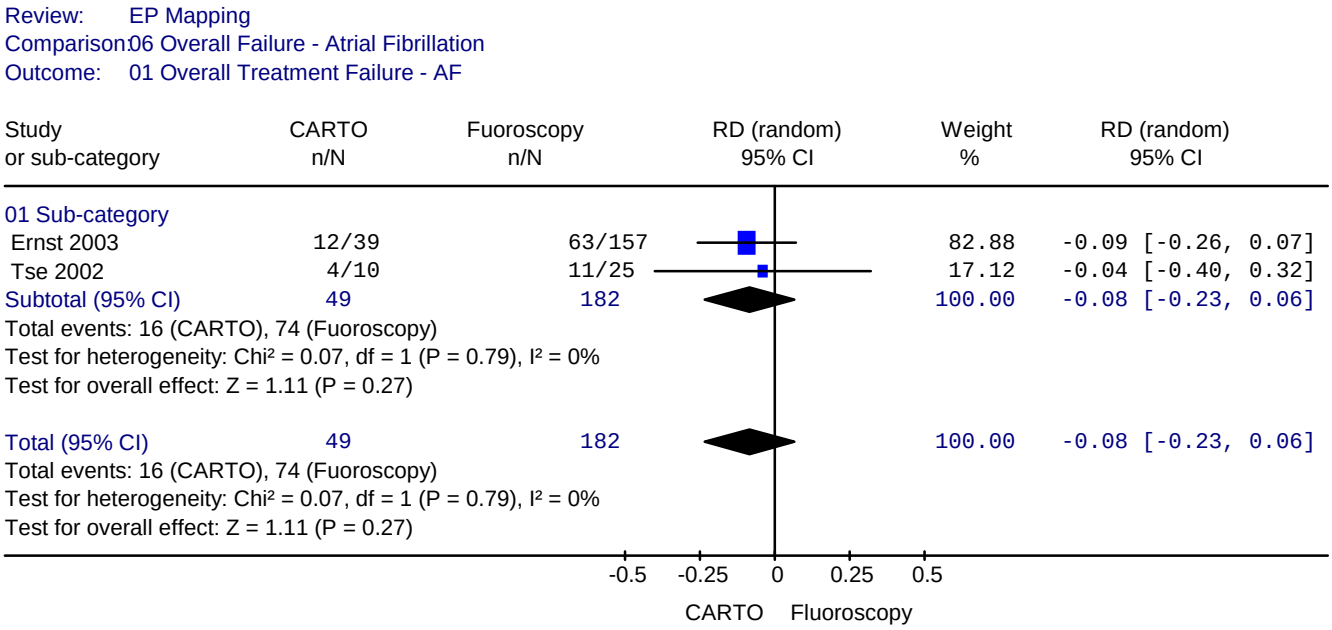


Figure 8: Forest Plot of Total Procedure Time: CARTO- Versus Fluoroscopy-Guided Pulmonary Vein Ablation for Atrial Fibrillation

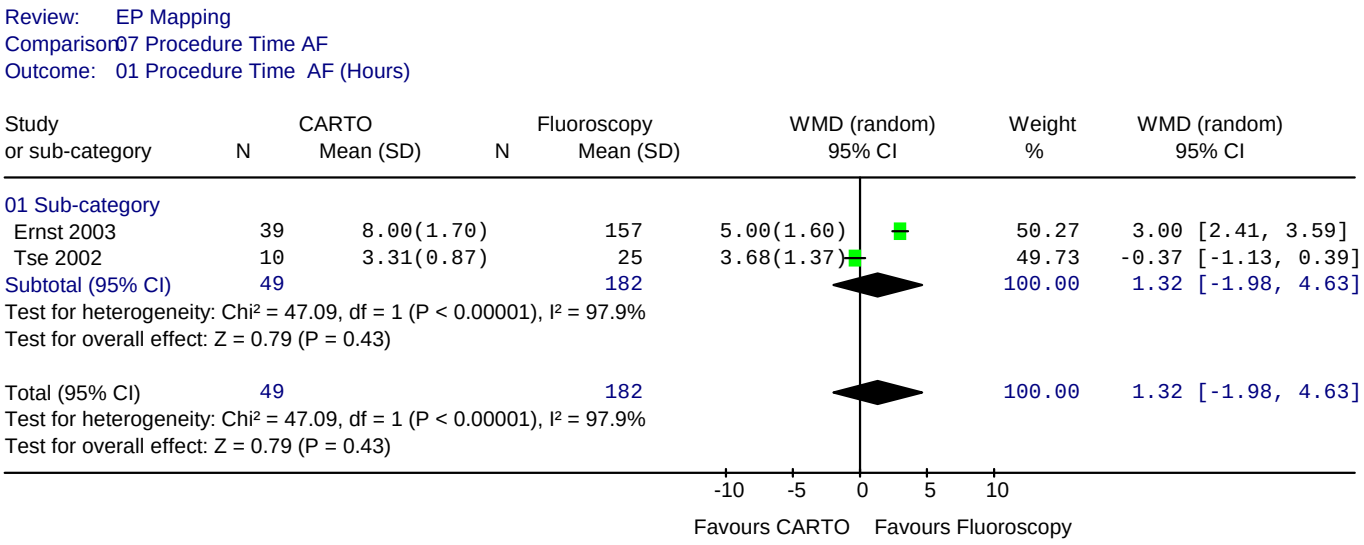
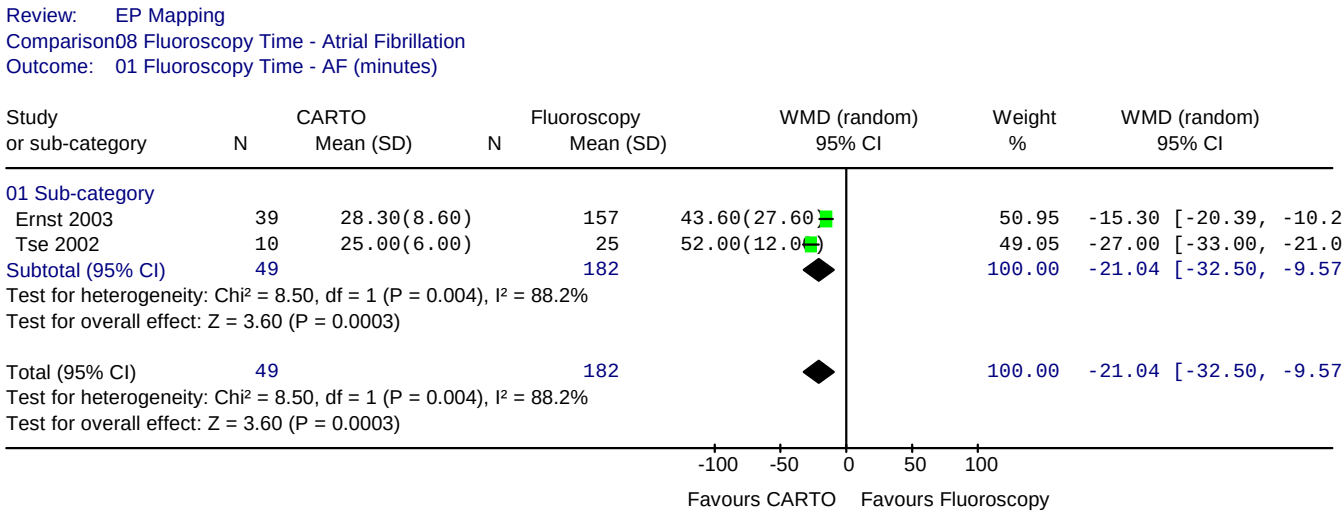


Figure 9: Forest Plot of Fluoroscopy Time: CARTO- Versus Fluoroscopy-Guided Pulmonary Vein Ablation for Atrial Fibrillation



CARTO Electroanatomic Mapping System Versus Fluoroscopy: Atrial Flutter

Six studies that compared CARTO-guided and fluoroscopy-guided ablation of AFL were found. All studies consisted of patients with AFL refractory to drug therapy. Three of the studies were RCTs and 3 were non-RCTs. The characteristics and outcomes of these studies are summarized in Table 8. Two of the RCTs had sample sizes of 50 and 80. In the RCT by Sporton et al., (30) the 16 patients with AFL were a subset of the entire sample that included other types of arrhythmias. This study had only 6 weeks follow-up, which was much shorter than that of the other studies (9–12 months). Hence the data of the 16 AFL patients were included in the pooled analysis for acute success and fluoroscopy time, but not for long-term success. The quality of the RCTs ranged from moderate to low (Appendix 3).

Of the 3 non-RCTs, the study by Leonelli et al. (33) had a sample size of 196 with uneven allocation to the 2 arms. The study by Khongaphattanayothin et al. (34) consisted of a subset of 59 patients out of 173 study subjects. The study by Delacretaz et al. (35) consisted of 20 adult patients who developed AFL with macro-re-entrant circuits after surgical repair of congenital heart disease. The follow-up period for these studies ranged from 3 to 19 months. Only 1of the 3 studies (33) reported consecutive enrolment. There were unbalanced allocations to the study and control groups in two studies, (33;34) and there was no blinding in any of the studies. Consequently, there were likely biases in patient selection and detection (Appendix 4).

Radiofrequency ablation was used in all studies. With the exception of 1 study, the end point was the achievement of bi-directional isthmus block.

Acute success rates and rates of arrhythmia recurrence at follow-up were similar in all but 1 study. Kottkamp et al. (36) reported significantly higher acute success rate for the CARTO group (96% for CARTO vs. 67% for fluoroscopy, $P < .05$), and Leonelli et al. reported a significantly lower recurrent rate for the CARTO group (1.1% for CARTO vs. 12.5% for fluoroscopy).

Only the study by Kottkamp et al. (36) reported a significantly lower procedure time for CARTO

compared with fluoroscopy (57.1 minutes vs. 75.5 minutes, $P < .05$). This was likely a result of the definition of success in this study, which limited the fluoroscopy time and RF pulses in both groups. All studies reported significantly lower fluoroscopy time for CARTO-guided ablation. Only 2 studies (30;37) reported radiation doses. Both demonstrated significantly lower radiation doses for the CARTO group.

Pooled analyses of the 6 studies are shown in Figures 10 to 13.

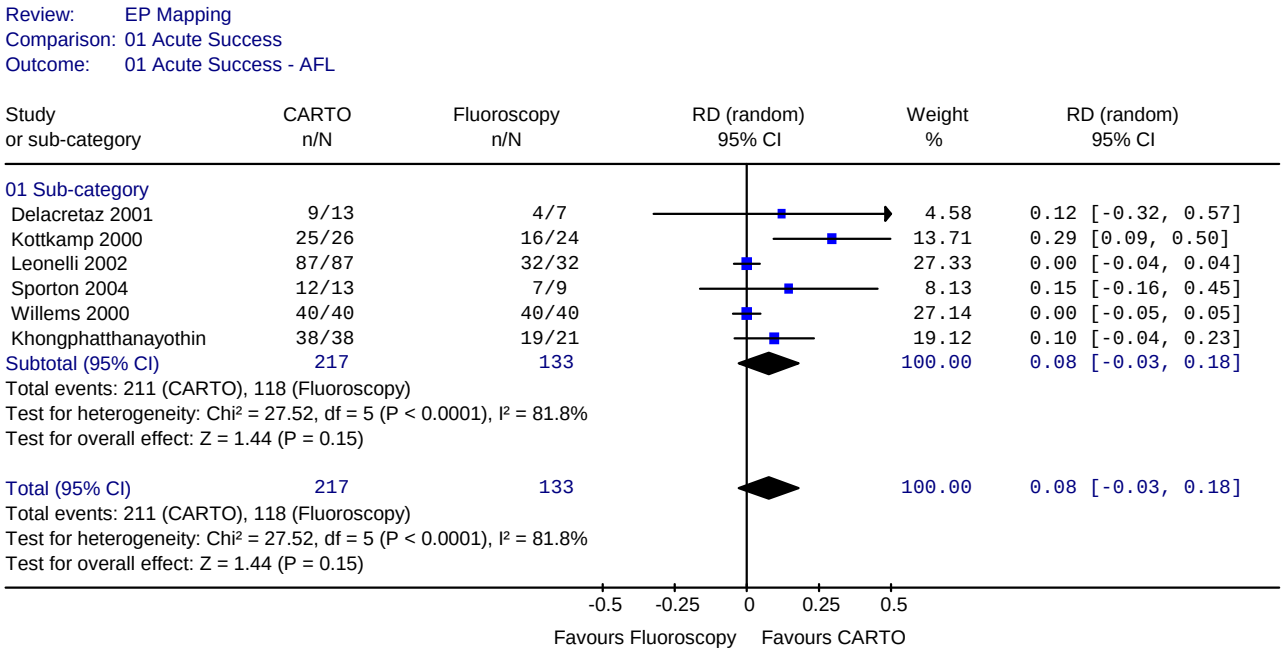
Table 8: Comparative Studies of CARTO-Guided Ablation Versus Fluoroscopy-Guided Ablation of Atrial Flutter

	Willems et al., 2000 (37)		**Kottkamp** et al., **2000 (36)**		**Sporton et al., 2004 (30)**		**Leonelli et al., 2002 (33)**		**Khongphatthanayothin et al., 2000(34)**		**Delacretaz et al., 2001(35)**	
Type of arrhythmia	AFL		AFL		AFL (subgroup)		Typical AFL		AFL & AT		IART (atrial flutter) Congenital heart disease	
Study design	RCT		RCT		RCT		Nonrandomized subgroup of 119 patients		Nonrandomized subgroup		Nonrandomized	
Definition of successful ablation	Complete bidirectional block in cavotricuspid isthmus		Complete bi-directional isthmus block ≤20 RF pulses or 25 min fluoroscopy		Bidirectional isthmus block		Successful conduction block		Non-inducibility; Isthmus block; no recurrence within 24 hours Failure = reablation within 3 months		No sustained monomorphic IART was inducible after ablation. Long-term: No spontaneous sustained IART during follow-up	
Mean (SD) follow-up, months	8.5 (2.8)		12 (5)		6 weeks		16.3 (2.2)		3		19 (14)	
Mapping technique	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**	**Entrainment + CARTO**	**Fluorosocpy entrainment mapping**
Sample size	40	40	26	24	9	7	87	32	38	21	13	7
Mean age, years	62.4 (9.8)	64.9 (8.2)	56.8 (11.7)	58.3 (10.7)		51 (20)		47(15)	51 (20)	47 (15)		43 (15)
Male, %	80	80	81	79		Nr		Nr	Nr	Nr	Nr	Nr
Ablation technique	RF	RF	RF	RF	RF	RF	RF	RF	RF	RF	RF	RF
Acute success, %	100	100	96	67 *P* < .05	8/9	6/7	100	100	100 (38/38)	90 (19/21)	69 (9/13) 77% of IART	57 (4/7) *P* = NS 86% of IART
Crossover, %	0	0	4	33	0	0	0	0	Nr	Nr	Nr	Nr

*AFL indicates atrial flutter; AF, atrial fibrillation; RCT, randomized controlled trial; RF, radiofrequency. Nr Not reported

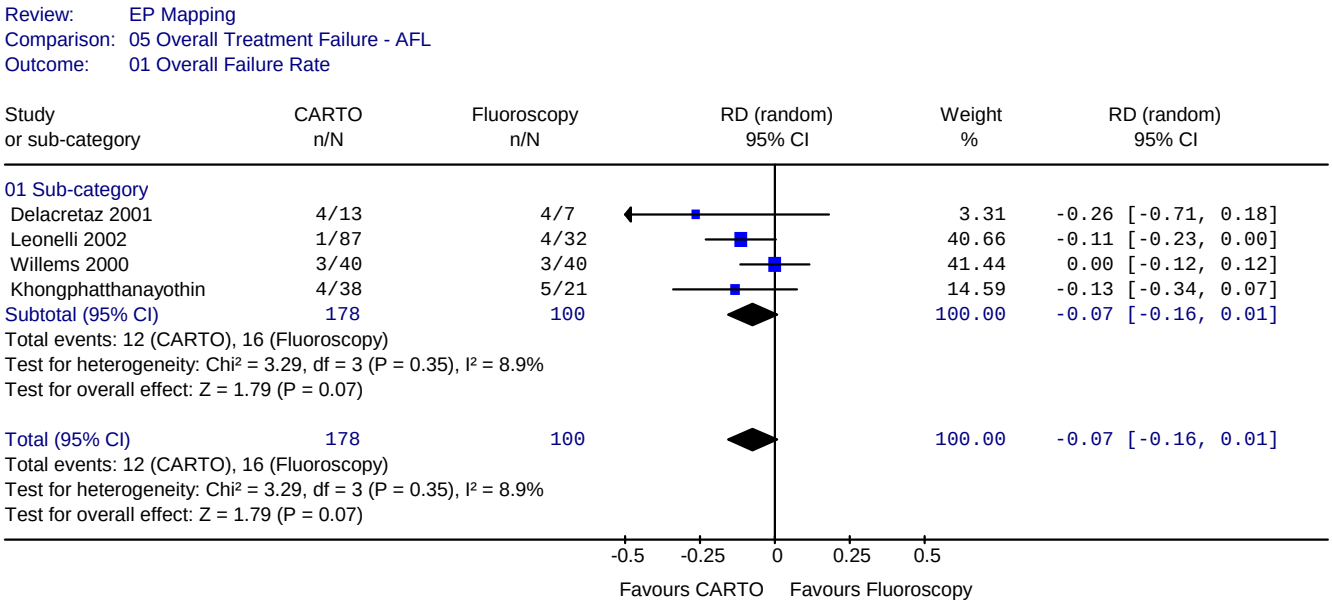
	Willems et al., 2000 (37)		Kottkamp et al., 2000 (36)		Sporton et al., 2004 (30)		Leonelli et al., 2002 (33)		Khongphatthanayothin et al., 2000(34)		Delacretaz et al., 2001 (35)	
	CARTO	**Fluoroscopy**	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**
Recurrence during follow-up (%)	9	9	4.3% of patients with complete isthmus block 66.7% of patients with partial block after ablation		33 (3/9)	14 (1/7)	1.1 (1/87)	12.5 (4/32) *P* < .01	10.5 (4/38)	23.8 (5/21)	31 (4/13)	57 (4/7)
Overall failure **%**	7.5 (3/40)	7.5 (3/40) NS			33	14	1.1	12.5	4/38	5/21	31	57 NS
Total procedure time (minutes)	169.3 (47.3)	172.5 (47.4) *P* = .7415	57.1 (24.2)	75.5 (27.1) *P* < .05	161 (56)	124 (40) *P* = .16	52 (11)	49 (18) *P* = NS	288 (102)	282 (120) *P* = NS		
Total fluoroscopy time (minutes)	7.7 (2.8)	29.2 (9.4) *P* = .0001	3.9 (1.5)	22 (6.3) *P* < .0001	11.4	40.1 *P* < .001	4.2 (1.5)	27.2 (8.2) *P* < .001	18(17)	44(23) *P* < .01	24 (9)	60 (30) *P* < .001
Radiation dose (Gray)		cGy.cm2 4,726 (1,934) *P* = .0001	-	-	8.9 (6.7)	23.9 (14) *P* = .01	-	-	-	-	-	-
Mean number of Radiofrequency pulse	13.2 (5.3)	16.7 (6.5) *P* = .2841	8 (4)	10 (5) *P* = NS	-	-	-	-	-	-		
Mean duration of RF pulse (seconds)	55.6 (4.3)	54.8 (4.9) *P* = .4812			-	-	-	-	-	-		
Procedure related Complications	Not reported	Not reported	0	0	0	0	None reported	None reported			0	0
Other information	All recurrences successfully ablated with CARTO™								**Failure 11% (4/38)**	**24% (5/21)**	Risk of recurrence (on drug) = 20%@ 2 yrs follow-up	
Authors' Conclusion	Same effectiveness & procedure duration with significant reduction in overall X-ray exposure with CARTO™		Higher acute success rate & 82.3% reduction in total fluoroscopy time & 99% reduction in isthmus mapping time with CARTO™.				CARTO™ resulted in a reduction of delayed AFL recurrence rate & marked decrease in radiation exposure for patient & operators				-total of 47 IART induced (RA 45, LA 2) -81% of all 20 patients remained arrhythmia free. Success similar for the two groups	

Figure 10: Forest Plot of Acute Success: CARTO- Versus Fluoroscopy-Guided Ablation for Atrial Flutter



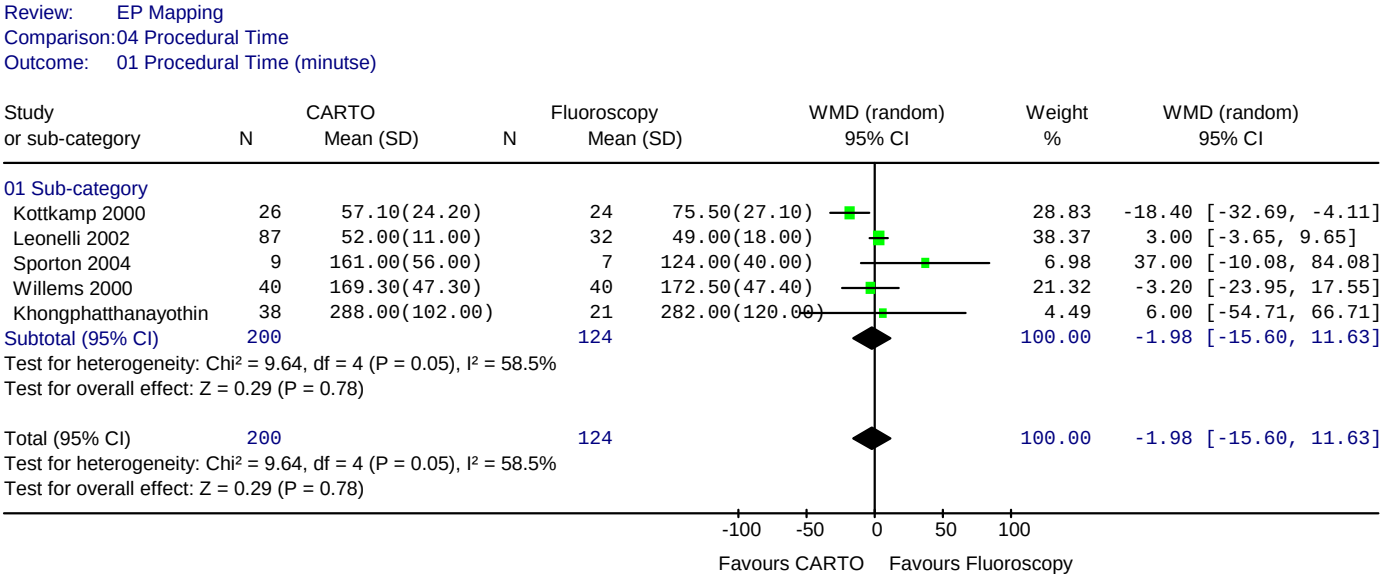
*There was no significant difference in the acute success rates between the CARTO group and the fluoroscopy group. However, there was significant heterogeneity in acute success rates among the studies.

Figure 11: Forest Plot of Treatment Failure: CARTO- Versus Fluoroscopy-Guided Ablation of Atrial Flutter



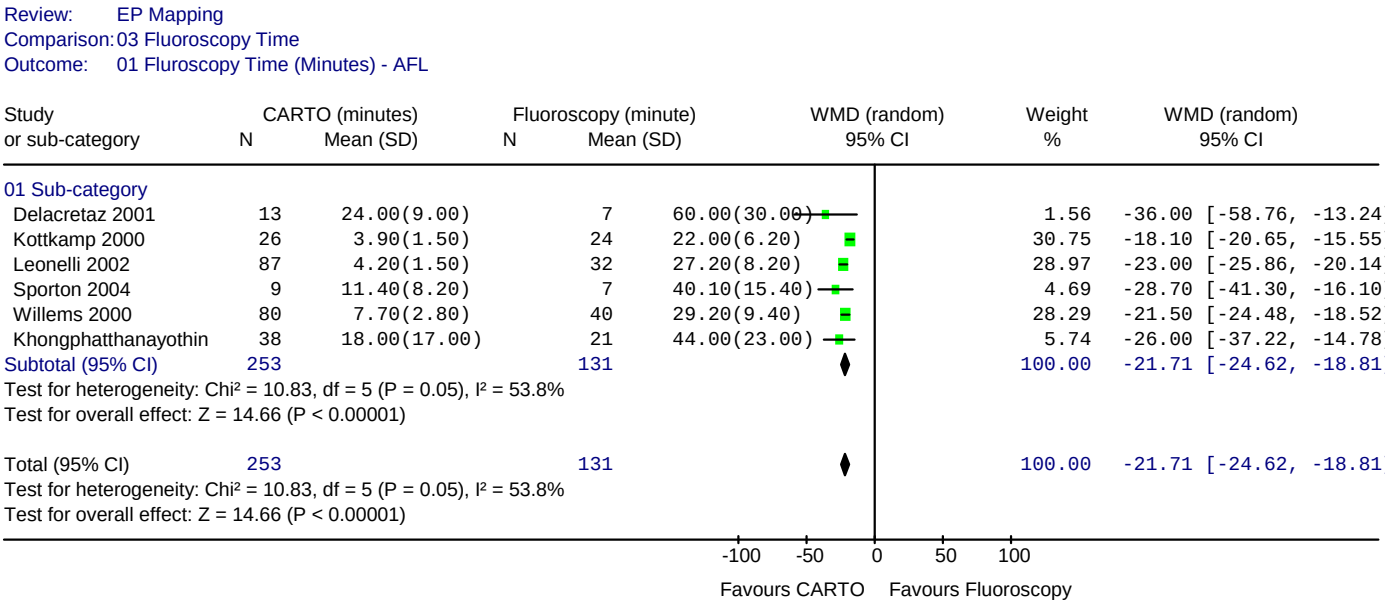
*The mean overall failure rate was not significantly different between the two groups.

Figure 12: Forest Plot of Procedure Time: CARTO- Versus Fluoroscopy-Guided Ablation of Atrial Flutter



*There was no significant difference between the total procedure time required for the CARTO group and that required by the fluoroscopy group.

Figure 13: Forest Plot of Fluoroscopy Time: CARTO™ Versus Fluoroscopy Guided Ablation of Atrial Flutter



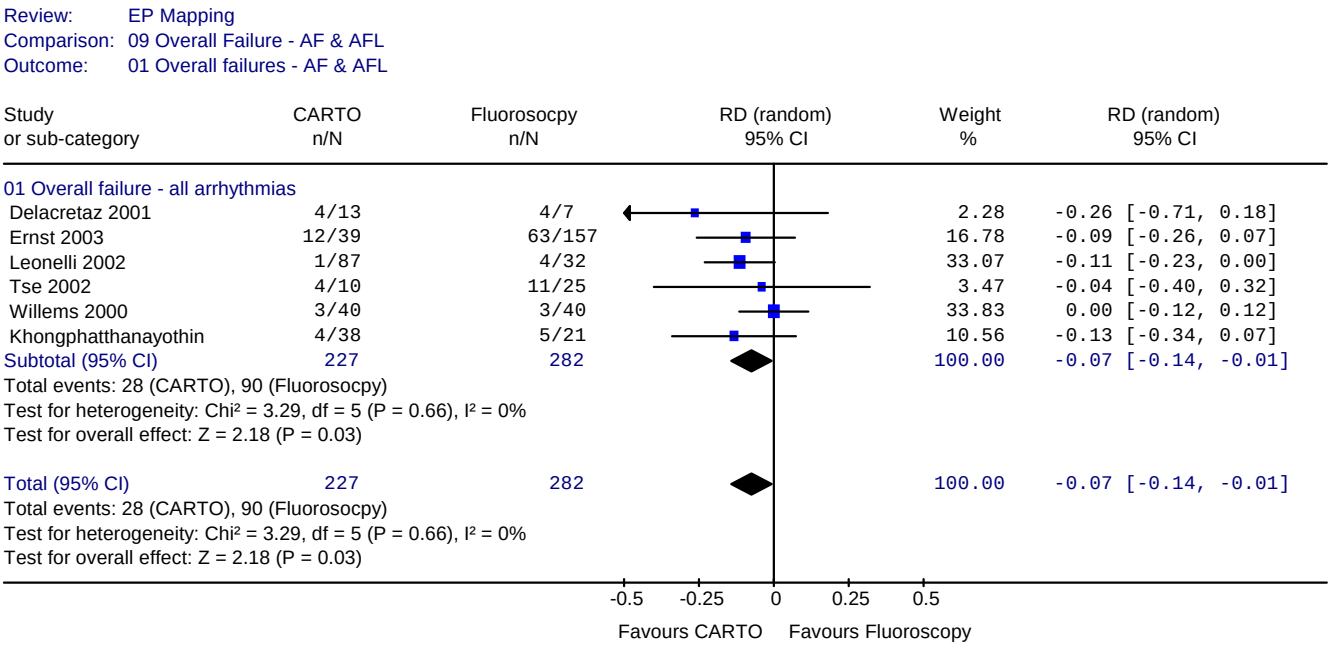
*The CARTO group had significant reduction in fluoroscopy time compared to the fluoroscopy group.

Forest plots of acute success rates, overall failure rate, and procedure time showed no significant differences between the CARTO group and the fluoroscopy group for AFL ablation (Figures 10–12). The only statistical difference was in fluoroscopy time, which was significantly shorter for the CARTO group (mean, 21.7 minutes; $P < .00001$). However, the forest plot also showed significant heterogeneity among the studies (Figure 13).

Pooled Analysis of Overall Failure Rate for Atrial Fibrillation and Atrial Flutter

The studies of AF or AFL alone might not have enough power to detect a difference in overall failure rate (% of people who had arrhythmia at follow-up). Thus, a pooled analysis of the overall failure rate for the 2 groups of studies was performed. The result suggests that CARTO demonstrated a beneficial effect on the long-term outcome of ablation for drug-refractory AFL and AF. The overall failure rate was 7% lower in the CARTO group compared with the fluoroscopy group. This was statistically significant ($P = .03$), but the upper limit of the 95% confidence interval is very close to 0 (point of no difference) (Figure 14).

Figure 14: Forest Plot of Overall Failure Rate: CARTO- Versus Fluoroscopy-Guided Ablation of Atrial Flutter and Atrial Fibrillation



CARTO Electroanatomic Mapping System Versus Fluoroscopy: Ventricular Tachycardia

There were no comparative studies that were devoted only to ventricular tachycardia (VT); however, 2 studies that reported on the comparison of CARTO and fluoroscopy had a subgroup of patients with VT. The characteristics of these studies and findings are summarized in Table 9.

Table 9: Summary of Comparative Studies on CARTO-Guided and Fluoroscopy-Guided Ablation of Ventricular Tachycardia

	Sporton et al., (30)		Khongphatthanayothin et al., 2000 (34)	
Type of arrhythmia	Ventricular tachycardia		Ventricular tachycardia	
Study design	Randomized controlled trial (subgroup)		Non-RCT comparative subgroup	
Definition of successful ablation	Termination of ventricular tachycardia & non inducible during follow=up			
Mean (SD) follow-up	6 weeks		3 months	
Ablation technique	Radiofrequency			
Mapping technique	**CARTO**	**Fluoroscopy**	**CARTO**	**Fluoroscopy**
Sample size, n	4	7	17	7
Mean (SD) age, years		51 (20)	51(20) entire cohort	47 (15) entire cohort
Males, %	NA	NA	NA	NA
Acute success rate, %	100 (4/4)	71 (5/7) *P* > .2	96 (16/17)	71 (5/7)
Asymptomatic @ follow-up (%)	75 (3/4)	60 (3/5) *P* > .5		
Overall Failure %	25 (1/4)	40 (2/5)	17 (3/17)	28 (2/7)
Mean (SD) total procedure time, minutes	156 (5)	176 (38) *P* = .52	5 (1.5) hours	5.2 (2) hours *P* = NS
Mean (SD) total fluoroscopy time, minutes	14.5 (12.8)	37.7 (29) *P* = .17	15 (12)	34 (31) *P* < .05
Mean (SD) Radiation dose (Gray)	10.8 (10.1)	58.7 (79.4) *P* = .27		
Complications	0	1/7 Cardiac tamponade	1/17 tamponade	1/7 tamponade

NA not available

In the RCT of a nonselected group of patients, Sporton et al. (30) included 11 patients with right ventricular tachycardia. Four of the patients were allocated to the CARTO, group and 7 were allocated to the fluoroscopy group. The end point of ablation was termination of the tachycardia during RF ablation and noninducibility of the arrhythmia during a mean 6 weeks of follow-up. There was no significant difference in immediate success, long-term failure, mean procedure time, and mean fluoroscopy time. The author of the study indicated that the study was not designed to detect a difference between CARTO and fluoroscopy ablation in these subgroups (Personal communication, August 15, 2005).

The non-RCT by Khongphatthanayothin et al. (34) included a subgroup of 24 patients who underwent RF ablation for right ventricular tachycardia. Seventeen of the patients had ablation guided by CARTO, and 7 patients had RF ablation guided by conventional fluoroscopy. The CARTO group had a higher acute success rate (96% vs. 71% for fluoroscopy) and a lower overall failure rate (17% vs. 28% for fluoroscopy). However, it was not clear whether these differences were statistically significant. The procedure times were similar in both groups (5 hours for CARTO and 5.2 hours for fluoroscopy), but the

fluoroscopy time was significantly shorter for patients in the CARTO group (15 minutes vs. 34 minutes, $P < .05$).

A pooled analysis showed a significant reduction in fluoroscopy time for the CARTO group compared with fluoroscopy (Figure 15), but there was no significant difference in acute success or overall failure between the 2 groups. However, because of the small sample size, a type 2 error could have been present (Figures 16 and 17).

Figure 15: Pooled Analysis of Fluoroscopy Time: CARTO Versus Fluoroscopy for Ventricular Tachycardia Ablation

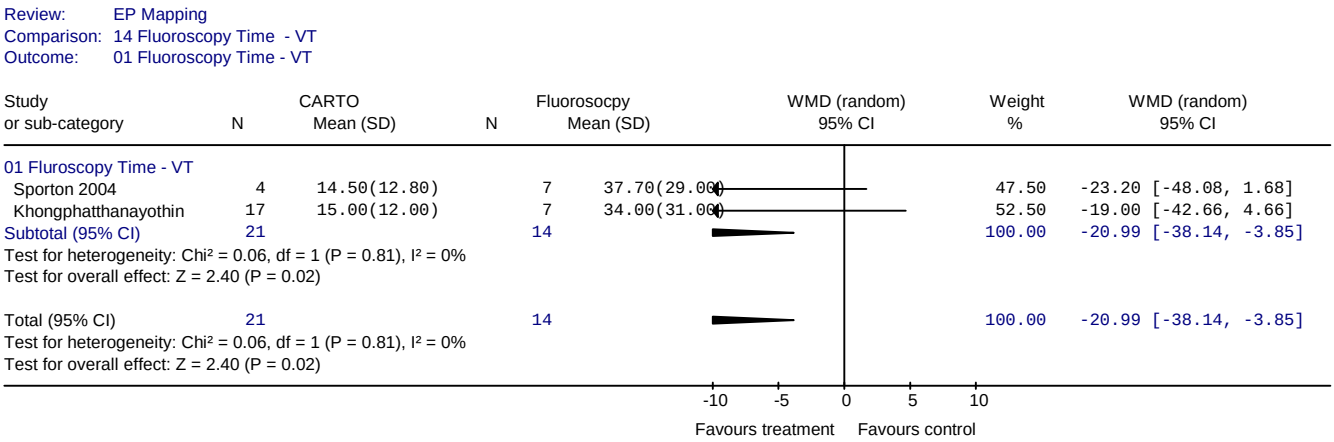


Figure 16: Pooled Analysis of Acute Success: CARTO Versus Fluoroscopy for Ventricular Tachycardia Ablation

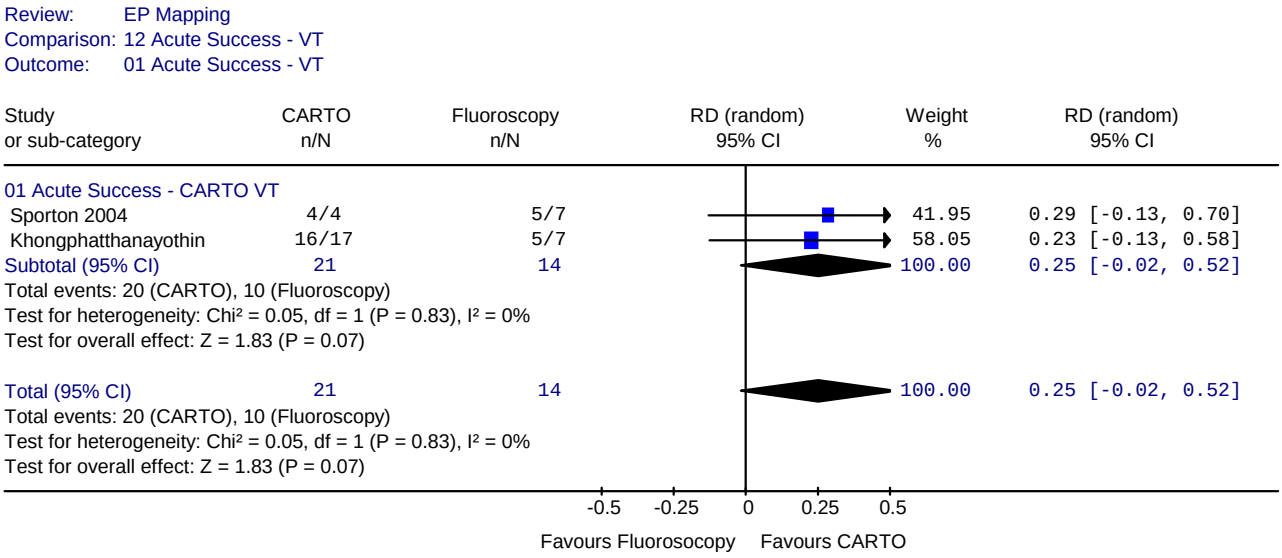
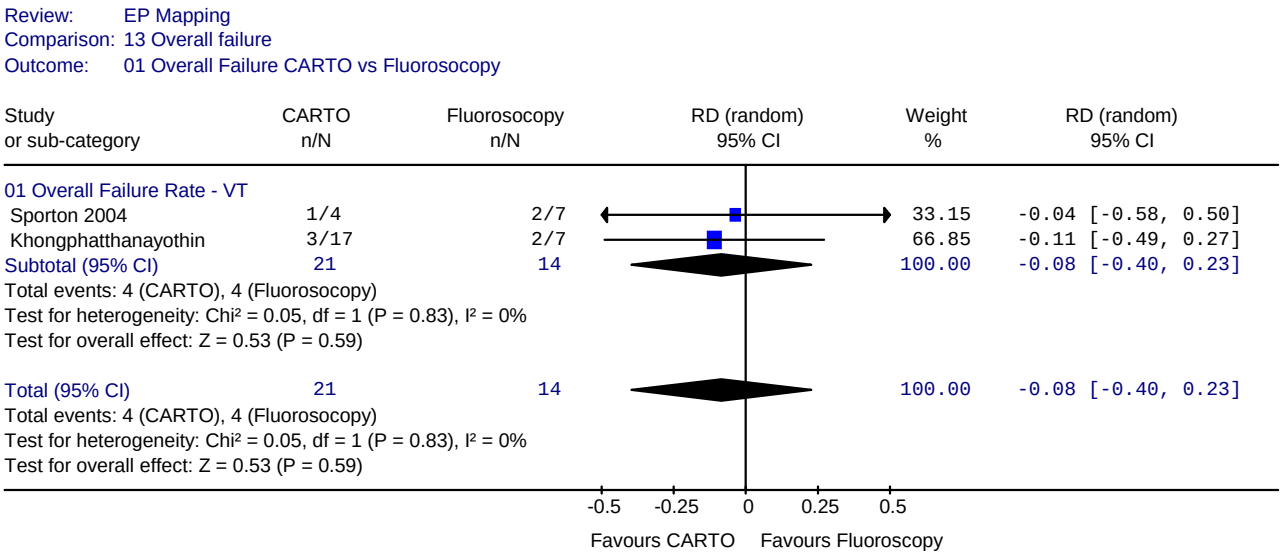


Figure 17: Overall Failure Rate: CARTO™ Versus Fluoroscopy for Ventricular Ablation



EnSite NavX Navigational System Versus Fluoroscopy: Atrial Fibrillation

Two RCTs compared ablation guided by the EnSite NavX navigational system with that guided by fluoroscopy to treat paroxysmal or persistent drug-refractory AF. Characteristics of these studies are summarized in Table 10.

Table 10: Studies That Compared EnSite NavX-Guided and Fluoroscopy-Guided Ablation of Atrial Fibrillation

	Rotter et al., 2005 (38)		**Tondo et al., 2005 (39)**	
Type of arrhythmia	Paroxysmal or persistent AF (PVI)		Paroxysmal or persistent AF (PVI)	
Study design	Randomized controlled trial		Randomized controlled trial	
Definition of successful ablation	Elimination or dissociation of PV potentials		Elimination of PV potentials	
Mean (SD) follow-up, months	EnSite: 7.2 Fluorosocopy : 6.2		7(2)	
Navigation technique	**EnSite NavX**	**Fluoroscopy**	**EnSite NavX**	**Fluoroscopy**
Sample size	35	37	30	30
Mean (SD) age, years	51 (9)	52 (10)		56 (8)
Male, %	89	86		52
Mean (SD) LVEF, %	65 (8)	67 (11)	58 (2)	57 (2)
Structural heart disease, %	11	5		
Acute success rate, %	—	—	100	100

	Rotter et al., 2005 (38)		Tondo et al., 2005 (39)	
Arrhythmia-free during follow-up, %	With or without AAD 74 (26/35)	With or without AAD 78 (29/37) *P* = .87	90 (27/30)	80 (24/30)
Overall failure rate, %	26 (9/35)	22 (8/37)	10 (3/30)	20 (6/30)
Mean (SD) procedure time, minutes (PV isolation)	52 (12)	61 (17) *P* = .02	-	-
Mean (SD) total procedure time, minutes	66.7	87.6	225 (15)	156 (10) *P* < .05
Mean (SD) fluoroscopy time minutes (PV isolation only)	15.4 (3.4)	21.3 (6.4) *P* < .001	-	-
Mean (SD) total fluoroscopy time (minutes)	21	31.2	22 (8)	56 (10) *P* < .05
Mean (SD) duration of RF pulse, seconds			5 (1)	10 (3)
Complications (**%)**	0	0	0	0

*AF indicates atrial fibrillation; PV, pulmonary vein; PVI, pulmonary vein isolation

In the study by Rotter et al., (38) atrial ablation outside the PV ostium was guided by EnSite NavX in 35 patients and by fluoroscopy in 37 patients. In addition, left atrial linear ablation was also performed in 51% of the EnSite group and 57% of the fluoroscopy group. In the RCT by Tondo et al., (39) atrial ablation outside the PV ostium was also performed, with 30 ablations guided by EnSite NavX and 30 by fluoroscopy. In this study, a left isthmus lesion between the mitral annulus and the inferior left PV was also created in patients with AF at the time of procedure. In addition, a roofline lesion in the left atrium was added in 5 patients. The mean follow-up time for the 2 studies ranged from 6 to 7 months. The end point in both studies was elimination of PV potentials.

The rate of acute success was available for the Tondo study; it was similar in the EnSite and fluoroscopy groups. The overall failure rate was higher in the fluoroscopy group in the Tondo study (20% vs. 10% for EnSite), but it was unclear whether this was significant. The mean total procedure time was shorter in the EnSite Group in one study (66.7 min vs. 87.6 min) (38), but longer in the EnSite group in the other study (225 min vs. 156 min; $P < .05$). (39) The total procedure time was much longer in both groups in the study by Tondo compared with that in the study by Rotter et al. This difference was likely due to the creation of an additional lesion in the mitral-inferior vena cava isthmus. Mean total fluoroscopy time was significantly shorter in the EnSite group in both studies.

EnSite NavX Versus Fluoroscopy: Atrial Flutter

One RCT compared EnSite NavX-guided and fluoroscopy-guided ablation in patients with symptomatic recurrent or persistent AFL (Table 11).

Table 11: EnSite NavX-Guided Ablation Compared With Fluoroscopy-Guided Radiofrequency Ablation for Atrial Flutter

	Ventura et al., 2004 (27)	
Type of arrhythmia	Recurrent or persistent typical atrial flutter	
Study design	Randomized controlled trial	
Definition of successful ablation	Bidirectional isthmus block	
Mean (SD) follow-up, months	7 (2)	
Navigation technique	**NavX**	**Fluoroscopy**
Sample size, n	20	20
Mean (SD) age, years	60 (11)	58 (13)
Male, %	75	85
Mean LVEF, %	58 (2)	57 (2)
Acute success rate, %	100	100
Recurrence during follow-up, %	0	0
Mean (SD) total procedure time minutes	144 (30)	137 (32) *P* = NS
Mean (SD) total fluoroscopy time, minutes	5.1 (1.4)	20 (11) *P* < .01)
Radiation dose Diagnostic Gycm^2	5.1 (3.1)	24.9 (1.6) (*P* < .01)
Mean (SD) number of radiofrequency pulses	12 (6)	12 (7) *P* = NS
Mean duration of radiofrequency pulses, seconds	-	-
Complications	Paroxysmal atrial fibrillation developed in 4 symptomatic patients	

In this study, Ventura et al. (27) randomized 40 consecutive patients with symptomatic AFL either to the NavX group (n = 20) or to the fluoroscopy group (n = 20). Baseline characteristics of patients in the 2 groups were similar. Radiofrequency ablation to create a lesion in the cavotricuspid isthmus was performed with an irrigated tip catheter. The end point of ablation was bidirectional isthmus block. All patients had ECG monitoring for at least 24 hours after ablation. Antiarrhythmic drug therapy was only continued in patients that also had AF. Holter monitoring and 12-lead ECG was repeated every 3 months during a mean follow-up period of 7 month. (27)

Complete acute success was achieved in both the EnSite and the fluoroscopy groups. No recurrence of AFL was found in either group. However, 4 patients developed AF during follow-up. No other complications were observed in either group. There were no significant differences in the total procedure time and number of radiofrequency pulses required by the 2 groups. EnSite NavX required significantly

shorter fluoroscopy duration (75% reduction) and lower radiation dose (80% reduction) than did fluoroscopy-guided ablation.

Efficacy of CARTO and EnSite in Complex Arrhythmias

Gurevitz et al. (40) conducted nonfluoroscopic mapping using either an EnSite noncontact mapping system (n = 17), CARTO (n = 36), or both (n = 15) in 68 patients in whom previous fluoroscopy-guided ablation had failed to cure the arrhythmia. Structural heart disease was present in 49% of the patients. Of the 68 patients, 22% had a corrected congenital cardiac malformation, 18% had coronary artery disease, and 3 had dilated cardiomyopathy. The results are summarized in Table 12.

Acute success, defined as a situation in which the clinical arrhythmia could no longer be induced 30 minutes or longer after ablation, was achieved in 79% of the patients, compared with a rate of 37% in the initial fluoroscopy-guided ablation. Of the 48 patients for whom nonfluoroscopic ablation was acutely successful and who were available for follow-up, 56% had recurrent arrhythmia. However, 69% had a smaller burden of arrhythmia symptoms than they had had before the ablation, 24% had a similar symptom burden, and 6% had an increased burden. Only 17% of the patients required antiarrhythmic drugs at follow-up. A third ablation was performed in 12% of the patients for whom nonfluoroscopic ablation was acutely successful. (40)

Table 12: Comparing Acute Success Rates of Repeat Ablation Using CARTO and/or EnSite Versus Initial Fluoroscopy Ablation*

	Initial Fluoroscopy-Guided Ablation (n = 68)	Second Ablation Guided by CARTO and/or EnSite (n = 68) Same Cohort
Types of arrhythmia	Ventricular tachycardia (12, 9/12 post-myocardial infarction), focal atrial tachycardia, atrial flutter, right ventricular outflow tachycardia, atrial ventricular node re-entrant tachycardia, etc	
Mean (SD) age, years	48 (17)	48 (17)
Mean (SD) follow-up, months	NA	20 (9)
Acute success, %	37	79
Recurrence during follow-up, %	100%	56 (of 48 successful with follow-up)
Reduced arrhythmic burden, %	N/A	69 (17% required antiarrhythmic drugs)
Mean (SD) procedure time, minutes	N/A	381 (138)
Mean (SD) fluoroscopy time, minutes	N/A	101 (48)
Procedure-related complications, %	N/A	7

*Guveritz (40)

Comparison Between CARTO and EnSite NavX: Atrial Fibrillation

One study was found that compared EnSite NavX with CARTO in guiding circumferential PV ablation for AF (Table 13). Liu et al. (25) randomized 75 patients with paroxysmal or chronic symptomatic drug-refractory AF to undergo PV ablation guided either by EnSite NavX (n = 40) or CARTO (n = 35). No details on the randomization procedure were provided. The 2 groups were similar in age, gender, mean left ventricular ejection fraction (LVEF), duration of AF, and presence of structural heart disease. RF was applied to ablate tissues circumferentially outside of the pulmonary veins' ostia. In patients with chronic AF, a linear lesion was also created to modify the substrate of the left atrium. The end point of the circumferential PV ablation was the elimination or dissociation of PV potentials as determined by circular mapping. Surface ECG, transthoracic echocardiography, and 24-hour Holter recording were performed 1 day after ablation. These were repeated after 1, 3, 6, and 12 months.

Compared with the CARTO group, the EnSite NavX group had a significantly higher acute success rate (65% vs. 31%, *P* = .004). More patients in the EnSite group were arrhythmia free during a mean follow-up period of 7 months, although this difference did not reach statistical significance (80% EnSite vs. 69% CARTO, *P* = .06). Another 3 people in the EnSite group and 4 people in the CARTO group had AF controlled by antiarrhythmic drugs. The mean total fluoroscopy times (18 vs. 25 minutes, *P* = .04) and procedural durations (150 vs. 170 minutes, *P* = .03) were significantly shorter guided by CARTO than by EnSite NavX. Liu et al. reported that EnSite provided a much higher resolution for the reconstructed geometry of the left atrium.

Complications included 1 (2.5%) case of hemothorax in the EnSite NavX group and 1 (5.7%) case each of pericardial effusion and suspected intestinal artery thrombosis in the CARTO group.

Table 13: Comparison of CARTO-Guided With EnSite NavX-Guided Ablation of the Pulmonary Vein in Atrial Fibrillation*

	Liu et al. 2005 (25)		
Type of arrhythmia	Atrial fibrillation		
Study design	Randomized controlled trial		
Quality			
Definition of successful ablation	End point of circumferential pulmonary vein ablation = elimination of dissociation of the pulmonary vein potential as determined by circular mapping End point of linear ablation was presence of a corridor of double potential during pacing adjacent to the line.		
Antiarrhythmic drugs	Amiodarone only, other antiarrhythmic drugs discontinued for at least 5 half-lives		
Mapping technique	**EnSite/NavX**	**CARTO**	***P***
Sample size	40	35	
Mean (SD) age, years	50.5 (14.7)	51.4 (13.2)	.36
Male, %	68	69	.56
Mean (SD) LVEF, %	57 (8)	60 (11)	.41
Mean (SD) atrial fibrillation duration, months	30 (18)	36 (14)	.24

Structural heart disease %	24	20	.49
Ablation technique	Circumferential with radiofrequency	Circumferential with radiofrequency	
Mean (SD) follow-up, months	7 (3)	7 (2)	
Acute success, % Immediate PV isolation	65	31	.004*
Arrhythmia free at follow-up, %	80	69	Log rank test .06
Linear LA ablation performed **[**	18	14	
Mean (SD) total procedure time, minutes	170 (34)	150 (23)	0.03*
Mean (SD) procedure time for geometry, minutes	16 (11)	14 (8)	0.06
Mean (SD) procedure time for ablation (CPVA), minutes	25 (10)	18 (11)	0.04
Mean (SD) total fluoroscopy time, minutes	25 (16)	18 (17)	0.04
Mean (SD) fluoroscopy time LV geometry, minutes	8 (4)	5 (4)	0.06
Mean (SD) fluoroscopy time for ablation (CPVA) minutes	15 (5)	10 (6)	0.05
RF power and temperature	RF 35–40 W @ 50^0C	RF 35–40 W @ 50^0C	
Procedure-related complications	Total: 2.5% Moderate hemothorax: 1/40 Atypical atrial flutter: 1/40	Total: 5.7% Pericardium effusion: 1/35 Suspected intestinal artery thrombosis: 1/35	
Authors' conclusion	All complications resolved following appropriate treatment. No pulmonary vein stenosis observed by echocardiography 3 months after the procedure. CPVA procedure for atrial fibrillation is effective and safe. Although there is difference between the CARTO and the EnSite/NavX system, the CPVA procedure guided by either of the systems yields similar results.		

*CPVA indicates circumferential pulmonary vein ablation; LV, left ventricular; RF, radiofrequency; SD, standard deviation; W, watts.
LA left atrial

LocaLisa Navigational System Versus Fluoroscopy

Four comparative studies on the LocaLisa navigational system (Metronic EP Systems, Minneapolis, MN, USA) were found. One study (41) was excluded because it is retrospective, and the report does not provide information on the participants, the arrhythmia, or duration of follow-up. The remaining 3 studies comprised 1 RCT on ablation of AFL and 2 non-RCTs on catheter ablation for AF.

Atrial Flutter

In an RCT Schneider et al. (42) compared the LocaLisa navigational system with fluoroscopy in ablation of AFL. They enrolled patients consecutively, used prospective randomization, and powered the study to measure a 40% reduction in fluoroscopy duration. Fifty patients with documented typical AFL were

randomly assigned to undergo isthmus ablation guided either by fluoroscopy (n = 24) or by LocaLisa (n = 26) (Table 14). Mapping was performed during spontaneous or induced AFL. Radiofrequency ablation was performed in both groups, and the end point for acute success was bidirectional isthmus block. For the fluoroscopy group, catheter manipulation and RF current deliveries were performed under guidance of the LocaLisa system without fluoroscopy. No patients were lost to follow-up.

Table 14: Characteristics of Study by Schneider et al.*

Type of arrhythmia	Atrial flutter	
Study design	Randomized controlled trial	
Definition of successful ablation	Bidirectional isthmus block	
Mean (SD) follow-up, months	6.2 (2)	
Mapping technique	**LocaLisa**	**Fluoroscopy**
Sample size	26	24
Mean (SD) age, years	64 (9)	65 (12)
Male, %	77	79
Mean left ventricular ejection fraction, %	n/r	n/r

*Schneider et al. (42); n/r. not reported

The difference in fluoroscopy time required for catheter deployment and diagnostics was not significantly between the 2 groups. However, the LocaLisa group showed a 40% reduction in fluoroscopy time compared with the fluoroscopy group during the ablation portion of the procedure. Total fluoroscopy time (7.5 minutes vs. 15.9 minutes for fluoroscopy, $P < .005$) and radiation dose (8.7 Gycm2 vs. 21 Gycm2 for fluoroscopy) were also significantly less in the LocaLisa group. The total procedure time and mean number of RF applications were not significantly different between groups. All patients in the 2 groups achieved bidirectional isthmus block and remained arrhythmia free without drug therapy during a mean follow-up of 6.2 (SD, 2) months (Table 15).

Table 15: Outcomes of Study by Schneider et al.*

	LocaLisa	**Fluoroscopy**
Type of Arrhythmia	AF	AF
Acute success, %	100	100
Recurrence during follow-up, %	0	0
Mean (SD) total procedure time, minutes	158 (60)	125 (48) P = NS
Mean (SD) total fluoroscopy time, minutes	7.5 (6.5)	15.9 (10.6) $P < .005$
Mean (SD) radiation dose (Gy cm^2)	8.7 (9.5)	21 (19.8) $P < .05$
Mean (SD) number of radiofrequency pulses	22 (15)	19 (15) P = NS
Procedure-related complications	Transient third-degree atrioventirucular block due to catheter dislocation in the LocaLisa group – resolved spontaneously.	

*Schneider et al. (42)

Atrial Fibrillation

Two non-RCTs that compared LocaLisa navigation with fluoroscopy navigation in catheter ablation of AF were found.

In a study by Macle et al., (43) 26 patients with symptomatic, drug-refractory paroxysmal AF underwent circumferential RF ablation around the PV ostium using a circular mapping catheter and guided by LocaLisa navigation. These patients were compared to 26 controls with similar demographic and clinical characteristics and had undergone catheter ablation using the same circular mapping catheter guided by fluoroscopy. Patient allocation to the study arms was based on patient preference. Successful ablation was defined as abolition or dissociation of PV potential in all PVs.

In another study, Wood et al. (44) compared 21 consecutive patients who underwent PV isolation using the LocaLisa navigation system to 11 patients who had undergone a similar ablation guided by fluoroscopy. All patients had a history of drug-refractory AF, and there were no significant demographic differences between the 2 groups. RF lesions were created at sites along the PV ostium that demonstrated PV potentials on a circular mapping catheter. The end point of the ablation was the complete elimination of PV potentials from all 4 PVs. Spiral chest CT was performed before and 3 months after ablation to monitor PV diameter. Patients were followed at 1 and 3 months, and then every 3 to 6 months after the ablation. Chronic success was defined as no recurrence of AF or a greater than 80% reduction in the frequency of AF episodes.

Characteristics of the 2 studies are summarized in Table 16.

Table 16: Characteristics of Studies Comparing LocaLisa-Guided and Fluoroscopy-Guided Ablation of Atrial Fibrillation*

	Macle et al., 2003 (43)		**Wood et al., 2004 (44)**	
Type of arrhythmia	Atrial fibrillation		Atrial fibrillation	
Study design	Nonrandomized controlled		Nonrandomized controlled	
Definition of successful ablation			Complete elimination of PV potentials from all 4 PV Chronic success: no AF recurrence or >/=80% reduction in frequency of AF	
Mean (SD) follow-up, months	4.6 (3.2)		7(4)	10 (4) *P* = .45
Mapping technique	LocaLisa	Fluoroscopy	LocaLisa	Fluoroscopy
Ablation strategy	RF Circumferential	RF Circumferential	RF PV isolation	RF PV isolation
Sample size	26	26	21	11
Mean (SD) age, years	52 (8)	53 (9)	54 (10)	53 (10) *P* = .82
Male, %	25/26	22/26	16/21	10/11 *P* = .31
Coronary artery disease	Structural heart disease HD 3/26	Structural heart disease 3/26	1/21	1/10
Paroxysmal AF			18/21	8/11
Mean (SD) duration of AF, years	7.1 (4.5)	6.0 (4.8)	6 (5)	5 (3) *P* = .45

*AF indicates atrial fibrillation; PV, pulmonary vein; RF, radiofrequency.

In both studies, PV disconnection was achieved in all PVs of patients in the LocaLisa and control group. Wood reported no statistically significant difference in total procedure time, but Macle et al reported a significantly shorter procedure time for the PV disconnection for individual PV or all PVs in the LocaLisa group. Both studies reported significantly shorter fluoroscopy time in the LocaLisa group, and both failed to detect any significant difference in long-term success. Macle et al reported that at a mean follow-up of

4.6 months, 73% of patients in the LocaLisa group versus 69% in the fluoroscopy group remained free of AF recurrence without antiarrhythmic drugs (*P* = .94). Wood reported that at follow-up (7 months for the LocaLisa group and 10 months for the control group), 81% of patients in the LocaLisa group had no or infrequent AF recurrences compared with 64% of control patients (*P* = .19). Of the patients that attained chronic success, 47% in the LocaLisa group and 43% in the control group remained on antiarrhythmic drugs. Macle et al did not report any complications and Wood et al. reported 1 case of pericardial tamponade and 1 case of pericardial effusion in the LocaLisa group, but none in the control group. (Table 17)

Table 17: Outcomes of Studies Comparing LocaLisa-Guided and Fluoroscopy-Guided Ablation for Atrial Fibrillation

	Macle et al., 2003 (43)		Wood et al., 2004 (44)	
Mapping technique	LocaLisa navigation	Fluoroscopy	LocaLisa navigation	Fluoroscopy
Acute success, %			100	100
AF free without drugs n/N n/N (%)	19/26 (73)	18/26 (69) *P* = .94	9/21	4/11
AF free with AAD n/N (%)	—	—	17/21 (81)	7/11(64) *P* = .19
Recurrence during follow-up (%)failure n/N	7/26	8/26	4/21	4/11
Mean (SD) total procedure time, minutes	PV disconnection 46.5 (12)	PV disconnection 66.3 (18.9) *P* < .0001	350 (64)	336 (82) *P* = .61
Mean (SD) total fluoroscopy time, minutes	8.4 (4.3)	23.7 (9.7) *P* < .0001	72 (29)	102 (37) *P* = .02
Mean (SD) number of radiofrequency pulses [			33 (17)	36 (20) *P* = .72
Mean (SD) duration of RF pulse (seconds)	34.8 (11.4)	38.2 (10.5) *P* = .28	—	—
Procedure-related Complications			2/21 pericardial tamponade, pericardial effusion	0 *P* = .42

Multielectrode Basket Catheter Mapping Versus Fluoroscopy

One RCT (45) was found that compared PV isolation using a multielectrode basket catheter (Polar Constellation, Boston Scientific, MA) and Astronoma navigation system with fluoroscopy ablation using a circular catheter (Lasso). Kumagai et al. (45) randomized 100 patients with symptomatic, drug-refractory paroxysmal AF either to the basket catheter group (n = 50) or to the fluoroscopy group (50). After ablation, patients received Warfarin for 3 months and follow-up with ECG and 24-hour Holter recordings at weekly then monthly intervals for 12 months. Three-dimensional CT was performed at 6 months and 1 year to assess PV stenosis. Success of the ablation was defined as the absence of clinical symptoms of AF without the need for antiarrhythmic drugs and documentation of stable sinus rhythm on 24-hour Holter monitoring (Table 18).

Table 18: Pulmonary Vein Isolation Guided by Basket Catheter System Compared With Fluoroscopy Circular Mapping

	Kumagai et al.,2005 (45)	
Sample size		100
Type of arrhythmia		Symptomatic drug-refractory atrial fibrillation
Mean (SD) follow-up, months		12
Study end point		Elimination of bidirectional pulmonary vein-LA conduction. [
Advanced mapping system	Basket catheter + astronoma navigation	Circular catheter with fluoroscopy navigation
Sample size	50	50
Ablation technique (RF)	Ostial pulmonary vein isolation	Pulmonary vein isolation
Mean (SD) age, years	57 (11)	58 (9)
Male, %	70	80
Structural heart disease %	4	4
Paroxysmal AF, %	100	100
Persistent AF, %	0	0
Mean (SD) duration of AF, years	69 (65)	89 (101) *P* = .5
Mean (SD) LVEF, %	65 (6)	66 (9) *P* = .8
Mean (SD) LA diameter, mm	38 (5)	40 (7) *P* =.2
Mean (SD) total procedure time, minutes	242 (70)	260 (71) NS
Mean (SD) total fluoroscopy time, minutes	69 (25)	86 (34) *P* < .01
AF free at follow-up without AAD, n/N (%)	40/50 (80)	31/50 (62)
AF free with or without AAD, n/N (%)	46/50 (92)	36/50 (72)

*AAD indicates antiarrhythmic drugs; AF, atrial fibrillation, LVEF, left ventricular ejection fraction; RF, radiofrequency. LA, left atrial

Table 19: Randomized Controlled Trial: Basket Catheter Compared With Fluoroscopy in Pulmonary Vein Isolation*

Study, Year	Sample size	Mean Follow-up, Months	Method of Ablation	AF free With or Without Drugs %	Long-Term Success		
					AF-Free Without Drugs %	AF-Free With Drugs, %	Failed (AF Recurrence),%
Kumagai et al., (45) 2005	100 Basket 50 50	12	PV Isolation	Basket catheter: 92 Circular catheter: 72	Basket catheter: 80 Circular catheter: 62 *P* < .05	Basket catheter: 12 Circular catheter: 10	Basket catheter: 8 Circular catheter: 28

*AF indicates atrial fibrillation; PV, pulmonary vein.

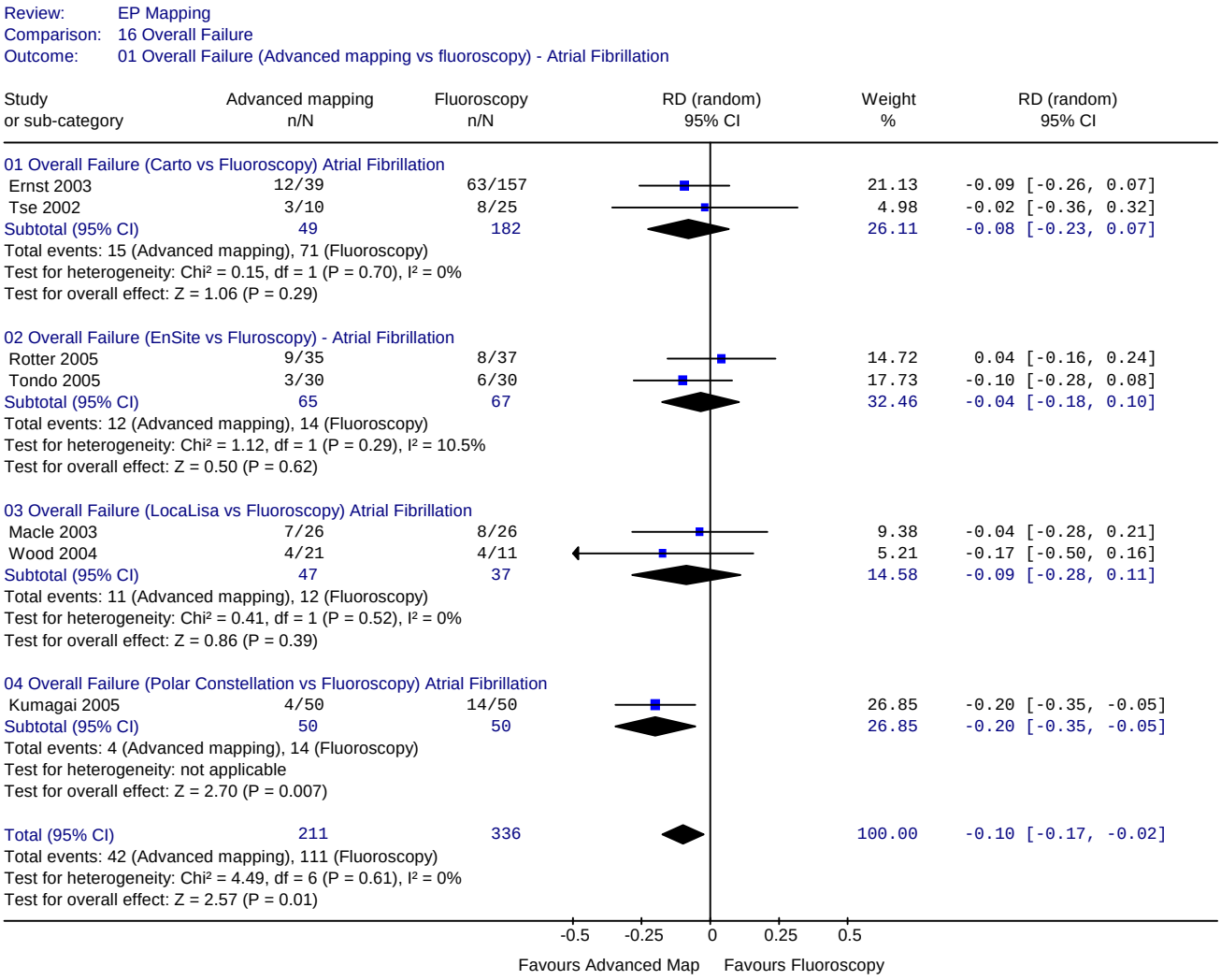
The results showed that nonfluoroscopy PV isolation using a multielectrode catheter and navigation system resulted in significantly reduced fluoroscopy time (Table 18). More patients in the fluoroscopy group had AF recurrence after the initial ablation compared with those in the basket catheter group (50% vs. 28%, *P* < .05), requiring repeat ablation in more patients (44% vs. 24%). At 12 month follow-up, the group that had had basket catheter mapping had significantly more patients that were AF-free without

antiarrhythmic drugs compared with the fluoroscopy group (80% vs. 62%, $P < .05$). Including patients who were AF-free with antiarrhythmic medication, the total AF-free rate was 92% in the basket catheter group and 72% in the fluoroscopy group. Pulmonary vein stenosis ($\leq$ 50%) was less frequent in the basket catheter group than in the fluoroscopy group (12% vs. 24%, $P < .01$). Other complications included 1 case each of pericardial effusion and unilateral quadrantopsia in the fluoroscopy group.

Meta-analysis: All Advanced Mapping versus Fluoroscopy Guidance – Ablation of Atrial Fibrillation

A pooled analysis was performed to compare the overall failure of AF ablation between all advanced mapping and fluoroscopy guidance. A Forest plot of the relative difference in overall failure rate showed that for 5 of the 7 studies there was a trend toward a lower failure rate for the advanced mapping system, but the difference did not reach statistical significance. For 1 study (38), the relative difference was 0.04 in favour of fluoroscopy, but this difference was not statistically significant either. Only 1 study (45) showed a 20% relative reduction in overall failure rate for the advanced mapping guided ablation compared with fluoroscopy-guided ablation (Relative difference –0.2, 95% CI –0.35, –0.5). This was statistically significant. A forest plot of all the studies comparing advanced mapping with fluoroscopy guidance in the ablation of AF showed no statistical heterogeneity and yielded a point estimate of -0.10 (95% CI, -0.17 to 0.02; $P = .01$), indicating that ablation guided by advanced mapping yielded an lower overall failure rate compared with fluoroscopy-guided ablation in people with AF. This result was mainly attributed to the Kumagai study. (45)

Figure 18: Forest Plot of Overall Failure of Advanced Mapping-Guided Versus Fluoroscopy-Guided Ablation of Atrial Fibrillation



Studies on Left Atrial Circumferential Pulmonary Vein Ablation Guided by an Advanced Mapping System

Because of the paucity of studies comparing ablation guided by advanced mapping with ablation guided by fluoroscopy, and given that advanced mapping systems are used most often in circumferential catheter ablation of PVs for the treatment of drug-refractory AF, it was decided to review RCTs and observational studies of these procedures in which an advanced mapping system was used. Seven studies were found that met previously reported inclusion criteria for observational studies on PV isolation. The characteristics of these studies and their subjects are summarized in Table 20.

Table 20: Studies on CARTO-Guided Circumferential Pulmonary Vein* Ablation

	Pappone et al., 2003 (46)	Kottkamp et al.,2004 (47)	Vasamreddy et al., 2005 (48)	Ouyang et al., 2004 (49)	Oral et al., 2004 (50)	Mansour et al., 2004 (51)	Arentz et al., 2005 (52)
Sample size	589	100	70	41	100	40	34
Paroxysmal/ persistent AF, %	69/0	80/20	30/31		100/0		100/0
Mean(SD) follow-up, months	29.5	12	6 (2.5)	6 (1)	8 (2)	11(3)	12
Study end point	No ECG confirmed symptomatic AF lasting > 10 min	% free of AF; time course & duration of AF pre & post procedure	Absence of symptomatic AF with no ADD after 1st month	PV isolation: elimination of spike potential	Noninducibility of AF without ADD	PV isolation & Free of AF at follow-up	Elimination of all PV potentials or sinus rhythm
Advanced mapping system	CARTO	CARTO	CARTO	CARTO	CARTO	CARTO	Constellation
Ablation technique	LACA around each PV ostium	LACA l + linear lesion connecting & to MiA	LACA+ linear lesions in CI, MiA & PLA	LACA around L & R PVs	LACA around L & R PVs + linear atrial lesions in 30 patients	LACA around L & R PVs +/- linear line to MiA	LACA around each PV ostium
Mean (SD) age, years	65 (9)	53 (10)	56 (10)	63 (9)	Range 54–56	55 (10)	52 (10)
Male, %	58	67	66	63 (9)	80	83	76
CAD	23	14		5/40	—		Structural HD 8/34
Mean (SD) duration of AF, years	5.5 (2.8)	7.3 (7)	9 (5.7)	7.6 (6.2)	Range 6–7	< 40% in 13% of patients	5.8 (3.2)
Mean (SD) LVEF, %	-	61 (7)	59 (10)		Range 53 –59		
Mean (SD) LA diameter, mm	-	40 (8)	43 (11)	42.6 (5.1)	Range 43–44	40.7 (4.1)	
Mean (SD) total procedure time, minutes	165 (22)	139 (31)	232 (60)		LACA: 169 (40) Linear: 25 (15)		273 (52)
Mean (SD) total fluoroscopy time, minutes	-	25 (10)			LACA 36 (11)		49 (17)
Mean (SD) RF time, minutes	59 (15)	35 (8)			LACA: 43 (10) Linear: 14 (12)	71.4 (26.6)	62 (22)

* AAD indicates antiarrhythmic drug; CI, cavotricuspid isthmus; LACA, left atrial circumferential ablation; MiA, mitral annulus; PAF, paroxysmal atrial fibrillation; PLA, posterior left atrium.

The 7 studies included 1 RCT (21) and 6 prospective observational studies. (46-49;51;52) Six of the studies were small, with circumferential PV ablation performed in 34 to 100 patients and a follow-up period ranging from 6 months to 1 year. The study by Pappone et al. (46) was the largest, comparing circumferential PV ablation performed in 589 patients to 582 medically treated controls with a mean follow-up period of 29.5 months. Six of the studies used CARTO to guide the circumferential PV ablation, and 1 study used the Constellation multielectrode basket catheter in conjunction with the Astronoma navigation system.

One (46) of the 7 studies compared circumferential PV ablation with medical therapy; 1 study (21;51) compared circumferential PV ablation with segmental PV isolation, and the remaining 5 studies (47-50;52) were studies on left atrial circumferential ablation alone.

The studies by Pappone (46) and Vasamreddy (48) included patients with any kind of AF, while Kottkamp et al. (47) and Mansour et al. (51) included paroxysmal and persistent AF. Ouyang (49) Oral et al., (50) and Arentz et al. (52) included only paroxysmal AF.

There were some variations in the ablation procedure among the studies. Pappone et al.and Arentz et al. created lesions to encircle each PV while the other studies had a lesion that encircled all right-sided PVs and another that encircled all left-sided PVs. The ablation in some studies also included linear lesions in the left atria in addition to the circular lesions around the PVs. (21;47;48;50;53) After initial left atrial circumferential ablation with lesions encircling the left and right PVs, Oral et al. randomized patients with inducible AF to either no further ablation or further ablation with additional linear atrial ablation along the left atrial septum, roof, and/or anterior wall where there were fractionated electrograms.

Table 21: Clinical Outcomes of Observational Studies on Circumferential Pulmonary Vein Ablation Guided by an Advanced Mapping System*

Study, Year	Sample Size (Using CARTO)	Mean Follow-up, Months	AF Free With or Without Drugs n/N (%)	Long-Term Success			Reduction in Risk of Death vs. Medical Therapy Alone
				AF-Free Without Drugs, n/N (%)	AF-Free With Drugs, n/N (%)	Failed (AF Recurrence), n/N (%)	
Pappone et al., 2003 (54)	589	28	469/589 (80)				↓54% (38/589 vs. 83/582) (P < .001)
Kottkamp et al., 2004 (47)	100	12	78/100 (78)	47/100 (47)	31/100 (31)	22/100 (22)	
Vasamreddy et al., 2005 (48)	70	6 (SD, 2.5)	53/70 (76)	39/70 (56)	14/70 (20)	17/70 (24)	
Ouyang et al., 2004 (49)	41	6	≥ 39/41 (95)	39/41 (95)	n/r	n/r	
Oral et al., 2004 (50)	100	6	n/r	80/100 (80)	n/r	n/r	
Mansour et al., 2004 (51)	40	11(SD, 3)	30/40 (75)	25/40 (63)	5/40 (12)	10/40 (25)	
Arentz et al., 2005(52)	34	12	29/34 (86)	21/34 (62)	8/34 (24)	5/34 (14)	

*AF indicates atrial fibrillation. n/r Not reported

Across studies, total procedure time ranged from 139 minutes to 273 minutes, and mean fluoroscopy time ranged from 25 minutes to 49 minutes (Table 20). There was a wide variation in the total RF time (35 minutes –71 minutes). The clinical outcomes are summarized in Table 21. The studies showed that circumferential PV ablation guided by a non-fluoroscopic electroanatomic mapping system resulted in an AF-free rate (with or without antiarrhythmic drugs) of 75% to 95% at follow-up ranging from 6 months to 1 year. At the longest follow-up of 29.5 months, the AF-free rate obtained by Pappone et al. was 80%. Kaplan-Meier analysis yielded freedom from AF recurrence in 84%, 79%, and 78% of patients at 1, 2, and 3 years respectively after circumferential PV ablation, compared with 61%, 47%, and 37% using medical therapy. Without antiarrhythmic drugs, the AF-free rate ranged from 47% to 95% (Table 15). Pappone et al. reported that circumferential PV ablation was effective in paroxysmal and chronic AF, and resulted in a 54% relative risk reduction in all-cause mortality compared with medical therapy (6% vs. 14%, $P < .001$), mainly due to a reduction in heart failure and ischemic stroke.

Oral et al. showed that in patients who still had inducible AF after left atrial circumferential ablation, 90% was rendered noninducible by additional linear atrial ablation at sites of fractionated electrograms. The noninducibility of AF attained might be associated with better midterm clinical outcomes compared to inducible AF after circumferential ablation alone.

Quality of Life

In the study by Pappone et al, (46) the ablation and the medically treated groups rated their baseline health status similarly and lower than people of the same sex in the general Italian population ($P < .001$). A significant time trend ($P = .007$) over 1 year was detected only in the patients that had received ablation ($P = .004$) who reached normative levels at 6 month, with no further changes at 1 year.

Safety

Complications of nonfluoroscopy-guided catheter ablation versus fluoroscopy-guided ablation are summarized in Table 22.

Table 22: Comparing Complications: Nonfluoroscopy–Guided and Fluoroscopy-Guided Ablation

Study	Arrhythmia	Nonfluoroscopy System	Complications in Nonfluoroscopy Group		Complications in Fluoroscopy Group	
			Total Rate, %	Type & Number of Complications	Total Rate, %	Type of Complication
Tse et al., 2002 (31)	AF	CARTO	0	—	4	PV ostium stenosis
Ernst et al., 2003(32)	AF	CARTO	2.5	Total PV occlusion	0.06	Severe PV stenosis
Willems et al., 2000 (37)	AFL	CARTO	NA		NA	
Kottkamp et al., 2000(36)	AFL	CARTO	0		0	
Sporton et al., 2004(30)	AFL	CARTO	0		0	
Leonnelli et al., 2002(33)	AFL	CARTO	0		0	
Khongphatthanayothin et al., 2000(34)		CARTO				

			Complications in Nonfluoroscopy Group		Complications in Fluoroscopy Group	
Delacretaz et al., 2001(35)	AFL	CARTO	0		0	
Sporton et al., 2004 (30)	VT	CARTO	0		1/7	Cardiac tamponade
Khongphatthanay othin 2000 (34)	VT	CARTO	6 (1/17)	Cardiac tamponade	1/7	Cardiac tamponade
Rotter 2004 (38)	AF	EnSite NavX	0		0	
Tondo et al., 2005 (39)	AF	EnSite NavX	0		0	
Ventura et al., 2004 (27)	AFL	EnSite NavX	4 pts	Paroxysmal AF	0	
Liu et al., 2005 (25)	AF	CARTO EnSite NavX	5.7 5	1 pericardial effusion 1 suspected intestinal artery thrombosis 1 pneumothorax 1 atypical AFL	-	-
Gurevitz et al., 2005(40)	AF	CARTO & EnSite NavX	7	2 pericardial effusion 1 femoral pseudo aneurysm 1 severe nose bleed & hypoxia 1 hypotension		
Wood et al., 2004 (44)	AF	LocaLisa	9.5	2/21 Pericardial temponade	0	
Schneider et al., 2003(42)	AFL	LocaLisa	NA		NA	

*AF indicates atrial fibrillation; AFL, atrial flutter; PV, pulmonary vein; VT, ventricular tachycardia

With the exception of the studies by Gurevitz et al. and Wood, procedure-related complication rates ranged from 0% to 6% for nonfluoroscopy-guided ablation and were not significantly different from those of fluoroscopy-guided ablations. Only 1 study on ablation of AFL reported complications. Most of the complications were associated with ablation for AF (PV ablation) and ventricular tachycardia. With AF ablation, the most common complication was PV stenosis. The study by Gurevitz et al. reported higher complication rates probably because the subjects had more complex arrhythmias that had already failed an initial fluoroscopy ablation.

Table 23: Procedure-Related Complications of Circumferential Pulmonary Vein Ablation Guided by an Advanced Mapping System (Not Compared With Fluoroscopy)*

Study, Year	Patients With Adverse Events, n/N (%)	PV Stenosis (> 50%), N (%)	Cardiac Tamponade / MI, N (%)	Stroke/TIA N (%)	Congestive Heart Failure N (%)	Others N (%)
Pappone et al., 2003 (46)	46/589 (8)	0	MI 7 (1.2) Tamponade 4 (0.7)	6 & 8 (2.4)	32 (5.4)	1
Kottkamp et al., 2004 (47)	4/100 (4)	0	0	0	0	0
Vasamreddy, 2005 (48)	4/70 (5.7)	2 (2.8)	1 (1.4)	1 (1.4)	0	0
Ouyang et al., 2004 (55)	3/41 (7)	1 (2)	0	0	0	2 noninfectious pericarditis
Oral et al., 2004 (50)	-	-	-	-	-	-
Mansour et al., 2004 (51)	4/40 (10)	0	1 (2.5) cardiac tamponade	1 (2.5)	0	2 (5) femoral vascular complications
Arentz et al., 2005 (52)	1/34 (3)	0	0	1 (3)	0	

*MI indicates myocardial infarction; PV, pulmonary vein; TIA, transient ischemic attack.

In the studies that examined circumferential PV ablation guided by an advanced mapping system (Table 23), the rate of adverse events ranged from 4% to 10%. Pappone et al reported that the rate of adverse events was lower in the ablation group compared with that in the medically treated group (8% vs.19%, respectively). Among the studies, the most frequent complications were stroke/transient ischemic event, myocardial infarction, and cardiac tamponade. Pulmonary vein stenosis, a common complication of focal PV ablation was reported in 2 of the 6 studies (2% and 2.8%) but few patients had symptoms or required treatment. For the largest series, Pappone et al. reported no occurrence of PV stenosis. They attributed this to deployment of the lesion line at more than 5 mm apart from each nearby PV ostium. Only Pappone et al. reported heart failure during follow-up (5.4%). In addition to the above adverse events, Kottkamp et al. reported the development of AFL in 5% of patients, and Oral et al. reported it in 21%, the majority (71%) resolved without ablation within 6 months. Pappone et al. reported incisional atrial tachycardia as the most frequent complication. It was treated by a repeat procedure. Although none was reported in the above studies, atrio-esophageal fistula following transcatheter ablation of AF had been reported. (56;57) Pappone et al (56) reported two patients who suffered gaseous and/or septic emboic events causing cerebral and myocardial damage attributed to an atrio esophageal fistula after undergoing circumferential pulmonary vein ablation. One of these cases was fatal. A single case had also been reported by Scanavacca et al. (57) and Sonmez et al. (58)It should be noted that this complication is not related to the use of the advanced mapping systems. Pappone et al (56) suggested that atrial esophageal fistula may be preventable by using lower power and temperature settings for applications of radiofrequency energy along the posterior left atrial wall.

Reduction in Radiation Exposure

According to the studies included in this health technology policy assessment, all nonfluoroscopy systems achieved statistically significant reductions in exposure to fluoroscopy. The reduction in fluoroscopy duration ranged from 32% to 85% with a median of 61%. The absolute reduction in fluoroscopy duration ranged from 10 minutes to 36 minutes with a median of 23 minutes.

Risk Associated With Fluoroscopy-Guided Mapping/Ablation

One of the risks of conventional mapping and ablation procedures arises from patients' prolonged exposure to ionizing radiation in the form of X-ray fluoroscopy. Moreover, medical personnel involved in the procedure are exposed to scattered radiation.

Effects of ionizing radiation are generally categorized as one of the following:

- Deterministic effect: This refers to an effect for which there is a threshold dose. The probability of such effects increases rapidly as the dose exceeds the threshold (e.g., erythema to the skin, sterility, and cataracts) (Table 24).

Table 24: Threshold Doses for Deterministic Effects to Skin*

Effect	Acute Dose Threshold (Gy)	Chronic Dose Threshold (Gy)	Time to Effect
Early transient erythema	2	—	Hours
Main erythema	6–8	30	3–6 weeks
Moist desquamation	10	—	4–6 weeks
Dermal necrosis	18	—	> 10 weeks
Dermal atrophy	—	35–40	14–20 weeks
Telangiectasia	—	40	> 1 year

*International Commission on Radiological Protection and the National Radiological Protection Board (United Kingdom)

Reproduced from the British Journal of Radiology, with permission from the British Institute of Radiology; McFadden SL, Mooney RB, Shepherd PH. X-ray dose and associated risks from radiofrequency catheter ablation procedures. Br J Radiol 2002; 75(891): 253-265

- Stochastic effects: Effects for which it is assumed that there is no threshold dose. These include malignant diseases and inherited defects in later generations. (59)

The thresholds for radiation doses recommended by the International Commission on Radiation Protection and National Commission on Radiation Protection (United Kingdom) are shown in Table 25.

Table 25: Recommended Limit for Annual Equivalent Radiation Doses*

	International Commission on Radiation Protection	National Commission on Radiation Protection
Skin, hands, and feet, mSv	500	—
Ocular lens, mSv	150	—
Head and trunk, mSv	—	50

*MSv indicates milli Sievert.

The risk of these deterministic and stochastic effects from X-ray exposure during mapping and catheter ablation were explored in 7 observational studies that are summarized in Appendix 8. (59-65) In these

studies, radiation exposure to patients and operators during EP studies and ablation procedures was measured using a thermoluminescent dosimeter and expressed as effective dose, mean skin dose, and/or dose area product. Based on the radiation dose, the risk of fatal malignancies was estimated in 3 studies, and genetic birth defects and skin injury in 3 studies.

Risk of Radiation Exposure to Patients

The sample sizes of the 7 observational studies (Appendix 8) ranged from 15 to 859. Fluoroscopy-guided ablation was performed in patients with Wolf Parkinson White Syndrome, re-entrant atrial tachycardia, AFL and ventricular tachycardia, or AF. Mean fluoroscopy time for AFL, AVNRT, and accessory pathways ranged from 20 to 67 minutes. The mean fluoroscopy duration for the ablation of AF ranged from 57 minutes to 129 minutes. Lickfett et al. (65) reported that the mean peak skin radiation dose in ablation of AF was at least 3-fold greater than in ablation of AFL and AVNRT.

Based on the mean radiation dose measured, the estimated lifelong risk of fatal malignancies from radiation exposure during an ablation procedure ranged from 0.7 per 1,000 patients to 1.3 per 1,000 patients. These were about 0.1% of the incidence of fatal malignancies in the general population. Rosenthal et al. (63) estimated the risk to be 1.4 per 1,000 females and 2.6 per 1,000 males. Similarly, Lickfett et al. estimated the incidence of fatal malignancies due to radiation exposure during PV ablation to be 1.5 per 1,000 females and 2.1 per 1,000 males. However, the estimated risk of fatal malignancies based on the maximum radiation exposure in one of the studies was 5 times higher (1 in 200 people). (59)

Calkins et al. (60) estimated the risk of genetic birth defects due to radiation exposure during ablation procedures as 20 per million births. Lindsay et al. estimated the risk of serious birth defects to be 12 per million births, about 0.1% of the incidence of birth defects in the general American population.

The proportion of adult patients in 3 studies who were found to have exceeded the radiation threshold for early radiation skin injury was 5.6 %, (66) 12% , (59) and 22%. (63) Rosenthal et al. (63) reported that 5% of 859 patients in their study had more than 2 hours of radiation exposure, and 1% exceeded the threshold dose needed to cause permanent destruction of the epithelium. However, no radiation skin injuries were reported in any of the studies.

Most studies concluded that the risks from radiation are low but should not be ignored. Patients who undergo catheter ablation for the treatment of AF are of particular concern because of the prolonged exposure to x-ray and the frequent need for reablation. All studies agreed that steps should be taken to minimize radiation exposure. These include reducing fluoroscopy time, using low-frame pulse fluoroscopy systems, using a lead glass shield between the patient and the operator, and using nonfluoroscopy mapping systems. (64;65)

Reported Radiation Skin Injury

Between January 1992 and October 1995, the United States Food and Drug Administration (FDA) received 26 reports of skin injury from fluoroscopy. Of these, 12 (46%) reports were related to injuries sustained from radiation exposure during RF cardiac catheter ablation. The injuries included skin breakdown, a second-degree skin burn, and a draining skin lesion. (67)

In September 1994, the FDA issued a public health advisory for avoiding serious X-ray-induced skin injuries to patients during fluoroscopically guided procedures including radiofrequency cardiac catheter ablation. The advisory cautioned that although the absorbed dose rate in the skin from a direct beam of a fluoroscopic X-ray system is typically between 0.02 Gy/minute and 0.05 Gy/minute, the actual dose may be higher, depending on the mode in which the equipment is operated and the size of the patient. The

advisory further indicates that even typical dose rates can result in skin injury after less than 1 hour of fluoroscopy. (FDA Public Health Advisory: Avoidance of Serious X-ray Induced Skin Injuries to Patients During fluoroscopy-Guided Procedures, September 30, 1994. (68)

The advisory suggests that facilities performing fluoroscopy-guided procedures observe the following principles:

- Establish standard operating procedures and clinical protocols for each specific type of procedure performed.
- Know the radiation dose rates (derived from measurements at the facility) for specific fluoroscopic systems and for each mode of operation used during the clinical protocol.
- Modify the protocol, such as using equipment as appropriate to limit the cumulative absorbed dose to any irradiated area of the skin to the minimum necessary for clinical tasks, particularly to avoid approaching cumulative doses that would induce unacceptable adverse effects.
- Enlist a qualified medical physicist to assist in implementing these principles in such a manner so as not to adversely affect the clinical objectives of the procedure.
- Note potential for injury in the patient's medical record for any procedure the facility determines could result in a cumulative absorbed dose in a specific area of skin equal to or greater than 1 Gy (100 rad).

Risk of Fluoroscopic Radiation Exposure to Operators

Radiation exposure to operators during catheter ablation was addressed in 4 studies. (59-61;64) All concluded that the radiation exposure received by medical personnel performing the ablation procedures is well below the limit established by the International Radiation Protection Commission.

Calkins et al. (60) determined that, based on radiation exposure to the head of the operator, the number of ablation procedures that would reach the radiation limit set by the International Radiation Protection Commission is 14 per month. Based on exposure to the hand, the number of procedures is 42 per month.

Lindsay et al. (61) determined that the effective radiation dose received by the physician was about 1.8 mrem per case. They further concluded that with the use of a lead collar and apron, the annual radiation exposure to the physician for 250 procedures would be equivalent to 9% of the recommended annual limit of 5 rem. The assisting personnel would receive an annual radiation dose equivalent to 5% of the recommended limit.

McFadden et al. (59) reported that the radiation exposure of the physician performing catheter ablation of arrhythmias was less than 0.15 mSv per month. The annual equivalent dose to the lens of the eye was 3.6 mV (allowed limit 150 mSv) and to the skin of the hand was 28.8 mSv (allowed limit 500 mSv).

Macle et al. (64) determined that the median radiation exposure to the physician for PV ablation was 66 uSv outside the collar, and 27 uSv in the waist level on the outside. The study also showed that the nurse assisting with the procedure received a median radiation exposure of 13 to 18 uSv in the mid-thorax on the outside. Macle et al. concluded that, even assuming 300 ablation procedures were performed annually, the radiation exposure to the physician would be below the recommended upper limit of the annual radiation dose.

Expert Opinion Regarding Risk of Radiation

An expert consultant advised the Medical Advisory Secretariat that the risk of radiation exposure has been reduced with the use of pulsed fluoroscopy and proper shielding. (Personal communications)

Emerging Techniques for Catheter Ablation of Complex Arrhythmias

Vagal ganglia ablation: Pappone et al. (69) abolished all evoked vagal reflexes around all PV ostia (complete vagal nerve denervation) in 34.3% of 297 patients undergoing circumferential PV ablation for paroxysmal AF to explore the role of vagal ganglia ablation in the treatment of AF. At 12-month follow-up, patients with reflexes and complete vagal denervation were less likely to have recurrent AF than those without reflexes. Multivariate analysis showed a large percentage of left atrial isolation and complete vagal denervation as independent predictors of AF recurrence. The authors suggested that complete vagal denervation adjunctive to circumferential PV ablation for paroxysmal AF confers added benefit in reducing AF recurrence.

Balloon catheter: Natale et al. (70) conducted a small study of 15 people on the feasibility and safety of a novel catheter for circumferential ultrasound ablation of AF. The system consists of an ultrasound transducer mounted at the tip of a catheter in a saline-filled balloon. The results were promising, but no further studies were found. (71)

Three-dimensional mapping systems: These, such as the CARTOMerge and the NavX DIF (Digital Image Fusion), are being developed to import MRI or CT images of the left atrium and PVs and navigate on real anatomy acquired, with simultaneous display of voltage and activation map. These new systems are designed to enhance the accuracy of and provide greater visual details of the anatomy. (54)

Emerging stereotaxis technology: This enables remote control of the mapping/ablation catheter on a variety of mapping systems. This robotic navigation system is intended to reduce the risk of major complications in the mapping and ablation of complex arrhythmias. It uses a fixed magnet to steer the tip of the catheter or wire and a catheter advancer system to advance and retract the catheter. An external magnetic field of a specified direction and magnitude is used to orient the tiny magnet in the tip of the catheter without pull or push effect. Other features in development include target navigation and semiautomatic electroanatomic map generation. (54)

Summary of Findings

- Evidence is based on a few small RCTS and non-RCTS that have flawed methods.
- Advanced nonfluoroscopy mapping/navigation systems appear to be safe; moreover, studies showed they consistently shortened the duration of fluoroscopy and radiation exposure.

- Advanced nonfluoroscopy mapping/navigation systems provide real time 3-dimensional images with integration of anatomic and electrical potential information that enables better visualization of the areas of interest for ablation
- Evidence suggests that nonfluoroscopy mapping and navigation systems may be used as adjuncts to rather than replacements for fluoroscopy in guiding the ablation of complex arrhythmias.
- Most studies showed a nonsignificant trend for a lower overall failure rate for advanced mapping-guided ablation compared with fluoroscopy-guided mapping.
- Pooled analyses of small RCTs and non-RCTs that compared fluoroscopy with nonfluoroscopy-guided ablation of AF and AFL suggest that advanced nonfluoroscopy mapping and navigational systems:

    - Yielded acute success rates of 69% to 100%, which is not significantly different from fluoroscopy ablation.
    - Had overall failure rates of 1% to 40% (median, 25%) at 3 to 19 months.

- Resulted in a 10% relative reduction in overall failure rate for advanced mapping guided-ablation compared with fluoroscopy-guided ablation for the treatment of AF.
- Yielded added benefit over fluoroscopy in guiding the ablation of complex arrhythmia. The advanced systems were shown to reduce the arrhythmia burden and the need for antiarrhythmic drugs in patients with complex arrhythmia for whom fluoroscopy-guided ablation had failed.

- Based on mostly observational studies, circumferential PV ablation guided by a nonfluoroscopy system was shown to do the following:

  - Result in freedom from AF (with or without antiarrhythmic drugs) in 75% to 95% of patients (median, 79%). This effect was maintained up to 28 months.
  - Result in freedom from AF without antiarrhythmic drugs in 47% to 95% of patients (median, 63%).
  - Improve patient survival at 28 months after the procedure compared with drug therapy.
  - Require special skills – patient outcomes are operator dependent, and there is a significant learning curve effect.

- Complication rates of PV ablation guided by an advanced mapping/navigation system ranged from 0% to 10% with a median of 6% during a follow-up period of 6 to 29 months.
- The complication rate of the study with the longest follow-up (28 months) was 8%.
- The most common complications of advanced catheter-guided ablation were stroke, transient ischemic attack, cardiac tamponade, myocardial infarction, AFL, congestive heart failure, and PV stenosis.

Limitations of Quality of Evidence

The quality of the studies ranged from moderate to poor. Most of the RCTs did not provide details on method of randomization and concealment, or do a power calculation. All studies had small sample sizes and thus likely not adequately powered to detect a difference in patient outcomes should one have existed. Blinding of the operator was not feasible, and there was no blinding of patients nor assessors reported in any of the studies. With the exception of 1 observational study, follow-up was short – generally under 2 years in most studies.

There was heterogeneity among the studies with respect to the following:

- Type of arrhythmias included – most the studies included paroxysmal AF, but some also included persistent and permanent AF.
- Duration of AF – Duration varied from months to years. Studies suggest that response to treatment decreases with duration of AF.
- Number of failed attempts at drug therapy – Some studies stipulate a that patients had to have failed a number of drug therapy attempts, ranging from 2 to 3 drugs.
- Presence of structural heart disease – Ablation is more difficult with the presence of structural heart disease. The proportion of patients with structural heart disease varied from study to study.
- Type of advanced mapping systems used -
  - Ablation procedure – A number of procedures were used for the ablation of PVs in people with AF. Some studies used lesions that encircled each PV ostium, while others used lesions that encircled a pair of PV ostium. Various types of additional linear lesions were also used in some of the studies.
- Definition of success – Some defined success as being arrhythmia-free without drugs, while others defined success as no significant AF.
- Anticoagulation therapy after ablation.

Indications for Atrial Fibrillation

The recommended uses of advanced nonfluoroscopic mapping systems have been summarized by Dr. Paul Friedman (22) and corroborated by expert consultants to the Medical Advisory Secretariat (Personal communications, November 24, 2005) (Table 26).

Table 26: Role of Advanced Mapping Systems Based on Arrhythmia*

Limited role for advanced mapping (high conventional success rate)	Advanced mapping shortens procedure, limits fluoroscopy, or enhances success	Advanced mapping extremely helpful or essential
AVNRT	Typical atrial flutter	Macro re-entrant atrial arrhythmias after surgical correction of congenital heart disease
Accessory pathway ablations	Idiopathic ventricular tachycardia (RVOT, LVOT, fascicular VT)	Transient/multiple focal atrial tachycardia
Atrioventricular junction ablations for rate control in atrial fibrillation	Repeat ablation after previously failed attempt	Atrial fibrillation; linear lesion for atrial compartmentalization procedure; also useful, but role less defined for encircling pulmonary vein isolation and non-pulmonary focal localization.
	Hemodynamically stable VT (nonidiopathic)	Hemodynamically unstable VT

*Friedman; (22) AVNRT indicates atrial ventricular nodal re-entrant tachycardia; VT, ventricular tachycardia; RVOT, right ventricular outflow tract tachycardia; LVOT, left ventricular outflow tract tachycardia.

Patient Selection for AF Catheter Ablation

There is no unanimous agreement among experts regarding the criteria for selecting patients for AF ablation. The following are factors often considered when determining whether a patient is a suitable candidate for catheter ablation of AF:

- Age: Pappone et al. (46) reported that age greater than 65 years was independently associated with a higher risk of dying after circumferential atrial catheter ablation for AF. The mean age of patients in the studies reviewed was mostly under 70 years.
- Type of AF: Some studies showed better AF-free rates in paroxysmal AF than persistent or permanent AF. However, Pappone et al. (46) showed that circumferential atrial ablation was effective in all 3 types of AF.
- Response to drug therapy: Most studies included subjects that had failed to respond to more than 1 antiarrhythmic drug.
- Symptoms of AF: Some studies stipulated that patients had to be symptomatic to be eligible.
- Comorbid conditions: History of ischemic heart disease was an independent predictor of death. Other contraindicated conditions are cardiac thrombus, thyroid dysfunction, and a history of stroke. (46)
- Functional status: Pappone et al. (46) excluded patients with New York Heart Association functional class IV.
- Left ventricular function: Left ventricular ejection fraction less than 45% was an independent predictor of death.

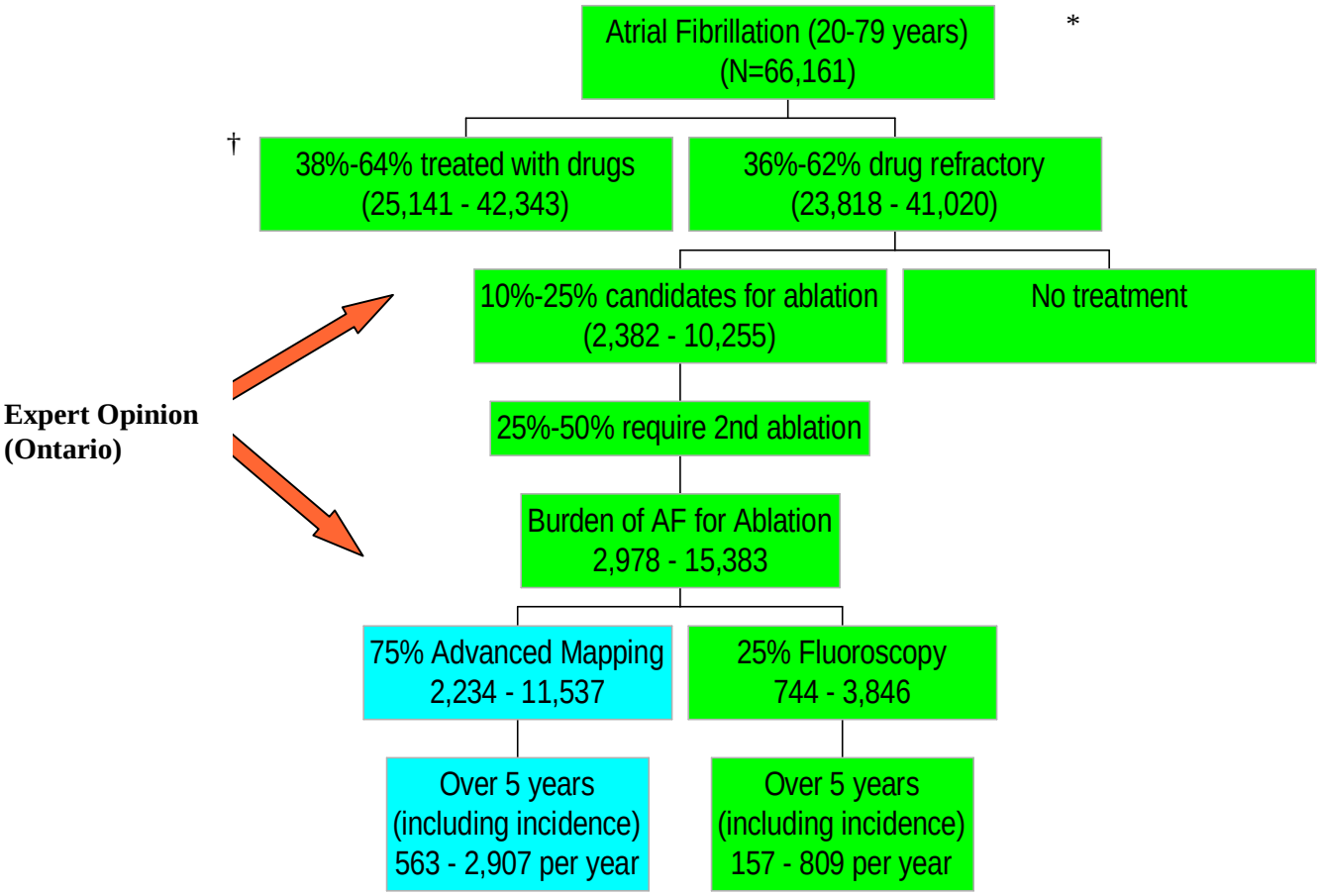
- Size of the atrium: An enlarged atrium has been shown to predict outcomes after catheter ablation in patients with AF. Some studies (46) stipulate that the left atrium should be less than 5.0 cm.
- Size of left ventricle: A left ventricular mass index greater than 125g/m^2 was an independent predictor of death. (46)

Estimated Need for Catheter Ablation Guided by Advanced Mapping in Ontario

People with AF comprise the largest group of patients requiring advanced mapping in catheter ablation procedures. Because catheter ablation is rarely performed in people aged over 80 years, the prevalence of patients (aged 20–79 years) with AF requiring catheter ablation was estimated in another systematic review conducted by the Medical Advisory Secretariat (link to report on Catheter Ablation). By applying the American overall prevalence rate of 0.95% (1) and response rate to drug therapy (34% to 68%) (2) to the Ontario population, it was estimated that about 23,818 to 41,020 people aged 20–79 years with AF would be refractory to antiarrhythmic drugs. Experts estimated that 10% to 25% of these people would be candidates for catheter ablation, and that 25% to 50% would require a second ablation, (72) bringing the need for catheter ablation based on total prevalence to about 3,000 to 15,300.

According to the experts, about 75% (2,234–11,537) of these ablations require guidance of advanced mapping. The annual incidence of AF in people aged 20-79 years was estimated to be 116 to 600 (from data in the Go 2001 study (1)). Assuming that need based on prevalence is addressed over 5 years, the annual need for advanced mapping-guided ablations of AF, which includes the incident cases, would be 563 to 2,907 (Figure 18). Total need might be higher because of other indications such as ventricular tachycardia and arrhythmia in postsurgical repair of congenital heart disease.

Figure 18: Need for Advanced Mapping Systems in Ontario Based on Prevalence and Incidence of Atrial Fibrillation



* Go et al. 2001(1);
† Wyse, 2002 (2).

Economic Analysis

Summary of Literature Review on Economic Analysis

Medical treatment (anticoagulants) compared with no treatment

Desbiens et al (73) found that Warfarin treatment is cost saving (i.e., more effective and less costly) than no treatment in younger populations that do not have comorbid conditions. In older populations that have comorbid conditions, it costs less than $30,000 (US) per quality adjusted life year.

Catheter ablation techniques (fluoroscopy and advanced mapping procedures) compared with medical treatment (anticoagulants and antiarrhythmics)

In general, studies (74-76) reported either that catheter ablation is cost saving or highly cost-effective compared with medical management. Cheng et al., (74) found that catheter ablation was cost saving compared with drug therapy in patient with severe ventricular tachycardia. Hogenhuis et al. (75) also found that catheter ablation was cost saving compared with drugs and open surgical ablation in survivors of cardiac arrest with symptomatic Wolf-Parkinson-White syndrome, but that it did not have a favourable cost-effectiveness profile for people with asymptomatic Wolf-Parkinson-White syndrome. Calkins et al (76) observed that catheter ablation had a cost-effectiveness of less than $33,000 (Cdn) per quality adjusted life year for people with both ventricular tachycardia and pre-existing ischemic coronary disease.

Ontario-Based Economic Analysis

Notes & Disclaimer

The Medical Advisory Secretariat uses a standardized costing methodology for all of its economic analyses of technologies. The main cost categories and the associated methodology from the province's perspective are as follows:

Hospital: Ontario Case Costing Initiative (OCCI) cost data is used for all program costs when there are 10 or more hospital separations, or one-third or more of hospital separations in the ministry's data warehouse are for the designated International Classification of Diseases-10 diagnosis codes and Canadian Classification of Health Interventions procedure codes. Where appropriate, costs are adjusted for hospital-specific or peer-specific effects. In cases where the technology under review falls outside the hospitals that report to the OCCI, PAC-10 weights converted into monetary units are used. Adjustments may need to be made to ensure the relevant case mix group is reflective of the diagnosis and procedures under consideration. Due to the difficulties of estimating indirect costs in hospitals associated with a particular diagnosis or procedure, the Medical Advisory Secretariat normally defaults to considering direct treatment costs only. Historical costs have been adjusted upward by 3% per annum, representing a 5% inflation rate assumption less a 2% implicit expectation of efficiency gains by hospitals.

Non-Hospital: These include physician services costs obtained from the Provider Services Branch of the Ontario Ministry of Health and Long-Term Care, device costs from the perspective of local health care institutions, and drug costs from the Ontario Drug Benefit formulary list price.

Discounting: For all cost-effective analyses, discount rates of 5% and 3% are used as per the Canadian Coordinating Office for Health Technology Assessment and the Washington Panel of Cost-Effectiveness, respectively.

Downstream cost savings: All cost avoidance and cost savings are based on assumptions of utilization, care patterns, funding, and other factors. These may or may not be realized by the system or individual institutions.

In cases where a deviation from this standard is used, an explanation has been given as to the reasons, the assumptions and the revised approach.

The economic analysis represents an estimate only, based on assumptions and costing methods that have been explicitly stated above. These estimates will change if different assumptions and costing methods are applied for the purpose of developing implementation plans for the technology.

Budget Impact Analysis

Hospitalization Costs

The Ontario Case Costing Initiative (OCCI) cost per hospitalization for mapping and ablation during fiscal year (FY) 2003 was $5,608 (Cdn).[1] This is the most current available cost data. Adjusting this cost by 3% per annum to reflect FY 2004 expected costs produced a cost estimate of $5,776 (Cdn). Since there

[1] (Search criteria: most responsible ICD-10 diagnosis code of I48.0 (atrial fibrillation) combined with a Canadian Classification of Health Interventions (CCI) principal procedure code of 1.HH.59.GP-AW.

is no separate procedure code for advanced mapping techniques, this cost estimate should be considered as a mean cost over all mapping techniques.

Based on data in the hospital discharge database for Ontario, there were 365 unique hospital separations for AF with a catheter procedure performed during FY 2004. Therefore, the total annual cost during FY 2004 of hospitalization associated with these mapping procedures was $2.1 million.

Physician Costs

Estimated first-year professional costs of $3,815 (Cdn) per treated patient are based on the numbers and calculations in Tables 27 A to C.

Table 27: Professional Costs Associated With EP Study and Ablation of Atrial Fibrillation

Source: Ontario Ministry of Health and Long-term Care - Physician Schedule of Benefits 2003
(Totals Adjusted by 2% to Reflect Latest OMA Agreement)

			Value Used in Calculation		
A. Advanced Mapping Procedure Fees	**Rate (Cdn)**	**Minimum (Cdn)**	**Minimum (Cdn)**		**Maximum (Cdn)**
+/- J021 - insertion of catheter	110.98		110.98		110.98
+/- Z437 Cardioversion (electrical) if applicable	65.99				65.99
# G178 - catheter ablation therapy	352.05		352.05		352.05
The following codes are paid at 50%					
# G176 - atrial Endocardial activation mapping	334.25	167.13	167.13		167.13
+/- G179 - repeated (up to three times)	111.18	55.59	55.59		166.77
# G249 Electrophysiologic measurements	231.64	115.82	115.82		115.82
# G261 - induction of atrial arrhythmias	331.04	165.52	165.52		165.52
+/- G297 Angiograms (one or two times)	109.65	54.83	54.83		109.65
# Z441 – transeptal	274.38	137.19	137.19		137.19
			1,159.00	to	1,391.00
				Mean	1,275.00

B. Perioperative Costs

Item	**Cost (Cdn)**	**Source**
CT chest scan + physician fee (x 407 = $76.60)	357	Ontario Schedule of Benefits
Physician fees for procedure	1,275	Table A
3 months postprocedure follow-up	1,442	1/4 of annual follow-up costs + CT scan
Total	**$ 3,074**	

C. First Year Costs		
Perioperative cost of ablation procedure	3,074	(Using Medium Success Rate 20% w/o catheter costs)
Annual follow-up cost for successful patients.	112	(Based on 1 specialist visit per year: A605)
Annual follow up cost for unsuccessful patients	3,257	(Based on annual costs of clinical tests and visits: first year is 0.75 yrs))
Weighted mean annual follow-up cost	741	(Based on 80% success rate)
Estimated first-year professional costs	3,815	(Perioperative + mean follow-up costs)

Device Costs

The cost of the catheters ranges from $1,800 to $2,500 (Cdn) for the 2 to 3 catheters needed for fluoroscopy procedures and from $5,700 to $6,900 (Cdn) for the 2 catheters plus patches needed for advanced mapping procedures (Personal Communication, September 22, 2005).

Downstream Cost Savings

Based on the prevalence of hospitalization for stroke and chronic heart failure in the population with AF, the Medical Advisory Secretariat estimated that there will be a mean annual cost savings of $971 (Cdn) per treated patient due to avoided hospitalizations with these diagnoses and about $700 (Cdn) per treated patient in annual cost savings due to reduced use of anticoagulant and antiarrhythmic drugs (Personal communications, December 13, 2005). Given that 78% (76,000/98,000) of population with AF is aged over 65 years, this savings will accrue directly to the Ontario Drug Benefits Program for most patients (1) (Personal communications, Ontario Ministry of Finance, December 2005).

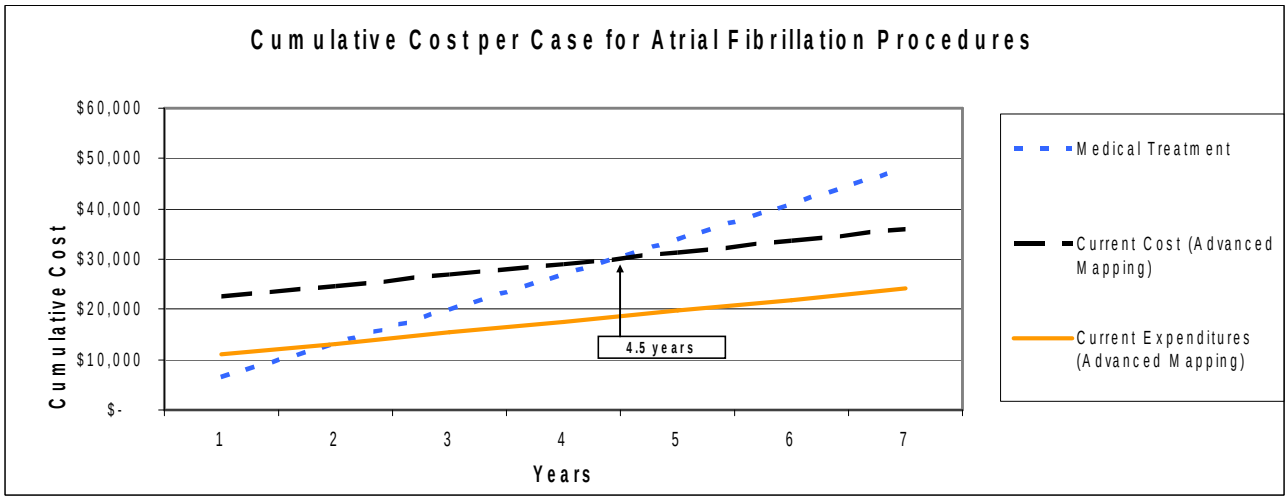
The ongoing costs per case of medical management versus catheter ablation guided by advanced mapping for the treatment of AF, including the downstream cost savings attributed to the latter, are presented in Table 28. Based on a model adapted from a vendor, the costing model includes upfront high-end estimates of the costs of hospitalizations, physician fees, device costs, drugs, labs, diagnostic radiology, repeat procedures for initial unsuccessful treatments, and attrition to medical management for patients who become refractory to ablation. A 2% annual inflation rate is assumed. The current Ministry of Health and Long-Term Care direct funding formula provides $1,000 (Cdn) for an EP study, and $1,600 (Cdn) for a catheter ablation procedure regardless of the mapping systems used.

Table 28: Comparison of Cumulative Costs of Ablation Guided by Advanced Mapping Versus Medical Therapy (Atrial Fibrillation)*

	Annual Cost		Cumulative Cost of Treatment by Procedure (Cdn)				
Treatment Path (high est. for advanced mapping)	Year 1 Cost	Annual Cost	Year 1	Year 2	Year 3	Year 4	Year 5
Medical treatment	6,475	6,475	6,475	13,080	19,817	26,688	33,697
Current cost (advanced mapping)	22,465	2,054	22,465	24,560	26,697	28,876	31,100
Current expenditures (advanced mapping)	11,068	2,054	11,068	13,163	15,299	17,479	19,702

*Note: Assume a 2% per annum inflation rate.

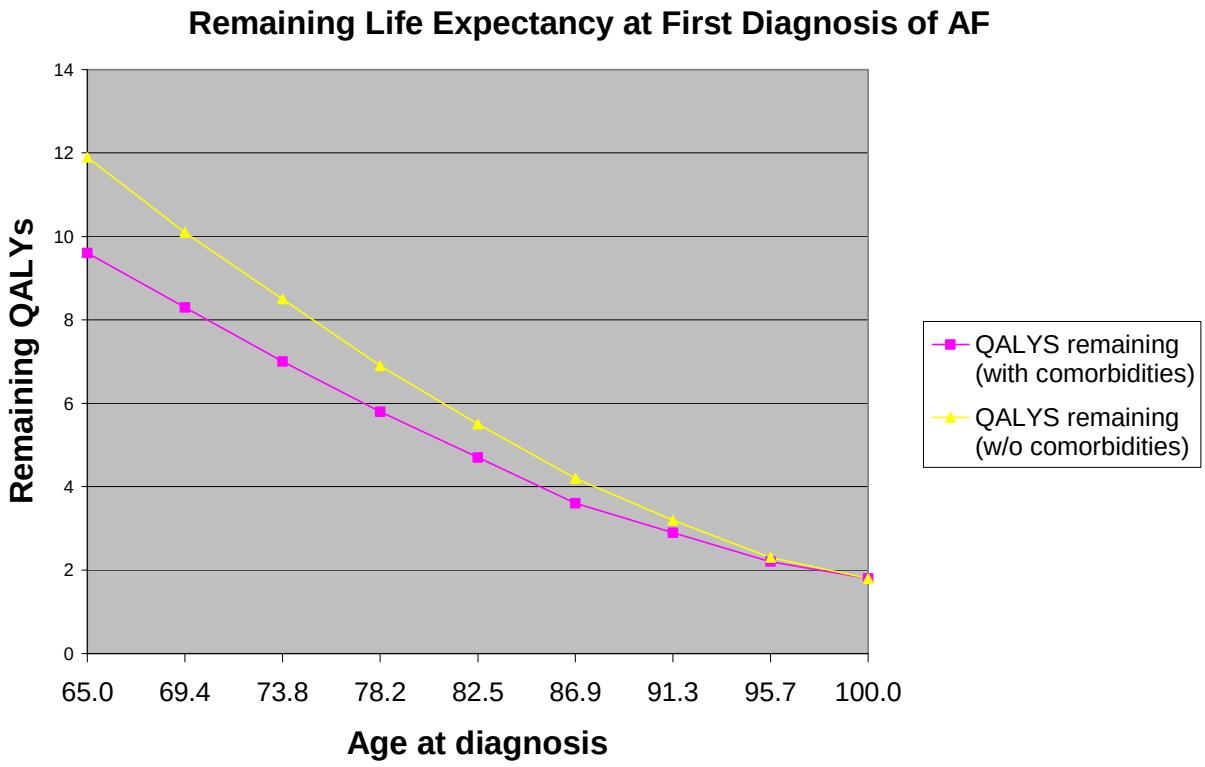
Figure 19: Comparison of Cumulative Costs of Ablation Guided by Advanced Mapping Versus Medical Therapy (Atrial Fibrillation)



The 3 scenarios include medical management with drugs, a high estimate for the current costs associated with advanced mapping (including $6,900 [Cdn] for catheters and patches), and the current amount funded for all mapping and ablation ablations ($2,600 [Cdn] per case for all costs associated with the procedure: catheters, patches, catheterization laboratory, etc.). Comparing medical management and advanced mapping ablation in the graph above, the added upfront cost of the latter are recouped – through reduced use of antiarrhythmics and anticoagulants, as well as fewer hospitalizations for stroke and congested heart failure – at 4.7 years after the procedure under the proposed funding formula. Using a more conservative estimate of the cost of the advanced mapping catheters and patches (e.g., $5,700 [Cdn]), this point of "break even" will occur at about 4 years. The current funding formula ($2,600 [Cdn]) is well below the level needed to fund the advanced mapping procedures (compare solid and hatched parallel lines in Figure 19).

To ensure the validity of the costing model, information about remaining life expectancy of those diagnosed with AF is needed. Evidence regarding baseline (i.e., without treatment) remaining life expectancy in terms of quality adjusted life years is given in Figure 20.

Figure 20: Remaining Life Expectancy at First Diagnosis of Atrial Fibrillation



Based on a concept by Desbiens NA. Deciding on anticoagulating the oldest old with atrial fibrillation: insights from cost-effectiveness analysis. J Am Geriatr Soc 2002; 50(5):863-869.

Because remaining life expectancy beginning at age 65 is always greater than or equal to the number of quality adjusted life years, Figure 20 presents a lower bound on remaining life expectancy. Given that baseline life expectancy remains in excess of 5 years until an age of diagnosis of 85 years, it is evident that most people with AF treated with advanced mapping ablation will survive beyond the point at which the added up front costs are recouped. (One would also expect that those diagnosed with AF at younger ages would also have remaining life expectancy in excess of five years given the trend lines according to age evident in the Figure 20.)

Appraisal

Expert Opinion

Expert consultants advised the Medical Advisory Secretariat of the following:

- Nonfluoroscopy mapping is not necessary for simple ablation procedures (e.g., typical flutter). However, it is essential in complex cases, including these:
    - Symptomatic drug-refractory AF
    - Arrhythmias in people who have had surgery for congenital heart disease (e.g., macro re-entrant tachycardia such as incisional atrial tachycardia)
    - Ventricular tachycardia due to myocardial infarction
    - Atypical AFL

- The studies were small, and some were only powered to detect a difference in fluoroscopy duration; therefore, there were likely type 2 errors.
- Comparative studies did not tell the whole story. Expert consultants advised the Medical Advisory Secretariat that the advanced mapping systems represent an enabling technology in the ablation of complex arrhythmias. The ablation of these complex cases would not have been feasible or advisable with fluoroscopy-guided ablation and, therefore, comparative studies would not be feasible or ethical in such cases.
- Many of the studies included patients with relatively noncomplex arrhythmias (e.g. typical AFL and atrial ventricular nodal re-entrant tachycardia), for which the success rates using the fluoroscopy approach were extremely high and unlikely to be improved upon using nonfluoroscopic mapping. Experts stated that higher success rates with advanced systems compared to fluoroscopy might be anticipated for the more complex arrhythmia substrates such as AF and scar-related AFL. (30)

Potential Benefits of Catheter Ablation

Atrial fibrillation, one of the main complex arrhythmias, is associated with a 5-fold increase in stroke and increased risk of congestive heart failure. There is indication that the prevalence of complex arrhythmias is increasing in Ontario. Average annual hospital admissions with a diagnosis of AF or AFL rose from 43,680 in 2000 to 50,640 in 2004. Atrial fibrillation and AFL were the most responsible diagnoses in about 19% of patients. Successful ablation offers a cure of the arrhythmia and, therefore, may decrease the downstream cost resulting from hospitalization for comorbid conditions of complex arrhythmias.

Funding Policy

Presently, all electrophysiologic mappings are funded at the rate of $1,000 (Cdn) per study regardless of the type of mapping systems used. For ablations using advanced mapping system, the hospital needs to make up the difference in the cost of the catheters (about $3,400 [Cdn]) from its global budget. As a result, hospitals have severely limited the number of ablations using advanced mapping systems.

Diffusion Pressure

- Atrial fibrillation, the most common complex arrhythmia, affects 99,000 Ontarians, and drug therapy has been shown to be effective in about 65% of these people.

- Atrial fibrillation increases with age; therefore, prevalence is expected to increase with the aging population.
- By age 50, almost 100% of people who have had surgery for congenital heart disease will develop arrhythmia, almost all of whom will require nonfluoroscopic mapping for ablation.
- The use of advanced mapping-guided ablation has been limited by the high cost of the single-use catheter (about $3,400 [Cdn] higher than fluoroscopy-guided ablation), and a shortage of EP laboratory time and nursing time. Experts advise that scheduling for such ablations can be challenging as the duration of the procedure is difficult to predict and may require nursing overtime. Presently, at 1 centre, the ablation may be cancelled if there is likelihood of nursing overtime.
- Some centres have greater demands for advanced mapping systems because of the type of patient population. For example, one of the EP centres is the referral centre for a high proportion of the adults who develop arrhythmia after having surgery to repair congenital heart disease in infancy.
- Hospitals have reported waiting times of up to 1 year for ablations requiring advanced mapping.

Diffusion in Ontario

The number of EP studies (fluoroscopy and nonfluoroscopy) and ablations that MOHLTC committed to funding and the actual number of EP studies and ablations performed and funded are shown in Table 29. Because EP studies are also performed for purposes other than ablation, the number EP studies performed was higher than the number of ablations performed. As can be seen from Table 29, there has been a progressive increase in mapping and ablations actually performed annually in Ontario between 2000/2001 and 2004/2005. During this period, the annual number of ablations performed rose by 63%, from 1,134 to 1,850. The number of ablations performed has been below the funded level in 4 of the last 4 fiscal years. The reason for this gap is not known; however, because all centres reported waiting lists for ablation procedures, this gap might be related to limitations in human resources or the availability of catheterization laboratory time. The volume of catheter ablations performed at each centre is shown in Table 30.

Table 29: Trends in Electrophysiology Studies and Ablations in Ontario (2000–2005)

	2000/2001	2001/2002	2002/2003	2003/2004	2004/2005	2005/2006
Number of EP studies with committed funding	1,173	1,909	2,409	2,283	2,712	2,674
Number of funded EP studies actually performed by year-end	1,691	2,167	2,110	2,228	2,492	—
Number of ablations with committed funding	1,359	1,512	1,680	1,573	1,965	2,063
Number of funded ablations actually performed by year-end	1,134	1,393	1,393	1,586	1,850	—

Table 30: Number of Catheter Ablations by Centre in Ontario (2004–2005)

Location	Actual Ablation (2004/2005)	% Of Total Ablations	Ablations for Atrial Fibrillation (2004/2005	% of AF Ablation
London Health Science Centre	351	19	93	26
Ottawa Heart Institute	232	12.5	53	15
University Health Network	361	19.5	54	15
Hamilton Health Sciences Centre	157	8.5	51	14
St. Michael's Hospital	306	16.5	17	5
Kingston General Hospital	88	4.8	16	4
Sunnybrook Health Sciences	73	4	9	2
Southlake Regional Health Centres	282	15.2	69	19
Total volumes (2004/2005)	**1,850**	**100**	**362**	**100**

The Ministry of Health and Long-Term Care was informed that all 8 centres that do EP mapping in the province are using 1 or more nonfluoroscopic mapping systems, the most common being the CARTO and EnSite systems. Because there is no separate fee code to differentiate between fluoroscopy-guided and nonfluoroscopy-guided ablations, the number of ablations guided by advanced mapping is not captured in ministry databases. The number of catheter ablations performed on adults with a diagnosis of AF was 362 in 2004/2005 (Table 30), accounting for about 20% of the total catheter ablations performed. Based on information from the field, the majority of these ablations likely were performed with the guidance of an advanced mapping/navigation system (Personal communications) The number of ablations that require advanced mapping could be higher, because it would include other indications for which advanced mapping-guided catheter ablation is deemed necessary, such as ventricular tachycardia.

Responses from a few EP centres to a ministry survey suggest that people who had ventricular tachycardia or who developed tachycardia after repair surgery for congenital heart disease had relatively short waiting times for catheter ablation (a few weeks), but the waiting times for people with AF were much longer, up to 1 year at 1 centre.

Learning Curve Effect

Pappone et al. (54) measured the learning curve effect on the outcome and duration of nonfluoroscopic mapping-guided circumferential PV ablation in 267 consecutive patients with AF. The results showed an indirect linear relation between total procedure time and number of procedures performed ($r = -0.59$) and between nonfluoroscopic mapping time and number of procedures performed ($r = -0.80$). Pappone et al. was unable to detect a relation between fluoroscopy time and operator experience. In univariate analysis, operator experience slightly predicted recurrence of AF in patients with persistent AF (hazard ratio, 1.56), but not in those with paroxysmal AF. Pappone et al. also reported that in an analysis of 6,442 patients, complications were predicted by an operator caseload of fewer than 150 procedures. (54)

Conclusions

- Advanced, nonfluoroscopic mapping systems enable the performance of some complex ablation procedures such as left atrial circumferential ablation.
- Small RCTs found significant reductions in fluoroscopy exposure in nonfluoroscopy-guided ablation, and a trend toward a lower overall failure rate that did not reach statistical significance, within the limitations of a small sample size and possibility of type 2 error.

- A pooled analysis suggests that advanced mapping systems may reduce the overall failure rate in the ablation of AF.
- Observational studies, including a large non-RCT with 29 months of follow-up, provided early evidence that nonfluoroscopy-guided circumferential PV ablation is a promising treatment for patients with symptomatic drug-refractory AF. The studies reported improved AF-free rates and reduced mortality and morbidity compared with medical therapy; however, there were wide variations in the results among studies.
- Experts advised that future large RCTs that compare advanced mapping to fluoroscopic mapping in complex arrhythmias are not likely because of ethical concerns.
- Although the incidence of life-threatening complications from ablation of complex arrhythmias was low, serious adverse events such as stroke, atrio-esophageal fistula, and PV stenosis could happen in PV ablation.
- For patients with symptomatic, drug-refractory AF who are otherwise healthy, catheter ablation offers a treatment option that is less invasive than open surgical ablation.
- Catheter ablation of AF is still evolving, and it appears that different ablative techniques may be appropriate depending on the characteristics of the patient and the AF.
- Experts advised that complex arrhythmias deemed appropriate for advanced mapping include the following conditions:
  - Highly symptomatic drug-refractory AF for which rate control is not an option
  - Hemodynamically unstable ventricular tachycardia from ischemic heart disease
  - Macro-re-entrant atrial tachycardia after surgical correction of congenital heart disease
  - Atypical AFL

- Data from centres that do EP mapping suggest that patients with drug-refractory AF may be the largest group with unmet need for advanced mapping-guided catheter ablation in Ontario.
- Because of the significant learning effect associated with advanced mapping-guided ablations of complex arrhythmias such as AF, it is advisable for the province to establish centres of excellence to ensure a critical volume, and to gain efficiency and minimize the need for antiarrhythmic drugs after ablation and the need for repeat ablation procedures.
- An Ontario-based economic analysis suggests that the cumulative, incremental, upfront costs of catheter ablation for AF guided by advanced nonfluoroscopy mapping may be recouped in 4.7 years through cost avoidance from reduced need for antiarrhythmic drugs and fewer hospitalizations due to stroke and heart failure.

Glossary

Accessory pathway	An abnormal muscular connection between the upper and lower chambers of the heart. Patients with accessory pathways may develop supraventricular tachycardias.
Arrhythmia	An irregular heart rhythm, or an abnormality in the timing or pattern of the heartbeat, causing the heart to beat too rapidly, too slowly, or irregularly.
Atrial fibrillation	Rapid, uncoordinated firing of electrical impulses from multiple sites in the upper chambers, which causes ineffective contractions.
Atrial flutter	A single "short circuit" in the atria that causes the atria to beat at about 300 beats per minute while the lower chambers of the heart (the ventricles) beat at a slower rate (often 75 or 150 beats per minute).
Atrial tachycardia	A sustained, irregular heart rhythm that occurs in the upper chamber of the heart and causes it to beat too rapidly.
AV nodal re-entrant tachycardia	An abrupt, rapid heartbeat that occurs when electrical impulses mistakenly enter an extra pathway in or near the AV node.
AV node	The normal electrical connection between the atria and the ventricles where electrical impulses are delayed for a fraction of a second to allow the lower chambers to fill completely with blood.
Cardioversion	A procedure used to shock the heart back into rhythm.
Catheter ablation	A procedure used to ablate areas of the heart that are causing arrhythmias. In a radiofrequency ablation, electrophysiologists pinpoint the area and then use radio wave energy to "cauterize" the tiny part of the heart muscle causing the heart rhythm abnormality.
Gray	A unit for measuring radiation exposure
Holter monitor	A wearable monitor used to obtain a continuous ECG recording, usually for 24 to 48 hours, useful for detecting abnormalities that may not occur during a resting ECG.
Paroxysmal supraventricular tachycardia	A "short circuit" arrhythmia that causes the heart to beat too rapidly.

Sinus node	A group of specialized cells in the right atrium where the electrical impulse in the heart normally begins. It functions as the heart's pacemaker, setting the pace for the heartbeat.
Supraventricular tachycardia	A series of rapid heartbeats arising from the upper chambers of the heart that can cause the heart to beat very rapidly or erratically and may lead to inadequate blood supplies to the body.
Ventricular tachycardia	A series of rapid heartbeats that originate in the lower chamber of the heart (the ventricles) that may cause the heart to beat inefficiently.
Wolff-Parkinson-White syndrome	A specific type of heart rhythm abnormality. Patients with WPW syndrome have an accessory pathway connecting the upper and lower chamber of the heart. These patients may develop a rapid heartbeat caused by a "short circuit" heart arrhythmia. The syndrome also may cause dangerous heart arrhythmias.

Appendices

Appendix 1: Literature Search Strategy

Search date: August 20, 2005
Databases searched: OVID MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, Cochrane CENTRAL and DSR, INAHTA

Database: Ovid MEDLINE(R) <1999 to August Week 2 2005>
Search Strategy:
---

1 exp Body Surface Potential Mapping/ (778)
2 exp Electrophysiologic Techniques, Cardiac/ (1275)
3 (CARTO or Ensite or Constellation or Localisa).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1258)
4 magnetic guidance system.mp. (3)
5 (map$ adj2 (endocardial or electrophysiologic$ or noncontact or electromagnetic or electromechanical or fluoroscopic$ or nonfluoroscopic$ or atrial or ventricular or cardiac or atrioventricular or biatrial or epicardial or electroanatomic$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (993)
6 or/1-5 (3654)
7 exp atrial fibrillation/ or exp tachycardia/ (12552)
8 exp Atrial Flutter/ (908)
9 exp Pulmonary Veins/ or pulmonary vein isolation.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1577)
10 or/7-9 (13945)
11 exp heart catheterization/ or exp catheter ablation/ or radiofrequency ablation.mp. or catheter.mp. or ablation.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (30900)
12 6 and 10 and 11 (850)
13 limit 12 to (humans and english language and yr="2000 - 2005") (723)
14 (systematic review$ or systematic overview$ or meta-analysis or metaanalysis).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (14131)
15 13 and 14 (0)
16 13 (723)
17 limit 16 to (case reports or comment or editorial or letter or "review" or review, multicase or "review of reported cases") (266)
18 16 not 17 (457)
19 15 or 18 (457)

Database: EMBASE <1996 to 2005 Week 34>
Search Strategy:
---
1 exp Epicardium Mapping/ (491)
2 exp Electrocardiography/ (14080)
3 (CARTO or Ensite or Constellation or Localisa).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1733)
4 magnetic guidance system.mp. (3)
5 (map$ adj2 (endocardial or electrophysiologic$ or noncontact or electromagnetic or electromechanical or fluoroscopic$ or nonfluoroscopic$ or atrial or ventricular or cardiac or atrioventricular or biatrial or epicardial or electroanatomic$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1360)
6 or/1-5 (17155)
7 exp Heart Atrium Fibrillation/ (12950)
8 exp Heart Atrium Flutter/ (1900)
9 exp TACHYCARDIA/ (18363)
10 exp Pulmonary Vein/ or pulmonary vein isolation.mp. (1527)
11 or/7-10 (30705)
12 exp Heart Catheterization/ (8017)
13 exp Catheter Ablation/ (5720)
14 exp Radiofrequency Ablation/ (533)
15 (catheter or ablation).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (46064)
16 or/12-15 (52661)
17 6 and 11 and 16 (1216)
18 limit 17 to (human and english language and yr="2000 - 2006") (791)
19 exp "Systematic Review"/ (5647)
20 Meta Analysis/ (19281)
21 (systematic review$ or systematic overview$ or meta-analysis or metaanalysis).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (28558)
22 18 and (19 or 20 or 21) (3)
23 18 (791)
24 limit 23 to (editorial or letter or note or "review") (118)
25 Case Report/ (365007)
26 23 not (24 or 25) (445)
27 22 or 26 (448)

Appendix 2: Quality Assessment of Non-Randomized Controlled Studies on CARTO in Ablation of Atrial Fibrillation

Criteria	Tse et al., 2002 (31)	Ernst et al., 2003(32)
Adequate sample size	35 CARTO 10 Fluoroscopy 25	193 CARTO 39 Fluoroscopy 157
Comparative	√	
Consecutive enrolment	√	
Treatment arms similar at baseline	√	Unclear
Performance		
Blinding of caregiver and patients	Not possible	Not possible
Standardized procedures	√	√
Clearly defined end points	√	√
Single operator for electrophysiologic study and ablation during study		
Detection		
Blinding of assessors	No	No
Clear definition of success	√	√
Mean follow-up	12 months	17 months
Attrition		
Crossover rate	0	0
Lost to follow-up	0	0
Intention-to-treat analysis	√	√
Limitations	Non-randomized, small sample. Two arms not concurrent	Non-randomized. Unclear if treatment arms were similar at baseline. Possible preselection bias. Unbalanced in sample sizes.
Medical Advisory Secretariat overall quality assessment	Moderate to low	

Appendix 3: Quality Assessment of Randomized Controlled Studies on CARTO in Ablation of Atrial Flutter

Criteria	Willems et al., 2000 (37)	Kottkamp et al., 2000 (36)	Sporton et al., 2004 (30)
Adequate sample size	80 Unclear. Power calculation not reported	50 Unclear. Power calculation not reported	102 Unclear, power calculation not reported
Appropriate randomization method	unclear	unclear	√ computer -generated random numbers
Selection			
Concealment of treatment allocation	unclear	unclear	√ Random number generated immediately before the procedure
Treatment arms similar at baseline	√	√	Not reported
Performance			
Blinding of caregiver and patients	Not possible	Not possible	Not possible
Clearly defined end points	√	√	√
Standardized procedures	√	√	√
Single operator for electrophysiologic study and ablation during study		√	
Detection			
Blinding of assessor	Not possible	Not possible	Not possible
Clear definition of success	√	√	√
Duration of follow-up	9 months	12 months	6 weeks
Attrition			
Lost to follow-up	0	0	11; results not reported
Intention-to-treat analysis	N/A	Yes	No
Limitations	Small sample	Small sample	Small sample; follow-up period unclear; no intention to treat analysis
Medical Advisory Secretariat overall quality assessment	Moderate	Moderate	Moderate to low

Appendix 4: Quality Assessment of Non-Randomized Controlled Studies on CARTO in Ablation of Atrial Fibrillation

Criteria	Khongphatthanayothin et al., 2000 (34)	Delacretaz et al., 2001 (35)	Leonelli 2002 et al., (33)
Adequate sample size	182 CARTO 79 Fluoroscopy 94	20 CARTO 13 Fluoroscopy 7	119 CARTO 87 Fluoroscopy 32
Comparative	√	√	√
Consecutive enrolment			√
Treatment arms similar at baseline	√	Unclear	Unclear
Blinding of caregiver and patients	Not possible	Not possible	Not possible
Standardized procedures	√	√	√
Clearly defined end points	√	√	
Single operator for electrophysiologic study and ablation during study	√		
Blinding of assessors	Not possible	Not possible	Not possible
Clear definition of success	√	√	√
Mean follow-up	3 months	19 months	16 months
Crossover rate	0	0	0
Lost to follow-up	0	0	0
Intention-to-treat analysis	NA	√	√
Limitations	Non-randomized, possible preselection bias. Two arms not concurrent. Only 3 months follow-up	Non-randomized, possible preselection bias. Two arms not concurrent. Very small sample	Fluoroscopy time was only based on a random selection of 14 patients from CARTO and 32 fluoroscopy patients.
Medical Advisory Secretariat overall quality assessment	Low	Low	Low

Appendix 5: Quality Assessment of Randomized Controlled Trials on EnSite NavX

Criteria	Ventura et al., 2004 (NavX)(27)	Rotter et al., 2005 (38)	Tondo et al., 2005 (NavX)(39)
Adequate sample size	40 Unclear	72 Powered to detect 30% reduction in fluoroscopy	60 Unclear
Selection			
Appropriate randomization method	Unclear	Unclear	Unclear
Concealment of treatment allocation	Unclear	Unclear	Unclear
Clear inclusion and exclusion criteria			
Treatment arms similar at baseline	√	√	Unclear
Performance			
Blinding of caregiver and patients	Not possible	Not possible	Not possible
Clearly defined end points	√	√	√
Standardized procedures	√	√	√
Single operator for electrophysiologic study and ablation during study			
Detection			
Blinding of assessor	No	No	No
Clear definition of success	√	√	√
Duration of follow-up	7 months	6	7 months
Attrition			
Lost to follow-up	0	0	0
Intention–to-treat analysis	N/A	N/A	N/A
Limitations	Small sample, no clear inclusion/exclusion criteria.	Study might not be powered to detect a difference in acute or long-term success rates	Small sample, short follow-up No clear inclusion/exclusion criteria
Medical Advisory Secretariat overall quality assessment	Moderate to low	Moderate to low	low

Appendix 6: Quality Assessment of RCT Comparing CARTO to EnSite Navigational System in Pulmonary Vein Ablation

Criteria	Liu et al., 2005 (25)
Adequate sample size	75
Appropriate randomization method	Unclear
Concealment of treatment allocation	Unclear
Clear inclusion and exclusion criteria	
Treatment arms similar at baseline	√
Blinding of caregiver and patients	Not possible
Clearly defined end points	√
Standardized procedures	√
Single operator for electrophysiologic study and ablation during study	
Blinding of assessor	Not possible
Clear definition of success	√
Duration of follow-up	7 months
Lost to follow-up	None
Intention to treat analysis	NA
Limitations	Small sample Unclear adequacy of randomization No blinding of patients or care provider
Medical Advisory Secretariat overall quality assessment	Moderate

Appendix 7: Quality Assessment of Studies on LocaLisa Navigational System

Criteria	Wood et al., 2004 (LocaLisa)(44) Non-Randomized	Schneider et al., 2003 (LocaLisa) (42) Randomized
Adequate sample size	32 Unclear	50 Unclear
Selection		
Appropriate randomization method	No randomization	Unclear
Concealment of treatment allocation	N/A	Unclear
Clear inclusion and exclusion criteria		
Treatment arms similar at baseline	√	√
Performance		
Blinding of caregiver and patients	Not possible	Not possible
Clearly defined end points	√	√
Standardized procedures	√	√
Single operator for electrophysiologic study and ablation during study	(Same 2 persons) √	
Detection		
Blinding of assessor	No	Not possible
Clear definition of success	√	√
Duration of follow-up	7 & 10 months	6 months
Attrition		
Lost to follow-up	0	0
Intention-to-treat analysis	N/A	N/A
Limitations	Small sample, no randomization short follow-up, no clear inclusion/exclusion criteria.	Small sample, short follow-up No clear inclusion/exclusion criteria
Medical Advisory Secretariat overall quality assessment	Low	Low

Appendix 8: Quality Assessment of Studies on Advance Mapping-Guided Circumferential Ablation for Treatment of Atrial Fibrillation

Criteria	Papponi et al., 2003 (46)	Kottkamp et al., 2004 (47)	Vasmreddy et al., 2005 (48)	Ouyamg et al., 2004 (49)	Oral et al., 2004 (50)	Mansour et al., 2004 (51)	Arentz et al., 2005 (52)
Adequate sample size	N = 1,171 No power calculation provided	Small (42 completed 12 month FU	Small (n = 70)	Small (n = 41)	(n = 100) No power calculation provided	(n = 40) No power calculation provided	(n = 34)
Design	Prospective Non-randomized	Prospective Case series	Prospective Case series	Prospective Case series	Prospective RCT	Prospective Non-randomized	Prospective case series
Consecutive enrolment	Yes	Yes	Yes	Yes	No	Yes	Yes
Comparison	Medical therapy	None	None	None	+ vs - linear ablation	Segmental PV isolation	None
Treatment arms similar at baseline	More severe in ablation group	NA	NA	NA	Yes	Yes	NA
Standardized procedures	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Clearly defined end points	?	Yes	Yes	Yes	Yes	Yes	Yes
Clear definition of success	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mean follow-up (months)	29.5	12	6 +/-2.5	6+/-1	6	11+/-3	12
Lost to follow-up	Yes	Not clear	None	None	None	None reported	None reported
Intention-to-reat analysis	Yes	Not clear	NA	NA	NA	NA	NA
Limitations	Selection bias No blinding	Small sample, selection bias. No blinding	Small sample, selection bias, Short follow-up, changed procedure during study, did not validate symptomatic AF recurrence	Small sample, selection bias. No blinding Short duration	No Holter recording, might not have detected asymptomatic PAF. Small sample Short duration	Small sample, follow-up initiated by patients; no randomization Not powered to determine superiority of techniques. Short follow-up time.	Small sample, selection bias, Short follow-up

Appendix 9: Studies on Risks of Radiation Exposure During Fluoroscopy-Guided Radiofrequency Catheter Ablation

	Calkins et al., 1991 (60)	Lindsay et al., 1992 (61)	Park et al., 1996 (62)	Rosenthal et al., 1998 (63)
Type of study	Prospective Observational	Prospective Observational	Prospective Observational	Multicentre prospective observational study
Number of patients	31	108	500	859
Type of arrhythmia	WPWS or PSVT	WPWS or AVNRT	SVT or VT	AVNRT, accessory pathway, AV junction
Mean (SD) age, years	35 (15)	WPWs 36 (19) AVNRT 43 (17)	40 (19.3)	36 (21)
Objective	Measure radiation & estimate resultant somatic & genetic risks	Measure radiation in phantom study & determine actual radiation dose based on each patient's exposure time.	Determine risk for acute or chronic radiation induced skin injuries	Measure radiation exposure & identify predictors of fluoroscopy duration
Mean Fluoroscopy time, minutes (SD)	44 (40)	WPWs 54 (37) AVNRT 45 (18)	46.5 (31)	53 (50) >150 min in >5% of patients
Radiation dose to patients	Median radiation dose Vertebral body posterior 7.26 rem Thyroid 0.46 rem Posterior iliac crest 2.46 rem	Effective dose for ablation 1.7 rem	Mean radiation exposure = 0.93 (62) Gy Dose area product – range 76 to 123 $Gycm^2$ Dose higher for accessory pathways & right- sided pathways.	Entrance radiation dose on skin = 1.3+/-1.3 Sv (0.03 – 11.1 Sv) Mean effective radiation dose = 0.025 Sv for females & 0.017 Sc for males
Risks of radiation exposure	Fatal malignancies: 0.7 per 1,000 patients Genetic birth defects: 20 per million births	Fatal malignancies 1 per 745 (1.3 per 1,000 pts) Serious birth defect: 12 per million births (0.1% of incidence in US)	5.6% of patients exceeded the threshold dose needed to cause the earliest signs of radiation skin injury (2 Gy, FDA) No clinical manifestation of acute radiation skin injury at time of discharge No patient received the threshold dose for irreversible skin injury	Fatal malignancies Female:1.4 per 1,000 males: 2.6 per 1,000 males 22% of adults & 11% of children exceeded the threshold dose for earliest sign of radiation skin injury (2 Sv) 1% of adults exceeded the threshold dose that causes permanent destruction in epithelium (7 Sv). The radiation exposure is greater in ablation of multiple targets
Other procedures	Fatal malignancies Heart catheterization 0.13 per 1,000 people PTCA 0.08 per 1,000 patients	Effective dose equivalent (rems) RF ablation (pt) 1.7 Recommended anuual Limit for rad. Worker 5.0 coronary angio 1.2 PCI 2.2 Thallium scan 2.1		
Radiation exposure to operators	Based on exposure to the head =14 /month Based on exposure to hand = 42/month	1.8 mrem/case With use of lead collar & apron, radiation exposure to MD for 250 procedures/year = 9% of recommended annual limit Assisting personnel<5%		

Risk without radiation exposure	Expected incidence of fatal malignancies = 200 per 1,000 pts	Expected incidence of fatal malignancies = 1 in 5 (US)	
Conclusion	Risks are relatively small compared with the risks associated with alternate approaches to management (drugs & surgery)	Radiation exposure is within established guidelines Collimation reduced exposure to patient & staff by 40%	Independent predictors of fluoroscopy duration: patient age, gender, success or failure of ablation & the institution at which the ablation was performed. Longer fluoroscopy exposure needed for men than women, adults than children.

Appendix 9: Studies on Risks of Radiation Exposure During Fluoroscopy-Guided Radiofrequency Catheter Ablation (continued)

	McFadden et al., 2002 (59)	Macle et al., 2003 (64)	Lickfett et al., 2004 (65)
Type of study	Prospective Observational	Prospective observational	
Number of patients	50	43	15
Type of arrhythmia	AV node ablation, R-sided pathways; AFL, left sided accessory pathways.	PAF Common Atrial flutter Accessory pathways	PAF 15 A Flutter 5 AVNRT 5
Mean (SD) age, years	Not available	49 (9)	AF 56 AFL 70 AVNRT 56
Objective	Quantify ionizing radiation to patients & operator during RF ablation & estimate risks	Measure radiation exposure (single electronic dosimeter)	Measure radiation exposure (thermoluminescent dosimeter vest)
Mean fluoroscopy time, minutes	67	PAF 57 (30) Common Aflutter 20 (10) Accessory pathway 22 (21)	PAF 129 (36.7) AFL 29.7 (10.5) AVNRT 17.1 (6.7)
Radiation dose to patients	Mean skin dose = 0.81 Gy Mean DAP 123 Gycm^2 Mean effective dose for = 17 mSv Max effective does for = 77 mSv	Median radiation exposure PAF 1,110 uSv (430–5330) Common Aflutter 500 (20–1,860) Accessory Pathways 560 (40–1,820) PAF 0.0011 Gy	Mean Effective Dose (mSv) AF : M 27.3 (8.9), F 18.7 (4.8) AFL: M 3.79 (1.2), F 15.8 AVNRT: M 3.37 (1.47), F 0.91 (0.70) PAF 1 – 1.48 Gy
Risks of radiation exposure	Mean fatal malignancies 1 in 1,000 (0.1%) Max fatal malignancies 1 in 200 (0.5%) 12% of patients exceeded threshold for radiation skin injury (2 Gy) No skin injuries were reported.		Fatal malignancies (exposure during AF ablation) Female 1.5 per 1,000 (0.15%) Male 2.1 per 1,000 (0.21%) 1/15 AF patient reached the threshold for transient erythema & epilation. No clinical evidence of radiation skin injury.
Other procedures	Mean effective dose for ablation = 17 mSv Abdominal CT = 10 mSv		
Radiation exposure to operators	<0.15 mSv/month Annual equivalent dose Lens of the eye 3.6 mSv (Allowed limit 150 mSv) Skin of the hand 28.8 mSv (Allowed limit 500 mSv)	Median radiation exposure - MD PAF 66 uSv (outside collar), 27 (waist), 2 (waist level inside) Common A flutter 28 (outside collar), 30 (waist level outside), 1 (waist level inside. Accessory pathways 33 (outside collar), 12 (waist level outside), <0.5 (waist level inside) Nurse 13 – 18 (mid thorax outside) 2–3 (mid thorax, inside) Assuming 300 procedures/year, radiation exposure to MD below the upper recommended annual dose limit	

Conclusion	Steps for reducing radiation exposure included reducing fluoroscopy time, use of pulse fluoroscopy system, judicious use of columnation & use of a lead glass shield between the patient & operator upper body, & use of non-fluoroscopic mapping systems. Particularly important for PAF ablation.	Mean peak skin dose in AF ablation was at least 3-fold greater than that in AFL & AVNRT ablation. Repeat procedures commonly required in AF patients. Needs to make every attempt to minimize radiation exposure e.g. low frame pulsed fluoroscopy & electromagnetic mapping systems.

** The absorbed radiation dose: 1 Gray = 100 rad 1 Gray is a dose equivalent of 1 Sievert (Sv)
1 rem is equivalent to 0.01 Sv (1 Sv = 100 rem) 1 rem = roentgen equivalent man PSD Peak skin dose

Appendix 10: Overall Quality Assessment Using GRADE (3)

Quality Assessment of Trials Comparing CARTO-Guided and Fluoroscopy-Guided Radiofrequency Ablation of Atrial Flutter

Quality Assessment						Summary of Findings					
						Number of Subjects		Effect			
No. Of Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	CARTO	Fluoroscopy	Relative (95% CI)	Absolute	Overall Quality	Outcome
Acute Success (% of patients with complete bi-directional isthmus block after procedure)											
Willems et al., (37) Kottkamp et al., (36) Sporton et al., (30)	RCT	*Some limitation	Some inconsistency	None	None	85	81			⊕⊕⊕O	Critical
GRADE Quality	High	Moderate	Moderate							Moderate	

*Unclear concealment and lack of blinding.

There is moderate evidence that high acute success rates (89%–100%) can be achieved in the ablation of AFL using CARTO. CARTO-guided ablation produced similarly high success rates as did fluoroscopy-guided ablation in 3 of 4 studies, and higher acute success rates than did fluoroscopy-guided ablation in 1 of 4 studies.

The difference in success rate of Kottkamp was probably due to difference in definition of acute success.

Chronic Success (Arrhythmia Free During Follow-up)

Quality Assessment						Summary of Findings					
						Number of Subjects		Effect			
No. Of Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	CARTO	Fluoroscopy	Relative (95% CI)	Absolute	Overall Quality	Outcome
Sustained success during following-up (Atrial Fibrillation)											
Willems et al., (37) Sporton et al., (30) Leonelli et al., (33)	RCT Non-RCT	*Some limitation	Some inconsistency	None	None	59	57			⊕⊕OO	Important
GRADE Quality	High	Moderate	Low	Low						Low	

*Unclear concealment and lack of blinding.
*Recurrence: 9%–25% for CARTO, similar to fluoroscopy in 2/3 studies; 25% vs. 0% (much higher) compared to fluoroscopy in 1 study.
Willems: isthmus dependent clockwise or counter clockwise AFL (atrial enlargement 45.8% vs. 50% of patients) structural heart disease 66.7% vs. 69.2%.

Overall Quality Assessment of Total Procedure Time (CARTO)

Quality Assessment						Summary of Findings					
						Number of Subjects		Effect			
No. Of Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	CARTO	Fluoroscopy	Relative (95% CI)	Absolute	Overall Quality	Outcome
Total Procedure Time (Atrial Fibrillation)											
Willems et al., (37) Sporton et al., (30) Leonelli et al., (33)	RCT Non-RCT	*Some limitation	None	None	None	59	57			⊕⊕⊕O	
GRADE Quality	High	Moderate	Moderate	Moderate	Moderate					Moderate	

*Unclear concealment and lack of blinding.

Overall Quality Assessment of Total Fluoroscopy Time (CARTO)

Quality Assessment						Summary of Findings					
						Number of Subjects		Effect			
No. Of Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	CARTO	Fluoroscopy	Relative (95% CI)	Absolute	Overall Quality	Out-come
Total Fluroscopy Time (Atrial Fibrillation)											
Willems et al., (37) Kottkamp et al., (36) Sporton et al., (30)	RCT	*Some limitation	None	None	None	85	81			⊕⊕⊕O	Import-ant
GRADE Quality	High	Moderate	Moderate	Moderate	Moderate					Moderate	

*Unclear concealment and lack of blinding.

Quality Profile of CARTO Versus Fluoroscopy in Mapping and Ablation of Atrial Fibrillation (Pulmonary Vein Ectopy Elimination)

Quality Assessment						Summary of Findings					
						Number of Subjects		Effect			
No. Of Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	CARTO	Fluoroscopy	Relative (95% CI)	Absolute	Overall Quality	Outcome
Acute Success (% of patients with complete bi-directional isthmus block after procedure)											
Tse et al., 2002 (31) Ernst et al., 2003 (55)	Observa-tional compare-ative	Some limitations*	None	None	None	49	182			⊕⊕OO	Critical
GRADE Quality	Moderate	Low	Low	Low	Low					Low	

*Small sample and no blinding.

Quality Profile of Chronic Success for CARTO Versus Fluoroscopy in Mapping and Ablation of Atrial Fibrillation (Pulmonary Vein Ectopy Elimination)

Quality Assessment						Summary of Findings					
						Number of Subjects		Effect			
No. Of Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	CARTO	Fluoroscopy	Relative (95% CI)	Absolute	Overall Quality	Outcome
Chronic success during following-up											
Tse et al.,2002 (31) Ernst et al.,2003 (32)	Observational comparative	*Some limitation	None	None	None	59	57			⊕OOO	Important
GRADE Quality	Moderate	Low	Low	Low	Low					Low	

Low quality evidence that there is no significant difference in the acute success rate between CARTO- and fluoroscopy-guided ablation of pulmonary vein ectopy in people with AF.

Quality Assessment						Summary of Findings					
						Number of Subjects		Effect			
No. Of Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	CARTO	Fluoroscopy	Relative (95% CI)	Absolute	Overall Quality	Outcome
Total Fluroscopy Time Tse et al.,2002 (31) Ernst et al.,2003 (32)	Observational comparative	*Some limitation	None	None	None	59	57			⊕⊕⊕O	Important
GRADE Quality	Moderate	Low	Low	Low	Low					Low	

Quality Profile of Fluoroscopy Time for CARTO Versus Fluoroscopy in Mapping and Ablation of Atrial Fibrillation (Pulmonary Vein Ectopy Elimination)

There is low quality evidence that fluoroscopy time is significantly lower in CARTO-guided ablation of pulmonary vein ectopy versus fluoroscopy-guided ablation for the treatment of paroxysmal AF.

References

1. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001; 285(18): 2370-2375

2. Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med 2002; 347(23): 1825-1833

3. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S et al. Grading quality of evidence and strength of recommendations. BMJ 2004; 328(7454): 1490

4. Pedersen OD, Brendorp B, Kober L, Torp-Pedersen C. Prevalence, prognostic significance, and treatment of atrial fibrillation in congestive heart failure with particular reference to the DIAMOND-CHF study. Congest Heart Fail 2003; 9(6): 333-340

5. Levy S, Camm AJ, Saksena S, Aliot E, Breithardt G, Crijns HJ et al. International consensus on nomenclature and classification of atrial fibrillation: A collaborative project of the Working Group on Arrhythmias and the Working Group of Cardiac Pacing of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. J Cardiovasc Electrophysiol 2003; 14(4): 443-445

6. Kerr CR, Humphries KH, Talajic M, Klein GJ, Connolly SJ, Green M et al. Progression to chronic atrial fibrillation after the initial diagnosis of paroxysmal atrial fibrillation: results from the Canadian Registry of Atrial Fibrillation. Am Heart J 2005; 149(3): 489-496

7. Haissaguerre M, Jais P, Shah DC, Garrigue S, Takahashi A, Lavergne T et al. Electrophysiological end point for catheter ablation of atrial fibrillation initiated from multiple pulmonary venous foci. Circulation 2000; 101(12): 1409-1417

8. Guerra PG, Skanes AC. Catheter ablation therapy for atrial fibrillation. Can J Cardiol 2005; 21 Suppl B: 31B-34B

9. Passman RS, Kadish AH, Dibs SR, Engelstein ED, Goldberger JJ. Radiofrequency ablation of atrial flutter: a randomized controlled study of two anatomic approaches. Pacing Clin Electrophysiol 2004; 27(1): 83-88

10. Sparks PB, Kalman JM. Is atrial flutter a risk factor for stroke? J Am Coll Cardiol 2001; 38(3): 785-788

11. Topol EJ, Califf RM, Isner J, Prystowsky EN, Swain J, Thomas J et al. Textbook of cardiovascular medicine. 2 ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2002.

12. Ceresne L, Upshur RE. Atrial fibrillation in a primary care practice: prevalence and management. BMC Fam Pract 2002; 3: 11

13. Humphries KH, Jackevicius C, Gong Y, Svensen L, Cox J, Tu JV et al. Population rates of hospitalization for atrial fibrillation/flutter in Canada. Can J Cardiol 2004; 20(9): 869-876

14. Chung MK, Shemanski L, Sherman DG, Greene HL, Hogan DB, Kellen JC et al. Functional status in rate- versus rhythm-control strategies for atrial fibrillation: results of the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Functional Status Substudy. J Am Coll Cardiol 2005; 46(10): 1891-1899

15. Cox JL, Schuessler RB, Cain ME, Corr PB, Stone CM, D'Agostino HJ, Jr. et al. Surgery for atrial fibrillation. Semin Thorac Cardiovasc Surg 1989; 1(1): 67-73

16. Medical Advisory Secretariat. Ablation for atrial fibrillation. Health technology literature review. 2006. Ministry of Health and Long-Term Care. In press.

17. Wood MA, Brown-Mahoney C, Kay GN, Ellenbogen KA. Clinical outcomes after ablation and pacing therapy for atrial fibrillation : a meta-analysis. Circulation 2000; 101(10): 1138-1144

18. Pappone C, Santinelli V. Atrial fibrillation ablation: state of the art. Am J Cardiol 2005; 96(12A): 59L-64L

19. Chen SA, Tai CT, Yu WC, Chen YJ, Tsai CF, Hsieh MH et al. Right atrial focal atrial fibrillation: electrophysiologic characteristics and radiofrequency catheter ablation. J Cardiovasc Electrophysiol 1999; 10(3): 328-335

20. Lemola K, Oral H, Chugh A, Hall B, Cheung P, Han J et al. Pulmonary vein isolation as an end point for left atrial circumferential ablation of atrial fibrillation. J Am Coll Cardiol 2005; 46(6): 1060-1066

21. Oral H, Scharf C, Chugh A, Hall B, Cheung P, Good E et al. Catheter ablation for paroxysmal atrial fibrillation: segmental pulmonary vein ostial ablation versus left atrial ablation. Circulation 2003; 108(19): 2355-2360

22. Friedman PA. Novel mapping techniques for cardiac electrophysiology. Heart 2002; 87(6): 575-582

23. Kumar GA, Maheshwari A, Thakur R, Lokhandwala YY. Cardiac mapping: utility or futility? Indian Pacing Electrophysiol J 2002; 2(1): 20-32

24. Wetzel U, Hindricks G, Dorszewski A, Schirdewahn P, Gerds-Li JH, Piorkowski C et al. Electroanatomic mapping of the endocardium. Implication for catheter ablation of ventricular tachycardia. Herz 2003; 28(7): 583-590

25. Liu X, Wang X-H, Gu J-N, Zhou L, Qiu J-H. Electroanatomical systems to guided circumferential pulmonary veins ablation for atrial fibrillation: Initial experience from comparison between the Ensite/NavX and CARTO system. Chin Med J 2005; 118(14): 1156-1160

26. Schneider MA, Ndrepepa G, Zrenner B, Karch MR, Schmieder S, Deisenhofer I et al. Noncontact mapping-guided ablation of atrial flutter and enhanced-density mapping of the inferior vena caval-tricuspid annulus isthmus. Pacing Clin Electrophysiol 2001; 24(12): 1755-1764

27. Ventura R. Catheter ablation of common-type atrial flutter guided by three-dimensional right atrial geometry reconstruction and catheter tracking using cutaneous patches: a randomized prospective study. J Cardiovasc Electrophysiol 2004; 15(10): 1157-1161

28. Arentz T, von Rosenthal J, Blum T, Stockinger J, Burkle G, Weber R et al. Feasibility and safety of pulmonary vein isolation using a new mapping and navigation system in patients with refractory atrial fibrillation. Circulation 2003; 108(20): 2484-2490

29. Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S et al. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. Circulation 2002; 105(9): 1077-1081

30. Sporton SC EMNASR. Electroanatomic versus fluoroscopic mapping for catheter ablation procedures: a prospective randomized study. J Cardiovasc Electrophysiol 2004; 15(3): 310-315

31. Tse H-F, Lee KLF, Fan K, Lau C-P. Nonfluoroscopic magnetic electroanatomic mapping to facilitate focal pulmonary veins ablation for paroxysmal atrial fibrillation. Pacing Clin Electrophysiol 2002; 25(1): 57-61

32. Ernst S, Antz M, Ouyang F, Vogtmann T, Goya M, Bansch D et al. Ostial PV isolation: is there a role for three-dimensional mapping? Pacing Clin Electrophysiol 2003; 26(7 Pt 2): 1624-1630

33. Leonelli FM, Tomassoni G, Richey M, Natale A. Usefulness of three-dimensional non-fluoroscopic mapping in the ablation of typical atrial flutter. Ital Heart J 2002; 3(6): 360-365

34. Khongphatthanayothin A. Nonfluoroscopic three-dimensional mapping for arrhythmia ablation: tool or toy? J Cardiovasc Electrophysiol 2000; 11(3): 239-243

35. Delacretaz E, Ganz LI, Soejima K, Friedman PL, Walsh EP, Triedman JK et al. Multi atrial maco-re-entry circuits in adults with repaired congenital heart disease: entrainment mapping combined with three-dimensional electroanatomic mapping. J Am Coll Cardiol 2001; 37(6): 1665-1676

36. Kottkamp H. Electromagnetic versus fluoroscopic mapping of the inferior isthmus for ablation of typical atrial flutter: A prospective randomized study. Circulation 2000; 102(17): 2082-2086

37. Willems S W. Catheter ablation of atrial flutter guided by electroanatomic mapping (CARTO): a randomized comparison to the conventional approach. J Cardiovasc Electrophysiol 2000; 11(11): 1223-1230

38. Rotter M, Scavee C, Sacher F, Sanders P, Takahashi Y, Hsu L-F et al. Correlation of atrial electrocardiographic amplitude with radiofrequency energy required to ablate cavotricuspid isthmus-dependent atrial flutter. Heart Rhythm 2005; 2(3): 263-269

39. Tondo C, Mantica M, Russo G, Karapatsoudi E, Lucchina A, Nigro F et al. A new nonfluoroscopic navigation system to guide pulmonary vein isolation. Pacing Clin Electrophysiol 2005; 28 Suppl 1: S102-S105

40. Gurevitz OT, Glikson M, Asirvatham S, Kester TA, Grice SK, Munger TM et al. Use of advanced mapping systems to guide ablation in complex cases: experience with noncontact mapping and electroanatomic mapping systems. Pacing Clin Electrophysiol 2005; 28(4): 316-323

41. Verbeet T, Castro J, Morissens M, Ngoc ET, Decoodt P. Use of a new non-fluoroscopic three-dimensional mapping system in type I atrial flutter ablation. Pacing Clin Electrophysiol 2005; 28(SUPPL. 1): S99-S101

42. Schneider MA NG. LocaLisa catheter navigation reduces fluoroscopy time and dosage in ablation of atrial flutter: a prospective randomized study. J Cardiovasc Electrophysiol 2003; 14(6): 587-590

43. Macle L, Jais P, Scavee C, Weerasooriya R, Hocini M, Shah DC et al. Pulmonary vein disconnection using the LocaLisa three-dimensional nonfluoroscopic catheter imaging system. J Cardiovasc Electrophysiol 2003; 14(7): 693-697

44. Wood MA, Christman PJ, Shepard RK, Ellenbogen KA. Use of a Non-Fluoroscopic Catheter Navigation System for Pulmonary Vein Isolation. J Interv Card Electrophysiol 2004; 10(2): 165-170

45. Kumagai K, Ogawa M, Noguchi H, Nakashima H, Zhang B, Miura S et al. Comparison of 2 mapping strategies for pulmonary vein isolation. Circ J 2005; 69(12): 1496-1502

46. Pappone C, Rosanio S, Augello G, Gallus G, Vicedomini G, Mazzone P et al. Mortality, morbidity, and quality of life after circumferential pulmonary vein ablation for atrial fibrillation: outcomes from a controlled nonrandomized long-term study. J Am Coll Cardiol 2003; 42(2): 185-197

47. Kottkamp H, Tanner H, Kobza R, Schirdewahn P, Dorszewski A, Gerds-Li JH et al. Time courses and quantitative analysis of atrial fibrillation episode number and duration after circular plus linear left atrial lesions: trigger elimination or substrate modification: early or delayed cure? J Am Coll Cardiol 2004; 44(4): 869-877

48. Vasamreddy CR, Dalal D, Eldadah Z, Dickfeld T, Jayam VK, Henrickson C et al. Safety and efficacy of circumferential pulmonary vein catheter ablation of atrial fibrillation. Heart Rhythm 2005; 2(1): 42-48

49. Ouyang F, Bansch D, Ernst S, Schaumann A, Hachiya H, Chen M et al. Complete isolation of left atrium surrounding the pulmonary veins: new insights from the double-Lasso technique in paroxysmal atrial fibrillation. Circulation 2004; 110(15): 2090-2096

50. Oral H, Chugh A, Lemola K, Cheung P, Hall B, Good E et al. Noninducibility of atrial fibrillation as an end point of left atrial circumferential ablation for paroxysmal atrial fibrillation: a randomized study. Circulation 2004; 110(18): 2797-2801

51. Mansour M, Ruskin J, Keane D. Efficacy and safety of segmental ostial versus circumferential extra-ostial pulmonary vein isolation for atrial fibrillation. J Cardiovasc Electrophysiol 2004; 15(5): 532-537

52. Arentz T, von Rosenthal J, Weber R, Burkle G, Blum T, Stockinger J et al. Effects of circumferential ostial radiofrequency lesions on pulmonary vein activation recorded with a multipolar basket catheter. J Cardiovasc Electrophysiol 2005; 16(3): 302-308

53. Fatemi M, Mansourati J, Rosu R, Blanc JJ. Value of entrainment mapping in determining the isthmus-dependent nature of atrial flutter in the presence of amiodarone. J Cardiovasc Electrophysiol 2004; 15(12): 1409-1415

54. Pappone C, Augello G, Santinelli V. Atrial fibrillation ablation. Ital Heart J 2005; 6(3): 190-199

55. Ernst S, Ouyang F, Lober F, Antz M, Kuck KH. Catheter-induced linear lesions in the left atrium in patients with atrial fibrillation: an electroanatomic study. J Am Coll Cardiol 2003; 42(7): 1271-1282

56. Pappone C, Oreto G, Rosanio S, Vicedomini G, Tocchi M, Gugliotta F et al. Atrial electroanatomic remodeling after circumferential radiofrequency pulmonary vein ablation efficacy of an anatomic approach in a large cohort of patients with atrial fibrillation. Circulation 2001; 104(21): 2539-2544

57. Scanavacca MI, D'Avila A, Parga J, Sosa E. Left atrial-esophageal fistula following radiofrequency catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol 2004; 15(8): 960-962

58. Sonmez B, Demirsoy E, Yagan N, Unal M, Arbatli H, Sener D et al. A fatal complication due to radiofrequency ablation for atrial fibrillation: atrio-esophageal fistula. Ann Thorac Surg 2003; 76(1): 281-283

59. McFadden SL, Mooney RB, Shepherd PH. X-ray dose and associated risks from radiofrequency catheter ablation procedures. Br J Radiol 2002; 75(891): 253-265

60. Calkins H, Niklason L, Sousa J, el Atassi R, Langberg J, Morady F. Radiation exposure during radiofrequency catheter ablation of accessory atrioventricular connections. Circulation 1991; 84(6): 2376-2382

61. Lindsay BD, Eichling JO, Ambos HD, Cain ME. Radiation exposure to patients and medical personnel during radiofrequency catheter ablation for supraventricular tachycardia. Am J Cardiol 1992; 70(2): 218-223

62. Park TH, Eichling JO, Schechtman KB, Bromberg BI, Smith JM, Lindsay BD. Risk of radiation induced skin injuries from arrhythmia ablation procedures. Pacing Clin Electrophysiol 1996; 19(9): 1363-1369

63. Rosenthal LS, Mahesh M, Beck TJ, Saul JP, Miller JM, Kay N et al. Predictors of fluoroscopy time and estimated radiation exposure during radiofrequency catheter ablation procedures. Am J Cardiol 1998; 82(4): 451-458

64. Macle L, Weerasooriya R, Jais P, Scavee C, Raybaud F, Choi KJ et al. Radiation exposure during radiofrequency catheter ablation for atrial fibrillation. Pacing Clin Electrophysiol 2003; 26(1 Pt 2): 288-291

65. Lickfett L, Mahesh M, Vasamreddy C, Bradley D, Jayam V, Eldadah Z et al. Radiation exposure during catheter ablation of atrial fibrillation. Circulation 2004; 110(19): 3003-3010

66. Boersma LVA, Garcia-Moran E, Mont L, Brugada J. Accessory pathway localization by QRS polarity in children with Wolff-Parkinson-White syndrome. J Cardiovasc Electrophysiol 2002; 13(12): 1222-1226

67. Shope TB. Radiation-induced skin injuries from fluoroscopy. Radiographics 1996; 16(5): 1195-1199

68. United States Food and Drug Administration. FDA Public Health Advisory: avoidance of serious x-ray-induced skin injuries to patients during fluoroscopically-guided procedures [Web page]. 1996. [cited 2006 Apr. 15]. Available at: http://www.fda.gov/cdrh/fluor.html

69. Pappone C, Santinelli V, Manguso F, Vicedomini G, Gugliotta F, Augello G et al. Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. Circulation 2004; 109(3): 327-334

70. Natale A, Pisano E, Shewchik J, Bash D, Fanelli R, Potenza D et al. First human experience with pulmonary vein isolation using a through-the-balloon circumferential ultrasound ablation system for recurrent atrial fibrillation. Circulation 2000; 102(16): 1879-1882

71. Marine JE, Schuger CD, Bogun F, Kalahasty G, Arnaldo F, Czerska B et al. Mechanism of atrial flutter occurring late after orthotopic heart transplantation with atrio-atrial anastomosis. Pacing Clin Electrophysiol 2005; 28(5): 412-420

72. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J et al. Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circulation 2005; 111(9): 1100-1105

73. Desbiens NA. Deciding on anticoagulating the oldest old with atrial fibrillation: insights from cost-effectiveness analysis. J Am Geriatr Soc 2002; 50(5): 863-869

74. Cheng CH, Sanders GD, Hlatky MA, Heidenreich P, McDonald KM, Lee BK et al. Cost-effectiveness of radiofrequency ablation for supraventricular tachycardia. Ann Intern Med 2000; 133(11): 864-876

75. Hogenhuis W, Stevens SK, Wang P, Wong JB, Manolis AS, Estes NA, III et al. Cost-effectiveness of radiofrequency ablation compared with other strategies in Wolff-Parkinson-White syndrome. Circulation 1993; 88(5 Pt 2): II437-II446

76. Calkins H, Bigger JT, Jr., Ackerman SJ, Duff SB, Wilber D, Kerr RA et al. Cost-effectiveness of catheter ablation in patients with ventricular tachycardia. Circulation 2000; 101(3): 280-288