Catheter Ablation Procedures
For Supraventricular Tachyarrhythmia
Including Atrial Flutter & Atrial Fibrillation

Draft Report - Peer Review

April 18, 2013
RESPONSES TO DRAFT REPORT

*Spectrum Research is an independent vendor contracted to produce evidence assessment reports for the Washington HTA program. For transparency, all comments received during the public comment period are included in this response document. Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only.*

This document responds to peer reviews from the following parties:

**Draft Report**

1. Jeanne Poole, MD; University of Washington, Harborview Medical Center, Seattle, Washington
2. Ramakota Reddy, MD; Sacred Heart Medical Center, Eugene, Oregon; Mackenzie-Willamette Hospital, Springfield, Oregon; Holy Family Hospital, Valley Hospital and Medical Center, Spokane, Washington

Specific responses pertaining to each comment are included in Table 1.
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<tr>
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The clinical trial results summarized in this document generally favor ablation over other approaches despite significant differences in patients studied (paroxysmal, persistent) and how outcomes were measured. While there are no mortality data available from any large randomized trial, the nonrandomized data are also favorable. The NIH/NHLBI on-going CABANA trial as previously noted, will examine a mortality endpoint in older patients with comorbidities. While the initial application of catheter ablation for AF was limited to highly selected patients with low co-morbid factors, the success rates in the hands of well-trained operators has resulted in extending the procedure to patients with highly symptomatic AF with greater co-morbid factors.

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**Page 238**

**QOL and Cost Effectiveness**  
The authors provide a compendium of studies available to examine QOL measures and cost effectiveness. The author’s carefully note that, *catheter ablation for SVTs is cost effective but this should be interpreted based upon how society is willing to consider cost for quality of life.* This is a critical issue and a full analysis of this question would and should require significant input from physicians caring for these patients if the cost benefit of an ablative approach is questioned by policy makers.  

**Thank you for your comments.**

**Concluding comments**  
This document provides important summaries of clinical studies addressing the technology of catheter ablation to mitigate or cure supraventricular tachyarrhythmias. These rhythms range from the congenital de novo rhythms utilizing accessory AV or dual AV nodal pathways to persistent atrial fibrillation in the setting of advanced cardiac disease. While the quality of many of these studies has been called into question in this document, the overall efficacy of catheter |

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<td>I had no idea what skeletonization surgery was for arrhythmias! It is a somewhat bizarre comparator to catheter ablation. I have been in the field for almost 20 years and I have to admit that I had to look up skeletonization to figure out what it referred to. I doubt there is a surgeon in the country (or world) who has done one for treatment of AVNRT in the last decade or more.</td>
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<td>As I would expect, it was found that RCT’s on SVT, WPW and (to a lesser extent) atrial flutter were difficult to find and not of excellent quality. I would caution that this should not be interpreted as suggesting that catheter ablation is not well proven</td>
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for these conditions. In fact, ablation has proven to be so obviously effective and relatively safe that large scale studies were never really contemplated for these arrhythmias. Much of the efficacy and safety data came from registries and personal experience and the data now is even better than registries suggest. It would now be almost too mundane to publish a series of 300 patients ablated for atrial flutter with <2% complications and >90% efficacy.

These statements do NOT apply to ablation for atrial fibrillation. A-fib ablation is and should be subject to much greater scrutiny and appropriate RCT’s than the other arrhythmias for a number of reasons outlined in the document.

The conclusions are generally valid for atrial fibrillation. For the other arrhythmias, they are also generally valid, but please see my comments above that the absence of data is not really relevant.

The report would have been **MUCH** easier to review and use if it was organized in such a way that each of the arrhythmias had its own major section, with the key questions as sub sections rather than the other way around. As it reads now, the preponderance of recent studies and techniques around atrial fibrillation make the other arrhythmias look like footnotes on every key question. For example Key question 2 only has to do with atrial fibrillation and is pretty irrelevant to the other arrhythmias. If the results section were rewritten in this way, I would rate the quality of the report as superior.

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**Gerhard Muelheims, MD, FACC**
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April 8, 2013

Robin E. Hashimoto, PhD
Spectrum Research, Inc.

Re: Catheter Ablation Procedures for Supraventricular Tachycardias (SVTA) including atrial flutter and atrial fibrillation

General Comments:

This document is a comprehensive review of clinical trial data meeting pre-specified author criteria for trial quality. It examines the efficacy, safety, quality of life and cost effectiveness of catheter ablation to treat supraventricular tachycardia (SVT), including atrial fibrillation (AF).

The extent of the document (over 300 pages with the appendix and over 100 references) limits an exhaustive critical review of each reference cited. I have however read the document and reviewed either the abstract or entire study cited and have provided below, a commentary on a number of points.

Overall, the authors are to be commended on this undertaking. The ultimate use of the information in this document is the critical issue. While the data included are important, they must be interpreted in the context of clinical practice guidelines, clinical experience and the progressive development of catheter ablation as a therapy for treatment of arrhythmias.

In many ways, the review of the clinical trials related to ablation of SVTs parallels the field of Electrophysiology. The historical development of ablation as a preferred treatment strategy must be considered. The early years (1970s and 1980s) were characterized by invasive electrophysiology studies which defined and described the normal electrical conduction system and gave birth to the initial understanding of abnormal reentrant and atrial based supraventricular arrhythmias. The application of ablation technology to the cure of certain SVTs followed initial approaches using open cardiac surgery procedures, which while adding to the basic understanding of these rhythm mechanisms, was associated with significant morbidity and mortality. Additionally, the reentrant arrhythmias were poorly suited to study with the randomized clinical trial model. Often the patient had intermittent and infrequent rhythm episodes, which would require either urgent care at the time of its event or subjecting the patient to daily doses of rhythm controlling medications to try to control an event that might occur only a few times per year. Many of these rhythms present in younger age groups (teens and 20s) making the tolerance of medications such as beta blockers or calcium channel blockers difficult, due to unacceptable side effects (impotence, depression, weight gain, fatigue, exercise heart rate limitations). Similarly, subjecting young individuals to a thoracotomy approach was ultimately considered inappropriate once a catheter based approach was available. The wide variation in presentation of the rhythms, the prolonged follow-up time that would be required and difficulty in adequately “matching” or controlling for adequate and similar clinical factors would make a robust, large, long follow-up and adequately powered randomized clinical trial approach difficult. What is known is that the collective experience of 4 decades of electrophysiologic experience, the reported and
clinically observed remarkable cure rate for these rhythms using catheter ablation, along with a low adverse event rate has resulted in ablative therapy preferable as first or second line therapy. The definition of evidence-based medical therapy incorporates both the best scientific evidence available and best physician judgment [Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn’t. British Medical Journal. 1996; 312(7023):71-72].

In contrast, AF is a rhythm most often occurring in the setting of significant cardiac or other organ system disease. Patients often have frequent episodes. The use of antiarrhythmic drug therapy has a long history of examination in clinical trials, including the AFFIRM trial [AFFIRM Investigators NEJM 347:1825,2002] which used a mortality endpoint to study rate or rhythm control (using antiarrhythmic drugs). A difference in mortality was not observed between the two treatment strategies. However, a sub-study of AFFIRM [Circulation 2004; 109:1509-1513] is suggestive or improved survival if patients can actually achieve maintenance of sinus rhythm. Non randomized trials using catheter ablation to achieve sinus rhythm also suggest mortality may be decreased. Mortality will be evaluated in the ongoing NIH/NHLBI trial randomizing older AF patients with significant co-morbidities to a treatment strategy of catheter ablation compared with rate or rhythm controlling medications [Catheter Ablation Versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA) NCT00911508]. Regardless of the mortality question improving symptoms and quality of life persist as important goals of AF therapy, including prevention of stroke. Antiarrhythmic drugs have in general, been disappointing and associated with poor rhythm control and/or significant side effects. [Crjins HJ et al, Am J Cardiol 1991, 68: 335–41, Kober L et al, N Engl J Med 2008; 358:2678-2687]

Whether or not an individual patient with their particular SVT should have catheter ablation as the first or second line of therapy v. treatment with antiarrhythmic medications is completely dependent upon the clinical presentation. The frequency of arrhythmia occurrence, the heart rate of the rhythm, the patient’s symptoms, and the impact on driving, job safety, risk for injury etc. are all important considerations. Other considerations include the risk of taking an antiarrhythmic medication, which is not trivial. The congenital reentrant SVTs are potentially curable rhythms using catheter ablation. The majority of these patients should be offered a curative medical therapy when available over a palliative one. That is just common sense and good medical practice. Catheter ablation for the atrial based rhythms (atrial fibrillation, atrial flutter, atrial tachycardia) will be driven by patient symptoms, location of rhythm (in the case of atrial tachycardia and atrial flutter) and ongoing studies examining treatment strategies.

The discipline of Clinical Cardiac Electrophysiology is an American Board of Internal Medicine subspecialty which requires physicians to undergo advanced and specialized training beyond three years of a general Cardiovascular Disease fellowship training program. Catheter ablation is an important aspect of this training which trains physicians in the procedural skill as well as patient evaluation and management to understand and execute the highest level of patient care.

Specific comments:

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RESULTS Section: Page 129

**Pulmonary vein isolation (PVI) Versus Anti-Arrhythmic Drugs (AADs)**

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*Concluding Comments:*

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State should be undertaken with specific plans for professional representation.

Sincerely,

Jeanne E. Poole, MD

Professor of Medicine
Director, Electrophysiology
Division of Cardiology
University of Washington, Seattle Washington
Tel: 206 685 4176
Fax: 206 616 1022
jpoole@u.washington.edu
Thank you for your willingness to read and comment on the Comprehensive Evidence-Based Health Technology Assessment Review for hip resurfacing. Your contribution and time are greatly appreciated.

This form can be filled out electronically on your personal computer. Enter your identification information and comments directly into the shaded areas; use the TAB key to move from field to field. Please enter the section, page, and line numbers where relevant. The shaded comment field will expand as you type, allowing for unlimited text. You have been provided comment fields in each section. Should you have more comments than this allows for, please continue with a blank page. Additionally, we are very interested in your evaluation of the ease of use of our Peer Review Form. Please use the last field to enter suggestions for improvement.

When the Peer Review form is complete, save it to your hard drive and return as an e-mail attachment to robin@specri.com

If you have questions or concerns please contact Robin Hashimoto, PhD at the email above.

**Reviewer Identification Information**

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<th>Reviewer Name</th>
<th>Ramakota Reddy, MD</th>
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<tr>
<td><strong>Address</strong></td>
<td>Street 3455 Spring Blvd</td>
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**INTRODUCTION Comments**

While reviewing this section please keep the following questions in mind, but please comment on any point:

- Overview of topic is adequate?
- Topic of assessment is important to address?
- Public policy and clinical relevance are well defined?

Good review of the types of arrhythmias. The ones that you put in bold are the most commonly ablated tachycardias. I suspect this is the reason they are in bold, although I don't see where that is said in the document text.
I had no idea what skeletonization surgery was for arrhythmias! It is a somewhat bizarre comparator to catheter ablation. I have been in the field for almost 20 years and I have to admit that I had to look up skeletonization to figure out what it referred to. I doubt there is a surgeon in the country (or world) who has done one for treatment of AVNRT in the last decade or more.

BACKGROUND Comments
While reviewing this section please keep the following questions in mind, but please comment on any point:
- Content of literature review/background is sufficient?

Very comprehensive and complete review of the literature

REPORT OBJECTIVES & KEY QUESTIONS Comments
While reviewing this section please keep the following questions in mind, but please comment on any point:
- Aims/objectives clearly address relevant policy and clinical issue?
- Key questions clearly defined and adequate for achieving aims?

The Key questions are well stated and relevant.

METHODS Comments
While reviewing this section please keep the following questions in mind, but please comment on any point:
- Method for identifying relevant studies is adequate?
- Criteria for the inclusion and exclusion of studies is appropriate?
- Method for Level of Evidence (LoE) rating is appropriate and clearly explained?
- Data abstraction and analysis/review are adequate?

Appropriate criteria for inclusion and exclusion were used. All relevant studies (and then some) were found, so the methods for identifying studies was adequate.

Data abstraction described here (and seen in the appendixes) is comprehensive and complete.
As I would expect, it was found that RCT’s on SVT, WPW and (to a lesser extent) atrial flutter were difficult to find and not of excellent quality. I would caution that this should not be interpreted as suggesting that catheter ablation is not well proven for these conditions. In fact, ablation has proven to be so obviously effective and relatively safe that large scale studies were never really contemplated for these arrhythmias. Much of the efficacy and safety data came from registries and personal experience and the data now is even better than registries suggest. It would now be almost too mundane to publish a series of 300 patients ablated for atrial flutter with <2% complications and >90% efficacy.

These statements do NOT apply to ablation for atrial fibrillation. A-fib ablation is and should be subject to much greater scrutiny and appropriate RCT’s than the other arrhythmias for a number of reasons outlined in the document.

**RESULTS Comments**

*While reviewing this section please keep the following questions in mind, but please comment on any point:*

- Amount of detail presented in the results section appropriate?
- Key questions are answered?
- Figures, tables and appendices clear and easy to read?
- Implications of the major findings clearly stated?
- Have gaps in the literature been dealt with adequately?
- Recommendations address limitations of literature?

The amount of detail is generally appropriate, although quite comprehensive. There are some pivotal papers and many fringe papers in the field and it would be difficult for a review such as this to be able to fairly separate these out. That being said, I think all of the pivotal trials have been included and were considered of high quality.

The figures and tables are clear and easy to read.

Gaps and limitations in the literature were dealt with adequately, although I would express some concern again that inadequate data for rhythms other than atrial fibrillation should NOT be interpreted as critical of the technique. The evolution and extremely positive experience with ablation for SVT, WPW and flutter made consideration of RCT’s somewhat unnecessary. This changed with atrial fibrillation and
the number of trials regarding atrial fibrillation is more reflection of the fact that this rhythm is not as obviously well treated with ablation as the other rhythms are, and that comparisons to AAD’s and surgery are necessary.

CONCLUSIONS Comments
While reviewing this section please keep the following questions in mind, but please comment on any point:

- Are the conclusions reached valid?

The conclusions are generally valid for atrial fibrillation. For the other arrhythmias, they are also generally valid, but please see my comments above that the absence of data is not really relevant.

OVERALL PRESENTATION and RELEVANCY Comments
While reviewing this section please keep the following questions in mind, but please comment on any point:

- Is the review well structured and organized?
- Are the main points clearly presented?
- Is it relevant to clinical medicine?
- Is it important for public policy or public health?

This is all very relevant to public policy and all of the points are clearly presented.

The report would have been MUCH easier to review and use if it was organized in such a way that each of the arrhythmias had its own major section, with the key questions as sub sections rather than the other way around. As it reads now, the preponderance of recent studies and techniques around atrial fibrillation make the other arrhythmias look like footnotes on every key question. For example Key question 2 only has to do with atrial fibrillation and is pretty irrelevant to the other arrhythmias. If the results section were rewritten in this way, I would rate the quality of the report as superior.

QUALITY OF REPORT
## Comprehensive Evidence-Based Health Technology Assessment

### Peer Review Form

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