



## Microvolt T-Wave Alternans Testing to Risk Stratify Patients for Implantable Cardioverter-Defibrillator Placement for Prevention of Sudden Cardiac Death

### *A Technology Assessment*

#### INTRODUCTION

The California Technology Assessment Forum has been asked to review the scientific literature on the safety and efficacy of using Microvolt T-Wave Alternans Testing to risk stratify patients for Implantable Cardioverter-Defibrillator placement for prevention of sudden cardiac death.

#### BACKGROUND

##### Heart Failure and Sudden Cardiac Death (SCD)

Congestive heart failure (CHF) is a common problem, affecting ten out of 1,000 people after the age of 65, with a prevalence in the United States of 4.8 million cases.<sup>1</sup> This may, in fact, be an under-estimation of the burden of disease since up to 50% of patients with decreased cardiac systolic function may be asymptomatic.<sup>2</sup> In addition, a diagnosis of CHF carries a 25% incidence of mortality over one year. Much of this mortality is attributable to SCD. Almost a half-million patients die of SCD per year in the United States alone.<sup>1</sup> Malignant arrhythmias, including ventricular tachycardia and ventricular fibrillation, are the final common pathway of cardiac arrest in the majority of cases. Worldwide, SCD comprises 50% of overall cardiac mortality in developed countries. <sup>1</sup> SCD is also the most common, and often first, manifestation of coronary artery disease, and out-of-hospital cardiac arrest almost always results in death. Individuals with CHF have a six to nine times higher likelihood of SCD than the average person. <sup>1, 3</sup> Other risk factors for SCD are a history of myocardial infarction, coronary artery disease, family history of sudden death, acquired or inherited cardiomyopathies and rare genetic defects related to cardiac conduction.<sup>4</sup>

##### Implantable Cardioverter-Defibrillators (ICD) and Risk Stratification

Two studies, the Multicenter Automatic Defibrillator Implantation Trial (MADIT) and the Multicenter Unsustained Tachycardia Trial (MUSTT), showed the benefits of electrophysiology (EP) study-guided ICD placement in high-risk patients.<sup>5, 6</sup> Subsequently, the Multicenter Automatic Defibrillator Implantation Trial II

(MADIT-II) focused on primary prevention of SCD for patients with ischemic cardiomyopathy and showed a reduction in mortality with ICD use.<sup>7</sup> ICD placement for primary prevention in patients with non-ischemic cardiomyopathy (NICM) has been more controversial, with only one of five trials which included patients with NICM showing a statistically significant benefit on all-cause mortality.<sup>8</sup> However, all studies showed a trend toward benefit, and a pooled analysis done in 2004 showed an overall reduction in all-cause mortality for primary prevention with ICD of 31%.<sup>8-13</sup>

Thus, two large studies, the Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) and the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), have shown a reduction in mortality with use of ICD in primary prevention for both patients with ischemic etiology of CHF and non-ischemic CHF.<sup>7, 8</sup> Although both studies had large relative risk reductions, they had much smaller absolute risk reductions (ARR); MADIT-II had an ARR of 5.6% and SCD-HeFT had an ARR of 6%. Additionally, ICDs are expensive and carry risks of their own, including procedural complications (bleeding, infection, death) and also device recalls, primarily for failed batteries.<sup>14-16</sup>

Over the past 25 years, experts have been actively searching for the best ways to risk stratify patients according to potential benefit from ICD placement. Various risk factors have been identified, such as ischemic heart disease, decreased left ventricular ejection fraction, and structural heart disease, and various risk stratification testing have been proposed, such as standard and signal average electrocardiogram (EKG) and EP testing with programmed electrical stimulation in the EP lab. However, these markers are often inaccurate and often fail to identify a substantial portion of high-risk patients, as well as falsely predict high risk in patients who never experience SCD.<sup>4</sup> In a meta-analytic evaluation of these methods, no single method appeared to perform better than the others; however, a stepwise use of non-invasive methods, followed by an invasive electrophysiology study was able to stratify the majority (92%) of the patients.<sup>17</sup>

#### Microvolt T-Wave Alternans (MTWA)

MTWA determined during ambulatory exercise stress testing has been proposed as an alternate, non-invasive way in which to predict risk of an arrhythmic event. Thus, MTWA can identify those patients who will benefit most from placement of an ICD, as well as those patients who are at low enough risk of SCD that they can avoid implantation of an ICD.<sup>18, 19</sup> MTWA can be tested for during outpatient exercise testing. T-wave alternans (TWA) is generally subtle, with variation in electrical amplitude to within a few microvolts. Therefore, TWA is generally undetectable on a standard ECG, but can be detected by elaborate signal processing techniques. New machines can detect TWA to within microvolts (called Microvolt TWA or MTWA). The MTWA device consists of a signal input (multi-lead ECG), digital amplifier, signal processor

and analysis module, computer, and screen display. The machine generates a printed report at the completion of a test.<sup>20</sup>

### Technology Assessment (TA)

**TA Criterion 1:** The technology must have the appropriate regulatory approval.

The Cambridge Heart, Inc. CH 2000 (Bedford, MA) was cleared through the FDA 510K process on April 12, 1999. Since that time, there have been several versions of the Cambridge Heart, Inc. device which have been approved. The most recent device, the Heartwave II Cardiac Diagnostic System, was approved on April 7, 2005. The Heartwave II Cardiac Diagnostic System is to be used only as an adjunct to clinical history and the results of other non-invasive and/or invasive tests. The Cambridge heart devices use the spectral analysis method for determining T-wave alternans.

The T-Wave Alternans (TWA) Algorithm Option (GE Medical Systems Information Technologies, Milwaukee, WI) received FDA 510K clearance on October 30, 2003. The T-Wave Alternans (TWA) Algorithm Option is intended for use in a hospital, doctor's office or clinic environment by competent healthcare professionals for recording ST-T wave morphology fluctuations for patients who are undergoing cardiovascular disease testing. The GE Medical Systems Information Technologies device does not use the spectral analysis method for determining T-wave alternans.

To our knowledge the data we are reviewing is only related to the Cambridge Heart technology.

TA Criterion 1 is met.

**TA Criterion 2:** The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.

The Medline database, Cochrane clinical trials database, Cochrane reviews database and the Database of Abstracts of Reviews of Effects (DARE) were searched using the key word 'microvolt t wave alternans'. These were cross-referenced with the keyword 'prognostic'. The bibliographies of reviews and key articles were manually searched for additional references. The search was performed for the period from 1966 through May 2006, and updated on September 13, 2006. The abstracts of citations were reviewed for relevance and all potentially relevant articles were reviewed in full.

The search identified 20 publications with data specifically on the prognostic value of MTWA for cardiac arrhythmias and/or SCD, 18 of which have been reported on extensively in a published meta-analysis and in a technology review done by the Technology Evaluation Center (TEC) of the Blue Cross and Blue Shield Association.<sup>21, 22</sup> The two remaining studies were of large prospective cohorts and were published in the first half of 2006<sup>23, 24</sup>

Level of evidence: 3 and 4.

TA Criterion 2 is met.

TA Criterion 3: The technology must improve the net health outcomes. For diagnostic tests, there is evidence that use of the test would result in improved medical management in a way that will benefit the patient.

## Benefit

### Recent Reviews

There have been multiple studies assessing the association of an MTWA test result with ventricular arrhythmia and/or SCD. Most of these have suggested that a positive or indeterminate MTWA test may be a good way to identify high risk patients, and that a negative test may be a good way to identify low-risk patients; but, because of their generally small size, varying patient populations and varying endpoints, the data have remained inconclusive. The bulk of these studies were included in a recent meta-analysis by Gehi et al.<sup>22</sup> This review included 19 studies (published in 18 papers) varying in size from 16 to 834 participants; had varying patient populations ranging from healthy athletes to patients with ischemic or non-ischemic CHF to those with ICD's already in place; and had varying endpoints, including syncope or ventricular tachycardia (VT), SCD or VT or ventricular fibrillation (VF), and appropriate ICD therapy. There was no inclusion criterion based on the ejection fraction of the enrolled patients; as a result, the included studies have mean LVEF's in their populations ranging from 23% to 71%. Of the 19 studies reviewed, the two largest focused on risk-stratification in post-MI patients, most of whom did not have a low LVEF and thus, would not have met MADIT-II criteria for ICD placement.<sup>25, 26</sup> This review found that the 12 studies which evaluated the predictive value of MTWA among patients with CHF over an average follow-up of 18 months had a summary estimate positive predictive value (PPV) of 25.5% and negative predictive value (NPV) of 93.8%.<sup>27-37</sup> The summary estimates of PPV and NPV were not substantially different among studies of non-ischemic or ischemic cardiomyopathy.<sup>22</sup> However, only two of these studies performed multivariate adjustment, including adjustment of other commonly used risk-stratification tests, such as LVEF,

signal-average EKG or non-sustained VT, to evaluate the independent prognostic value of MTWA.<sup>27, 32</sup> Although both found MTWA to be an independent predictor of arrhythmic events, these were relatively small studies of 53 and 83 subjects, respectively. Gehi et al.<sup>22</sup> conclude that MTWA appears to be as good a risk-predictor as other methods, but it is still unclear what incremental prognostic value it provides<sup>22</sup>.

In October 2005, the TEC of the Blue Cross and Blue Shield Association conducted its own review of the subject.<sup>21</sup> This review included all of the studies in the Gehi review, as well as four others, which studied mixed populations referred for electrophysiology testing<sup>19, 38-40</sup>, one which studied a population with a history of ventricular arrhythmias<sup>41</sup> and one which studied a small group of patients with the Brugada Syndrome.<sup>42</sup> Similar to the Gehi review, the TEC review concluded that the data are insufficient to assess whether the use of MTWA improves health outcomes or is as beneficial as any established alternatives.<sup>21</sup>

### Newer Studies

Since the TEC and Gehi reviews, two prospective cohort trials using the spectral analysis method of MTWA testing have been published, both of which enrolled patients from the community who were likely to be eligible for ICD placement as primary prevention of SCD (Table 1). The first of these, by Bloomfield et al<sup>23</sup>, studied 549 patients between November 1996 and March 2003 who were enrolled at 11 clinical centers in the United States, the majority of which were large community-based private cardiology practices. The study enrolled 587 patients, but 38 either withdrew or died before MTWA testing, leaving a total of 549 enrolled patients. One-half were recruited from academic heart failure centers, a quarter from community based private practices and a quarter from other academic cardiology groups. Patients were included if they either had ischemic heart disease or non-ischemic cardiomyopathy and their LVEF was less than or equal to 40%. Participants were categorized as having either an abnormal MTWA result (including positive and indeterminate) or a normal MTWA result. Unlike in prior studies, participants underwent MTWA testing while taking all of their usual cardiovascular medications, including beta-blockers. Participants were followed for up to 24 months, with a primary combined endpoint of all cause mortality and non-fatal sustained ventricular arrhythmias. This study found a two-year actuarial event rate of 15% (47 events) among patients with an abnormal MTWA test, versus a two-year actuarial event rate of 2.5% (four events) among patients with a normal MTWA test. (Table 2) Event rates were higher for patients with an indeterminate MTWA test (17.5%) than for those with an abnormal MTWA test (12.3%), giving a combined event rate for an abnormal MTWA test of 15%. This combined event rate resulted in a 6.5 times higher hazard of having an event (all cause mortality or non-fatal sustained ventricular arrhythmia) for patients with an abnormal MTWA test versus those with a normal test. This hazard was decreased, but still significant, after adjusting for age, gender, cardiomyopathy type (ischemic/ non-ischemic), past CHF admission, New York Heart Association

(NYHA) functional class, LVEF and diabetes (HR 5.5; 95% CI 2.0-15.3). Male gender (HR 2.67; 95% CI 1.2-5.9), having had a past CHF admission (HR 3.1; 95% CI 1.6-6.2) and not being on beta-blockers (HR 4.2; 95% CI 2.4-7.4) each independently increased the hazard of having an event. Abnormal MTWA was associated with mortality in the subgroups of LVEF  $\leq$  31% and LVEF 31%-40% (HR 5.0; 95% CI 1.8-14.1 in low LVEF sub-group, and non-calculable in the higher LVEF group because there were no events among patients with a normal MTWA test in this subgroup). There were 189 participants with a normal MTWA result, four of whom had events, giving a negative predictive value (NPV) of 97.9% over the two-years of follow-up. There were 360 participants with an abnormal (positive or indeterminate) MTWA result, 47 of whom had events, giving a positive predictive value (PV) of 13.1% over the two-years of follow-up.

The second study, by Chow et al<sup>24</sup>, evaluated 768 patients with ischemic cardiomyopathy and LVEF  $\leq$  35% enrolled at four outpatient cardiology clinics between March 2001 and June 2004 (Table 1). This study did not include patients with non-ischemic cardiomyopathy. MTWA results were categorized as positive, negative or indeterminate. The positive and indeterminate groups were combined for the primary outcome into a 'non-negative' MTWA group and compared to the negative MTWA group. Unlike the Bloomfield et al study<sup>23</sup>, participants had beta-blockers and non-dihydropyridine calcium-channel blockers withheld for >24 hours prior to MTWA testing. Participants were followed for up to 18 months after testing, with a primary endpoint of all-cause mortality, and secondary endpoints of cause-specific mortality, and appropriate ICD shock delivery. Participants were also stratified by whether or not they had an ICD placed. (Table 2) The overall all-cause mortality rate (primary endpoint) for the non-negative MTWA group was 15.2%, compared to 8.3% for the non-negative MTWA group. Participants with a non-negative MTWA test had a higher hazard of all-cause mortality (HR 2.51; 95% CI 1.5-4.2); this increased hazard persisted after adjustment for co-variables (HR 2.2; 95% CI 1.3-3.8), although it is unclear which co-variables were actually included in the final model. When stratified by ICD placement group, those with a non-negative MTWA and no ICD had an all-cause mortality rate of 21.8% compared to 11% for those with a non-negative MTWA and an ICD. The mortality rates for arrhythmic deaths for the non-negative MTWA group without ICDs was 11.2%; whereas, this rate was 3.4% for this same group with ICDs, which was similar to the rates for the negative MTWA group with ICDs (4.0%) and without ICDs (3.4%). Thus, the bulk of this increased risk of all-cause mortality appeared to result from an increased risk of arrhythmic deaths. However, when examined by LVEF category and adjusted for other co-variables, only the group of patients with an LVEF  $\leq$  30% were at increased risk for all-cause mortality (HR 2.1; 95% CI 1.2-3.7); those with LVEF 31%-35% had only a non-significant trend toward increased risk (HR 3.0; 95% CI 0.9-9.7). The negative predictive value of the MTWA test in this study was 91.7%. The positive predictive value was 30.7%.

## Harms

The question of harm is particularly crucial for those patients who have a negative test. Both the studies examined above<sup>23, 24</sup> provide data that is helpful in assessing harms. In Bloomfield et al, the group with a normal (or negative) MTWA test have a 2.5% two-year rate of all cause mortality or appropriate ICD shock (two deaths and two appropriate ICD shocks)<sup>23</sup>. The question of possible harm to the group that would potentially not receive an ICD based on a negative MTWA test result can be looked at most directly, however, in the study by Chow et al<sup>24</sup>, because many more participants had ICDs. In the Bloomfield study, only 69 participants had ICDs placed either before or over the course of the study, with equal proportions in the abnormal and normal MTWA test groups. In the Chow study, 376 (49%) of the participants had an ICD placed, allowing for stratified analyses. Among participants in this study who had a negative MTWA result, those who did not have an ICD had only 0.4% higher mortality rate than those with an ICD, resulting in a NNH by non-placement of an ICD of 250 over 18 months.

Having an ICD is not risk-free. Initial implantation requires anesthesia and a dye load, carrying risks with both of these as well as the risk of a wound infection. Device failure is a small, but not insignificant issue – a recent study found 31 deaths over a 12 year period directly attributable to device malfunction.<sup>16</sup> Replacing a potentially defective ICD also carries risk – another study found that over a one-year recall period from October 2004 to October 2005, 31 patients (5.8% of those studied) undergoing device replacement experienced a major complication, including two deaths.<sup>14</sup> Another, perhaps even more significant, area of concern is related to quality of life. Inappropriate shocks occur as a result of atrial fibrillation or flutter, sinus tachycardia during exercise, oversensing and lead failures. For every 100 patients receiving an ICD, 30 will die anyway, seven to eight will be saved by the ICD, ten to twenty will have an inappropriate shock, five to fifteen will have other complications, and the remainder will not experience their devices at all.<sup>43</sup>

## Improvement of Medical Management

Recent joint professional guidelines from the American College of Cardiology, American Heart Association, and European Society of Cardiology gave MTWA a level of evidence of Class IIa, “weight of the evidence/opinion is in favor of usefulness/efficacy.”<sup>47</sup> The guidelines point out that MTWA appears to have a high NPV, but that it may also be used for its PPV in the right population. Unfortunately, the societies do not give any guidance or reference any data on how best to incorporate MTWA into clinical practice in a way that will improve medical management and benefit patients. Another recent review of MTWA suggests an algorithm for its use; however, there has not been any study to support this or any other particular algorithm.<sup>44</sup> Many questions remain as to how best to utilize this prognostic test in clinical practice. Published studies have only followed patients for up to two years. Although longer-studies are underway,

that data has not yet been published. Thus, it remains unclear if risk-stratification with an MTWA test needs to be repeated, and if it does, at what interval and how frequently. It is also unclear if this test is best used alone or if the low-risk MTWA group can, or should, be further risk stratified by additional testing to avoid the potential harm of not implanting an ICD, or if the high-risk MTWA group can, or should, be further risk stratified by additional testing to avoid the potential harm of implanting an ICD unnecessarily. The cohort studies reported on here have shown MTWA to be an independent predictor of events, but they have not tested the incremental benefit of combining MTWA with other tests.

TA Criterion 3 is not met

TABLE 1: DESCRIPTION OF RECENT COHORT STUDIES OF PATIENTS WITH CARDIOMYOPATHY UNDERGOING MTWA TESTING

Study	Patient Population	Inclusion / Exclusion Criteria	MTWA test	Definition of MTWA Result	Endpoint	Other Risk Predictors / Confounders Assessed
<b>Bloomfield 2006</b>	Ischemic heart disease (n=267) <i>or</i> Non-ischemic cardiomyopathy (n=282)	<u>Inclusion:</u> · LVEF ≤ 40% · ≥ age 18  <u>Exclusion:</u> · Prior sustained ventricular arrhythmia · Persistent a-fib/flutter · Unstable CAD · NYHA class IV CHF · Unable to exercise on treadmill or bicycle	Exercise test (bike or treadmill) while taking regular cardiovascular medications (including beta-blockers)  CH2000 or Heartwave systems	<u>Positive:</u> Onset HR is ≤ 110 beats/min  <u>Negative:</u> Maximum negative HR ≥ 105 beats /min  <u>Indeterminate:</u> All others	All cause mortality <i>and</i> non-fatal sustained ventricular arrhythmias  (adjudicated by external events committee blinded to MTWA result)	Age Gender Race Ischemic vs. non-ischemic Past CHF admission NYHA functional class LVEF QRS duration Use of beta-blockers Diabetes ICD placement
<b>Chow 2006</b>	Ischemic heart disease (N=768)	<u>Inclusion:</u> · LVEF ≤ 35% · ≥ age 21  <u>Exclusion:</u> · Prior sustained ventricular arrhythmia · Not in sinus rhythm	Exercise test (treadmill) while taking regular cardiovascular medications ( <i>except</i> , beta-blockers and non-dihydropyridine calcium channel blockers held for >24 hours before test)	<u>Positive:</u> Onset HR is ≤ 110 beats/min  <u>Negative:</u> Maximum negative HR ≥ 105 beats /min  <u>Indeterminate:</u> All others	<u>Primary Endpoint:</u> All cause mortality  <u>Secondary Endpoints:</u> Cause-specific mortality; Appropriate ICD shock delivery; Comparison of MTWA positive, negative and indeterminate groups	Age Gender LVEF Symptomatic heart failure ICD placement QRS duration Holter monitoring History of MI, revascularization Co-morbidities (diabetes, HTN, COPD, CRI, PVD, CVA, TIA, a-fib, unexplained syncope)

TABLE 2: RESULTS OF RECENT COHORT STUDIES OF PATIENTS WITH CARDIOMYOPATHY UNDERGOING MTWA TESTING

<b>Study</b>	<b>MTWA Results</b>	<b>Endpoint Results</b>	<b>Event Rates</b>	<b>Positive and Negative Predictive Values</b>
<b>Bloomfield 2006</b> (N=549)	<u>Abnormal</u> (positive or indeterminate) 360 (66%)  <u>Normal</u> (negative) 189 (34%)	<u>Overall 24 months</u> 51 events --40 deaths --11 non-fatal sustained ventricular arrhythmias  <u>Abnormal MTWA</u> --47 events  <u>Normal MTWA</u> --4 events	<u>Abnormal MTWA</u> : 15.0%  <u>Normal MTWA</u> : 2.5%	<u>PPV</u> 47/360= 13.1%  <u>NPV</u> 185/189=97.9%
<b>Chow 2006</b> (N=768)	<u>Non-negative</u> (positive or indeterminate) 514 (67%)  <u>Negative</u> 254 (33%)	<u>Overall 18 months</u> 99 deaths  <u>Non-ICD</u> Non-negative MTWA --43 deaths Negative MTWA --15 deaths  <u>ICD</u> Non-negative MTWA --35 deaths --6 deaths	<u>Non-negative MTWA</u> : Non-ICD: 21.8% ICD: 11.0%  <u>Negative MTWA</u> : Non-ICD: 8.4% ICD: 8.0%	<u>PPV</u> 78/254 =30.7%  <u>NPV</u> 233/254.= 91.7%

**TA Criterion 4: The technology must be as beneficial as any established alternatives.**

Beyond LVEF as used in MADIT-II and SCD-HeFT, there are no clearly established alternatives to adequately risk-stratify patients with cardiomyopathy to receive, or not receive, an ICD. A meta-analysis of published literature on specific tests (not including MTWA) used to risk stratify patients for ICD placement found that no one test was better than any other; however it did find that a step-wise approach of three tests, with the final test being an invasive EP study, was able to stratify patients into a low-risk category (2.9% two-year risk of a major arrhythmic event) and a high-risk category (41% two-year risk of a major arrhythmic event).<sup>17</sup> The low-risk group in that meta-analysis had a similar two-year event risk as the low-risk group (MTWA normal) in the Bloomfield study (2.5%).<sup>23</sup>

TA Criterion 4 is not met.

**TA Criterion 5: The improvement must be attainable outside the investigational settings.**

Both of the recent cohort studies tested patients in outpatient clinic settings, some of which were in the community, using non-invasive exercise testing. The Bloomfield<sup>23</sup> study also allowed patients to continue their beta-blocker therapy, thus making this an even more feasible test to use in a non-investigational setting. However, because MTWA has not been proven in clinical trials to result in improved medical management in a way that will benefit the patient, improvement cannot be attained outside the investigational setting.

TA Criterion 5 is not met.

## Conclusion

Although MTWA testing with the spectral analysis method has been shown in cohort studies to have a good NPV for sudden cardiac death, and thus may prove helpful in counseling patients with both ischemic and non-ischemic cardiomyopathy who meet criteria for ICD placement to not elect to use the device, it remains unclear how best to use the test in medical management in a way that will benefit the patient. Ongoing trials will likely contribute more information about how MTWA testing compares to EP testing, as well as the utility of MTWA testing at different LVEF cutoffs.<sup>45, 46</sup> However, the gold standard study, a randomized controlled trial that compares use of MTWA in ICD placement decision-making to current standard practice, has not been undertaken.

## RECOMMENDATION

It is recommended that the use of Microvolt T-Wave Alternans testing to risk-stratify patients for Implantable Cardioverter-Defibrillator placement for prevention of sudden cardiac death does not meet CTAF criteria 3-5 because it is unclear, as of yet, how to use this test to improve medical management in a way that will benefit the patient.

*The California Technology Assessment Forum Panel voted unanimously to accept the recommendation as written.*

October 18, 2006

## RECOMMENDATIONS OF OTHERS

### Blue Cross Blue Shield Association (BCBSA)

The BCBSA TEC Medical Advisory Panel reviewed this technology in 2005 and found that TEC criteria were not met.

### Centers for Medicare and Medicaid Services (CMS)

In March 2006 CMS developed a National Coverage Determination providing for the use of T-wave Alternans. "Microvolt T-WAVE ALTERNANS diagnostic testing is covered for the evaluation of patients at risk for SCD, only when the spectral analysis method is used."

### American College of Cardiology, California Chapter (ACCCA)

The ACC California Chapter has been invited to participate in the meeting and to provide an opinion statement. The ACC/AHA/ESC 2006 Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death – Executive Summary can be found at:  
<http://www.acc.org/qualityandscience/clinical/pdfs/VASCDEExecSum.FINAL.8.14.06.pdf>.

### Heart Rhythm Society (HRS)

The HRS has provided an opinion statement noting that more research is needed to further delineate MTWA's role in selecting patients for an ICD. However, at this time, HRS believes that MTWA is one of several diagnostic tools that a physician may find useful in evaluating a patient at risk for SCD and determining the best therapy for that patient.

**ABBREVIATIONS USED IN THIS ASSESSMENT:**

CHF: Congestive Heart Failure

SCD: Sudden Cardiac Death

ICD: Implantable Cardioverter-Defibrillators

EP: electrophysiology

MUSTT: Multicenter Unsustained Tachycardia Trial

MADIT-II: Multicenter Automatic Defibrillator Implantation Trial II

SCD-HeFT: Sudden Cardiac Death in Heart Failure Trial

EKG: Electrocardiogram

TWA: T-Wave Alternans

MTWA: Microvolt T-Wave Alternans

TEC: Technology Evaluation Center

VT: Ventricular Tachycardia

VF: Ventricular Fibrillation

PPV: Positive Predictive Value

NPV: Negative Predictive Value

LVEF: Left Ventricular Ejection Fraction

NYHA: New York Heart Association

NNT: Number Needed to Treat

NNH: Number Needed to Harm

EF: Ejection Fraction

NICM: non-ischemic cardiomyopathy

ARR: absolute risk reduction

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