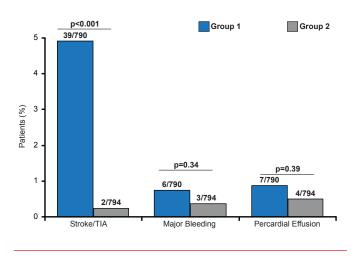
## CLINICAL TRIAL HIGHLIGHTS



## Figure 1. Periprocedural Events and Complications

TIA=transient ischemic attack.

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Warfarin use during ablation for AF was associated with relative risk reduction of 95% for stroke/TIA, 81% for minor bleeding, and 50% for major bleeding. Warfarin discontinuation, high CHADS<sub>2</sub> score, and AF type (nonparoxysmal) were significant predictors of thromboembolic events (Figure 2).

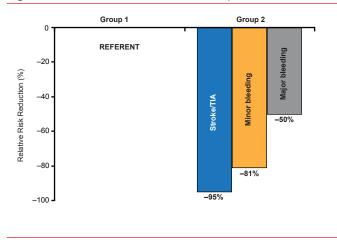


Figure 2. Relative Risk Reduction of Periprocedural Events

TIA=transient ischemic attack.

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Dr. Di Biase noted that periprocedural thromboembolic and hemorrhagic events are worrisome complications of catheter ablation for AF, particularly in patients with LSP AF, and with high CHADS<sub>2</sub> scores [Scherr D et al. *J Cardiovasc Electrophysiol* 2009]. These findings support other data suggesting that the combination of an open irrigation ablation catheter and periprocedural therapeutic anticoagulation with warfarin may reduce the risk of periprocedural stroke without increasing the risk of pericardial effusion or other bleeding complications [Di Biase L et al. *Circulation* 2010].

Dr. Di Biase concluded that the use of the newer anticoagulants during AF ablation procedures should be investigated in these high-risk patients and only compared with strategies that did not discontinue warfarin.

## DE-MRI Quantification of Atrial Fibrosis Predicts Ablation Outcome in Patients With Atrial Fibrillation

Written by Emma Hitt, PhD

Nassir F. Marrouche, MD, University of Utah, Salt Lake City, Utah, USA, presented data from the Delayed-Enhancement Magnetic Resonance Imaging (DE-MRI) Determinant of Successful Radiofrequency Catheter Ablation for Atrial Fibrillation trial [DECAAF; NCT01150214].

Previous studies demonstrated that the structural changes to the heart that are associated with atrial fibrillation (AF) can be quantified using DE-MRI [Oakes RS et al. *Circulation* 2009]. The DECAAF trial tested the hypothesis that DE-MRI can be used to determine the amount of left atrial fibrosis and/or remodeling, which predicts the patient's response to AF ablation.

In the international, prospective, multicenter, blinded, follow-up DECAAF trial, 330 patients that were undergoing their first AF ablation procedure were enrolled. Data from 261 patients were analyzed, as 57 MRIs were of poor quality and could not be analyzed and 12 patients were lost to follow-up. Patients were excluded from the study if they had a prior left atrial catheter or surgical ablation, were contraindicated for the DE-MRI contrast agent, were morbidly obese, and/or were too large for the MRI structure.

The follow-up period consisted of electrocardiogram, or Holter or event monitoring at 3, 6, and 12 months, as well as any additional follow-ups after 12 months, following the ablation procedure. The MARREK DE-MRI software sequence was installed at each participating center, and the staff was trained on five patients prior to enrolling for the DECAAF study. The primary endpoint for the DECAAF trial was recurrence of atrial arrhythmias following a 90-day blanking period.

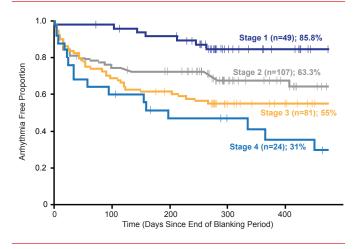
Quantification of atrial fibrosis by DE-MRI was categorized based on the Utah Classification System of Left Atrial Structural Remodeling, where stage 1 consists of <10% fibrosis/remodeling, stage 2 ≥10% to <20%, stage 3 ≥20% to <30%, and stage 4 ≥30% fibrosis/remodeling. The DECAAF trial results indicate that performing DE-MRI on patients prior to atrial ablation is feasible and produces reproducible data around the world. Interestingly, all



patients in the trial had posterior wall involvement, which accounted for about 57% of the total fibrotic tissue in the left atrium. The only predictor of atrial fibrosis was history of hypertension.

Atrial fibrosis and/or structural remodeling, as quantified by DE-MRI, was demonstrated in multivariate analysis to be the only independent predictor of ablation outcome (Figure 1).

Figure 1. DE-MRI-Based Atrial Fibrillation Staging Is Associated With Ablation Procedure Outcome



Reproduced with permission from NF Marrouche, MD.

Dr. Marrouche concluded that, in his opinion, the data from the DECAAF trial indicates that DE-MRI quantification of atrial fibrosis is a very strong predictor of AF ablation outcome and can be reproduced around the world. He added that DECAAF data would promote DE-MRI based individualized management of the AF and help triaging patients to the appropriate treatment option based on the amount of atrial disease. In the future this would not only help procedural success, but also avoid unnecessary ablation procedures.

## FIRM-Guided Ablation of Stable Rotors and Focal Sources Can Eliminate PAF Without PVI

Written by Mary Beth Nierengarten

In patients with paroxysmal atrial fibrillation (PAF), disease can be eliminated by targeting ablation to its primary sustaining mechanism alone without the need to ablate triggers. This is the conclusion of the Precise Rotor Elimination without Concomitant pulmonary vein Isolation for the Successful Elimination of Paroxysmal Atrial Fibrillation study [PRECISE-PAF; NCT01248156] presented in a late-breaking clinical trial session. The study results also confirm recently published evidence that the primary sustaining mechanisms of PAF is by stable rotors and focal sources revealed by Focal Impulse and Rotor Map (FIRM) in patient-specific bi-atrial locations [Narayan SM et al. *J Am Coll Cardiol* 2012], and offers data that elimination of rotors or focal sources either directly by FIRM-guided ablation, or coincidentally when anatomical ablation passes through them, may explain the success of different AF ablation approaches [Narayan SM et al. *J Am Coll Cardiol* 2013. In press].

Sanjiv M. Narayan, MD, PhD, University of California, San Diego School of Medicine, Veterans Affairs Medical Center, San Diego, California, USA, and colleagues undertook the PRECISE-PAF trial to test their hypothesis that prospective targeted ablation of stable rotors and focal sources alone would eliminate PAF over the long term without the need for pulmonary vein isolation (PVI).

The study included 31 consecutive PAF patients undergoing FIRM-guided ablation in five centers in the United States. Patients included in the study were aged >21 years, had indications for PAF ablation, discontinued antiarrhythmics >5 half-lives, and amiodarone >30 days. The only patients excluded were those unable or unwilling to provide informed consent. The primary endpoint was single procedure freedom from AF.

Most of the study participants were male (n=28); the average age was 59 years; AF had been present for ~4 years; the average CHADS<sub>2</sub> score was 1.5; and 38.7% (n=12) had a CHADS<sub>2</sub> >2. Overall, 74.2% (n=23) had hypertension and 32.3% (n=10) had coronary disease.

The primary endpoints of the study were acute elimination of diagnosed AF rotors and focal sources based on repeated mapping, as well as long-term freedom of AF (ie, using standard criteria defined as <30 seconds on external intermittent monitors or <1% in patients with continuous monitoring). Monitoring was done quarterly and antiarrhythmic drugs were discontinued after a 90-day blanking period.

For each patient, the investigators delivered FIRMguided ablation at each source to achieve termination of AF with noninducibility or to eliminate sources on repeat FIRM-maps. Residual tachycardias were also ablated. PVI was not done.

The study found that stable rotors and focal sources arose in all 31 patients, with 2.5 AF rotor/focal sources per patient. Overall, the sources arose in the left atrium in 66.3% of the patients and in the right atrium in 33.7%.

Median FIRM-guided ablation was  $17.4\pm8.2$  minutes, and total case ablation including typical atrial flutter ablation, was a median of  $22.7\pm9.1$  minutes. Although PVI showed potential in all patients, they were not isolated.

On follow-up for a median of 223 days, using more rigorous monitoring than typically used in AF trials, 82.6%