

# FIRM SUBSTRATE MAPPING APPROACH: outcome data update

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# NO CONFLICT OF INTEREST TO DECLARE

# GOALS

- Discuss the initial FIRM mapping data

   Very promising
- Discuss new data on FIRM mapping

   Less clear, somewhat conflicting
- Discuss the need for further prospective multicenter data
  - Further data on FIRM alone vs PVI
  - ?comparison of different technologies for rotor mapping

### PV CAN BE PASSIVE: PVI IS A BENEFITICAL BUT IMPERFECT ABLATION STRATEGY



#### Incidence of pulmonary vein conduction recovery in patients without clinical recurrence after ablation of paroxysmal atrial fibrillation: Mechanistic implications



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**BACKGROUND** Pulmonary vein (PV) isolation has become the mainstay acute procedural end point for paroxysmal atrial fibrillation (AF) ablation.

OBJECTIVE To examine the incidence of conduction recovery in the PVs in patients without clinical recurrence of AF after paroxysmal AF ablation.

METHODS From August 2008 to March 2011, 392 patients with drugrefractory PAF underwent catheter ablation in our center, a wide area circumferential ablation approach guided with a circular mapping catheter was performed with the intended endpoint of entrance block in all PVs. 276 (70.4%) of them were free from recurrence at one year follow-up, and 32 of them were enrolled to assess the incidence of PV reconnection. Forty-three patients with clinical recurrence after ablation were analyzed for comparison. The regions of gap were mapped and characterized in all of the reconnected PVs.

RESULTS Among patients without recurrence, recovery of PV conduction was observed in 29 of 32 (90.6%) patients: 10/32 (31.2%) reconnection in 4 veins, 7/32 (21.9%) in 3 veins, 10/32 (31.2%) in 2 veins, and 2/32 (6.2%) in 1 vein. No anatomic propensity was seen because reconnection was evenly distributed throughout all veins. (left superior pulmonary vein 21, left inferior pulmonary vein 20, right superior pulmonary vein 19, and right inferior pulmonary vein 23). When compared to patients with recurrence, no significant differences were seen in the proportion of patients with reconnection (P = 1.0) or in left atrium-PV intervals (73.4  $\pm$  43.3 ms vs 61.9  $\pm$  31.8 ms; P > .05).

CONCLUSION A high incidence of PV reconnection was similarly observed in patients with and without recurrence of AF, suggesting that sustained PV isolation may not be required for freedom from clinical recurrence of AF.

KEYWORDS Atrial fibrillation; Ablation; Pulmonary vein; Conduction recovery; Reconnection; Recurrence

ABBREVIATIONS AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia; EP = electrophysiological; GP = ganglionated plexus; LA = left atrium/atrial; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; PV = pulmonary vein; RIPV = right inferior pulmonary vein

(Heart Rhythm 2014;11:969-976) © 2014 Heart Rhythm Society. All rights reserved.

Amongst patients without recurrence, recovery of PV conduction was observed in 29/32 (90.6%) of patients: 31.2% reconnection in 4 veins, 21.9% in 3 veins, 31.2% in 2 veins, and 6.2% in 1 vein.

### SUBSTRATE ABLATION for PERSISTENT AF: STAR AF II

### CFAE arm



# Linear ablation arm



Verma, *NEJM* 2015; 372:1812

### **SUBSTRATE ABLATION: STAR AF II**



Verma, NEJM 2015; 372:1812

### **ATRIAL FIBRILLATION INTERPRETATION OF MAPPING STUDIES**



Shivkumar K, Buch E, Boyle NG: Non-Pharmacological Management Of Atrial Fibrillation: Role Of Pulmonary Veins And The Posterior Left Atrium. <u>Heart Rhythm 2009;6:S5–S11</u>





# **Experimental Evidence of Rotors**

In 20X20 mm preparation of homogeneous ventricular tissue, selfsustaining vortices rotating around a singularity were induced



Davidenko, PNAS 1990; 87:8785

### Stable Microreentrant Sources as a Mechanism of Atrial Fibrillation in the Isolated Sheep Heart

Ravi Mandapati, MD; Allan Skanes, MD; Jay Chen, BSc; Omer Berenfeld, PhD; José Jalife, MD

- Background—Atrial fibrillation (AF) has traditionally been described as aperiodic or random. Yet, ongoing sources of high-frequency periodic activity have recently been suggested to underlie AF in the sheep heart. Our objective was to use a combination of optical and bipolar electrode recordings to identify sites of periodic activity during AF and elucidate their mechanism.
- Methods and Results—AF was induced by rapid pacing in the presence of 0.1 to 0.5 μmol/L acetylcholine in 7 Langendorff-perfused sheep hearts. We used simultaneous optical mapping of the right and left atria (RA and LA) and frequency sampling of optical and bipolar electrode recordings (including a roving electrode) to identify sites having the highest dominant frequency (DF). Rotors were identified from optical recordings, and their rotation period, core area, and perimeter were measured. In all, 35 AF episodes were analyzed. Mean LA and RA DFs were 14.7±3.8 and 10.3±2.1 Hz, respectively. Spatiotemporal periodicity was seen in the LA during all episodes. In 5 of 7 experiments, a single site having periodic activity at the highest DF was localized. The highest DF was most often (80%) localized to the posterior LA, near or at the pulmonary vein ostium. Rotors (n=14) were localized on the LA. The mean core perimeter and area were 10.4±2.8 mm and 3.8±2.8 mm<sup>2</sup>, respectively.
- Conclusions—Frequency sampling allows rapid identification of discrete sites of high-frequency periodic activity during AF. Stable microreentrant sources are the most likely underlying mechanism of AF in this model. (Circulation. 2000;101:194-199.)

### LA Isochrone Map



Mandapati R, Skanes A, Chen J, Berenfeld O, Jalife J. *Stable microreentrant* sources as a mechanism of atrial fibrillation in the isolated sheep heart. *Circulation.* 2000;101(2):194-199.

A recent debate has centered on whether the CONFIRM trial (Narayan et al, JACC 60: 628–36, 2012) supports the Mother Rotor hypothesis as the mechanism of human AF

**CROSSTALK (**J Physiol, 592:3163-70, 2014) **Proposal:** *Rotors have been demonstrated to drive human AF* **Opposing view:** *Rotors have not been demonstrated to be the drivers of human AF* 

### **Pro: Jalife & Narayan**

- It works! CONFIRM trial\*: FIRM+Standard RX (82% success) vs Standard Rx (45% success)
- Low spatial resolution 'panoramic' phase mapping (64 RA + LA basket electrodes) identified a mean of 2.1 rotors in 97% of patients, precessing over 2-3 cm<sup>2</sup> area

### **Con: Allessie & de Groot**

- High resolution human AF mapping studies have not identified rotors consistently & neither has 'panoramic' body surface ECG
- A trial of PVI alone versus FIRM alone is needed

# **CURRENT FIRM DATA**

# **FIRM TECHNIQUE**

- Mapping performed with Rhythm View, Topera, Inc system
  - Basket cathter Electrograms filtered to exclude noise and far-field signals using previous work on rate dynamics of atrial action potential duration to estimate minimum activation time and conduction velocity
  - These properties are used by the system to identify physiologic propagation paths
  - Isopotential movies are constructed of AF cycles
  - The predicted wobble of a rotor is calculated into the localization of the rotor
  - Rotors are identified only if stable for ~10 minutes

# **FIRM TECHNIQUE**





Narayan et al, JACC 2012;60:628

# **Rotor Mapping During Human AF**



# THE PROMISE: to avoid extensive LA destruction



# **FIRM DATA AVAILABLE TO DATE**

# <u>CON</u>ventional Ablation for Atrial Fibrillation With Or Without <u>Focal Impulse and Rotor Modulation</u> The CONFIRM Trial

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JACC 2012;60:628

### Methods: CONFIRM Trial Protocol

### Endpoints

 (1) Acute AF Termination/slowing≥10% (<30 mins); (2) Long-Term AF-Freedom defined as AF/AT < 1% on implanted monitoring devices or < 30 seconds on Holter/Event Monitor</li>

### Followup in Clinic at 1, 3, 6, 9, 12, (18), 24 months, Plus

- Anti-arrhythmic medications discontinued after 90 d blanking
- Implanted Loop Recorder with automatic AF detection algorithm
- Or Holter/Event Monitor



### **CONFIRM ACUTE PROCEDURAL RESULTS**

- Patients prospectively enrolled to either conventional ablation (FIRM-blinded) or AF rotor mapping/ablation followed by conventional ablation (FIRM-guided)
- In FIRM-guided arm, 56% had AF termination during ablation, additional 30% showed AFCL slowing

Characteristic	<b>Conventional Ablation</b>	FIRM-Guided Ablation	p Value
Cases with intraprocedural sustained AF	65/71 (92%)	36/36 (100%)	0.10
Subjects with AF sources	63/65 (97%)	35/36 (97%)	1.00
Acute endpoint achieved	13/65 (20%)	31/36 (86%)	<0.001
AF termination endpoint	6/65 (9%)	20/36 (56%)	<0.001
Ablation time, min, at primary source	-	2.5 (1.0-3.1)	
To sinus rhythm/atrial tachycardia	3/3	16/4	0.29

### **CONFIRM Outcomes: Long-Term Off-Drug Efficacy**



### Initial Independent Outcomes from Focal Impulse and Rotor Modulation Ablation for Atrial Fibrillation: Multicenter FIRM Registry

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**Methods** — We prospectively enrolled n = 78 consecutive patients (61 ± 10 years) undergoing FIRM guided ablation for persistent (n = 48), longstanding persistent (n = 7), or paroxysmal (n = 23) AF. AF recordings from both atria with a 64-pole basket catheter were analyzed using a novel

**Results**—Each institution recruited a median of 6 patients, each of whom showed  $2.3 \pm 0.9$  AF rotors/focal sources in diverse locations. 25.3% of all sources were right atrial (RA), and 50.0% of patients had  $\geq 1$  RA source. Ablation of all sources required a total of  $16.6 \pm 11.7$  minutes, followed by PVI. On >1 year follow-up with a 3-month blanking period, 1 patient lost to follow-up (median time to 1st recurrence: 245 days, IQR 145–354), single-procedure freedom from AF was 87.5% (patients without prior ablation; 35/40) and 80.5% (all patients; 62/77) and similar for persistent and paroxysmal AF (P = 0.89).

### **MULTICENTER FIRM REGISTRY RESULTS**



#### Figure 3.

Freedom from atrial fibrillation after single (index) FIRM + PVI procedure for all cases (green) and patients at their first ablation (blue).



#### Figure 4.

Freedom from all atrial arrhythmias (atrial fibrillation and atrial tachycardia) after a single (index) FIRM + PVI procedure for all cases (green) and patients at their first ablation (blue). J Am Coll Cardiol. 2014 May 6; 63(17): 1761-1768. doi:10.1016/j.jacc.2014.02.543.

### Ablation of Rotor and Focal Sources Reduces Late Recurrence of Atrial Fibrillation Compared to Trigger Ablation Alone

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Objectives — To determine if ablation that targets patient-specific AF-sustaining substrates (rotors or focal sources) is more durable than trigger ablation alone at preventing late AF recurrences.

Background-Late recurrence substantially limits the efficacy of pulmonary vein (PV) isolation for AF, and is associated with PV reconnection and the emergence of new triggers.

Methods — We performed 3 year follow-up of the CONFIRM trial, in which 92 consecutive AF patients (70.7% persistent) underwent novel computational mapping to reveal a median of 2 (IQR 1–2) rotors or focal sources in 97.7% of patients during AF. Ablation comprised source (Focal Impulse and Rotor Modulation, FIRM) then conventional ablation in n=27 (FIRM-guided), and conventional ablation alone in n=65 (FIRM-blinded). Patients were followed with implanted ECG monitors when possible (85.2% FIRM guided, 23.1% FIRM-blinded).

**Results** — On 890 days follow-up (median; IQR 224–1563) compared FIRM-blinded therapy, patients receiving FIRM-guided ablation maintained higher freedom from AF after 1.2±0.4 procedures (median 1, IQR 1–1) (77.8% vs 38.5%; p=0.001) and a single procedure (p>0.001), and higher freedom from all atrial arrhythmias (p=0.003). Freedom from AF was higher when ablation directly or coincidentally passed through sources than when it missed sources (p>0.001).



Figure 3. Freedom from the Secondary End Point (all Atrial Arrhythmias) Freedom from the Secondary End Point (all Atrial Arrhythmias) for FIRM-guided ablation (blue) and conventional ablation (red: p=0.01).

# **PRECISE-PAF**

Prospective Targeted Ablation of Stable Rotors/

**Focal Sources Will Eliminate Paroxysmal AF Long** 

### **Term Without PVI**

• **PRECISE-PAF:** <u>Precise</u> <u>Rotor</u> <u>Elimination</u> without <u>Concomitant</u> pulmonary

vein <u>I</u>solation for the <u>S</u>uccessful <u>E</u>limination of <u>P</u>aroxysmal <u>AF</u>

• (clinicaltrials.gov: NCT 01248156, 2010)

Narayan S.M., Krummen D.E., Donsky A., Swarup V., Miller J.M.; Precise Rotor Elimination without Concomitant pulmonary vein Isolation for the Successful Elimination of Paroxysmal Atrial Fibrillation. PRECISE-PAF. *Heart Rhythm*. 2013;10:LBCT4

# **PRECISE-PAF**

- Previous reported data:
- ~30 patients enrolled
- 100% with sources
- 82.6% freedom from AT/AF at median f/u of 223 days

# **ADDITIONAL DATA**

#### SINGLE CENTER EXPERIENCE WITH FIRM ABLATION: A CASE SERIES OF 125 PATIENTS

Jason R. Foreman, DO, Benzy J. Padanilam, MD, Jeff A. Olson, DO, Girlsh V. Nair, MD and Eric N. Prystowsky, MD, FHRS. St. Vincent Hospital, Indianapolis, IN, St Vincent Medical Group, Indianapolis, IN

Introduction: Focal impulse and rotor modulation (FIRM, Topera Inc.) is a novel computational mapping of localized sources that

may maintain atrial fibrillation (AF). Only limited studies have been reported about the safety and efficacy of ablations directed by FIRM mapping.

Methodis: Between February and December 2014, 125 patients presenting in AF or having inducible sustained AF underwent FIRM ablation and pulmonary vein isolation (PVI). Procedural details and complications are reported for all patients. Outcomes are reported for all patients with > 6 months follow-up. Results: Among 125 patients evaluated, 66.4% were men, and the mean age was 62.75 years. The mean number of rolors per patient was 5.2, with an average of 2.0 in the right atrium and 3.2. in the left atrium. Atrial fibrillation was classified as paroxysmal in 53 (42.4%), persistent in 61 (48.8%), and long-standing persistent in 11 (8.8%) patients. Termination of atrial fibrillation during the procedure occurred in 49 of 125 (39.2%) patients with 33 (67.3%) terminations in the paroxysmal group, 15 (30.6%) in persistent, and 1 (2%) in long-standing persistent atrial fibrillation. A total of 52 (41.6%) patients had at least 6 months of clinical follow-up. After the initial 90 day blanking period, 34 of 52 (65.4%) patients had no recurrent AF or atrial tachycardia. (AT): 47.1 % for paroxysmal and 47.1 % for persistent. Of note: of 24 patients with termination during AF only 3 had recurrent AF. There were 2 (1.6%) strokes, 1 (0.8%) major bleeding event and no deaths. Both strokes were small with full neurologic recovery and occurred during rivaroxaban anticoagulation. Conclusions: in this large single-center series of patients undergoing FIRM abiation with PVI, the safety of the procedure is comparable to historic controls. Termination occurred in 46.2 % of patients and augured a good clinical outcome.

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Methods: Between February and December 2014, 125 patients presenting in AF or having inducible sustained AF underwent FIRM ablation and pulmonary vein isolation (PVI). Procedural details and complications are reported for all patients. Outcomes are reported for all patients with a 6 months follow-up. Results: Among 125 patients evaluated, 66.4% were men, and

125 pts. 39% termination rate (2x more frequent in paroxysmal group), 65% of those with f/u (52 pts) were free of AF/AT.

There were 2 (1.6%) strokes, 1 (0.8%) major bleeding event and no deaths. Both strokes were small with full neurologic recovery and occurred during rivaroxaban anticoagulation. Conclusions: In this large single-center series of patients undergoing FIRM ablation with PVI, the safety of the procedure is comparable to historic controls. Termination occurred in 46.2 % of patients and augured a good clinical outcome.

# **RECENT ABSTRACT**

#### Abstract: P192

Nine months outcomes following focal impulse and rotor modulation for the treatment of atrial fibrillation using the novel 64-electrode basket catheter

#### Authors:

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#### Topic(s):

Catheter ablation (Atrial Fibrillation)

#### Citation:

Europace Abstracts Supplement ( 2015 ) 17 ( Supplement 3 ), iii16

The mechanism for AF maintenance is still controversial. The concept of rapidly-activating spiral rotors perpetuating AF has lead to the development of several rotor-mapping systems.

We present the 9-month outcomes of focal impulse and rotor modulation (FIRM) ablation using the novel 64-electrode basket catheter and computational system and evaluate its feasibility in conjunction with PVI to treat AF.

25 patients underwent FIRM mapping and ablation to treat AF (paroxysmal AF, n = 10, 40%). A novel basket catheter was used for rotor identification within the right atrium (RA) followed by the left atrium (LA). Radiofrequency energy was applied at and around each rotor core for 300s and rotor-mapping was repeated until all rotors were eliminated before PVI was performed.

A mean of 2.9±1.6 rotors were identified per patient, predominantly in the LA (n = 59). 7/59 (11%) left-sided rotors were located in the PVs. Total median FIRM ablation time was 925.0 (651.0, 980.0) seconds. Clinical follow-up outcomes after 9±1 months were as follows: Recurrence occurring after a three-month blanking period was seen in 6/25 (24%) patients. Recurrent rhythms included AF in 3 patients and AT in 3 patients. Of these 6 patients, 4/6 underwent re-ablation procedures. After the last procedure, 23/25 (92%) patients remained in sinus rhythm. Of the 19 patients without AF/AT recurrence outside the blanking period, 10/19 (53%) patients had AF termination or CL prolongation by ≥10%. AF termination occurred more often in male compared to female patients (11/16 (68.8%) vs. 1/9 (11.1%) patients; p=0.01), and in patients with induced AF compared to spontaneous AF (11/14 (78.6%) vs. 1/11 (9.1%); p=0.01). No single baseline characteristic or procedural parameter including AF termination or CL prolongation predicted recurrence using univariate prediction models.

Elimination of all AF rotors can be achieved by catheter ablation and leads to AF termination or CL prolongation in approximately every second patient. Nine months clinical outcomes following PVI and rotor ablation using the novel basket catheter are promising and in line with previous reports. No baseline or procedural parameter including AF termination or CL prolongation predicted arrhythmia recurrence.

#### Tilz R, EHRA Annual Sessions 2015, presentation P192, Milan

# **ROTOR ONLY ABLATION**

#### Abstract: P462

FIRM only ablation in patients with persistent atrial fibrillation: acute and medium term results

#### Authors:

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Topic(s): Catheter ablation (Atrial Fibrillation)

#### Citation:

Europace Abstracts Supplement ( 2015 ) 17 ( Supplement 3 ), iii68

Modulation of focal impulses and rotors (FIRM) has been described to be highly effective in preventing AF recurrences if added to pulmonary vein Isolation (PVI). The aim of the present study is to evaluate safety and efficacy of such an ablation without PVI in persistent AF cases. We present acute and medium term results of the patients (pt)included already.

Patients (pt) with persistent AF undergo FIRM ablation supported by EnSite<sup>TM</sup> NavX<sup>TM</sup> (St. Jude).Endocardial Mapping of focal and rotational activity is performed using RhythmviewTM (Topera Inc). Routine cerebral MRI and esophageal endoscopy are performed to notice silent cerebral lesions (SCL) and silent endoscopically detected esophageal lesions (EDEL). Follow up is performed every 3 months including 48h Holter and event recorder in case of palpitations without documentation in the Holter ECG.

Twenty one patients were included already (mean age 62±10 years, 72% men, mean LA diameter 42 ±4 mm). Median rate of sources was 1 [0-3] in RA and 3 [1-4] in LA. In none of the patients AF termination in sinus rhythm could be observed. CL prolongation occurred in 10/21 pt (47%) with conversion in a regular AT in 2/21 pt (11%). Mean procedure duration, fluoroscopy time, LAtime and RF time were 227 ±47 min, 26 ±8, 137 ±31 and 36 ±14 min. Minor or major complications occurred in one patient (1 late pericardial tamponade), EDEL have been observed in 1/21 pt (4.8%) and SCL in 4/17 pt (25%), whereas pre-existing SCL could be detected in 10/17 pt (59%). Rate of early recurrences was 10/15 (67%). Regular AT was observed in 7/10 recurrences (70%). Two of these patients showed both, AF and AT. In June 2015 we will present complete 6 months follow up of all the presented cases.

FIRM only ablation seems to be safe regarding silent and overt complications. Rate of SCL is comparable to published rates of RF ablation. The rate of EDEL is very low due to avoidance of posterior ablations. Procedural parameters seem to be comparable to that of conventional ablation concepts for persistent AF cases. Early recurrences occur often as regular AT. Inclusion of linear ablations might be a useful concept in case of extensive regional ablation which might have created critical isthmus sites.

#### Schade, EHRA Annual Sessions 2015, presentation P462, Milan

### **ROTOR ONLY ABLATION**

#### PO01-58

ACUTE AND SHORT-TERM OUTCOMES IN PERSISTENT AND LONG-STANDING PERSISTENT PATIENTS UNDERGOING ROTORS ONLY ABLATION

Carola Gianni, MD, Luigi Di Blase, MD, PhD, Thomas Deneke, MD, PhD, Tami Metz, BSN, RN FA, Philipp Halofass, MD, Patrick Müller, MD, Anja Schade, MD, Sanghamitra Mohanty, MD, Chintan Trivedi, MD, Rong Bai, MD, Amin Al-Ahmad, MD, FHRS, J. David Burkhardt, MD, G. Joseph Gallinghouse, MD, Rodney P. Horton, MD. Patrick M. Hranitzky, MD. FHRS, Javier E. Sanchez, MD, Gery F. Tomassoni, MD, FHRS and Andrea Natale, MO, FHRS, Texas Cardiac Antrythmia Institute at St. David's Medical Center and Department of Clinical Sciences and Community Health at University of Milan, Austin, TX, Texas Cardiac Anthythmia Institute at St. David's Medical Center and Albert Einstein College of Medicine at Montetione Medical Center, Austin, TX, Heart-Center Bad Neustadt, Bad Neustadt. Germany, Texas Cardiac Anhythmia Institute at St. David's Medical Center, Austin, 7X, Klinikum Coburg, Coburg, Germany, Ruhr-University Bochum, Bochum, Germany, Lexington Cardiology Consultants, Lexington, KY

Introduction: Focal impulse and rotor modulation (FIRM) guided abiation targets localized sources that are thought to sustain AF and has been shown to be superior to conventional abiation alone in patients with paroxysmal and persistent AF. Few data are available on long standing persistent (LSP) AF. We sought to evaluate the acute and short-term outcomes of FIRM-only abiation in persistent and LSP AF patients.

Methods: This was a prospective observational study of consecutive non-paroxysmal AF patients undergoing FIFMonly ablation in 3 centers (2 in the US, 1 in the EU). Acute success was defined as AF termination or ≥ 10% AF slowing. Short-term efficacy was defined as freedom from AF/AT during hospitalization and initial follow-up (including the 2-month blanking period).

Results: A total of 30 patients were enrolled (20 persistent, 10 LSP), in 1 LSP AF patient the procedure was aborted because of anatomical reasons (persistent left superior and inferior vena cava). There were no major periprocedutal adverse events. Rotors were present in all patients (a mean of 4 sources per patient; 61% were left atnal) and were ablated as confirmed by their absence during remapping. These were no AF terminations, and overall acute success, driven by AF slowing, was achieved in 25% of patients with persistent AF and 56% of patients with LSP AF, in the short term follow-up, single-procedure freedom from AT/AF recurrence was 40% in persistent AF patients (all of these patients were on short-term amiodarone to prevent early

arrhythmias following ablation). In the LSP AF population, singleprocedure freedom from AT/AF recurrence was 0% **Conclusions:** Targeted ablation of stable AF rotors in persistent and LSP AF proved to be safe but not effective in obtaining AF organization/termination during the procedure. In LSP AF patients, rotors alone ablation was not effective in maintaining sinus rhythm in the short-term follow-up.

#### PO01-58

#### ACUTE AND SHORT-TERM OUTCOMES IN PERSISTENT AND LONG-STANDING PERSISTENT PATIENTS UNDERGOING ROTORS ONLY ABLATION

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Introduction: Focal impulse and rotor modulation (FIRM) guided abiation targets localized sources that are thought to sustain AF and has been shown to be superior to conventional abiation alone in patients with paroxysmal and persistent AF. Few data are available on long standing persistent (LSP) AF. We sought to evaluate the acute and short-term outcomes of FIRM-only abiation in persistent and LSP AF patients.

Methods: This was a prospective observational study of consecutive non-paroxysmal AF patients undergoing FIRMonly ablation in 3 centers (2 in the US, 1 in the EU). Acute success was defined as AF termination or > 10% AF slowing. Short-term efficiecy was defined as treedom from AF/AT during bostituitization and initial follow up (includion the 2-month)

Rotors in all 30 patients, No terminations, 25% slowing in persistent AF and 56% in longstanding persistent AF, 40% freedom from AT/

### AF in short-term f/u

AF organization/termination during the procedure. In LSP AF patients, rotors alone ablation was not effective in maintaining sinus rhythm in the short-term follow-up.

### Quantitative Analysis of Localized Sources Identified by Focal Impulse and Rotor Modulation Mapping in Atrial Fibrillation

Peyman Benharash, MD; Eric Buch, MD; Paul Frank, MD; Michael Share, MD; Roderick Tung, MD; Kalyanam Shivkumar, MD, PhD; Ravi Mandapati, MD

> Circ Arrhythm Electrophysiol Volume 8(3):554-561 June 16, 2015



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# QUANTITATIVE ANALYSIS OF UCLA FIRM CASES

Based on prior mechanistic studies, we hypothesized that rotor sites would exhibit features distinguishing them from other atrial sites:

- Evidence of rotational activity on electroanatomic mapping
- Distinctive quantitative characteristics
  - Frequency domain
  - Shannon entropy

# QUANTITATIVE ANALYSIS OF FIRM CASES

- Quantitative analysis of EGM's when FIRM rotors were detected
  - Assessment of multipolar basket catheter
    - Coverage of atrial surface
    - Electrogram quality
  - Electroanatomic activation maps of rotor sites
  - Frequency domain and entropy analysis
- FIRM rotor ablation results
  - Acute
  - Intermediate
  - Long term (2 Centers)

### **BASELINE CHARACTERISTICS**

	All patients (n=24)	Acute Procedural Success (n = 12)	No Acute Procedural Success (n = 12)	<u>p value</u>
Age	64 ± 10	66 ± 11	61 ± 10	0.33
Male gender (%)	14 (61)	9 (75)	5 (42)	0.11
Paroxysmal pattern of AF (%)	12 (50)	6 (50)	6 (50)	1.00
AF duration (years from diagnosis)	7.8 ± 5.5	9.0 ± 4.3	6.5 ± 6.5	0.28
Prior AF ablation (%)	15 (63)	8 (67)	7 (58)	0.69
Number of previous AF ablations	1.2 ± 1.1	1.4 ± 1.3	0.9 ± 0.9	0.29
Number of failed antiarrhythmic drugs	1.7 ± 1.0	1.5 ± 0.9	1.8 ± 1.0	0.41
CHA2DS2-VaSC score	1.7 ± 1.0	1.8 ± 1.1	1.6 ± 1.0	0.57
LVEF (%)	63 ± 6.9	64 ± 5.7	61 ± 8.0	0.31
LA volume on MRI (ml)	76 ± 32	79 ± 31	73 ± 33	0.64

Benharash P, Buch E, Frank P, Share M, Tung R, Shivkumar K & Mandapati R. Quantitative Analysis Of Localized Sources Identified By Focal Impulse And Rotor Modulation Mapping In Atrial Fibrillation 2015 (submitted-in review)



Benharash P, Buch E, Frank P, Share M, Tung R, Shivkumar K & Mandapati R. Quantitative Analysis Of Localized Sources Identified By Focal Impulse And Rotor Modulation Mapping In Atrial Fibrillation 2015 (submitted-in review)

### LEFT ATRIAL BASKET CATHETER COVERAGE



LA surface was segmented to calculate total surface area outside pulmonary veins

1 cm fill threshold was set to calculate surface area near any basket electrode

**Proportion of LA surface area** mapped  $54\% \pm 15\%$ 

EAM SA always an underestimate

Benharash P, Buch E, Frank P, Share M, Tung R, Shivkumar K & Mandapati R. Quantitative Analysis Of Localized Sources Identified By Focal Impulse And Rotor Modulation Mapping In Atrial Fibrillation 2015 (submitted-in review)

### **DISORGANIZED PATTERN AT ROTOR SITES**



# ONLY CASE WITH ROTATIONAL ACTIVITY

### LA rotors/pt :**1.6 ± 0.8**

RA rotors/pt :0.6 ± 0.8



Benharash P, Buch E, Frank P, Share M, Tung R, Shivkumar K & Mandapati R. Quantitative Analysis Of Localized Sources Identified By Focal Impulse And Rotor Modulation Mapping In Atrial Fibrillation 2015 (submitted-in review)

## **SUMMARY OF RESULTS**

All procedures (n=24)Procedural Success (n = 12)Procedural Success (n = 12)Procedural Success (n = 12)Number LA rotors identified $1.6 \pm 0.8$ $1.7 \pm 0.9$ $1.5 \pm 0.7$ $0.61$ Number RA rotors identified $0.6 \pm 0.8$ $0.7 \pm 0.9$ $0.6 \pm 0.8$ $0.81$ Proportion of LA surface area mapped with basket catheter $54\% \pm 15\%$ $56\% \pm 16\%$ $53\% \pm 15\%$ $0.75$ Number of basket electrodes with adequate $54\% \pm 15\%$ $56\% \pm 16\%$ $53\% \pm 15\%$ $0.75$		All	Acute	No Acute	$\frown$
Number LA rotors identified $1.6 \pm 0.8$ $1.7 \pm 0.9$ $1.5 \pm 0.7$ $0.61$ Number RA rotors identified $0.6 \pm 0.8$ $0.7 \pm 0.9$ $0.6 \pm 0.8$ $0.81$ Proportion of LA surface area mapped with basket catheter $54\% \pm 15\%$ $56\% \pm 16\%$ $53\% \pm 15\%$ $0.75$ Number of basket electrodes with adequate $0.6 \pm 0.8$ $0.75$		<u>All procedures</u> (n=24)	<u>(n = 12)</u>	<u>(n = 12)</u>	<u>p value</u>
Number RA rotors identified0.6 ± 0.80.7 ± 0.90.6 ± 0.80.81Proportion of LA surface area mapped with basket catheter54% ± 15%56% ± 16%53% ± 15%0.75Number of basket electrodes with adequate	Number LA rotors identified	1.6 ± 0.8	1.7 ± 0.9	1.5 ± 0.7	0.61
Proportion of LA surface area mapped with basket catheter54% ± 15%56% ± 16%53% ± 15%0.75Number of basket electrodes with adequate	Number RA rotors identified	0.6 ± 0.8	0.7 ± 0.9	0.6 ± 0.8	0.81
Number of basket electrodes with adequate	Proportion of LA surface area mapped with basket catheter	54% ± 15%	56% ± 16%	53% ± 15%	0.75
atrial electrogram         31 ± 17         27 ± 18         35 ± 16         0.28	Number of basket electrodes with adequate atrial electrogram	31 ± 17	27 ± 18	35 ± 16	0.28
Dominant frequency at rotor sites (Hz)         4.9 ± 1.3         4.8 ± 1.4         5.0 ± 1.3         0.62	Dominant frequency at rotor sites (Hz)	4.9 ± 1.3	4.8 ± 1.4	5.0 ± 1.3	0.62
Dominant frequency at non-rotor sites (Hz)         4.7 ± 1.6         4.8 ± 1.6         4.6 ± 1.7         0.06	Dominant frequency at non-rotor sites (Hz)	4.7 ± 1.6	4.8 ± 1.6	4.6 ± 1.7	0.06
Shannon entropy at rotor sites         4.8 ± 0.5         4.8 ± 0.3         4.9 ± 0.7         0.35	Shannon entropy at rotor sites	4.8 ± 0.5	4.8 ± 0.3	4.9 ± 0.7	0.35
Shannon entropy at non-rotor sites         4.9 ± 0.6         4.8 ± 0.5         5.0 ± 0.6         0.08	Shannon entropy at non-rotor sites	4.9 ± 0.6	4.8 ± 0.5	5.0 ± 0.6	0.08
Patients with rotational activity or focal source at rotor site on electroanatomic	Patients with rotational activity or focal source at rotor site on electroanatomic				
<u>mapping</u> 1 (4%) 0 (0) 1 (8%) 0.34	mapping	1 (4%)	0 (0)	1 (8%)	0.34

# **ACUTE PROCEDURAL OUTCOMES**

- Acute endpoint:
  - AF termination to sinus rhythm
  - AF organization
  - >10% slowing of AF cycle length (measured in coronary sinus)
- Acute success in 12/24 (50%)
  - AF termination: 1/24
  - AF organization: 3/24
  - AFCL slowing: 8/24
- No significant difference in number of rotors, ablation time, age, or prior ablation in those with acute success vs. failure

None of the patients with AF at the start of the procedure had AF termination or organization -- all acute success was due to CL slowing.

### **FREEDOM FROM ATA OF AAD**



<u>Michael Share MD</u>, Ravi Mandapati MD, Kalyanam Shivkumar MD PhD, Eric Buch MD; Clinical Outcomes of Focal Impulse and Rotor Modulation (FIRM) for Treatment of Atrial Fibrillation: Single Center Experience; AHA 2014

### **ROTORS IN HUMANS: recent studies**

#### Technical challenges of rotor identification during atrial fibrillation using phase singul...

#### Abstract: P257

Technical challenges of rotor identification during atrial fibrillation using phase singularity detection

#### Authors

P. Kuklk<sup>1</sup>, A. Van Humsk<sup>1</sup>, S. Zoemering<sup>1</sup>, B. Maesen<sup>2</sup>, L. Pison<sup>2</sup>, H.J. Crijns<sup>2</sup>, S. Willema<sup>3</sup>, U. Schotten<sup>1</sup>, <sup>1</sup>Maastricht University, Department of Physiology - Massricht -Netherlands, <sup>2</sup>Maastricht University Medical Center (MUMC), Department of Cardiology - Maastricht - Netherlands, <sup>3</sup>University Medical Center Hamburg Eppendorf, Department of Cardiology, Electrophysiology - Hamburg - Germany,

#### Topicisie

Mechanisms & Computer modelling (Atrial Fibrillation)

#### Citationi

Europace Abstracts Supplement ( 2015 ) 17 ( Supplement 3 ), iii20

Recent studies report presence of stable rotors during persistent strial fibrillation (PersAF) defined as phase singularities (PS) mapped using basket type catheters. Purpose of this study is to explore technical difficulties inherent to this type of mapping approach.

Two mapping approaches were used to map both attiz: (i) endocardial mapping using 64-electrode mapping cathetar (Constellation, Boston Scientific) in N=19 pts undergoing cathetar ablation of PersAF and (ii) high-density epicardial mapping in N=21 pts undergoing CABG surgery (12 pts with PersAysmal AF (PAF) and 9 with PersAF) using 16x16 electrodes armys with 1.5 mm inter-electrode spacing (10 s recordings). Electrogram phase was reconstructed using Hilbert transform preceded by simusoidal recomposition. Rotors were detected as PS at a set of four neighboring electrodes with a condition of lifespan geneter than 1 cycle length of AF. Endocardial mapping coverage was assessed using atrial geometry reconstructed using NavX system and defined as the % of total area within 1 cm from the basket electrodes.

Following problems were identified with respect to sensitivity and specificity for detection of rotors: (i) low attail coverage using a basket catheter: in the most optimal position the coverage was 43a16% in LA and 60a21% in RA, (ii) lack of objective method to determine basket electrode contact with attail wall resulting in potential inclusion of noncontact electrograms into analysis, (iii) short lifespan of detected PS in high-density mapping: 1.8a0.6 rotations (max: 6.8 rotations) and their mignatory behaviour: drift length 12.6a8.0 mm (max: 71 mm), (iv) poor specificity of PS detection using a grid of 4 electrodes. Analysis performed on an extended detection grid (each PS point was confirmed or rejected based on assessment on 4x4 electrodes grid around PS point) resulted in only 9% of PS points confirmed as rotating waves.

Identification of rotational waves using phase singularity detection in endocardial maps recorded with basket catheters has multiple limitations which should be addressed before use in ablation strategies.

#### Kuklik P, EHRA Annual Sessions 2015, presentation P257, Milan

### **IN PRESS- HEART RHYTHM**

### LONG-TERM CLINICAL OUTCOMES OF FOCAL IMPULSE AND ROTOR MODULATION FOR TREATMENT OF ATRIAL FIBRILLATION: A MULTI-CENTER EXPERIENCE

Eric Buch MD FHRS<sup>1</sup>, Michael Share MD<sup>1</sup>, Roderick Tung MD FHRS<sup>1</sup>, Peyman Benharash MD<sup>1</sup>, Parikshit Sharma MD<sup>3</sup>, Jayanthi Koneru MD FHRS<sup>3</sup>, Ravi Mandapati MD FHRS<sup>1,2</sup>, Kenneth A. Ellenbogen MD FHRS<sup>3</sup>, Kalyanam Shivkumar MD PhD FHRS<sup>1</sup>

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#### LONG-TERM CLINICAL OUTCOMES OF FOCAL IMPULSE AND ROTOR MODULATION FOR TREATMENT OF ATRIAL FIBRILLATION: A MULTI-CENTER EXPERIENCE

BASELINE	All Patients (n=43)	Clinical Success (n = 16)	AF Recurrence (n = 27)	p value
Age	61 ± 11	62 ± 11	61 ± 12	0.79
Male gender (%)	32 (74)	13 (81)	19 (70)	0.43
Paroxysmal pattern of AF (%)	24 (56)	7 (44)	17 (63)	0.22
AF duration (years from diagnosis)	7.3 ± 5.4	7.9 ± 5.6	6.9 ± 5.3	0.56
Prior AF ablation (%)	29 (67)	11 (69)	18 (67)	0.89
Number of previous AF ablations	1.2 ± 1.0	1.3 ± 1.0	1.1 ± 1.1	0.55
Number of failed antiarrhythmic drugs	1.6 ± 0.8	1.7 ± 0.9	1.6 ± 0.7	0.69
CHA2DS2-VaSC score	1.7 ± 1.1	1.5 ± 1.1	1.9 ± 1.2	0.28
LVEF (%)	59 ± 6.4	59 ± 5.0	59 ± 7.1	1.00

Buch E, Share M, Turng R, Benharash P, Mandapati R, Ellenbogen K, Shivkumar K- Long-term *Clinical Outcomes Of Focal Impulse And Rotor Modulation For Treatment Of Atrial Fibrillation: A Multi-center Experience* –(in revision) 2015

#### LONG-TERM CLINICAL OUTCOMES OF FOCAL IMPULSE AND ROTOR MODULATION FOR TREATMENT OF ATRIAL FIBRILLATION: A MULTI-CENTER EXPERIENCE

ACUTE RESULTS	All Patients (n=43)	Clinical Success (n = 16)	AF Recurrence (n = 27)	p value
Number LA rotors targeted	2.0 ± 1.0	1.8 ± 0.9	2.1 ± 1.1	0.36
Number RA rotors targeted	0.6 ± 0.8	0.7 ± 0.7	0.6 ± 0.8	0.68
Procedure time (min)	314 ± 82	336 ± 70	301 ± 88	0.18
Fluoroscopy time (min)	55 ± 24	58 ± 27	53 ± 23	0.52
Total RF ablation time (min)	39 ± 18	41 ± 16	37 ± 20	0.50
Acute procedural success	20 (47%)	10 (63%)	10 (37%)	0.11

Buch E, Share M, Turng R, Benharash P, Mandapati R, Ellenbogen K, Shivkumar K- *Long-term Clinical Outcomes Of Focal Impulse And Rotor Modulation For Treatment Of Atrial Fibrillation: A Multi-center Experience* –(in revision) 2015

# LONG-TERM OUTCOMES OF FIRM: MULTI-CENTER



The mean follow-up was  $527 \pm 190$  days. Single-procedure freedom from AF, all ATA and all ATA off AAD were 37.2%, 30.2% and 20.9%, respectively. Subgroup analysis showed no significant differences based on the type of AF, whether or not PVI was performed, or whether this was a first or repeat ablation.

# **SUMMARY OF UCLA FIRM DATA**

1) The multipolar basket catheter provides inadequate coverage of the LA, with half the surface area unsampled, and decipherable atrial electrograms from only 48% of electrodes

2) FIRM-identified rotor sites do not exhibit distinctive electrophysiological characteristics with regard to dominant frequency or Shannon entropy

3) Rotational activation (>1 rotation) on electroanatomic mapping was not observed at FIRM-identified rotor sites

4) Ablation of rotor sites, even when accompanied by PVI, did not result in AF termination in the majority of patients

5) Long term follow up results (2 centers) were disappointing. Singleprocedure freedom from AF, all ATA and all ATA off AAD were 37%, 30% and 21%

# WHAT IS NEEDED

- Our entire training and career to date have centered on understanding electrograms: interpreting and making sense of a logical sequence of events and electrogram relationships. This is what drew many of us to the field
- FIRM mapping does not allow us to make these deductions with currently available recording systems and we must trust the proprietary algorhythms that produce possible rotor targets in virtually all patients.
  - We must trust it because "it worked" in CONFIRM
- PVI +FIRM has some early promising data, but If FIRM alone can outperform PVI then this will be the true test.
  - The promise was limited ablation
  - But will we get it?

# FIRMAT: will we get the clinical data we need?

### ClinicalTrials.gov

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#### Focal Impulse and Rotor Modulation Ablation Trial for Treatment of Paroxysmal Atrial Fibrillation (FIRMAT-PAF)

This study has been terminated. ClinicalTrials.gov Identifier: NCT01925885 (+Terminated: mon-thing an enrolling participants has halted prematurely and will not resume; participants are no longer being examined or treated) First received: August 5, 2013 Last updated: March 23, 2015 Sponsor: Last verified: March 2015 Indiana University History of Changes Collaborators: University of California, Los Angeles Indiana University Health/Indiana University School of Medicine Strategic Research Initiative Topera, Medical Information provided by (Responsible Party): Indiana University

### **REAFFIRM Trial**

### ClinicalTrials.gov

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Home > Find Studies > Study Record Detail

#### Randomized Evaluation of Atrial Fibrillation Treatment With Focal Impulse and Rotor Modulation Guided Procedures (REAFFIRM)

This study is currently recruiting participants. (see Contacts and Locations)

Verified December 2014 by Topera, No.

Sponsor Topera, Inc.

Information provided by (Responsible Party): Topona, Inc. ClinicalTrials.gov Identifier: NCT02274857

First received: October 22, 2014 Last updated: December 18, 2014 Last verified: December 2014 History of Changes

Clinicaltrials.gov, accessed 8/1/2015

# FIRM STUDY OSLO (stand alone)

		Trial record 2 of 8 for:	focal impulse a	nd rotor
		Previous Study   Retu	rn to List   N	lext Study ►
IRM as a Stand-	alone Procedure	e in the Treatment of	Atrial Fibril	lation
This study is currer	ntly recruiting partic	ipants. (see Contacts and L	ocations)	ClinicalTrials.gov Identifier:
Verified October 2014	by Oslo University Hos	pital		NCT02101541
Sponsor:				First received: February 28, 2014
Oslo University Ho	ospital			Last updated: October 22, 2014
Information provided	by (Responsible Par	ty):		History of Changes
Rolf Franck Berntser	, Oslo University Hos	pital		
Full Text View	Tabular View	No Study Results Posted	Disclaimer	How to Read a Study Record

#### Purpose

The FIRM Study Oslo will in two sequential within-patient trials investigate the efficacy of **focal impulse and rotor** modulation (FIRM) as a standalone procedure in the treatment of paroxysmal and persistent atrial fibrillation, evaluated by continuous pre- and post-procedural heart rhythm monitoring.

Intervention

SENTREHEA

### **FIRM vs PVI - UCSD**

Trial record 5 of 8 for: focal im Previous Study   Return to List ubstrate Versus Trigger Ablation for Atrial Fibrillation This study is not yet open for participant recruitment. (see Contacts and Le Verified June 2014 by University of California, San Diego Sponsor:	apulse and rotor t   Next Study ► .ocations) ClinicalTrials.gov Identifier: NCT02169037
Previous Study   Return to List Ubstrate Versus Trigger Ablation for Atrial Fibrillation This study is not yet open for participant recruitment. (see Contacts and Le Verified June 2014 by University of California, San Diego Sponsor:	t   Next Study ► .ocations) ClinicalTrials.gov Identifier: NCT02169037
ubstrate Versus Trigger Ablation for Atrial Fibrillation This study is not yet open for participant recruitment. (see Contacts and Lo Verified June 2014 by University of California, San Diego Sponsor:	Ocations) ClinicalTrials.gov Identifier: NCT02169037
This study is not yet open for participant recruitment. (see Contacts and Le Verified June 2014 by University of California, San Diego Sponsor:	Ocations) ClinicalTrials.gov Identifier: NCT02169037
Verified June 2014 by University of California, San Diego Sponsor:	NCT02169037
Sponsor:	
	First received: June 18, 2014
University of California, San Diego	Last updated: NA
Collaborators:	History: No changes posted
National Institutes of Health (NIH)	
National Heart, Lung, and Blood Institute (NHLBI)	
Information provided by (Responsible Party):	
Sanjiv Narayan, MD, PhD, University of California, San Diego	
Full Text View Tabular View No Study Results Posted Discl	aimer 2 How to Read a Study Record

#### Purpose

This is a prospective randomized study to assess the safety and efficacy of FIRM (Focal Impulse and Rotor Modulation)-guided ablation for the treatment of symptomatic atrial fibrillation (AF). The study hypothesis is that the efficacy of AF elimination at 1 year will be higher by ablating patient-specific AF-sustaining rotors and focal sources only by Focal Impulse and Rotor Modulation (FIRM) compared to conventional ablation (including PV isolation).

	Condition	Intervention
	Atrial Fibrillation	Procedure: FIRM Ablation Procedure: Conventional AF ablation with PVI
Study Type:	Interventional	
Study Design:	Allocation: Randomized	
	Endpoint Classification: Efficacy	y Study
	Masking: Open Label	agiment
	Primary Purpose: Treatment	
Official Title:	Substrate Ablation ( <b>Focal Impu</b> Fibrillation: A Randomized Clini	<mark>ilse and Rotor</mark> Modulation) Compared to Pulmonary Vein Isolation to Eliminate Human Atria cal Trial
Resource links	provided by NLM:	

HEAR

Genetics Home Reference related topics: familial atrial fibrillation

MedlinePlus related topics: Atrial Fibrillation

U.S. FDA Resources

Further study details as provided by University of California, San Diego:

#### Primary Outcome Measures:

Long term success [ Time Frame: 12 months ] [ Designated as safety issue: No ]

# **SUMMARY**

"You must be sincerely committed to what's right and not who's right." John R. Wooden (1920-2010) UCLA Basketball Coach and Presidential Medal of Freedom Recipient, 2003

- Rotor mapping for AFIB ablation has gained significant interest along with other techniques/technologies developed to localize these possible drivers
- Early data showed remarkable results utilizing FIRM mapping in addition to PVI
- More recent data has been more tempered
- Further multicenter experience and FIRM alone vs PVI is essential. Otherwise FIRM runs the risk of becoming another version of PVI+ for persistent AF.



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slides on rotors-modeling



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Coach John R. Wooden

1910-2010

