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David D. McManus University of Massachusetts Medical School

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Plasma microRNAs are associated with atrial fibrillation (the miRhythm Study) and change after catheter-ablation

David D. McManus, MD, MSc;^{1,2,3} Kahraman Tanriverdi, PhD;¹ Honghuang Lin PhD;^{2,4} Nada Esa MD;¹ Menhel Kinno MD;¹ Rosalind Lee, MS;⁸ Divakar Mandapati MD, Stanley Tam MD, MBA, Patrick T. Ellinor MD, PhD,^{9,10} John F. Keaney, Jr. MD;¹ Emelia J. Benjamin MD, MSc;^{5,6,7} Victor Ambros, PhD;⁸ Jane E. Freedman, MD^{1,2}

- ¹ Cardiology Division, Department of Medicine, University of Massachusetts Medical School, Worcester, MA, USA
- ² National Heart Lung and Blood Institute's and Boston University's Framingham Heart Study, Framingham, MA, USA
- ³ Epidemiology Division, Department of Quantitative Health Sciences, University of Massachusetts Medical School Worcester, MA
- ⁴ Computational Biomedicine Section, Department of Medicine, Boston University School of Medicine, Boston, MA, USA
- ⁵ Section of Cardiovascular Medicine, Department of Medicine, Boston University, Boston, MA, USA
- ⁶ Preventive Medicine Section, Department of Medicine, Boston University School of Medicine, Boston, MA, USA
- ⁷ Epidemiology Department, Boston University School of Public Health, Boston, MA, USA
- 8 Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA, USA
- ⁹ Cardiac Arrhythmia Service, Massachusetts General Hospital, Boston, MA, USA
- ¹⁰ Cardiovascular Research Center, Massachusetts General Hospital, Charlestown, MA, USA

Short title: Circulating microRNAs and Atrial Fibrillation

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Corresponding author:

David D. McManus, MD ScM Assistant Professor of Medicine Cardiology Division University of Massachusetts Medical School Worcester, MA 01655 tel 774-441-6611; fax 774-442-6959 mcmanusd@ummhc.org **Background:** Atrial fibrillation (AF) is the most common dysrhythmia in the U.S. and Europe. Few biomarkers exist to identify individuals at risk for AF. Cardiac microRNAs (miRNAs) have been implicated in susceptibility to AF and are detectable in the circulation. Nevertheless, data are limited on how circulating levels of miRNAs relate to AF or change over time after catheter- ablation.

Methods: In 211 miRhythm participants (112 with paroxysmal or persistent AF; 99 without AF), we quantified plasma expression of 86 miRNAs associated with cardiac remodeling or disease by high-throughput quantitative reverse-transcriptase polymerase chain reaction (qRT-PCR). We used qRT-PCR to examine change in plasma miRNA expression from baseline to 1-month after ablation in 47 participants. We also quantified expression of the 20 most variable miRNAs in atrial tissue in 31 participants undergoing cardiac surgery.

Results: The mean age of the miRhythm cohort was 59 years and 58% of participants were men. 21 miRNAs differed significantly between participants with AF and those with no AF in regression models adjusting for known AF risk factors (p value of ≤ 0.0006). Several miRNAs associated with AF, including miR-21, miR-29a, miR-122, miR-150, miR-320, and miR-92a, regulate expression of genes implicated in the pathogenesis of AF. Levels of 33 miRNAs, including 14 associated with AF, changed significantly between baseline and 1-month after catheter ablation (p value of ≤ 0.0006). Although all AF-related plasma miRNAs were expressed in atrial tissue, only miR-21 and miR-411 differed significantly with respect to preoperative AF status.

Conclusions: Plasma levels of miRNAs associated with heart disease and cardiac remodeling were related to AF and changed after catheter-ablation. Our study suggests that AF has a unique circulating miRNA profile and that this profile is influenced by catheter-ablation.