Circulation Research: A new method to improve treatment of atrial fibrillation

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The new study was conducted by investigators at the CNIC, the Hospital Clínico San Carlos in Madrid, and the CiberCV research network and is featured on the cover of the latest edition of the journal Circulation Research

Researchers at the *Centro Nacional de Investigaciones Cardiovasculares* (CNIC), the *Hospital Clínico San Carlos* in Madrid, and the Spanish cardiovascular research network (CiberCV) have discovered a new method to optimize ablation of atrial fibrillation (AFib), one of the most common forms of irregular heartbeat (arrhythmia). The study is featured on the cover of the latest edition of the prestigious journal *Circulation Research.*

When a cardiac arrhythmia does not respond to drug therapy, the standard treatment is catheter ablation to isolate the pulmonary veins from the left atrium. However, the results of ablation are disappointing in patients with a complex AFib that is not limited to the pulmonary veins but also involves other atrial regions. “This is especially common in persistent AFib lasting months or years,” exlained study coordinator Dr David Filgueiras, who leads a research group at the CNIC and is a cardiologist at the the *Hospital Clínico San Carlos*.

First author Dr Jorge García Quintanilla explained that the new method “allows ablation procedures to be tailored to the specific needs of individual patients with persistent AFib, identifying the key regions to treat with high precision.” Dr Filgueiras added that the new method “costs no more than the conventional procedure and there is thus no obstacle to its use by most centers experienced in AFib ablation.”

AFib affects more than 30 million people worldwide, and in Spain an estimated 600000 people have this condition. An estimated 37% of people older than 40 years will develop AFib at some stage during their lives. Nevertheless, despite more than 100 years of research, understanding remains limited about the mechanisms that initiate and maintain AFib, and this likely explains the disappointing treatment outcomes to date.

Arrhythmias arise because the waves of electricity that activate the heart can follow different patterns. For example, they can start from a fixed point and radiate outward (focal activity) or they can turn around a center of rotation that can be fixed or can move through the cardiac tissue (rotational activity). In AFib, the electrical wave patterns are complex, combining focal and rotational patterns moving at high speed. This makes it difficult to pinpoint the origin of the arrhythmia and target the ablation to this site, as can be done in the case of other arrhythmias with simpler patterns.

Atrial fibrillation affects more than 30 million people worldwide, including an estimated 600000 in Spain

To treat persistent AFib, clinical practitioners have begun to use closed systems that guide the ablation to regions with rotational or focal electrical activity. However, these systems are very expensive and, as Dr Filgueiras explained, “often do not establish the spatiotemporal stability of the electrical foci with sufficient rigor and do not take account of the hierarchical organization underlying the arrhythmia.” Moreover, these systems have important technical limitations and require the use of expensive single-use consumables as well as the purchase of the equipment needed to process the information acquired with these consumables. As Dr García Quintanilla explained, “For the few centers that use these systems, the cost per procedure is very high, making this approach unfeasible for general use with large numbers of AFib patients.”

Reduced costs

“Our method,” said Dr Filgueiras, “requires no additional equipment or consumables; instead, it simply uses a computer program that can be implemented in any standard electroanatomical navigator. The method thus allows patient-tailored ablation of complex AFib at no additional cost compared with current procedures for isolating the pulmonary veins.”

In the course of the study, the team discovered that the electric potentials in the heart atria during AFib are characterized by amplitude modulation and frequency modulation (AM and FM), similar to the established systems for radio broadcasts. “Detailed analysis of these modulations allowed us to track rotational activity with high precision and to pinpoint the regions that maintain the arrhythmia, in which rotational activity may not be evident.” The study also helps to resolve a longstanding controversy in the field, by demonstrating that “rotational activity is sensitive to but not specific to the regions that maintain AFib”, explained Dr Filgueiras.

The new method allows guided ablation to isolate the pulmonary veins from the left atrium, enabling this procedure to be tailored to the specific situation of patients with persistent atrial fibrillation

The study followed a fully translational approach. The authors first analyzed data obtained by cardiac optical mapping of the electrical activity in hearts isolated from an animal model of persistent AFib. Cardiac optical mapping records cardiac electrical activity at high spatiotemporal resolution. The authors also analyzed cardiac optical mapping in computer simulations of AFib in the animal model and in humans.

A unique model

Cardiac optical mapping is not possible in human patients. Therefore, the authors adapted the modulation analysis algorithms to the electrical signals obtained in vivo using conventional catheters (which give lower spatial resolution) and conducted further tests with conventional electrophysiological tools. For this, the team used a pig animal model of persistent AFib that is remarkable for its long duration (several months) and its similarity to clinical human AFib. The model was developed at the CNIC over the past 5 years since Dr Filgueiras joined the center.

Using this approach, the authors were able to demonstrate that the atrial regions that sustain fibrillation are those with high mean FM, that these regions are stable in space and time, and that their ablation efficiently terminates the arrhythmia. Moreover, the study detected rotational activity both inside and outside of these regions, indicating that not all rotational activity should be ablated.

The authors used this innovative technology to guide the treatment of patients with complex AFib at the *Hospital Clínico San Carlos*, a leading center for advanced treatment of complex arrhythmias. These patients had not responded to conventional treatment by electrical isolation of the pulmonary veins. This study confirmed that the new technology is able to identify patients in whom a minimally invasive catheter ablation strategy will be ineffective because the regions contributing to AFib maintenance encompass too large an area.

Julián Pérez Villacastín, Director of the Cardiovascular Institute at the Hospital Clínico San Carlos, summarized the importance of the study findings. “Our achievement is a good example of the importance of organizing multidisciplinary teams. This will allow the studies performed at the CNIC to be translated into new treatments for patients with difficult arrhythmias at the *Hospital Clínico San Carlos* arrhythmia unit and hopefully at many other centers. We are still unable to completely cure these arrhythmias, but this new technology will greatly improve quality of life for our patients.”

The investigators propose that the algorithms for AM and FM analysis could be easily incorporated into conventional electroanatomical navigation systems, increasing the precision and reducing the cost of patient-specific procedures for the ablation of persistent AFib.

- Quintanilla, J. G., Alfonso-Almazan, J. M., Perez-Castellano, N., Pandit, S. V., Jalife, J., Perez-Villacastin, J., & Filgueiras-Rama, D. (2019). Instantaneous Amplitude and Frequency Modulations Detect The Footprint of Rotational Activity and Reveal Stable Driver Regions as Targets for Persistent Atrial Fibrillation Ablation. *Circulation Research, 125*(6), 609-627. doi:10.1161/CIRCRESAHA.119.314930