EDITORIAL

First Evidence of Clinical Benefit of Robotically Driven Catheter Ablation or an Outlayer?

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Results of catheter ablation of atrial fibrillation (AF) are far from optimal at the present time. Even in paroxysmal AF, where there is general agreement on the crucial role of the atrial muscle around the pulmonary vein ostial region in the genesis of AF,[1] antral pulmonary vein isolation not infrequently fails in providing long-term AF free status.

One of the possibilities to explain the failures is venoatrial conduction recovery. In fact, a universal finding when patients come back to the electrophysiology laboratory because of AF recurrence after a first ablation procedure is venoatrial electrical reconnection.[2,3] And just by reisolating the pulmonary veins the majority of patients obtain significant clinical benefit.[2,3]

A likely hypothesis for such a clinical scenario is that the initial ablation is not "good enough," i.e., the lesions acutely deteriorate electrical conduction to the point of conduction block (electrical isolation of the pulmonary veins) but somehow reduce in size during the healing process and conduction recovers. When discussing this phenomenon with my patients, I used to tell them "we are electro-physiologists; we know when we change the *function* of the conduction in your heart, but we do not *see* the lesions we are creating."

If we consider how we create lesions, with a catheter introduced and manipulated 70–80 cm away from the heart, the heart chamber beating and changing dimensions every second, and the thoracic volume changing every inspiratory excursion, it may even be surprising that we are able to create lesions at all.

Several technological improvements have been developed in recent years in order to improve lesion creation. In particular, in relation to radiofrequency ablation, two of the most important developments are robotic catheter navigation and contact force measurement.

Robotic navigation, either by "attracting" the tip of a catheter containing a magnetic sensor[4] or by the use of a robotically controlled steerable sheath that contains and guides an otherwise regular catheter,[5] has the final purpose of catheter stabilization to maintain the catheter at the same spot during the time of radiofrequency delivery.

However, even if the purpose is obtained, catheter stability does not ensure by itself lesion formation. Catheter contact with the endocardium is another necessary requirement for lesion formation.

It has been known for years in experimental settings that the contact force between the catheter and the heart is an important determinant of the size of the lesion that can be created in the heart wall.[6,7] In recent years, catheters have been developed that can measure, in clinical grounds, contact force between the catheter tip and the endocardium.[8,9] Initial results with the use of these catheters seem promising.[10–18]

Theoretically speaking, the association of the stability provided by a robotically driven catheter and the assurance of good contact force provided by catheters that measure contact force is probably the best combination to ensure the physical conditions that can produce an adequate lesion.

In this context, the study by Ullah et al., in this issue of the *Journal*,[19] could be particularly relevant. They compared four groups of 50 patients each that underwent catheter ablation of persistent AF at six hospitals from two countries. Two prospective groups, with either manual or robotically controlled steerable sheath navigation, included patients in whom the catheters used had contact force sensing technology. The two other groups were historic controls of patients with either manual or robotic (with the same system) navigation, but in whom the ablation catheter did not have contact force sensing technology. The ablation procedure included wide area circumferential ablation of the pulmonary veins

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with documentation of bidirectional electrical conduction block in all patients and a right atrial isthmus flutter line in the cases with common flutter documented. Other lines of block and ablation of areas with fractionated activity were left to the discretion of the operator.

The main finding of the study is that with a single ablation procedure and after a 12-month follow-up period, a significantly higher proportion of patients in the robotic/contact force arm was free of AF recurrences as compared with both the manual/contact force arm and the robotic/no contact force arm. The crude numbers for the proportion of AF-free patients were 64% for the robotic/contact force arm, 36% for the manual/contact force arm, 36% for the robotic/no contact force arm, and 38% for manual/no contact force arm.[19]

Can we conclude from this study, as it appears, that robotic navigation with catheters with contact force sensing technology is superior in terms of clinical results than other forms of point-by-point radiofrequency ablation for patients with AF? Before reaching this conclusion, several considerations are necessary:

(1) The design of the study is not randomized, even in the prospective arms that included catheters with contact force sensing technology in all patients. The authors provide certain clinical information about the patients and the procedures. There are no significant differences in variables such as AF duration and left atrial diameter, which are known to influence the success rate. There are no significant differences in procedural variables such as proportion of cases in whom a roof or mitral isthmus line were performed. Interestingly enough, more patients in the robotic arm underwent cavotricuspid isthmus ablation. The authors acknowledge this result but mention that there was no difference in the proportion of recurrences as atrial tachycardia or flutter versus AF. However, other sources of bias may still be present: we have no information about the operators and it may be that more experienced operators were more familiar with the robotic system and their patients were more often assigned to the robotic arm, resulting in better results.

(2) The historical controls may have even more bias as comparative groups than the prospective groups. It is conceivable that robotic navigation in the control group might have represented the initial experience in some groups/operators participating in the study, and it is well known that robotic navigation needs a learning curve before optimal results can be achieved.[20]

(3) We do not know to what extent these results could apply to paroxysmal AF. In paroxysmal AF most electrophysiologists perform only circumferential pulmonary vein isolation. However, the investigators in these patients with persistent AF performed procedures other than pulmonary vein isolation in more than half of the patients. It is not possible to know if the additional benefit found in the robotic group was due to a better pulmonary vein isolation procedure or a better creation of roof and mitral lines. Furthermore, the authors do not mention in what proportion of patients of each group complex fractionated electrograms were ablated, adding more uncertainty as to the reason for the observed results.

(4) Finally it has to be recognized that superiority of robotic over manual navigation with the same catheter has never been reported before. Two randomized trials, comparing manual versus robotically controlled steerable sheath navigation, have shown similar results with both navigation modalities in terms of AF-free survival. One study included 60 patients with paroxysmal AF, and showed that after 6 months of follow-up 77% and 73% (manual and robotic, respectively, P = NS) were AF-free without antiarrhythmic drugs.[21] A more recent and larger trial randomized 157 patients with all types of AF (74% persistent, and 58% of those longstanding persistent) and showed that after a single procedure and 12 months of follow-up, 33% and 24% (manual and robotic, respectively, P = NS) were arrhythmia-free without antiarrhythmic drugs.[22] Interestingly enough, this trial comes in part from the same investigators as the manuscript by Ullah et al.[19] In addition, several other nonrandomized comparisons between manual navigation and either robotically controlled steerable sheath or magnetic robotic navigation have systematically shown similar effectiveness with manual and robotic systems,[23–29] and noncomparative trials show figures that can be considered comparable to what can be expected with manual ablation.[30–32]

What is the difference, then, between the study by Ullah et al.[19] and all these other "negative" trials? There are three possibilities: (1) the authors have not been able to detect certain bias that make the groups not comparable; (2) the robotic system works better for the ablation of substrates other than the pulmonary vein antra, and since in the majority of the other trials most patients had paroxysmal AF and only the pulmonary veins were treated, the difference went unnoticed; and (3) the contact force sensing technology included in the catheter, in association with robotic navigation, makes the difference. At the present time, we cannot decide which of these possibilities is most likely. However, the third

possibility merits special attention. The robotic system used in the study by Ullah et al.[19] already incorporates contact force sensing technology that can be used with all catheters. However, this system reads the contact force from the robotic arm rather than from the catheter tip, as catheters with contact force sensing capabilities do, and it is conceivable that the latter is more precise. Could this make the difference to the point of decreasing the clinical arrhythmia recurrence rate by almost half?

More studies are necessary to clarify the above issues, but certainly Ullah et al. should be congratulated for having detected a technological combination that could be clinically superior to what is at the present time the most frequently used technology for catheter ablation of AF, and also for being able to show clinical results that suggest a substantial benefit for the patients as a result of the use of this technology. I am sure that the issues presented in their manuscript will inspire important research in the coming years.

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