# Relevance of electrical connectivity between the coronary sinus and the left atrial appendage for the intentional electrical isolation of the left atrial appendage in treating persistent atrial fibrillation: Insights from the LEIO-AF study

Mokhtar Ibrahim, MRCP, PhD,[*†] Sandeep Panikker, MRCP, PhD,[*] Eric Lim, MRCP,[*] Vias Markides, FRCP, MD,[*] Tom Wong, FRCP, MD, FHRS[*]

*From the* [*]*Cardiology Department, Royal Brompton and Harefield, London, United Kingdom, and* [†]*Cardiology Department, Ain Shams University, Cairo, Egypt.*

## Introduction

Catheter ablation is an accepted therapeutic option for paroxysmal atrial fibrillation (AF), but its role is less certain in patients with persistent AF.[1] The difference in response to pulmonary vein (PV) isolation (PVI) between paroxysmal and persistent forms of AF may arise because of triggers from non-PV sites or alterations in atrial substrate favoring maintenance of AF that are unaffected by PVI alone.[2] In support of this statement, adjunctive ablation of certain sites (including the superior vena cava, ligament of Marshall [LOM], crista terminalis, coronary sinus [CS], posterior wall of the left atrium [LA], and left atrial appendage [LAA]) as well as more widespread ablation aimed at modifying substrate has been shown to improve the success of catheter ablation of persistent AF.

In the case of the LAA, the BELIEF study (Effect of Empirical Left Atrial Appendage Isolation on Long-term Procedure Outcome in Patients With Persistent or Long-standing Persistent Atrial Fibrillation Undergoing Catheter Ablation)[3] recently showed that in patients with long-standing persistent AF, empirical electrical isolation of the LAA together with extensive atrial ablation markedly improved freedom from AF at 1 year compared to an extensive atrial ablation strategy alone. However, electrical isolation of the LAA can be challenging and is sometimes impossible to achieve. This may be partly because the electrical connections of the LAA are not completely understood.

Here we report 2 patients showing that the CS can be an important electrical conduit to the LAA.

**KEYWORDS** Catheter ablation; Coronary sinus; Electrical isolation; Left atrial appendage; Persistent atrial fibrillation
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This work was supported by the Royal Brompton and Harefield. **Address reprint requests and correspondence:** Dr Tom Wong, Heart Rhythm Centre, The Royal Brompton and Harefield Hospitals, Sydney St, London SW3 6NP, United Kingdom. E-mail address: t.wong2@rbht.nhs.uk.

## Case reports

We report 2 patients enrolled as part of the LEIO-AF (Left Atrial Appendage Electrical Isolation and Occlusion to Treat Persistent Atrial Fibrillation: A Safety and Feasibility) study. In this study, all patients had long-standing persistent AF and underwent extensive atrial ablation and empirical LAA electrical isolation together with LAA occlusion by means of a Watchman device (Boston Scientific, Marlborough, MA).[4]

After routine PVI and additional lines, ostial electrical isolation of the LAA was then attempted at the atrial side of its ostium, in view of the potentially greater tissue thickness in this area, to minimize the risk of perforation (Figure 1). The target contact force and power were 15–20 g and 35 W, respectively. Additional ablation was performed at the left superior PV–LAA ridge at the pulmonary venous and LAA sides as necessary to achieve electrical isolation. Ablation within the CS was permitted if the remaining electrical connection to the LAA was found to be within the CS after extensive ostial LAA ablation. Radiofrequency energy was limited to 20–25 W in the CS with an irrigation rate of 30 mL/min.

If electrical isolation of the LAA was successfully achieved, the LAA was occluded with an appropriately sized Watchman device. Even in the case of incomplete LAA isolation, because of potential reduction in LAA contraction from extensive ablation, closure of the LAA may play an important role in reducing the risk of thrombus formation and subsequent stroke. Rillig et al[5] recently confirmed that after LAA isolation, there was an unexpectedly high incidence of LAA thrombus formation and stroke despite oral anticoagulant therapy.

## Case 1

A 77-year-old male patient was referred with symptomatic long-standing persistent AF despite oral antiarrhythmic therapy. Catheter ablation of AF was performed as per the LEIO-AF protocol. The initial step of wide circumferential isolation


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## KEY TEACHING POINTS

- In many cases of long-standing persistent atrial fibrillation (AF), the left atrial appendage (LAA) is important in maintaining AF.
- Electrical isolation of the LAA can occur during AF ablation both intentionally and unintentionally.
- Intentional electrical isolation of the LAA is feasible in most cases but sometimes quite challenging. Ablation from within the coronary sinus may be an essential step in some cases to achieve electrical isolation of the LAA.
- A muscular sleeve around the coronary sinus, vein of Marshall, and other venous atrial branches may exist in some cases and act as an electrical conduit between the LAA and the left atrium.
- Electrical isolation of the LAA may have adverse consequences such as increased thromboembolic risk; currently, the role of intentional electrical isolation of the LAA during AF ablation is uncertain and is the subject of ongoing studies.

of the PVs did not result in termination of AF, which also persisted following further roof, endocardial floor, and mitral isthmus lines. The mapping Lasso catheter placed at the LAA ostium showed organized firing from within the LAA at a shorter cycle length than that placed elsewhere in the LA and at a similar cycle length as of the mid- and distal CS catheter (Figure 2A). Radiofrequency energy was then delivered to encircle the LAA ostium.

Although this initially resulted in slowing and electrical isolation of the LAA, LAA reconnection occurred soon after (Figure 2B and C). The ablation catheter was subsequently moved to the CS and advanced into an atrial branch of the distal CS. This brought the ablation catheter into proximity to the LAA ostium (6 mm on 3-dimensional mapping), which was confirmed by fluoroscopy (Figure 2D and E).

### Case 2

A 75-year-old female patient was referred for catheter ablation of symptomatic long-standing persistent AF. Initially, PVI and roof, endocardial floor, and mitral isthmus line ablation were performed, but these did not result in termination of AF (Figure 3A). After LAA ostial ablation, earliest potentials appeared to be deep within the body of the LAA and a residual sleeve of electrical activity in the anterosuperior LAA was present. Because of failure to durably isolate the LAA through

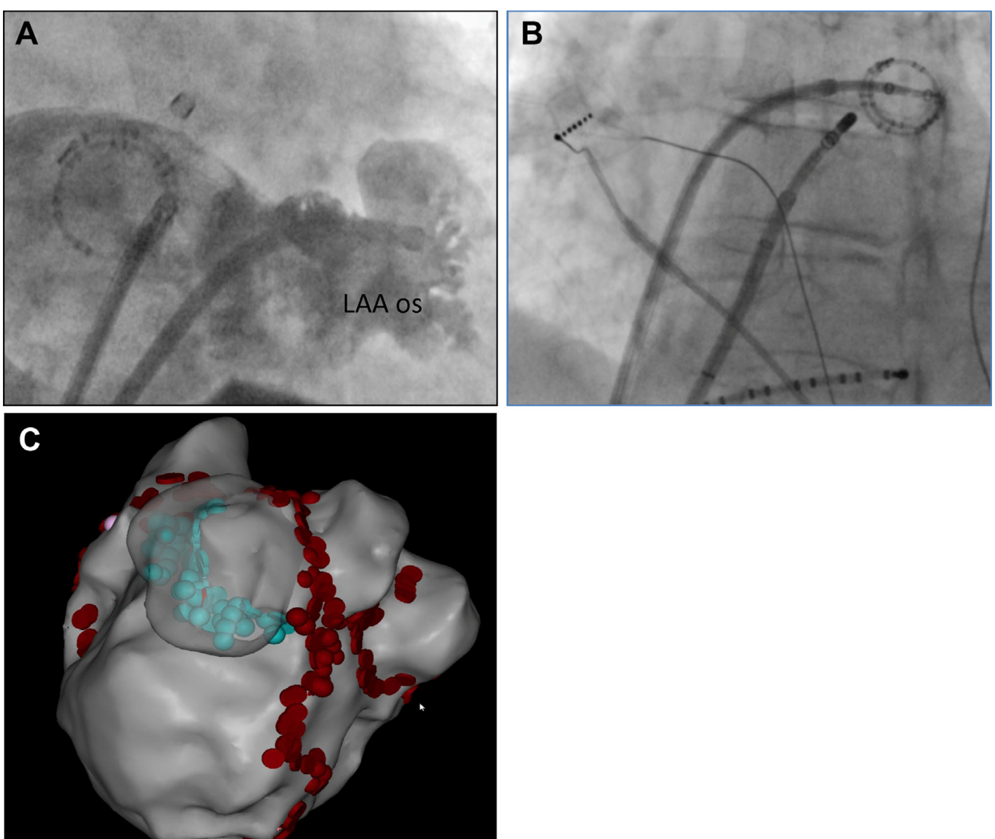


**Figure 1** Case 1. **A:** Contrast was used to define the LAA. **B:** The Lasso catheter is situated at the LAA os. **C:** Circumferential ablation was performed along the atrial aspect of the LAA (CARTO anatomical shell, left lateral view). LAA os = left atrial appendage ostium.

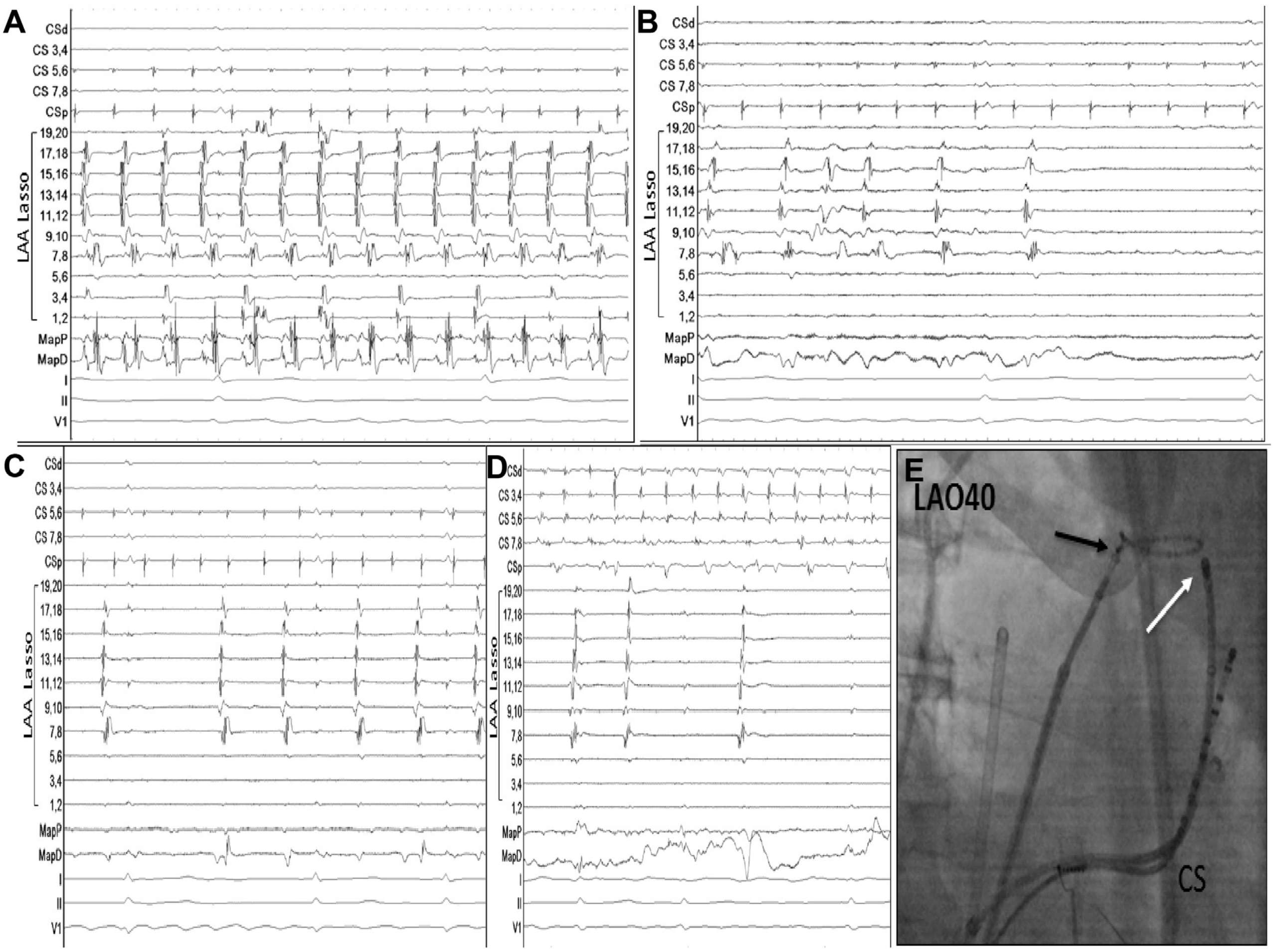


**Figure 2** Case 1. **A:** Recordings after pulmonary vein isolation and linear ablation. **B:** Recording after initial endocardial LAA ablation. **C, E:** Ablation within atrial branch of the CS (*white arrow*). **D:** Isolation of the LAA. CS = coronary sinus; LAA = left atrial appendage; LAO = left anterior oblique.

ostial ablation (Figure 3B and C), the ablation catheter was moved to the CS. Unlike the previous case, CS venography showed that there was only a small calibre communication between the distal CS and the LAA, and it was not possible to advance the ablation catheter near the ostium of the LAA. Therefore, ablation energy was applied to the mid-CS instead (Figure 3D and E) and this led to successful electrical isolation of the LAA (even though the ablation site was 28 mm remote, on 3-dimensional mapping, from the LAA).

Before ablation within the CS in both cases, high-output pacing via the mapping catheter did not result in phrenic nerve capture. Although we did not perform coronary angiography to delineate the left circumflex artery anatomy, 12-lead electrocardiograms were continuously monitored during and after ablation to rule out any ischemic changes.

In both cases, AF did not terminate with ablation, so direct current cardioversion was performed to restore sinus rhythm. A Watchman LAA occlusion device was then deployed uneventfully.

Both cases did not experience any symptomatic episodes of atrial tachycardia or AF at 3 and 12 months of follow-up. A repeat transoesophageal echocardiogram at 3 months revealed complete occlusion of the LAA.

## Discussion

These 2 cases highlight the CS as a distinct electrical conduit to the LAA. We discuss here the relevance of the LAA in AF pathogenesis and the electrical connection of the LAA more generally.

Di Biase et al[3] first reported a 27% prevalence of LAA firing in a consecutive series of 987 patients undergoing repeat catheter ablation for symptomatic and drug-resistant AF. In 8.7%, LAA firing was the only documented target of ablation; this was particularly common in nonparoxysmal forms of AF (81 of 86 patients). This early study showed that LAA firing is involved in the initiation or perpetuation of AF in a subset of patients and is more important in persistent compared to paroxysmal form of AF.

In the LEIO-AF study[4] (in which both patients reported here were enrolled), we showed that it is feasible to electrically isolate the LAA in approximately 90% (ie, 20 of the 22 patients enrolled), with adjunctive ablation within the CS necessary in about 9% (ie, these 2 reported patients).

Understanding the electrical connectivity of the LAA is therefore essential for its successful isolation, as well as preventing inadvertent isolation.

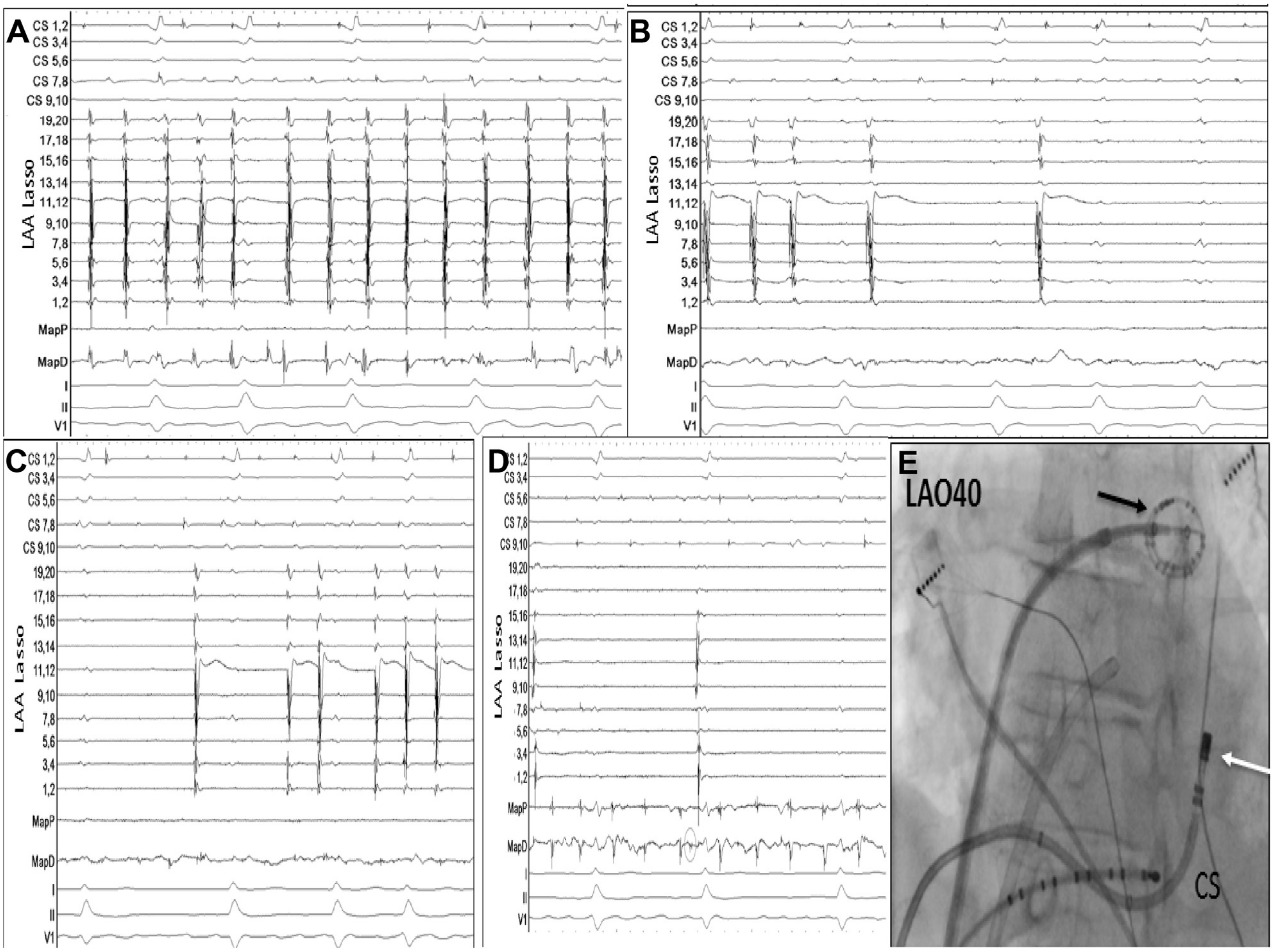


**Figure 3** Case 2. **A:** Recordings after pulmonary vein isolation and linear ablation. **B:** Recording after initial endocardial LAA ablation. **C:** Isolation was not durable (reconnection). **D, E:** Radiofrequency delivery in the mid-distal CS (panel E, *white arrow*) led to the isolation of the LAA (panel D). CS = coronary sinus; LAA = left atrial appendage; LAO = left anterior oblique.

The base of the LAA is the major electrical conduit connecting the LA to the body of the LAA. The LAA ostium is surrounded by circumferentially oriented muscle fibers tracing their origin from the leftward extension of the Bachmann bundle (BB). BB starts as an extension of the anterior internodal tract at the level of the superior vena cava. It then stretches subepicardially across the interatrial groove. Its rightward and leftward extensions bifurcate to pass to either side of the right and left atrial appendages. Leftward, BB buttressing part of the anterior atrial wall is still traceable to where it encircles the neck of the LAA and blends in with the lateral atrial wall. The superior part traverses in the infolding of the atrial wall, known as the left lateral ridge, to pass in front of the orifices of the left PVs. The inferior part descends toward the atrial vestibule to combine with the circumferentially aligned myocardial strands in the subepicardium of the inferior wall.[6]

As a result, interruption of conduction to the LAA during catheter ablation has been described when radiofrequency energy is applied in the region of BB, the base of the LAA, as well as points in between, such as the mitral isthmus.[7]

The cases in this report show that there are also important posterior electrical connections to the LAA. In case 1, isolation was achieved by application of radiofrequency energy in the distal CS branches near the LAA ostium, and in case 2, isolation occurred during ablation in the mid-CS, remote from the LAA ostium. It is important to mention that in both cases, electrical connections of the LAA persisted despite a routine endocardial circumferential ablation at the base of the LAA. Hence, the final epicardial ablation from within CS seems to be complementary but an essential step for electrical isolation of the LAA.

Di Biase et al also discussed the unusual patterns of isolation of the LAA during a study of 488 patients undergoing catheter ablation for persistent and long-standing persistent AF. After attempting endocardial ablation of the LAA, 34 patients (7%) and 39 patients (8%) required epicardial ablation at the mid- and distal CS, respectively, suggesting the presence of a distinct electrical connection between the CS and the LAA.[8]

Jiang et al[9] further corroborated the anterior and posterior connections to the LA and LAA. In a large series of 201 patients with persistent AF, they showed an 11% incidence of

LAA activation delay complicating aggressive septal ablation. In a subset of these patients, activation mapping was performed, showing that the earliest breakthrough to the LA changed to the CS in 86%. Together, these observations suggest that the major route of electrical connectivity to the LAA lies in the anterior LA, but they also confirm the existence and importance of myocardial bridges that link the muscular coat of the CS to the base of the LAA in at least some patients (10%–20%).

It is well known that the myocardial coat of the CS is contiguous with the left atrial myocardium, but to our knowledge, only Barcelo et al[10] have described a specific muscular connection between the LAA and the CS, which they call the "atriocoronary sinus bundle." After arising from the base of the LAA, this striated muscle bundle enters the left atrioventricular groove and, after approximately 30–40 mm, divides into fibers that interdigitate with those of the superior surface of the myocardial coat of the CS at the level of the entrance of the left oblique vein of Marshall (VOM).

In his recent editorial commentary, Valderrábano[11] highlighted the role of the VOM and LOM in the pathogenesis of atrial tachycardia and AF. Furthermore, Chugh et al[12] demonstrated that the LOM-PV connection was found in 18 patients (32%) of AF and related atrial arrhythmias. It may be ablated at any point along its course, at the mitral annulus, at the lateral ridge/PV antrum, and epicardially in the CS and the VOM itself. Ethanol ablation of the VOM may be an adjunctive strategy in patients with refractory perimitral reentry. In our cases, although we may not have ablated within the VOM, it is plausible that the ablation targeted the muscular sleeve that accompanied the VOM in case 2 and a more distal atrial branch in case 1. Therefore, it appears that the sleeves may represent a direct communication with the LAA rather than the PVs.

## Conclusion

The LAA is an important site of AF initiation or perpetuation, and LAA ablation is required in some cases for successful catheter ablation of AF. To enable efficient isolation of the LAA as well as to avoid inadvertent isolation of the LAA, it is necessary to understand the electrical connectivity of the LAA. These 2 cases highlight the existence of a muscular sleeve around the CS, VOM, and other venous atrial branches in some patients that acts as an electrical conduit between the LAA and the LA.

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