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EDITORIAL

The atavistic problem of identifying atrial fibrosis to perform a tailored RF ablation of persistent atrial fibrillation

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Persistent AF is mostly associated with triggers and mechanisms localized both at the level of the pulmonary veins and in other anatomical regions of the left atrium. Atrial fibrosis plays an important role in the genesis and perpetuation of AF. Detection of atrial fibrosis by imaging modalities is challenging and suboptimal for the detection of scars in thin wall atria, resulting in center-to-center non-reproducibility. Endocardial voltage mapping by acquiring thousands of voltage points (HD mapping) has been increasingly used in clinical practice for defining AF substrates[1]. Indeed, during RF ablation procedures identification of left atrial anatomical areas of low-voltage electrical activity (LVZs), is commonly considered a surrogate marker of atrial fibrosis. Rolf et al. first proposed a "tailored ablation" in patients with persistent AF based on the results of bipolar HD mapping[2] and Kircher et al. demonstrated that pulmonary vein isolation (PVI) plus ablation of LVZs <0.5 mV in sinus rhythm improved outcomes in this patients compared with PVI only or PVI plus posterior wall isolation[3]. In these studies, the electrical signals recorded by catheters are converted by 3d mapping systems into color-coded voltage maps. These maps, however, may vary according to the catheters and 3d systems used. The approach has limitations because while the terms "low voltage" and "scar/fibrosis" are used interchangeably, there is a fundamental difference between these 2 terms and voltage amplitude should not be used as a reference to quantify myocardial tissue fibrosis[4]. In addition, in their editorial commentary Anter and Josephson have focused their attention on the distinction between interstitial fibrosis and reparative fibrosis, highlighting that only the latter replaces dead cardiomyocytes, interfering with electric continuity, resulting in slow conduction and discontinuous conduction[4]. This nonuniform anisotropic conduction promotes reentry. Furthermore, activation direction, electrode spacing, electrode size, filter settings, point density, and tissue contact are all factors that potentially influence HD maps. In particular the relationship between the orientation of the recording bipole and the wave-front bipole may influence the arrival time of the activating wave-front at each electrode; this can mean that electrical signals may not be recorded even when they are present[5] bringing out false LVZs. A solution to this problem may be provided by a new mapping technique, known as omnipolar mapping; this is based on the use of a 3d mapping system and a multi-electrode catheter that allows simultaneous recordings of unipolar electrograms, and spans 2d and 3d space to derive conduction velocity and wave-front direction[6], and in this way enables detailed characterization of myocardial activation that is insensitive to catheter orientation. Identifying LVZs also depends on the recording window specified for analysis and on the related voltage

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thresholds chosen for the definition of LVZs, since these factors can cause HD maps to vary markedly. Data on the relationships between pre-ablation atrial fibrosis and atrial voltage thresholds are not currently available, and no true voltage threshold for atrial anomalies has been established. However, most studies have used a voltage of <0.05 or <0.2 mV to identify scar areas and a value of >0.5 mV to identify normal tissues, while the range between 0.05/0.2 mV and 0.5 mV is commonly used to define the low voltage that identifies the presence of underlying anomalies in the atrial structure. Our group identified a range of LVZs that was more suited to representing atrial fibrosis[7]. This was because the omnipolar catheter differs from multipolar catheter in terms of its ability to select the bipolar electrograms. The relative increase in electrogram amplitude with the omnipolar catheter has been shown to change the voltage threshold by which tissue can be histologically defined as scar[8]. In our view, the 0.3–0.6 mV range we described, offers a simple method of searching for potential and selective electro-anatomical substrates underlying AF. Indeed, in our study a distinction between scar, compact fibrosis, and non-compact fibrosis was done, with different imaging patterns, useful for a more correct interpretation of the atrial substrates. It has been proposed that reentry mechanisms do not occur in densely fibrotic areas or scar tissue because there are not enough cardiomyocytes to allow impulse propagation, nor does it occur in mostly normal tissue, because any reentry circuits that are established are unstable and self-terminate promptly. The range 0.3–0.6 mV allows an easy interpretation, clearly distinguishing between scar/compact fibrosis, healthy tissue and non-compact fibrosis, and drastically reducing false LVZs that can merge even with omnipolar recordings, if different ranges are used. These characteristics of the 0.3–0.6 mV voltage range have been confirmed with our recent experience using the 3d Ensite X system and new tools near field and emphasis map. **Figure 1** highlights the difference between the voltage maps with the range 0.3–0.6 mV and the range 0.05–0.5 mV. The range helped us to identify potential non-compact fibrosis through the "rainbow color" that could represent local non-pulmonary vein conductive alterations that influence anisotropy. This substrate probably plays a critical role in giving rise to AF mechanisms. Finally, Butcher et al.[9] in their recent study used omnipolar voltage mapping during AF and compared LVZs < 0.5 mV in AF with LVZs < 0.5 mV in sinus rhythm. As Jadidi and Loewe reported in their editorial comment published on JACC: Clinical Electrophysiology[10], this suggested approach brings the advantage of revealing smaller LVZs in sinus rhythm than during ongoing clinical AF, irrespective of the independent question regarding the best threshold in sinus rhythm to guide ablation. However, in our experience, the maps do not change, both in sinus rhythm and in AF, whatever voltage range and whatever recording mode is used (bipolar or omnipolar), if the atrial tissue is completely healthy, as in the case of paroxysmal lone AF (see **Figures 2** and **3** that clearly show these findings). The difference between sinus rhythm maps and AF maps continues to be represented by wider LVZs during AF, suggesting that AF determines them. Therefore, the problem of correct identification of the LVZs continues to be present when the left atrium is not healthy whether the identification of the LVZs should be done in AF or in sinus rhythm. In our opinion, until this dilemma is completely resolved, the holy grail of persistent tailored ablation AF cannot be found.

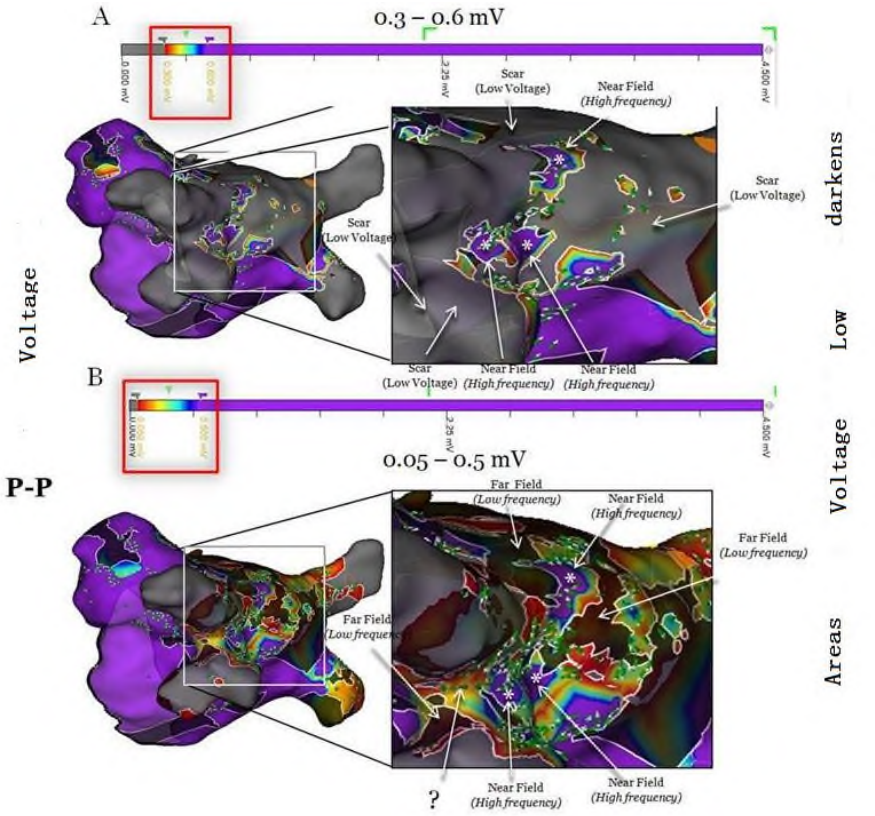

Figure 1. EnSite™ OT Voltage and Emphasis Map: 0.03–0.6 mV and 0.05–0.5 mV ranges in comparison.
A: The 0.3–0.6 mV voltage map shows islands of healthy tissue (purple color), inside a clearly scar (grey color) and non-compact fibrotic tissue (raimbow color).
B: The 0.05–0.5 mV voltage map allow to identify islands of healthy tissue inside a complex substrate of low voltage compatible with large areas of non-compact tissue. This map is difficult to interpret.

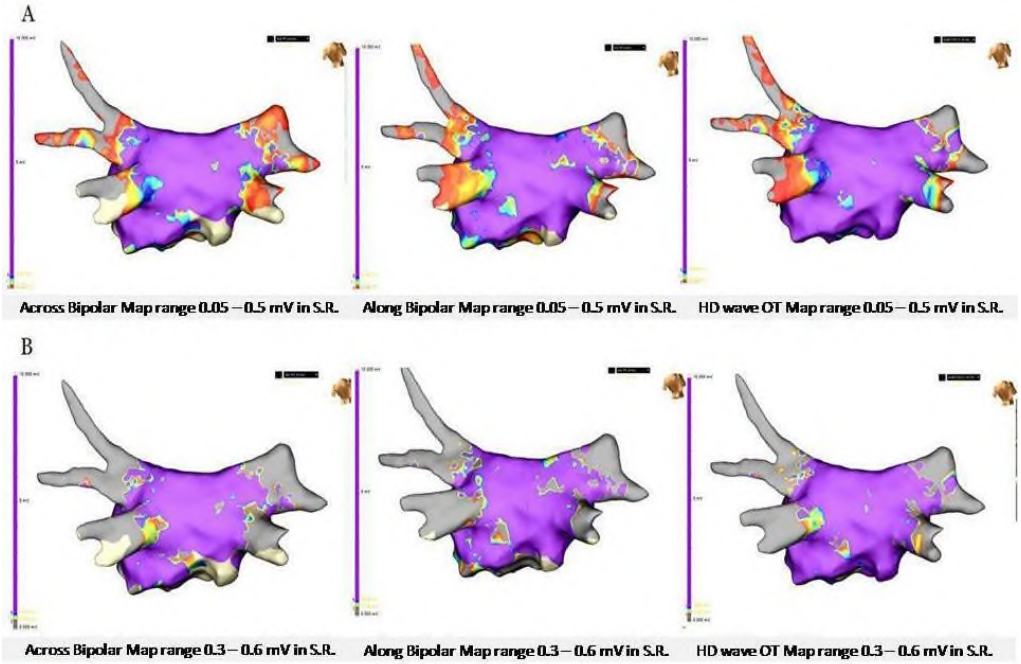

Figure 2. EnSite™ OT and Bipolar Voltage maps: the ranges 0.05–0.5 mV and 0.3–0.6 mV are compared in sinus rhythm.
A: Intra-patient post processing voltage maps in sinus rhythm using 0.05–0.5 mV. Very small differences are detectable both in bipolar mode (Across and Along) and in OT mode (HD-wave). Note the dominant purple color representing healthy tissue.
B: Same patient in A. intra-patient post processing voltage maps in sinus rhythm using 0.3–0.6 mV. Very small differences are detectable both in bipolar mode (Across and Along) and in OT mode (HD-wave), and both using the 0.3–0.6 mV and 0.05–0.5 mV ranges.

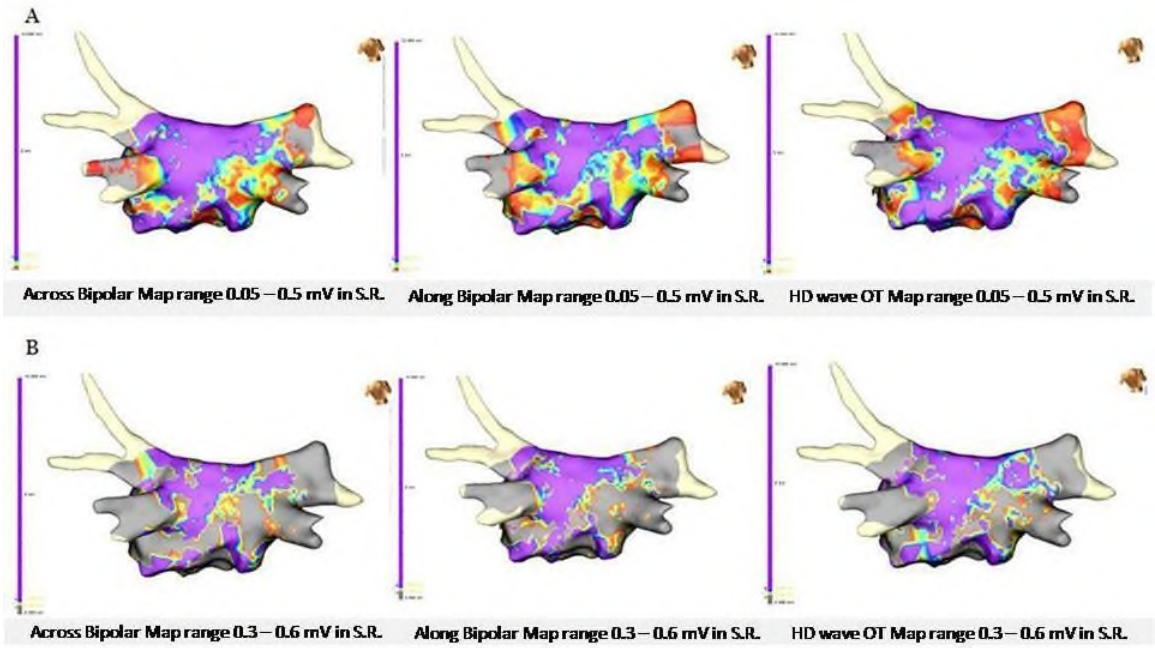

Figure 3. EnSite™ OT and Bipolar Voltage maps: the ranges 0.05–0.5 mV and 0.3–0.6 mV are compared during atrial fibrillation. A: Same patient in Figure 1. Intra-patient post processing voltage maps in atrial fibrillation using 0.05–0.5 mV. Very small differences are detectable both in bipolar mode (Across and Along) and in OT mode (HD-wave).
B: Same patient in A. Intra-patient post processing voltage maps in atrial fibrillation using 0.3–0.6 mV. Very small differences are detectable both in bipolar mode (Across and Along) and in OT mode (HD-wave). Similarly, minimal differences were observed comparing the range 0.3–0.6 with the range 0.05–0.5. Note more scar (grey color) and non-compact fibrosis (raimbow color) with respect the map in sinus rhythm, probably related to the arrhythmia and not to the substrates.

Conflict of interest

The authors declare no conflict of interest.

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