Scar identification, quantification, and characterization in complex atrial tachycardia: a path to targeted ablation?

Decebal Gabriel Laţcu1*, Sok-Sithikun Bun1, Ruben Casado Arroyo2, Ahmed Moustfa Wedn1, Fatima Azzahrae Benaich1, Karim Hasni1, Bogdan Enache1, and Nadir Saoudi1

1Service de Cardiologie, Centre Hospitalier Princesse Grace, Avenue Pasteur 98000, Monaco; and 2Department of Cardiology, Erasme University Hospital, Université Libre de Bruxelles, Brussels, Belgium

Successful catheter ablation of scar-related atrial tachycardia depends on correct identification of the critical isthmus. Often, this is represented by a small bundle of viable conducting tissue within a low-voltage area. Its identification depends on the magnitude of the signal/noise ratio. Ultra-high density mapping, multipolar catheters with small (eventually unidirectional) and closely-spaced electrodes improves low-voltage electrogram detection. Background noise limitation is also of major importance for improving the signal/noise ratio. Electrophysiological properties of the critical isthmus and the characteristics of the local bipolar electrograms have been recently demonstrated as hallmarks of successful ablation sites in the setting of scar-related atrial tachycardia.

Keywords
Scar • Fibrosis • Atrial tachycardia • Electroanatomical mapping

Introduction

Complex atrial tachycardia (AT) are frequently scar-related, either after atrial fibrillation (AF) ablation or incisional. The success of catheter ablation depends on the precise diagnosis of the AT mechanism, which is sometimes very challenging1 despite reliable electrocardiogram (ECG)-based algorithms that have been proposed and are used in everyday practice.2–5 Recent advances in mapping resolution and precise automatic annotation of intracardiac electrograms (EGM) are major steps in the evolution of electro-anatomical mapping systems.6 Entrainment mapping remains very useful to select the chamber to be mapped, to diagnose/confirm the AT mechanism and to rule out passive loops.7

On top of these techniques precise knowledge of previously created lesions (ablation reports, previous maps with ablation tags, and surgical reports) along with substrate imaging contribute to scar identification. This step plays a key role since critical areas of arrhythmogenesis occur often in diseased tissue where voltage is attenuated. In this article, we will review the particularities of scar identification at the atrial level and of the detection of viable tissue within scars by improving the signal/noise ratio.

Pathophysiology of atrial scar

Electrical8 and structural9 remodelling are, in many cases, the substrate of atrial tachyarrhythmias. Fibrosis is the hallmark of structural remodelling10, replacement fibrosis (e.g. post-myocardial infarction) and interstitial fibrosis (reactive—due to ageing, hypertension, obstructive sleep apnoea, or infiltrative—such as in amyloidosis) are commonly described, with both types coexisting in many late-stage conditions.11 They all have in common an increase of the extracellular matrix at the expense of cardiomyocytes. Myofibroblasts of various origins synthesize collagen, which is deposited in the extracellular space.12 Various factors such as pressure and volume overload induce an imbalance between matrix metalloproteinase13 and tissue inhibitor of metalloproteinases, leading to an insufficient degradation of the extracellular matrix, and finally myocardial fibrosis.14

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* Corresponding author. Tel: +377 97 98 97 71; fax: +377 97 98 97 32. E-mail address: dglatcu@yahoo.com

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Iatrogenic scar may be created in the atria by previous ablation (with radiofrequency or other energy sources) or surgical incisions (Figure 1). Radiofrequency catheter ablation induces acute (coagulation necrosis), mid-term (fatty infiltration surrounded by chronic inflammation), and long-term (fibrotic scar with uniform linear scars after linear ablation) pathological modifications. The uniformity of these chronic lesions explain the lack of proarrhythmic effect in the absence of ablation gaps.

Cryotherapy, through ice crystals formation and thawing yields cellular destruction in the acute phase. Ischaemic necrosis follows (through haemorrhage, inflammation, and cell-membrane disruptions) and finally, replacement fibrosis give rise to the mature cryolesion within weeks.

Data about healing of post-operative cardiac wounds is scarce in the literature. Proliferation of collagen epicardially, weakness due to lack of adhesion between sutured edges, and slow development of a neointima have been reported for atrial wall incisions.

Clinical diagnostic methods of cardiac fibrosis include serum markers, various imaging modalities, and histology of endomyocardial biopsy. When assessing a proarrhythmic substrate, localization is capital and is only provided by imaging techniques. Of these, late-gadolinium enhancement (LGE) in cardiac magnetic resonance (CMR) imaging detects patchy and focal areas of fibrosis while measurement of the extra-cellular volume fraction by T₁ mapping detects diffuse and microscopic cardiac fibrosis.

Analysis of atrial-wave amplitude on standard 12-lead surface ECG also informs on the extent of atrial fibrosis. Shrinking of the F-wave amplitude on the surface ECG is related to the magnitude of the underlying atrial voltage, which is also related to the amount of viable atrial muscle. It has been associated with AF duration and patient’s age, both in V₁ and II, with lower values (<0.12 mV in V₁) linked to AF recurrence after catheter ablation. Our group proposed a fibrillatory wave computation in multiple leads that improved the non-invasive prediction of ablation outcome in persistent AF.

**Preprocedural imaging**

While ventricular fibrosis assessment has achieved excellent results with LGE-CMR, imaging of atrial fibrosis remains delicate. Several publications with a strong scientific impact proposed LGE-CMR for detection of both pre-existing and post-ablation induced atrial fibrosis. The extent of baseline LGE has been shown to predict AF recurrence after ablation and may improve patient selection for ablation procedures. LGE-CMR may also provide information about gaps in previous ablation lines; integration of these images in 3D mapping systems may facilitate ablation procedures by targeting the breaks visualized in the previous lesion sets.

Nevertheless, LGE-CMR for detection of atrial scar has not been wildly adopted in clinical practice, mainly because of insufficient reproducibility. Late-gadolinium enhancement sites on CMR were

**Figure 1** (A) Voltage mapping of the right atrium (inferior view) for recurring right AT in a patient with a previous cavo-tricuspid isthmus (CTI) linear RF ablation. Complete endocardial block at the CTI is suggested by the local low voltage and widely separated double potentials (bipolar EGM) along the line. (B) Activation mapping of the left atrium (LA) in sinus rhythm (right lateral view) in a patient with an ancient mitral valve repair. The surgical report indicated a direct incision of the LA posterior to the septum, in front of the right pulmonary veins, in the Sondergaard groove. The local block line indicated by the activation mapping (with double potentials) helps localizing the surgical scar. AT, atrial tachycardia; A/V, atrial/ventricular EGM; EGM, electrograms; LAA, left atrial appendage; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.
Detection of atrial scar in the electrophysiology lab: how to choose the right catheter in order to maximize the electrical signals

While mapping a scar-related AT, viable tissue within scars should be detected as it may represent the critical isthmus (CI) of a re-entrant circuit. Detection of low-amplitude signals is thus mandatory for successful diagnosis. The lower threshold of recordable physiological electric signals will be represented by the amplitude of electronic noise, which should be minimized in order to improve the signal/noise ratio.

The morphology and amplitude of the recorded EGM depends on myocardial properties, wavefront direction, conducting medium, catheter-tissue contact and orientation, catheter electrodes size, composition, shape and inter-electrode spacing. The fundamentals of unipolar and bipolar EGM recording are beyond the scope of this overview article. Nevertheless data exists proving that mapping with small closely spaced electrodes can improve mapping resolution, which is of capital importance within areas of low voltage.

Until a very recent past (e.g. 5 years) the standard catheter for mapping was (and still is in a number of centres and/or clinical situations) a linear catheter with a 3.5 mm tip electrode separated by 2 mm for a proximal 2 mm electrode (i.e. Navistar/ThermoCool/SmartTouch, Biosense-Webster; BW). This results in an interelectrode distance (centre-to-centre) of 4.75 mm. More recently, multielectrode mapping using 1 mm electrode catheters with a 2 mm interelectrode spacing (3 mm centre-to-centre; PentaRay, BW) have been introduced and widely used along with the advent of automatic electrode mapping using 1 mm electrode catheters with a 2 mm interelectrode distance (centre-to-centre) of 4.75 mm. More recently, multielectrode mapping using 1 mm electrode catheters with a 2 mm interelectrode spacing (3 mm centre-to-centre; PentaRay, BW) have been introduced and widely used along with the advent of automatic annotation of EGM. A comparative study in normal atria with simultaneous mapping by both catheters found a very similar normal cut-off for bipolar voltage for both catheters (0.48 vs. 0.52 mV, \( P = 0.65 \)) in the right atrium and 0.50 vs. 0.52 mV, \( P = 0.80 \) in the left atrium\(^\text{45} \)), suggestive that the inferior limit of the bipolar voltage EGM is independent of the mapping electrode dipole size and spacing (within these above-mentioned ranges).

If a higher mapping density was expected with the multipolar catheter, several other results\(^\text{41} \) emphasize the importance of smaller size—closely-spaced electrodes when mapping scar-related AT. In these conditions, EGM duration is shorter (by eliminating far-fields and minimizing the mapped area by each point), delineation of low-voltage areas is improved (abnormal, low-voltage, as well as dense-scar areas are smaller), late potentials and EGM fractionation are more frequently recorded. The authors\(^\text{41} \) elegantly demonstrated that not the mapping density, but the smaller electrode size and inter-electrode spacing were responsible for the resolution improvement, especially within scarred tissue. Another important finding was that mapping with a linear ablation catheter (3.5-2-2 mm dipole) demonstrated lower mean voltage of the fractionated EGM, limiting accurate activation time annotation. Overall, in severely scarred atria, 54.4% of all data points recorded with 2-2-2 mm dipoles had distinct EGM that allowed annotation vs. 21.4% of all low-voltage points recorded with linear catheters (\( P = 0.02 \)).\(^\text{41} \) A lower atrial pacing threshold was also demonstrated with this type of catheter.

The more recent 64-pole basket mapping catheter (IntellaMap Orion\textsuperscript{TM}, Boston Scientific; BS) further improved these aspects (Figure 2). It incorporates very small, flat (0.4 mm\(^2\); 2.5 mm spacing), unidirectional electrodes.\(^\text{43,44} \) Owing to their exclusive location on the external side of the splines, they are structurally less influenced by noise and far-field signals. Maps produced experimentally with the Rhythmia mapping system (BS) using this catheter had an unprecedented EGM resolution (2.6 mm), the noise was very low (<0.01 mV) and were highly accurate, without need for manual reannotation. EGM along the lines of conduction block demonstrated double potentials while EGM recorded at the level of gaps exhibited fusion of double potentials. The initial experimental results have been validated clinically in a prospective setting,\(^\text{1} \) with a mapping resolution of 2.09 ± 128 points/cm\(^2\). By recording higher bipolar voltage EGM, it has also been reported that, compared with Lasso (BW), the minibasket catheter has improved sensitivity in detecting PV potentials after RF ablation.\(^\text{45} \)

Background noise limitation

Electrical noise is the other aspect of the signal/noise ratio; artefacts may have various origins and may bias EGM interpretation. Electromagnetic fields and intermittent connections are the main causes of noise interference in the electrophysiology lab. If poor cable connections, surface ECG leads and catheter handles can be easily managed, electromagnetic noise sources are more difficult to suppress. A set of measures contribute to noise reduction before the signal amplification process: correct routing of the intracardiac, radiofrequency and ECG cables without floor contact, isolation of power cables away from signal cables, and careful skin preparation. Intracardiac noise may also be reduced by using an indiffedunipolar electrode inside the inferior vena cava, deep sedation, or general anaesthesia.

Despite all these measures, in many laboratories background noise (BGN) still persists at levels that might be comparable to the magnitude of the smallest electrical signals from viable tissue within the scar (Figures 2 and 3). Noise levels have rarely been the subject of published research. In a recent study from our group,\(^\text{1} \) we measured the electronic noise on the Rhythmia system using the voltage calipers with adequate amplification and speed. From the bipolar EGM acquired during scar-related AT with the Orion catheter, BGN was assessed at six pre-specified sites for the left atrium (mid-roof, mid-posterior wall, posterior mitral annulus, inter-atrial septum, mid-anterior wall, and appendage) and four pre-specified sites for the RA (cavo-tricuspid isthmus, septum, appendage, and crista terminalis). The BGN was also assessed on the bipolar EGM recorded with a standard decapolar catheter (2 mm rings electrodes and spacing) and on the surface ECG.

Background noise ranged from 10 to 12 μV (0.011 ± 0.004 mV) for the basket catheter EGM, without significant differences between sites (Figure 2). It is worth noting that this value is much lower than
**Figure 2** The fully deployed 64-pole basket mapping catheter (Intellamap Orion™, Boston Scientific; BS) and size/spacing of the unidirectional electrodes. Examples of intracardiac EGM and bipolar noise level at various atrial sites. A/V, atrial/ventricular EGM.

**Figure 3** (A) Anterior view of left atrial (LA) voltage (upper image) and activation mapping (lower image) during clockwise perimital flutter (cycle length 490 ms) in a patient with previous pulmonary vein isolation and severe dilation of the LA. The map was acquired with the PentaRay catheter and the Confidense module of Carto 3 (Biosense-Webster). The dense scar threshold was lowered to 0.01 mV. A wide scar area is visualized at the level of the anterior wall, without distinguishable endocardial gap at this level. Entrainment confirmed that both septal and lateral aspects of the mitral valve were in the circuit and endo-epi ablation at the mitral isthmus was successful. (B) Antero-superior view of left atrial (LA) voltage (upper image) and activation mapping (lower image) during anterior wall clockwise macro-re-entrant AT (cycle length 460 ms). The map was acquired with the Orion catheter and the Rhythmia system (Boston-Scientific). The dense scar threshold was also set to 0.01 mV. There is a large scar on the anterior wall of the LA extending to the roof with a low-voltage gap in its superior part (despite very low bipolar EGM amplitude of 0.08 mV at this level, the signal/noise ratio = 10). Ablation at this level successfully terminated the tachycardia. LAA, left atrial appendage; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.
nominal setting of ‘dense scar’ in the mapping systems (generally 0.03–0.05 mV). The small, flat (unidirectional) and closely spaced electrodes of the Orthon had less noise than that of the standard decapolar catheter (0.016 ± 0.019 mV) and the surface ECG leads (0.02 ± 0.01 mV) acquired on the Rhythmia system (P = 0.00009). 1

This unprecedented low level of BGN opens new possibilities for efficient mapping of viable tissue within scar, by appropriated thresholding of ‘dense scar’ to lower levels, closer to BGN.

**Scar detection by bipolar voltage mapping and scar thresholding**

Ventricular cut-offs for scar detection by endocardial bipolar voltage mapping were proposed by Marchlinski et al.,46 but limited data exists for the atria. A recent study39 reported values for delineating inexorable dense scars in patients undergoing AF ablation ranging from 0.15 mV to 0.45 mV using the Carto system (BW). Ultra-high density mapping data for scar detection has even less been reported. In a ventricular scar animal model, scar detected by the Rhythmia system using the basket for mapping correlated best with the magnetic resonance imaging.6 A small series50 found an excellent correlation between scar-distribution on CMR and high-density voltage mapping using the Rhythmia system during AT, with a bipolar cut-off of 0.5 mV.

In the previously mentioned scar-related AT series,1 using a bipolar cut-off of 0.5 mV the extent of low-voltage areas was very important [58 ± 25% of the left atrial (LA) surface]. A commonly used dense-scar thresholding approach (e.g. with a cut-off of 0.05 mV) yielded a result of the ‘dense-scar’ extent of 22 ± 16% of the LA surface. We proposed a patient-specific scar-thresholding process. Thus, after map completion, dense scar thresholding was performed in each case wherever necessary (Figure 3B). The ‘confidence mask’ parameter was than fine-tuned and lowered as much as needed (but above the BGN) to visualize the entire circuit for each AT. Dense scar threshold (‘confidence mask’) was established at 0.016 ± 0.009 mV (median 0.015 mV). Only 12 ± 8% of the LA surface remained inferior to the patient-specific dense scar threshold: a supplemental 10% of the LA surface became thus accessible to analysis and activation interpretation compared with the standard 0.05 mV threshold.

A recently developed technology may bring new insights into scar detection through electrical coupling analysis.50 The measure of the local (bipolar) impedance provides information about the catheter-tissue contact and its decrease is experimentally correlated with the lesion size.50 The ongoing LOCALIZE study (ClinicalTrials.gov Identifier: NCT03232645) will correlate these innovative parameters with gap localization after PV ablation in paroxysmal AF patients. Above these features, local impedance values have informative potential about the stiffness of the tissue and may indirectly assess the extent of fibrosis.

**Detection of critical isthmus of atrial tachycardia allows targeted ablation**

Critical isthmus of macro-re-entrant AT is a region of significant narrowing and/or slowing of the wavefront. The hallmark characteristics of the CI are lower voltage and slower conduction.40,51,52 Ultra-high density mapping brought new insights into these characteristics. We demonstrated that bipolar EGM at the CI systematically show low voltage (0.08 ± 0.11 mV), prolonged duration with multicomponent signals (100 ± 63 ms, covering 35 ± 18% of the cycle length), and significantly lower conduction velocity than the adjacent segments of the circuit: 0.27 ± 0.19 m/s, lower than orthodromically before (1 ± 0.49 m/s, P < 0001) or after the CI (1 ± 0.73 m/s, P < 0001).1

Interestingly, in our series, 50% of the AT had bipolar EGM amplitude within the CI of less than 0.05 mV, and in 27% of less than 0.03 mV: activation mapping would not have been diagnostic in these cases with the higher bipolar dense scar threshold (such as 0.03 mV or 0.05 mV, which are generally used).

A recent very elegant study53 based on ultra-high density activation mapping of AT demonstrated that the association of low voltage (0.07 ± 0.05 mV) and long duration (121 ± 11 ms) of bipolar EGM is specific for slow conduction areas (0.08 ± 0.02 mV) and help discriminate fractionated potential due to slow conduction from wavefront collision/friction and pivot sites (e.g. at the extremity of a block line).

Ablation at the CI is highly successful.1,54 On top of entrainment mapping techniques, identification of CI within scars by activation mapping and EGM characteristics may be particularly helpful.

**Conclusion**

Scar characterization in complex AT aims to detect viable conducting tissue in a low-voltage area. All the technical measures improving the signal/noise ratio address this objective. Critical area of arrhythmogenesis are often located in theses area, and their ablation, after confirmation of their critical role in scar-related AT, is highly successful.

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**References**


