Ablation for Atrial Fibrillation

Electroanatomic properties of pulmonary vein antral regions enclosed by encircling ablation lesions

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Aims

Encircling ablation of the right and left pulmonary venous antra is commonly practiced. The importance to procedure outcome of electrical isolation of unablated myocardium enclosed by the encircling lesions is increasingly clear. The safe and effective achievement of isolation is dependent on a thorough comprehension of the ‘electroanatomic’ ablation substrate. We sought to improve comprehension of this substrate by examining relationships between anatomy and electrogram amplitude and timing after encircling ablation.

Methods and results

After deployment of encircling antral ablation lesions, detailed, echocardiographically guided mapping of endocardial regions enclosed by the lesions was performed. Among patients in whom the encircling lesion did not produce electrical isolation of the enclosed region (143 of 199 left antra and 37 of 198 right antra), separate electrograms generated by enclosed atrial myocardium (EM) and contiguous non-enclosed myocardium (NEM) were apparent at most mapped sites. Non-enclosed myocardium electrogram amplitudes demonstrated a spatial pattern which could be understood by considering contiguous atrial anatomy. Enclosed myocardium electrogram amplitudes demonstrated distinct spatial patterns that were more variable and not related to contiguous anatomy; they guided one or more additional ablation lesions within the enclosed region, which produced isolation. Among patients in whom the encircling lesion did produce isolation of the enclosed region, only NEM electrograms were consistently observed.

Conclusion

The relationships between anatomy and electrogram amplitude and timing detailed herein may be helpful during the conduct of encircling ablation with a goal of isolation of EM.

Keywords

Atrial fibrillation • Intra-cardiac echocardiography • Catheter ablation

Introduction

The importance of the posterior left atrium for the initiation and perpetuation of atrial fibrillation (AF) has been demonstrated. Recognition of this fact led to demonstration of the feasibility and utility of ablation-induced electrical isolation of otherwise viable myocardium investing pulmonary vein walls.1 Since then, ablation lesions have been migrated proximally to ‘encircle’ the pulmonary venous antra, in order to enclose a larger region of posterior left atrial myocardium. Many practitioners now believe that electrical isolation of the enclosed region is essential for a favourable ablation outcome. Early studies by Keith and Flack2 and Papez,3 with more recent elaborations by Ho et al.1,4 and Platonov et al.6 illustrate the posterior left atrial anatomic substrate. Anatomy, however, is an imperfect predictor of electrophysiological behaviour.

Early in our experience, it became apparent that the encircling antral lesion commonly did not achieve electrical isolation of the myocardium enclosed by it.7 In such cases, delayed conduction between myocardium not enclosed by the lesion and myocardium enclosed by the lesion produced a separation between electrograms generated by these respective myocardial masses, which was not present prior to ablation. Electrograms representing activation of each mass could be recorded during mapping within the enclosed region, and their amplitudes and timing thus analysed separately. Using intra-left atrial echocardiography to pinpoint the
anatomical location of each mapped site, and by aggregating data from sites throughout the enclosed regions, we were able to create anatomical maps of electrogram amplitude and timing in individual patients. These data have informed us as to the necessity and location of additional lesions within the enclosed regions to achieve isolation. Although inter-individual variability was observed, patterns were apparent. In order to rigorously illustrate these patterns, this report attempts to coalesce data from a large cohort.

**Methods**

This analysis was approved by the Institutional Review Board of the University of Pittsburgh Medical Centre. Informed consent was obtained from each patient.

**Patients**

Two hundred consecutive patients who underwent catheter ablation intended to cure an established syndrome of paroxysmal or persistent AF were included. This is an elaboration on previous reports that contain a detailed characterization of this cohort, operative technique, and medium-term clinical outcomes. Elements of particular relevance include young age (54 ± 7 years), preponderance of paroxysmal AF (64%), small LA volume (86 ± 7 cc), preserved LV systolic and valvular function, no prior atrial ablation or incision, and absence of type VIII anti-arrhythmic agents at the time of the ablation procedure.

**Operative procedure**

A detailed description of the operative technique has been published previously. Important elements included cardiac computed tomography (CT) prior to each procedure, from which multidimensional left atrial images were generated for each patient, as well as general anaesthesia using jet ventilation, which maximized spatial precision during mapping and ablation. Intra-cardiac navigation involved a collaboration between intra-LA echocardiography (ICE; UltraCETM, Boston Scientific, Natick, MA, USA) and magnetic tracking (CARTOTM; Biosense Webster, Diamond Bar, CA, USA). Intra-cardiac echocardiography permitted direct, real-time visualization of the endocardial surfaces of both antra, contiguous atrial and extra-atrial anatomy, and the location of a mapping/ablation electrode in situ; anatomical accuracy for the latter purpose has been previously demonstrated. Mapping and ablation were performed during sinus rhythm or right atrial pacing, with anatomical demarcation at each site based on the point of endocardial contact of the distal electrode. The distal electrode was 7 Fr, 4 mm length, non-irrigation. Radiofrequency power titration during focal ablation lesion applications was guided by electrogram amplitude reduction where possible, which usually required stable electrode-endocardial contact for 30 s at a peak power of 25–35 W. Bipolar electrograms (ablation electrode to 2 mm length ring electrode with 2 mm inter-electrode spacing, 30–500 Hz filtering, and 1–2 cm/mV gain) were recorded using commercial systems (EP Medsystems, NJ, USA or Prucka/GE Healthcare, Chalfont St Giles, UK). Pacing to assess for exit block was unipolar, through the distal electrode, and long cycle length.

The procedure began with ICE-guided encircling lesions of each antrum. Each encircling lesion was comprised a series of focal lesions applied contiguously (defined by uninterrupted contact of 2 mm diameter spherical CARTO spatial ‘icons’, each representing a focal lesion). The encircling lesion path was located at least 1 cm from any venoatrial junction, with one exception: defined using ICE, in 37 patients (19%) proximity of the intervenous ridge insertion to the apex of the anterior wall caused the encircling lesion path in this area to come within 1 cm of the anterior wall aspect of the venoatrial junctions. Myocardium enclosed within the encircling lesion was termed as ‘enclosed myocardium (EM)’; remaining atrial myocardium was termed as ‘non-enclosed myocardium (NEM).’ Typical examples are shown in Figures 1 and 2.

Intra-cardiac echocardiography-guided mapping of the enclosed region was then performed. If electrical isolation (below) was not observed, then one or more ‘secondary’ lesions were delivered at sites within the enclosed region guided by activation mapping of impulses entering the region (below). After each secondary lesion was applied, mapping of the enclosed region was repeated to reassess the presence and pattern of conduction into the enclosed region. The procedural endpoint was electrical isolation of both enclosed regions, defined by entrance block into and exit block from their entirities.

**Analytical methods**

The peak-to-peak amplitude and timing of the major deflection of each electrogram were measured offline, each as the mean of three non-consecutive beats, by non-blinded personnel. To minimize error in the local electrogram analysis caused by contiguity of the encircling lesion, in each antrum an empiric, 5 mm-width (defined using ICE) ‘no-measurement’ zones were used to separate the lesion from enclosed tissue from which electrogram data was included; points located in this zone were not included in the analysis. Electrogram timing was measured relative to earliest evidence of the surface P-wave.

Data are reported as mean ± standard deviation, unless otherwise stated. Comparisons of continuous variables were performed using a t-test or repeated measures ANOVA and of categorical variables using a χ² test. Correlations were performed using the Pearson product moment correlation. For each test, a P-value of <0.05 was considered significant.

**Results**

In two patients, the procedure was aborted due to anaesthesia intolerance; in one of these patients, left enclosed region isolation was achieved prior to procedure termination. The data are thus a coalescence of left antrum ablation in 199 patients and right antrum ablation in 198 patients: successful isolation of enclosed regions was achieved in all antra. There were no other procedural complications. The veins were common on the left in 32 patients (16%). There were supernumerary veins on the left in 2 patients (1%) and on the right in 67 patients (34%). Atrial wall thickness, defined using ICE, was variable but ≤5 mm along the entire encircling lesion path (Figures 1 and 2). Contiguous structures, notably appendage complex, superior caval vein, and contiguous right atrial septum were readily imaged (Figures 1 and 2).

Immediate post-ablation mapping of the encircling lesion demonstrated that electrogram amplitudes and slopes were reliably <10% of their pre-ablation baselines along the entire lesion paths. Mapping within the enclosed regions then demonstrated that electrical isolation of the left enclosed region was achieved in 56 patients (27%), and of the right enclosed region in 161 patients (81%). Among the 143 patients in whom left
enclosed region isolation was not achieved, one (32 patients) or more (111 patients; average of five lesions) secondary lesions within the left enclosed region were required to achieve isolation. Among the 37 patients in whom right enclosed region isolation was not achieved, one (18 patients) or more (19 patients; average of two lesions) secondary lesions within the right enclosed region were required to achieve isolation. No significant differences in the likelihood of encircling lesion success nor in secondary lesion number/locations were correlated with AF syndrome (paroxysmal vs. persistent), LA volume (CT), or number of individual veins. Observations are described separately below for left and right enclosed regions.

Figure 1 The top and bottom rows demonstrate typical intra-cardiac echocardiography images obtained with the transducer in various locations within the left enclosed region. The centre row uses computed tomography images to illustrate how the intra-cardiac echocardiography images were used to integrate electrograms with anatomy and to demarcate myocardium enclosed by the encircling lesion (highlighted in blue) from myocardium which is not enclosed: (A) whole-heart, left-lateral vantage; (B) left atrial, viewed from a posterior extra-cardiac vantage; (C) left atrial, with the left antrum viewed from an intra-cardiac vantage; (D) the two endocardial halves of (C) resulting from a cleavage plane along the red line shown in (C). On all computed tomography images, the dotted lines show the encircling lesion, and solid lines the venoatrial junctions. Numbered locations on the computed tomography images correspond to those on the intra-cardiac echocardiography images. The enclosed region was conceptualized as having four ‘walls’: 1, posterior; 2, inferior; 3, anterior; and 4, superior. The confluence of superior and inferior veins was defined as the intervenous ridge (5→6). The asterisks on the intra-cardiac echocardiography images represent sites where wall thickness was measured. aAo, ascending aorta; MPA, main pulmonary artery; LAAd, distal portion of appendage complex; LAAp, proximal portion of appendage complex; LAAo, ostium of LAAp, defined as the region of transition between smooth (LAAp) and trabeculated (LAAd) endocardial contours; CS, coronary sinus; Cx, circumflex coronary artery; LV, left ventricle; RV, right ventricle; LA, body of left atrium; LPV, left pulmonary venous antrum; LAD, left anterior descending coronary artery; SCV, superior caval vein; LS, left superior pulmonary vein; LS’, branch of left superior pulmonary vein; LI, left inferior pulmonary vein; RS, right superior pulmonary vein; RI, right inferior pulmonary vein; dAo, descending aorta; LPA, left pulmonary artery; eso, oesophagus; P, pericardial recess; MA, mitral annulus; T, intra-cardiac echocardiography transducer; Tr, muscular trabeculum in appendage; †, tissue bridging left atrial body and contiguous left superior vein roof.
Left enclosed region

Isolation not achieved by the encircling lesion (143 patients)

An average of 42 ± 11 mapped sites per patient were required to encompass the enclosed region. At most sites, both EM and NEM electrograms were recorded. Representative examples are shown in Figure 3.

Non-enclosed myocardium electrogram amplitudes were highest along the anterior wall, although among patients there was variation in this area, which appeared to be influenced by proximity of the enclosed and appendage regions (Figure 4). Electrogram timing suggested craniocaudal activation, anterior wall in advance of posterior wall, the former coinciding with the activation of the contiguous appendage region (Figures 3 and 5). Activation began in the latter half of the P-wave and ended prior to its completion; total activation time was 28 ± 13 ms.

Enclosed myocardium electrograms were rarely apparent before the termination of the P-wave (Figure 3). Their amplitudes were more symmetrically distributed and (at individual sites) larger than NEM amplitudes (P < 0.008; Figure 5). Electrogram timing suggested a variable sequence of activation within the enclosed region among individuals, dependent on the location(s) of conduction remaining after the encircling lesion (see below); this produced spatial variation in NEM–EM electrogram intervals (Figure 3).
Secondary lesions targeted the earliest EM electrogram timing. The anterior wall, particularly in the area of its junction with the intervenous ridge, was a disproportionately frequent site (Figure 5). Secondary sites commonly did not abut the encircling lesion. On occasion, they were located within the superior pulmonary vein, and such sites could have an echocardiographically distinct anatomical corroborate (Figure 1). Among the 111 patients in whom more than one secondary lesion was necessary, ablation in more than one area was commonly necessary, with a later-activating area becoming apparent after ablation in an earlier-activating area. In most patients, isolation of EM was an all-or-none phenomenon. However, in 18 patients (13%), during secondary lesions we observed the occurrence of isolation of only the pulmonary vein(s) (superior only, \( n = 9 \); inferior only, \( n = 7 \); both, \( n = 2 \)) prior to an additional lesion(s) which achieved isolation of the entire enclosed region. After isolation was achieved, dissociated EM electrograms were observed in 89 patients, with electrical quiescence in the remainder.
Isolation achieved by the encircling lesion (56 patients)
An average of 33 ± 8 mapped sites per patient were required to encompass the enclosed region. Compared with patients who required secondary lesions, there were no apparent differences in NEM electrograms. Dissociated EM electrograms were observed in 38 patients.

Right enclosed region
Isolation not achieved by the encircling lesion (37 patients)
An average of 45 ± 8 mapped sites per patient were required to encompass the enclosed region. At most sites, both EM and NEM electrograms were recorded. Representative examples are shown in Figure 3.

Non-enclosed myocardium electrogram amplitude was asymmetrically distributed, favouring the upper half of the anterior and contiguous superior walls, areas adjacent to the superior caval-right atrial septal junction (Figures 2, 3, and 6). In addition to being more spatially discrete, on average, amplitude was significantly smaller than in the left enclosed region ($P < 0.001$; Figures 5 and 6). Electrogram timing suggested craniocaudal activation; activity began immediately after P-wave onset, and total activation time was 34 ± 18 ms.

Enclosed myocardium electrograms were also generally confined to the P-wave. Their amplitudes were more symmetrically distributed and (at individual sites) larger than NEM amplitudes ($P < 0.001$; Figure 6). As in the left enclosed region, EM electrogram timing and thus NEM–EM intervals were variable.
Secondary lesions favoured anterior and superior walls (Figure 6), in most patients limited to a single area. In four patients (11%), during secondary lesions we observed the occurrence of isolation of only the pulmonary vein(s) (superior only, \( n = 3 \); inferior only, \( n = 1 \)) prior to an additional lesion(s) which achieved isolation of the entire enclosed region. After isolation was achieved, dissociated EM electrograms were observed in 12 patients, with electrical quiescence in the remainder.

**Isolation achieved by the encircling lesion (161 patients)**

This occurred significantly more commonly than on the left side (\( \beta < 0.01 \)). An average of 42 ± 11 mapped sites per patient were required to encompass the enclosed region. Compared with patients who required secondary lesions, there were no apparent differences in NEM electrograms. Dissociated EM electrograms were observed in 49 patients.

**Discussion**

We used intra-left atrial echocardiography to pinpoint the anatomical location of an endocardial mapping electrode in antral regions enclosed by encircling ablation lesions and integrated location with recorded electrograms. In antra where the encircling lesion did not produce electrical isolation of EM, conduction delay resulted in separation between NEM and EM electrograms, which were superimposed prior to ablation (Figure 3). This separation provided an opportunity to gain insight into the electroanatomic properties of the enclosed antral regions.

**Left enclosed region**

**Non-enclosed myocardium electrograms**

The observed spatial (anatomical) pattern of amplitudes suggests that electrograms were derived primarily from myocardium of
the appendage region. Although electrographic activity of ‘appendage’ derivation recorded within the left pulmonary vein region is well described, our data provide important extensions. First, previous reports were limited to electrograms recorded within the pulmonary veins, whereas we provide data from the entire enclosed region. Second, previous reports did not illustrate or incorporate the anatomical complexity of the appendage apparatus, which covers a large geographic territory and includes both smooth and trabeculated regions. Third, techniques used in previous reports were limited in their ability to resolve anatomic locations of the mapping electrode, and thus provided little spatial detail. Such data have practical value: as is demonstrated in Figure 3, apparently small changes in mapping electrode location can cause major changes in electrogram morphology, yielding interpretive confusion. Finally, herein we report, for the first time, that a specific electroanatomical relationship, proximity of enclosed and appendage regions.

The observed timing of NEM electrograms is consistent with the activation of myocardium surrounding the enclosed region by a wavefront dominated by the inter-atrial bundle, fibres of which invest the anterior wall more directly than the posterior wall.

**Enclosed myocardium electrograms**

After the encircling lesion, residual conduction into the enclosed region was common, as reported previously. The observed anatomical pattern of amplitudes in the region is consistent with a progressive increase in myocardial thickness moving from within the veins towards the encircling lesion. Residual conduction presumably proceeded via myocyte tracts which survived the encircling lesion and bridged between the enclosed region and contiguous NEM. The detailed anatomical characterization of residual conduction provided in the present report is an extension of prior reports. The commonness of residual conduction along the anterior wall of the enclosed region is consistent with previous morphological characterization of a broad tract bridging this wall with the contiguous appendage region, supporting the notion that encircling lesion breadth was inadequate to fully encompass the tract in many patients. Additional support is derived from a report demonstrating a higher rate of initial enclosed region isolation using an ablation technique which includes lesion within the enclosed region in the area where the intervenous ridge joins the anterior wall. Less consistently implicated areas of the residual conduction were located primarily in the upper portion of the appendage region. The observed anatomical pattern of amplitudes in the region is consistent with a progressive increase in myocardial thickness moving from within the veins towards the encircling lesion. Residual conduction presumably proceeded via myocyte tracts which survived the encircling lesion and bridged between the enclosed region and contiguous NEM. The detailed anatomical characterization of residual conduction provided in the present report is an extension of prior reports. The commonness of residual conduction along the anterior wall of the enclosed region is consistent with previous morphological characterization of a broad tract bridging this wall with the contiguous appendage region, supporting the notion that encircling lesion breadth was inadequate to fully encompass the tract in many patients. Additional support is derived from a report demonstrating a higher rate of initial enclosed region isolation using an ablation technique which includes lesion within the enclosed region in the area where the intervenous ridge joins the anterior wall. Less consistently implicated areas of the residual conduction were located primarily in the upper portion of the appendage region. The observed anatomical pattern of amplitudes in the region is consistent with a progressive increase in myocardial thickness moving from within the veins towards the encircling lesion. Residual conduction presumably proceeded via myocyte tracts which survived the encircling lesion and bridged between the enclosed region and contiguous NEM. The detailed anatomical characterization of residual conduction provided in the present report is an extension of prior reports. The commonness of residual conduction along the anterior wall of the enclosed region is consistent with previous morphological characterization of a broad tract bridging this wall with the contiguous appendage region, supporting the notion that encircling lesion breadth was inadequate to fully encompass the tract in many patients. Additional support is derived from a report demonstrating a higher rate of initial enclosed region isolation using an ablation technique which includes lesion within the enclosed region in the area where the intervenous ridge joins the anterior wall. Less consistently implicated areas of the residual conduction were located primarily in the upper portion of the appendage region.
of the enclosed region, suggesting that conduction in these areas were mediated by tracts projecting from the inter-atrial bundle; such tracts have been described previously.5

Right enclosed region
Non-enclosed myocardium electrograms
The observed anatomical pattern of amplitudes suggests that electrograms were derived primarily from myocardium comprising the contiguous areas of atrial septum, caval vein, and inter-atrial bundle. Although electrographic activity of ‘caval’ derivation recorded within the right superior pulmonary vein is previously reported;23 our data provide an important extension, for reasons similar to those described above for the left enclosed region. We hypothesize that the smaller amplitude of electrograms recorded in the right vs. left enclosed region was attributable primarily to closer proximity of the NEM-generating myocardial mass in the latter. The observed timing of NEM electrograms is consistent with the activation of myocardium surrounding the enclosed region by a wavefront emanating from atrial septum near its junction with the caval vein.4 5,6,24,25

Enclosed myocardium electrograms
Considering our findings in the context of those of previous anatomical and electrographic investigations of the right antral region,5,6,24,25 we hypothesize that residual conduction was attributable to tracts projecting from the inter-atrial bundle onto the anterior or superior walls, the breadth or depth of which protected them from the encircling lesion. Although prior reports have suggested that inter-atrial conduction commonly occurs via tracts bridging Waterston’s groove,5,24 our data would suggest otherwise.

Limitations
There are important limitations to these data. First, they are likely influenced by patient selection, which if linked to the magnitude of atrial structural disease (e.g. fibrosis), might affect the likelihood of isolation after the encircling lesion and/or the number and location of secondary lesions. Second, the electrogram data were likely specific to the construction of the recording bipolar. Third, our use of an empiric ‘no-measurement’ zone, which was an effort to minimize measurement error due to contiguous effects of the encircling lesion, may be challenged. Fourth, given a paucity of consistent anatomic landmarks along the posterior wall, there was likely variation in the location of the encircling lesions in this area, which could have impacted our findings. The infrequency of residual conduction observed in this area limits the importance of this variation. Fifth, there is no way to prove that the encircling lesions were uniformly transmural. Non-transmurality could have led to misinterpretation of the mode of residual conduction. We support our assumption of transmurality on the following: (i) wall thickness along the lesion paths was consistently 5 mm or less; (ii) observed magnitude of ablation-induced electrogram amplitude reduction was consistent with transmurality;13,26 (iii) isolation of the left enclosed region by the encircling lesion was not uncommon and was the rule for the right enclosed region; and (iv) secondary lesion sites often did not abut the encircling lesion, which would have been expected if residual conduction was due to non-transmurality. Sixth, our findings were likely influenced by the breadth of the encircling lesion and were thus likely specific to the radiofrequency power titration methodology utilized. For example, there are reports describing higher rates of isolation after encircling lesions using more aggressive power titration techniques, which may be seen to diminish the importance of our findings.19,27,28 However, our goal was less to achieve isolation than to capitalize on non-isolation as an window through which to gain insight into the electroanatomic properties of the antral regions. Given the nature of these properties, such insights could not be gained by differential pacing prior to the encircling lesion. With the inevitable development of new ablation tools and techniques, these insights may prove valuable. Finally, our assay of conduction was performed during long-cycle length atrial activation, conditions which likely differ substantively from those operational during AF triggering and sustenance.

Conflict of interest: none declared.

References


