54.8% of first time ICD recipients were candidates for S-ICD.¹

REFERENCE
Isthmus sites identified by Ripple Mapping are usually anatomically stable: A novel method to guide atrial substrate ablation?

Vishal Luther PhD MRCP, Norman Qureshi PhD MRCP, Phang Boon Lim PhD MRCP, Michael Koa-Wing PhD MRCP, Shahnaz Jamil-Copley PhD MRCP, Fu Siong Ng PhD MRCP, Zachary Whinnett PhD MRCP, D. Wyn Davies MD, FRCP, FHRS, Nicholas S. Peters MD, FRCP, FHRS, Prapa Kanagaratnam FRCP, PhD, Nick Linton MEng, MRCP, PhD

Imperial College Healthcare, London, UK;

Address for correspondence: Dr Nick Linton,

Department of Cardiology, Hammersmith Hospital, Imperial College Healthcare NHS Trust, Du Cane Road, London W12 0HS, United Kingdom.

Telephone: +44 (0) 203 313 1000; Fax: +44 (0) 203 312 1657

Email: n.linton@imperial.ac.uk

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jce.13425.

This article is protected by copyright. All rights reserved.
VL is funded by a British Heart Foundation Clinical Research Training Fellowship award (FS/15/12/31239). NL is funded by a British Heart Foundation Intermediate Clinical Research Fellowship award (FS/15/25/31423).

Imperial Innovations holds Intellectual Property relating to Ripple Mapping on behalf of PK and NL, who have also received royalties from Biosense Webster. PK, NL, and VL have received consulting fees with respect to Ripple Mapping from Biosense-Webster. Other authors: No disclosures.

Abstract
**Background:** Post ablation reentrant ATs depend upon conducting isthmuses bordered by scar. Bipolar voltage maps highlight scar as sites of low voltage, but the voltage amplitude of an electrogram depends upon the myocardial activation sequence. Furthermore, a voltage threshold that defines atrial scar is unknown. We used Ripple Mapping (RM) to test whether these isthmuses were anatomically fixed between different activation vectors and atrial rates.

**Methods:** We studied post-AF ablation ATs where >1 rhythm was mapped. Multipolar catheters were used with CARTO ConfiDENSE for high-density mapping. RM visualized the pattern of activation, and the voltage threshold below which no activation was seen. Isthmuses were characterized at this threshold between maps for each patient.

**Results:** Ten patients were studied (Map1 was AT1; Map2: sinus 1/10, LA paced 2/10, AT2 with reverse CS activation 3/10; AT2 CL difference 50±30ms). Point density was similar between maps (Map1:2589±1330; Map2:2214±1384; p=0.31). RM activation threshold was 0.16±0.08mV. 31 isthmuses were identified in Map1 (median 3 per map; width 27±15mm; 7 anterior; 6 roof; 8 mitral; 9 septal; 1 posterior). Importantly, 7/31 (23%) isthmuses were unexpectedly identified within regions without prior ablation. AT1 was treated following ablation of 11/31 (35%) isthmuses. Of the remaining 20 isthmuses, 14/16 isthmuses (88%) were consistent between the two maps (4 were inadequately mapped). Wave-front collision caused variation in low voltage distribution in 2/16 (12%).

**Conclusions:** The distribution of isthmuses and non-conducting tissue within the ablated left atrium, as defined by RM, appear concordant between rhythms. This could guide a substrate ablative approach.
Keywords:
Atrial tachycardia
3D mapping
CARTO
Scar
Ablation

Introduction

Electrophysiologists commonly use bipolar voltage maps to highlight areas of low voltage that might be considered as scar or electrically inert tissue.\textsuperscript{1-3} It is frequently these areas that form the substrate for reentrant arrhythmias, and therefore they may be a target for ablation.\textsuperscript{4} In cases of ventricular tachycardia, there is consensus that substrate modification is appropriate even after successful ablation of the presenting tachycardia.\textsuperscript{5} However, in the atria it is unclear how to assess the arrhythmia substrate based upon electrogram recordings.

The mechanism of atrial tachycardia (AT) is often iatrogenic in origin – either due to previous AF ablation or cardiac surgery.\textsuperscript{6-9} Bipolar voltage maps during tachycardia may help to identify isthmuses of conducting tissue bordered by scar that support activation.\textsuperscript{10-14} Whether the same scar distribution is seen with a change in activation vector or rate has not been studied in patients with AT following AF ablation. This is important, as if the isthmus locations remain concordant independent of the rhythm mapped, then this could guide
substrate ablation outside of tachycardia for symptomatic patients non-inducible on the day of their procedure or even at the time of their initial AF ablation procedure.

Such an empirical ablation approach requires an accurate method of defining scar and isthmuses. In relating bipolar voltage to scar in the ventricle, early work demonstrated that voltages <0.5mV and >1.5mV correlated well with histo-pathological specimens. However, the bipolar voltage amplitude may depend upon the myocardial activation sequence. Changes in amplitude can occur with variations in activation direction with respect to anisotropic tissue characteristics, or when variations in activation direction lead to wavefront collision. Furthermore, unlike in the ventricle, a consensus for a bipolar voltage threshold that defines atrial scar does not exist.

We have described previously how Ripple Mapping (RM) can be used to determine electrically functional tissue, without a fixed bipolar voltage threshold, for the purposes of guiding activation mapping during atrial tachycardia in patients with previous AF ablation. RM is uniquely suited as it the only mapping system that presents both voltage and activation simultaneously. In this study we retrospectively considered the hypothesis that the isthmuses of active tissue identified using Ripple Mapping are concordant and anatomically fixed between rhythms with different activation direction vector or atrial rate.
Methods

Study population: The cases in this study were patients who underwent ablation for atrial tachycardia using Ripple Mapping, and in whom Ripple Maps for more than one atrial rhythm were collected over an approximate 12-month period in our institute. The reasons for additional map collection were clinical: either to map a second tachycardia or to check for block of an ablation line. Only maps where electro-anatomical data throughout all of the left atrium in both maps were considered. Consecutive patients were included, in whom these criteria were fulfilled. All participants gave informed consent and ethical approval was obtained from the National Research Ethics Service.

Procedures were performed under general anesthesia and with femoral vein access. Transesophageal echocardiography was used to exclude left atrial appendage thrombus and to guide transseptal puncture. A decapolar catheter was placed into the coronary sinus for use as a reference. An electroanatomical mapping system was used (CARTO3v4, Biosense Webster, Inc., Diamond Bar, CA). A multi-electrode mapping catheter (Lasso Nav or PentaRay Nav, Biosense Webster, Inc., Diamond Bar, CA) was placed through sheaths into the LA and used for mapping the LA body and the pulmonary veins. Low voltage area <0.3mV was defined for each map as a percentage of the total LA surface area (excluding the pulmonary veins) using the CARTO surface area tool.
Data collection: The mapping catheter and method of data collection was identical for all maps acquired for each patient. The Color threshold was set below 5mm to ensure a dense and even spread of electrogram data across the map. To avoid the inclusion of erroneous or non-contact points on the map, several different functions of the map were selected. First, both internalized points >10mm and non-respiratory gated points were removed. Second, a series of filters that review each passing EGM picked up by the mapping catheters was activated (CARTO CONFIDENSE Continuous Mapping); this included a “cycle length range” filter that measured the cycle length between 2 beats and accepted those within 5% of the mapped cycle length, an “LAT stability” filter that compares the LAT of each new beat to the previous beat, and rejected those with LAT more than 3ms, and a “position stability” filter that rejected points collected more than 2mm away from a previous beat. Finally a “tissue proximity” filter was activated that uses impedance measurements to determine an electrode's proximity to the cardiac surface and rejects those points collected when greater than the radius of the electrode (assumed not to be in contact).

Ripple map analysis: RM is part of the mapping module in CARTO3v4 (Biosense Webster). RM presents each EGM as a moving bar on the surface geometry. The height of the bar corresponds to the EGM voltage amplitude at that time-point and every bipolar EGM from each projected point is aligned temporally to the fiducial reference signal. The RM of all points is presented as a movie, and we set it to play from 1 tachycardia cycle length before the reference electrogram to 1 cycle length after the reference electrogram. When multiple points are collected over an area, a “ripple” effect is seen as the movement of bars traverses...
from one area to the next. Unlike LAT mapping, where activation is represented visually relative to the “window-of-interest”, the ripple bars are analyzed in relation to each other. Local activation direction is established by the local sequence of bar movement; therefore, there is no concept of ‘early’ or ‘late’ but only of local activation direction. Deflections less than 0.03mV were considered to be noise and not shown. The bars were clipped above 0.30mV to allow low voltage bars to be seen without being obscured by large bars from areas of healthy tissue. The RM was played as a continuous loop and used to characterize every potential wavefront and isthmus on the bipolar voltage map.

Active Tissue Thresholding and Isthmus Identification: During RM viewing, the atrial geometry was colored according to the interpolated bipolar voltage. At the start of the case, a voltage threshold of 0.3mV was arbitrarily assigned (i.e., areas with voltage <0.3mV displayed as red, otherwise purple). When the Ripple map was played, the voltage threshold was then adjusted such that if activation wavefronts were observed in areas deemed inactive according to the interpolated voltage color (i.e., red), then the voltage threshold was reduced. Therefore, after completing this process, the bipolar voltage threshold resulted in areas with active Ripple wavefronts being shown in purple, and areas with no discernible activity in red.

This approach was used to characterize every possible conducting isthmus bordered by inactive areas or anatomical obstructions. All isthmuses were defined over an 8 segment model of the LA (1=anterior, 2=lateral, 3=LAA, 4, roof, 5=posterior, 6=mitral isthmus, 7=roof, 8=septum). Isthmuses were characterized by their borders as either “non-conducting–non-conducting” (NC-NC), or “non-conducting–anatomical” (NC-A).
Some isthmuses exist in all patients because of PVI. These are at the roof, left mitral isthmus, and right mitral isthmus (Figure 1). Isthmuses that were in these positions were sub-classified as 'expected', and otherwise 'unexpected'.

**Ablation:** Power controlled (25–35W) radiofrequency (RF) energy was delivered (Stockert70 RF generator, Biosense Webster) through an irrigated ablation catheter (SmartTouch Thermocool) targeting the critical isthmus supporting the tachycardia circuit as part of the clinical procedure prior to remapping.

**Statistical analysis:** Categorical variables were expressed as percentages. Continuous variables were expressed as mean ± 1 standard deviation for parametric data and/or median (lower quartile – upper quartile) for non-parametric data. Paired data were analyzed using the Wilcoxon Signed Ranks and unpaired data were analyzed using a Mann-Whitney U-Test for non-parametric data. A two-sided p value was determined where applicable and a value of p≤0.05 was considered significant. SPSS Version 22 (IBM) was used for statistical analysis.

**Results**

Ten patients (68+-7 yrs, 8 male) were studied with mapping of >1 left atrial activation pattern. All patients had undergone previous pulmonary vein isolation for AF. Previous ablation sometimes included a roof line (5/10 (50%)), mitral isthmus ablation (4/10 (40%)), and electrogram defragmentation (6/10 (60%)). There were 7/10 (70%) patients who had
undergone 2 or more ablation procedures, including 3 patients who had been treated previously for an AT with ablation. Patient demographics are summarized in Table 1.

A dense map of AT1 was collected in each patient (median 2265points (1554-4308). The median AT cycle length was 250ms (238-300ms). Low voltage area (<0.3mV) encompassed 25% (14–53%) of the total left atrial surface. The bipolar voltage map was adjusted for Active Tissue Thresholding (see Methods), and the median threshold was 0.16±0.08mV. A total of 31 isthmuses were identified in AT1 (median 3 per map; width 27±15mm). The isthmuses were bordered by non-conductive tissue on either side (NC-NC) in 14/31 (45%), and an anatomical structure on one side (NC-A) in 17/31 (55%). Isthmus width was 20mm (14-25) in the NC-NC isthmuses, and 25mm (20-50) in the NC-A isthmuses (p=0.03). The majority of these isthmuses were expected types post AF ablation (as illustrated in figure 1) – there were 6 along the roof, 8 between the left inferior pulmonary vein and mitral annulus, and 9 between the right lower pulmonary vein and septum. The remaining 7/31 (23%) isthmuses were considered “un-expected,” as they could not have been predicted based on the history of previous ablation. An example of an unexpected isthmus is seen as figure 2 and supplementary video 1.

These maps were used during the clinical procedure and 11/31 (35%) isthmuses were ablated resulting in a change or termination of AT1 (2 anterior; 4 roof; 5 mitral). In one patient, owing to a dual loop roof and mitral dependent tachycardia, both isthmuses required ablation prior to tachycardia termination.
For the second map, 3/10 (30%) patients were mapped with either sinus rhythm, LAA pacing, or CS pacing. The remaining 7/10 (70%) patients had a second tachycardia, occurring either as a transition from AT1, or induced following atrial burst pacing. The median CL was 260ms (245-280). This tachycardia was found to be CTI dependent flutter in 2 patients with passive activation over the left atrium. A comparison between map 1 and 2 is presented in table 2.

There was no difference in point density between the maps for each patient (1722 points in Map 2 (1390-2670), p=0.58). Low voltage area <0.3mV encompassed 33% (19-53%) of the LA surface area (p=0.63). After ablation of 11/31 isthmuses from AT1, at these sites of ablation there was low voltage present in the data for Map 2. Therefore, these sites were not included in further analysis and the remaining 20 isthmuses were analyzed. Four of 20 isthmuses (adjacent to the transseptal puncture site) were incompletely mapped and could not be used in the comparison. Of the remaining 16 isthmuses, 14/16 (88%) matched Map 1 for location and width (4 anterior; 2 roof; 3 mitral; 5 septal). These matching isthmuses were NC-NC type in 5/14 (36%), and NC-A in 8/14 (64%). Examples of matching isthmuses are seen in figure 3 and figure 4, and in supplementary video 2.

Two isthmuses did not correspond well between Map 1 and Map2. In both of these cases, RM revealed that there was wavefront collision at the isthmus site (1 anterior; 1 posterior). An
example of this is presented in figure 5 and in supplementary video 3. Table 3 summarizes a comparison of the isthmus characteristics between Map 1 and Map 2.

**Discussion**

We have investigated the use of RM to define the isthmuses of active tissues supporting AT in the context of previous AF ablation. We assessed the reproducibility of these isthmuses in the presence of different atrial activation sequences. This study demonstrates general concordance in their distribution. Where there was not concordance then this was due to wavefront collision, and this can be identified using RM.

During ablation procedures, it can be difficult to differentiate scar from conducting tissue objectively. Predetermined voltage thresholds have not been useful in identifying atrial scar. We have previously developed a simple method for Active Tissue Thresholding by using RM to personalize the bipolar voltage threshold for each patient. This current study was necessary to investigate its reproducibility: as each tachycardia is somewhat unique in its direction of activation and rate, repeat mapping of the same atrium might not necessarily create the same voltage.

This is the first study attempting to understand whether LA voltage maps are concordant in the same individual, when obtained in different rhythms (with different activation vectors or rate). The patients included had all undergone previous ablation for persistent AF and AT.
High density mapping was used to characterize the substrate in detail (>2000 points). Contact with the endocardial surface was reliable, determined using a tissue proximity filter based on impedance, and application of stringent point collection filters. Multi-polar catheters with smaller tips and narrower inter-electrode spacing were used for mapping to record accurate EGMs from smaller tissue diameter.

The concordance in isthmus locations observed in this study is important for those patients with paroxysmal arrhythmia planned for ablation and non-inducible on the day of their procedure, precluding effective mapping. Ablation of all isthmuses within the atrial substrate mapped outside of tachycardia may be considered an alternative strategy for long-term abolition of atrial arrhythmia. Feasibility of such an approach has been previously described. The bipolar voltage and LAT display of a single tachycardia was used to ablate all putative isthmuses thought related to otherwise un-mappable ATs post-surgical atriotomy, achieving high rates of acute non-inducibility and low recurrence at 1-year follow-up.

Atrial “scar” was identified by a bipolar voltage of $\leq0.05-0.1\text{mV}$ - this threshold originating from the baseline noise in early electro-anatomic mapping systems, and points below this threshold were hidden behind grey “scar” tags when LAT mapping was used. However, atrial based substrate ablation approaches have yet to be routinely adopted, owing to absence of a universally accepted voltage threshold to define atrial scar. Furthermore, interpretation of LAT propagation in areas of low voltage can be misleading due to interpolation algorithms within unmapped sites (which assumes activation is uniform), and concern that incorrect assignment of LAT for a small number of low-amplitude fractionated EGMs can invalidate the entire activation map. Extensive ablation can prolong the intra-atrial conduction time such that it exceeds the window of interest, and the timing of the true latest activation site
displayed as early in the window with respect to the next cycle of activation. Ripple Mapping is not reliant upon annotation of activation time or setting a window of interest, as the bars are analyzed in relation to each other to establish the activation direction, and avoids interpolation within unmapped sites - an example of the benefit of RM over LAT interpretation is illustrated in figure 2.19-21

In this study, we consider an approach to define atrial scar using Ripple Mapping.19 RM offers a means of differentiating areas of electrically active tissue – inactive tissue being devoid of Ripple wavefronts. Underlying voltage maps were adjusted to display inactive tissue in red, and active tissue as purple. Using a combination of RM Active Tissue Thresholding to define all isthmuses when mapping an AT, and remapping to define all concordant isthmuses, a novel substrate target could be considered. This approach is summarized in figure 6. An empirical substrate ablation approach based on the isthmuses identified in one map alone would not be recommended, as we infrequently observed non-conductive tissue in one rhythm appear conductive in another. This was a consequence of changes in activation direction or timing, and subsequent wavefront collision, resulting in electrogram amplitude attenuation. The co-display of activation overlying the voltage map with RM allowed us to understand the nature of wavefront collision on the underlying voltage map.

After PVI, patients often develop AT with prototypical macroreentrant circuits – usually 'roof-dependent' or 'mitral isthmus dependent'. These tachycardias pass through isthmuses that result from non-conducting ablated tissue and anatomical obstructions. Often detailed
mapping is not required for these tachycardias to be ablated, and the isthmuses are 'expected' as a consequence of the previous ablation. In contrast, other AT circuits may involve isthmuses that are not in prototypical locations and we denote these as 'unexpected'. Unexpected isthmuses are more difficult to map and successfully ablate. While many of the isthmuses identified in this study were “expected”, Ripple Mapping activation threshold helped identify “unexpected isthmuses” bordered by idiopathic non-conductive tissue not obviously related to prior ablation delivery. These isthmuses formed the critical isthmus of an AT in some cases, hence would have been a likely cause for arrhythmia recurrence without identification using RM in this manner.

Substrate-guided AF ablation studies have shown benefit in targeting low voltage areas, presumed atrial fibrosis. The voltage threshold used to define these low voltage areas for ablation in these studies was arbitrary, and high recurrence rate at 1 year may reflect this arbitrary classification. Accepting that low voltage atrial fibrosis in the pre-ablated atrium may be different to post-ablation myocardium, our approach to identifying non-conducting tissue may offer a more individualized approach to identify this low voltage substrate for AF ablation as well, and requires further study. While we hypothesize that a strategy based on systematic ablation of all isthmuses might reduce future atrial arrhythmia burden, it also increases tissue destruction. However, in an era where LA voltage substrate ablation for persistent AF is under evaluation, a method that involves isthmus ablation is potentially less destructive than voltage alone, and requires further study.
Limitations

This was a retrospective study with a small sample size, though the concept is hypothesis generating for future prospective studies. The absolute value of the activation threshold determined by this method of identifying conducting tissue is dependent on the recording technique and noise threshold of the recording system, which will influence the resolution and quality of the electrograms that are used for the Ripple maps. Thus, these areas of scar are not necessarily dense fibrosis, but regions where some of the signals were low amplitude such that a propagating wave through the region could not be identified.

Conclusions

This study demonstrates that there is general concordance in the distribution of conducting isthmuses and non-conducting regions in the ablated left atrium, as depicted with Ripple Mapping and active tissue thresholding, despite altering the activation vector or atrial rate. This method requires further study, but potentially allows the isthmuses for tachycardias to be identified from maps of different atrial rhythms. Using Ripple mapping active tissue thresholding to define all isthmuses when mapping an AT might allow further pro-arrhythmic substrate to be targeted.

References


This article is protected by copyright. All rights reserved.


This article is protected by copyright. All rights reserved.


Tables

Table 1: Baseline demographics

<table>
<thead>
<tr>
<th>Pt no</th>
<th>Age</th>
<th>Gender</th>
<th>Previous Ablation history</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>M</td>
<td>1. PVI and CFAE. MI, Roof</td>
</tr>
<tr>
<td>2</td>
<td>77</td>
<td>M</td>
<td>1. PVI; 2. Redo PVI + Roof + CFAE</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>M</td>
<td>1. PVI + CFAE</td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>M</td>
<td>1. PVI; 2. Redo PVI + CTI</td>
</tr>
<tr>
<td>5</td>
<td>72</td>
<td>M</td>
<td>1. PVI + CTI. 2. Redo PVI, Roof + MI, 3. Focal AT from anterior LA</td>
</tr>
<tr>
<td>6</td>
<td>69</td>
<td>M</td>
<td>1. PVI, 2. Roof + MI</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>M</td>
<td>1. Surgical AF abl. (with MVR)</td>
</tr>
<tr>
<td>8</td>
<td>77</td>
<td>M</td>
<td>1. PVI + MI + CFAE</td>
</tr>
<tr>
<td>9</td>
<td>73</td>
<td>F</td>
<td>1. PVI x2 and CFAE</td>
</tr>
</tbody>
</table>
Table 2: Map data

<table>
<thead>
<tr>
<th>No</th>
<th>CL/ms</th>
<th>CS activation</th>
<th>Points</th>
<th>Activation Threshold/mV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>240</td>
<td>D-P</td>
<td>2103</td>
<td>0.15</td>
</tr>
<tr>
<td>2</td>
<td>240</td>
<td>P-D</td>
<td>1618</td>
<td>0.15</td>
</tr>
<tr>
<td>3</td>
<td>255</td>
<td>P-D</td>
<td>1696</td>
<td>0.40</td>
</tr>
<tr>
<td>4</td>
<td>300</td>
<td>P-D</td>
<td>4328</td>
<td>0.15</td>
</tr>
<tr>
<td>5</td>
<td>240</td>
<td>P-D</td>
<td>1362</td>
<td>0.2</td>
</tr>
<tr>
<td>6</td>
<td>300</td>
<td>P-D</td>
<td>4406</td>
<td>0.07</td>
</tr>
<tr>
<td>7</td>
<td>260</td>
<td>P-D</td>
<td>2426</td>
<td>0.06</td>
</tr>
<tr>
<td>8</td>
<td>360</td>
<td>D-P</td>
<td>832</td>
<td>0.2</td>
</tr>
<tr>
<td>9</td>
<td>230</td>
<td>D-P</td>
<td>2823</td>
<td>0.2</td>
</tr>
<tr>
<td>10</td>
<td>220</td>
<td>D-P</td>
<td>4301</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Abbreviations:
CL – cycle length; ms – milliseconds; CS – coronary sinus; D-P – distal to proximal;
P-D – proximal to distal; LAA – left atrial appendage

Table 3: Isthmus characteristics between Map 1 and Map 2

| P-D – proximal to distal; LAA – | MAP 1 | MAP 2 |

This article is protected by copyright. All rights reserved.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Non Conducting – Non Conducting</th>
<th>Non Conducting – Anatomical</th>
<th>Non Conducting – Non Conducting</th>
<th>Non Conducting – Anatomical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N. o.</td>
<td>Width</td>
<td>Location</td>
<td>N. o.</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>15</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>21</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>6</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>20</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>8</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>20</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>20</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>6</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>10</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>30</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>1</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>10</td>
<td></td>
<td>Functional</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>25</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>1</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>15</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>8</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Figure 1: Isthmus types**

The LA geometry is shown in AP. PVI has been performed (red circles represent spot ablation lesions). Following this ablation, three isthmuses can be expected (blue cross) as activation is constrained between regions of non-conducting ablated tissue along the roof, around the septum, and between the LLPV and mitral annulus. A further unexpected isthmus is seen (yellow cross) on the anterior wall, consequent to unconventional ablation along the anterior wall, or from of idiopathic low voltage tissue at this site.

**Figure 2: Mapping the critical isthmus (see supplementary video 1)**

Left: A high density LA map was collected in AT1, and is displayed in PA at the active tissue threshold (0.06mV). At this value, areas supporting active Ripple wavefronts were colored purple, and areas with no discernible activity in red. An island of “red” non-conducting tissue was unexpectedly identified on the posterior wall. The Ripple map revealed counterclockwise activation around the island, and an unexpected critical isthmus between this island and red non-conduction tissue adjacent to the left PVs (see location of ripple bars on static frame). This isthmus was ablated, interrupting the AT circuit. Right: The corresponding automated LAT map, with window of interest set either side of the p wave, did not allow identification of a critical isthmus.

**Figure 3: Fixed isthmus patterns**
High-density LA bipolar voltage maps were collected in AT1 and AT2 (CTI dependent flutter). RM demonstrated activation wavefronts above 0.4mV. Both maps are displayed in the same PA orientation, at this voltage setting. In AT1, a wavefront of Ripple bars travelled down the posterior wall from the roof, bordered on either side by low voltage non-conducting tissue secondary to prior PVI. In AT2, Ripple bars travelled up the posterior wall towards the roof, bordered on either side by the same “fixed” low voltage non-conducting tissue.

**Figure 4: Fixed isthmus patterns (see also supplementary video 2)**

High-density LA bipolar voltage maps were collected in AT1 and sinus rhythm. RM demonstrated activation wavefronts above 0.15mV. Both maps are displayed in modified AP. In AT1, a wavefront of Ripple bars was seen to travel across the anterior surface, from the septum to lateral wall. Activation was contained between an isthmus on the anterior wall formed of non-conductive tissue from previous right PVI and on the anterior wall adjacent to the mitral annulus. In sinus rhythm, activation remained constrained between the same non-conductive borders.

**Figure 5: Isthmus block secondary to change in activation direction and wavefront collision (see also supplementary video 3)**

RM demonstrated activation wavefronts above 0.15mV. Both maps are displayed in AP. In AT1, two distinct wavefronts were seen travelling in a cranio-caudal direction from the roof, and caudo-cranial direction from the floor. The two wavefronts collided on the anterior wall,
adjacent to the mitral annulus, and coalesced to form a single body of activation towards the RPVs. In AT2, both wavefronts are again present; however, the timing of the caudo-cranial wavefront is earlier resulting in wavefront collision in the mid anterior wall. Bipolar electrograms within the anterior wall measured >0.5mV. Electrograms from the site of collision in AT2 revealed very low voltage signal along the anterior wall, which were healthy in AT1, creating distinct voltage maps.

Figure 6: Atrial substrate ablation workflow

HRA – high right atrium; LAA – Left atrial appendage.

Figure 1

Figure 2
Figure 3

Figure 4
Figure 5

AT1: CL 240ms, CS activation: Dist-Prox
Points: 2103

Sinus rhythm: ~1000ms,
CS activation: Prox-Dist. Points: 1039
Figure 6
High density map in Rhythm 1 – paced map from LAA with short cycle length

RM Scar Threshold

Identify isthmuses

High density map in Rhythm 2 – paced map from HRA with longer cycle length

Analyse isthmuses at same scar threshold

Highlight fixed isthmuses

Ablate all fixed isthmuses