Validation of a novel high resolution mapping system for panoramic mapping of the left atrium: potential for mapping drivers in AF

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ABSTRACT

Background-

The success rate of catheter ablation for persistent atrial fibrillation (AF) remains variable. Identification of drivers in persistent AF remains challenging. This study sought to validate a novel wavefront mapping system (CARTOFINDER, Biosense Webster) and apply it to persistent AF.

Methods-

Patients undergoing catheter ablation for left sided atrial tachycardia (AT) and persistent AF were included in this study. A 64 pole-basket catheter was used to acquire unipolar signals over 30 seconds. Processing of these signals by CARTOFINDER generates high-resolution wavefront propagation maps. The system was used prospectively in all patients and validated initially with atrial pacing from four different sites and secondarily for ATs with the mechanism confirmed by conventional activation mapping and entrainment as well as the response to ablation. The system was then used to identify potential drivers in AF, with the effect of ablation at these sites assessed.

Results-

Thirty patients (15 AT, 15 AF) were included in the study with 209 maps created by the system. The system correctly identified atrial-pacing sites in all paced maps. It also accurately mapped 9 focal/micro re-entrant and 14 macro re-entrant ATs. One AT patient had spontaneous AF that was also mapped. Eighteen drivers of AF were identified in sixteen patients. On ablation of these drivers, 5 terminated to sinus rhythm, 6 organized into an AT, and 7 resulted in cycle length slowing. All procedures were performed without any complications.

Conclusion-

This study provides independent clinical validation of the novel CARTOFINDER mapping software in mapping atrial paced beats and ATs. The results of this study also suggest the potential for the system to be utilized in mapping AF to guide ablation.

INTRODUCTION

Recent data suggest current methods to ablate drivers of atrial fibrillation (AF) beyond the pulmonary veins are ineffective (1). Although conventional mapping taking consecutive points or localized collections of points works well for mapping organised tachycardias, this is of limited use for mapping rhythms with beat to beat variation like AF. Recent technologies for so called 'panoramic atrial mapping' have had some reported success (2-4). There is therefore great interest in additional techniques and technologies to facilitate mapping drivers in AF.

A novel-mapping software (CARTOFINDER (CF), Biosense Webster Inc, CA) that uses CARTO electroanatomical mapping system (Biosense Webster, Inc, CA) as its foundation has been developed to specifically map potential drivers in AF through identifying repetitive activation patterns that are either focal, re-entrant or rotor like activity. To achieve panoramic mapping the system uses a 64 pole-basket catheter to acquire 30 seconds of unipolar signals through CARTO. Processing of these signals using the CF software results in high-resolution wavefront propagation maps in an open format where points and electrograms can be scrutinized. This system has not been previously subjected to independent clinical validation or prospectively used to guide AF ablation.

This study aimed to validate the CF mapping software in terms of (1) localizing focal activation patterns through atrial pacing, (2) mapping atrial tachycardias (AT) where the mechanism is confirmed by conventional mapping, entrainment, and ablation. The system was then applied to AF to determine its potential for identifying drivers in AF. The response to ablation at sites identified as possible drivers was then assessed.

METHOD

Patients undergoing catheter ablation for AT (*de novo* or post previous catheter ablation for AF) and persistent AF (<24 months and no previous AF ablation) were prospectively included in this study. All procedures were performed with un-interrupted anticoagulation therapy and intravenous heparin administration to achieve an ACT of >300ms. The procedures were performed either under conscious sedation

or general anaesthesia. Patients provided informed consent for their involvement in this study, and the study was approved by the UK National Research Ethics Service (16/LO/1379) and was registered on clinicaltrials.gov as a sub-study of another ongoing trial (NCT02950844).

Electrophysiology Procedure

All cases were performed with CARTO electroanatomical mapping system. Right and left atrial (LA) geometries were created in all patients. A high-density bipolar voltage map was created in all patients to establish the relationship between drivers and sites of remodeling and scar. Points were taken using a pentaray catheter with 2-6-2mm spacing (Biosense Webster, Inc, CA) and all points were manually checked to ensure accuracy. An interpolation threshold of 5mm was used for surface colour projection and bipolar electrograms were filtered at 30 to 500Hz. Bipolar voltage of <0.05mV were defined as sites of low voltage zones (5). To collect the wavefront maps, a 60mm or 50mm 64-pole basket catheter of eight spines each with eight electrodes spaced 5mm apart was used to record bipolar and unipolar signals (Constellation, Boston Scientific, Natick, MA and FIRMap Abbott, CA, USA). The catheter was sized from the transverse and longitudinal diameter of the LA obtained from a transthoracic echocardiogram performed on the day of the procedure as advised by the manufacturer. The basket catheter was positioned in the LA through an 8 Fr Mullens (Medtronic, Inc, MN) or 8.5 Fr SL1 sheath (Daig Medical, MN) under fluoroscopy guidance. A decapolar catheter (Biosense Webster, Inc, CA) was positioned in the coronary sinus (CS). A Thermacool SmartTouch or Thermacool SmartTouch Surround Flow catheter (Biosense Webster, Inc, CA) was used for ablation and atrial pacing.

Through catheter manipulation the basket catheter was positioned to achieve the best possible LA and right atrial (RA) coverage and electrode contact. Once the catheter was in a stable position a recording was taken with the CF software. A minimum of two recording was taken per patient. If the coverage and contact was limited the basket catheter was repositioned before the second recording. The CF software provides an evaluation of the coverage achieved as a percentage of the chamber surface area. As the system calculates the surface area by including the LA appendage and vascular structures collected as part of the geometry (i.e. the pulmonary veins for

the LA and vena cava in the RA) the coverage will be an underestimation of the actual cover achieved however, the value given does allow coverage to be compared between positions and so quantitatively guide catheter repositioning.

If the patient was in sinus rhythm at the start of the case AT or AF was induced through incremental burst pacing from the CS. Pacing was started at a cycle length of 400ms and reduced by 10ms until the arrhythmia was induced or until 200ms was reached.

CARTOFINDER software

The CF software records 30 seconds of unipolar signals obtained from the 64-poles of the basket catheters, with the latter referenced to Wilson's Central Terminal (WCT). The ventricular far field signals are then filtered. This is done through initially measuring the ventricular far field morphology over 30 seconds and averaging to allow the morphology that represents pure ventricular signals to be identified. This is then subtracted from the unipolar data leaving behind only atrial signals. Following this, for each unipolar signal two bipolar signals are created by pairing the electrode with the nearest two basket electrodes. This creates a bipolar electrogram window that ranges from the earliest onset to the latest offset of the two bipolar electrograms. This is then applied to the unipolar signals and any atrial signals identified within this window of interest are annotated and areas outside are excluded (Supplementary figure 1).

The local activation time is then determined from the annotated unipolar signals through wavelet analysis (6). This is then used to create propagation maps whereby the site of earliest activation time is labeled red through to blue. The timing from the annotated signals is then projected onto the anatomical map. The window of interest then moves through the 30 seconds recording and the map then changes in a dynamic fashion to show wavefront propagation (Figure 1).

Following annotation of the atrial signals, the spline and pole numbers of the basket are displayed on the LA/RA geometry to allow the location of the recorded unipolar data to be visualized on the anatomical map. Grey areas on the map represent areas of no atrial signals (whether through poor contact or atrial scarring). The unipolar

electrograms with annotated atrial signals can also be scrutinized whilst reviewing the maps displayed.

Validation with Atrial pacing

To validate the software in terms of identifying focal activations, atrial pacing was performed in sinus rhythm at a cycle length of 600ms from four different sites: proximal and distal CS (endocardialy), LA roof and LA appendage. A recording with the CF software was taken during pacing at each site. Two operators performed procedures, but a 3rd and 4th blinded observer evaluated the maps offline (independent to each other) to ensure they effectively demonstrated the site of pacing.

Validation in AT

To validate the system in terms of identifying complex circulating wavefronts, CF maps were created during AT. CF maps were reviewed prospectively to predict the mechanism of the AT. This was then compared with the actual AT mechanisms as determined by a combination of detailed conventional LAT maps, entrainment of the tachycardia and response to ablation. If a further AT was induced following ablation this was also mapped with CF software and evaluated as above.

Mapping drivers in AF

All AF patients underwent wide area circumferential ablation of the pulmonary veins (PV) to achieve PV isolation. Recordings were taken with the CF software both before and after PV isolation to allow comparison of activation patterns. Recordings taken following PV isolation were used to guide ablation at sites identified as potential drivers by the system.

The maps post PV isolation were assessed for potential drivers by the two operators performing the case and later scrutinized separately by the two-blinded observers offline to assess the plausibility of the potential drivers identified. A potential driver was defined as repetitive patterns of activation that was either focal with radial activation over ≥2 consecutive wavefronts or rotational activity with ≥1.5 rotations of 360 degrees (as these definitions have been used by others previously, NCT0211376). Other wavefront properties were defined along similar lines to previous definitions: planar activation was defined as a single broad wavefront with linear activation,

whereas disorganized activity was defined as the absence of clear wavefont propagation (7).

To monitor the effect of ablation at these sites the cycle length of AF was monitored through a Lasso catheter (Biosense Webster, Inc, CA) positioned in the LA appendage. Clusters of ablation lesions were delivered at the sites of potential drivers and the duration of radiofrequency ablation at these sites was recorded. Cycle lengths were measured in all patients over 30 cycles before and after ablation at potential driver sites. Although small changes in cycle length (usually 5-6ms) have been used previously to determine a response to ablation (8, 9), it was thought that ablation of a clear driver ought to have a more significant effect. Confirmed drivers were therefore defined as sites where ablation resulted in slowing of the cycle length of ≥30ms, organization of the rhythm to an AT, or termination to sinus rhythm.

Statistical analysis

All statistical analyses were performed using SPSS (IBM SPSS Statistics, Version 20 IBM Corp, Armonk, NY, USA). Continuous variables are displayed as mean ± standard deviation (SD). Categorical variables are presented as a number and percentage. Kappa was used to examine interobserver agreement between the 3rd and 4th blinded observer. Chi-square was used for the comparison of nominal variables. The student t-test, or its non-parametric equivalent, Mann-Whitney when appropriate, was used for comparison of continuous variables.

RESULTS

Thirty patients were included in this study (mean age 64 ± 10 yrs., 63% Male). Baseline characteristics are shown in Table 1.

All procedures were performed successfully without any complications. The average procedural duration was 250.5 ± 56.5 min and mean fluoroscopy time of 4.6 ± 4.6 min.

Of the 30 patients included in the study, 15 had AT and 15 had AF (Figure 2). Of the 15 AT patients, one degenerated into AF. This patient therefore also had AF mapped

and drivers targeted. Of the 15 AF patients, five reverted to AT during ablation and had these mapped with CF, as did the AT patient who had degenerated into AF (Figure 2).

Thirteen of the 15 patients undergoing ablation for AT had undergone previous radiofrequency ablation for persistent AF which included PV isolation in all cases. Five of these patients had also undergone previous ablation for AT (33%) which included cavotricuspid isthmus (CTI) dependent flutter in all patients.

A total of 219 CF maps were constructed with the system, of which 111 CF maps were created in AF. This was an average of 5.4 ± 2.3 maps in AT and 6.9 ± 1.3 maps in AF. These maps were available to be analyzed within an average of 58 ± 6 seconds of being collected. Twenty-one of these maps were created in the RA (9.5%) out of which only four were during AF.

Pacing validation

Validation with pacing at the four sites was performed in all patients. In two patients consistent capture along the roof was not achieved despite pacing at maximum output and pulse width. In these two patients pacing was performed at the mid anterior wall. The CF maps were effective in demonstrating the site of focal atrial activation in all patients. The two-blinded observers were asked to determine the site of pacing. There was a 100% agreement between the 3rd and 4th blinded observers. Manual analysis also confirmed that the poles closest to the pacing site were the sites of earliest activation (Figure 3A-D).

AT mapping (figure 4A-D and 5A-C)

Eighteen ATs were mapped in the 14 AT patients. The AT patient who degenerated into AF also reverted to AT during ablation and had this AT mapped with CF. Five further patients in the AF group reverted to AT during ablation and had these mapped with CF. Thus, 24 ATs were mapped in 20 patients. One AT in one patient was not effectively mapped with the software, as the recording of electrograms with the basket catheter was very limited despite catheter repositioning. This generated limited maps making it difficult to make an accurate assessment of the AT mechanism. The LA coverage in this patient was only 21% of the chamber surface area despite catheter

repositioning and the LA contact was limited to 25% of poles recording data. The LA was severely dilated (volume 78ml) and had a mean bipolar voltage of 0.18 ± 0.08mV, so although electrode contact was likely limited, some poles might feasibly have been in contact but recording no signal.

In the remaining 19 patients in whom AT was effectively mapped, the LA coverage was 68.0 ± 10.2% and the proportion of poles recording LA signal were 74.2 ± 13.2%. The 26 CF maps created in these patients correlated to the conventional CARTO LAT maps in all cases with the mechanisms confirmed by entrainment (Figure 5A-C). Further to this, the mechanisms were confirmed by ablation that terminated the AT to sinus rhythm in all cases. Attempts were made to re-induce the AT with burst atrial pacing and extra-stimuli, but the clinical AT was non-inducible in all cases. Table 2 demonstrates the mechanism of the 23 ATs effectively mapped with CF software. The AT that could not be mapped with the CF software was confirmed to be mitral isthmus dependent. Notably four other mitral isthmus-dependent ATs were correctly identified by the software.

AF mapping

i) Pre PV isolation

A total of 30 CF maps were created pre PV isolation (2.1 ± 0.6 maps per patient). No continuous stable rotational activity or stable focal drivers were seen in any of the AF maps (before or after PV isolation). In nine out of the 15 patients (60.0%) at least one driver was identified that met the study definition. The nine patients had a total of 27 maps out of which 16 maps demonstrated the presence of a driver (59.3%). In patients where a potential driver was identified this was seen in 65 ± 17% of the pre PV isolation maps.

In each of the 16 maps thought to demonstrate a driver, these were seen to recur 2.4 ± 0.44 times per 30 second recording. These predominantly demonstrated rotational activity (n=8, 66.7%). The remaining 20 maps pre PV isolation demonstrated no discernable rotational or focal activity. These maps showed a combination of multiple broad linear wavefronts which circulated seemingly randomly, and sites of disorganized activity with no clear discernable wavefronts. There were no significant difference in mean bipolar voltage (0.35 ± 0.10mV vs. 0.35 ± 0.18mV; p=1.00), LA

volume (55.4 ± 10.0ml vs. 57.3 ± 10.3ml; p=0.66) and duration of AF (13.4 ± 7.1 months vs. 14.1 ± 5.6 months; p=0.84) in those patients in whom drivers were seen on pre PV isolation maps compared to those where no drivers were seen.

ii) Post PV isolation

In one of the 15 AF patients the CF maps were generated with inappropriate annotation of atrial signals due to excessive noise on many of the unipolar electrograms presumably due to damage to the basket. The maps generated in this patient post PV isolation were therefore limited and did not allow successful driver identification. A total of 32 CF maps were created post PV isolation in the remaining 14 patients (2.3 ± 0.8 maps per patient). All patients had at least 1 potential driver identified (range 1-2). A total of 17 drivers were successfully mapped (1.2 ± 0.4 per patient). These drivers were reproducible and occurred on 75.8 ± 14.2% of the CF maps. Of these 17 drivers, nine had been identified on the pre-PV isolation maps (Table 3). Of note, all drivers identified pre PV isolation were also seen post PV isolation. 47

The drivers were predominantly of rotational activity (n=12, Figure 6A-D) out of which nine occurred at sites of low voltage zones LVZs (75%). The remaining five drivers were of a focal nature and occurred in areas of normal bipolar voltage. The anatomical location of these drivers is demonstrated in table 3. Over the 34 recordings of 30 second each, the rotational activity as per study definition occurred 3.5 ± 1.4 times per recording with a mean of 2.5 ± 1.0 consecutive rotations. This was reproducible on a per patient basis: the rotational activity occurred with a mean of 2.7 ± 0.9 consecutive rotations. In those with focal activations, these occurred 3.8 ± 0.5 times per recording with a mean of 3.2 ± 1.1 consecutive focal activations (Figure 7). Only 6% of drivers were ever stable for >5 consecutive cycles (across all the recordings), and none were seen to complete more than six cycles (Figure 7).

Ablation at the 17 sites identified as drivers on the post PV isolation maps resulted in an effect in all cases (Table 3, Figure 8). AF terminated in 10 of the 14 patients mapped with targeting of these drivers (five terminated to sinus rhythm and five to AT). Ablation at the remaining driver sites resulted in cycle length prolongation of ≥30ms. Termination of AF occurred for eight of the nine drivers that had also been

identified pre PV isolation compared to two of eight drivers that were not identified pre PV isolation (p=0.015). An average of 3.4 ± 0.9 minutes of ablation was delivered at each driver site.

Examining all maps of AF, comparing to the original identification of drivers by the two operators performing cases, blinded observer one identified the same drivers in 94% of instances and observer two identified the same drivers in 100%. When examining the drivers identified live at the time of the procedure, here was a strong agreement between the two-blinded observers in terms of whether they identified the same drivers (Kappa 0.9; 95% CI 0.7-1.0).

iii) AT patients with spontaneous AF mapped

In one of the AT patients the AT spontaneously degenerated into AF and this was mapped with the CF system. In this patient the CF maps revealed repetitive rotational activity at the low anteroseptum. Ablation here resulted in organization to a typical right atrial flutter (Table 3).

DISCUSSION

This novel CARTOFINDER mapping software proved effective in the validation phase of this study, identifying focal sources of activation during atrial pacing at different sites. The mechanism of AT was also correctly identified in a majority of patients, hindered in a small proportion by the challenges achieving adequate LA coverage in patients with dilated scarred atria. The system effectively identified focal or localized reentrant activity in a majority (93.8%) of patients with AF. Targeting these sites had a significant effect in all patients where such drivers were identified, terminating AF in two thirds of patients and slowing cycle length markedly (≥30 ms) in the remainder.

Mapping with the basket catheter and the CF software

As the CF software is incorporated into the CARTO system, this facilitates use by physicians already familiar with CARTO. The operators were experienced electrophysiologists but were novices to the CF system, and despite the latter were still able to operate CF effectively with a limited learning curve. The CF software

further allows unipolar electrogram and location data to be obtained during the study from all 64-poles and an additional 14-poles from the mapping and decapolar catheter. This thereby allows an additional 18 electrode poles over which signals can be obtained during the study. As a result ablation could potentially be performed simultaneously to having the basket catheter in situ and thereby allowing repeat mapping with the basket catheter. This was not performed in the current study as this early experience was intended to validate the system and explore it's utility in AF, but could be useful to re-map during ablation as AF organises and changes.

The CF software uses a 64-pole basket catheter with the aim of achieving panoramic mapping, at least for one atrium at a time. However, the quality of the CF maps is highly dependent on the electrogram data that can be recorded with the basket catheter. Mapping with the basket is very dependent on the degree of LA contact, the ability to record signal when in contact (i.e. the absence of widespread scar), and the LA coverage achieved with the basket catheter. Skeptics of mapping with basket catheters point to the low spatial resolution of electrodes and the poor contact and coverage of the LA achieved (10, 11). One study using basket catheters found that the coverage was limited by electrodes being positioned in the blood pool and there being clustering of basket splines (10). These authors found that only 52% of electrodes recorded signal and only 54% of the LA surface was within 10mm of an electrode. Temporal-spatial stability of the basket catheter is also a recognized limitation of these catheters (10). In one of the 15 AT patients the LA contact and coverage achieved was very limited which affected the maps created. This patient had a scarred and severely dilated LA that would account for the sub-optimal recording obtained with the basket and thereby suboptimal CF maps. LA coverage in the remaining patients was a little higher than these other published studies at 64%. The ability to rapidly create multiple maps enabled catheter repositioning to achieve optimal coverage and repeat mapping, without a great impact on procedure duration. Utilizing the additional tool that specifies LA coverage enabled a quantitative evaluation when repositioning the basket catheter. CF maps were effectively created in the RA in nine patients indicating that the software can be used for both left and right-sided arrhythmias.

A total of 16 patients had AF mapped (one from the AT cohort), although one patient had incorrect atrial signal annotation due to noise on the unipolar signals. Of the remaining 15 patients all had at least one driver successfully identified. The majority of these drivers were repetitive during a 30 second recording and detected on repeat maps performed. This provides internal validation of the drivers identified. There was a response to ablation in all patients, with ablation of 11 out of 18 drivers causing termination of AF and cycle length prolongation occurring for the remainder. This suggests clinical validity for the driver activity identified. It is possible that additional drivers might have been identified with re-mapping and that targeting these could have terminated AF in the remaining patients. It is noteworthy that several studies have also identified drivers in the RA which was only mapped in four patients with AF. It is of course possible though that more drivers were not identified in this study due to limitations in the CF software to detect them.

During electrogram analysis the system works to identify only high quality atrial signals. Finding the right balance in excluding noise but retaining true atrial signal is essential, as together with the inevitable loss of some data through poor LA contact and limitations to coverage with the basket, this will clearly have an impact on the CF maps created. Inappropriate annotation of atrial signals where there was noise, as was seen in one patient, led to CF maps that were un-interpretable. Nevertheless, in a majority of cases the system struck a balance that resulted in useful maps.

Daoud EG et al. (12), reported on the mapping of AF with the CF system. In contrast to their findings, we were able to identify drivers on CF maps created pre PV isolation in less than 60% of maps and only 64% of patients contrary to their 85.7% of patients. In the remaining patients a combination of broad planar wavefronts and disorganized, chaotic activity were seen. Several studies have shown an organising effect of PV isolation (8, 13, 14). In our study the drivers were demonstrated in a much greater proportion of maps post PV isolation. It seems unlikely that drivers would be more prevalent following PV isolation. This observation might be due to difficulty mapping localized sources at the conical PV ostia with a spherical basket in the body of the LA. Alternatively, it may be that the limitations of mapping with the current generation of basket catheters do not allow identification of drivers in rapid disorganized AF, or that the CF software may not be capable of mapping drivers

under these conditions. These data suggest CF might be most useful in facilitating mapping and ablation of drivers following PV isolation. Notably, targeting the drivers identified on both pre and post PV isolation CF maps more frequently resulted in termination of AF, suggesting that greater stability might suggest greater mechanistic importance.

The mechanisms sustaining AF remain a controversial. Another group using similar 64-pole basket catheters has reported the presence of continuous stable rotors (2, 3). Others have found little or no evidence of rotors (7, 15). Non-invasive mapping with the ECG-I system has suggested that AF is maintained by a combination of focal discharges and rotors that, whilst transient in nature, seem to recur at the same sites (4). The current study is most compatible with the findings of this latter study. A majority of drivers identified were reentrant with a small proportion being focal discharges. Those with reentrant mechanisms were predominantly located in low voltage zones suggestive of remodeling and, although transient, recurred at the same sites repeatedly. Furthermore we were able to confirm the functional importance of both mechanisms in terms of maintaining AF by demonstrating a significant response to ablation in all cases. Whilst the reentry mechanisms observed were potentially compatible with rotors, with the limited mapping resolution and the transient nature of the phenomena it was difficult to be sure of this from the maps obtained. It is also recognized that the focal discharges seen on endocardial mapping may not have been truly focal and could well represent endocardial breakthrough due to dissociation of the endocardial and epicardial layers (16).

Limitations

This study targeted drivers after CF maps at a fixed time point and did not remap in a dynamic way. Furthermore the RA was only mapped in four patients, which other studies suggest might have missed approximately a quarter of drivers. This early study on this technology focused on feasibility and electrophysiologic end points. A larger study with clinical follow up is needed to determine whether targeting of drivers impacts on the long-term success rates for the ablation of persistent AF.

CONCLUSION

This novel mapping system was effectively validated by mapping focal activation patterns from atrial paced beats and mapping more complex wavefront activations in AT. Transient focal and reentrant sources were identified in AF which recurred frequently at the same sites. These drivers were observed repeatedly providing internal validation of the maps and their mechanistic importance was confirmed by the response to ablation. These early results suggest clear potential for this system to facilitate the mapping and ablation of drivers in AF.

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Table 1- Demonstrates the baseline characteristics of the cohort

Baseline characteristics	**Cohort n=30**
Age yrs. mean ± SD	64 ± 10
Male n (%)	19 (63)
Diabetes mellitus n (%)	0
Hypertension n (%)	13 (43)
TIA/CVA n (%)	2 (7)
Ischaemic heart disease n (%)	2 (7)
Cardiac surgery n (%)	3 (10)
Left ventricular EF ≥ 55% n (%)	26 (87)
LA size cm^2	
20-30	21 (70)
30-40	9 (30)
>40	0
Persistent AF n (%)	15 (50)
Previous AF ablation n (%)	
WACAs	13 (87)
CFAEs	6 (40)
Roof line	4 (27)
Mitral isthmus line	5 (33)
Previous AT ablation (including AT and AF patients) n (%)	
Cavo-tricuspid isthmus dependent flutter	5 (17)
Focal or micro re-entrant	2 (7)
Current medical strategy	
Beta-blockers including Sotalol	22 (73)
Amiodarone	4 (13)
Flecainide	5 (17)

Table 2- Demonstrates the mechanism of the ATs mapped by CARTOFINDER with confirmation by conventional means, entrainment and response to ablation.

ATs mapped and ablated	
AT n	17
Mitral isthmus-dependent flutter	3
Roof-dependent flutter	4
Focal/micro re-entrant	9
LA mid anterior	2
LA mid roof	3
LA low antero-septal	1
Right focal/micro re-entrant around scar	2
LA low posterior	1
CTI dependent flutter	1
AF organised to AT n	6
CTI dependent flutter	3
Mitral isthmus dependent flutter	1
Roof dependent flutter	2

Table 3- Demonstrates the characteristics of the AF drivers mapped with the CF software and the response to and duration of ablation at the driver site

Driver type	Driver location in LA	Consecutive repeats in 30sec mean ± SD	Proportion of maps with driver %	Visible on pre PV maps	Ablation response	Ablation duration min
Focal	Posterolateral	2.3 ± 0.6	100	Yes	SCL	2.8
Focal	Lateral	4.0 ± 0.8	67	Yes	Sinus	1.8
Rotational	Anterior LAA	2.3 ± 0.4	100	Yes	AT	4.4
Focal	Posterolateral	4.0 ± 2.7	60	Yes	AT	4.2
Rotational	Posterolateral	1.8 ± 0.4	100	No	Sinus	4.0
Rotational	Mid anterior	2.2 ± 0.7	75	No	SCL	3.3
Rotational	Mid posterior	4.0 ± 0	100	No	SCL	4.1
Focal	Inferior RLPV	3.0 ± 0.8	67	Yes	Sinus	3.8
Rotational	Mid roof	2.9 ± 1.0	100	Yes	Sinus	4.0
Rotational	Posterior LAA	2.3 ± 1.1	75	No	SCL	4.6
Rotational	Anteroseptal	2.5 ± 0.7	50	Yes	AT	3.4
Focal	Mid anterior	2.75 ± 1.0	100	No	SCL	2.5
Rotational	Roof	2.3 ± 0.9	67	Yes	Sinus	2.2
Rotational	Anterolateral	2.4 ± 0.8	67	No	SLC	4.7
Rotational	Anterior LAA	3.0 ± 1.3	100	Yes	AT	2.2
Rotational	Posteroseptal	4.5 ± 2.1	50	No	SCL	3.1
Rotational	Mid Roof	2.8 ± 0.9	67	No	AT	2.7
Rotational	Anteroseptal	2.5 ± 0.6	67	N/A*	AT	2.4

SCL denotes slowing cycle length
* denotes the AT patient that degenerated to AF

FIGURE LEGEND

Figure 1A-C- Demonstrates Ai-ii) Coloured window of interest moving through selected atrial unipolar signals which is a representative of early through to late activation of each electrode pole in relation to each other (star highlighting the earliest part of the wavefront) B) the basket catheter on a transparent LA map C) the basket catheter on a transparent RA map.

Figure 2- A flowchart indicating the number of patients that had AT and AF ablation and the number of these that had mapping done with the CF system.

Figure 3A-D- Shows a still CF map, in anterior view, created in the LA during LA appendage pacing with the basket and mapping catheter positions visualized. The earliest activation is seen at the basket poles closest to the pacing site followed by the propagation of the wavefront through the LA.

MVA- Mitral valve annulus

RUPV- Right upper pulmonary vein

LUPV- Left upper pulmonary vein

Figure 4A-D- Shows still CF maps demonstrating a focal AT mapped to the LA septum (A-C) in an area of low voltage zone as demonstrated on the bipolar voltage map (D). The white circle on the voltage map highlights the site of ablation leading to AT termination. The corresponding electrograms demonstrates the annotation of the atrial signals (yellow dots) on selected 64-pole electrodes.

MVA- Mitral valve annulus

RUPV- Right upper pulmonary vein

LUPV- Left upper pulmonary vein

Figure 5A-C- Shows a still CF map of a left sided roof dependent flutter and the corresponding LAT maps A-B) Anterior and posterior views of still CF maps demonstrating wavefront propagation in a roof dependent flutter C) Anterior and posterior LAT views supporting a roof dependent flutter. White arrows on the CF map demonstrate the direction of the wavefront.

MVA- Mitral valve annulus

RUPV- Right upper pulmonary vein

LUPV- Left upper pulmonary vein

Figure 6A-D- Shows a still CF map demonstrating an AF driver with rotational activity along the anterior wall and the corresponding unipolar electrograms obtained from the 64-pole basket catheter

MVA- Mitral valve annulus

RUPV- Right upper pulmonary vein

LUPV- Left upper pulmonary vein

Figure 7- Demonstrates the number of times an AF driver with either rotational activity (dark grey) or focal with radial activation (light grey) was seen consecutively in a 30 second recording.

Figure 8A-D- Demonstrates a still CF map with an AF driver with focal activity at the lateral wall of the LA (A-B) and the ablation lesion delivered (C) to achieve sinus rhythm as shown on the electrograms (D)

LAA- Left atrial appendage

RUPV- Right upper pulmonary vein

LUPV- Left upper pulmonary vein

SUPPLEMENTARY FIGURES

Figure 1A-C-

A) Demonstrates the pure atrial unipolar signals following far field ventricular signal filtering. The faint grey line demonstrates the initial signal prior to filtering.

B) Shows the bipolar electrogram window made up of two bipolar electrograms created by pairing the electrode with the nearest two basket electrodes. Red and blue electrograms represents each bipole and the bipolar electrogram window ranges from the earliest onset to the latest offset of the two bipolar electrograms.

C) Atrial signals that are within the bipolar eletrogram window are then annotated and through wavelet analysis sites of earliest activation in relation to the other electrodes are identified.