The impact of image integration on catheter ablation of atrial fibrillation using electroanatomic mapping: a prospective randomized study

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Aims
A detailed appreciation of the left atrial/pulmonary venous (LA/PV) anatomy may be important in improving the safety and success of catheter ablation for AF. The aim of this randomized study was to determine the impact of computed tomographic (CT) integration into an electroanatomic mapping (EAM) system on clinical outcome in patients undergoing catheter ablation for atrial fibrillation (AF).

Methods and results
Eighty patients with AF were randomized to undergo first-time wide encirclement of ipsilateral PV pairs using EAM alone (40 patients) or with CT (40 patients, Cartomerge®). Wide encirclement of the pulmonary veins was performed using irrigated radiofrequency ablation with the electrophysiological endpoint of electrical isolation (EI). The primary endpoint was single-procedure success at 6 month follow up. Acute and long-term procedural outcomes were also determined. There was no significant difference in single procedure success between EAM (56%) and cavotricuspid isthmus image (CTI) (50%) groups (P = 0.9). Acute procedural outcomes (EI, PV reconnection, sinus rhythm restored by ablation in persistent AF), fluoroscopy, and procedure durations (EI of right PVs, EI of left PVs, total) did not differ significantly between EAM and CTI groups.

Conclusion
Image integration to guide catheter ablation for AF did not significantly improve the clinical outcome. Achieving PV EI is the critical determinant of procedural success rather than the mapping tools used to achieve it.

Keywords
Atrial fibrillation • 3D mapping • Ablation

Introduction
Catheter ablation has become the treatment of choice for patients with symptomatic drug refractory AF. Electrical isolation (EI) of the pulmonary veins (PVs) forms the cornerstone of the current ablation strategies.1–3 Over the last decade, ablation has evolved from targeting foci deep within the PVs4 to a segmental ostial approach,5 and then further proximal to ablation of the cuff of surrounding atrium or PV antrum.6,7 Isolation of larger areas around the PVs is associated with a higher rate of success than segmental ostial ablation.7 Wide encirclement of the PVs in ipsilateral pairs involves long, continuous ablation lines with the predominant cause of arrhythmia recurrence due to recovery of PV conduction or gaps in the ablation line.8,9 The advent of 3D mapping systems has greatly facilitated the ability to successfully and safely complete complex ablation strategies. In addition with the exponential increase in AF ablation10 and the broadening indications, the demand for less experienced operators to competently complete the procedure increases. This requirement to encircle completely the PVs is made more complex by the considerable anatomic variation in the PV anatomy.11 A detailed representation of the anatomy can be provided by integration of a computed tomographic (CT) or magnetic resonance imaging (MRI) scan of the LA to assist in guiding catheter manipulation.12,13 Although there are a number of pitfalls to overcome in extracting and registering the image,14 image integration has the
potential to improve the clinical outcomes of PV isolation and AF ablation. To date, there is a lack of randomized data to support this. In a non-randomized retrospective analysis of 94 patients who had undergone catheter ablation for AF into an electroanatomic mapping (EAM) system, we reported a reduction in fluoroscopy time, arrhythmia recurrence, and increased restoration of sinus rhythm in patients where ablation was guided by CT integration compared with a 3D mapping system alone. However, the observational non-randomized nature of this study meant that we were unable to account for a learning curve effect. The aim of the present study was to perform a randomized controlled trial to determine the impact of image integration into a 3D mapping system on clinical outcome in patients undergoing catheter ablation for AF.

Methods

Study population and randomization procedure
The study population consisted of 80 patients who underwent first-time catheter ablation of AF at a single institution between April and October 2006. All patients had symptomatic documented AF and had failed at least two antiarrhythmic drugs. The inclusion criteria were patients undergoing catheter ablation for atrial fibrillation (AF) with the exclusion criteria being: an unwillingness to be involved in the research study (n = 0) or previous AF ablation (n = 7). Prior to the procedure, patients were randomized to catheter ablation guided by EAM alone or by EAM with cavotricuspid isthmus image (CTI) (Cartomerge™, Biosense Webster, Inc., Diamond Bar, CA, USA). The randomization schedule involved closed envelopes containing the allocation to either 3D mapping (n = 40) or CT integration (n = 40). The envelope was opened on the morning of the procedure by the operator after receiving consent from the patient to inclusion in the randomized trial. Randomization was single blinded with the patient not informed of the allocation. The nature of the study did not allow blinding of the operator although analysis of the 7 day Holter was performed by an arrhythmia nurse in a blinded fashion. All patients underwent CT imaging 1–3 days prior to the procedure. The study was approved by the East London and the City research and ethics committee, London, UK. All patients gave written informed consent. The patient selection and recruitment are presented in Figure 1.

Electrophysiological study and radiofrequency ablation
Transoesophageal echocardiography was performed in all patients within 24 h of the procedure to exclude left atrial (LA) thrombus. Antiarrhythmic drugs were continued until the day of the procedure. Patients already on oral anticoagulants had this exchanged for low-molecular-weight heparin 5 days before the procedure, for the remainder anticoagulation was started only after the procedure.

Electrophysiological study was performed in the post-absorptive state under conscious sedation. A 6F quadripolar or decapolar (for persistent AF patients) catheter was positioned in the coronary sinus. A double-transseptal puncture (Cook Mullins sheath with Endry’s transeptal needle) was performed, and intravenous heparin was administered to maintain an activated clotting time of between 300 and 400 s. A circumferential steerable 14-pole catheter was positioned as close as possible to the PV ostium (Orbiter PV, Bard EP, Lowell, MA, USA).

Computed tomography
A multislice helical CT (GE Lightspeed Ultra 64-slice scanner) was typically performed 24 h prior to the procedure. The imaging technique

Figure 1 Flow diagram of the progress through the phases of the randomized trial.
has been described previously. In brief, following a test bolus, 80 mL of non-ionic contrast (omnipaque 300, Amersham Health, Oslo, Norway) was injected at 5 mL/s through an antecubital vein. Scanning was performed in a single inspiratory breath hold in the crano-caudal direction at the level of the atrium with retrospective ECG gating. Contiguous axial CT slices were reconstructed from the CT data using a soft-tissue algorithm, and the resulting DICOM data were recorded onto CD Rom.

Electroanatomic mapping
A standard protocol was instituted for the creation of the geometry for the electroanatomic map. The ostia of all PVs were identified and four points tagged at the anterior, posterior, superior, and inferior margins using PV angiography and the drop off point during catheter withdrawal from the PV (Figure 2). An LA shell was not routinely created. The total duration required to identify and annotate the ostia of all PVs was calculated as the ‘registration time’. The CT image was available for viewing by the operator but the image was not integrated into the mapping system.

Three-dimensional mapping with computed tomography integration
The segmentation and registration of the CT image into the EAM system using custom-designed software (Cartomerge™) has been previously described in detail. In brief, using proprietary software tools, segmentation of the cardiac image was performed to separate the LA and PVs from surrounding structures. Registration of the CT image was performed using landmark and surface mapping (Figure 3). Landmark registration involved the identification of at least three points at or before the first-order branches of each of the three PVs. Locations were confirmed using selective PV angiography. Next, surface registration was performed with at least 30 widely spaced points predominantly from the lateral, septal, roof, inferior, and posterior LA walls. Catheter contact was ensured by fluoroscopic visualization of catheter mobility in relation to cardiac motion and a discrete atrial electrogram. Next, the overall closeness of fit was assessed using customized software that provides a point-by-point review of registration accuracy. If necessary, the points were deleted and additional landmark and surface registration points were taken to achieve an overall accuracy of <3 mm. The total duration required to accurately register the CT image was calculated as the registration time.

Catheter ablation
Ablation was performed to encircle the left- and right-sided PVs in pairs 1–2 cm from their ostia as defined by PV angiography and the 3D map. At the anterior aspect of the left PVs, ablation was performed along the ridge between the left atrial appendage (LAA) and the PV ostia. Energy was delivered through a 3.5 mm irrigated tip catheter (Navistar Thermocool, Biosense Webster) with power limited to 30 W and temperature to 50°C for LA ablation. Flow was limited to 2 mL/min unless blood cooling was insufficient to allow >20 W delivery in which case flow was titrated up until sufficient energy was delivered to achieve ablation. Energy was delivered until the amplitude of the local bipolar atrial electrogram had been reduced by >80% or was <0.1 mV. The PVs were continuously assessed for electrical disconnection using the circular mapping catheter. If veno-atrial electrical connections persisted, further ablation was performed at the ablation line guided by the activation sequence on 14-pole circular catheter until EI was achieved. If this was not successful, then further applications (power, 20–25 W and temperature 50°C) were made at the veno-atrial junction typically in the region of the intervenous ridge. This process was then repeated for the contralateral PVs. The catheter ablation point successful in achieving EI was annotated on the Carto system with anatomic tags. The sites of EI were then collated, viewing the PV ostia internally as a modified clockface. The time taken (in min) for ipsilateral PV isolation was

Figure 2. Upper panel demonstrates registration in the three-dimensional mapping group. The ostia of all pulmonary veins were identified and four points tagged at the anterior, posterior, superior, and inferior margins using pulmonary venous angiography and the drop off point during catheter withdrawal from the pulmonary vein. Lower panel demonstrates ablation (brown dots) encircling the left-sided pulmonary veins. LSPV, left superior pulmonary vein; LIPV, left inferior PV.
determined from the start of the first ablation point to the completion of PV EI of the ipsilateral PV pair.

If AF continued following PV EI, a combination of the following was performed: (i) linear ablation—a roof line joining the superior aspects of each wide encirclement ablation ring and a coronary sinus (CS) line joining the inferior aspects of the right and left wide encirclement ablation lines in close proximity to the CS as fluoroscopically guided by the CS EP catheter. Additional ablation was performed within the CS (20 W, 50°C) with the aim of electrical disconnection of the CS and (ii) complex fractionated electrograms—left and right atria were mapped systematically for fractionated potentials that were then targeted for ablation.22 If, at any stage, AF organized to atrial tachycardia (AT), activation mapping was performed. If AF continued following the linear ablation and targeting of fractionated electrograms, internal cardioversion was performed. The procedure was completed with a cavotricuspid isthmus ablation (power 50 W; temperature 45°C; flow 30 mL/min) in all patients requiring cardioversion and also in patients where typical atrial flutter had been previously documented. Unidirectional conduction block was confirmed by differential pacing techniques and by the demonstration of widely spaced double potentials along the CTI. Re-testing of PV disconnection and an angiogram was performed for all four PVs at the end of the procedure.

Total procedure duration (in min) was determined from the needle to skin time for femoral venous access until the removal of all catheters. Fluroscopy time was recorded for both PV isolation and for the complete procedure.

**Post-ablation management**

Patients were discharged the day following the procedure without antiarrhythmic medication and reviewed at 3, 6, and 12 months. They were given loading doses of warfarin and self-administered low-molecular-weight heparin until their INR is >2. A dedicated arrhythmia nurse was allotted for follow-up and immediate ECG or monitoring for any patients with symptoms suggestive of arrhythmia recurrence. At 6 months, a 7 day Holter monitor was performed to assess arrhythmia burden. Arrhythmia recurrence was defined as any atrial tachycardia or fibrillation episode lasting >30 s that persisted after a 4 week blanking period from the day of the procedure. A repeat procedure was offered to patients with recurrent atrial arrhythmia who required ongoing antiarrhythmic medication beyond 6 weeks. For repeat procedures, a double-transseptal puncture and assessment for PV EI was performed. If PV electrical reconnection was demonstrated, the number of reconnected PVs was recorded and mapping was performed along the prior ablation lines and gaps targeted.

The primary endpoint of the study was single procedure success of antiarrhythmic drugs at 7 day Holter monitor at 6 months. The secondary endpoints were fluoroscopy time, procedure duration, and long-term restoration of sinus rhythm.

**Statistical analysis**

All variables are expressed as mean ± SD. Comparisons between groups were performed with either an unpaired Student’s t-test or where a normal distribution could not be assumed the Mann–Whitney U-test. A sample size of 38 was calculated based on an earlier retrospective study15 for a difference of 30% at a desired power of 0.8 for a significant difference of <0.05. Tests were one-sided with a Bonferroni correction included for the three secondary endpoints to account for a potential type 1 error due to multiple comparisons. A log-rank survival analysis was included to account for censored data. Categorical variables expressed as numbers and percentages were compared with a Fisher’s exact test as for the primary endpoint. A P-value of <0.05 was considered statistically significant.

**Results**

**Patient characteristics**

The study population consisted of 80 consecutive patients who underwent first-time catheter ablation for AF between April and
October 2006. Patient characteristics for the EAM and CT groups are presented in Table 1.

**Procedure characteristics**

The acute procedural outcomes are presented in Table 2. A trend to a reduction in fluoroscopy time for the completion of PV EI was demonstrated in the CT group (43 ± 22 min) compared with the EAM group (52 ± 21 min, \( P = 0.1 \)). Otherwise, there was no significant difference in the procedure duration (registration, EI of right and left PVs, and total) between the CT and 3D mapping groups. The mean surface registration error in the CT group was 2.3 ± 0.5 mm with a standard deviation of 1.7 ± 0.4 mm.

**Electrical isolation: right PVs**

There was no significant difference in achieving EI of the right PVs [39/40 (97%) patients in CT group vs. 37/40 (92%) in EAM group] \( P = 0.6 \) (Figure 4). There was no significant difference in the anatomic distribution of the successful sites for EI (Figure 5). Simultaneous isolation of the ipsilateral right PVs was achieved in 13/40 (33%) of the CT group and 15/40 (38%) of the EAM group \( P > 0.99 \).

**Electrical isolation: left PVs**

No significant difference was demonstrated in achieving EI of the left PVs between the two groups \( P > 0.99 \) (Figure 4). There was no significant difference in the anatomic distribution of the successful sites for EI (Figure 5). Simultaneous isolation of the ipsilateral left PVs was achieved in 12 (31%) of the CT group and 14 (35%) of the EAM group.

There was no significant difference in acute reconnection of PVs \( P = 0.5 \) during the index procedure.

**Complications**

There were two pericardial effusions requiring drainage in the CT group. Pulmonary vein stenosis occurred in the right middle branch in one patient in the EAM group.

**Clinical outcome**

The long-term outcomes are presented in Table 3. There was no significant difference in the primary endpoint of single procedure success off antiarrhythmic drugs at 7 day Holter monitor at 6 months between the two groups [22/39 (56%) in EAM group vs. 19/38 (50%) in the CTI group, \( P > 0.99 \)]. One patient was lost to follow up in each group. There was one unrelated death in the CTI group prior to 6 months follow-up.

Recurrence was defined as any atrial tachyarrhythmia of >30 s at anytime during the follow up period. Recurrent atrial tachyarrhythmias were demonstrated in 20/39 (51%) patients in the EAM group vs. 22/38 (58%) patients in the CTI group \( P > 0.99 \). Repeat procedures were performed in 14 patients (AF in 12 and AT in two patients) in the EAM group and 16 patients (AF in 10 and AT in six patients) in the CTI group. Pulmonary vein reconnection was demonstrated in 100% of patients with all patients undergoing repeat EI. A second procedure was not performed in six patients in the EAM group (controlled on medication in five) and six patients in the CTI group (controlled on medication in six patients).

At a mean follow-up of 59 ± 12 weeks, sinus rhythm was maintained without antiarrhythmic medication in 30 patients (77%) in the EAM group compared with 27 patients (71%) in the CTI group. Survival analysis using a log-rank test did not demonstrate a significant difference between the two groups \( P = -0.62 \).

**Discussion**

This randomized controlled study reports the short- and long-term outcomes of patients undergoing first-time catheter ablation for AF guided by an EAM system alone compared with the addition of CTI. The main findings were no significant differences in:

1. single procedure success at 7 day Holter monitor at 6 months follow-up.

| Table 1 | Patient characteristics |
|---|---|---|
| EAM (\( n = 40 \)) | CT integration (\( n = 39 \)) | \( P \)-value |
| Age (years) | 56 ± 10 | 56 ± 13 | 0.8 |
| Paroxysmal AF | 58% | 62% | 0.9 |
| AF duration (months) | 69 ± 45 | 83 ± 74 | 0.9 |
| Number of failed antiarrhythmic medications | 2.7 ± 1.0 | 2.3 ± 1.0 | 0.2 |
| Structural heart disease | 30% | 28% | 0.9 |

| Table 2 | Acute procedural outcomes |
|---|---|---|
| EAM (\( n = 40 \)) | CT integration (\( n = 39 \)) | \( P \)-value |
| PV electrical isolation | | | |
| RPVs | 92% | 97% | 0.6 |
| LPVs | 100% | 100% | \( > 0.99 \) |
| Procedure duration (min) | 225 ± 56 | 232 ± 65 | 0.6 |
| Skin to double LA access (min) | 26 ± 12 | 26 ± 11 | \( > 0.99 \) |
| Registration (min) | 28 ± 14 | 24 ± 13 | 0.2 |
| RPV electrical isolation (min) | 57 ± 24 | 66 ± 35 | 0.2 |
| LPV electrical isolation (min) | 46 ± 25 | 49 ± 18 | 0.5 |
| Fluoroscopy time (Total (min)) | 57 ± 23 | 53 ± 18 | 0.4 |
| For PVI | 52 ± 21 | 43 ± 22 | 0.1 |
| PV reconnection (% patients) | 14 (35%) | 10 (26%) | 0.5 |
Figure 4 Internal images of the right (left panel) and left (right panel) pulmonary venous pairs demonstrating the sites at which electrical isolation was achieved in the electroanatomic mapping (red dots) and image integration (yellow dots) groups. LSPV, left superior pulmonary vein; LIPV, left inferior PV; RSPV, right superior pulmonary vein; RIPV, right inferior PV.

Figure 5 Sites of electrical isolation in the study population according to pulmonary venous quadrant. There was no significant difference in the sites of electrical isolation in patients where catheter ablation was guided by electroanatomic mapping alone vs. image integration. SUP, superior; INF, inferior; ANT, anterior; POST, posterior.
Impact of image integration on catheter ablation

### Table 3 Long-term outcomes

<table>
<thead>
<tr>
<th></th>
<th>EAM (n = 39)</th>
<th>CT integration (n = 38)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single procedure success at 6 month Holter (total)</td>
<td>22/39 (56%)</td>
<td>19/38 (50%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Recurrent AT/AF during 12 month follow-up</td>
<td>20/39 (51%)</td>
<td>22/38 (58%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Second procedure</td>
<td>14/39 (36%)</td>
<td>16/38 (42%)</td>
<td>0.64</td>
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<tr>
<td>Rhythm at second procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial tachycardia</td>
<td>2</td>
<td>6</td>
<td>0.23</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>12</td>
<td>10</td>
<td>0.23</td>
</tr>
<tr>
<td>PV reconnection</td>
<td>100%</td>
<td>100%</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>1–2 PVs</td>
<td>6 (43%)</td>
<td>11 (69%)</td>
<td>0.27</td>
</tr>
<tr>
<td>3–4 PVs</td>
<td>8 (57%)</td>
<td>5 (31%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Long-term success</td>
<td>30/39 (77%)</td>
<td>27/38 (71%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Follow-up (weeks)</td>
<td>59 ± 11</td>
<td>59 ± 13</td>
<td>&gt;0.99</td>
</tr>
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Comparisons performed using Fisher’s exact test.

2. arrhythmia recurrence at a mean follow-up of 59 ± 12 weeks.
3. the successful restoration of sinus rhythm at a mean follow-up of 59 ± 12 weeks.

### Potential advantages of image integration

Image integration has widely been validated in animal and human studies and has established widespread use to assist in catheter navigation for AF ablation. The pulmonary venous (PV) anatomy demonstrates tremendous inter- and intra-individual variation. Common PV anatomic variations include a left common PV or an additional right-sided PV. These findings may have direct implications on the ablation strategy to achieve EI. Improved visualization of the PV anatomy and surrounding atrium has provided the opportunity to tailor the ablation strategy to an individual’s anatomy. This is particularly relevant in the region of the atrial fold between the LA appendage where visualization of a sufficiently broad ridge may permit ablation en face rather than on the venous aspect preferred for catheter stability. The importance of anatomic structures beyond the PVs in patients with longstanding persistent AF is becomingly increasingly appreciated. Haissaguerre et al. demonstrated the critical role of targeting fractionated activity at discrete locations at the interatrial septum, coronary sinus, and LAA in successfully restoring sinus rhythm. Ablation involving a combination of PV EI, disconnection of other thoracic veins, complex atrial activity, and linear ablation restored sinus rhythm in 95% of patients with 38% requiring a second procedure. In addition, complex atrial activity does not occur randomly throughout the atria but at pre-defined anatomic locations.

### Safety

Image integration may contribute to an improvement in the safety of the procedure for patient and operator alike. Radiation exposure is of considerable concern for complex ablation procedures with repeat procedures required in up to 40% of patients. In the present study, there was a trend to a reduction in fluoroscopy times for the completion of PV EI in the CTI group compared with the EAM group. The procedural fluoroscopy time does not reflect the radiation exposure from the CT performed in all patients in the present study. Radiation exposure to the patient may be further reduced by the choice of MRI rather than CT although this is largely determined by the expertise of the individual centre. Prospective or non-ECG-gated CT image acquisition also provides a reduction in radiation dose. The fluoroscopy time remains considerable as the EAM system displays only the ablation catheter, and X-ray is often required to visualize the circular mapping catheter to assist in the achievement of EI should this not have been achieved with an apparently complete circumferential lesion set. The EnSite NavX system (St Jude Medical) has the potential advantage of a further reduction in fluoroscopy time by displaying all electrophysiological catheters. Arentz et al. reported a reduction in fluoroscopy time for wide encirclement of the PVs guided by the NavX system (40 ± 12 min) compared with individual segmental ostial ablation of the PVs (53 ± 18 min, P < 0.001) guided by X-ray alone. The fluoroscopy times were similar between the NavX-guided approach reported by Arentz et al. and that of CT integration in the present study. It is possible that image integration into the NavX system may result in further reduction in fluoroscopy time.

In the present study, only one case of moderate pulmonary vein stenosis was reported in the EAM group. The incidence of PV stenosis has been substantially reduced with the cuff of surrounding atrial myocardium, the target for catheter ablation. Nonetheless, a more accurate representation provided by image integration of the veno-atrial junction helps avoid inadvertent ablation at or beyond the PV ostia.

### Prior studies

Few studies have compared the impact of more detailed imaging on clinical outcomes of patients undergoing catheter ablation for AF. Our present study is in contrast to previous data that we have published of a retrospective analysis of the clinical outcomes of patients undergoing catheter ablation guided by CT integration compared with an EAM or non-contact mapping system. Patients who underwent CA guided by CT integration demonstrated a significant reduction in recurrent atrial arrhythmias and improved clinical success at a mean follow-up of 25 ± 5 weeks. The difference in the outcomes has a number of potential explanations:

1. visualization of the patient’s LA on a CT is sufficient to significantly improve the operators understanding of the anatomy without the need for the CT to be registered and guide ablation.
2. using CT integration for a period of time teaches the operator enough about the LA anatomy and the way that the ablation catheter behaves, that CT integration is no longer necessary after completing this learning curve.
3. the clear differences in study design and primary endpoint.
Study limitations

The ability of the operator to visualize the LA anatomy on CT may have biased the results of the EAM group. This seems unlikely as the anatomy of the LA was also routinely defined by angiograms of all PVs as part of the procedure protocol. The present study may not have demonstrated a difference in the occurrence of PV stenosis due to the absence of routine postoperative imaging of the PVs. However, 40% of patients underwent a second procedure that necessarily involves repeat imaging of the PVs, and these findings were included in the study follow-up.

Conclusion

In a randomized prospective study, image integration to guide catheter ablation for AF did not significantly improve the clinical outcome. Although a more detailed representation of the left atrium remains a useful adjunct to catheter ablation for AF, it appears that operator skill and experience are most important in determining clinical outcome.

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References


