**Clinical Research Protocol**

**Study Title:** Biatrial global high-density electroanatomical mapping of atrial fibrillation – a prospective mechanistic registry study.

**Internal Reference Number / Short title:** BiMAP-AF

**Ethics Ref:** 18/SC/0409

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| **Sponsor:**  | Oxford University Hospitals NHS Foundation Trust |
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| **Chief Investigator Signature:**  |  |

Dr Tim Betts and Dr Michael Pope have no potential conflicts of interest.

**Confidentiality Statement**

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, HRA, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

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# SYNOPSIS

|  |  |
| --- | --- |
| **Study Title** | Biatrial global high-density electroanatomical mapping of atrial fibrillation – a prospective mechanistic registry study. |
| **Internal ref. no. / short title** | Biatrial mapping of atrial fibrillation – BiMAP-AF |
| **Study Design** | Prospective non-randomised registry investigation |
| **Study Participants** | Adults aged ≥18 with atrial fibrillation undergoing catheter ablation |
| **Planned Sample Size** | 22 patients  |
| **Planned Study Period** | 18 months |
|  | **Objectives** | **Outcome Measures** |
| **Primary** | To identify the electrophysiological mechanisms of atrial fibrillation, the role of the right atrium, and how these relate to additional anatomical, clinical and demographic features. | Presence and number of pre-defined electrophysiological phenomena such as “rotors” and “focal firing”. |
| **Secondary** | Determine the impact of catheter ablation of the electrophysiological mechanisms on the maintenance of sinus rhythm | Freedom from recurrent atrial fibrillation or tachycardia, defined as that seen on 12 lead ECG recording or >30 seconds on ambulatory monitoring at 9-12 months. |

# ABBREVIATIONS

|  |  |
| --- | --- |
| CI | Chief Investigator |
| CRF | Case Report Form |
| GCP | Good Clinical Practice |
| GP | General Practitioner |
| HRA | Health Research Authority |
| ICF | Informed Consent Form |
| NHS | National Health Service |
| NRES | National Research Ethics Service |
| PI | Principal Investigator |
| PIL | Participant/ Patient Information Leaflet |
| R&D | NHS Trust R&D Department |
| REC | Research Ethics Committee |
| SOP | Standard Operating Procedure |

# BACKGROUND AND RATIONALE

Atrial fibrillation (AFib) is the most common sustained arrhythmia, with increasing prevalence seen within an aging population. It is associated with significant morbidity and mortality including stroke and heart failure, as well as burdensome symptoms, which all contributes to frequent hospitalisation and thus significant socioeconomic impact. Current management options are based around either control of heart rate or maintenance of sinus rhythm. Drugs to maintain sinus rhythm are often ineffective, poorly tolerated and associated with significant toxicity. Invasive catheter ablation procedures aiming to electrophysiologically isolate the pulmonary veins are increasingly widely performed for patients with significant drug-refractory symptoms. Efficacy however is often poor. Although multiple procedures can achieve success rates of 70-80% for patients with paroxysmal AFib, those with more persistent arrhythmia experience far less positive results.(1-3) This is in part due to an incomplete understanding of the electrophysiological mechanisms of the arrhythmia. Although ectopy arising in the pulmonary veins is well recognised as a fundamental trigger for AFib and forms the basis for the role of pulmonary vein isolation, non-pulmonary vein triggers are poorly characterised and additional mechanisms involved in propagating and sustaining arrhythmia are likely to exist, yet may vary considerably between individuals. (4) The reduced efficacy of pulmonary vein isolation alone in patients with persistent AFib highlights the importance of these additional mechanisms. Furthermore, the focus to date has been on the role of the left atrium in initiating and maintaining the arrhythmia, with the right atrium largely ignored. Recent work by Miller et al. using a 64 pole basket catheter to conduct sequential left and right atrial endocardial contact mapping to identify focal impulses and rotors (thought to act as AFib drivers) identified right atrial rotors in 85% of patients with persistent AFib, and 22% required ablation within the right atrium to terminate the arrhythmia.(5) However, simultaneous biatrial electroanatomical mapping using interventional catheter techniques has not previously been performed.

ACUTUS medical has developed a novel non-contact high-density global electroanatomical mapping system (AcQMap) of which Oxford has access to 1 of only a few worldwide. This system allows visualisation of whole chamber activation, which can be employed during AFib to reveal complex mechanisms such as focal impulses, rotational activity or re-entry circuits that may serve to maintain the arrhythmia. Feasibility and validation of this system have previously been demonstrated in a small registry of 125 patients in the UK and Europe, in which Oxford was involved. The ability to link 2 systems to facilitate simultaneous mapping of the entire left and right atrium has been demonstrated in the engineering lab using bench models, but not yet been performed in-vivo.

This study aims to be the first to employ 2 linked ACUTUS AcQMap systems to conduct simultaneous high-density global biatrial mapping in patients with AFib. This will further delineate the electrophysiological mechanisms responsible for rhythm propagation and maintenance and be the first to explore the interaction of the two atria in the initiation and perpetuation of the complex rhythm. Knowledge gained will guide further studies of additional targets or strategies for ablation in order to improve clinical outcomes.

# OBJECTIVES AND OUTCOME MEASURES

|  |  |  |
| --- | --- | --- |
| **Objectives** | **Outcome Measures**  | **Timepoint(s) of evaluation of this outcome measure (if applicable)** |
| **Primary Objective**To identify the electrophysiological mechanisms of atrial fibrillation, the role of the right atrium, and how these relate to additional anatomical, biochemical and clinical features. | Presence and number of pre-defined electrophysiological phenomena such as “rotors” and “focal firing”. | N/A |
| **Secondary Objectives**Determine the impact of catheter ablation of the electrophysiological mechanisms on the maintenance of sinus rhythm | Freedom from recurrent atrial fibrillation, defined as that seen on 12 lead ECG recording or >30 seconds on ambulatory monitoring. | 9-12 months from the date of ablation |

# STUDY DESIGN

This a prospective open-label observational registry study.

Participants will be undergoing elective catheter ablation procedures for atrial fibrillation. They will be identified in clinic or following listing for the procedure prior to formal recruitment. The main research element is a mechanistic evaluation of atrial fibrillation mechanisms through the use of simultaneous global biatrial electroanatomical mapping using AcQMap systems. The electrophysiological mapping results form the study data that will then be analysed. Patients will be seen for follow up 3 months and 9-12 months following the procedure, which will mark the end of study involvement.

# PARTICIPANT IDENTIFICATION

## Study Participants

Patients with atrial fibrillation undergoing a de-novo catheter ablation procedure.

## Inclusion Criteria

* Participant is willing and able to give informed consent for participation in the trial.
* Male or Female, aged 18 years or above.
* Diagnosed with paroxysmal or persistent atrial fibrillation and planned for a catheter ablation procedure.
* In the Investigator’s opinion is able and willing to comply with all trial requirements.

## Exclusion Criteria

The participant may not enter the trial if ANY of the following apply:

* Physical or anatomical barriers to the use of two simultaneous mapping catheters
* Previous cardiac surgery
* Previous ablation (catheter or surgical)
* Female participant who is pregnant, lactating or planning pregnancy during the course of the trial.
* Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participants at risk because of participation in the trial, or may influence the result of the trial, or the participant’s ability to participate in the trial.
* Participants who have participated in another research trial involving an investigational medicinal product in the past 12 weeks. (Involvement in *any* other research trial is not a contraindication per se.)

# STUDY PROCEDURES

## Recruitment

Study participants will be identified by medical staff in the outpatient clinic at the time of listing for catheter ablation, or by review of patients electronically listed for this procedure. If patients are in the clinic and give consent then they may be approached by a member of the research team at this stage. If identified by medical staff through listing for the procedure, they will be approached by telephone. An information leaflet will then be provided by post if this has not been provided in clinic with contact details for the research team. If willing to participate then formal screening and recruitment will take place at the time of attendance for standard pre-procedure assessment. Information must have been provided with sufficient time for the potential participant to fully consider involvement prior to formal recruitment and consent (generally expected to be at least 24 hours).

## Informed consent

The participant must personally sign and date the latest approved version of the Informed Consent form before any trial specific procedures are performed. It is anticipated that this is done at the initial visit, which will serve as both the screening and baseline study visit.

Written and verbal versions of the Participant Information and Informed Consent will be presented to the participants detailing no less than: the exact nature of the trial; what it will involve for the participant; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the trial at any time for any reason without prejudice to future care, without affecting their legal rights and with no obligation to give the reason for withdrawal.

The participant will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the trial. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the Informed Consent. The person who obtained the consent must be suitably qualified and experienced, and have been authorised to do so by the Chief/Principal Investigator. A copy of the signed Informed Consent will be given to the participant and a copy placed in the medical records. The original signed form will be retained at the trial site.

## Screening and Eligibility Assessment

As there is no randomisation, there is no time limit between screening and formal recruitment. It is anticipated that these will occur at the same visit to coincide with standard clinical care. Screening procedures include a review of medical history, demographics, and physical examination for exclusion criteria.

## Baseline Assessments

Baseline assessments include medical history; current medications and any recently stopped medications (with particular reference to anti-arrhythmic drugs and anticoagulants), smoking history, alcohol use, illicit drugs use, and a physical examination. Measurements taken should include height, weight, body mass index and waist circumference. Data collected from imaging performed as part of standard clinical care should include left ventricular ejection fraction, diastolic function (including average E/E’), significant valvular disease (defined as at least moderate stenosis or regurgitation), left atrial diameter, left atrial volume (including indexed for body surface area), and presence of significant coronary disease at angiography (invasive or CT)(if performed). Laboratory test results recorded should include haemoglobin, urea, creatinine, and creatinine clearance (estimated by Cockroft and Gault formula). A 12 lead ECG should be performed.

## Study Visit

As part of standard care a 12 lead ECG will be performed for all patients following arrival on the day of their procedure. In line with standard practice in this institution all procedures will be undertaken under general anaesthesia.

Venous access, trans-septal puncture and placement of standard electrophysiology (mapping and ablation) catheters will be undertaken at the discretion of the operator. Anticoagulation will be administered following trans-septal puncture in line with standard protocols.

**Patients with paroxysmal atrial fibrillation**

Patients with paroxysmal atrial fibrillation will undergo voltage mapping in standard fashion of both the left and right atrium followed by the insertion of 2 AcQMap catheters, 1 into the left atrium, and one into the right atrium. Geometry analyses will be undertaken for both chambers. Simultaneous electrical activation recordings will then be conducted in both atria to perform biatrial mapping of sinus rhythm. This will consist of 30 seconds of recording, with maps created for the first 10 seconds and the last 10 seconds. Biatrial mapping will be repeated during pacing. Atrial fibrillation will then be induced by incremental burst atrial pacing and ACUTUS biatrial mapping repeated with the same protocol. Standard pulmonary vein (PV) isolation will then be performed using the Abbott EnSite Precision mapping software and contact-force-guided irrigated-tip radiofrequency energy ablation. PV isolation will be confirmed with a circular mapping catheter. If sinus rhythm is achieved, the case will end. If the patient remains in atrial fibrillation, Acutus biatrial mapping will be repeated. Any further ablation may be performed at the discretion of the operator prior to direct current cardioversion and the end of the case.

**Patients with persistent atrial fibrillation**

For patients with persistent atrial fibrillation, irrespective of presenting rhythm, 2 AcQMap catheters will be advanced, 1 into the left atrium and 1 into the right atrium. Geometry analyses will be undertaken for both chambers. Simultaneous electrical activation recordings will then be conducted in both atria to perform ACUTUS biatrial mapping of the presenting rhythm. This will consist of 30 seconds of recording with maps created for the first 10 seconds and last 10 seconds. For those patients presenting in sinus rhythm ACUTUS biatrial mapping will be repeated during pacing (see appendix 1b) and voltage maps of the left and right atria will be obtained in sinus rhythm. Patients presenting in atrial fibrillation will undergo external direct current cardioversion. If sinus rhythm is restored, voltage maps of the left and right atria will be obtained followed by ACUTUS biatrial mapping of sinus rhythm and during pacing (see appendix 1b). Atrial fibrillation will then be induced by incremental burst atrial pacing and ACUTUS biatrial mapping will be repeated as described above. If sinus rhythm cannot be restored, then the case continues as below.

The procedure is then carried out in line with standard techniques for pulmonary vein (PV) isolation using the Abbott EnSite Precision mapping software and contact-force-guided irrigated-tip radiofrequency energy ablation. PV isolation will be confirmed with a circular mapping catheter. ACUTUS biatrial mapping will then be repeated as described above.

Ablation of any further targets of AFib substrate can be undertaken at this stage at the discretion of the operator using electrophysiological data obtained from the ACUTUS maps using contact-force-guided irrigated-tip radiofrequency energy until local electrograms at target sites are abolished. Biatrial mapping will be repeated following ablation of each substrate targeted prior to moving onto the next target. This will continue until either sinus rhythm is restored, the arrhythmia organises into a stable re-entrant arrhythmia, or all areas of substrate in both atria are targeted. In the case of organisation into a stable re-entrant arrhythmia this will then be mapped and further ablation performed until sinus rhythm is achieved. If atrial fibrillation persists after ablation of all targets deemed appropriate by the operator, direct current cardioversion will be performed to restore sinus rhythm. PV isolation will be confirmed after return to sinus rhythm followed by repeat biatrial mapping as described above including during pacing. Isoproterenol will then be infused and any spontaneous ectopic beats that initiate AFib or atrial tachycardia will be mapped and targeted with ablation. If AFib recurs then this should be managed at the discretion of the operator.

See appendix 1 for a flowchart of procedures during catheter ablation. Appendix 1b outlines the details of mapping procedures to follow.

A blanking period of 90 days post-procedure will occur. During this time recurrent arrhythmias will be documented but not included in any outcome assessment. They will be treated using cardioversion and/or antiarrhythmic drugs in line with standard clinical practice. Patients will undergo initial follow up at 3 months post procedure, with additional clinic follow up at 9-12 months. At each visit, symptom burden will be assessed. Patients with recurrent symptoms of arrhythmia will undergo standard investigation, which would be expected to include ambulatory monitoring as indicated.

**Table distinguishing standard care vs research procedure.**

|  |  |
| --- | --- |
| **Standard care** | **Research procedure** |
| Venous access and insertion of electrophysiological catheters including 1 AcQMap catheter | Venous access and insertion of 2nd AcQMap catheter |
| Transeptal puncture | Concurrent right atrial mapping during all recordings |
| Voltage mapping | Simultaneous left and right atrial mapping (AcQMap) during sinus rhythm and pacing |
| Left atrial mapping of atrial fibrillation |  |
| Direct current cardioversion |  |
| Pulmonary vein isolation |  |
| Additional ablation guided by AcQMap data |  |
| Mapping and ablation of observed stable rhythms |  |
| Isoproterenol infusion and ablation of ectopy |  |

## Subsequent Visits

Visit 1: Clinic visit at 3 months (with a window of 1 month after but not before) following catheter ablation in line with standard clinical practice. A 12 lead ECG will be recorded. An up to date drugs history will be documented. Documented arrhythmias occurring prior to 90 days post-procedure will be recorded but not included as part of any outcome assessment as this forms the designated blanking period. Any adverse events should be documented.

Visit 2: Clinic visit 9-12 months following catheter ablation. This is the final study visit aimed to coincide with clinical follow-up. A 12 lead ECG is recorded. A 72 hour ambulatory monitor will be worn for assessment of sub-clinical arrhythmia. An up to date drugs history will be recorded. Any adverse events should be documented. The ambulatory monitor will be returned after use by depositing it either in the clinic or in a designated returns box but there is no formal visit at this stage.

## Discontinuation/Withdrawal of Participants from Study

Each participant has the right to withdraw from the trial at any time. In addition, the Investigator may discontinue a participant from the trial at any time if the Investigator considers it necessary for any reason including:

* Pregnancy
* Ineligibility (either arising during the trial or retrospectively having been overlooked at screening)
* Significant protocol deviation
* An adverse event which requires discontinuation of the catheter ablation or results in inability to continue to comply with trial procedures
* Withdrawal of Consent

If a patient is withdrawn or voluntarily withdraws from the trial at any period following the procedure then data collected up to that point will still be analysed. If any event during the procedure results in necessary deviation from the study protocol on grounds of clinical necessity then any data collected up to that point will be analysed. It may be required to recruit additional patients if this occurs depending on the extent to which data had been collected. This is at the discretion of the chief investigator.

The reason for withdrawal will be recorded in the CRF.

If the participant is withdrawn due to an adverse event related to ACUTUS mapping, the Investigator will arrange for follow-up visits or telephone calls until the adverse event has resolved or stabilised.

## Definition of End of Study

The end of trial is the date of the last visit of the last participant.

# SAFETY REPORTING

## Definition of Serious Adverse Events

A serious adverse event is any untoward medical occurrence that:

* results in death
* is life-threatening
* requires inpatient hospitalisation or prolongation of existing hospitalisation
* results in persistent or significant disability/incapacity
* consists of a congenital anomaly or birth defect.

Other ‘important medical events’ may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

## Reporting Procedures for Serious Adverse Events

A serious adverse event (SAE) occurring to a participant should be reported to the REC that gave a favourable opinion of the study where in the opinion of the Chief Investigator the event was ‘related’ (resulted from administration of any of the research procedures) and ‘unexpected’ in relation to those procedures. Reports of related and unexpected SAEs should be submitted within 15 working days of the Chief Investigator becoming aware of the event, using the HRA [report of serious adverse event](http://www.nres.npsa.nhs.uk/docs/forms/Safety_Report_Form_%28non-CTIMPs%29.doc%22%20%5Ct%20%22_blank) form (see HRA website).

# STATISTICS AND ANALYSIS

As this is a mechanistic study there is no primary outcome measure requiring statistical analysis. Retrospective analyses may be conducted to explore trends in electrophysiological mechanisms identified and their relation to demographic, anatomical, or clinical features recorded and in line with secondary outcome measures.

# DATA MANAGEMENT

## Access to Data

Direct access will be granted to authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations.

## Data Recording and Record Keeping

The participants will be identified by a unique trial specific number and/or code in any database. The name and any other identifying detail will NOT be included in any trial data electronic file. A paper form assigning patient details to study codes will be kept in the study master file only.

Electroanatomical mapping data forms the majority of study data collected. Participants will be identified by their unique trial number on any data exported from the catheter laboratory computers. ACUTUS mapping data together with all procedure data will be stored on secure trust servers in a password-protected folder in line with standard practice for all such clinical procedures. This system is a designated ACUTUS workstation on which all clinical cases are stored. Study data for analysis will be exported at the time of the procedure in an anonymised form identifiable by study code onto a separate computer workstation to allow analysis of the mapping data. Analysis work is done within the research office using this designated system, which is password protected and accessible by the study team only.

Analysis results will then be recorded using a purpose designed Excel database.

# QUALITY ASSURANCE PROCEDURES

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

# ETHICAL AND REGULATORY CONSIDERATIONS

## Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

## Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in accordance with relevant regulations and with Good Clinical Practice.

## Approvals

The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC), and HRA for written approval.

The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

## Reporting

The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC Committee, HRA (where required) host organisation and Sponsor. In addition, an End of Study notification and final report will be submitted to the same parties.

## Participant Confidentiality

The trial staff will ensure that the participants’ anonymity is maintained. The participants will be identified only by a participant ID number on all trial documents and any electronic database, with the exception of the CRF, where participant initials may be added. All documents will be stored securely and only accessible by trial staff and authorised personnel. The trial will comply with the Data Protection Act, which requires data to be anonymised as soon as it is practical to do so.

## Expenses and Benefits

Reasonable travel expenses for any visits additional to normal care will be reimbursed on production of receipts, or a mileage allowance provided as appropriate.

# FINANCE AND INSURANCE

## Funding

Initial study funding is through the CRM Hub. Further research grant funding will be applied for to cover the ongoing study costs. This is required to cover the purchase of AcQMap catheters beyond those used for standard care, reimburse travel costs where visits are required in addition to routine care, and fund follow up ambulatory monitors.

## Insurance

NHS bodies are legally liable for the negligent acts and omissions of their employees. If you are harmed whilst taking part in a clinical research study as a result of negligence on the part of a member of the study team this liability cover would apply.

Non-negligent harm is not covered by the NHS indemnity scheme. The Oxford University Hospitals NHS Foundation Trust, therefore, cannot agree in advance to pay compensation in these circumstances.

In exceptional circumstances an ex-gratia payment may be offered.

# PUBLICATION POLICY

The results will be presented at scientific meetings and published in peer-reviewed scientific journals. The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by Heart Research UK (if becomes applicable). Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged. Participating patients will be offered a copy of any publications arising from the study.

# REFERENCES

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# APPENDIX 1: Ablation procedure flow-charts

1. Persistent atrial fibrillation
2. Paroxysmal atrial fibrillation

# APPENDIX 1b: Mapping protocols

## Sinus rhythm contact mapping

This is performed using the Abbott EnSite Precision electroanatomic mapping system and a circular mapping catheter with an Inquiry decapolar catheter placed in the coronary sinus and the proximal electrode located at the coronary sinus ostium. Geometry and bipolar voltage data should be collected concurrently for the right atria and then left atria sequentially during sinus rhythm. Voltage scale should be set to clearly differentiate areas of voltage <0.05mv (scar), <0.4mv (low voltage area) and >1.5mv. Effective refractory periods (ERP) should then be determined by pacing at twice the diastolic threshold from the right atrial appendage, left atrial appendage and mid-coronary sinus respectively. This should be done using an 8 beat drive train at cycle lengths of 600ms and 450ms followed by a decrementing extra-stimulus starting at 100ms faster than the drive train cycle length down to ERP. If atrial fibrillation is induced then measurement of ERPs should be abandoned and the procedure continued. If necessary then DCCV may be performed.

## Acutus mapping during sinus rhythm and pacing

Following insertion of AcQMap catheters to both the left and right atria, geometry is obtained from each chamber in turn (if not already done in atrial fibrillation). Electrophysiological recordings are carried out for both atria simultaneously for 30 seconds. These are time aligned in each recording. The first 10 seconds following time alignment and the last 10seconds of recording are processed for dipole density activation mapping. Separate recordings are then taken during an 8 beat pacing drive train from the right atrial appendage, mid coronary sinus and left atrial appendage at cycle lengths of 600ms, and 450ms with a coupled S2 extra-stimulus starting at 100ms faster than the drive train cycle length and decrementing in 50ms intervals until within 50ms of the ERP at that site at which point the decrement is reduced to 10ms. Pacing output should be set at the shortest pulse width and voltage that consistently achieves capture. Time alignment during pacing is taken from the onset of the pacing stimulus.

## Acutus mapping during atrial fibrillation

Following insertion of AcQMap catheters to both the left and right atria, geometry is obtained from each chamber in turn (if not already done in sinus rhythm). Electrophysiological recordings are carried out for both atria simultaneously for 30 seconds. These are time aligned and the first 10seconds following time alignment and the last 10seconds of recording are processed for dipole density activation mapping. AcQTrack automated analysis should be carried out on each segment of dipole density mapping.

# APPENDIX 2: SCHEDULE OF PROCEDURES

|  |  |
| --- | --- |
| **Procedures** | **Visits** |
| **At procedure pre-assessment** | **Study visit** | **3 months post procedure** | **9-12 months post procedure** |
| **Screening** | **Baseline**  |  | **Visit 1** | **Final visit** |
| Informed consent | √ |  |  |  |  |
| Eligibility assessment | √ |  |  |  |  |
| Demographics | √ |  |  |  |  |
| Medical history | √ |  |  | √ | √ |
| Concomitant medications |  | √ | √ | √ | √ |
| Physical examination | √ |  |  |  |  |
| Height, weight, BMI, waist circumference |  | √ |  | √ | √ |
| Imaging results |  | √ |  |  |  |
| 12 lead ECG |  | √ | √ | √ | √ |
| Laboratory test results |  | √ |  |  |  |
| Catheter ablation with simultaneous biatrial mapping |  |  | √ |  |  |
| 72 hour ambulatory monitor |  |  |  |  | √ |
| Adverse event assessments  |  |  |  | √ | √ |

# APPENDIX C: AMENDMENT HISTORY

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Amendment No.** | **Protocol Version No.** | **Date issued** | **Author(s) of changes** | **Details of Changes made** |