16th Atrial Fibrillation Symposium
23-24 March 2017
The Hague, The Netherlands
trial fibrillation (AF) currently affects 2 % of the population, with estimates that by 2030, 14–17 million people in Europe will experience AF. This debilitating condition is fast becoming a critical public health issue. To improve education and care in this area, Biosense Webster has developed ground-breaking innovations and has sponsored this educational symposium for 16 years. This year’s symposium took place on 22–24 March 2017 in The Hague, the Netherlands, and welcomed an international faculty to present an agenda that reflected the newest developments, research and perspectives in AF treatment.

The Atrial Fibrillation Practical Sessions were conducted on the first day and focused on all aspects of the AF ablation procedure and the practical usage of new technologies in the field of AF ablation. The high-level lectures were case-based and geared towards improving procedure workflow and, ultimately, improving patient care. International expert faculty shared experiences from their practice, as well as tips and tricks. The target audience was physicians looking to perfect their procedure workflows, enhancing efficacy, efficiency and safety through the sharing of knowledge.

The next two days comprised the Atrial Fibrillation Symposium, where international faculties presented the newest developments and research results, some prior to publication. The target audience was skilled AF practitioners seeking the most progressive information in this field to advance their knowledge and practice. Interactive polling via handheld devices provided real-time insights, in addition to engagement through Q&A sessions during each panel discussion. Attendees received up to 10 hours of CME for their participation.

In welcoming attendees to the 16th Atrial Fibrillation Symposium, Prof Dipen Shah of Geneva, Switzerland, said: “This year’s programme has been put together to emphasise currently relevant themes and threads in the field of AF and its treatment by catheter ablation. Although AF has an undeniably characteristic electrical signature, the increasing awareness and understanding of causative sequelae and associated structural abnormalities in the atria have led to the acknowledgement of atrial cardiomyopathy as a distinct entity. The symposium’s scientific intent will therefore kick off with an exposition of this. It is my sincere hope that you will enjoy the proceedings as much as I and my colleagues in the scientific committee did putting the programme together.”
Dr Stanley Nattel from Montreal, Canada, began with an overview of the history of the term atrial cardiomyopathy and its use in conjunction with atrial fibrillation (AF), setting the stage for their present-day definitions.

The European Heart Rhythm Association (EHRA), the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Association and the Latin American Society for Cardiac Stimulation and Electrophysiology attempted to standardise the definition, characterisation and clinical implications of the term atrial cardiomyopathy in 2016. In the resulting consensus document, atrial cardiomyopathy was defined as “any complex of structural, architectural, contractile or electrophysiological changes affecting the atria with the potential to produce clinically relevant manifestations”.2

The consensus document also produced definitions for four classes of atrial cardiomyopathies (see Figure 1). This histological classification has many limitations.

However, it is a useful beginning that will help clinicians consider the histopathology of atrial cardiomyopathy in a more organised way. Dr Nattel believes that it will be possible in the relatively short term to create a more meaningful classification and to use it to define clinically relevant predictive factors and therapeutic decisions. The next step will be to test the classification to evaluate whether it can be used to guide clinical care in practice.

Atrial cardiomyopathy is an evolving concept. There is evidence that consideration of atrial cardiomyopathy may add value to patient management. A more clinically relevant classification considering aetiological factors and indices of electrical, mechanical and structural remodelling would help in identifying practical applications of the concept.

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**Figure 1. Classification of Atrial Cardiomyopathies (EHRA-HRS-APHRS-SOLEACE – EHRAS Class I-IV)**

- Primarily Cardiomyocyte-dependent (Class I)
  - lone AF
  - genetic diseases
  - diabetes mellitus

- Primarily Fibroblast-dependent (Class II)
  - aging
  - cigarette smoking

- Mixed Cardiomyocyte-Fibroblast-dependent (Class III)
  - CHF
  - valvular diseases

- Primarily Non-Collagen Deposits (Class IV)
  - isolated atrial amyloidosis
  - granulomatosis
  - inflammatory Infiltrates
  - glycosphingolipids

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**Introduction**

**Atrial Cardiomyopathy and Atrial Fibrillation**

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This session explored the underlying cause of atrial abnormalities by looking downstream of the atria at the ventricles. The recognition of focal triggers provided the earliest and strongest clinical insights into electrophysiology and the electropathology of AF, and the session reviewed the current understanding of mechanisms of focal triggers. The session ended with a reconciliatory overview of current AF mapping data from different techniques, from inside and outside – and even through – the walls of the heart.

Role of the Ventricle in Atrial Fibrillation
Dr Rohan Wijesurendra and colleagues at Oxford University have designed a prospective, longitudinal clinical study of patients with AF undergoing catheter ablation to help answer the question, “What is the precise nature of the link between AF and left ventricular dysfunction?” The study excluded those with inadequate ventricular rate control in AF and significant cardiovascular comorbidities to focus on ‘lone’ AF. The study also included several matched control subjects in sinus rhythm (SR). The researchers used cardiac magnetic resonance as a gold-standard method for determining left ventricular volumes and systolic function. The results showed:

- In patients with AF, left ventricular (LV) function and myocardial energetics are impaired compared to matched controls in SR.
- Before ablation, AF at the time of the scan (compared to SR) is associated with lower left ventricular ejection fraction (LVEF), but energetics are equally impaired irrespective of the intra-scan rhythm.
- Post-ablation, LVEF improves modestly, but, like left atrial ejection fraction, does not normalise.
- The improvement in LV function is driven by the switch to SR at the time of the scan, rather than by a reduction in AF burden over time.
- Myocardial energetics are unchanged post-ablation, despite the substantial and sustained reduction in AF burden.

Focal Triggers
Dr Nattel considered focal triggers as an aspect of mechanisms of AF, and provided some new perspectives on this topic. He began with a simplified scheme of arrhythmia mechanisms in AF, involving ectopic activity, triggers and a re-entry substrate. Over 90% of AF episodes are initiated by premature atrial contractions, which act as initiators on a vulnerable substrate. However, in addition, sustained ectopic activity can itself lead to AF.

Both long-standing persistent AF and paroxysmal AF patients manifest delayed afterdepolarisations due to abnormal calcium handling, but with distinct mechanisms. Novel mechanistic approaches may need to be developed to target patient-specific pathophysiology. Importantly, delayed afterdepolarisations and triggered activity are likely the principal source of atrial premature complex generation.

Not all focal firing is due to focal ectopic activity, as shown by the use of wave mapping. A recently published paper delineates the zones of epicardial and endocardial dissociation along the opposite surface, resulting in breakthrough activity. Thus, focal firing on the endo- or epicardial surface may be due to breakthrough instead of ectopy, and endo-epicardial interaction may multiply AF-maintaining sources. This may be a form of AF-maintaining activity that does not involve true ectopy or re-entry.
In 2016, a core group formulated and published the most recent European Society of Cardiology (ESC) guidelines for the management of AF. These guidelines were the focus of their own session, starting with an overview and then a closer look at some of the significantly modified recommendations pertaining to the treatment of AF.

**General Management and Gaps in Evidence**

There are five domains of integrated AF management, and these interventions should lead to haemodynamic stability, cardiovascular risk reduction and stroke prevention, and provide improved life expectancy. Together, they should result in symptom improvement, and improved quality of life, autonomy and social functioning.

“The guidelines put a strong focus on integrated AF management,” said Prof Harry Crijns of Maastricht, the Netherlands. “It’s a top priority. That’s about patient involvement in multidisciplinary teams. It’s also cooperating in multidisciplinary chronic AF care teams when patients are simple, and working together in AF heart teams when patients need complex decisions.”

However, there are many gaps in the evidence, mostly with regard to antithrombotic or anticoagulation treatments, such as left atrial appendage occlusion for stroke prevention, or anticoagulation in AF after intracerebral bleeds. These are mainly the result of the lack of patients needed to sufficiently power clinical trials.

Prof Crijns reviewed the results of several studies that help to address these gaps in the evidence, although they do not offer definitive guidance, and highlighted the need for further study. For example, more studies are needed to evaluate the impact of stopping anticoagulation after ablation in lower-risk patients, for instance in patients with heart failure due to tachycardiomyopathy, or with a mixed heart failure pattern (e.g. congestive heart failure, tachycardiomyopathy). Another example is the need for new studies in patients who have contraindications for anticoagulation, and especially also patients who have had an ischaemic stroke while on anticoagulant therapy, which is an important part of the Maastricht University patient population.

Concerning research into producing permanent transmural and longitudinal continuous lesions, researchers at Maastricht are studying a hybrid thoracoscopic surgical and transvenous catheter ablation approach. This pilot trial, called the Hybrid Versus Catheter Ablation in Persistent AF (HARTCAP-AF) study, may eventually indicate that the hybrid approach is more effective than stand-alone percutaneous catheter ablation approach. Other evidence gaps relate to the value of opportunistic screening for AF, and AF screening for early detection, as well as how much AF constitutes a mandate for antithrombotic therapy in patients with pacemakers. Prof Crijns also discussed the temporal disconnect between arrhythmia and stroke, the evidence in time-of-calamity studies, and the correspondence between CHA2DS2-VASC score and use of non-vitamin K antagonist oral anticoagulants (NOACs).

He also described work in progress at Maastricht to compare cardioversion with a ‘wait-and-see’ approach (see Figure 3). Prof Crijns thinks that the wait-and-see approach is often successful, because a lot of patients convert without intervention. It gives the clinician time to diagnose these patients.

**First-line AF Ablation: Should Be Considered or May Be Considered?**

Is first-line ablation of AF a ‘should’ or ‘maybe’ when compared with anti-arrhythmia drugs? According to a 5-year follow-up of first-line ablation patients with a mean of 1.5 procedures and a median of 1 procedure, approximately 80 % will remain in SR. This statistic is actually not bad, said Prof Gian-Battista Chierchia of Brussels, Belgium. Ablation is significantly better than antiarrhythmic drugs (AADs) in keeping patients who failed an AAD in SR. And, he notes, it is probably age-dependent – the younger, the better.

So why not ablate earlier? Or, alternately, why should ablation occur earlier? There are various reasons. First is safety – ablation is considered less safe than AADs, but in fact higher overall death rates are seen with AADs than in early-ablation patients. The second reason is disease progression. If not tackled quickly, paroxysmal AF progresses quickly, in one study, approximately 15 % progressed from paroxysmal to persistent AF within 1 year. It has also been shown that ablation tends to delay the progression of the pathology.
“If you ablate, the patients will more likely not progress to persistent AF if they initially presented as paroxysmal AF,” said Prof Chierchia.

Another reason is procedure complexity. The more the pathology advances, the more it tends to be complex to treat the patient.

Trials and literature indicate that ablation is more effective than AADs for extending time to recurrence of asymptomatic AF after radiofrequency (RF), and comes with a lower rate of symptomatic AF after RF. Furthermore, the new ESC guidelines state that catheter ablation is the recommended treatment for symptomatic paroxysmal AF, which is refractory to at least one Class I or Class III antiarrhythmic drug.

The key addition to these guidelines is that patient choice should be fundamental to the decision, provided that it is performed in expert centres, justifying catheter ablation as first-line treatment in selected patients with paroxysmal AF who ask for interventional therapy. The patient should be thoroughly informed about the procedure as part of this component.

**Stand-alone AF Surgery: Do the Risks Justify a Class IIa Indication?**

Member of the 2016 ESC guideline committee, Dr Bart P van Putte of Nieuwegein and Amsterdam, the Netherlands, spoke about how the risks and benefits of the different ablation recommendations should be balanced if there is a Class IIa or a Class I indication.

Dr van Putte started by highlighting the three surgical recommendations with a Class IIa indication in the guidelines:

1. Catheter or surgical ablation should be considered for patients suffering from symptomatic, persistent, or longstanding persistent AF refractory to drugs to improve symptoms.
2. Surgery should be considered when catheter ablation has failed.
3. Minimally invasive surgery should be considered for patients suffering from persistent or post-ablation AF.

Dr van Putte defined the meaning of stand-alone AF surgery. This term comprises three different types of surgery – thoracoscopic Maze surgery (a thoracoscopic procedure without extracorporeal circulation); a Maze-IV procedure done by sternotomy, necessitating extracorporeal circulation (a somewhat invasive procedure); and the Maze-IV procedure performed through port access, i.e. a mini-thoractomy necessitating extracorporeal circulation (becoming more of a priority treatment in hospitals). He compared these three procedures with AF ablation, including short- and long-term results, and complication rates.

The overall 1-to-5-year success rates are at least comparable with catheter ablation, which means that the freedom-from-AF rates after 1 to 5 years vary from 65 to 80 %. In addition, overall complication rates in most papers are approximately 9 %, which is comparable with 11 % for patients who undergo a single-catheter ablation.

Dr van Putte believes that the risks do justify a Class IIa indication. There seems to be a balanced relationship between risks and benefits. What is the consequence of this Class IIa indication for stand-alone AF surgery for the near future? He thinks more patients will be referred for this treatment, and secondly, more trials will be done. More evidence will result in a change of indication.
Session 3
Should Persistent AF Be Treated by Pulmonary Vein Isolation?

The field of AF has had to contend with an evolving landscape following the publication of the Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II (STAR AF II) trial. This session focused on persistent AF and the issues regarding how best to treat it. Instead of examining pulmonary vein isolation (PVI) alone, speakers critically questioned the current evidence and looked beyond the pulmonary veins as therapeutic targets.

Limitations of the Current Definitions of Persistent AF

The term ‘persistent AF’ was first used in 1997. The ‘3 P’ definition (see Figure 4) has been in use since then and has not changed drastically over the intervening years. Prof John Camm from St George’s, University of London and Imperial College London, UK, was one of the authors who helped create the definition. At the time, they were looking for a ‘P’ between paroxysmal and permanent, building on the then-evolving discussion around acute and chronic. The co-authors split the concepts into first-onset (paroxysmal), recurrent (persistent) and permanent.

The concept of long-standing persistent AF was introduced in the 2014 guidelines. Persistent AF is defined as continuous AF sustained for greater than 7 days and long-standing persistent AF is continuous AF that is longer than 12 months in duration.15

Prof Camm said that we cannot look at persistent AF without considering the definitions of paroxysmal AF (a shorter-duration arrhythmia), while long-standing and permanent AF are termed continuous arrhythmia. Paroxysmal AF can be described as self-terminating – within 48 hours in most cases – although some paroxysmal AF can last up to 7 days. This can be further broken down into short episodes of paroxysmal AF, episodes of paroxysmal AF that terminate soon, and episodes of paroxysmal AF that terminate after a long time. Persistent AF requires induced termination, which is sometimes divided into earlier termination and later episodes of termination.

New concepts are evolving these definitions within AF in ways that make the terminology more precise, if somewhat more complicated (see Table 1). This is important because of the progressive nature of AF and because the definitions used are critical for dictating future treatment intention. There are also differences in hazard ratios depending on how the patient condition is stratified, even within the different levels of persistent and paroxysmal AF.

![Figure 4. The ‘3 P’ Classification](image)

Table 1. AHA/ACC/HRS AF Guidelines 2014

<table>
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<tr>
<th>Term</th>
<th>Definition</th>
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| Paroxysmal AF      | • AF that terminates spontaneously or with intervention within 7 days of onset  
• Episodes may recur with variable frequency                                                                                                   |
| Persistent AF      | • Continuous AF that is sustained >7 days                                                                                                      |
| Long-standing      | • Continuous AF >12 months in duration                                                                                                          |
| permanent AF       |                                                                                                                                                                                                          |
| Permanent AF       | • The term “permanent AF” is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm  
• Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of AF  
• Acceptance of AF may change as symptoms, efficacy of therapeutic interventions, and patient and clinician preferences evolve |

Adapted from January et al., 201415

The temporal classification of a single AF episode is clinically useful, but definitions are numerous and unclear. The temporal pattern has been used in the clinic and in clinical trials to choose therapy or to stratify patients, but the temporal classification must be replaced, improved or supplemented to facilitate treatment decisions. Multidimensional classifications of AF (e.g. CHADS-VASC, EHRA score, 7P classification), and clinical- and device-derived AF classifications may be helpful to supplement the definitions, but more work needs to be done in these areas.
There is growing evidence for the role of extrapulmonary vein (extra-PV) substrate in AF; that is, atrial fibrosis is a key pathophysiological player in the progress of AF. Prof Hans Kottkamp of Hirslanden Hospital in Zurich, Switzerland, highlighted the research he and his colleagues have been carrying out in this area. Atrial fibrillation does not beget atrial fibrosis, nor is atrial fibrosis related to increased age of the patient. Atrial fibrosis is a complex process involving triggers, fibrotic substrate and modulators, and may be caused by multiple potential mechanisms. However, Prof Kottkamp says that it is becoming more and more clear that atrial fibrosis is the pathophysiological key player of the AF substrate, but we simply do not agree where it comes from (see Figure 5). Prof Kottkamp hypothesises that arrhythmia is a manifestation of fibrotic disease and not the other way around, but acknowledges this concept is controversial.

Atrial fibrosis is the pathophysiological key player of the AF substrate

Voltage mapping and electrogram morphology can be used as surrogates for atrial fibrosis, and used to determine a fibrotic atrial cardiomyopathy (FACM) score: FACM 0 = purple (voltage >1.5 mV), FACM 4 = almost all parts red (voltage <0.5 mV) (see Figure 6). The fourth score, dubbed the strawberry, is the most massively and diffusely affected left atrium. “When this is affected, whatever you do, you will not get the patient back to sinus rhythm,” said Prof Kottkamp.

What, then, is to be done with respect to extra-PV substrate in AF? Prof Kottkamp discussed approaches depending on the presentation of the patient. For example, in a patient with persistent AF who has FACM 0, only a PVI is performed. In contrast, for FACM 1, 2 and 3 patients, box isolation of fibrotic areas performed in the first ablation procedure has led to good results.

Prof Kottkamp has also been working with a new ‘globe’ ablation technology that may help combine stable, multi-electrode contact mapping with ablation in a single tool, and he feels it shows promise with respect to treating atrial fibrosis in the context of AF.

How Can We Explain Recent Trials Indicating No Benefit of Extra-PV Ablation?

Prof Gerhard Hindricks from University of Leipzig began his presentation by describing the different treatment strategies for extra-PV ablation. Durable PVI is the cornerstone of treatment strategies for the clear majority of patients with the various forms and presentations of AF. Add-on strategies that have been evaluated include deployment of linear lesions, complex fractionated atrial electrograms, AF termination, ablation of focal targets and left atrial appendage isolation, rotor detection and ablation, ablation of cardiac ganglia, and ablation of renal nerves. The latter three strategies were not discussed in detail, in favour of the classic moulds of extra-PV ablation.

In reviewing the treatment results, Prof Hindricks focused on several outcome measures, with the primary one being freedom from AF recurrence after ablation. Secondary outcomes parameters include complications, procedural data and resource utilisation. For all treatment strategies, positive effects on the main outcome measure (i.e. reduced AF recurrence rate attributed to the use of the extra-PV ablation strategy) can be found in the literature. However, whenever the treatment strategies had been evaluated in the setting of larger, multicentre studies, structured meta-analyses, or in the few randomised clinical trials available, most add-on strategies have failed to give solid and significant benefits.

After 20 years of AF ablation, no treatment strategy for extra-PV ablation received a recommendation in recent ESC guidelines for catheter ablation of AF, said Prof Hindricks. There is no strong evidence to advocate anything beyond PVI for any subclass of AF population, aside from solid PVI.
When interpreting the current clinical results, it is important to understand some key points and questions:

- Therapy allocation was mainly based on ECG phenotyping.
- There was no personalised approach in most studies.
- Most studies have been too small and underpowered.
- Most studies were carried out without clearly defined endpoints.
- Is the effect of additional ablation the same for all patient entities with AF?
- Did we induce both benefit and harm with a net-to-neutral effect?
- Did we apply acceptable standardisation of treatment strategies and follow-up?

Outcome after catheter ablation is a complex scenario, and numerous factors play into the risk of recurrence (see Figure 7).

“We have to realise that the technique applied is an important part of the whole set-up that defines the recurrence rate, but it’s just one part among various factors that define the risk of recurrence after catheter ablation of atrial fibrillation,” concluded Prof Hindricks.

Is There an Optimal Extra-PV Substrate Ablation Strategy?
Procedural success for AF is affected by a range of factors – the type of AF, the substrate of the AF, if there is scar tissue, triggers, gender, the presence of valvular disease, left atrial size, and the technique. Dr Amin Al-Ahmad from the Texas Cardiac Arrhythmia Institute in Austin, US, explained that the treatment goal is electrical silence, to eliminate all electrical activity in the posterior wall, as part of the pulmonary vein (PV) ablation strategy.

Isolation is achieved in his practice at about 40 W, and typically with 5–10 g contact force (CF), but the catheter must continuously move and areas must be revisited. This approach to isolating the PV wall has been validated in meta-analyses for both paroxysmal and, even more so, persistent AF patients. Mitigating the risk to the oesophagus can be achieved by using a temperature probe that provides enough coverage of the oesophagus to be accurate, or even to move the oesophagus (although researchers are still trying to understand the safety and efficacy of this technique).

However, the question remains as to whether isolating the PV posterior wall is enough. Dr Al-Ahmad presented a case study that showed three of four PVs completely isolated after cryoablation. He asked attendees how they would manage the recurrence, and the audience was split between ablating the PV only, and ablating and looking for triggers.

“If you’re able to provoke arrhythmias, and you target those specific focal triggers, then you do indeed have some benefit in arrhythmia reduction. That’s been our strategy,” said Dr Al-Ahmad. “As we finish our AF ablation, we always look for PV triggers, and we document what they are. Now, if you take them for a third procedure, there are new PV triggers that are occurring – that tells us that this is a progressive disease. It makes sense. You can hit it for a while but ultimately new substrate does appear.”

In addition, pulmonary vein triggers are probably more important earlier in the disease progression and, as the disease progresses, non-PV triggers become more important. Techniques for eliciting them become the biggest challenge, along with how to target them for ablation successfully, efficaciously and safely.

Dr Al-Ahmad said the optimal extra-PV substrate ablation is complete isolation of the PVs, and his group includes the posterior wall of the left atrium. Then they identify triggers using high-dose isoproterenol and, if they can elicit triggers, they completely isolate the trigger substrate.
The availability of technologies for real-time contact for sensing has significantly advanced and invigorated techniques of catheter ablation of AF, particularly with RF energy. This session was an in-depth look at contact force and included a critical perspective of the head-to-head with cryoballoon ablation. The experts discussed their opinions on the use of contact for sensing to reduce or avoid lesion gaps, and highlighted the significant and evolving body of evidence of clinical outcomes, as well as the caveats of too much contact force during the AF procedure.

Relevance of Fire and Ice

AF is the most common arrhythmia with a prevalence >33 million patients. Approximately 40% are asymptomatic, and another 30% are effectively treated with anti-arrhythmia drugs (AAD). Of the remaining 30% who are symptomatic and with failed AAD treatment, just 4% are treated annually – amounting to 396,000 treated with catheter ablation, and leaving 22.7 million patients who have not been effectively treated by drugs or undergone catheter ablation.

There is a lack of consistency across Europe in numbers and rates of catheter ablation procedures. In these countries, said Prof Karl-Heinz Kuck of Asklepios Klinik St. Georg in Hamburg, Germany, electrophysiologists are discussing what to add to PVI. Countries with lower rates do not have access to catheter ablation or, if they have access, there are no clinicians available who know how to do it.

The development of balloon-based PVI is on the upswing, Prof Kuck suggested, because of the long learning curve, complexity, and challenge to create transmural, contiguous and permanent lesions with point-by-point ablation. He stressed that he is a strong supporter of CF-based catheter ablation, but this technique may not be optimal for every provider, especially given the widespread nature of AF.

There is no randomised controlled trial showing superiority of catheter ablation with contact force, compared to conventional RF catheter ablation, Prof Kuck explained. The only randomised trial that has compared a control group with a contact force group, aiming at non-inferiority, showed the same success rate when comparing the primary endpoints.

Ablation strategies that target the PVs and/or PV antrum are the cornerstone of most ablation procedures and, if the PVs are targeted, electrical isolation should be the goal. Furthermore, the new ESC guidelines recommend that catheter ablation should target isolation of the pulmonary veins using RF ablation or cryoballoon catheters. The radiofrequency catheter uses heat in a focal point-by-point delivery guided by electro-anatomical mapping, and cryoballoon uses freezing in a balloon single-step delivery guided by fluoroscopy without mapping. Prof Kuck explained the parameters for use of both techniques, and discussed the results of the largest cryoballoon versus RF ablation study ever performed and published. Cryoballoon ablation resulted in non-inferior mid-term efficacy compared with RF ablation at a median follow-up of 14 months, with significantly lower mean procedure times and lower left atrial (LA) dwell-time and lower costs. Pericardial effusion was higher in RF patients compared with cryoballoon, but phrenic nerve injury was higher in cryoballoon and there were no incidences of phrenic nerve injury in the RF group. Mean fluoroscopy time was 2 minutes lower in the RF group.

“The cryoballoon-based PVI approach in paroxysmal AF is non-inferior to the radiofrequency-based PVI with regard to frequency and safety, and superior with regard to re-hospitalization and re-ablation,” Prof Kuck concluded. “Novel balloon-based radiofrequency ablation systems combine direct visualisation of the anatomical substrate and, thereby, also new technologies for lesion formation. Permanent PVI can potentially be achieved to a high extent with a balloon technology… to my understanding, it’s the future of catheter ablation of AF, and the future is now.”

CF: What Does it Mean and How Does it Affect Lesion?

Traditional parameters of RF lesion control have been the target electrode temperature, delivered radiofrequency power in the power control mode, RF durattimes impedance-based control, and electrode-tissue contact – an important but hitherto unquantified parameter. In the previous era, contact was evaluated in various semi-quantitative ways: fluoroscopy, tactile feedback, electrograms, electrode temperature and impedance, and intracardiac echo.
"It is only over the last 7 or 8 years that real-time contact force sensing has been available, which has given precise control of lesion creation," said Prof Dipen Shah, from University Hospitals Geneva, Switzerland. Electrode tissue contact can be thought of as comprising of two components. The most important is the magnitude of the surface area of the electrode in direct contact with the tissue – the contact footprint.

Atrial tissue and the ventricle and myocardial tissue are soft, and as a rigid electrode is pushed into it, it gets more and more enveloped into the tissue. The second component is the stability of this contact, which can be considered as being composed of spatial stability (sliding of the tip electrode over the endocardium), and temporal stability, maintaining the intensity of the contact over time.

To quantify the contact pressure a catheter tip exerts on the tissue, the operator needs to know the exact surface area of contact. However, this cannot be assessed precisely. Experiments on ex vivo, porcine left atria showed that the same amount of force applied to different parts of the left atrium reduced the wall thickness by different amounts, depending on the thickness and tissue composition of the wall.27

A dynamic situation exists in vivo, including the effects of both cardiac and respiratory movement. To estimate a dynamically changing contact force over time, or at least its intensity, Prof Shah’s team formulated the area under the real-time contact force curve, termed the ‘force-time integral’, as a cumulative index of the amount of force over time. This allows, in one sense, a good measure of temporal stability whereas spatial stability requires precise, two-dimensional localisation capabilities with respect not to a stable extra-cardiac spatial reference such as a back patch, but with reference to the intra-cardiac endocardia, which we do not yet have.

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Research by Prof Shah and his colleagues determined the general effects of increased CF: increased electrode-tissue interface surface area; reduced electrode surface area exposed to (low impedance) blood; reduced electrode tip-sliding; tissue compression and thinning; tissue trauma; and higher tissue temperatures during RF delivery, including higher probability of a ‘pop’ and higher probability of extracardiac heating.28

To mitigate for risk, contact force sensors should be appropriately zeroed and re-zeroed after every reintroduction into the vascular system or through a sheath. It should be kept in mind that electromagnetic interference is likely to reduce the accuracy of this form of CF sensing. Catheter stability is important, and the composition of the atrial tissue should be kept in mind to reduce variances in lesion size.

Measuring CF remains important for recognising instances of absence of contact, reduction of ineffective ablations, better control of lesion size and repeatability, better arrhythmia-free outcome after PVI for paroxysmal atrial fibrillation (pAF) with optimal contact force, improved specificity for low-voltage substrate, reduced tissue trauma during catheter manipulation, and monitoring influence of respiration on contact, which Prof Shah thinks is an often-underestimated advantage of real-time CF sensing.

**Determinants of Gap in CF-guided PV Encircling**

Next, Prof Mattias Duytschaever from Bruges, Belgium, discussed CF-guided point-by-point PV encircling, and what determines a gap when CF has been used according to the ‘rules’. That is, if a patient has a reconnection in one or more veins, what has caused the gap, was there a weak link in the initial ablation chain and, finally, is it clinically relevant?

Prof Duytschaever presented an analysis of research on 42 paroxysmal AF patients who underwent contact force-guided PV encirclement. In the resulting 84 circles, 840 segments were identified, 44 of which had a gap. Segments with a gap were compared to durable segments without a gap.

Prof Duytschaever’s analysis defined the weakest link within each segment as the minimal time of application, power, delta impedance, CF, force-time integral and ablation index, and the maximal inter-lesion distance.

The ablation index is a formula that integrates power and contact force over time, taking into account the rapid rise of the lesion in the first seconds of the ablation, and a greater contribution of power.

"Inter-lesion distance seems straightforward, but don’t forget this is a new tool," said Prof Duytschaever. "Before, we could not reliably measure inter-lesion distance because we were just putting tags during our ablation."
“The key finding: the difference between a segment with a gap and no gap is a lower ablation index. Vice versa, where all the ablation indexes were to a high level of specificity, the difference between segments with gap and no gap is the inter-lesion distance. They are independent; if you combine both parameters, if inter-lesion distance and the ablation index are more than 400 at the posterior wall and more than 550 on the anterior wall, you have a 93 % specificity for predicting a durable segment.”

Building on these data, Prof Duytschaever’s research group explored the use of enclosing the PVs with ablation index-guided RF applications with an inter-lesion distance of <6 mm and found the reproducible, perfect circle “invariably leading to PV isolation, and that makes a big difference. We [also] consider the presence of the oesophagus – an ablation index of 300 is enough if I have signs of oesophageal injury. That is most of the time an application of around 8 seconds.”

There were two complications in 250 patients using this approach, neither conclusively linked to the procedure, and no significant adverse events.

Prof Duytschaever’s group has submitted a paper on the comparative data of the last 50 CF-guided patients versus the first 50 close-guided ablations with the strict criteria. They have reached near-100 % acute isolation rate.

This is very reproducible; colleagues who are now using this technique, all acknowledge that this is reproducible and superior to CF-guided ablation, he said. Prof Duytschaever’s results show rates of freedom from AF at 3, 6, and 12 months of 92 % in the close-guided group.

Prof Duytschaever concluded that acute and late gaps in contact force–guided PV encircling are due to insufficient lesion depth and/or discontiguity. The use of the strict-criteria ablation protocol results in a significant improvement in acute durability and arrhythmia-free survival. Nevertheless, real-time assessment of lesion formation remains one of the most important unmet needs in cardiac electrophysiology.

**Randomised Trials of CF Efficacy: A Critical Look at the Literature**

There have been five studies that have randomised patients to having the CF data either available to the operator or blinded to the operator (see Table 2). CF targets in each of the studies were ‘fairly modest’ at 5–20 g, and all except one involved a long waiting period of 60 minutes to watch for spontaneous reconnection. Most of these studies showed that using contact force shortened ablation time, decreased fluoroscopy time, and resulted in significantly fewer sites of acute reconnection. Complication rates did not differ significantly, but then these were infrequent overall.

**Table 2. Study Design**

<table>
<thead>
<tr>
<th>Patients/centres</th>
<th>Design</th>
<th>Target CF (g)</th>
<th>Wait time/Adenosine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimura et al. 30</td>
<td>CARTO-ST, blinded</td>
<td>10–20</td>
<td>Adenosine</td>
</tr>
<tr>
<td>Nakamura et al. 31</td>
<td>CARTO-ST, blinded</td>
<td>&gt;20</td>
<td>60 min+ Adenosine</td>
</tr>
<tr>
<td>Pedrote et al. 32</td>
<td>CARTO-ST, blinded No Lasso</td>
<td>&gt;10</td>
<td>30 min+ Adenosine</td>
</tr>
<tr>
<td>Reddy et al. 33</td>
<td>Tacticath+NAVX versus Navistar+ CARTO</td>
<td>≥ 10</td>
<td>30 min</td>
</tr>
<tr>
<td>Ullah et al. 34</td>
<td>CARTO-ST, blinded</td>
<td>None</td>
<td>60 min+ Adenosine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients/centres</th>
<th>Design</th>
<th>MDs</th>
<th>Prior PVI Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kimura et al. 30</td>
<td>CARTO-ST, blinded</td>
<td>2</td>
<td>&gt;200/ S CF cases</td>
</tr>
<tr>
<td>Nakamura et al. 31</td>
<td>CARTO-ST, blinded</td>
<td>4</td>
<td>Variable</td>
</tr>
<tr>
<td>Pedrote et al. 32</td>
<td>CARTO-ST, blinded No Lasso</td>
<td>2</td>
<td>&gt;300 CF cases</td>
</tr>
<tr>
<td>Reddy et al. 33</td>
<td>Tacticath+NAVX versus Navistar+ CARTO</td>
<td>47</td>
<td>–</td>
</tr>
<tr>
<td>Ullah et al. 34</td>
<td>CARTO-ST, blinded</td>
<td>7</td>
<td>'Experienced'/ &gt;30 CF cases</td>
</tr>
</tbody>
</table>

Source: Kimura et al., 2014; Nakamura et al., 2015; Pedrote et al., 2016; Reddy et al., 2015; Ullah et al., 2016

“However, what really matters is how these patients did on follow-up, and [the existing randomised studies show] absolutely no improvement in clinical outcomes,” said Dr Dhiraj Gupta of Liverpool Heart and Chest Hospital in the UK.

“That’s really a big disappointment. Why have contact force trials not shown clinical success? Why couldn’t they prove what most operators believe strongly to be true?”

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Dr Shinsuke Miyazaki of Tsuchiura Kyodo Hospital in Tokyo, Japan, explored the upper limits of contact force through the existing literature and the experience of his research colleagues.

The first study to investigate the catheter tip force required for mechanical perforation was performed on ex vivo porcine hearts. Researchers found that the perforation force was significantly lower in the RA than LA. In addition, the perforation force was significantly lower through the ablated tissue than through unablated tissue. The minimal perforation force was found to be 40 g. In another study using swine atrial chambers, 111 perforations were created in the RA and LA wall, with or without preceding RA delivery. Perforation of the atrial wall was seen over a wide range of contact force values, and the lowest perforation force was 77 g. RF ablation reduced the perforation force by 23 %.35

Another study investigated the perforation force of atrial tissue using a human heart and a porcine cardiac specimen and found similar results: the perforation force was lower in the RA than the LA; perforation after RF delivery required lesser force than after cryoablation and in ablated tissue; the use of larger tip size catheters significantly decreased the risk of perforation. Most importantly, the human atrial perforation force differed from those in porcine hearts: 38 g in the RA and 63 g in the LA, even in healthy human atrial tissue.36

Studies on the incidence of steam pop have found that, under constant RF power and RF duration, lesion size correlates with the contact force, and the incidence of steam pop increases with increasing contact force.37 Other studies have shown that, without knowledge from real-time contact force monitoring, transient high-contact force of >100 g was commonly observed, even among the experienced operators.38 In other trials, results indicate that >40 g of contact force should be avoided during RF ablation to prevent cardiac tamponade.39

Analysis of the five trials raised two issues:

- long waiting time (30–60 minutes) – poorer quality lesions created without contact force got a chance to manifest themselves and be re-ablated, thereby negating much of the benefit; and
- mandating either no CF targets or low CF targets (<20g) – this meant that in most trials, the average CF between the two groups was similar.

“If we’re just concentrating on contact force alone we’re missing the point,” said Dr Gupta. “Contact force data help determine how deep each lesion is, but it is equally important to have good contiguity between adjacent lesions. We know that force time integral is superior to contact force as a marker of lesion size. And power is an important component of lesion creation. If you use high power, contact force becomes less and less relevant. And that’s where ablation index comes in. Contact force is critical in ablation delivery but, at the end of the day, it’s only one ingredient in what is a very complex recipe.”

How much CF is too much force?

Dr Shinsuke Miyazaki of Tsuchiura Kyodo Hospital in Tokyo, Japan, explored the upper limits of contact force through the existing literature and the experience of his research colleagues.

After describing these published results, Dr Miyazaki turned to the experience at his institution, where in 3,483 patients and 5,222 procedures from 2002 to 2016, there have been 51 episodes of cardiac tamponade (0.98 %). CF-sensing catheters were used in 526 cases, 11 of which had cardiac tamponade (2.1 %). In all cases, two patients required surgical repair of tamponade (0.038 %). Based on this experience and the literature, Dr Miyazaki’s institution was able to determine parameters potentially associated with the risk of cardiac tamponade:

- CF during RF applications (power, duration) >40g;
- ablated tissue by RF;
- regional variations (tissue composition, underlying tissue);
- wall thickness and stiffness;
- catheter tip configuration and size, and type of catheter;
- catheter-tissue orientation;
- patient background, underlying atrial disease, scar tissue; and
- heart movement associated with contractions and respirations.

“We need to control the lesion size to avoid collateral damage, such as oesophageal injury,” said Dr Miyazaki. “And predicting the lesion sites in the vicinity of our already-ablated areas seems to be difficult due to the tissue oedema. So, we do not know exactly how deep of a lesion is necessary to obtain a durable lesion. There are multiple variable factors that impact on the risk of a perforation and steam pops during AF ablation. Therefore, an optimal CF range should be carefully adjusted considering these factors in individual situations.”
The first day’s final session put front and centre a debate that addresses an important clinical economical issue: can we discharge our AF ablation patient the same day instead of keeping him or her overnight?

The debate opened by asking the audience to use their interactive, hand-held devices and respond to the question: ‘Are we ready to move to 1-day hospitalisation?’ (see Figure 10).

**Protagonist**

Reasons for staying in hospital include rest and recuperation, the need for supportive therapy not available at home (e.g. IV pain relief, fluid), monitoring for serious complications, and cardiac rhythm monitoring. However, argues Prof Richard Schilling from Barts Heart Centre London, UK, this kind of support is rarely needed in some patients. For these appropriately selected patients, with the right planning, same-day discharge should become the norm.

Same-day discharge will help make AF more cost-effective and, therefore, more accessible. The median cost of AF ablation is $20,600 in the US, with the most expensive procedures costing more than $77,000. Analysis of US data has shown outcomes are not associated with cost and, in fact, the less-expensive procedures tend to be safer. Thus, for patients with limited lesions in the left atrium, same-day discharge could be employed to free up resources to be reinvested in more complex patients.

The most common serious complications of AF ablation are cardiac tamponade and vascular complications, and many other issues that cannot be prevented by keeping patients in overnight. “Monitoring alone isn’t a reason to keep them in,” said Prof Schilling.

In his practice, Prof Schilling selects only the least complicated patients for same-day ablation, and gives them the choice about how they would like to approach their procedures. If the patients are travelling a long distance, they are encouraged to stay in a nearby hotel before and after their procedures. The procedures are performed in a small, local hospital catheterisation lab by operators trained in a standardised method, using standardised equipment.

The observed 4.8 % complication rate with same-day AF ablation comprises five phrenic nerve palsies (1.9 %), two tamponades (0.7 %), three groin complications (1.1 %), two pericardial effusion with no drainage (0.7 %), and one temporary wire (0.4 %). At 3-month follow-up 58.0 % of patients had complete resolution, 30.4 % had improvement in their conditions, and 19.6 % requested repeat procedures for ongoing symptoms.

“IT’s not suitable for everyone, but day-case AF ablation is feasible for some patients,” said Prof Schilling. “It has significantly impacted our waiting times and ability to treat these patients earlier, and earlier AF ablation may result in better outcomes.”

**Antagonist**

Dr Helmut Pürerfellner from Linz, Austria, acknowledged that same-day AF ablation would be inherently less expensive, and it would be useful to free up money to take care of more patients. However, there is no good clinical data for same-day AF ablation, as it is being performed only in a limited capacity in a few countries, including Canada, the US, the UK and Switzerland. Furthermore, there is no support from any guidelines for same-day ablation, and there are “too many and too-complex potential risks”, especially those that are often delayed, including:

- bleeding (vascular access);
- tamponade;
- transient ischaemic attack/stroke;
- congestive heart failure;
- pericardial chest pain;
- nausea/vomiting;
- migraine;
- phrenic nerve palsy; and
- gastroparesis.

There could also be recurrent arrhythmias, including atrial tachycardia/AF, inappropriate sinus tachycardia, and sick sinus syndrome with bradycardia or pauses. The human factor, too, should not be discounted, for answering questions, providing reassurance and comfort, enhancing patient satisfaction and ensuring physician satisfaction.

“Seeing how my patient is faring the next day is something I need as a person and a physician,” said Dr Pürerfellner. “Should we adopt same-day discharge as standard clinical practice for AF ablation? In short, no.”

The follow-up audience vote was 31 % yes, 69 % no.
The first session of Day 2 focused on the importance of the target atrial tissue as opposed to the ablation energy of the tool, because wall thickness and tissue composition play almost an important a role as the energy. Presentations described lesion efficacy and disease substrate, information derived from electrograms, and innovative approaches to speeding of ablation times.

**Atrial Wall Thickness: The Missing Ingredient for Effective Tailored Ablation**

Left atrial wall thickness varies with atrial location, pathological state and age. It is a potential early marker of adverse atrial remodelling and the atrial wall is the primary ablation target, making wall thickness a relevant consideration in RF ablation success, said Prof Mark O’Neill from London, UK, opening Day 2.

Based on the available literature, the thickness of the atrial wall may have a role to play in perpetuation of AF. In limited studies of patients with AF recurrence, the atrial wall has been demonstrated to be thicker in some zones than in patients without recurrence, and as the degree of fibrosis (as estimated by voltage) increases, so too does atrial wall thickness. In addition, many studies of lesion formation show that lesion depth is at least 3–4 mm, sometimes 4–6 mm at powers, contact force and durations typically employed for AF ablation.41–45 The atrial wall may be 2–3 mm thick, and this must be taken into consideration.

To assess and validate atrial wall thickness, 3D atrial wall thickness maps were created to inform catheter ablation procedures for AF (see Figure 11). Prof O’Neill and his team have validated their method for measurements in porcine hearts.46 CT is currently the best non-invasive modality for wall-thickness assessment, a calculation that may provide a reproducible means for assessment of disease progression. Awareness of local wall thickness is likely to encourage less rather than more ablation in most locations.

“We have been able to demonstrate that the atrial wall thickness pertaining to the appendage is greater at the anterior aspect of the appendage followed by the superior, inferior and posterior aspects,” said Prof O’Neill.

The sites of reconnection are most commonly at the thickest site, the anterior site, followed by the next thickest, and so on. Where there was acute reconnection, this was more commonly seen in thicker than thinner atrial sites. More work is needed before recommending ablation targets identified using MR or CT-derived wall thickness information. There’s also a new area to explore. It is possible that an increase in left atrial wall thickness may in fact be an early marker of propensity to AF – earlier than fibrosis detected on an MRI scan – and something that could be more widely applicable to early detection of patients at risk of AF.

**Bipolar and Unipolar Electrogram Changes as In Vivo Marker for Transmural Lesion**

Dr Agustín Bortone of Service de Cardiologie Hôpital Privé les Franciscaines in Nîmes, France, spoke on unipolar and bipolar electrogram changes as in vivo markers of transmural creation. Several publications have shown that local electrogram amplitude reduction greater than 50 % is associated with the formation of transmural lesions (TL).47,48 However, the monitored bipolar (most commonly) electrogram from the tip to the first recording ring (tip-ring) extends beyond ablated tissues, reducing the effect of RF application on the monitored electrogram. In addition, other studies do not confirm the relationship between a halving of the electrogram amplitude and the creation of TL. Some show that achievement of split potentials rather than electrogram amplitude reduction is predictive of TL, while others argue that a signal amplitude reduction of 80% or even 90% is a marker of TL, rather than 50 %.49–51

Dr Bortone said that it seems logical to consider that the decrease in the amplitude of electrogram – either unipolar or bipolar – is correlated with the depth of the lesion and thus to TL achievement. However, with conventional catheters the electrogram analysed takes account of information that exceeds the treated tissue. There is a lack of specificity, and the percentage of exact reduction of the electrogram amplitude defining a TL is not clear.

Dr Bortone discussed and summarised the literature regarding these issues, and his analysis concluded that bipolar electrogram (BE) and unipolar electrogram amplitude reduction monitored by conventional catheters does not allow accurate TL creation assessment, in part because the perfect percentage reduction value is unknown. Bipolar
electrogram amplitude reduction monitored by mini electrodes appears
promising as a marker of TL creation. Unipolar electrogram morphologic
changes to complete a positive signal are clear, reproducible and
accurate markers of TL creation. BE morphologic changes are highly
variable and, therefore, very difficult to use as real-time markers
of TL creation. Transmurality is either functional and reversible, or
corresponds to a necrotic and irreversible state.

In conclusion, the association of the monitored BE reduction (plateau)
monitored by mini electrodes and the analysis of the morphologic
changes of the unipolar electrogram may improve our ability to assess
TL creation. The CF-sensing technology, as well as short-duration and
high-power RF applications may increase the probability of creating
transmural and necrotic (irreversible) lesions. The whole challenge lies
in creating transmural, irreversible and non-extramural lesions.

Can Short-duration and High-power RF Delivery be Safe and Effective?
Dr Elad Anter of Beth Israel Deaconess Medical Center in Boston, US,
asked why the incidence of PV reconnection remains high despite
adequate energy and tissue CF, and speculated that inadequate catheter
stability, especially over a relatively long duration of 20 to 30 seconds
may play a role by not necessarily creating tissue oedema. The answer
may lie in higher energy for a shorter duration, which could provide
more effective energy and, potentially reduced collateral injury.

Summarising numerous experiments in a thigh muscle preparation,
Dr Anter said: “The combination of 90 W for 4 seconds at 10–20 g
appeared to be effective and safe. These are the parameters that we
have taken to the beating heart.”

He has focused on applying these findings using the QDot Micro
Thermocoool Smarttouch SF. Dr Anter has found that high power and
short duration – 90 W and 4 seconds – of ablation can be effective
in atrial tissue. It produces full-thickness, irreversible cellular damage
that, in all PVs, including the left PV, are wider and more contiguous,
compared to standard energy delivery. The safety of this technology
requires real-time temperature monitoring, limited to 65°C, plus an
advanced irrigation technology. Collateral damage appears to be smaller
compared to conventional ablation, probably due to reduced conductive
heating.

Multimodality Assessment of the Atrial Fibrillation Substrate: Fat, Fractionation and LGE
Dr Saman Nazarian from the University of Pennsylvania, in Philadelphia,
US, explored the impact of the substrate components. He noted that
epicardial fat is associated with AF. Fat is metabolically active, releases
inflammatory cytokines and adipokines into the adjacent myocardium,
and exhibits rich innervation from ganglionated plexi in the proximity of the
PV ostia.

He and his team studied the epicardial fat distribution and examined
its association with electrogram properties. They noted that epicardial
adipose tissue is very strongly associated with bipolar voltage, and
it has a regional character, meaning that where there is epicardial
adipose tissue overlying that region, the bipolar voltage amplitude is
decreased. The geographic distribution of fractionated electrograms
also has a strong association with overlying epicardial fat.

Fibrosis is also associated with AF. There are different modes of
fibrosis: reactive interstitial fibrosis that separates muscle bundles,
and reparative fibrosis (final) that replaces dead cardiomyocytes.
The presence of fibrosis interferes with electrical continuity due
to non-conductive patches, slows conduction due to longer paths,
alters the balance of refractory and excitability properties, and may
anchor re-entry. Furthermore, due to fibroblast electrical coupling with
cardiomyocytes, fibrosis may promote ectopic activity.

“Surprisingly, right atrial fibrosis is also quite common; in fact, there’s
more fibrosis in the right atrial appendage compared to the left atrial
appendage. This brings into question the forgotten chamber when we’re ablating AF and the potential role of fibrosis in the right atrium,”
Dr Nazarian commented.

He went on to explain his work in image-based arrhythmia substrate
assessment, and its promise as a tool for arrhythmia management in the
era of ‘precision medicine’. Late gadolinium enhancement (LGE) on
CMR is associated with reduced voltage, decreased atrial function, and
decreased conduction velocity. The association of AF persistence with AF
recurrence post ablation is entirely mediated by the extent of fibrosis at
baseline. However, LGE on CMR does not distinguish reactive fibrosis (i.e.
potentially transient) versus replacement fibrosis, which is permanent.

“I wasn’t fully convinced of gadolinium imaging, but we started to see
these beautiful linear lesions following ablation, that not only show
ablation related scar but also highlight areas of pre-existing fibrosis,”
said Dr Nazarian. “Atrial function also closely associates with fibrosis
as measured by LGE. Passive atrial EF is closely associated with
fibrosis based on our data. Active EF is just on the border of statistical
significance. All strain parameters are also strongly associated with
the extent of late gadolinium enhancement.” These associations have
obvious implications for stroke risk stratification in the setting of AF.
Anticoagulation is a mainstay of the treatment of AF, particularly in the context of an ablation procedure. NOACs are used in the majority of patients today, and the presentations in this session discussed effective integration of anticoagulants into everyday practice, including catheter ablation. The recent availability of antidotes to these increasingly popular drugs has provided reassurance to providers, and attendees learned from expert opinion on when and how to use them.

Uninterrupted NOAC: What Does It Mean?
Dr Luigi Di Biase from New York, US, summarised primary studies on NOACs to date. He stressed that, either where uninterrupted warfarin or NOACs are used, heparin is still needed during the procedure. In the heart of his presentation, Dr Di Biase presented his anticoagulation protocol. First, all patients are on warfarin before the procedures to achieve 4–6 weeks of therapeutic international normalised ratio (INR) before ablation is performed. Patients undergo ablation procedure on warfarin with INR ranges from 2–3.

The protocol steps (see Figure 12):

- A bolus of 10,000 units unfractionated heparin in males and 8,000 in females is given before the trans-septal puncture.
- During the procedure, effort is taken to keep the activated clotting time (ACT) above 350 seconds.
- During the procedure, the trans-septal sheaths are continuously infused with heparinised saline.
- Every effort is taken to avoid air embolism.

In a multicentre, randomised study, use of this protocol showed that therapeutic INR protects against peri-procedural thromboembolic events in higher-risk patients. The risk of these complications during AF ablation is predominantly confined to patients with non-paroxysmal AF and, in particular, long-standing persistent AF. Therefore, Dr Di Biase said that future studies assessing the protecting value of newer anticoagulants should be performed in comparison with warfarin treatment, and should enrol patients with non-paroxysmal AF, as these events are relatively rare in paroxysmal AF patients. Recent data seem to suggest that, in patients undergoing AF ablation, uninterrupted rivaroxaban and apixaban provide similar stroke protection to warfarin. The results of another recent study showed fewer bleeding complications with uninterrupted dabigatran than uninterrupted warfarin and similar thromboembolic events.

“With the use of uninterrupted NOACs, a higher amount of heparin is necessary to maintain ACT above 350 seconds during the procedure,” concluded Dr Di Biase. “However, more data are needed with the newer anticoagulants to understand the safety in the presence of major bleeding complications and the role of other upcoming drugs.”

Figure 12. Anticoagulation Protocol

ACT = activated clotting time; AF = atrial fibrillation; INR = international normalised ratio; TOE = trans-oesophageal echocardiogram. Adapted from Di Biase et al., 2010.
The symposium’s final session was an overview of new technology, giving a teaser of upcoming evolutions to catheter ablation and AF management including new energies; individualised, patient-tailored modelling of ablation and disease therapy; truly high-density mapping; thermal modelling; and the latest innovations for PV isolation.

**Electroporation-assisted PVI**

Electroporation is a technology that Dr Fred Wittkampf, from Utrecht, the Netherlands, has been developing for 8 years. This is a method of creating holes in cell membranes; mainly electrically active cells in particular are targeted.

“It has been suggested that we are using a high-energy shock, but I can assure you that is an alternative fact,” joked Dr Wittkampf. “The energy we are using to isolate the PVs is only 14 joules per electrode, equivalent to approximately 0.5 seconds of RF.”

The non-thermal lesions are half-dome shaped, unlike RF lesions that are narrower at the surface of the tissue.

As with RF, tissue contact is essential. The electrode interface impedance is affected by tissue contact and can be measured in real time using a small bipolar current between neighbouring electrode pairs. Mechanical pressure sensors are not required.

During the circular electroporation impulse, the current density decreases linearly with distance from the electrodes as compared to an exponential decay with a point source as with conventional RF ablation. This difference explains the much deeper lesions that can be created with circular electroporation ablation. With sufficient circular contact, pulmonary vein can be isolated with one shot.

Electroporation can create stunning and transient block without recurrence within 30 minutes or an hour. The disadvantage, he pointed out, “is that you don’t know when to stop ablation. The advantage however, is that you don’t have to wait 30 minutes.”

There have been no incidents of pulmonary vein stenosis or other complications in animal studies during the development of this technology. Technical development, testing and approval has been completed; the protocol for a first human feasibility study, scheduled for the end of 2017, has been submitted to the Institutional Review Board, and a safety and efficacy study will take place thereafter.

**Computational Modelling to Guide Interventional Management of Atrial Fibrillation and Atrial Tachycardia**

At Johns Hopkins in Baltimore, US, Prof Natalia Trayanova and colleagues are trying to develop a non-invasive predictor of the targets for ablation of flutter or fibrillation. To achieve this, the patient undergoes pre-ablation MRI.

Image processing is done to outline the areas of fibrosis and structural remodelling, which lets the team create a computational model that helps predict the targets for eliminating the arrhythmia. The algorithm for creation of the model is based on the evidence of how electrophysiological remodelling affects persistent AF.

Prof Trayanova’s team is using this modelling technique predominantly for substrate modification in patients with severe fibrotic disease, particularly repeat patients who have fibrosis or structural remodelling from previous ablations. The goal is to create 3D, patient-specific models.

For example, in an atrial model, the team generates the model segmenting the geometry of the atria, delineating the fibrotic and non-fibrotic tissues. Patient-specific fibre orientations are incorporated, and the geometrical model is populated with all the different cell types.

“I can visualise everything from the dynamic of the proteins all the way to the whole organ,” Prof Trayanova explained.

“We can see when the fibrosis does not extend to the endocardia surface, and the other way around. The algorithm places points for pacing – at least 40 locations – and then we deliver stimuli from there to see whether arrhythmia has developed and what it looks like.”

Prof Trayanova then gave an overview of her team’s research. She presented case studies in which the model was able to accurately and non-invasively predict targets for ablation, including in patients who had undergone previous failed ablation.

She also discussed some of the challenges, including finding the best way to terminate a re-entrant driver with ablation. Over the course of research, the team has worked out the technical difficulties, and is now focused on improving the precision of target prediction.

**High-density Mapping: Too Much of a Good Thing?**

There may be some confusion in the definitions of mapping density and mapping resolution in the field of AF treatment. Dr Elad Anter of Beth Israel Deaconess Medical Center in Boston, US, explained the terms. Mapping density relies on the number of times the operator footprint goes over a surface.

Mapping resolution is influenced by electrode size and interelectrode spacing, so mapping with small, closely spaced electrode catheters can improve mapping resolution within areas of low voltage. High-density mapping allows the operator to better identify the entire circuit in a small area that otherwise would be difficult to record distinct electrograms within.
An interpolation limited to 5 mm or below will probably supply sufficient mapping densities, he said. However, for mapping resolution, notably with respect to electrode size and intra-electrode spacing, the point at which you get meaningful information needs to be studied separately.

Dr Anter questioned how much density and resolution we need in practice. Moving from 100 points to 500 points and 800 points provides a lot of information. Now, new mapping technologies are providing 10,000 points. Is this necessary? In many difficult cases, increased resolution enables us to determine where the circuit is, explained Dr Anter, but mapping resolution alone is often not sufficient for understanding the arrhythmia.

Dr Anter discussed a new algorithm that incorporates calculation of vectors and velocities in addition to activation mapping, in order to understand the global propagation of the arrhythmia. This algorithm is called CoherenceMap. The software, made by Biosense Webster, can improve mapping of scar-related AT, he said, noting that its novelty relies on its ability to identify areas of non-continuity.

**The Concept of Thermal Modelling**

The development of contact force has allowed a better understanding about what type of lesions are being created. However, there are still unknown variables with this new technology, for example angulation of the catheter, the catheter’s interface with the tissue, and temperature.

“Temperature is the result of everything else you do,” said Dr Tom De Potter, from Aalst, Belgium. “If you think about lesion formation as a thermodynamic process, you have certain input variables: energy, contact, interaction of the catheter to the tissue. Then there are modifying variables: tissue characteristics, tissue thickness, blocked flow. A temperature is the result of all this, ultimately leading to the necrosis you want to generate.”

Thermal modelling aims to understand this process, determine the temperature evolution within the tissue, measure tissue temperature and impedance, and estimate catheter-to-tissue pose and temperature field. Software simulates the temperature field based on different models of reality, models of human tissue, and on observed parameters such as contact force and catheter position.

Not only does this give a simulation model of what may be happening in the real world, it tries to make the most accurate prediction of the actual ablation forming under the catheter tip. By using the measured temperature as an input variable for the model, it has the potential to simulate on-going lesion formation and to better guide physicians in optimal energy delivery.

Dr De Potter described in depth his experience with the use of thermal modelling system, integration with existing 3-D visualisation technology, its validation of ablation targets, and the research and literature supporting its use.

“We’ve shown that it’s possible for software to make a thermodynamic model of RF lesion formation that correlates really nicely with animal data,” said Dr De Potter. “A closed-loop system can solve the unknown variable of tip-tissue interaction by using the measured temperature at the tip/tissue interface. Initial clinical experience has improved the algorithm and led to very insightful new research in biophysics. Ultimately, if we can accurately model lesion formation, we should be able to optimise energy titration in individual positions.”

**Latest Innovations for PVI Tools**

Prof Vivek Reddy of Mount Sinai Hospital in New York, US, described and recapped the newest technologies available for PVI, in four categories: balloons, advances in point-ablation technology, novel global ablation systems, and irreversible electroporation.

A multicentre, single-arm, first-in-human feasibility study recently showed the RF balloon catheter could deliver directionally tailored energy using multiple electrodes for efficient acute PVI in patients with paroxysmal AF. Results showed the RF balloon catheter was able to achieve electrical isolation of all pulmonary veins with a high rate of first-pass isolation and low evidence of latent pulmonary vein re-conduction. The procedural performance with the device was favourable, with 100% of the treated pulmonary veins electrically isolated without the need for a focal ablation catheter.

“Existing balloon catheters are limited in a number of ways, the most significant limitation being a single ablative element that delivers identical amounts of energy along the full pulmonary vein ostium circumference,” said Prof Reddy. “This can lead to over-ablation of thin tissue, under-ablation of thick tissue, and unnecessary complications. The investigational RF balloon is designed to both optimise safety and efficacy and reduce procedure time.”

The emerging technologies discussed in the symposium show great promise for advancing efficacy of PVI, speed of lesion creation, more accurate target predictions and more. Despite the excitement generated by these innovations, Prof Reddy reminded the audience that, with technological improvements come learning curves and potential for complications.

“My biggest concern is oesophageal damage, and my very strong recommendation for that, based on evidence and experience is mechanical oesophageal deviation,” said Prof Reddy. “In addition, how much ablation is too much? We all want 100% success with one procedure, and may believe we should ablate more potential targets. But I think we must start thinking about the cost to left atrial function. At some point, we’re going to have to ask: If you get a 5% or 10% increase in success, how much atrial function can you lose to justify that? And does it make sense to subject everybody to a very extensive strategy if only a subset need the strategy?”

Weighing the costs and benefits in terms of LA function will be a necessary focus of research and practice as technology continues to develop and evolve in this era of patient-specific ‘precision medicine’.
Prof Mattias Duytschaever from Bruges, Belgium, closed the 16th Atrial Fibrillation Symposium by thanking the presenters and attendees for the fruitful discussions, and interactive and insightful learning.

“We’ve had two exciting, fascinating days of research, a mixture of basic and clinical electrophysiology of atrial fibrillation with these very interactive and dynamic panel discussions,” he said. “It is clear that there are large gaps in the evidence regarding treatment of persistent or permanent atrial fibrillation, or whatever ‘P’ you use in your taxonomy. We still have to go a long way in persistent, permanent atrial fibrillation. For me, it’s clear that we need advanced, electro-anatomical mapping. But I do believe that we are closing the gap towards durable PVI.”

Prof Duytschaever thanked Biosense Webster for their continuing efforts to improve catheter ablation, support of trials, and commitment to education that moves the field forward. He thanked his colleagues on the planning committee, Prof Mark O’Neill from London, UK, and Prof Dipen Shah of Geneva, Switzerland.

“We hope to see you next year for the 2018 Atrial Fibrillation Symposium, on 7-9 February in Prague,” he concluded.
Save the date!

10th Atrial Fibrillation Symposium Practical Sessions
17th Atrial Fibrillation Symposium

Edition 2018
7-8-9 February, Prague
Atrial Fibrillation Symposium


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1. Luther, V. et al. A Prospective Study of Ripple Mapping in Atrial Tachycardias. CIRCEP. 2016

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