Electrophysiological Evaluation of Pulmonary Vein Isolation

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Abstract
Since the pulmonary veins (PVs) were identified as a major source of AF triggers, ablation strategies targeting the PVs have evolved from focal ablation inside the PVs to wide area circumferential PV isolation (PVI) which at this juncture is the standard approach. Despite the widespread popularity of PVI, a universal definition is lacking. While “entrance block” is a generally accepted endpoint for PVI, the role of “exit block” has yet to be determined. Inexcitability of the circular ablation line has been introduced as a promising additional endpoint for PVI and was associated with an improved clinical outcome in a randomized trial. Correct interpretation of PV electrograms during an ablation procedure is critical in terms of efficacy and safety. A variety of electrophysiological techniques help to correctly differentiate components of complex PV electrograms. Resumption of PV conduction after initially successful PVI leading to AF recurrence remains a major problem and confirmation of bi-directional conduction block does not exclude reversible tissue damage along the ablation line. Prolongation of post-PVI monitoring and application of provocative procedures such as the administration of adenosine after initial PVI to unmask dormant PV conduction may improve clinical outcome although there is lack of valid data supporting these strategies. This article aims on clarifying the electrophysiological criteria for complete pulmonary vein isolation and the explain the importance of this cornerstone in almost all atrial fibrillation ablation procedures.

Introduction
Percutaneous catheter ablation has emerged as an established treatment option for symptomatic, drug-refractory atrial fibrillation (AF). Since the pulmonary veins (PVs) were identified as a major source of ectopic foci initiating AF, catheter ablation strategies aimed at PV trigger elimination have evolved from focal ablation inside the PVs to wide-area circumferential PV isolation (PVI) which at this juncture is the most widely accepted strategy. The popularity of PVI is related to several factors, including a clear pathophysiological explanation, the reproducibility of the procedure, and the convincing performance of PVI which is documented in clinical trials. This review will focus on electrophysiological principles and techniques relevant to the evaluation of PVI in daily clinical practice.

Role of Pulmonary Veins in AF
It is well known that the PVs are a main source of ectopic foci capable of triggering episodes of AF. These focal discharges may emanate from multiple sites within a given PV or from multiple PVs in one individual. Several lines of evidence indicate that the PVs not only act as triggers of AF that continue independently after initiation but also participate in the maintenance of AF. Jais et al. reported on a small series of patients with AF resulting from a sustained episode of focal rapid firing (so-called “focal AF”) that could be successfully eliminated by discrete radiofrequency (RF) ablation. Another mechanism by which the PVs may perpetuate AF is the occurrence of intermittent bursts of rapid electrical activity (also referred to as “PV tachycardia”) during ongoing episodes of AF which act as drivers of the fibrillatory process. These PV tachycardias are characterized by shorter cycle lengths compared to the adjacent LA. Further evidence of the key role of the PV in maintaining AF is derived from the observation that AF reproducibly terminates during RF application at the LA-PV junction. The presence of sleeves of left atrial musculature extending onto the outer aspect of the PVs to a variable length has long been recognized. These extensions can be found on all PVs and exhibit a highly variable architecture with frequent circumferential discontinuities. The thickness of the sleeves is highest at the LA-PV junction and then gradually decreases distally. The sleeves are comprised of predominantly circularly or spirally arranged bundles of myocytes interacting with additional bundles showing a longitudinal or oblique orientation, occasionally forming a “mesh-like” arrangement. Although yet not fully understood, PV arrhythmogenicity is related to the complex arrangement of myocardial fibers and specific electrophysiological properties of myocytes within the sleeves. A variety of experimental and clinical studies suggest spontaneous impulse formation due to abnormal automaticity or triggered activity, and (micro-) reentry as potential mechanisms of PV activity.
Historical Considerations

Since Haïssaguerre and co-workers described the pivotal role of PV triggers in the initiation of AF, ablation strategies targeting the PVs have undergone profound modifications. Initially, focal trigger elimination was performed within the PVs at the site of earliest activation. This concept of “focal ablation”, however, has been largely abandoned due to a low long-term success rate, the considerable risk of PV stenosis, and the lack of a clearly defined procedural endpoint. These limitations have encouraged the development of two alternate ablation strategies: (1) segmental ostial PVI and (2) circumferential PV ablation (CPVA). Segmental ostial PVI is an electrophysiologically guided technique aimed at electrical disconnection of the PVs at the level of the PV ostium. PVI is achieved by sequential RF delivery at ostial sites showing the earliest bipolar PV potential or the most rapid intrinsic deflections in the unipolar electrograms. With this technique, approximately 50% of the ostial circumference is targeted. CPVA, initially described by Pappone et al., is an anatomical approach to encircle the PVs by ablating on the atrial aspect of the LA-PV junction under the guidance of a non-fluoroscopic 3-dimensional electroanatomical mapping system. Ablation line continuity was originally defined by voltage abatement within the encircled areas and a pre-defined activation delay between contiguous points lying in the same axial plane inside and outside the ablation line. This approach by design does not involve verification of PVI, and it could be demonstrated that only 55% of PVs were isolated after CPVA. Subsequently, Ouyang et al. demonstrated the feasibility of complete isolation of the PVs with continuous circular lesions placed around the ipsilateral PV pairs guided by the double-Lasso technique and 3-dimensional mapping. Comparisons between different ablation strategies are limited. Two randomized studies comparing segmental ostial PVI and CPVA showed conflicting results. In a randomized study by Arentz et al., circumferential PVI was associated with a significantly higher clinical success rate than segmental ostial PVI. The superiority of circumferential PVI was related to the larger left atrial area encompassed by the circumferential lines containing proximal AF triggers, rotors that may act as drivers of AF, and autonomic plexi. The recognition that the PV antrum plays an essential role in the generation and perpetuation of AF and that targeting the tubular portion of the PV is still associated with risk of PV stenosis led to a shift of the lesion set away from the PV ostia towards the left atrium (LA) thereby including portions of the LA posterior wall, of the posterior septum, and of the LA roof. However, the exact mechanisms underlying the effect of PVI on AF arrhythmogenesis remain to be established. An explanation for this effect must take into account the complex and poorly understood nature of AF initiation and perpetuation, especially in patients with persistent or long-standing persistent AF. Although controversy still exists regarding the strategy for catheter ablation of AF, circumferential/antral PVI is preferentially performed in the majority of centers.

Endpoints of Pulmonary Vein Isolation

There is consensus that ablation strategies targeting the PVs or the PV antrum form the cornerstone for the majority of AF ablation procedures and that PVI should be the primary endpoint of these procedures. In patients with paroxysmal AF, PVI alone is the most commonly applied technique to isolate PV triggers and modify the substrate within the PV antrum. In patients with persistent or long-standing persistent AF however, a more extensive ablation protocol may be necessary to improve rhythm outcome because triggers and perpetuators outside the PV antra are additional, dominant factors for arrhythmogenesis. PVI may be combined with additive strategies of substrate modification including the placement of additional linear lesions, the ablation of non-PV triggers in both atria, the ablation of complex fractionated atrial electrograms, and the ablation of ganglionic plexi. However, the incremental therapeutic benefit of these adjuvant strategies has not been determined. Despite the central role of PVI during an AF ablation procedure, However, a universal definition of PVI is lacking. While “entrance block” into the PV is well defined as elimination of PV potentials distal from the ablation line, and is generally accepted as an endpoint for PVI (see figure 1), “exit block” is not. Only a minority of leading electrophysiologists rely on the value of the additional evaluation of “exit block”, i.e. failure to capture the LA during sinus rhythm while pacing at high output from the biopoles of a circular mapping catheter (CMC) placed distally from the ablated area. There are several explanations for this real-world scenario. Entrance block is frequently considered indicative of bidirectional conduction block which renders evaluation of exit conduction dispensable. Appropriate evaluation of exit block (see figure 2) may be impeded.

Figure 1: Electrograms during PV isolation. Map 1-2 is the bipolar electrogram from the tip of the ablation catheter, Map 1 is the unipolar electrogram. Before ablation (I), during ablation (II-III) and after achieving entrance block the PV (IV). Note: already after few minutes of ablation the LA-PV junction may be crossed (II). The ablation catheter is placed at the ostium of the PV; the bipolar electrogram in (III) is already suggestive for isolation, but on spiral catheter there still is a delayed PV spike on “Lasso 5/6” recorded.
beats or sustained tachycardias, within the isolated PVs is generally accepted as valid surrogate of exit block (see figure 3). However, dissociated rhythms are not constantly present throughout an ablation procedure. It might be assumed that verification of exit block may be helpful to overcome these uncertainties. The controversy of “exit block” assessment is reflected by the recommendation by current Expert Consensus “that achievement of electrical isolation requires, at a minimum, assessment and demonstration of entrance block into the PV”.

A novel pacing technique to assess ablation line completeness has been independently proposed by two feasibility studies. After initial encircling of the ipsilateral PV pairs at the antral level, high-output pacing was employed during sinus rhythm from the tip of the ablation/mapping catheter to detect residual excitable gaps while following the circumferential lesion set. If capture to the LA occurred during pacing at a certain point of the ablation line, additional RF energy was applied until loss of capture could be demonstrated. After the whole circumference of the circles had been rendered unexcitable, the endpoint of “loss of capture” was validated against conventional evaluation of bi-directional conduction block using a CMC. In the study by Eitel et al. including 147 patients with symptomatic paroxysmal and persistent AF, the mapping/ablation catheter and CMC were sequentially advanced into the LA via a single transseptal access. Bi-directional conduction block was found in 95 % of patients after loss-of capture along the circles had been achieved. Similar results were found by Steven et al. who reported that bi-directional conduction block confirmed by a CMC was found in 95 % of vein pairs after loss-of capture along the circles had been achieved.

The clinical significance of this new technique could be demonstrated in a subsequent two-center study including 102 patients with symptomatic, drug-refractory paroxysmal AF. After entrance block had been achieved, capture to the LA during pacing on the encircling ablation line could be found in 50 % of vein pairs suggesting that residual gaps in the ablation line that may promote AF recurrences or increase the risk of iatrogenic macro-reentrant tachycardia would have been left if entrance block would have been applied as the only criterion to define PVI. The validity of entrance block depends upon precise detection of electrical activity from residual bi-directionally conducting myocardial connections and correct interpretation of PV electrograms. Additionally, dissociated activity, i.e. single ectopic

Figure 2: Pacing from spiral catheter (Lasso, red arrows). The atrium (decapolar catheter in the coronary sinus, CS) is not capturing the frequency of stimulation. On spiral 7/8 an electrogram ("local capture") can be recorded after every stimulus (blue arrows). This means that the antral musculature distal to the ablation line is excited by the stimulus, but this is no longer transmitted to the atrial myocytes.
pacing along the ablation line (see figure 4). After a mean follow-up of 18 ± 6 months, significantly more patients in the pace-guided group were free from AF recurrence or atrial tachycardias after a single procedure as compared to the conventional group, without additional use of class I or III antiarrhythmic drugs in either group (83 % versus 52 %, \( p=0.001 \)). Procedure duration was significantly longer in the pace-guided group whereas no statistically significant difference could be found for fluoroscopy time. Loss of capture along the lesion set was confirmed by a CMC in 97 % of PV pairs.

The results of these studies consistently demonstrate the feasibility of achieving bi-directional conduction block with the technique of “pace-guided” RF delivery along the ablation line, also referred to as “pace-and-ablate” approach.\(^{35,38}\) Furthermore, unexcitability along the circles seems to be superior to a conventional approach using a CMC for the assessment of bi-directional conduction in terms of freedom from arrhythmia relapses. As AF recurrence predominantly result from PV reconnection after initial PVI the considerable difference in clinical outcome may at least be partially explained by the creation of more durable lesions when unexcitability is applied as an additional endpoint.\(^{36,40}\) This is supported by an animal study that demonstrated that loss of pace capture was significantly associated with uniform and transmural lesions.\(^{41}\) Interestingly, local electrogram characteristics were not able to reliably identify sites of pace capture due to a substantial overlap of amplitudes between excitable and non-excitable sites.\(^{35,39}\) This is in line with the observation that pace capture after ablation is often still encountered in locations with significantly decreased or fractionated potentials.\(^{42}\) In summary, available data strongly suggest the incorporation of “loss of capture” as an additional endpoint of ablation procedures.

### Pulmonary Vein Electrograms

Usually, PVI is assessed using a variable loop CMC placed distally to the ablation line at various levels within the PV-LA continuity. Closely spaced bipolar CMCs have the advantage of a more effective far-field rejection and better discrimination of near-field potentials from far-field potentials, but at the expense of an increased risk for underdetection of PV potentials.\(^{43}\) Correct positioning of the CMC within the PV and stable contact to the PV wall are crucial for proper recording of PV electrograms. Since knowledge of the highly variable PV anatomy greatly facilitates PV mapping, pre-procedural (e.g. computed tomography, magnetic resonance imaging) or intra-procedural (e.g. selective venography, rotational angiography, intracardiac ultrasound) imaging is helpful to define the complex 3D anatomy of the PV antra and the LA-PV junction.\(^{44}\)

Precise understanding of PV electrograms prior to and after lesion placement is critical to verify conduction block and to avoid unnecessary ablation that may increase the risk of peri-interventional complications such as PV stenosis, thromboembolic events, or phrenic nerve injury. During sinus rhythm or atrial pacing, the activation of neighboring structures usually precedes PV activation. This electrical activity of non-PV sources can be recorded from within the PV. Therefore, a PV electrogram composed of at least two components can be recorded on a mapping catheter placed in the PV. The initial component is a far-field potential representing electrical activation of adjacent myocardium that is followed by the PV potential after an isoelectric period of variable duration (“delay”).\(^{43}\) Bipolar PV potentials display typical near-field characteristics, i.e. a high-frequency electrogram with a sharp upstroke, a short duration (< 50 msec), and an amplitude > 0.05 mV.\(^{45,46}\) In sinus rhythm or during atrial pacing, PV potentials demonstrate a proximal-to-distal activation sequence that is reversed in the event of spontaneous ectopic activity originating in the PV or during distal PV pacing. PV potentials can be recorded on a CMC circumferentially or at segments distant from potential far-field sources.\(^{31}\) As opposed to PV potentials, non-PV sources exhibit far-field characteristics with lower amplitudes and slopes, typically a non-circumferential distribution on a CMC determined by the anatomic relationship of

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**Figure 3:** 2 forms of dissociated activity in the PV after isolation (red arrow). In the left panel a slow “idio-venous” rhythm is recorded (frequent), in the right panel there is an ongoing PV-tachycardia with no conduction to the atrium.
PVs to surrounding cardiac structures, and stable activation timing when mapping is performed more distally within the PVs.31,45,46

Due to the close anatomic proximity of PVs and adjacent electrically active cardiac structures, far-field potentials may arise from the ipsilateral PVs, both atrial, the SVC, and the ventricles. As the left superior PV (LSPV) is situated behind the posterior wall of the LAA, far-field potentials predominantly originate from this wall and are restricted to the anterior bipoles of the CMC. In left inferior PV (LIPV) extra-PV signals mainly arise from the low lateral LA and less commonly from the LAA as this vein takes off below the level of the LAA.31 As the right superior PV (RSPV) passes next to the posterior aspect of the right atrial-SVC junction, myocardial sleeves covering this structure are the major source of far-field signals and can be recorded from the anterior-superior aspect of this vein.47

The right inferior PV usually projects downward and backward remote from electrically active tissue and thus extra-PV sources rarely contribute to PV electrograms.31 In the left-sided PVs, PV potentials have a higher amplitude and slope and as compared to the atrial components, however, due to significant overlap of amplitudes and slopes these parameters do not reliably differentiate between these two components.45 As for the left PV’s, PV potentials in the RSPV were greater than those of the atrial component. Additionally, in the left-sided PVs, atrial potentials were significantly wider than PV potentials, have a negative polarity in bipolar electrograms, and have slower upstrokes and downstrokes than the PV potentials in unipolar electrograms.46

**Electrophysiological Techniques to Distinguish PV Electrogram Components**

During an ablation procedure, correct interpretations of PV electrograms may provide considerable challenges to the electrophysiologist as PV electrograms frequently do not show the above mentioned “standard” pattern with a clear separation of components by an isoelectric interval. This summation of simultaneous electrical activity of PVs and extra-PV structures may produce a single potential, closely spaced double potential, or complex fragmented electrograms rendering appropriate distinction of potentials difficult. Additionally, PV electrogram morphology may change during an ablation procedure thereby resembling far-field potential characteristics. Technical obstacles for proper signal interpretation such as poor mapping catheter contact or mapping too distally in the PV should be carefully excluded.

Activation mapping is a useful tool that can easily be applied by placing a mapping catheter at the anatomical site suspected to be the origin of far-field potentials.43 If, for example, far-field signals from the LAA are present during mapping of the LSPV, only potentials recorded from a mapping catheter placed at the posterior wall of the LAA coincide with the far-field signal of the LSPV electrogram.45 Similar maneuvers can be performed for the LIPV and the RSPV by placing the mapping catheter at the low LA or at the posterior aspect of the SVC. In a prospective study including 114 patients undergoing electrophysiologically guided ostial PVI, low-amplitude far-field signals originating from the SVC were recorded in 23 % of patients.45 Due to the close anatomical relationship, sinus node and SVC activation is almost simultaneous whereas the activation of the RSPV occurs after a delay of 20-50ms.31,47 An SVC potential could be identified by a deflection earlier than 30 ms from onset of the sinus P wave with a sensitivity of 92 %, a specificity of 100 %, a positive predictive value of 100 %, and a negative predictive value of 89 %.

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**Figure 4:** Principle of “Pace & Ablate”-approach: a stimulus (10V/1ms) is given from the ablation catheter (green tip), ablation is initiated, after 3 stimuli with conduction to the LA the 4th and 5th stimulus is blocked. Simultaneously, the small remaining PV electrogram on Spiral 5/6 is disappearing (blue arrows) at beat 4 and isolation is completed. In the map the CS catheter (yellow) and the esophageal probe for assessment of intraluminal temperature (light blue) are visualized.
In case of uncertainty, dedicated pacing maneuvers can help to identify the components of a fused signal or the origin of a given single potential [Asirvatham, 2007; Shah 2002]. These maneuvers include (1) decremental pacing, (2) pacing maneuvers modifying the atrial activation sequence, and (3) pacing maneuvers to identify the extra-PV contributor of PV electrograms. Decremental pacing, i.e., pacing from the atria or the coronary sinus (CS) at increasingly shorter cycle lengths, may split the components of a fused signal or delay a PV potential as the PV ostium frequently exhibits decremental conduction properties. Alternatively, programmed atrial stimulation with a single extra-stimulus may be applied in order to produce or accentuate a delay between potentials. Separation of electrogram components may be also achieved by changing the direction of the propagation wavefront as variations in the interval between recorded potentials are related to differences in relative activation times from the atrial pacing site into the PVs and extra-PV locations, respectively. This might be accomplished by pacing from different sites in the atria at the same cycle length (differential pacing) or by pacing from the CS and the LAA. Identification of the contributing non-PV source may be achieved by pacing from an atrial site close to the PV or at/in the suspected extra-PV source. When pacing from a site generating a far-field potential is performed, this signal moves closer to or merges with the pacing stimulus.

In a study by Shah et al., single potentials were found in 63% of patients in the LSPV and in 70% of patients in the LIPV during sinus rhythm. During CS pacing, separation of potentials could be produced in the LSPV in all patients and in the LIPV in 80% of patients. For the LSPV, distal CS pacing was associated with a shorter activation time of the far-field component and a more pronounced separation of the signals as compared to proximal CS pacing. Pacing from the LAA led to fusion of the far-field component with the pacing artifact and to a greater separation of the recorded electrograms compared to distal CS pacing. For the LIPV, no significant difference with respect to separation of the signals could be observed for either CS pacing sites or LAA pacing. Contrarily, CS pacing is associated with a significant increase in the percentage of RSPVs with overlapping signals. In a study by Iwasa et al., identification of PV potentials in the RSPV could be significantly more often accomplished during sinus rhythm or pacing from the high right atrium as compared to pacing from the CS. Additionally, pacing from within the PVs has been shown to be highly effective in identifying PV potentials. The reproducibility of this approach, however, is limited as capture of the PV musculature can be difficult particularly after (inadvertent) ablation within the PVs had been performed.

Evaluation of PVI should be preferentially performed during sinus rhythm as it facilitates discrimination of potentials and allows for the evaluation of exit conduction or pace capture along the ablation line (if desired). Occasionally, stable sinus rhythm cannot be restored after encircling of one or both PV pairs, thus PVI has to be studied during ongoing AF or atrial tachycardia. If far-field potentials are absent, entrance can be easily ascertained by the electrical silence on the CMC with or without interspersion of dissociated electrical activity. Of note, dissociated activity should not be confused with high-grade conduction block from the LA into the PVs. Identification of the contributing non-PV source may be achieved by pacing from an atrial site close to the PV or at/in the suspected extra-PV source. When pacing from a site generating a far-field potential is performed, this signal moves closer to or merges with the pacing stimulus.

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Figure 5: Screenshot from a PVI procedure: the registered 3D reconstructed CT (grey shell) is displayed; the spiral catheter (red) is placed in the RSPV, the red electrograms show a regular PV tachycardia after administration of adenosin; the CS is in stable sinus rhythm (yellow electrograms); the RSPV is isolated.
by activation mapping as described above, i.e. by placing a second mapping catheter at or close to the suspected source to search for coincidental potentials. Nevertheless, PVI should be carefully re-evaluated after restoration of sinus rhythm.

Assessment of Early Reconduction

Despite the well-established clinical efficacy of ablation procedures targeting the PVs there is still a substantial rate of AF recurrence after index complete PVI necessitating repeat interventions to achieve long-term success. During “traditional” point-by-point RF ablation, single focal lesions were sequentially placed in the complex 3D anatomy of the PV-LA junction and the PV antra, respectively. Thus, among other factors, anatomic challenges and inappropriate catheter-tissue contact may impede durable disruption of PV conduction. There is a large body of evidence that recovery of conduction to and from previously isolated PVs constitutes the major mechanism of AF recurrence rather than new arrhythmogenic substrates. PV reconnection occurred in about 80% of patients with AF recurrence who underwent repeat ablation after successful PVI during the index procedure. Interestingly, no recovery of PV conduction was observed in volunteers who were free from arrhythmia recurrence after the first ablation procedure. The discrepancy between the incidence of acute PVI and chronic PVI may be explained by ablation-mediated reversible tissue injury with edema or thermal stunning leading to transient conduction block across the ablation line. It is evident that RF delivery leads to depolarization of the resting membrane potential thereby rendering the myocytes unexcitable. Studies on human and porcine models indicate that tissue edema may extend beyond the site of ablation. In a cohort of 25 patients undergoing AF ablation, sequential MRI scans revealed that electrical PVI defined as entrance block into the PVs was achieved by a combination of reversible and irreversible tissue injury. The hypothesis that acute electrical PVI results from an interplay of temporary and permanent tissue injury is supported by findings from a study by Miller et al. including 28 patients undergoing catheter ablation for paroxysmal or persistent AF. Contiguous RF lesions were placed in a point-by-point fashion circumferentially around the ipsilateral PV pairs. RF application was halted as soon as entrance block was documented on a CMC and intentional “visual gaps” were left in the ablation line. After confirmation of exit block, pace capture along the visual gaps could be observed in 68% of tested PVs and two-thirds of adenosine-induced PV reconnections were through the visual gaps. These data strongly suggest that established techniques to define PVI are unable to identify reversible hyperthermal tissue image. Two strategies have been reported for the early detection of PV re-conduction after an initially successful PVI. One consists of re-evaluating conduction over primarily isolated PVs after a pre-defined wait period (usually 30 to 60 minutes after PVI). During that waiting period early PV reconnection has been observed in up to 50% of PVs with the majority of recurrences occurring within 30 minutes. It therefore seems quite logical that identification of acute PV reconnection by prolonging the monitoring period followed by additional ablation of conduction gaps may improve lesion durability and rhythm outcome. However, data from two randomized trials investigating the clinical benefit of a post PVI waiting period showed inconsistent results. In the study by Wang et al., 90 patients with paroxysmal AF were randomly assigned to a waiting period of 30 and 60 minutes, respectively, with re-isolation of reconnected PVs, or to no prolonged monitoring after antral PVI had been achieved. During a mean follow-up of 6.7 ± 2.3 months, significantly more patients were free from atrial tachycardias in the “waiting groups” as compared to those without prolonged monitoring (84% and 87%, respectively, versus 61%, p=0.04). These results could not be confirmed by Baensch et al. who randomized 107 consecutive AF patients to a waiting period of 60 minutes or to immediate termination of the procedure after PVI. After 9.6 ± 4.3 times follow-up, similar rates of freedom from any arrhythmia could be observed in both groups. Generally, the potential benefits of adding a waiting period after PVI have to be balanced against the risk of prolonged procedure duration and practical considerations including the workflow in the electrophysiological laboratories. Current Expert Consensus recommends that “monitoring for PV reconnection for 20 minutes following initial PV isolation should be considered”. The second strategy is based on pharmacological provocative maneuvers to unmask latent PV conduction. Adenosine, isoproterenol, and ATP have been used to reveal dormant PV conduction. Adenosine and isoproterenol reverse RF-mediated depolarization and restore excitability of the myocytes by hyperpolarizing the resting membrane potential. Whilst adenosine-induced hyperpolarization of the resting membrane potentials is mediated by selective activation of the IK Ado inward rectifier current, isoproterenol actions on the resting membrane potential are related to multi-channel effects. Adenosine is superior to isoproterenol in uncovering dormant PV conduction clinically and experimentally because of greater adenosine-induced hyperpolarization. A recently published meta-analysis of non-randomized studies suggests that patients undergoing routine testing without adenosine/ATP (see figure 5) followed by ablation of conduction gaps have a higher freedom from AF relapses compared to patients without drug challenge. Nevertheless, only a minority of leading electrophysiologists employ provocative means as a routine clinical tool, which is at least partially related to the lack of randomized clinical trials.

Conclusions:

AF ablation strategies targeting the PVs have evolved from focal ablation inside the PVs to wide area circumferential PVI which today is the most commonly applied approach. Despite the widespread popularity of PVI a universal definition is lacking. While “entrance block” into the PVs is a generally accepted endpoint evaluation of exit conduction from the PVs remains controversial. Unexcitability of the circular ablation line has been introduced as a new promising endpoint and was associated with an improved clinical outcome in a randomized trial. Precise understanding of PV electrograms during an ablation procedure is crucial with respect to efficacy and safety. A variety of electrophysiological techniques help to correctly interpret components of complex electrograms. PV reconnection leading to AF recurrence remains an unresolved problem and conventional confirmation of bi-directional conduction block does not exclude reversible tissue damage. Prolongation of post-PVI monitoring and application of provocative maneuvers such as the administration of adenosine after initial PVI to uncover latent PV conduction may improve clinical outcome although robust data supporting these strategies are lacking.

References:

1. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and


