Modified phased radiofrequency ablation of atrial fibrillation reduces the number of cerebral microembolic signals

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Aims
Phased radiofrequency (RF) ablation for atrial fibrillation is associated with an increased number of silent cerebral lesions on magnetic resonance imaging and cerebral microembolic signals (MESs) on transcranial Doppler ultrasound imaging compared with irrigated RF. The increased rate of embolic events may be due to a specific electrical interference of ablation electrodes attributed to the catheter design. The purpose of this study was to elucidate the effect of deactivating the culprit electrodes on cerebral MESs.

Methods and results
Twenty-nine consecutive patients (60 ± 11 years, 10 female) underwent their first pulmonary vein isolation using phased RF energy. Electrode pairs 1 or 5 were deactivated to avoid electrical interference between electrodes 1 and 10 (‘modified’). Detection of MESs by transcranial Doppler ultrasound was performed throughout the procedure to assess cerebral microembolism. Results were compared with the numbers of MESs in 31 patients ablated using all available electrodes (‘conventional’) and to 30 patients undergoing irrigated RF ablation of a previous randomized study. Ablation with ‘modified’ phased RF was associated with a marked decrease in MESs when compared with ‘conventional’ phased RF (566 ± 332 vs. 1530 ± 980; P < 0.001). This difference was mainly triggered by the reduction of MES during delivery of phased RF energy, resulting in MES numbers comparable to irrigated RF ablation (646 ± 449; P = 0.7). Total procedure duration as well as time of RF delivery was comparable between phased RF groups. Both times, however, were significantly shorter compared with the irrigated RF group (123 ± 28 vs. 195 ± 38; 15 ± 4 vs. 30 ± 9; P < 0.001, respectively).

Conclusion
Pulmonary vein isolation with ‘modified’ phased RF is associated with a decreased number of cerebral microembolism especially during the delivery of ablation impulses, supporting the significance of electrical interference between ablation electrodes 1 and 10. Deactivation of electrode pairs 1 or 5 might increase the safety of this approach without an increase in procedure duration or RF delivery time.

Keywords
Atrial fibrillation • Ablation • Complications

Introduction
Catheter ablation of atrial fibrillation is a well-established treatment option for symptomatic patients and numbers of interventions are rising. Various technical tools such as the ‘pulmonary vein ablation catheter’ (PVAC®; Medtronic Inc.) have been developed to facilitate pulmonary vein isolation (PVI). Concerns have been raised about an increased incidence of silent cerebral embolism using this phased radiofrequency (RF) ablation device in comparison with irrigated tip RF ablation or cryoablation. Our group confirmed these findings...
in terms of an increased rate of microembolic signals (MESs) detected by transcranial Doppler ultrasound (TCD) as a valid marker of embolic activity in patients undergoing PVAC® ablation compared with irrigated tip RF ablation in a prospective randomized study.4 This increased formation of embolic material may be due to a specific electrical interference between electrodes 1 and 10 while used phased unipolar and bipolar RF ablation.5 Therefore, we investigated the number of MESs during PVI in patients undergoing ‘modified’ phased RF with deactivated electrode pairs 1 or 5 in comparison with ‘conventional’ phased RF with all 10 electrodes activated and conventional irrigated RF.

### Materials and methods

#### Study protocol

We performed a prospective, single centre study. Patients with symptomatic, persistent, or paroxysmal atrial fibrillation undergoing solely PVI were considered for the study. Exclusion criteria were longstanding persistent atrial fibrillation, former surgical or non-surgical left atrial ablation, including former PVI, presence of other atrial tachycardia, prior cardiac surgery, moderate or severe mitral valve stenosis or regurgitation, heart failure with a NYHA class III or IV, left ventricular ejection fraction ≤40%, severe chronic pulmonary disease, left atrial thrombus, contraindication to oral anticoagulation, significant stenosis of the brain supplying arteries, and pregnancy. The local ethics committee approved the study protocol.

After obtaining written, informed consent patients underwent ‘modified’ phased RF PVI. Bridging with weight adjusted low molecular weight heparin was done in patients on Vitamin K antagonists, if an international normalized ratio (INR) value < 2.0 was documented at admission to our hospital. New oral anticoagulants (Dabigatran, Rivaroxaban) were discontinued one day prior to the ablation procedure. In general, oral anticoagulation was prescribed according to the current guidelines, hence there was no routine treatment in all patients.1 A transesophageal echocardiography was performed in all patients prior to ablation to exclude left atrial thrombus formation within one day prior to the ablation. According to the current consensus statement on AF ablation, all patients received oral anticoagulation for two months after ablation.6 Further, long-term oral anticoagulation was done as indicated by the current guidelines.1 In all patients a computed tomography of the heart was performed and the anatomy of the left atrium (LA) and the PVs were reconstructed (EnSite Verismo; St. Jude Medical).

During the ablation, surface electrocardiograms and bipolar intracardiac electrograms were registered using a digital recording system (Axiom Sensis XP, Siemens AG, or a Prucka GE Medical The General Electric Company). Signals were sampled at 1 kHz, filtered at 0.1–100 Hz for surface electrocardiograms and at 30–250 Hz for intracardiac signals.

All subjects received a full colour-coded duplex investigation of their extracranial neck and intracranial arteries to exclude significant stenosis as alternative active source of cerebral microemboli and to determine whether a suitable bone window for the monitoring studies existed, as reported previously.4 Patients with significant stenosis of the brain supplying arteries were excluded.

Safety endpoints were stroke, transient ischemic attack, myocardial infarction, mortality, and significant hemorrhage (decreases in hemoglobin levels of ≥ 2 g/deciliter).

#### Ablation procedure

The ablation protocol of our facility for phased and irrigated RF ablation has been described in detail previously.7 In brief, ablation was performed as follows:

**‘Modified’ phased radiofrequency ablation**

After gaining femoral venous access, a steerable decapolar catheter (Livewire; St. Jude Medical) was placed in the coronary sinus. A single transseptal puncture (TSP) was done using a non-steerable sheath (Daig SL1, St Jude Medical) under fluoroscopic imaging and pressure monitoring. Subsequently, a bodyweight adjusted heparin bolus was applied. The target activated clotting time (ACT) was 250–350 s with half-hourly controls and managed with additional heparin boluses if necessary. Thereafter, selective angiography of the PVs was performed with about 40 mL of nonionic contrast (Ultravist 370; Bayer), in posterior-anterior and left anterior oblique 60° projections. The SL1-sheath was then replaced by a non-deflectable 12 Fr long sheath (Frontier Advance, Medtronic Inc.) for advancing the PVAC® catheter. The long sheath was perfused with heparinized saline solution.

The 10 pole phased RF catheter (PVAC®, Medtronic Inc.) was positioned at the ostium of each PV in an over-the-wire technique (PV-Tracker; Medtronic Inc.) and ablation was done exclusively with a 4:1 bipolar/unipolar ratio and a maximum power of 8 W for 1 min while electrode pairs 1 or 5 were deactivated throughout the procedure. Temperature limit was set to 40°C. After each ablation, conduction into the PV was checked and ablation was repeated at sites with remaining conduction. Electrode pairs without tissue contact or positioned at sites without conduction were deactivated at the operators’ discretion. This procedure was repeated until no remaining conduction was detected. Complete isolation of the PVs was confirmed during sinus rhythm and using differential pacing maneuvers. If AF persisted after ablation sinus rhythm was restored by electrical cardioversion.

**‘Conventional’ phased radiofrequency ablation**

Materials, procedural techniques, and settings equal those used during ‘modified’ phased RF ablation, save that electrode pairs 1 or 5 were not deactivated.

#### Irrigated tip radiofrequency ablation

In contrast to the phased RF ablation groups, access to the LA was achieved by performing two separate TSPs. A non-steerable sheath...
(Daig SL; St. Jude Medical) for advancing the diagnostic circular decapolar catheter (Inquiry Optima; St. Jude Medical), and a deflectable long sheath (Agilis; St. Jude Medical) for the ablation catheter were placed in the LA. Management of anticoagulation including ACT measurements and heparin dosage were identical with the phased RF groups.

After selective, simultaneous angiography of the ipsilateral PVs and acquisition of the individual three-dimensional anatomy of the LA (Ensite NavX Velocity; St. Jude Medical, with image integration), antral circumferential RF ablation around ipsilateral PVs using a 4 mm open-tip irrigated catheter (IBI Therapy Coolpath Duo; St. Jude Medical) was performed. Maximum power was set to 30 W, going selectively up to 40 W if PVI could not be achieved, especially at the anterior ridge border of the lateral PVs. Temperature was limited to 43°C. Irrigation was adjusted manually between 17 and 30 mL/min. Electrical cardioversion was performed if the patient remained in AF after PVI.

**Microembolus detection**

The detection and evaluation procedure was performed according to international consensus recommendations. The same TCD device (Doppler-Box; Compumedics DWL) was used for all studies and for the blinded off-line evaluation of the data. Both medial cerebral arteries were continuously insonated through the temporal window from the start of the procedure (groin puncture) until the end of the ablation procedure (withdraw through the interatrial septum) in all patients (Figure 1A and B). A continuous MES registration of at least one medial cerebral artery throughout the ablation procedure could be achieved in all patients. The investigations were well tolerated by the subjects, without any side effect.

Three different observers (F.G., P.L., and M.A.R.) analysed the tapes off-line. Analysis of MES comprised (i) listening to each signal and (ii) watching each signal on screen at highest speed. As the implemented solid/gaseous differentiation algorithm of the software proved unreliable in pre-study examinations, no differentiation between gaseous and solid signals was attempted. Embolic signals were evaluated by three observers according to standard criteria. Ratings were made without using a decibel threshold. All signals not classified as artefacts but as MESs were counted in each patient. Single countable MESs were summed up to a total MES-count.

**Comparison of microembolic signal rates**

The overall MES rate and the itemized MES numbers were subsequently compared with the results of 31 patients undergoing ‘conventional’ phased RF ablation and 30 patients undergoing conventional irrigated RF ablation using the same MES detection protocol.

**Statistics**

All statistical analyses were performed using SPSS 21.0 (IBM Corporation). Continuous variables are presented as mean ± SD. Statistical comparison between the numbers of MESs was performed using a one-way analysis of variance. Inter-rater agreement on MES was tested using a methodology described in detail elsewhere. In brief, inter-observer agreement was expressed as proportions of specific agreement for positive ratings (ps±). Ps± values are comparable with widely used κ-statistics. However, κ values are not meaningful in the case of MES, because no specific negative rating is made during MES analysis.

**Results**

**Patient and procedural characteristics**

A total number of 29 patients were included into the study. There was no significant difference concerning the baseline characteristics and the cardiovascular risk factors (Table 1). The total duration of the procedure, the total fluoroscopic time, and the ablation duration were significantly lower when using ‘conventional’ and ‘modified’ phased RF compared with irrigated RF (Table 2).

**Microembolus detection**

The total amount of MES occurring during the whole ablation procedure (time from TSP to removal of the sheaths from the LA) was significantly lower in the ‘modified’ phased RF group compared with the ‘conventional’ phased RF group [566 ± 332 (‘modified’ phased RF) vs. 1530 ± 980 (‘conventional’ phased RF), \(P < 0.001\), Figure 2A]. The reduction in MES in ‘modified’ phased RF ablation was mainly attributed to a decrease of MES during ablation itself as displayed by the amount of MES per minute ablation [45 ± 34 (‘conventional’ phased RF) vs. 1.9 ± 1.6 (irrigated RF) vs. 15 ± 13 (‘modified’ phased RF), \(P < 0.001\), also see Figure 2B]. Owing to a significantly lower embolic load during the procedure steps prior to ablation in the ‘modified’ phased RF group compared to the irrigated RF group, the overall amount of MES was similar to the irrigated RF group [566 ± 332 (‘modified’ phased RF) vs. 646 ± 449 (irrigated RF), \(P = 0.7\), Figure 2A]. Symptomatic cerebral embolism did not occur. No safety endpoints had been reached in any patient treated by the ‘modified’ phased RF protocol.
Discussion

Employing phased RF ablation in PVI has been associated with an increased number of silent cerebral lesions detected by magnetic resonance imaging.\(^2,3\) By using transcranial Doppler imaging, we were able to confirm these results in terms of an increased microembolic load in 61 patients randomly assigned to irrigated RF ablation (30 patients) and 'conventional' phased RF ablation (31 patients).\(^4\) Data from animal studies suggest that the development of MESs is mainly attributed to the ablation itself due to a specific electrical interference between electrodes 1 and 10, which are out of phase during bipolar energy delivery and might get into too close proximity during ablation, thereby generating gas bubbles and coagulation particles.\(^5\) Utilizing the same MES detection protocol, a significant reduction in MES could be observed in 29 consecutive patients undergoing PVI using the PVAC device with deactivated electrode pairs 1 or 5. This was driven by a significant abatement of MES generation during phased RF itself, confirming animal data. These findings are also in line with the recent work of Wieczorek et al., who found less cerebral lesions on magnetic resonance imaging in patients who underwent a 'modified' phased RF ablation.\(^11\) In contrast, there was no prolongation in RF application or procedure time with our approach. Based on our data of similar MES in 'modified' phased RF compared to irrigated point-by-point ablation exclusion of additional PVAC-electrodes remain questionable as long as this diminished the procedural advantages of the phased RF system. The higher rate of pre-ablation MES in irrigated RF group might be attributed to the double TSP and two left atrial sheaths despite a careful sheath management including perfusion with heparinized saline solution. Further reduction of MES might be accomplished by changes in the procedural management, e.g. performing PVI under therapeutic INR, which reduces stroke as well as bleeding complications.\(^12\)

Limitations

We are presenting a cohort of 29 consecutive patients rather than performing a randomized study. This was due to the observation of increased number of MESs in conventional-phased RF in our previous, randomized study as well as first results in an animal model...
Modified phased radiofrequency ablation of AF reduces the number of cerebral MESs

However, incidence of MES prior to left atrial access was low and not different between the three groups.

**Conclusion**

The avoidance of an electrode 1–10 interaction by deactivating electrode pairs 1 or 5, resulted in a significant reduction in cerebral MES in comparison to ‘conventional’ phased RF ablation. This was attributed to a significant reduction in MES during ablation itself, supporting the hypothesis of electrical interference of electrodes 1 and 10. The resulting overall MES rate using ‘modified’ phased RF ablation was comparable to conventional irrigated RF ablation. In light of these results and especially because of the unknown long-term effects of cerebral microembolism during catheter ablation for AF, a mandatory deactivation of electrode pairs 1 or 5 should be strongly considered while using the PVAC® device. Further clinical studies are needed to evaluate the efficiency and safety of this ‘modified’ phased RF ablation.

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**References**


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**Superior vena cava isolation by right pulmonary vein ablation**

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Case

A 77-year-old female patient with paroxysmal atrial fibrillation was referred for catheter ablation. Before the right superior pulmonary vein isolation (RSPV), two components of potentials were recorded at a circular mapping catheter placed in the antrum of RSPV (figure). The first component consisted of high-frequency and low-amplitude signals, followed by a high-frequency and high-amplitude signals (second component). After disappearance of the second component during right PV ablation, the first component was present without any conduction delay. Radiofrequency energy applied at an anterior edge of the RSPV made the first component delay and ultimately disappeared. However, the first component reappeared shortly after termination of radiofrequency energy delivery. Then, a circular mapping catheter was placed in superior vena cava (SVC), where large and high-frequency signals synchronous with the first component in the RSPV were recorded. Electrical isolation of SVC by only one radiofrequency application at the septal aspect of SVC eliminated the remaining potential in the right PV. This case is unique in that SVC isolation was identified by the disappearance of the far-field SVC potential in RSPV during RSPV ablation.

The full-length version of this report can be viewed at: http://www.escardio.org/communities/EHRA/publications/Documents/Superior-vena-cava-isolation.pdf.