Radiofrequency catheter ablation (RFA) for atrial fibrillation (AF) has evolved as standard of care in selected patients. Periprocedural thromboembolic events and bleeding complications are among the most important and insidious complications of AF ablation. A proper periprocedural anticoagulation management is mandatory to minimize the thromboembolic and bleeding risk. Clinical Perspective on p 582

Optimal periprocedural anticoagulation protocols to minimize these complications are still under discussion. Uninterrupted periprocedural anticoagulation with warfarin has been shown to be safe and effective when using an international normalized ratio between 2 and 2.5. A proper periprocedural anticoagulation management is mandatory to minimize the thromboembolic and bleeding risk.

Methods

The study cohort included 544 patients (mean age, 63±10 years) who underwent left atrial RFA procedures between February 2012 and May 2013. All patients receiving uninterrupted periprocedural rivaroxaban 15 or 20 mg/d before the procedure were matched by age, sex, and type of rhythm disorder with an equal number of patients managed with uninterrupted vitamin K antagonist phenprocoumon (international normalized ratio, 2–3). During RFA, heparin was given intravenously to maintain an activated clotting time at 270 to 300 s. The safety end point was a composite of bleeding, thromboembolic events, and death. There were no thromboembolic complications and no deaths in either group. The prevalence of major bleeding complications was similar in both groups (1 tamponade in RivG and 1 groin hematoma requiring transfusion in phenprocoumon). Minor bleeding complications occurred equally in both groups (20 of 272; 7% in the rivaroxaban versus 33 of 272, 12% in the phenprocoumon; P=0.08). In multivariable analyses, female sex was associated with a greater risk of complications (odds ratio, 1.96; 95% confidence interval, 1.10–3.49).

Conclusions

In patients undergoing left atrial RFA, continuous periprocedural rivaroxaban use seems to be as safe as uninterrupted periprocedural phenprocoumon administration.

Key Words: atrial fibrillation ♦ catheter ablation ♦ hemorrhage ♦ rivaroxaban

Background

This study aimed to evaluate the safety of continuous periprocedural rivaroxaban administration during left atrial radiofrequency ablation (RFA) in comparison with uninterrupted oral vitamin K antagonist administration. Data about the use of rivaroxaban in the setting of left atrial RFA procedures are lacking.

Methods and Results

The study cohort included 544 patients (mean age, 63±10 years) who underwent left atrial RFA procedures between February 2012 and May 2013. All patients receiving uninterrupted periprocedural rivaroxaban 15 or 20 mg/d before the procedure were matched by age, sex, and type of rhythm disorder with an equal number of patients managed with uninterrupted vitamin K antagonist phenprocoumon (international normalized ratio, 2–3). During RFA, heparin was given intravenously to maintain an activated clotting time at 270 to 300 s. The safety end point was a composite of bleeding, thromboembolic events, and death. There were no thromboembolic complications and no deaths in either group. The prevalence of major bleeding complications was similar in both groups (1 tamponade in RivG and 1 groin hematoma requiring transfusion in phenprocoumon). Minor bleeding complications occurred equally in both groups (20 of 272; 7% in the rivaroxaban versus 33 of 272, 12% in the phenprocoumon; P=0.08). In multivariable analyses, female sex was associated with a greater risk of complications (odds ratio, 1.96; 95% confidence interval, 1.10–3.49).

Conclusions

In patients undergoing left atrial RFA, continuous periprocedural rivaroxaban use seems to be as safe as uninterrupted periprocedural phenprocoumon administration. (Circ Arrhythm Electrophysiol. 2014;7:576-582.)

Key Words: atrial fibrillation ♦ catheter ablation ♦ hemorrhage ♦ rivaroxaban

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per day (o.d.). The morning or evening administration according to patients habit was continued. A total of 57% of patients received rivaroxaban 2 to 6 hours before the procedure and 43% of patients 6 to 12 hours before the procedure.

Phenprocoumon Group
An equal number of patients matched for age, sex, and type of rhythm disorder were included who received therapeutic (international normalized ratio, 2.0–3.0) anticoagulation with the VKA phenprocoumon (Marcumar).

In both groups, oral anticoagulation therapy was started 24 weeks before RFA and was administered periprocedurally without interruption.

Ablation Procedure
In all patients, transesophageal echocardiography or dual-source computer tomographic scan was performed before RFA to rule out LA appendage thrombus. There was no LA appendage thrombus detected on transesophageal echocardiography or dual-source computer tomographic scan in any of the patients in either group.

Ablation procedures were performed in the fasting state under conscious analgo-sedation (fentanyl sodium and midazolam or disoprivan) using a 3-dimensional mapping system for anatomy and catheter visualization (NavX; St. Jude Medical, St Paul, MN, or Carto; Biosense Webster, Diamond Bar, CA). Vascular access was obtained through a femoral vein. A 4-F femoral arterial sheath for invasive blood pressure recording was at the discretion of the operator. A steerable 8-polar catheter was placed in the coronary sinus (CS; XPT; C.R. Bard, Lowell, MA). The LA was accessed by single transeptal puncture or via a patent foramen ovale. In both groups, after access to the LA, an intravenous bolus of unfractionated heparin (50 IU/kg body weight if baseline activated clotting time [ACT] was >170 s or 60 IU/kg body weight if baseline ACT was ≤170 s) was given. Although catheters remained in the LA, the ACT was checked 15 minutes after the bolus and every 30 minutes thereafter to maintain an ACT of 270 to 300 s with a continuous infusion of unfractionated heparin.

In paroxysmal AF, a circumferential pulmonary vein isolation was performed 2 by 2 as described before. In persistent AF, a sequential ablation strategy was used as described by others.10 In both groups, atrial tachycardias as presenting rhythm for ablation or arising after complex fractionated atrial electrograms were used as described by our group.11,12 For all ablations, cooled radiofrequency energy using a 3.5-mm open irrigated tip ablation catheter was delivered with a maximum temperature of 43°C and a maximum power of 30 to 40 W.

If no sinus rhythm was achieved with ablation, direct current cardioversion or drug intervention was performed at the end of the procedure.

The same operators performed the ablation procedures in both groups. Vascular access, ablation strategy, and ablation techniques were similar between the 2 groups.

Postprocedural Management
The sheaths were removed once the activated partial thromboplastin time was <150 s. Rivaroxaban 15 or 20 mg orally daily or phenprocoumon were given 24 hours after the last intake preprocedurally. Each oral anticoagulant was continued for 23 months. After RFA, all patients had a physical examination, an electrocardiographic monitoring, a transthoracic echocardiography, and a duplex ultrasonography of the vascular access site.

Safety End Point
The safety end point was a composite of bleeding, thromboembolic events, and death during hospitalization. The bleedings were classified according to the REPLACE-2 (Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events) bleeding definition13 with the inclusion of pericardial effusion.

Major Bleeding Complications Included
- Any bleeding requiring blood transfusion.
- Retropertitoneal bleedings and hematomas requiring surgical intervention.
- Pericardial effusions requiring drainage or surgical intervention (tamponade).
- Intracranial hemorrhage.

Minor Bleeding Complications Included
- Hematomas (>5 cm) not requiring blood transfusion or surgical intervention.
- Pericardial effusions (>5 mm) not requiring an intervention (nontamponade).

Thromboembolic Events Included
- Cerebrovascular accidents and transient ischemic attacks. In case of a suspected cerebrovascular event, a cranial computer tomographic scan or MRI of the brain was performed and the diagnosis had to be confirmed by a neurologist.
- Deep vein thrombosis and pulmonary embolism.
- Peripheral arterial embolism.

Statistical Analysis
Data are presented as mean values and SDs for continuous variables with normal Gaussian distribution; non-normally distributed continuous variables are presented as median (interquartile range); categorical data are presented as exact numbers and percentages. Both groups were compared using the independent Student t test for continuous variables, nonparametric Wilcoxon tests for non-normally distributed traits, and the χ² test or Fisher exact test where appropriate for categorical variables. A multivariable logistic regression analysis was performed to determine predictors of complications. All potential confounders were included in a stepwise regression analysis based on clinical significance or observed univariable association. The odds ratio and 95% confidence interval (CI) of composite bleeding and thromboembolic complications were computed. A 2-tailed P value <0.05 was considered statistically significant. All analyses were performed using SPSS version 21 for Windows (SPSS, Inc, Chicago, IL).

Results
Baseline Characteristics
The baseline characteristics of the 2 groups are shown in Table 1. The mean age of the patients was similar in both groups (62.5±10.6 years in the rivaroxaban and 63.7±9.6 years in the phenprocoumon; P=0.18) with 68% being men in each group. The treated arrhythmia was AF in 77% of patients of each group. There were no significant differences in the individual components of the CHADS₂VASc score, the mean CHADS₂ score, LA size, and the presenting rhythm on arrival at the electrophysiology laboratory between both groups.

Procedural Data
The mean international normalized ratio on the day of the procedure was 1.2±0.2 (rivaroxaban) and 2.1±0.4 (phenprocoumon; P<0.001). The baseline ACT was significantly higher in the rivaroxaban (156±37 s) than in the phenprocoumon (142±20 s; P<0.001). The mean ACT during the procedure
Tables

Demographics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>RivG (n=272)</th>
<th>PhenG (n=272)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62.5±10.6</td>
<td>63.7±9.6</td>
<td>0.18</td>
</tr>
<tr>
<td>Age ≥75 y</td>
<td>26 (10)</td>
<td>31 (11)</td>
<td>0.71</td>
</tr>
<tr>
<td>Men</td>
<td>185 (68)</td>
<td>185 (68)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.3±4.5</td>
<td>27.5±4.4</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Medical history

- **AF type**
  - Paroxysmal: 133 (49) vs. 126 (46), P=0.61
  - Persistent: 76 (28) vs. 83 (31), P=0.57

- **AT**
  - 63 (23) vs. 63 (23), P=0.99

Redo procedure: 64 (24) vs. 128 (47), <0.001

Duration of AF/AT, mo (mean): 26±38 vs. 37±41, <0.001

Heart failure (LVEF<40%): 9 (3) vs. 13 (5), 0.52

Hypertension: 173 (64) vs. 162 (60), 0.86

Diabetes mellitus: 26 (10) vs. 32 (12), 0.49

Previous TIA or stroke: 16 (6) vs. 19 (7), 0.73

Coronary artery disease: 35 (13) vs. 32 (12), 0.70

Chronic renal insufficiency: 17 (6) vs. 9 (3), 0.23

CHADS₂, mean: 0.9±0.8 vs. 1.0±0.9, 0.25

CHA₂DS₂-VASc score, mean: 1.8±1.4 vs. 2.0±1.5, 0.22

0: 50 (18) vs. 50 (18), >0.99

1: 73 (27) vs. 67 (25), 0.62

≥2: 149 (55) vs. 155 (57), 0.67

Mean left atrial size, mm: 44±6 vs. 45±7, 0.09

Mean LVEF, %: 60±37 vs. 56±7, 0.05

Medication use

- Aspirin: 41 (15) vs. 39 (14), 0.90
- Clopidogrel: 6 (2) vs. 5 (2), >0.99
- Aspirin and clopidogrel: 4 (1) vs. 3 (1), >0.99
- ACE inhibitor/ARB: 121 (44) vs. 142 (52), 0.09
- β-blocker: 221 (81) vs. 257 (94), <0.001
- Calcium-channel blocker: 5 (2) vs. 30 (11), <0.001
- Digoxin: 9 (3) vs. 18 (7), 0.11
- Statins: 75 (28) vs. 73 (27), 0.85
- Diuretic: 61 (22) vs. 85 (31), 0.03

Values are mean±SD or n (%). ACE indicates angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blocker; AT, atrial tachycardias; LVEF, left ventricular ejection fraction; PhenG, phenprocoumon group; RivG, rivaroxaban group; and TIA, transient ischemic attack.

was significantly lower in the rivaroxaban than in the phenprocoumon (278±32 versus 289±35 s; P<0.001). There was no difference in the mean of maximum ACT during the procedure between the 2 groups (307±47 versus 311±44 s; P=0.31; Tables 2 and 3).

The median of total unfractionated heparin required to maintain a therapeutic ACT during RFA was significantly higher in the rivaroxaban (116 IU/kg) than in the phenprocoumon (99 IU/kg; P<0.001; Table 3); however, this difference was abolished after accounting for body weight and procedure duration.

Safety End Point

No deaths and no thromboembolic complications occurred in either group. Periprocedural complications primarily consisted of bleeding complications that occurred in 55 of 544 (10%) patients (Table 4).

The prevalence of total bleeding complications between rivaroxaban (8%) and the phenprocoumon (13%; 5% difference in rates; 95% CI, −0.5% to 10.1%; P=0.09), as well as the composite end point of bleeding and embolic complications (8% versus 13%; P=0.09), did not differ significantly. In the rivaroxaban, the timing of drug administration relative to the procedure did not result in a significant difference in the safety end point (<6 versus ≥6 h; P=0.37).

Major bleeding complications occurred in 1 of 272 (0.4%) patients in the rivaroxaban (cardiac tamponade requiring surgery of an obvious perforation of the posterior LA and the transfusion of 3 U of packed red blood cells) and 1 of 272 (0.4%) patients in the phenprocoumon (groin hematoma requiring 2 U of packed red blood cells transfusion; P>0.99). Both patients had uneventful recovery after intervention. None of the patients with major bleeding complications received coagulation factor complexes.

Minor bleeding complications occurred in a similar proportion of patients in the rivaroxaban (20 of 272; 7%) and phenprocoumon (33 of 272; 12%), respectively (P=0.08).

Pericardial effusion without tamponade occurred more often in the phenprocoumon (22 of 272; 8%) than in the rivaroxaban (9 of 272; 3%; P=0.03). Groin hematomas requiring
The incidence of major and minor bleeding complications after LA RFA is significantly higher with 12.2% to 20%.16–18 It was recently shown that uninterrupted therapeutic warfarin administration during the periprocedural RFA period is associated with a significant reduction of embolic events without an increased bleeding risk.1,19 Continuation of oral anticoagulation therapy with VKA is also recommended in the recent HRS/EHRA/APHRS (Heart Rhythm Society/European Heart Rhythm Association/Asia Pacific Heart Rhythm Society) consensus statement20 on AF ablation.

The introduction of new oral anticoagulants 3 years ago for patients with nonvalvular AF has changed the anticoagulation landscape. Till date, there are only limited and conflicting data about the periprocedural use of dabigatran during LA RFA.7,8 About rivaroxaban, 1 prospective observational study from Eitel et al21 shows that anticoagulation with new oral anticoagulants, including rivaroxaban, after AF catheter ablation is safe and effective. A recently published post hoc analysis of a ROCKET AF (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) substudy22 showed that rivaroxaban (n=36) could be continued periprocedurally for RFA with no differences in long-term stroke rates or survival when compared with periprocedural warfarin therapy (n=43). There are no randomized data to support the use of rivaroxaban as the periprocedural anticoagulant for RFA.6

In our study, no deaths or thromboembolic complications occurred with rivaroxaban. The overall bleeding rate of 10% corresponds to previously published studies dealing only with phenprocoumon15–17 and was not significantly different between both groups. There was a tendency toward less minor bleeding complications with rivaroxaban (7%) when compared with VKA (12%). However, this was because of a higher rate of nontamponade pericardial effusions in the phenprocoumon group. These small pericardial effusions occur more frequently after extensive LA ablation and a differentiation between an inflammatory reaction and a bleeding complication is difficult.23

In the multivariable regression analysis, female sex was associated with complications as also shown in other studies.24,25 Persistent AF and atrial tachycardias as presenting rhythm were associated with bleeding complications.

On multivariable regression analysis, including age, sex, CHA2DS2-VASc score, type of presenting rhythm disorder, aspirin use, and rivaroxaban use, the independent predictors of the safety end point were female sex (odds ratio, 1.96; 95% CI, 1.10–3.49) and persistent AF or atrial tachycardias as presenting rhythm disorder (odds ratio, 3.25; 95% CI, 1.74–6.08). Rivaroxaban was not an independent predictor of the safety end point (odds ratio, 1.652; 95% CI, 0.92–2.96).

**Discussion**

This study systematically evaluates the safety of uninterrupted periprocedural rivaroxaban during LA RFA in a large group of patients. The main finding of the study is that uninterrupted rivaroxaban is not associated with thromboembolic events or with an increased bleeding risk when compared with uninterrupted vitamin K antagonist (phenprocoumon) administration.

**Periprocedural Anticoagulation and Complications**

The risk of thromboembolic, as well as bleeding complications during or after RFA procedures, remains a significant concern. Whereas the incidence of periprocedural thromboembolic events is reported in the range of 0.1% to 1.1%,14–16

| Table 3. Comparison of Intraprocedural Anticoagulative Data Between Patients on RivG (Xarelto) and PhenG (Marcumar) |
|--------------------------------------------------|---------------------------------|-----------------|
| Intraprocedural Anticoagulative Data              | RivG (n=272)                   | PhenG (n=272)   |
|貧IR (s)                                          | 1.2±0.2                        | 2.1±0.4         |
| Baseline ACT, s                                  | 156±37                         | 142±20          |
| Maximum ACT, s                                   | 307±47                         | 311±44          |
| Mean ACT, s                                      | 278±32                         | 289±35          |
| Any ACT value >300 s (%)                         | 139 (51)                       | 157 (58)        |
| Total heparin dosage, IU                         | 9550 (7375 to 12225)           | 8075 (6250 to 10800) |
| Median (25th and 75th percentile)                | 116 (90 and 141)               | 99 (78 and 124) |
| Total heparin dosage/body weight, IU/kg          | 45 (36 and 60)                 | 44 (33 and 59)  |
| Median (25th and 75th percentile)                | 45 (36 and 60)                 | 44 (33 and 59)  |
| Values are mean±SD or n (%) or median (25th and 75th percentile). ACT indicates activated clotting time; INR, international normalized ratio; PhenG, phenprocoumon group; and RivG, rivaroxaban group. |

Predictors of Bleeding Complications

On univariable analysis, a higher CHA2DS2-VASc score (2.3±1.3 versus 1.8±1.4; P=0.03), a larger LA size (47±6 versus 44±7 mm; P=0.04), arterial hypertension (75% versus 60%; P=0.03), persistent AF ablation (71% versus 50%; P<0.01), intraprocedural cardioversion (42% versus 23%; P<0.01), complex fractionated atrial electrogram ablation (45% versus 26%; P<0.01), and persistent AF or atrial tachycardias as presenting rhythm (73% versus 47%; P<0.001) were associated with bleeding complications.

On multivariable regression analysis, including age, sex, CHA2DS2-VASc score, type of presenting rhythm disorder, aspirin use, and rivaroxaban use, the independent predictors of the safety end point were female sex (odds ratio, 1.96; 95% CI, 1.10–3.49) and persistent AF or atrial tachycardias as presenting rhythm disorder (odds ratio, 3.25; 95% CI, 1.74–6.08). Rivaroxaban was not an independent predictor of the safety end point (odds ratio, 1.652; 95% CI, 0.92–2.96).
immediately be restarted with full anticoagulant effect once a hemostatic state is established after sheath removal. The most concerning disadvantage is the lack of a specific antidote to reverse the anticoagulant effect acutely. Prothrombin complex concentrate and activated prothrombin complex concentrate have been used and completely reverse the anticoagulant effect of rivaroxaban.

In our study, there was 1 periprocedural cardiac tamponade in the rivaroxaban group, which had to be managed surgically. Using continuous periprocedural rivaroxaban in RFA procedures may, therefore, necessitate prothrombin complex concentrate administration or surgical intervention to manage bleeding complications, which are not inherent to the type of anticoagulant.

The question remains whether the bleeding risk outweighs the other advantages using rivaroxaban for LA RFA procedures. Consistent with the findings by Piccini et al. and Lakkireddy et al., we found evidence of neither an increased risk of stroke or systemic embolism nor of an increased bleeding risk in patients treated periprocedurally with rivaroxaban when compared with continued VKA. Knowing the overall safety profile and predictable pharmacokinetics, rivaroxaban might represent an optimal anticoagulant agent during LA RFA.

### Intraprocedural ACT Measurement and Heparin Administration During Continuous Rivaroxaban Therapy

For intraprocedural heparinization, we choose to target an ACT of 270 to 300 s. In the recent consensus statement, it was recommended to maintain a target ACT of ≥300 to 350 s. This recommendation is based on studies that showed that thrombi can form on the transseptal sheath and electrode catheter almost immediately after crossing the septum and that early heparinization substantially decreases this risk. However, these studies were conducted under warfarin discontinuation and periprocedural bridging with heparin.

The recent meta-analysis showed variable ACT target numbers and the individual use of protamine. There is no clear recommendation about the target ACT in patients under continuous oral anticoagulation.

In a multicenter registry evaluating the safety of continuous dabigatran with a target ACT of 300 to 400 s, the incidence of major bleeding was as high as 6%. In another large study in which dabigatran was stopped on the evening before the procedure and ACT targeted at 300 to 350 s, major bleeding occurred in 2% of patients without thromboembolic complications. This shows that a slightly lower ACT could decrease bleeding complications without increasing thromboembolic events. In our experience, procedural heparin infusion with a target ACT of 270 to 300 s in patients under continuous oral anticoagulation represented a safe and effective protocol.

Patients who were treated with rivaroxaban received a 15% increased heparin dose when compared with patients receiving phenprocoumon; however, this difference was no longer significant after accounting for body weight and procedure duration. Nevertheless, despite comparable heparin dose, the mean ACTs achieved during the RFA procedure were significantly lower in the rivaroxaban group. ACT measurement does not seem to reflect the true anticoagulative status of the patient under continuous rivaroxaban therapy appropriately. Similar findings were described using periprocedural dabigatran. Further investigation is needed to understand this mechanism. Upcoming alternative anticoagulation assays, such as drug-specific antifactor Xa activity measurements, may prove useful assessing anticoagulant activity and potentially helping to guide intraprocedural heparin administration.

### Limitations

The present study is a nonrandomized single-center study. However, the study includes a large patient group treated with rivaroxaban or phenprocoumon, and patients were well matched for age, sex, and type of rhythm disorder.

Given the size of the study and the low event rate for thromboembolic complications, we are limited in drawing final conclusions about the efficacy in the prevention of thromboembolic events. In addition, in view of our intraprocedural ACT and heparin measurements, the optimal heparin dosage seems to require further investigation.

### Conclusions

In patients undergoing LA catheter ablation, periprocedural continuation of rivaroxaban seems to be as safe as the uninterrupted therapeutic use of VKA (phenprocoumon). Large, randomized trials are required to confirm these results and identify the optimal periprocedural anticoagulation protocol for LA ablation procedures.

### Disclosures

None.
References


New oral anticoagulants for nonvalvular atrial fibrillation have changed the management landscape. For radiofrequency catheter ablation of atrial fibrillation uninterrupted anticoagulation with vitamin K antagonists, aiming for an international normalized ratio of 2 to 2.5 is recommended in the recent HRS/EHRA/APHRS (Heart Rhythm Society/European Heart Rhythm Association/Asia Pacific Heart Rhythm Society) consensus statement on left atrial radiofrequency ablation. The optimal management of periprocedural anticoagulation in patients on new oral anticoagulants is unclear. In the present cohort study, we compared the safety profile of radiofrequency ablation in patients under continuous periprocedural anticoagulation with rivaroxaban (15 or 20 mg/d) versus uninterrupted therapeutic anticoagulation with a vitamin K antagonist (phenprocoumon). A total of 544 patients (272 in each group) were followed up during hospitalization. We observed no significant differences in major and minor bleeding complications between rivaroxaban and phenprocoumon patients. Moreover, there were no thromboembolic complications in either group. This study suggests that periprocedural continuation of rivaroxaban is as safe as the uninterrupted therapeutic use of vitamin K antagonist (phenprocoumon) in left atrial radiofrequency ablation. Nevertheless, larger, randomized trials are required to confirm our findings and identify the optimal periprocedural anticoagulation protocol for left atrial ablation procedures in patients on rivaroxaban before overall recommendations can be given for daily clinical practice.
Safety of Continuous Periprocedural Rivaroxaban for Patients Undergoing Left Atrial Catheter Ablation Procedures

Roger Dillier, Sonia Ammar, Gabriele Hessling, Bernhard Kaess, Herribert Pavaci, Alessandra Buiatti, Verena Semmler, Susanne Kathan, Monika Hofmann, Carsten Lennerz, Christof Kolb, Tilko Reents and Isabel Deisenhofer

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