


3D mapping of phrenic nerve course for radiofrequency pulmonary vein isolation

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Abstract

Introduction: Phrenic nerve (PN) injury is a rare but severe complication of radiofrequency (RF) pulmonary vein isolation (PVI). The objective of this study was to characterize the typical intracardiac course of the PN with a three-dimensional electroanatomic mapping system, to quantify the need for modification of the ablation trajectory to avoid delivering an ablation lesion on sites with PN capture, and to identify very circumscribed areas of common PNC on the routine ablation trajectory of a RF-PVI, allowing fast and effective PN screening for everyday usage.

Methods: We enrolled 137 consecutive patients (63 ± 9 years, 64% men) undergoing PVI. A detailed high output (20 mA) pace-mapping protocol was performed in the right (RA) and left atrium (LA) and adjacent vasculature.

Results: The right PN was most commonly captured in the superior vena cava at a lateral (50%) or posterolateral (23%) position before descending along the RA either straight (29%) or with a posterolateral bend (20%). In the LA, beginning deep within the right superior pulmonary vein (RSPV), the right PN is most frequently detectable anterolateral (31%), then descends to the lateral proximal RSPV (23%), and further towards the lateral antral region (15%) onto the medial LA wall (12%). To avoid delivering an ablation lesion on sites with PN capture, modification of ablation trajectory was necessary in 23% of cases, most commonly in the lateral RSPV antrum (81%). No PN injury occurred.

Conclusion: PN mapping frequently reveals the close proximity of the PN to the ablation trajectory during PVI, particularly in the lateral RSPV antrum. Routine PN pacing should be considered during RF PVI procedures.

KEYWORDS

atrial fibrillation, catheter ablation, phrenic nerve injury, phrenic nerve palsy, pulmonary vein isolation, radiofrequency energy

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1 | INTRODUCTION

The number of catheter ablation procedures for atrial fibrillation (AF) using radiofrequency (RF) energy is continuously increasing.¹ While phrenic nerve (PN) injury is rather frequent during cryoballoon AF ablation (4.2%),² it is a rare complication when using RF energy, ranging from 0.11% to 0.48%.³⁻⁵

In recent years, scientific research addressed the durability of pulmonary vein isolation (PVI)⁶ by focusing on transmural lesions as well as minimizing interlesion distance.⁷ However, since introducing the CLOSE protocol⁷ in 2019 at our institution we have seen three cases of symptomatic PN injuries in about 2100 procedures for AF (0.14%), presenting with exertional dyspnea, fatigue, and diminished quality of life. Particularly, dyspnea can be very agonizing, especially for patients already trying to cope with this symptom before PVI, namely adipose and heart failure patients. Both patient groups increasingly receive PVI for AF rhythm control, thus PNI should be strictly avoided in those patients. Additionally, symptomatic PNI can be long-lasting⁵ potentially aggravating the primary condition and diminishing quality of life over a long period of time. Although it is a well-known complication, preventive measures are not taken routinely during RF PVI procedures.

Therefore, the aim of this study was to analyze the intracardiac course of the PN in detail by marking phrenic nerve capture (PNC) sites on a biatrial electroanatomic map during RF PVI procedures. We sought to identify the most common anatomical PN course in our cohort as well as its interpatient variability. The main focus was set to identify PNC in the vicinity of routine PVI ablation sites, to assess the proportion needing modification of the ablation trajectory, to analyze the resulting distance between the ablation lesion sets and PNC, and most importantly, to identify very circumscribed areas of common PNC on the routine ablation trajectory of a RF antral PVI approach, to allow a fast and effective PN screening for everyday usage.

2 | METHODS

In this study, patients undergoing a left atrial RF ablation procedure for paroxysmal or persistent AF between March 2020 and March 2021 were enrolled in an electronic database. The database included demographic and procedural information, along with mapping and PN pacing times. Before the procedure, all patients had a detailed history taken, physical examination, laboratory testing, electrocardiogram and transthoracic echocardiography. The study protocol was reviewed and approved by our institutional review board (registration number 22-1061).

2.1 | Catheter ablation procedure

The ablation procedures were carried out under general anesthesia, as previously described in detail.⁸ In brief, after obtaining access to the right femoral vein, two 63 cm, standard 8F long sheaths (Swartz™

Braided Transseptal Series Guiding Introducer, LAMP™ 45°, Abbott, USA) were placed in the right atrium (RA), which served as support for a 7 F, 3.5-mm tip, open-irrigated ablation catheter (ThermoCool Smarttouch®, Biosense Webster) and a 20-polar circular mapping catheter (Lasso®, Biosense Webster, spacing 2-6-2, electrode size 1 mm).

2.2 | Right atrial pace mapping of the right PN

The workflow of PN mapping, as described in the following subsections, was standard of care during the selected period (March 2020 and March 2021). After catheter placement, a high-density fast anatomical map of the RA and its adjacent caval veins was obtained using the Lasso catheter and the CARTO® 3D electroanatomic mapping system (CARTO® 3 System, Biosense Webster). The regional detail level was set to at least 15, to achieve high mapping resolution. Special attention was taken to obtain highly detailed anatomy of the superior and inferior vena cava (SVC/IVC) as well as the posterior and lateral wall of the RA. To pace-map the intracardiac course of the PN, the distal bipolar electrode of the ablation catheter was used. Pace mapping was started at the SVC and was continued in small steps toward the IVC. Pacing was performed with high output (20 mA, 2.0 ms pulse width) at a cycle length of 600 ms and contact force between 5 and 15 g. In a subset of patients, additional low-output pacing (10 mA) was performed at sites with high-output PNC.

If at a location no PNC could be obtained, the ablation catheter was navigated inferiorly in a sinusoidal fashion, carefully mapping the circumference of the SVC, the lateral to posterior RA wall and the RA-IVC junction. Capture of PN was monitored by palpating the presence or absence of diaphragmatic twitching. The sites of PNC were tagged on the 3D map approximately every 5 mm.

2.3 | Left atrial pace mapping of the right and left PN

After transseptal puncture, a high-density fast anatomical voltage map of the left atrium (LA) was created, with a special focus to obtain highly detailed anatomy of the right and left pulmonary veins and the left atrial appendage (LAA). The regional detail level was set to at least 17. After completion of the LA geometry, both atria were visualized in the 3D-mapping system. PN pace mapping was commenced in the right superior pulmonary vein (RSPV). Again, the course of the PN was followed inferiorly, using adjacent RA PNC sites as a rough guide for the PN course. If no PN capture could be obtained, the RSPV, the entire LA medial wall with an emphasis on antral PV regions and the carina between the right superior and right inferior pulmonary vein were mapped to assure the absence of PN capture.

Pace mapping of the left PN, was started in the apex of the LAA and continued according to the PN course. The entire orifice of the

LAA was mapped, including the ridge towards the left superior pulmonary vein (LSPV) as well as the transition to the LA medial wall.

2.4 | Catheter ablation

Catheter ablation for PVI was utilized using the “CLOSE”-protocol.⁷ In our study, the following criteria were applied: interlesion distance ≤ 5 mm, RF energy was set to 35 Watts aiming for an ablation index of ≥ 550 at the anterior, septal, medial and lateral aspects of the LA wall and to 30 W aiming for an ablation index of ≥ 400 at the roof and posterior LA wall regions.

The prerequisite to not deliver an ablation lesion on sites with PNC was formulated. In case of PNC, the ablation trajectory was modified to deliver lesions only at sites without PNC.

2.5 | Postprocedural analysis of the 3D electroanatomic map

The course of intracardiac PNC on the 3D electroanatomic map was outlined on schematic maps of the RA and LA (Supporting Information: Figure S1). PNC in the SVC and RSPV was considered to be relevant for ablation and thus included in the analysis, if it occurred within a 20 mm margin of the venoatrial junction. All measurements were made with the CARTO[®] 3 software, using the “distance measurement” or “design line” tool.

2.6 | Statistical analysis

The normality of data distribution was tested using the Kolmogorov–Smirnov and Shapiro–Wilk test. If formal testing was not significant normality was accepted otherwise graphs, skewness, and kurtosis were used to confirm nonnormality.

Categorical variables are expressed as number (percentage). Continuous variables are expressed as mean \pm standard deviation or median (interquartile range) as appropriate. Group differences were assessed using a Chi-square/Fisher's Exact test, a two sample t-test, or a Mann–Whitney U-test as appropriate. All tests were 2-sided, and a *p*-value of < 0.05 was considered statistically significant. SPSS Statistics 25 (IBM Corporation) was used for statistical analysis.

3 | RESULTS

One hundred and thirty-seven consecutive patients who underwent catheter ablation for AF were included in the analysis (Table 1). Patients were 63 ± 9 years old, predominantly male, overweight, and having a history of arterial hypertension, but only

TABLE 1 Clinical parameters (*n* = 137)

Variable	Value	
Age (years)	63	± 9
Male gender	88	(64%)
Structural heart disease	22	(16%)
Coronary artery disease	24	(18%)
Obstructive sleep apnea	14	(10%)
Arterial hypertension	100	(73%)
Diabetes mellitus	14	(10%)
Prior cerebrovascular event	15	(11%)
Body mass index (kg/m ²)	29	± 4
<i>Atrial fibrillation type</i>		
- Paroxysmal	54	(39%)
- Persistent	83	(61%)

Note: Data are displayed as *n* (%) or mean \pm SD.

TABLE 2 Procedural parameters (*n* = 137)

Variable	Value	
Re-do, <i>n</i> (%)	45	(33%)
<i>Ablation lesion set, <i>n</i> (%)</i>		
- PVI	88	(64%)
- Re-PVI RSPV	12	(9%)
- Re-PVI RIPV	7	(5%)
- Re-PVI LSPV	11	(8%)
- Antral Re-PVI	31	(23%)
- Other	2	(2%)
Right atrial mapping time (min)	6	(5–8)
RA PN Pacing time (min)	3	(2–4)
Left atrial mapping time (min)	12	(10–15)
LA PN Pacing time (min)	2	(1.5–3)

Note: Data are displayed as *n* (%) or median (interquartile range). Abbreviations: LA, left atrium; LSPV, left superior pulmonary vein; PN, phrenic nerve; RA, right atrium; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.

few having structural heart disease and/or coronary artery disease. Thirty-nine percent presented with paroxysmal and 61% with persistent AF.

Anatomic mapping of the RA was feasible within six (5–8) min (Table 2), whereas acquisition of the anatomic voltage map of the LA required 12 (10–15) min ($p < 0.001$). The time pacing of the PN in the RA was significantly longer than in the left atrium (3 [2–4] min vs. 2 [1.5–3] min; $p < 0.001$).

TABLE 3 Phrenic nerve parameters

Variable	Value	Value
Right PN capture	136/137	(99%)
Left PN capture	25/65	(39%)
Max. distance RA - LA PNC High (mm)	9	(6–10)
<i>Superior vena cava</i>		
High output capture	119/137	(87%)
SVC: Length PNC line high (mm)	20	(16–20)
<i>Right atrium</i>		
High output capture	85/137	(62%)
RA: Length PNC line high (mm)	39.5	(11.25–54)
<i>RSPV with medial wall LA</i>		
High output capture	78/137	(57%)
RSPV/LA: Length PNC line high (mm)	13	(6.5–22)
<i>Left atrial appendage</i>		
High output capture	25/65	(39%)
LAA: Length PNC line high (mm)	8	(4–13)

Note: Data are displayed as *n* (%) or median (interquartile range). Abbreviations: IVC, inferior vena cava; LA, left atrium; LAA, left atrial appendage; PN, phrenic nerve; PNC, phrenic nerve capture; RA, right atrium; RSPV, right superior pulmonary vein; SVC, superior vena cava.

3.1 | PN capture

We were able to capture the right PN in 136 of 137 patients (99%), including pacing sites high in the SVC. Exclusive capture deep in the SVC and deep in the RSPV (>20 mm from the venoatrial junction and >20 mm from RSPV orifice, respectively) was excluded from the analysis being irrelevant for the ablation procedure. The superior vena cava within a 20 mm margin of the RA was the most frequent site of PNC in 87% of patients (Table 3). In the SVC, PNC could be demonstrated over a median length of 20 (16–20) mm. In the RA, the PN could be captured with high output pacing in 62% of patients over a median length of 39.5 (11.25–54) mm.

In the RSPV and adjacent medial wall of the LA, the PN could be captured in 57% of patients. Here a rather short course of PNC with a median length of 13 (6.5–22) mm was seen.

In a subset of 58 (42%) patients, additional low-output pacing (10 mA) was performed at sites with high-output PNC (20 mA). In the RSPV and adjacent LA, 36/58 patients (62%) demonstrated high output PNC and 25/58 (43%) low output PNC. The rates of high and low-output PNC inside the RSPV were significantly higher than PNC in the antrum/LA (Table 4). The rates at the LA sidewall were lower (Table 4).

TABLE 4 Phrenic nerve parameters of subset of patients with additional low output PN pacing

Variable	Value	Value	p
High output pacing			
PNC within RSPV	36/58	(62%)	<0.001
PNC within antrum	12/58	(21%)	
PNC at LA sidewall	8/58	(14%)	
Low output pacing			
PNC within RSPV	23/58	(40%)	<0.001
PNC within antrum	3/58	(5%)	
PNC at LA sidewall	1/58	(2%)	

Note: Data are displayed as *n* (%). Abbreviations: LA, left atrium; PNC, phrenic nerve capture; RSPV, right superior pulmonary vein.

3.2 | Intracardiac course of PN

3.2.1 | Right PN capture in the RA

The typical course of the right PN in the RA started in the SVC at a lateral (50%) or posterolateral (23%) position before descending downwards either straight or with a slight bend towards the posterolateral wall of the RA (Figure 1B). In 12% of patients, we found an anterolateral course of PNC in the SVC. Very rarely (2%), patients showed a posterior course of the PN in the RA. PNC could neither be demonstrated in the posterior part of the SVC, nor in the anterolateral region of the RA.

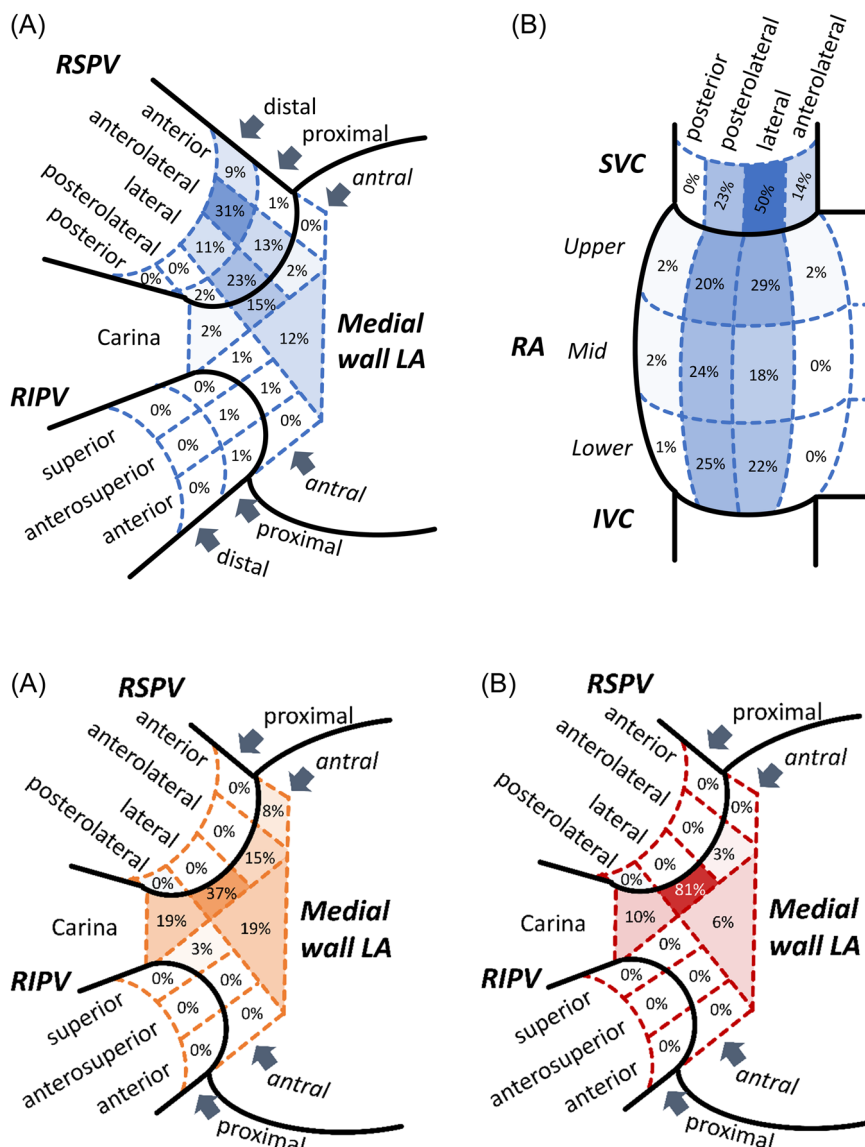
3.2.2 | Right PN capture in the LA

In the LA deep within the RSPV, the right PN most commonly runs anterolateral (31%). It then descends to the lateral aspect of the proximal RSPV (23%), over the lateral antral region (15%) onto the medial LA wall (12%; Figure 1A). A more anterior and anterolateral course in the distal and proximal RSPV could be found in 9% and 13% of cases, respectively. A more posterolateral course along the RSPV, then running over the carina and even leading to PN capture in the antral region of the RSPV was very rare, however, was seen in 2% and 1% of patients, respectively.

PNC in the antrum of the RSPV was found in 19% (26/137) of patients. Specifically, PNC was found in 2% in the carina, 15% in the lateral RSPV antrum, and 2% in the anterolateral RSPV antrum (Figure 1A).

3.2.3 | Left PN capture

Pacing of the left PN was attempted in 63 patients, with PNC in only 25 patients (40%). The left PN could solely be captured deep inside



the LAA, namely in its apex or at its roof. There was neither PNC around the circumference of the LAA nor the antral region of the left pulmonary veins. The course of PNC was rather short with a length of 8 (4–13) mm (Table 3).

3.3 | Ablation line modification

In 31 patients (23%) modification of the ablation lesion set in the RSPV antrum and medial wall of the LA was needed to comply with the self-made prerequisite of not delivering an ablation lesion on sites with PNC. PVI was achieved in all cases where ablation line was modified. The rate of first-pass isolation of the right PVs were 84%. There was no significant difference regarding rates of first-past isolation whether or not modification of the ablation trajectory was necessary (83% vs. 85%, $p = 1$). The lateral RSPV antrum was by far the most common site needing modification of the anticipated ablation trajectory in 81% (25 patients) of these cases (Figure 2B).

The carina (10%), the anterolateral RSPV antrum (3%) as well as the medial wall of the LA (6%) were further sites of PNC necessitating modification of the ablation trajectory.

In the subset of 58 (42%) patients in whom high and low output PN pacing was performed, 15 patients (26%) needed modification of the ablation trajectory due to PNC. Of these locations, 10 (67%) demonstrating exclusive high-output PNC, and five (33%) demonstrating additional low-output PNC.

Figure 3, for the left PN, none of the patients needed modification of the ablation line due to PNC.

3.4 | Minimal distance between PN capture and ablation lesion

In this study, the minimal distances between sites PNC and ablation lesions were 5 mm (three cases), 6 mm (three cases), 7 mm (three cases), and 8 mm (eight cases). For the right PN, frequent locations of

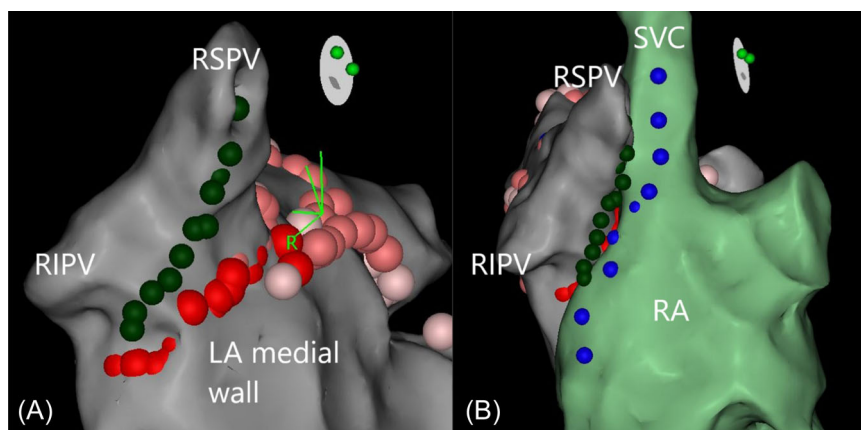


FIGURE 3 (A) View of the LA medial wall from a right medial position in a patient needing modification of the pulmonary vein isolation ablation trajectory due to right phrenic nerve (PN) course, (B) same patient additionally showing the RA highlighting the close spatial relationship of right PN course and both atria in selective patients. IVC, inferior vena cava; LA, left atrium; RA, right atrium; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; SVC, superior vena cava.

the minimal distance between PNC and ablation lesions were in the antral region of the RSPV and the medial wall of the LA (Figure 2A), the most frequent being again the lateral antral region of the RSPV.

For the left PN, we found a minimal distance of PNC to ablation lesion to be 9 mm. The location of the minimal distance was the ridge between LSPV and LAA in all cases (25 patients, 100%).

For the patients with high and low output PN pacing, the resulting minimal distance between the modified ablation lesion and site of PNC was significantly smaller for high output PNC (median 8 [IQR 6–10], $n = 15$) than for additional low output PNC (12 [7–16] mm, $n = 10$, $p = 0.012$).

No cases of PN injury occurred in this study, as confirmed by postinterventional bilateral PN pacing.

4 | DISCUSSION

This study shows that the course of the PNs can be easily mapped and visualized on a 3D electroanatomic map and that knowledge of its course provides important guidance for the trajectory of catheter ablation.

Most importantly, we identified very circumscribed areas of common PNC on the routine ablation trajectory of a RF antral PVI approach, allowing a fast and effective PN screening for everyday usage. These areas are: anterolateral and lateral RSPV antrum, carina, and LA right lateral wall.

The most common course of the right PN in the LA is along the distal anterolateral and proximal lateral RSPV over the lateral antral region to the right medial wall (Figure 1B). However, there can be considerable variation to the right PN course, namely running more anteriorly or posteriorly.

To comply with the prerequisite of not delivering an ablation lesion on sites with PNC, about one-quarter of patients needed modification of the ablation lesion set due to the course of the right

PN. The lateral RSPV antrum was the most common site of PNC necessitating modification of the ablation trajectory (Figure 2B).

The minimal distance between PNC and ablation lesion was 5 mm (three cases), 6 mm (three cases), 7 mm (three cases), and 8 mm (eight cases) with no case of PN injury in this study.

4.1 | Anatomic course of the PNs in the atria

4.1.1 | Course of the right PN in the RA

An anatomical study by Sánchez-Quintana et al.⁹ dissecting the course of the right and left PN in 19 cadavers, found that the right PN descends along the right anterolateral border of the SVC veering posteriorly as it approaches the superior cavoatrial junction. Since we analyzed PNC in the SVC within a margin of 20 mm above the superior cavoatrial junction, we can confirm that PN course in a large clinical patient cohort. Accordingly, in our study, the most common course of the PN in the distal SVC was lateral or posterolateral.

In 2008, Schmidt et al.¹⁰ published a preliminary study in a cohort of 18 patients, reconstructing the 3D anatomic course of the right PN by pace mapping with “maximum output” (10 V, 2.9 ms). Using a clockwise annotation of the SVC in the superior view to track the course of the right PN in the SVC and RA, they found the PN course to be strictly lateral (9 o’clock) in 4 of 15 patients (26%), posterolateral (10 and 11 o’clock) in 8 of 15 patients (53%), and anterolateral (8 o’clock) in 3 of 15 patients (20%). Additionally, they found the PN course in the RA to be straight in a craniocaudal direction with regard to the SVC annotation.

Our results differ from their findings: We found a rather lateral course of the PN in the SVC, running down the RA lateral wall in a variable course, either straight lateral or with a slightly posterior bend into a posterolateral course.

4.1.2 | Course of the right PN in the LA

The anatomical study by Sánchez-Quintana et al.⁹ demonstrated the right PN runs anterior to the superior and inferior right pulmonary veins. It is particular close to the RSPV, with a mean minimum distance of 2.1 ± 0.4 mm and a distance of <2 mm in a third of cases. Unfortunately, the exact location of that minimal distance and a detailed anatomic course of the PN in the LA, both being relevant for the electrophysiologist, is neither described nor depicted in the mentioned publication.

The PN pacing study by Schmidt et al.¹⁰ reported right PNC in only 7 of 18 patients (39%) in the RSPV and only one patient in the LA (6%). These numbers appear to be relatively low, considering we were able to achieve right PNC in the RSPV and LA in 85 patients (62%, Table 3).

Another PN pacing study (high output pacing with 20 mA) by Ji et al.¹¹ did not visualize the entire PN course but checked for PNC on the ablation trajectory. They subdivided the LA course of the right PN into three segments: the anterior aspect of the RSPV, carina, and RIPV. Of the 30 patients (30%) with right PNC in the LA, the anterior aspect of the right carina was the most common site that demonstrated PNC (85% of patients with PNC), followed by the anterior RSPV ostium (70%) and, the anterior RIPV ostium (30%).

We could show that in 62% of patients the right PN runs near the RSPV/LA (Table 3). Furthermore, we could delineate in detail the most common course of the right PN in the LA as follows: descending from the distal anterolateral RSPV to a lateral position in the proximal RSPV, the right PN then moves onto the lateral antral region and further to the medial wall of the LA (Figure 1B). We also showed, that there is a considerable variation to the right PN course, namely a more anterior or posterior course. Additionally, we could characterize the locations needing modification of the ablation trajectory to avoid ablation on sites with PNC.

4.1.3 | Course of the left PN in the LA

On the left side, the PN runs inferiorly over the aortic arch, pulmonary trunk and continues along the lateral wall of the LAA onto the high anterolateral left ventricular free wall.⁹

An anatomical study¹² outlining the spatial relationship between the left PN and key cardiac structures showed that there are three types of courses of the left PN in relation to the LAA: an anterior, a lateral, and an inferior course. While the anterior course does not cross the LAA, the lateral PN course descends close to the apex of the LAA, and the inferior PN course passes with a close relationship to the roof of the LAA. Romero et al.¹³ found that the left PN can be captured within the LAA in 74% of cases and in only 4.5% at the proximal LAA or the LAA ostium. Huemer et al.¹⁴ demonstrated PNC by high-output pacing (20 mA) in the ostial part of the LAA in 5% of patients.

Concordantly, we only found PNC in the apex and roof of the LAA. Regions as the antrum of both left pulmonary veins and the circumference of the LAA did not demonstrate PNC.

4.2 | Catheter Ablation and the course of the PNs

In 2013, Ji et al.¹¹ reported that the PN lies along a wide-area circumferential ablation line trajectory in 30% of patients. This is similar to our finding of 23% needing modification of the ablation lesion set, to comply with the prerequisite of not applying an ablation lesion on sites with PNC. However, we could describe in detail the lateral RSPV antrum as the most common but not exclusive site for modification and we could highlight that the entire RSPV antrum and medial wall of the LA can be in close proximity to the right PN (Figure 2A).

Fukumoto et al.¹⁵ reported that in 68% of patients the right PN was captured (low output pacing with 10 mA) from the RSPV, while only 1 of 40 cases (2.5%) demonstrated right PN capture 6 mm outside the RSPV in the left atrial antrum, a finding, which may be explained by the low pacing output alone. This suggests, that ablating in the RSPV antrum is not accompanied by an increased risk of PN injury. On the other hand, we could show that right PN capture in the RSPV antrum and LA medial wall is much more common with 19% and 12% of cases, respectively.

Furthermore, our data on high and low-output PNC shows, when pacing as well as ablating inside vascular structures (RSPV) the PNC threshold is lower, hence, the PN may be closer and the risk for PN injury higher. Pursuing an antral PVI approach with ablation strictly in the RSPV antrum should reduce the risk of PNI, however, does not eliminate it. Thus, the safest approach would be to apply the same rules for the LA as for the RA, where it is common practice to avoid ablation at sites with PNC.

4.3 | Minimal distance between site of PNC and ablation lesion—What is a safe distance to PNC for ablation?

For high-output PNC the minimal distance to an ablation lesion was 5 mm (three cases), 6 mm (three cases), 7 mm (three cases), and 8 mm (eight cases) in our study.

Although there were no cases of PN injury in this study, the conclusion of 5 mm being a safe distance for catheter ablation is not valid due to the small sample size and the rareness of this complication.

4.4 | How to explain the discrepancy between common PNC and low incidence of PN injury?

From an anatomical standpoint, the thickness of the muscular LA sidewall ranges between 2.5 and 4.9 mm (mean 3.9 ± 0.7 mm).¹⁶

Additionally, the mean thickness of the fibrous pericardium measured on histology is reported to be 0.5 ± 0.1 mm (range 0.2–1 mm).¹² Last, the PN itself runs within the pericardiophrenic neurovascular bundle, which is surrounded by a fat pad of variable thickness (0.1–1.2 mm).¹² Thus, estimating the mean thickness of tissue between PN and directly opposed ablation catheter in the LA would be about 5.0 mm.

The thickness of superior pulmonary veins wall was measured to be 2.3 ± 0.9 mm.¹² Again, adding the thickness of the fat pad around the pericardiophrenic neurovascular bundle, the estimated mean thickness of tissue between PN and directly opposed ablation catheter in the RSPV would be about 3.0 mm, explaining the higher rate of low output PNC in the RSPV as well as the higher incidence of PNI when ablating inside a pulmonary vein.

Biophysical data shows a lesion diameter of 11.7 mm (radius 5.85 mm) when applying RF energy with a 7F, 3.5-mm tip, open-irrigated ablation catheter at 30 W with 20 g of contact force for 60 s,¹⁷ which is marginally above the estimated tissue thickness in the LA. Additionally, ablation lesion lines generated with RF are not homogeneous and may differ in diameter and depth, as for low-power or high-power, short-duration lesions. Furthermore, the accompanying artery and vein may have an additional convective cooling effect on the PN. Another factor may be the lack of systematic assessment for PNI after RF PVI procedures, thus those patients may be underdiagnosed.

To conclude, as long as PN injury seems possible at a desired ablation site, either ablation at this site should be avoided or monitoring of PN integrity during ablation should be performed.

4.5 | Implications for catheter ablation procedures

Due to the high percentage of PNC in the antral region of the right pulmonary veins and the severe complication of a PN palsy, we suggest the following routine approach for PVI:

- (A) As a routine approach, PN pacing before ablation should be mandatory in the following circumscribed regions: the anterolateral and lateral RSPV antrum, carina, and LA right lateral wall. When not delineating the PN course in detail, this is feasible in 10–20 s.
- (B) As an additional safety measure, PN pacing also in the SVC and RA may be considered. Exclusive PN pacing in the RSPV and LA could theoretically miss the PN course, if not done very thoroughly. Knowledge of the right PN course in the SVC and RA enables the interventionalist to specifically and easily target adjacent sites for PN pacing in the LA. With this approach, it seems safer that all PNC sites are identified in LA.

Regarding time constraints, acquiring the entire RA geometry as in this study would not be necessary for everyday usage. Focusing on the SVC as well as the lateral and posterolateral RA would be

sufficient. PN pacing itself is quickly applicable and took about 2.25 min per atrium.

For a simple circumferential PVI procedure, pacing the left PN is not necessary. However, when performing an LAA isolation procedure or targeting focal atrial tachycardias from the LAA this may differ.

4.6 | Limitations

Owing to the increased risk of perforation, PN mapping inside the LAA was not forced. Thus, some sites of PNC inside the LAA may have been missed. Pace mapping of the left PN deep inside the LSPV was not performed. Although this is a known rare site of PN capture,¹⁵ this location is not of clinical relevance for catheter ablation. Furthermore, the sample size was too small to make a statement whether or not PN injury can be effectively prevented with the described method. However, when treating arrhythmias in the RA (SVC isolation, focal atrial tachycardia arising from crista terminalis), similarly no ablation is performed at locations with PNC.

5 | CONCLUSION

This study delineates in detail the most common course of the right and left PN in the RA and LA and identifies very circumscribed areas of common PNC on the routine ablation trajectory of an RF antral PVI approach, trying to bridge the gap between theoretical anatomical course and the practice-oriented visualization of the PNs in a descriptive schematic and ultimately allowing a fast and effective PN screening for everyday usage.

The most common course of the right PN in the LA is along the distal anterolateral and proximal lateral RSPV over the lateral antral region to the right lateral wall (Figure 1B). However, there can be considerable variation to the right PN course, namely running more anteriorly or posteriorly.

Thirty-one patients (23%) needed modification of the ablation lesion set to avoid ablation on the course of the right PN in the antrum of RSPV and right lateral wall of the LA. The lateral RSPV antrum was the most common site of PNC necessitating modification of the ablation trajectory (Figure 2B).

While pacing and monitoring the right PN during cryoballoon PVI is an integral part of the procedure, it should also be routinely used during RF PVI procedures.

CONFLICTS OF INTEREST

Franz-Josef Neumann reports lecture fees paid to his institution from Amgen, Bayer Healthcare, Boehringer Ingelheim, Boston Scientific, Daiichi Sankyo, Edwards Lifesciences, Ferrer, Pfizer, Novartis; consultancy fees paid to his institution from Boehringer Ingelheim, Novartis and grant support from Bayer Healthcare, Boston Scientific, Biotronik, Edwards Lifesciences, GlaxoSmithKline, Medtronic, Pfizer,

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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