Cardioneuroablation as Therapy to Neurally Mediated Bradycardia

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Background

- Reverse remodeling of sinus node function after catheter ablation of atrial fibrillation in patients with prolonged sinus pauses and/or sinus bradycardia has been observed since 1995.

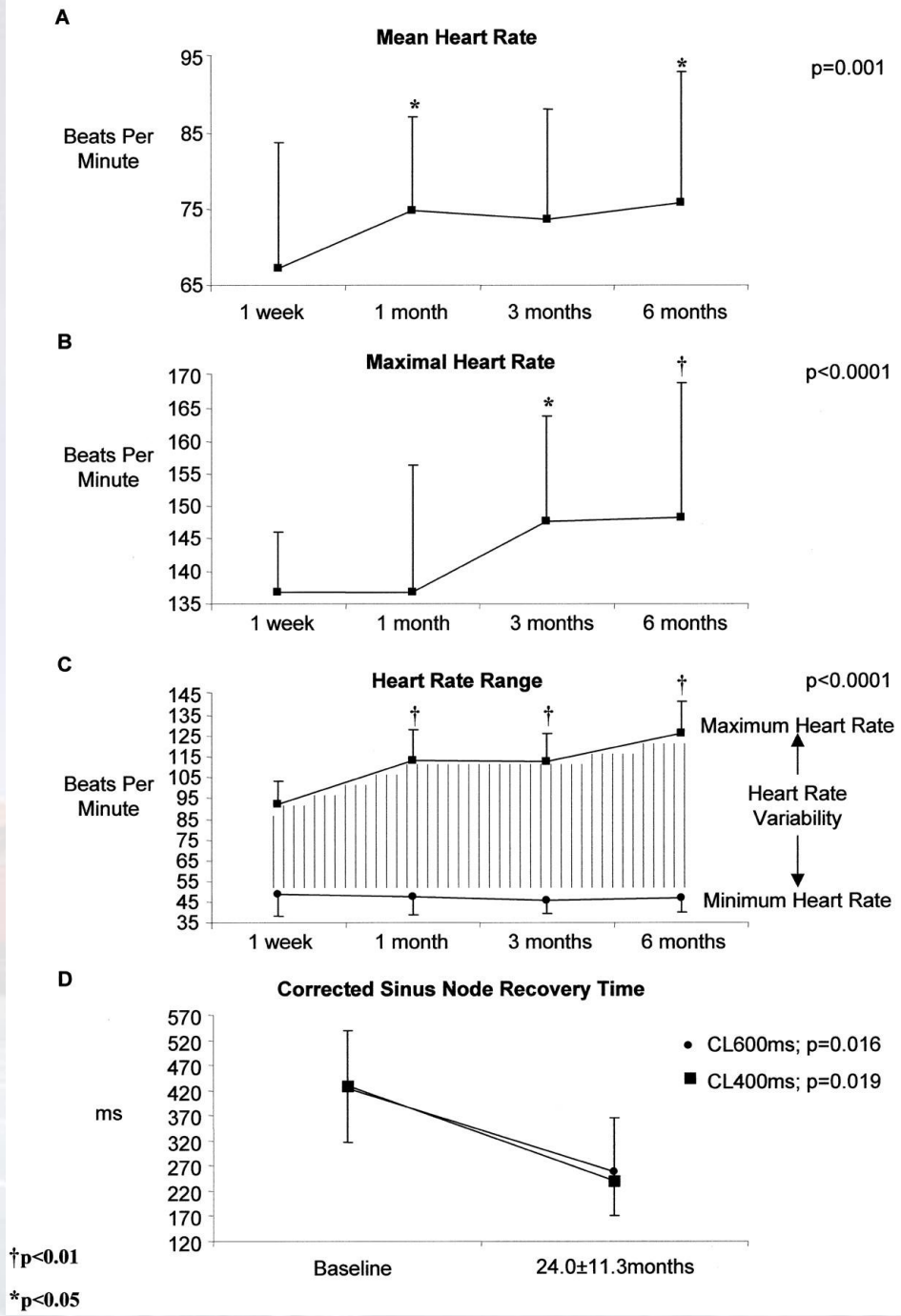
Circulation. 2003;108:1172-1175

- The increasement of sinus rate post PV isolation of paroxysmal AF may last 1 year.

Europace 2005 415–420

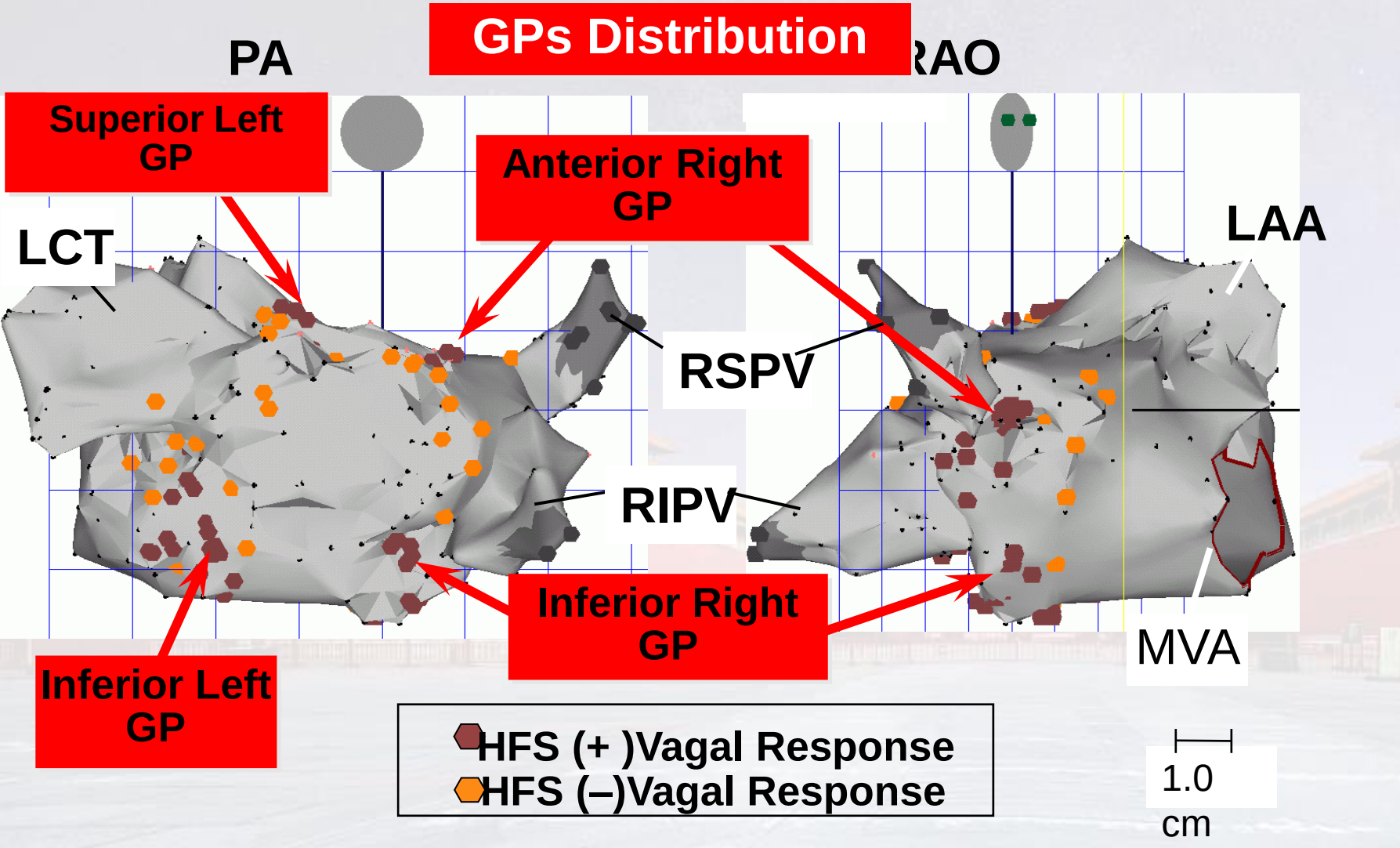
- Cryo-PVI causes a significant rise of sinus rate that is more pronounced in subjects with previous sinus bradycardia.

Clin Res Cardiol. 2021

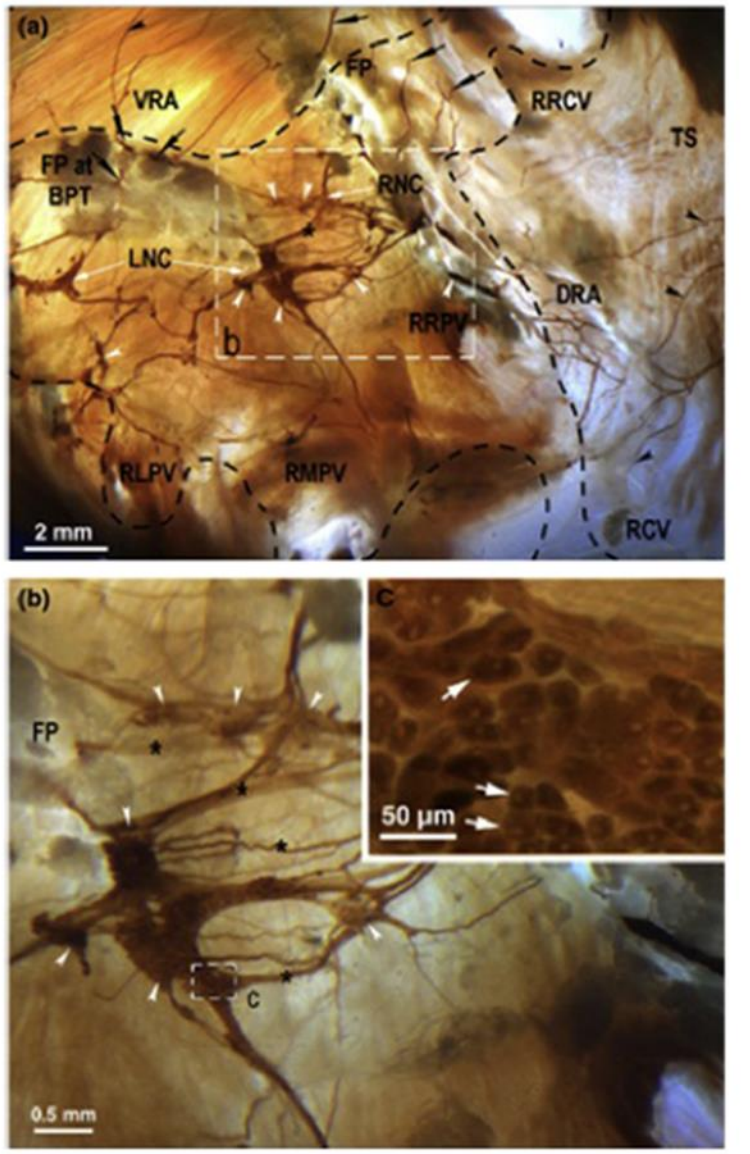


Circulation. 2003;108:1172-1175

GPs of the left atrium

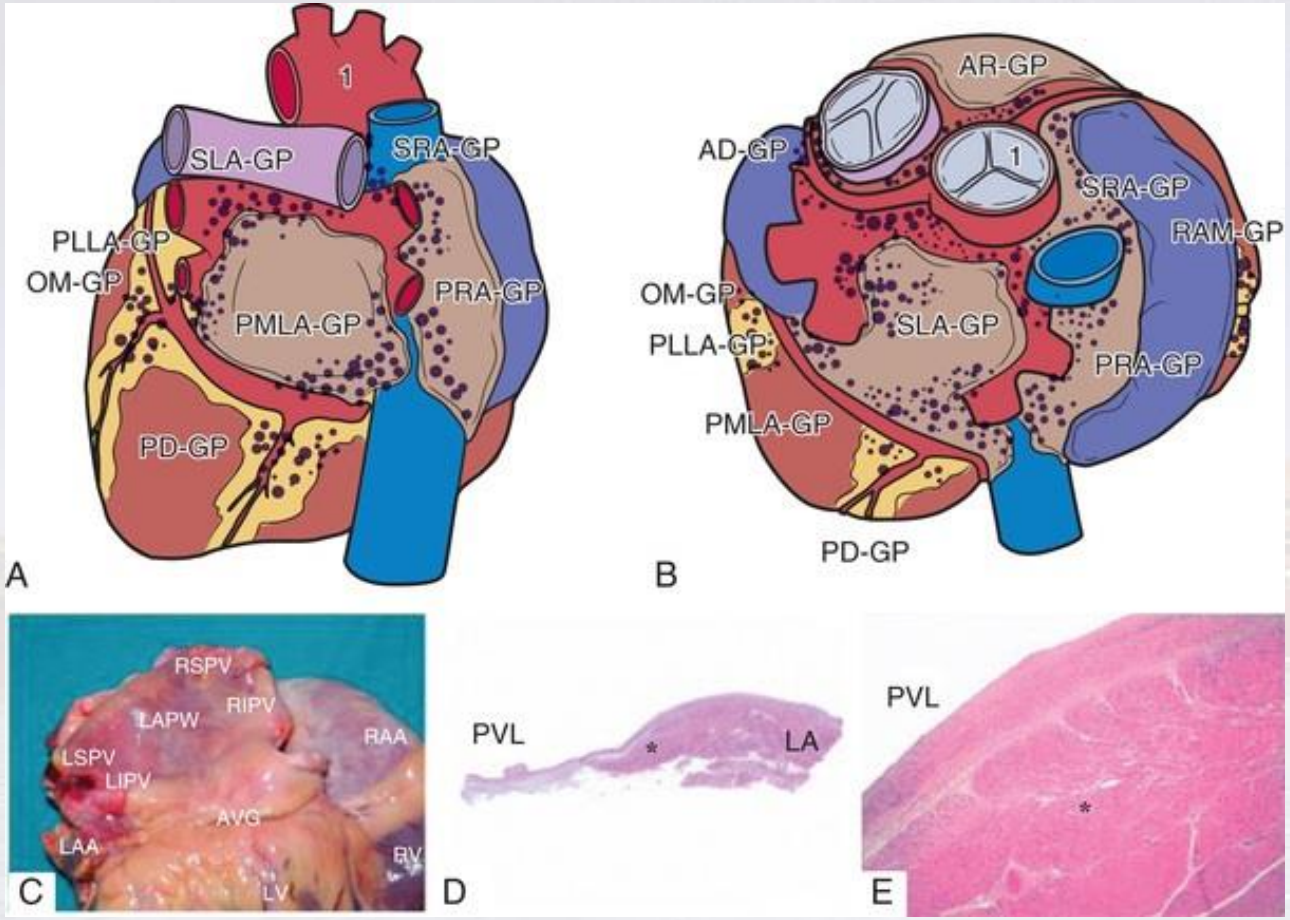


Po S, 2009



Autonomic Neuroscience: Basic and Clinical 199 (2016) 3–16

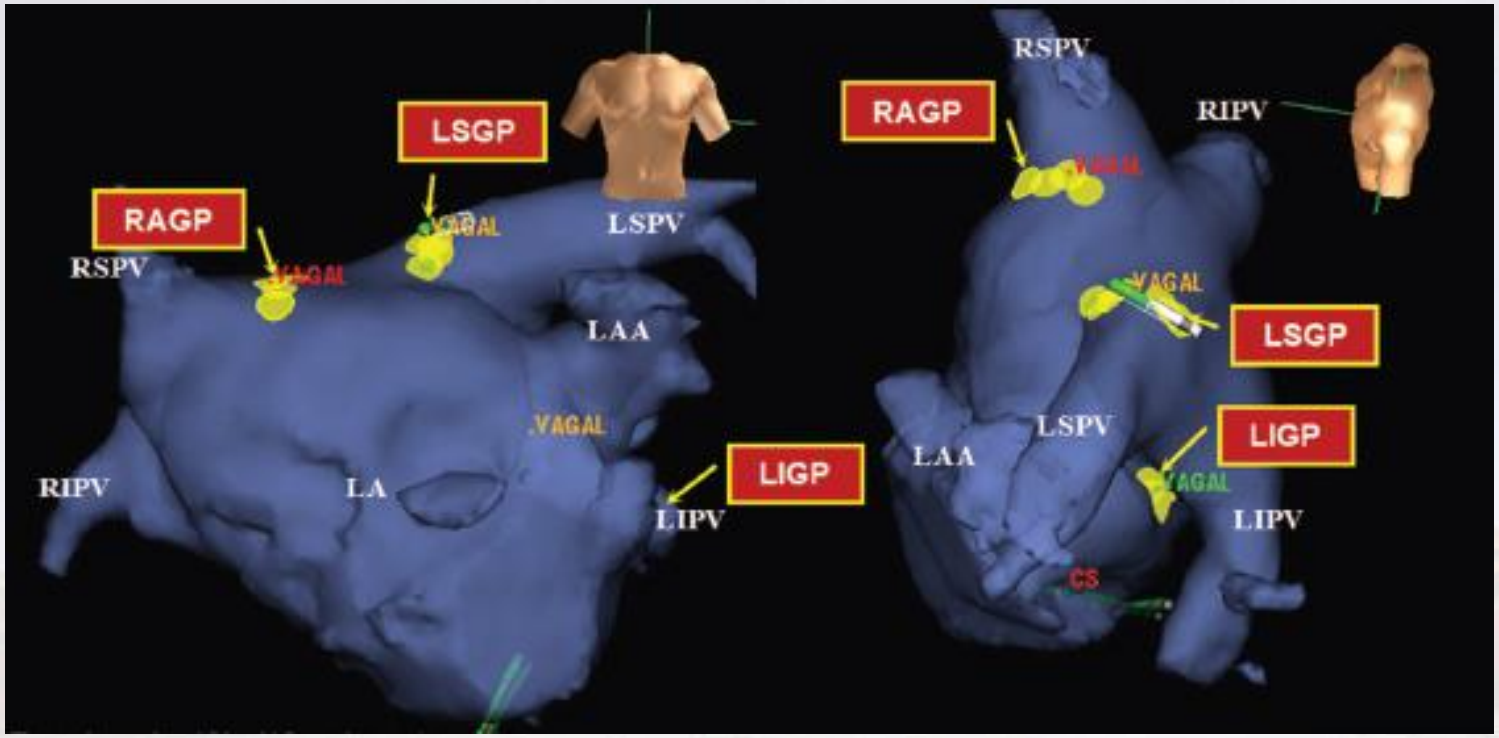
Anatomic Locations of Ganglionated Plexus (GPs)



- Tissues between LA and pulmonary veins
- Tissues between RA and SVC / IVC
- Interatrial tissues
- Marshall vein
- CS
- Tissues adjacent to coronary arteries
- Interventricular tissues

Corradi D et al. Int J Cardiol 2013;168:1769-78.

Concept of Cardioneuroablation



Potential Indications:

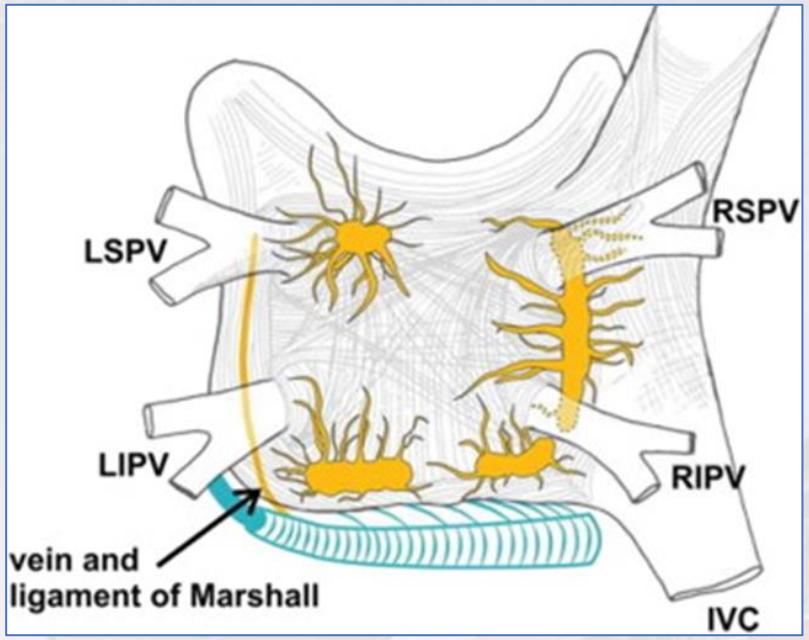
- Vasovagal syncope (VVS)
- Brady arrhythmias
- Atrial fibrillation

The GPs could be abolished by catheter ablation

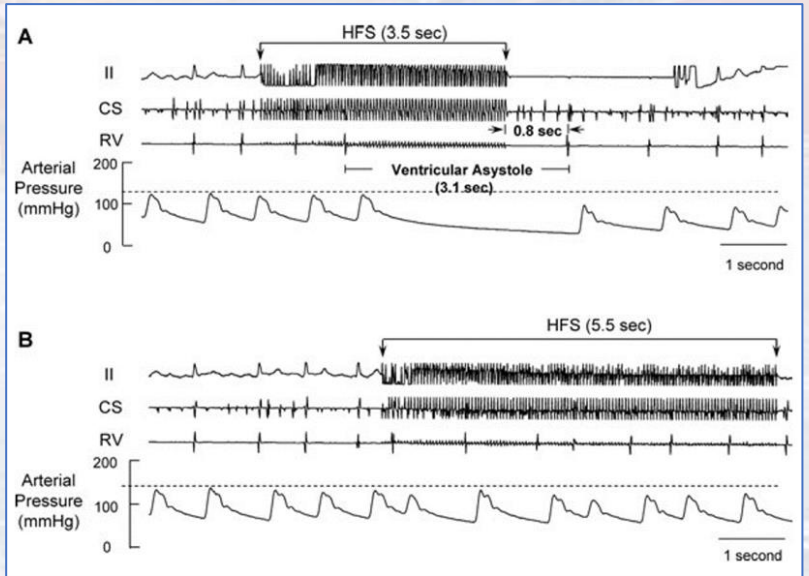
It may rebalance the due to the physiological function of GPs' and also anatomical location which can be targeted easily by ablation catheter.

Methods for GPs Targeting

- Anatomic
- EGM Mapping
- High Frequency stimulation（HFS）

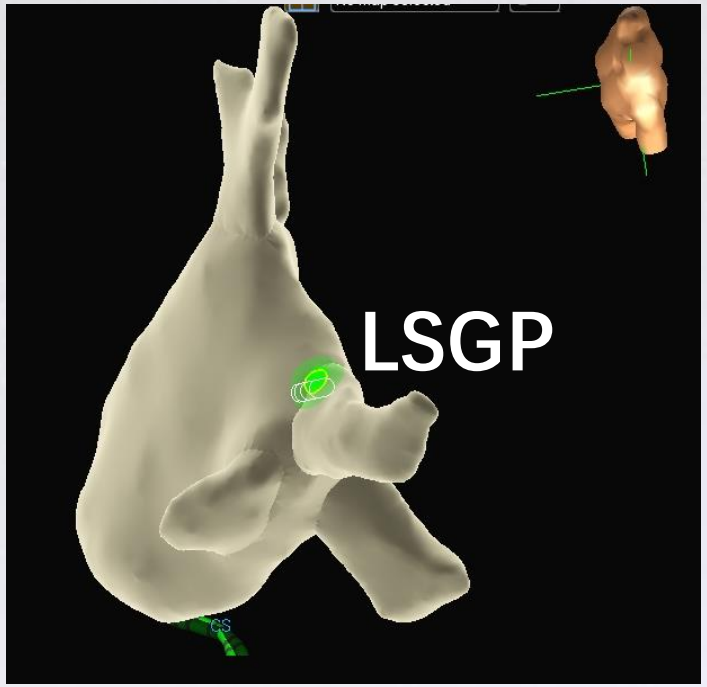


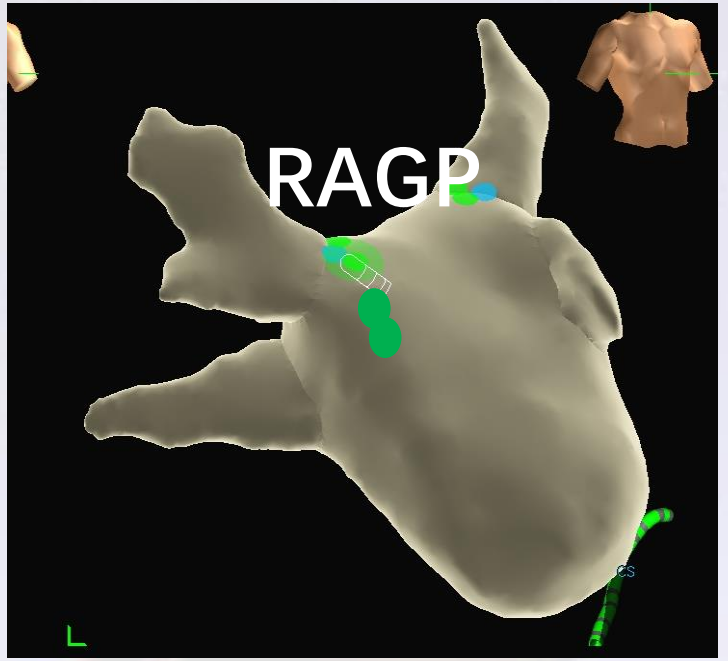
Europace, 14 (2012), pp. 528-606

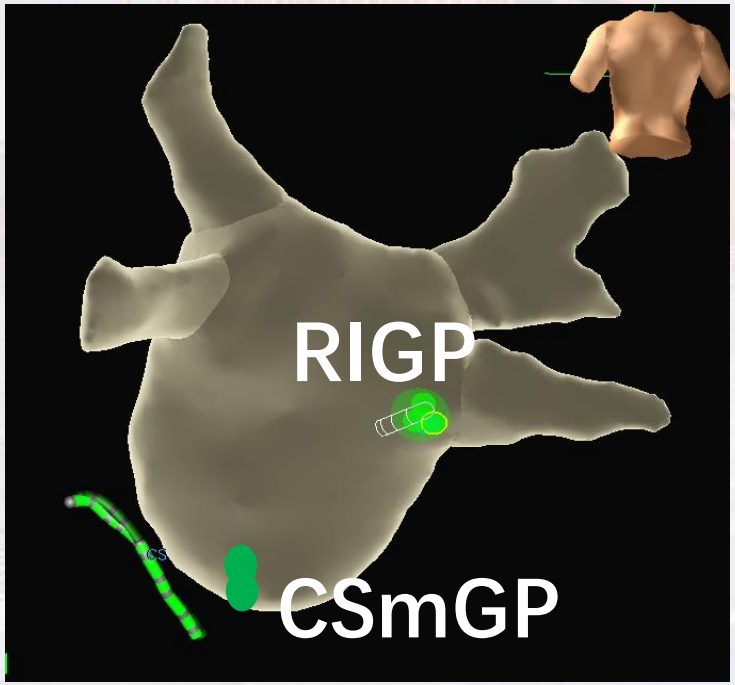


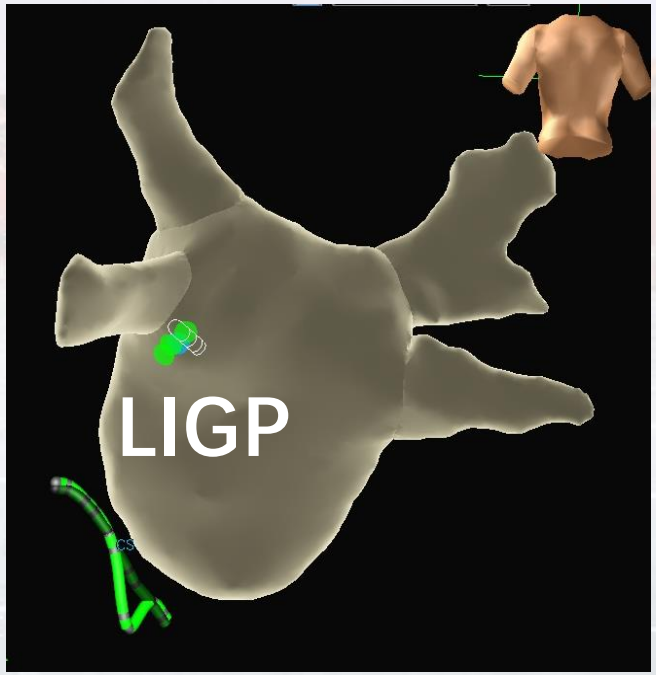
Po S, JCE 2009

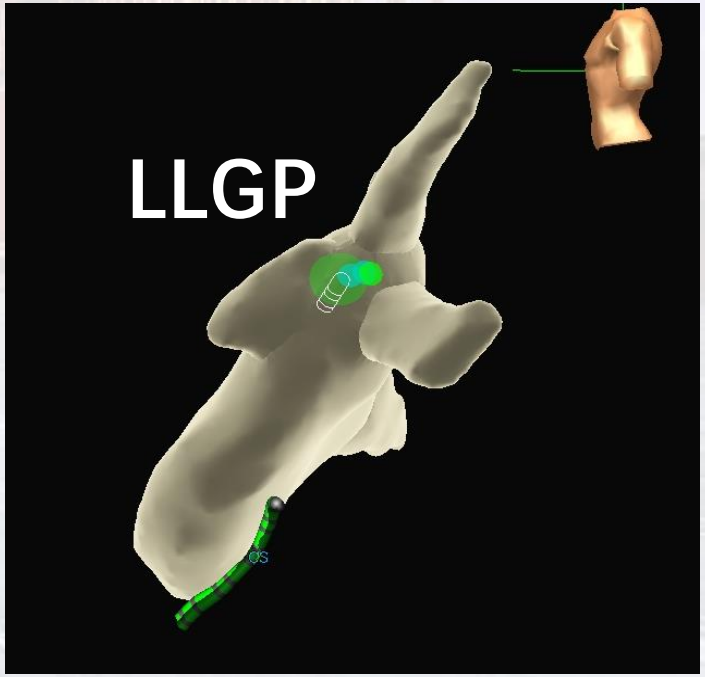
Anatomic targets of GPs





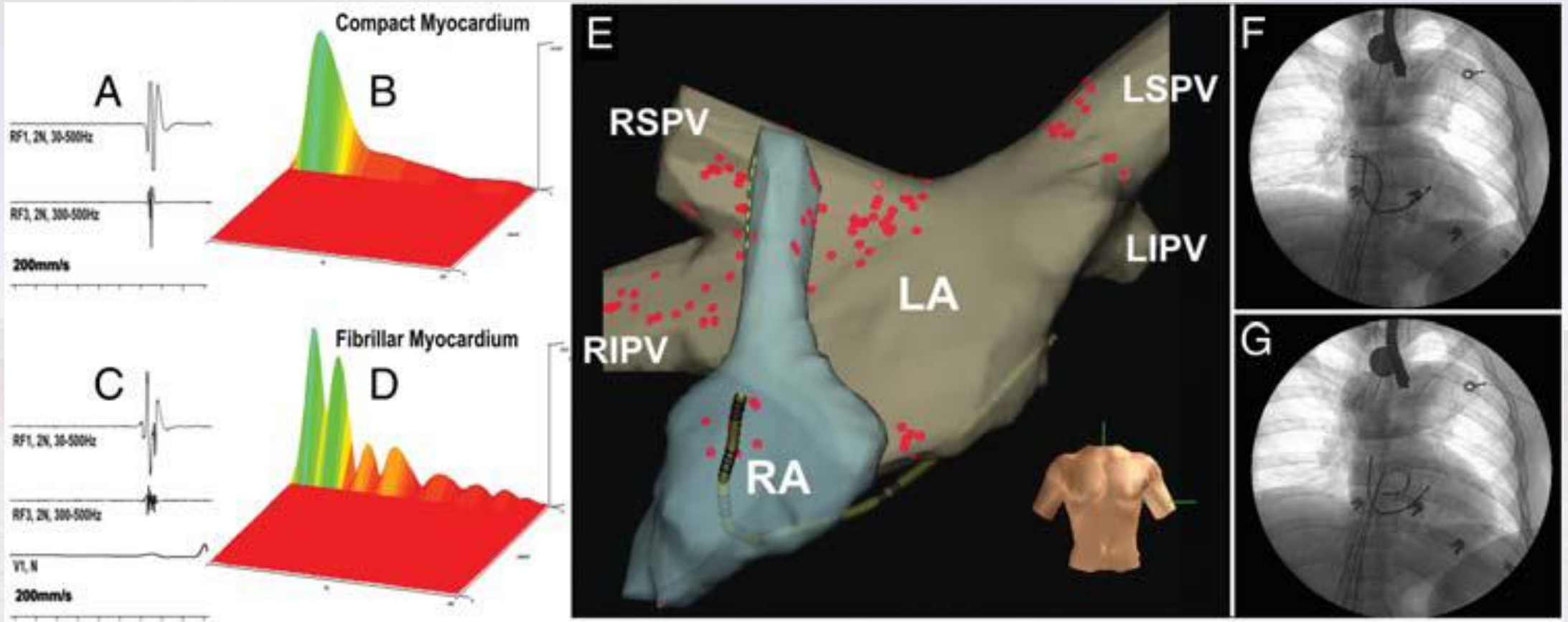






Methods for Targeting: 1

Jose Carlos Pachon （Brazil）： RA + LA

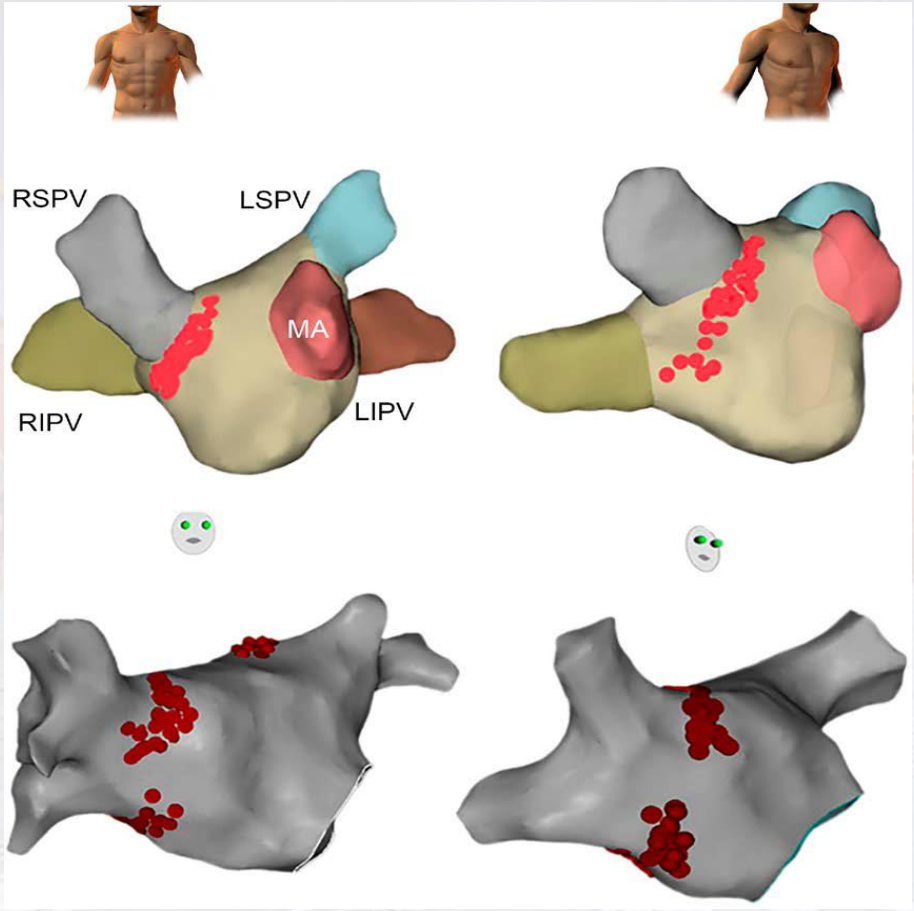


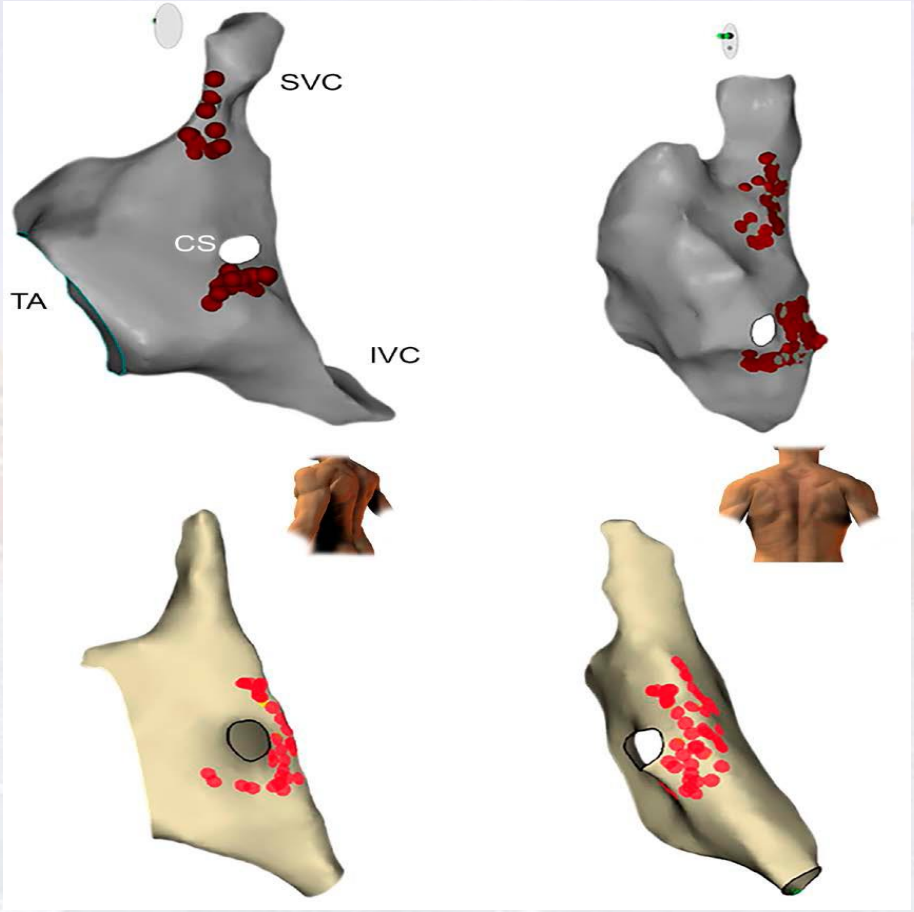
Europace (2011) 13, 1231–1242

Methods for Targeting: 2

Esteban W. Rivarola （Brazil）：

RA + LA

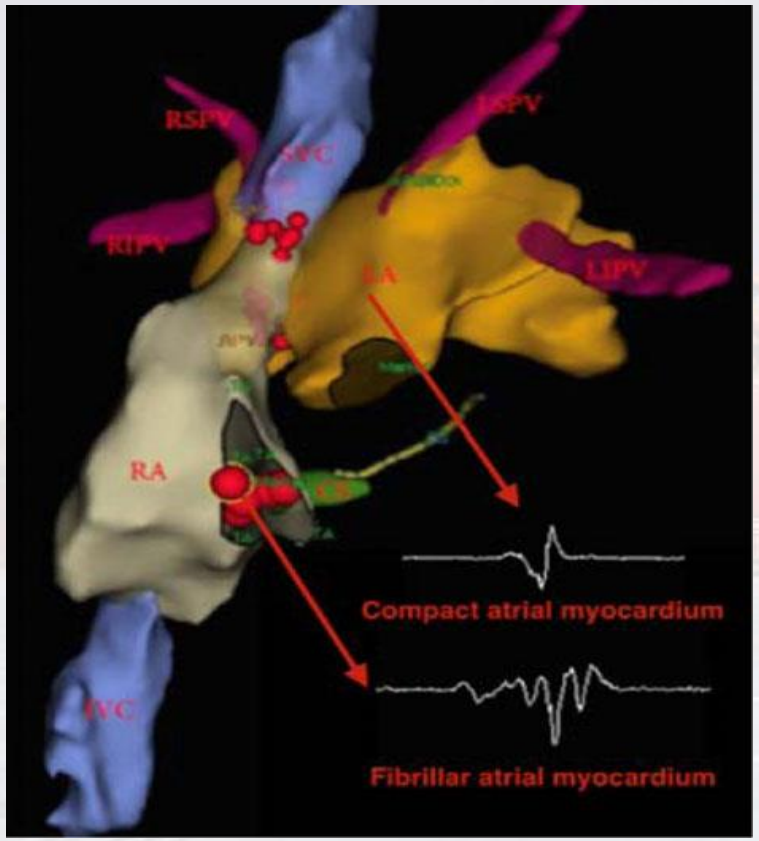


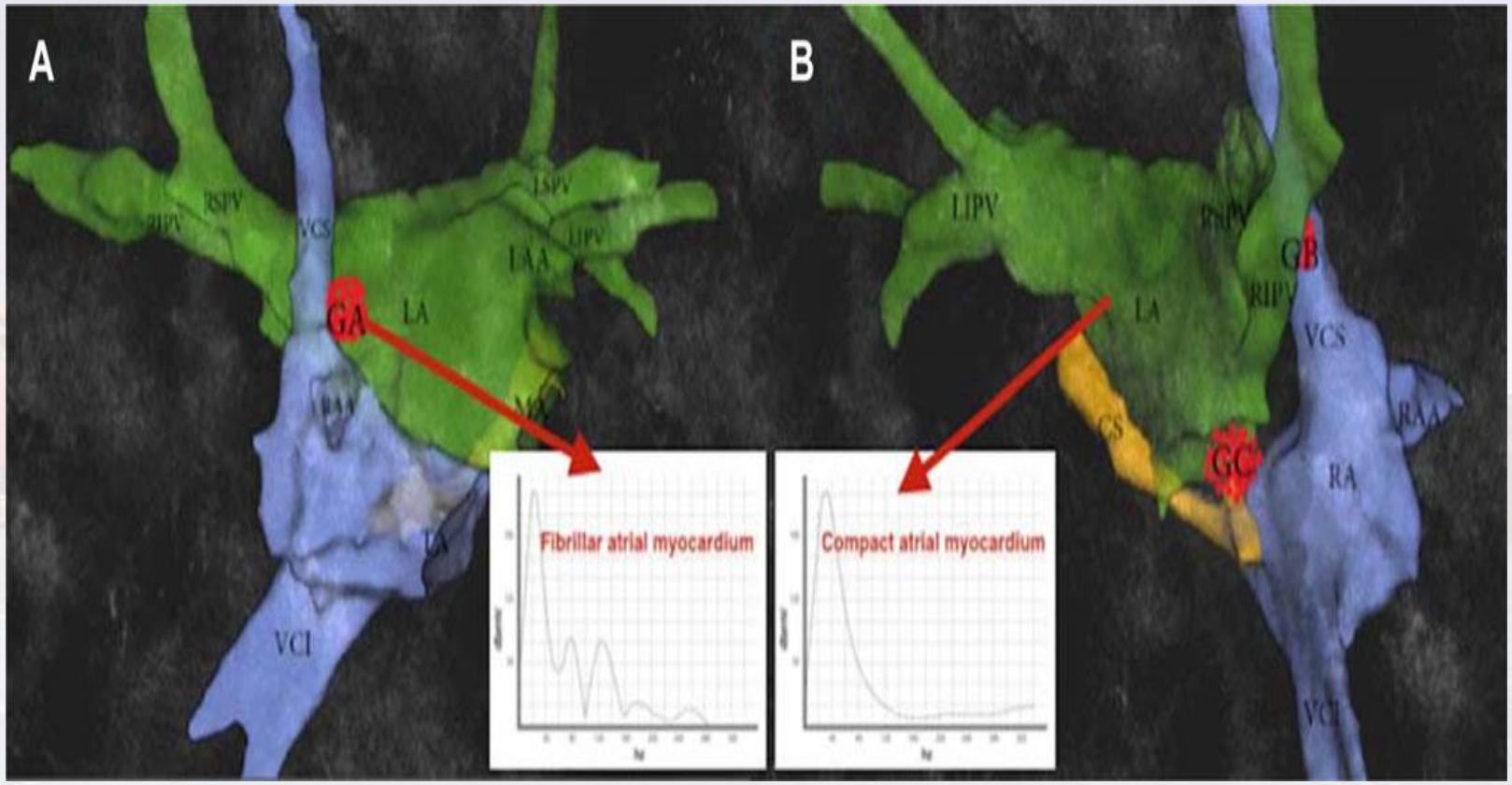


Circ Arrhythm Electrophysiol. 2017 Feb;10(2):e004638.

Methods for Targetting: 3

Tolga Aksu （Turkey）：　　RA + LA



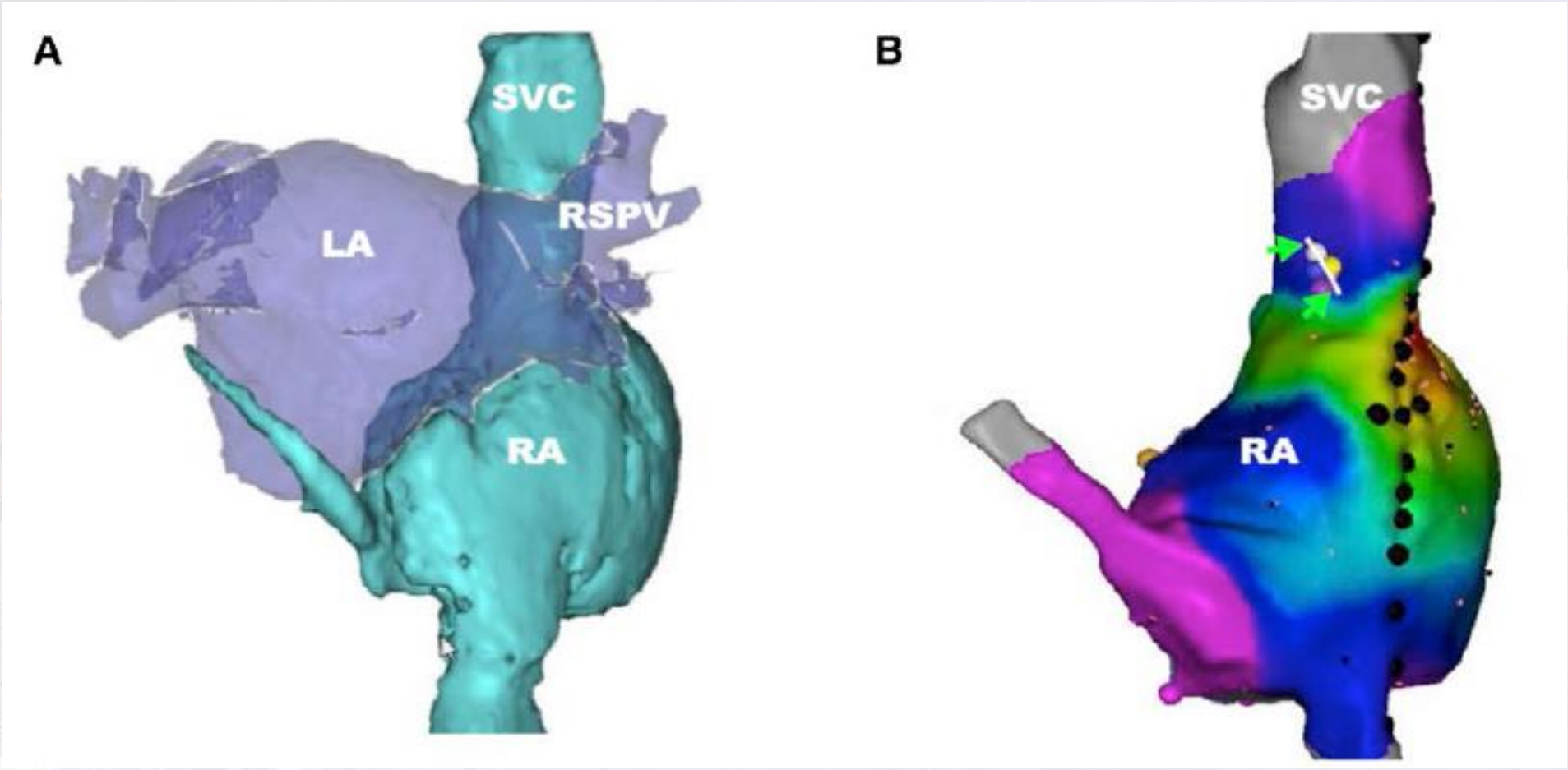


Pacing Clin Electrophysiol. 2016 Jan;39(1):42-53

J Cardiovasc Electrophysiol 2020 Dec;31(12):3326-3329.

Methods for Targeting: 4

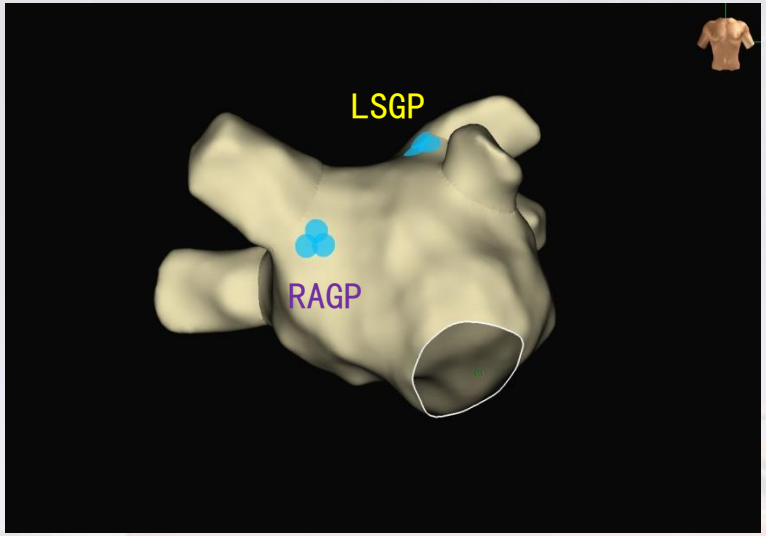
Philippe Debruyne (Belgium）：　　RA

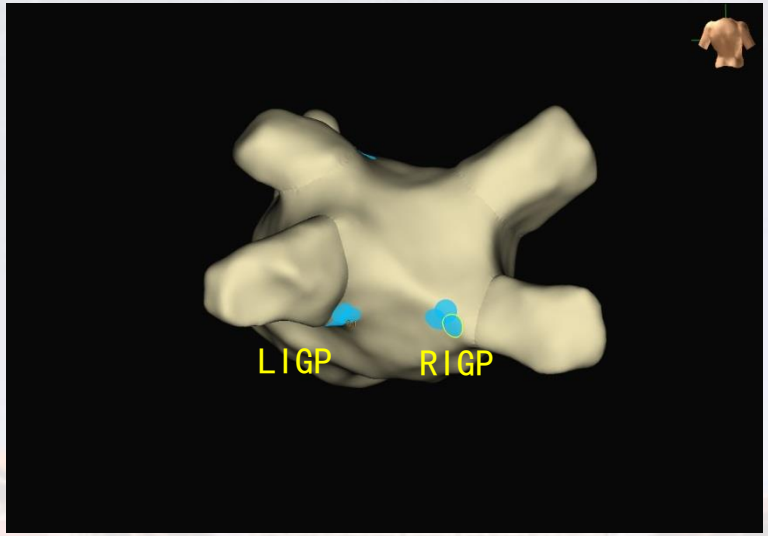


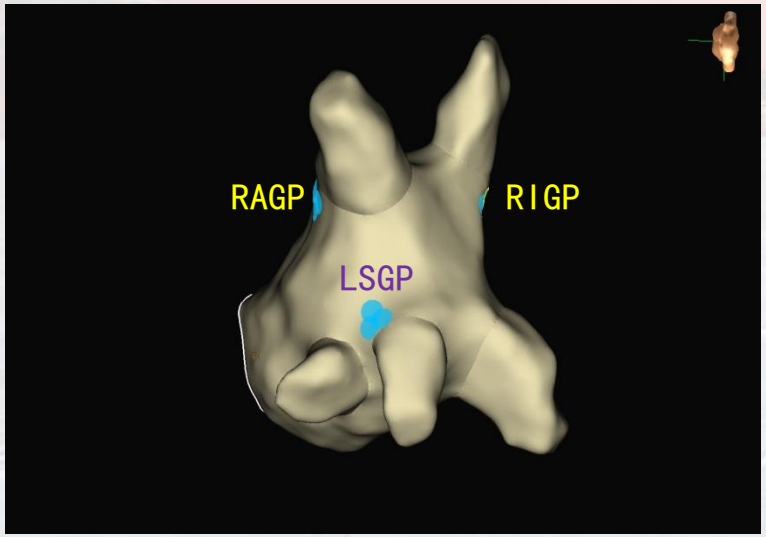
Circ Arrhythm Electrophysiol 2018;11:e006604

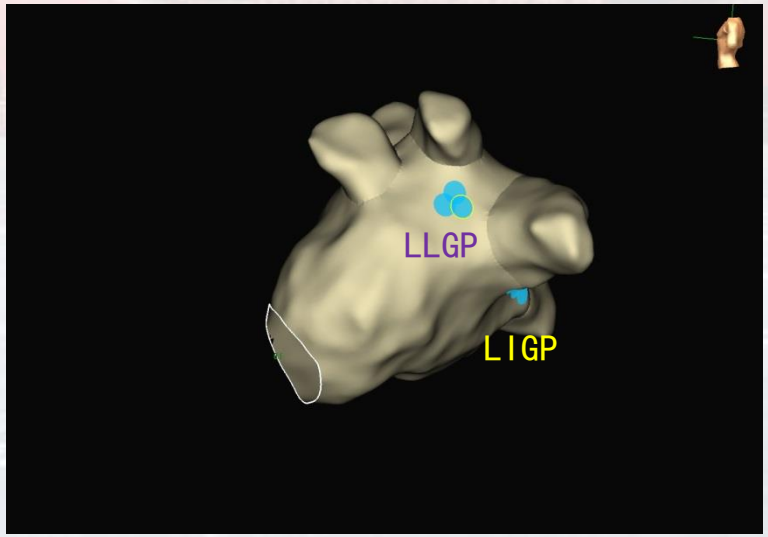
Methods for Targeting: 5

Yan Yao (China）：　　LA



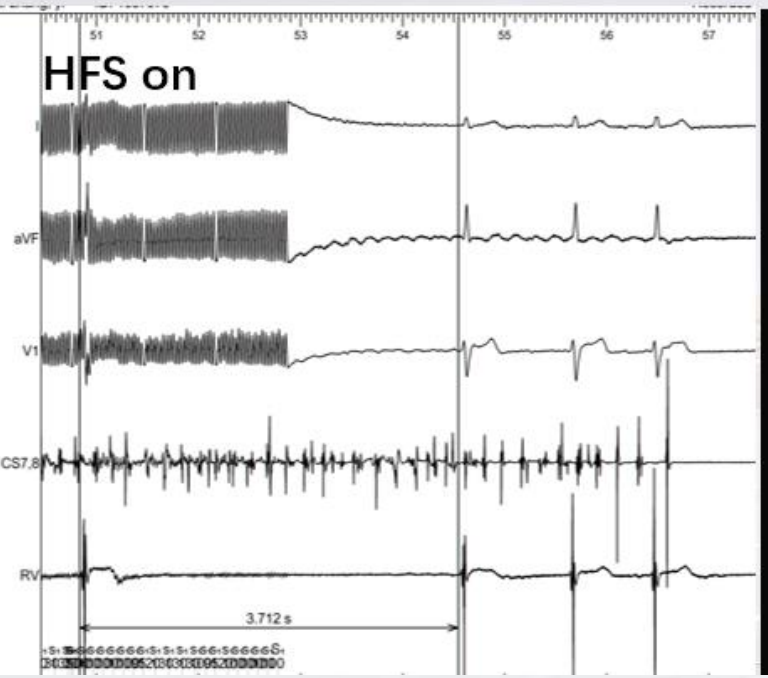


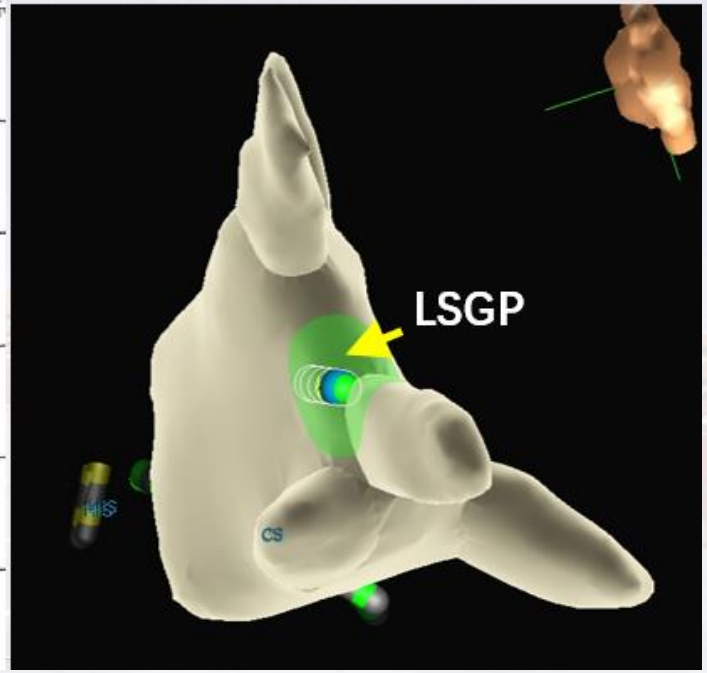




- RAGP： Right anterior GP
- LSGP： Left superior GP
- LIGP： Left inferior GP
- LLGP： Left lateral GP
- RIGP： Right inferior GP

Method for Targeting:
High Frequency Stimulation (HFS)





High frequency stimulation (HFS):

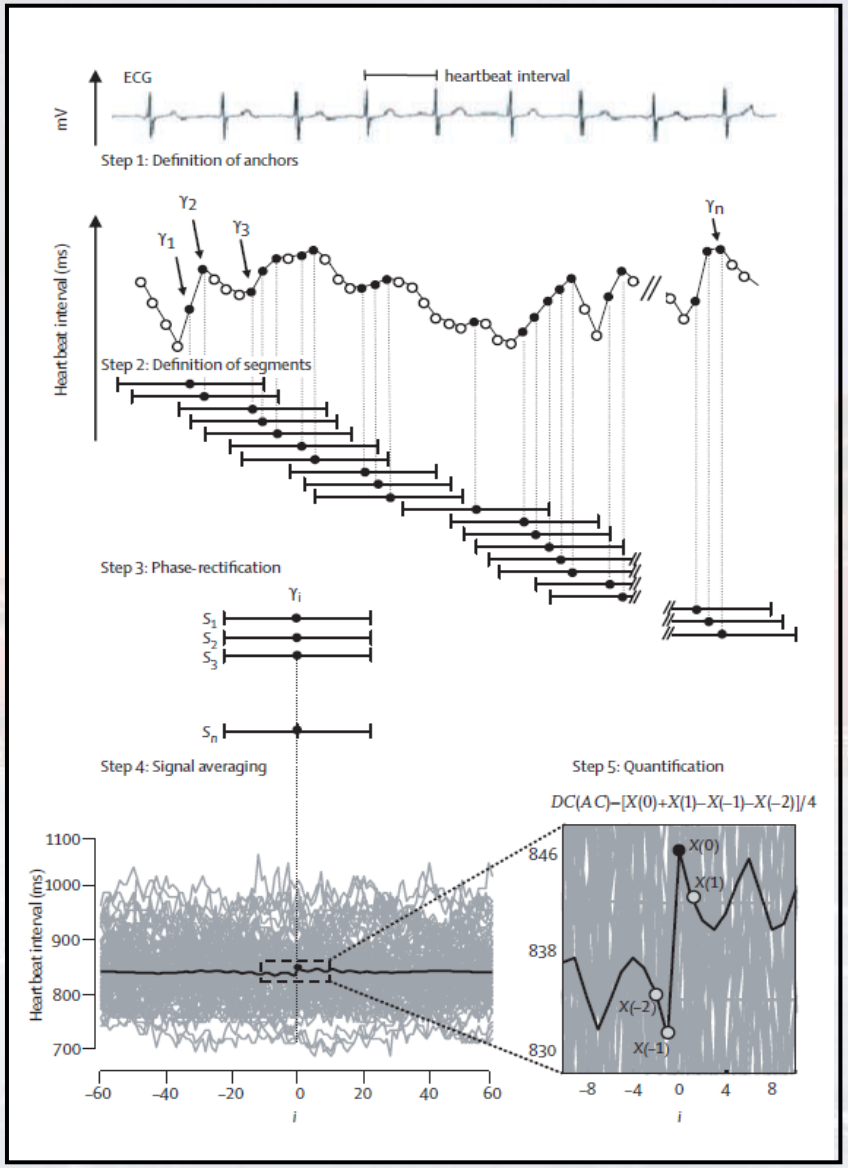
Frequency: 20-50Hz
Output: 10-150V
PW: 10ms
Duration: 2-5 Sec.

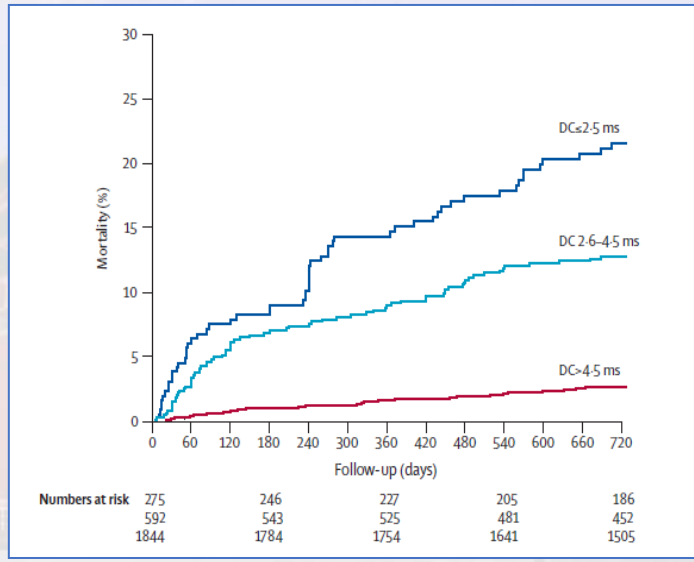
Positive HFS:
SR decrease>50%, sinus pause or AVB>2.0 Sec.

Po SS. J Cardiovasc Electrophysiol. 2009;20:1186-1189

Value of Deceleration Capacity (DC)

- Deceleration capacity(DC) is derived by PRSA(phase-rectified signal averaging) technique;
- Quantitative assessment of cardiac vagal tone;
- Risk stratification evaluation in AMI patients;
- DC:
  - ✓Overall DC(ODC):24 h
  - ✓Daytime DC(DDC):6:00-23:00
  - ✓Nighttime DC(NDC):23:00-06:00





1. Bauer A. Physica A. 2006;364:423-434.
2. Bauer A. Lancet. 2006;367:1674-1681.

DC > 7.5 could be used to diagnose VVS & increased vagal tone

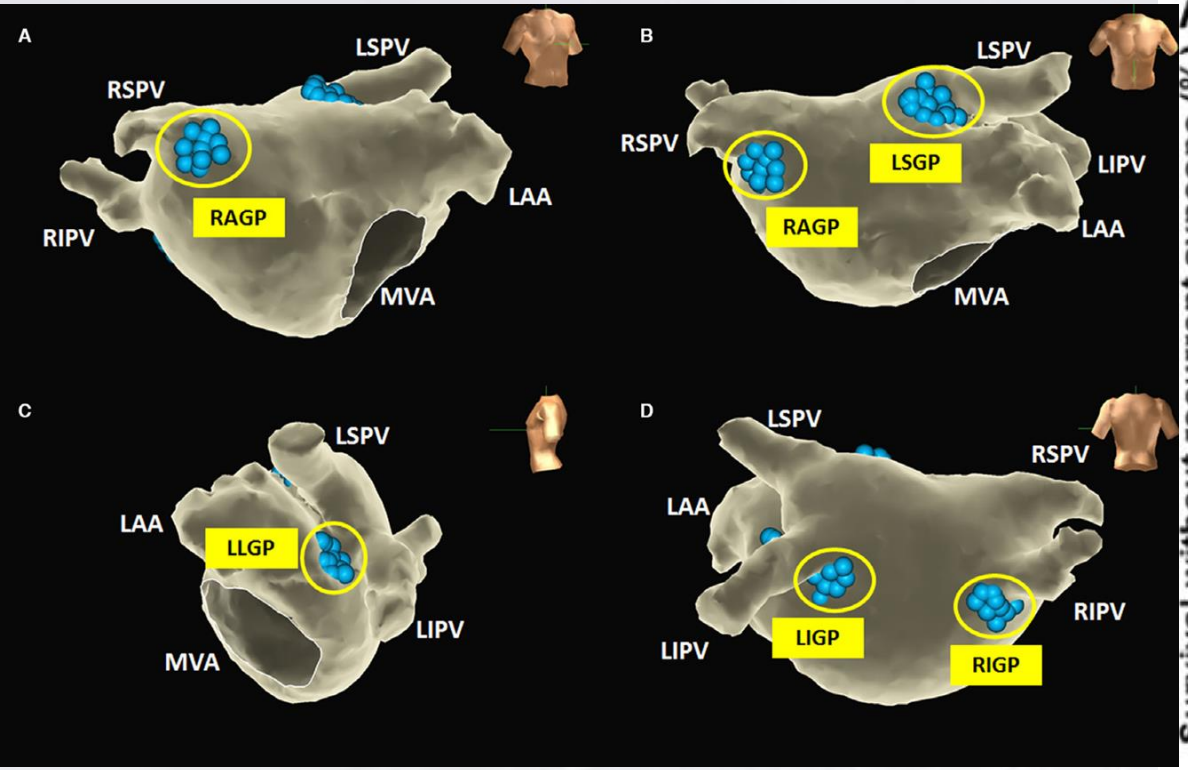
▪ Table 4 ROC curve analysis of DC, SDSD, SDNN and RMSSD

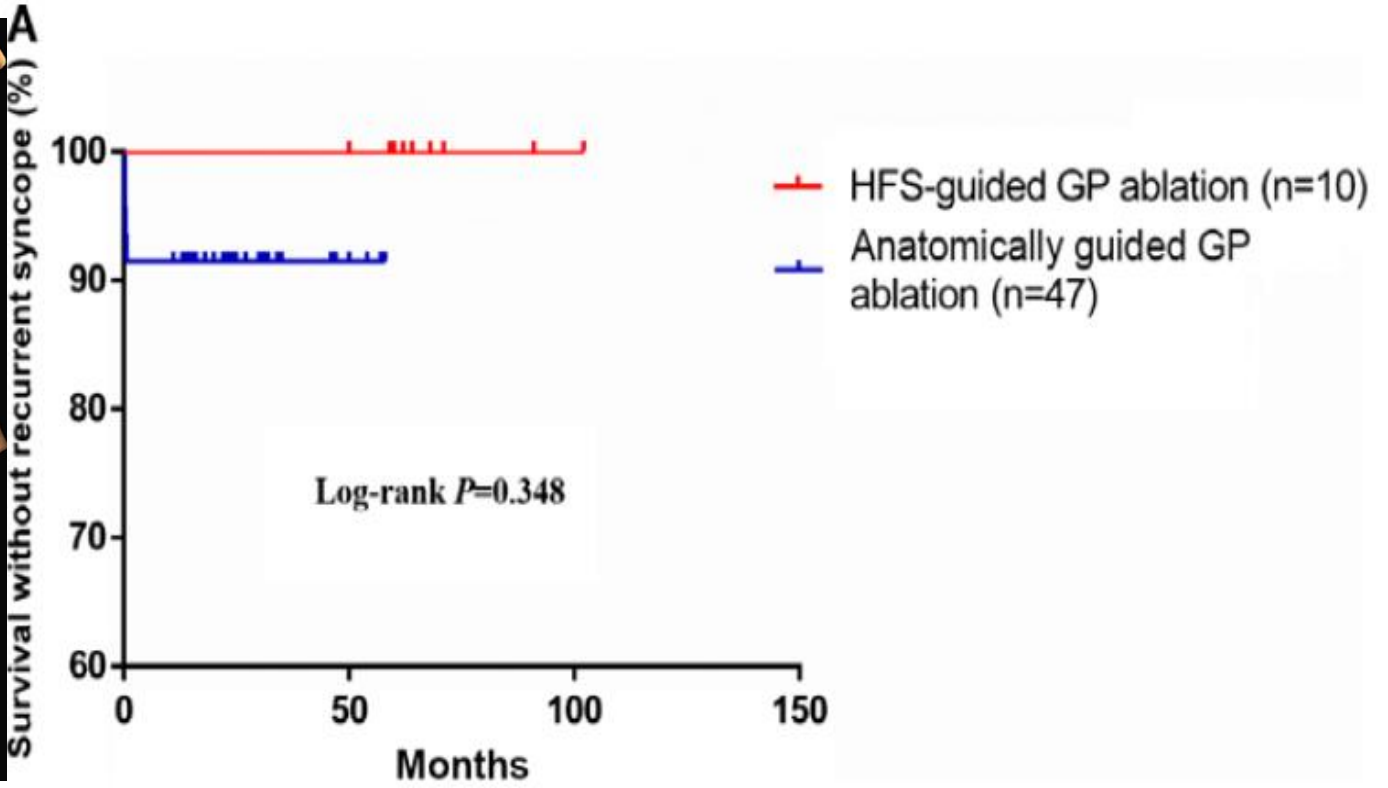
	AUC	Cutoff value (ms)	Sensitivity (%)	Specificity (%)
DC	0.863(0.801-0.924)	6.78	81.3	88.5
SDSD	0.624(0.528-0.720)	28	79.2	52.5
SDNN	0.683 (0.601-0.765)	131	49.0	86
RMSSD	0.605(0.517-0.693)	34	42.7	87

AUC=area under curve; DC=deceleration capacity; SDSD=standard deviation of difference between adjacent normal-to-normal intervals; SDNN= standard deviations of all average normal-to-normal intervals; RMSSD= root mean square of all successive differences of all normal-to-normal intervals.

Zheng LH, Yao Y, et al. Circ AE, *2020*

Long-term Effectiveness of Cardioneuroablation in VVS with HFS vs Anatomic Targeting





Sun W, …Yao Y, et al. JAHA 2016

Underlying Mechanism:

Role of RAGP in Cardioneuroablation

ELSEVIER

Heart Rhythm

Volume 16, Issue 10, October 2019, Pages 1545-1551

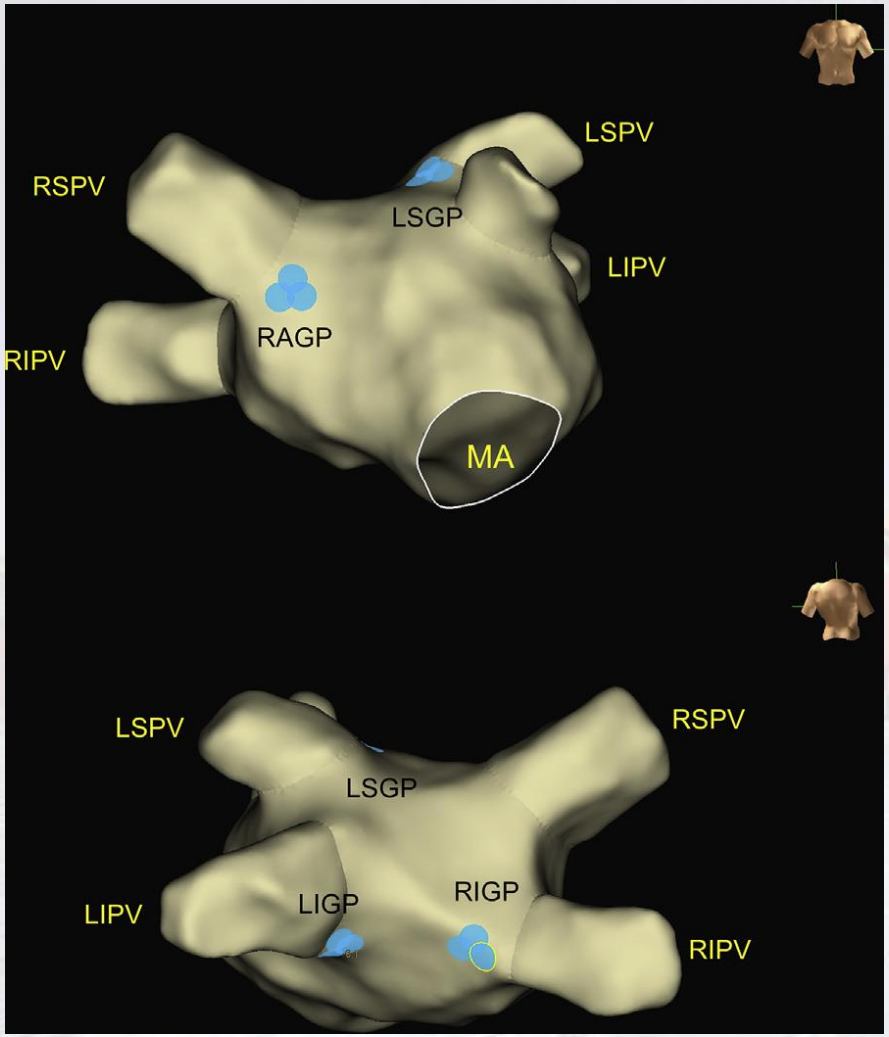
Clinical

Ablation

Right anterior ganglionated plexus: The primary target of cardioneuroablation?

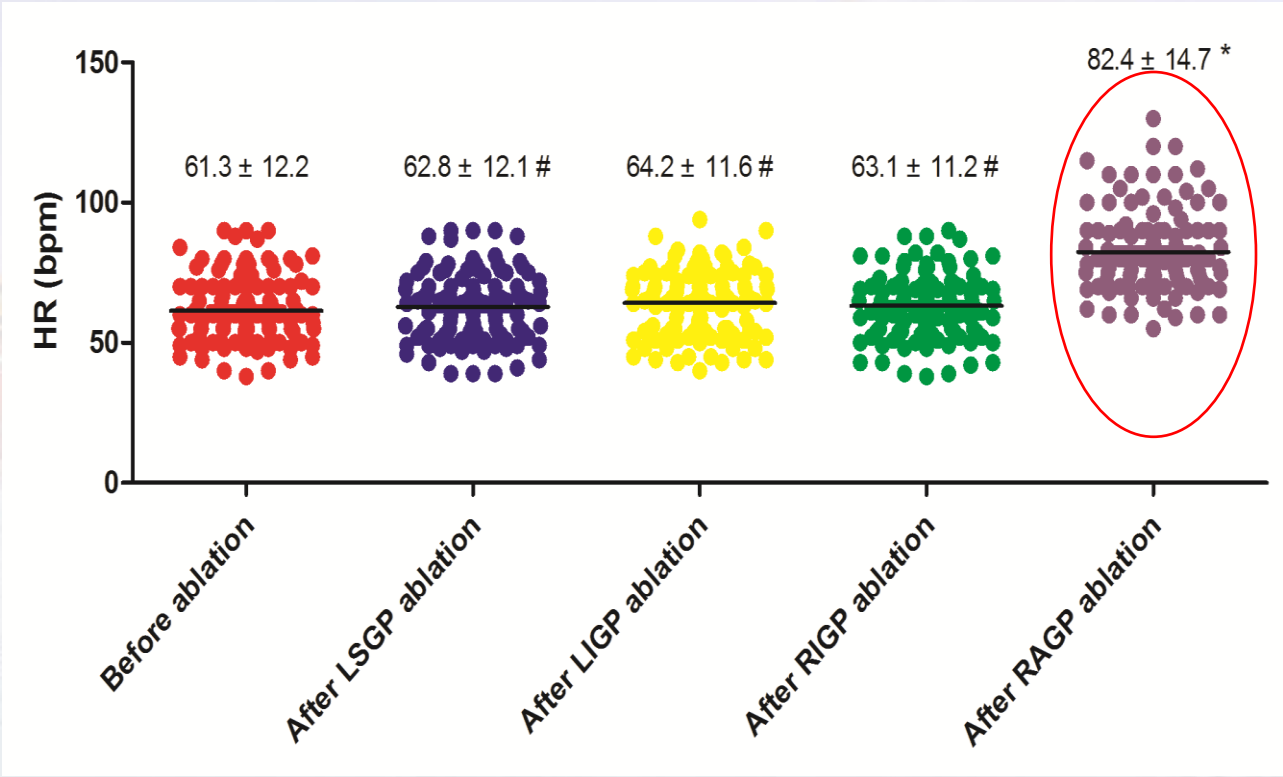
Feng Hu MD, Lihui Zheng MD, PhD, Erpeng Liang MD, Ligang Ding MD, PhD, Lingmin Wu MD, Gang Chen MD, Xiaohan Fan MD, PhD, Yan Yao MD, PhD, FHRS

Role of RAGP in Cardioneuroablation



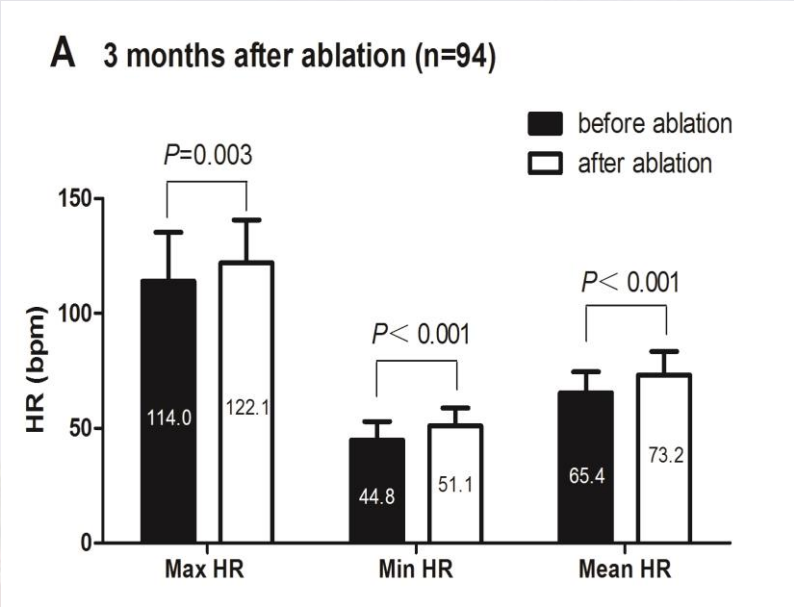
115 consecutive VVS patients (retrospective study)

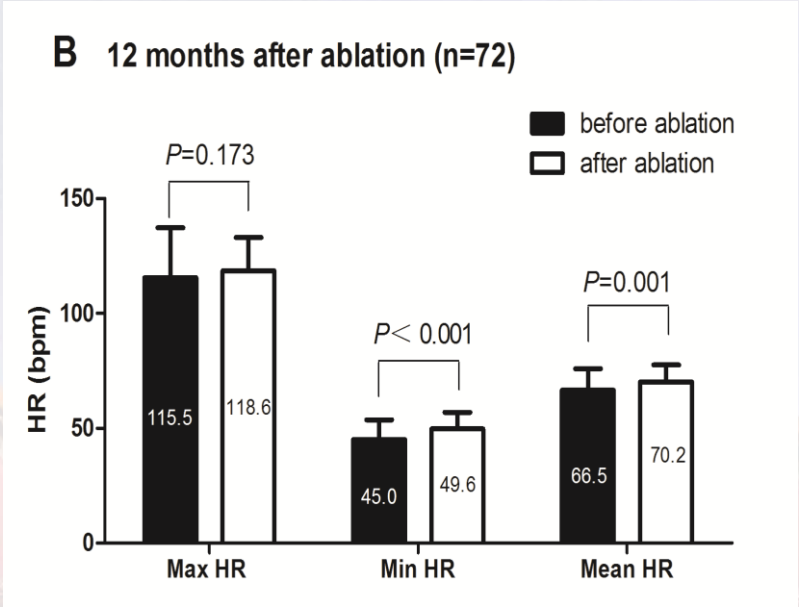
Ablation sequence: LSGP - LIGP - RIGP - RAGP

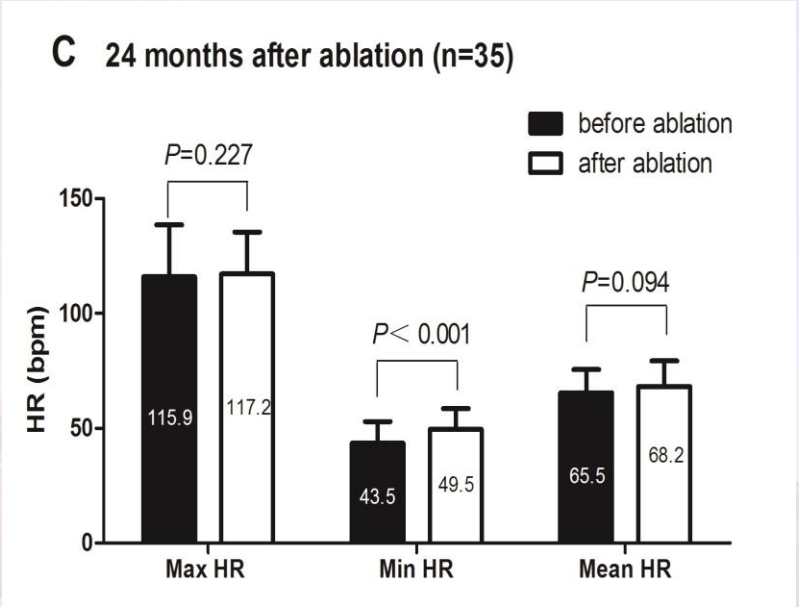


Hu F, …Yao Y, et al. Heart Rhythm 2019

Long-term Effectiveness on Hear Rate







3 months **12 months** **24 months**

Hu F, …Yao Y, et al. Heart Rhythm 2019

GPs Ablation as therapy to Sinus Bradycardia

Atrial Ganglionated Plexus Modification

A Novel Approach to Treat Symptomatic Sinus Bradycardia

Mu Qin, MD,[a] Yu Zhang, MD,[a] Xu Liu, PhD,[a] Wei-Feng Jiang, MD,[a] Shao-Hui Wu, MD,[a] Sunny Po, MD, PhD[b]

ABSTRACT

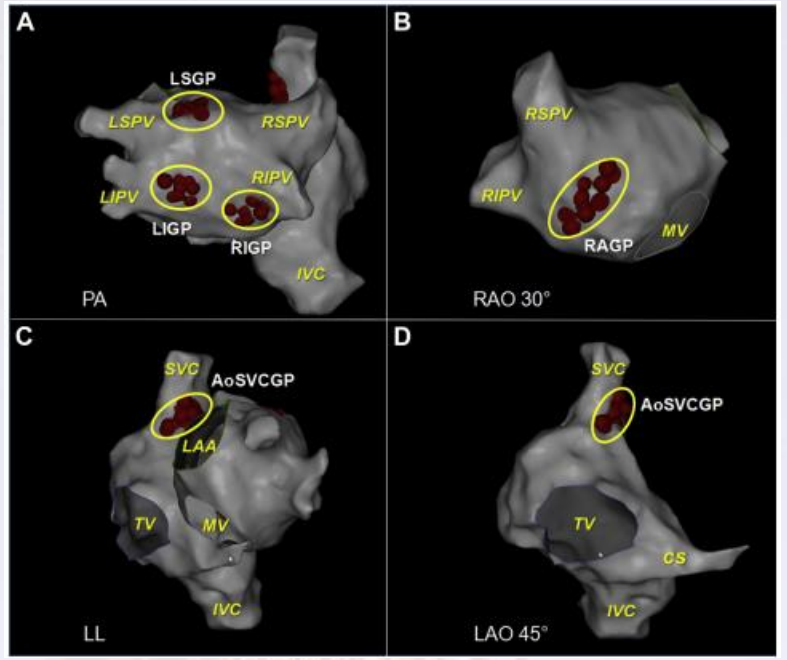
OBJECTIVES This study sought to determine if anatomic atrial ganglionated plexus (GP) ablation leads to long-term sinus rate (SR) increase and improves quality of life in patients with symptomatic sinus bradycardia (SB).

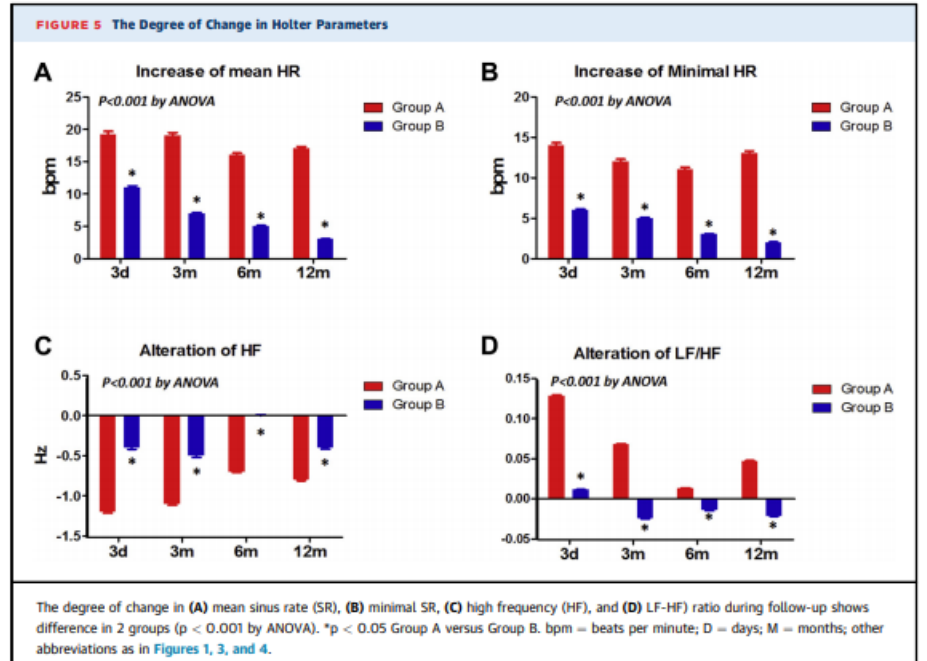
BACKGROUND Atrial GP ablation has been demonstrated to increase SR in our previous study. Atrial GP ablation may also be effective in treating patients with symptomatic SB.

METHODS Sixty-two patients with symptomatic SB were recruited: Group A included patients <50 years of age (n = 40); Group B included patients ≥50 years of age (n = 22). All patients underwent anatomic ablation of the main atrial GP, and 24-h Holter monitoring and quality-of-life assessment were performed during 1 year of follow-up. Quality of life was accessed by the Medical Outcomes Study Short-Form 36 Health Survey.

RESULTS Although SR markedly increased in all patients after GP ablation, the increase was significantly greater in patients <50 years of age than in patients ≥50 years of age (19.3 ± 9.9 beats/min vs. 10.8 ± 5.4 beats/min; p = 0.001). The right anterior GP and the GP at the junction of the aorta and superior vena cava made the greatest contributions to SR increase among all GP. The mean and minimal SR increased significantly after ablation and remained elevated for 12 months only in Group A patients. Although symptoms and quality of life improved in all patients, 5 of the 8 domains of the Medical Outcomes Study Short-Form 36 Health Survey did not show obvious improvements in patients of Group B at 12 months.

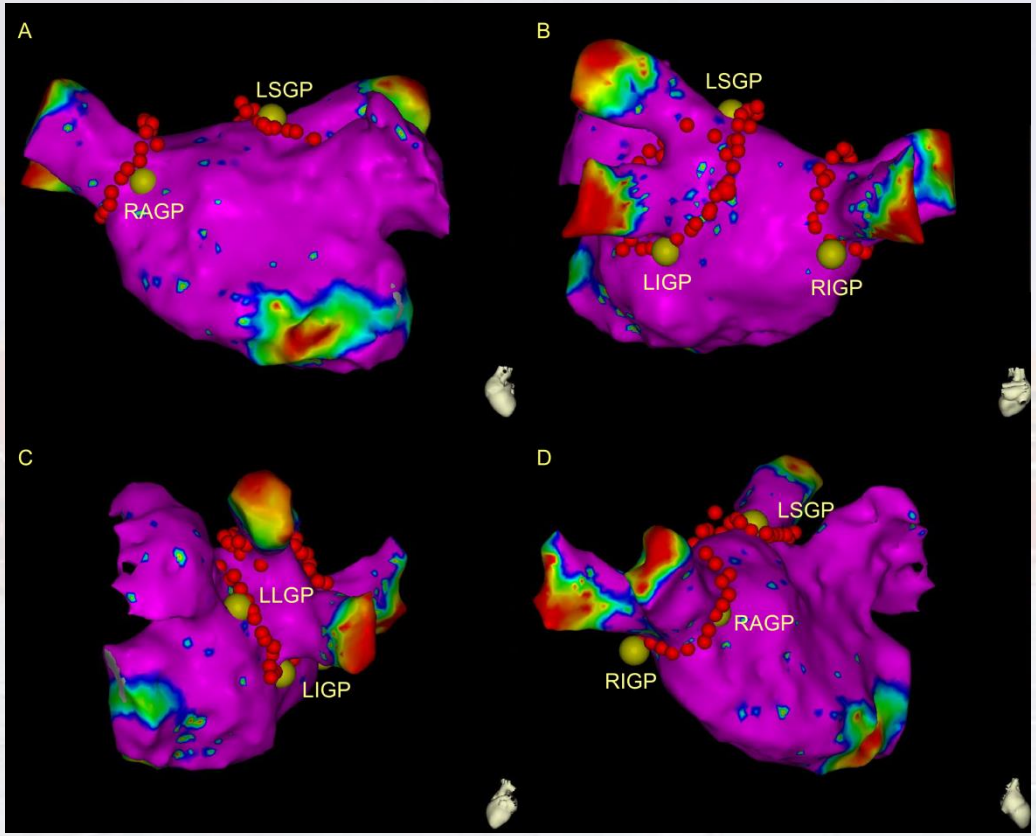
CONCLUSIONS Anatomic atrial GP ablation effectively increased SR and improved quality of life in patients <50 years of age with symptomatic SB. (J Am Coll Cardiol EP 2017;3:950-9) © 2017 by the American College of Cardiology Foundation.

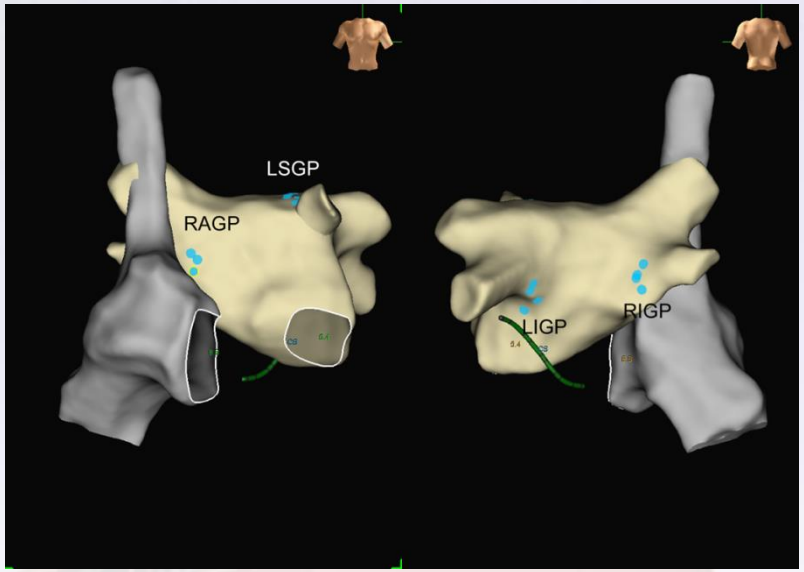


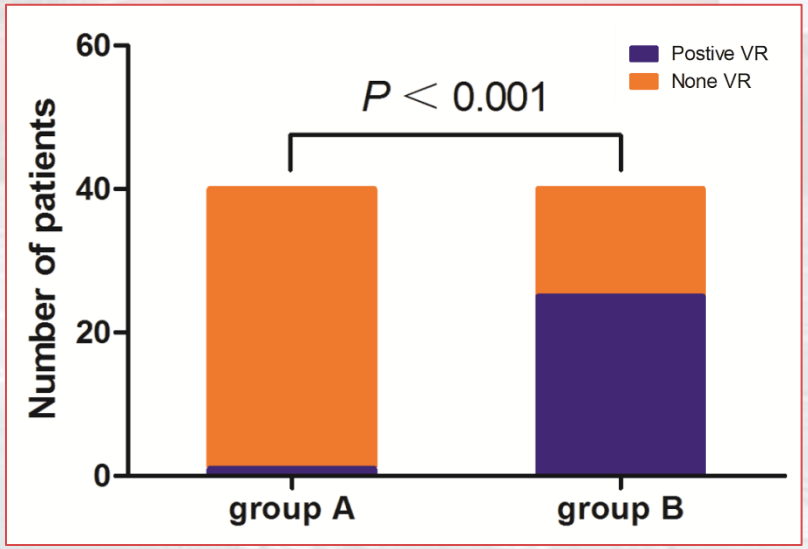


The degree of change in **(A)** mean sinus rate (SR), **(B)** minimal SR, **(C)** high frequency (HF), and **(D)** LF-HF) ratio during follow-up shows difference in 2 groups ($p < 0.001$ by ANOVA). *$p < 0.05$ Group A versus Group B. bpm = beats per minute; D = days; M = months; other abbreviations as in Figures 1, 3, and 4.

RAGP as the first target may suppress VR during AF ablation

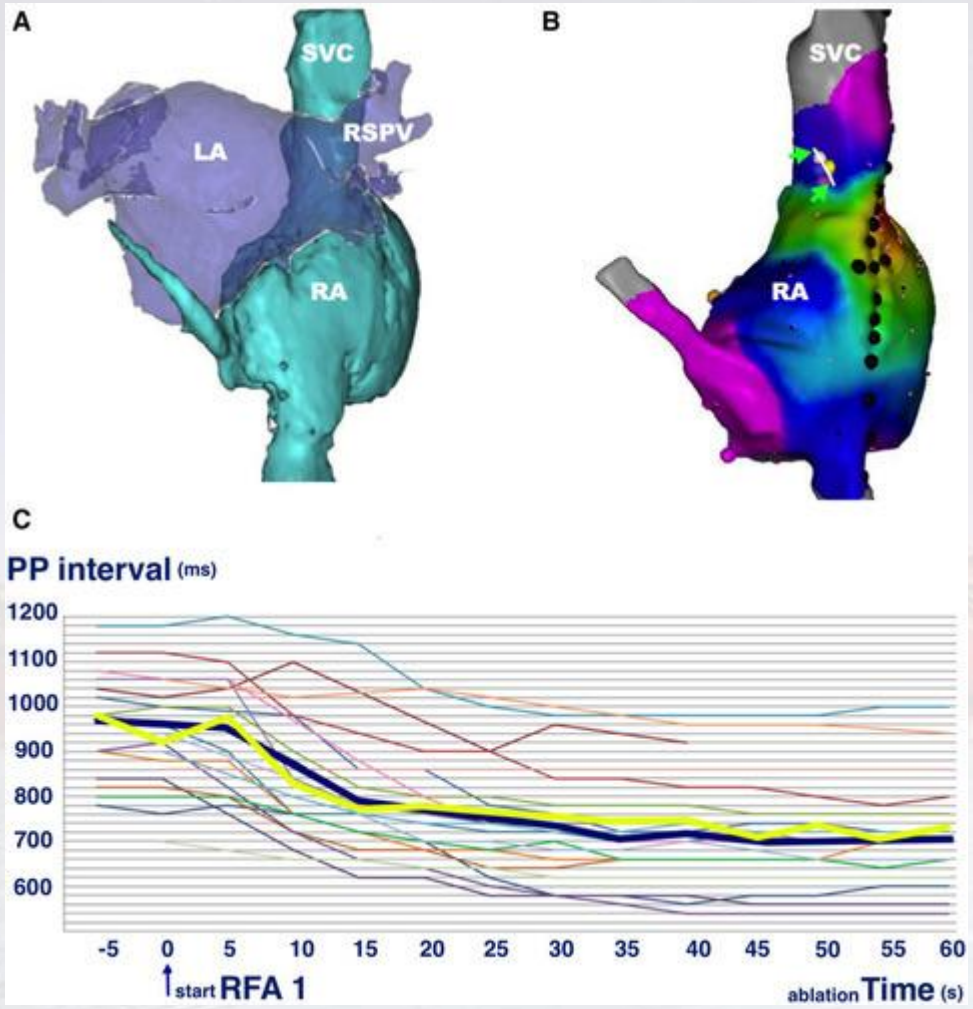


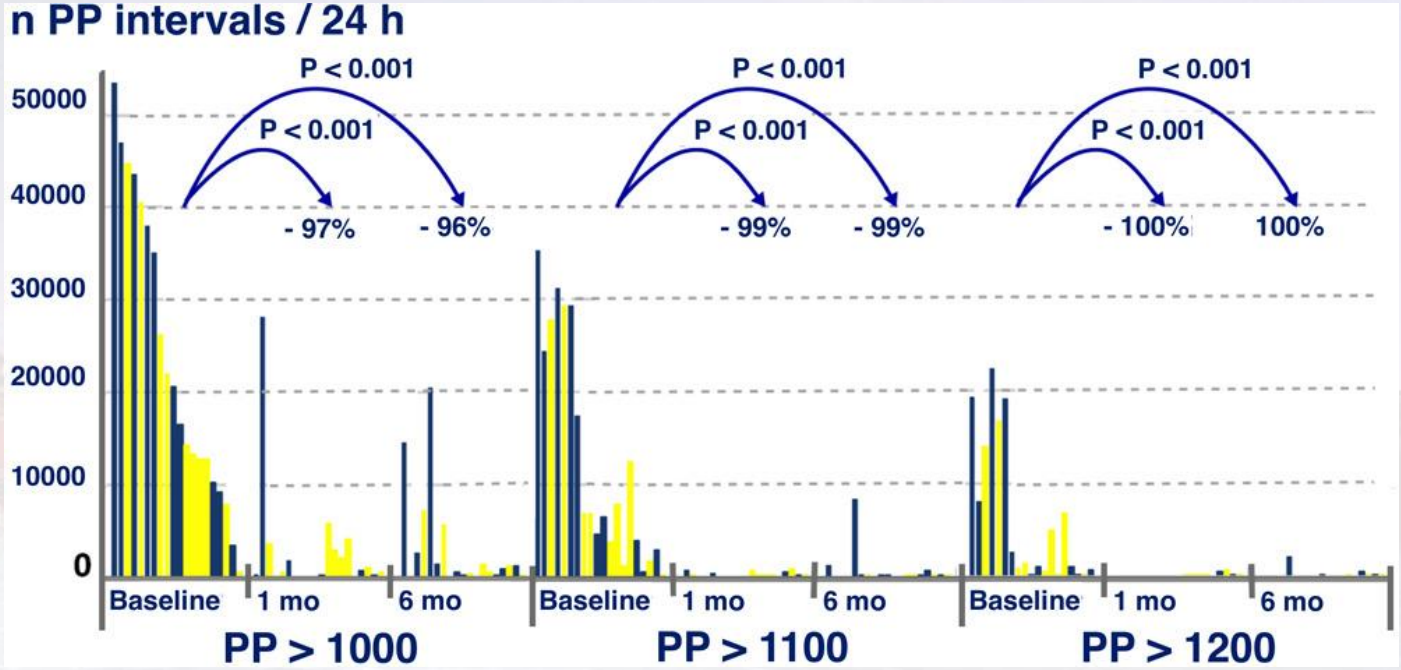




Hu F, Yao Y, et al, Circulation: AE. 2019

Unifocal Right-Sided RAGP Ablation





Debruyne P, Circ AE. 2018 Sep;11(9):e006604

Patients Selection

Discrimination of intrinsic SSS or AVB from those with high vagal tone

- Assessment of the contribution of parasympathetic system:
  - **Atropine Test**: 0.04 mg/kg I.V. for 15 min. An increase of ≥25% or sinus rate ≥90 bpm in the first 15 min is considered as a positive response
  - **Deceleration Capacity (DC)**: ≥ 7.5 indicates high vagal tone;
  - (For AVB, EP study, adenosine and atropine are all helpful to exclude the intrinsic or extrinsic AVB)
- **Contraindications:**
  - Patients with underlying heart disease, especially with heart failure;
  - Patients with severe hypertension, diabetes or any disease which require β blocker;

Cardioneuroablation in the treatment of vagal mediated bradycardias

- **38 patients （2017.12-2020.01）**

  intermittent advanced AV block (AVB)：25 (65.8%)

  intermittent sinus arrest (SA)：11 (28.9%)

  symptomatic related sinus bradycardia (SB)：7 (18.4%)

Atropine test and DC performed,
No vasovagal syncope or AF

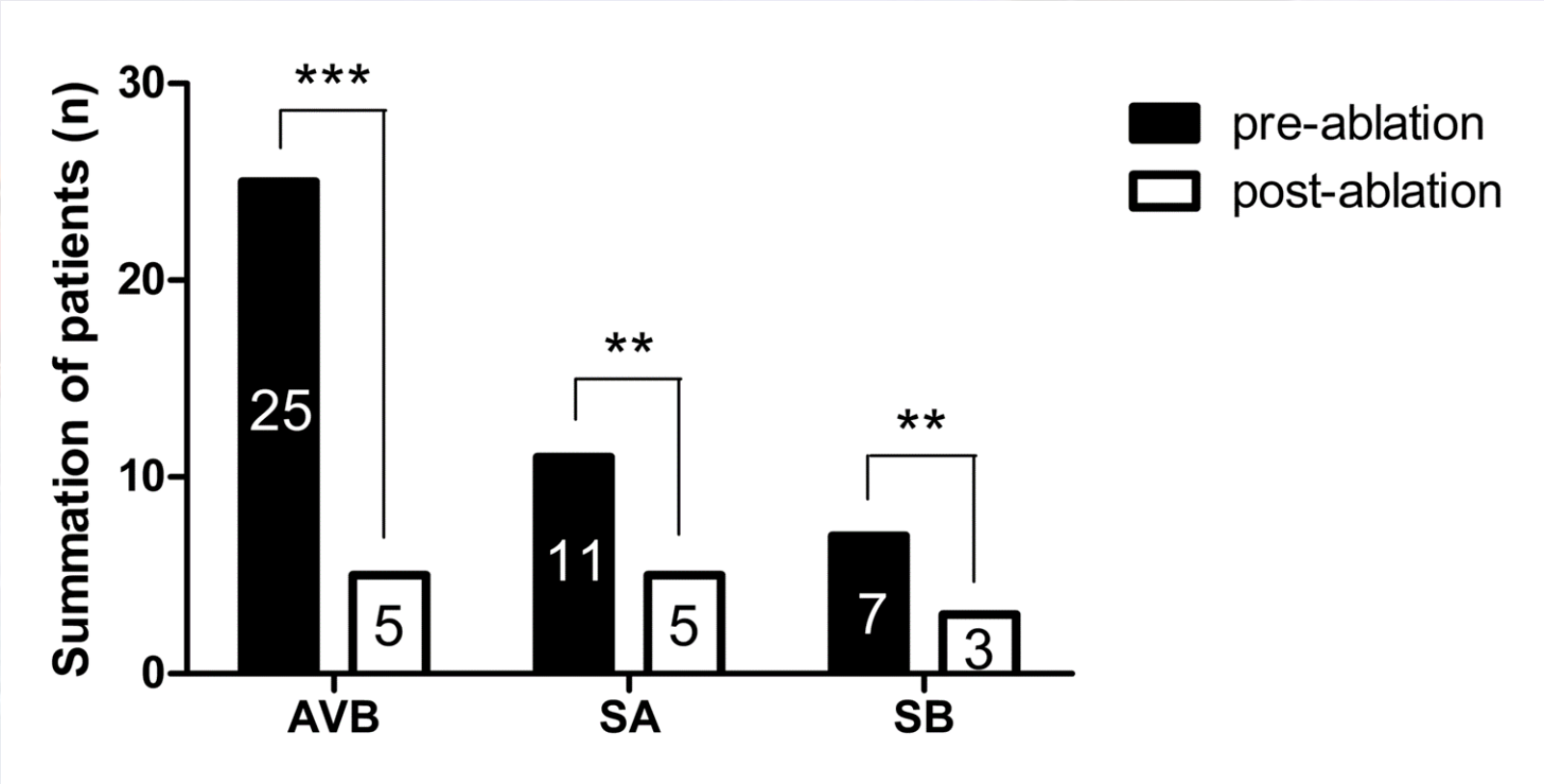
Baseline Characteristics of Patients (n= 38)

Age(year)	36.1±15.3
Sex, Male, n (%)	20 (52.6%)
Follow up time (month)	30.6±23.5
HUT result	
Only heart rate decreased, n (%)	7 (18.4%)
Only blood pressure decreased, n (%)	3 (7.9%)
Both heart rate and blood pressure decreased, n (%)	28 (73.7%)
Left atrium diameter (mm)	31.4±4.5
Left ventricle diameter (mm)	47.1±4.3
Left ventricular ejection fraction (%)	64.1±3.8

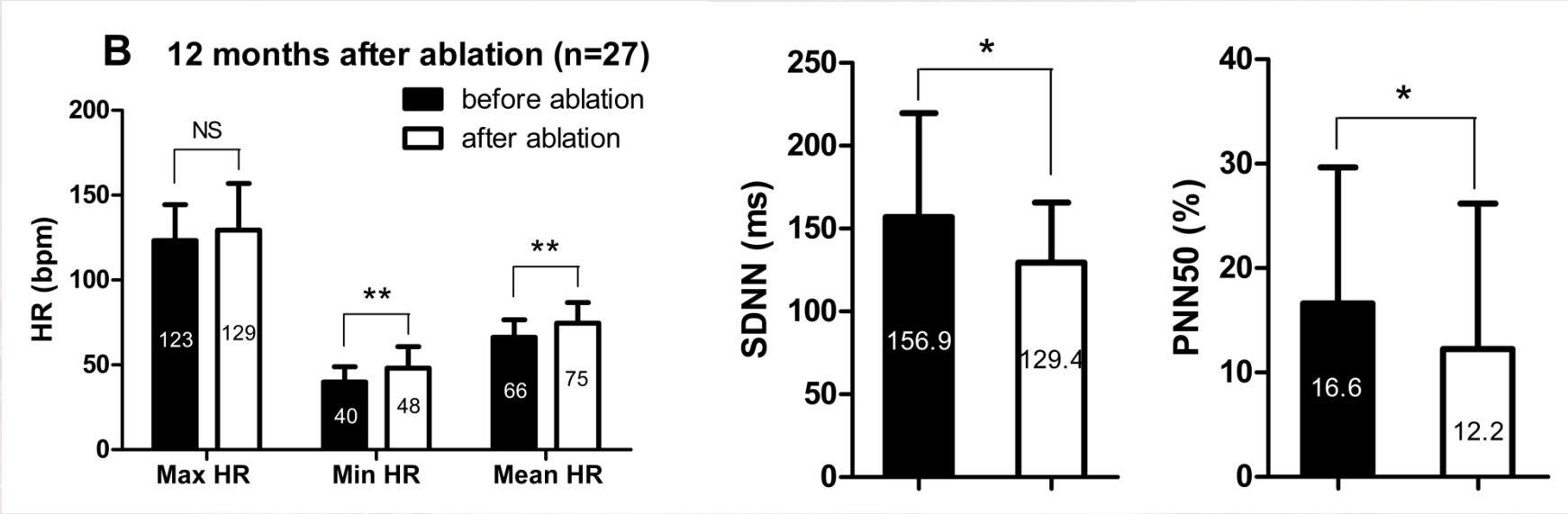
Clinical outcomes

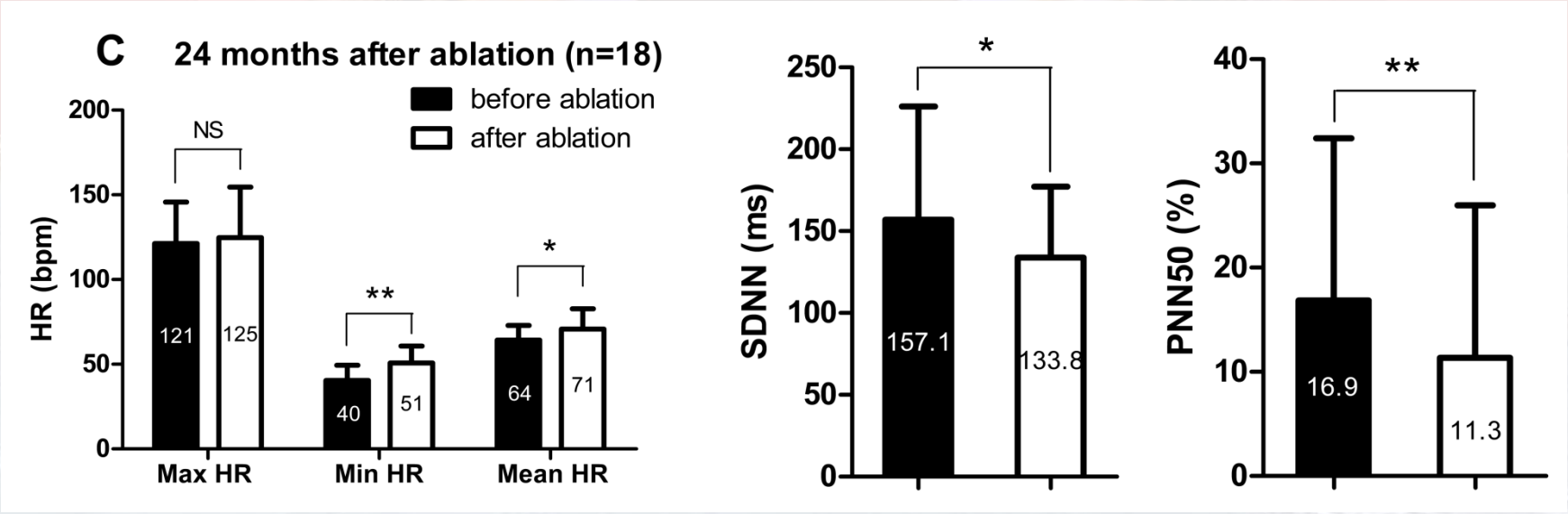
- *30 participants had no recurrence of any types of bradycardiac arrhythmia*
- *8 patients had recurrent bradycardiac arrhythmias*
  - *Only 2 participants accepted pacemaker implantation during follow-up*

Recurrent cases:
2 pts with AVB;
1 with SA;
1 with SB;
1 with AVB+SA+SB;
2 pts with AVB+SA;
1 with SA+SB;



Holter during follow-up





Unpublished data

Case

33 y, Female,

recurrent syncope (intermittent sinus arrest , frequent junctional escape rhythm)

DC: 30

Baseline

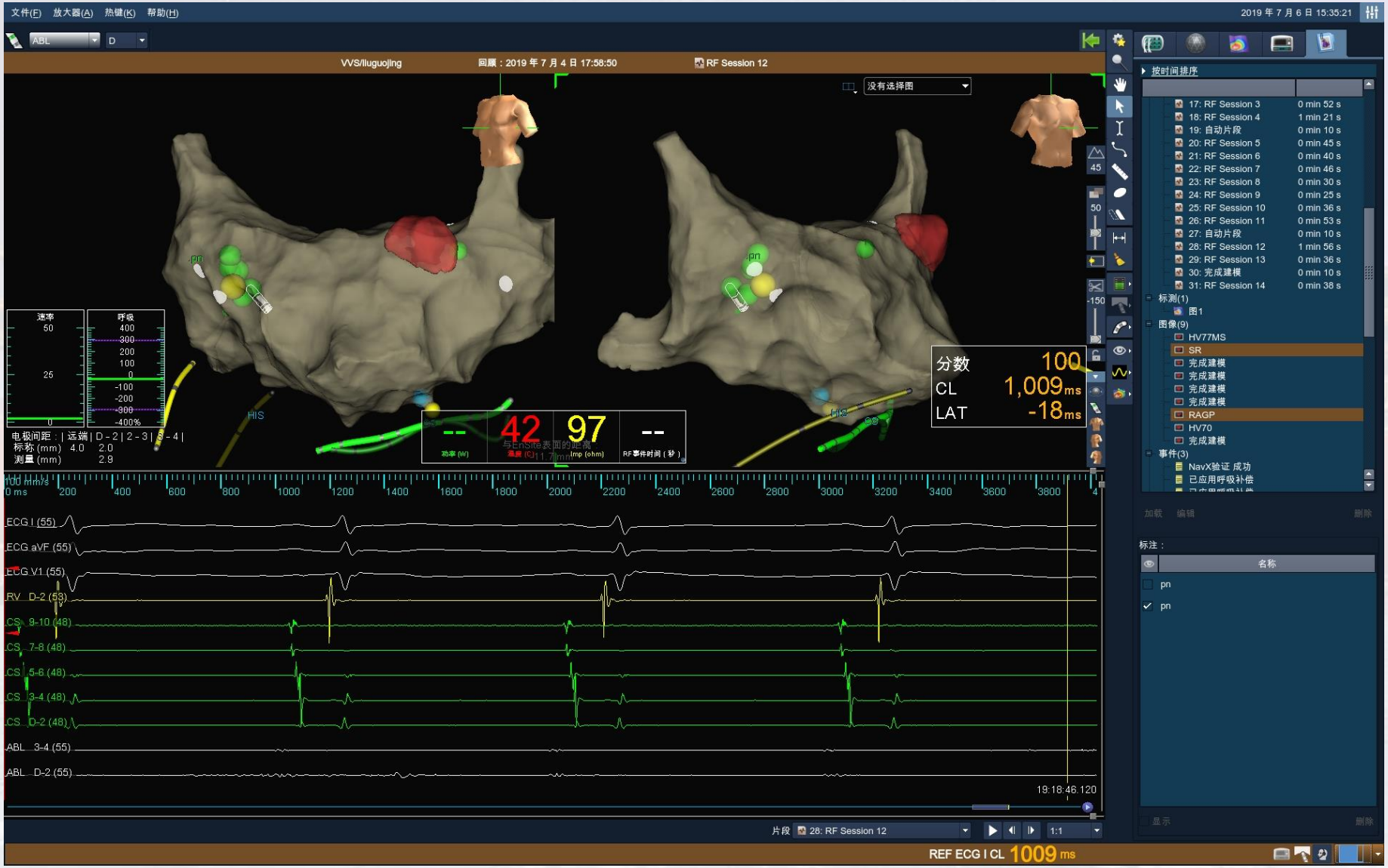
SNRT: 2.3s;

AH 97ms;

HV 77ms

Ablation at RAGP

Ablation other GPs in left atrium



Ablation from RA

Electrophysiological parameters

	Before Cardioneuroablation	After Cardioneuroablation
SANRT (s)	2.3	1.174
AH (ms)	97	93
HV (ms)	77	70
AVN Wenckebach (ms)	480	380
AVNERP (ms)	1000/300	800/280

Summary

- Cardioneuroablation may effectively modify the bradycardic arrhythmias caused by hyper vagal tone, which should be confirmed by atropine or DC test;
- RAGP is the only targeted GP to increase heart rate and may achieved from both RA & LA approaches;
- The indications, methods and endpoints need to be established by further studies.

Thank you! Welcome to visit Beijing