Deterioration effect of gaps and extrapulmonary vein trigger on pulmonary vein isolation: A computational modeling study

Taehyun Hwang, MD, Ze Jin, MD; Daehoon Kim, MD; Byounghyun Lim, PhD; Oh-Seok Kwon, PhD; Je-Wook Park, MD; Hee-Tae Yu, MD, PhD; Tae-Hoon Kim, MD; Jae-Sun Uhm, MD, PhD; Boyoung Joung, MD, PhD; Moon-Hyoung Lee, MD, PhD; Hui-Nam Pak, MD, PhD

Division of Cardiology, Department of Internal Medicine,
Yonsei University College of Medicine, Yonsei University Health System,
Seoul, Republic of Korea

Korean Heart Rhythm Society

COI Disclosure

Name of First Author: Taehyun Hwang

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Background – PVI

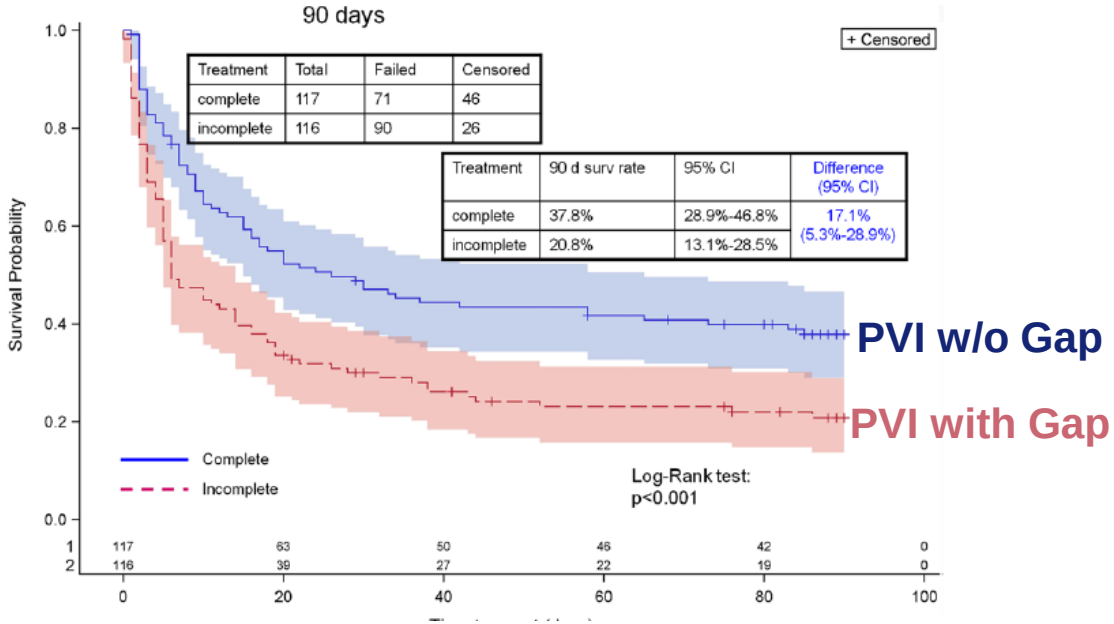
Pulmonary vein isolation (PVI) is the cornerstone of AFCA.

CENTRAL ILLUSTRATION: PVI Compared to Non-PVI Ablation

Study and Year	Active Therapy	Events	N	Control Therapy	Events	N	Weight (%)	Relative Risk [95% CI]
Risk of recurrence at 12 months								
Di Biase, 2009	PVI + CFAE	3	34	CFAE	26	34	10.5	0.12 [0.04, 0.35]
STAR AF, 2010	PVI + CFAE	9	34	CFAE	26	34	16.6	0.35 [0.19, 0.62]
Chen, 2011	PVI	17	60	CFAE	25	58	17.8	0.66 [0.40, 1.08]
Katritsis, 2013	PVI + GP	19	80	GP	28	68	18	0.58 [0.36, 0.94]
Mamchur, 2014	PVI	18	40	GP	20	36	18.5	0.81 [0.52, 1.27]
RADAR-AF, 2014	PVI	24	58	HFSA	22	54	18.5	1.02 [0.65, 1.58]
Random effects model (Q = 18.93, df = 5, p for heterogeneity = 0.00; I^2 = 79.7%)								0.54 [0.33, 0.89]
								p for overall effect = 0.0147

Sau A, et al. Meta-analysis of randomized controlled trials of atrial fibrillation ablation with pulmonary vein isolation versus without. JACC Clin Electrophysiol 2019;5:968–76.

PVI gap between the PV-LA has a critical role in acute success of PVI and recurrence after AFCA.

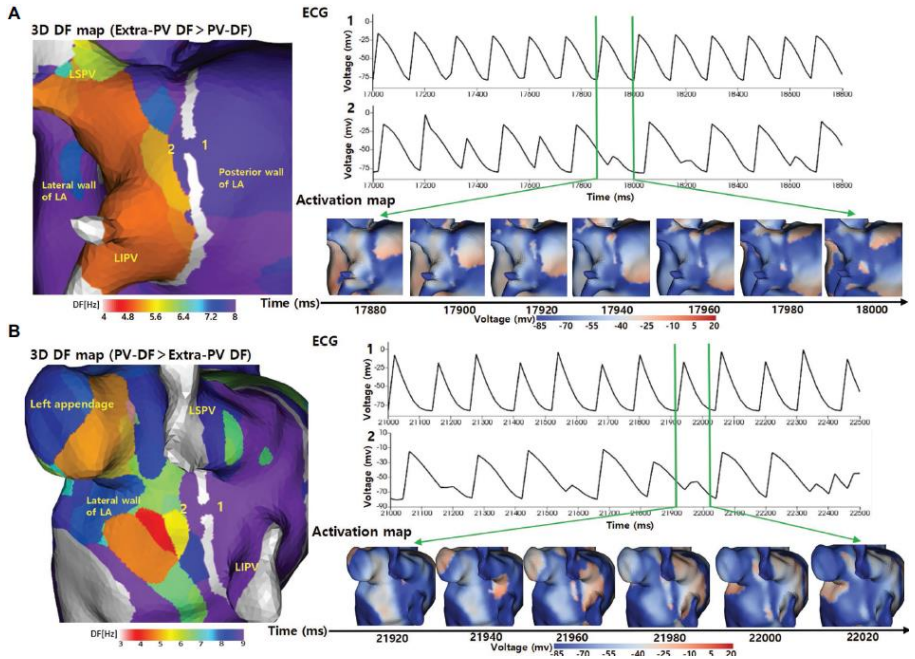


Kuck KH, et al. mpact of Complete Versus Incomplete Circumferential Lines Around the Pulmonary Veins During Catheter Ablation of Paroxysmal Atrial Fibrillation: Results From the Gap-Atrial Fibrillation-German Atrial Fibrillation Competence Network 1 Trial. Circ Arrhythm Electrophysiol. 2016 Jan;9(1):e003337

Background – Gap numbers

During AF, wave-breaks commonly occurred at the wavelet exit of the gaps

Additional virtual ablation of wave-breaking PVI gaps had a greater anti-AF effect than virtual DF ablation or virtual flecainide.
No. of PVI gap = 4

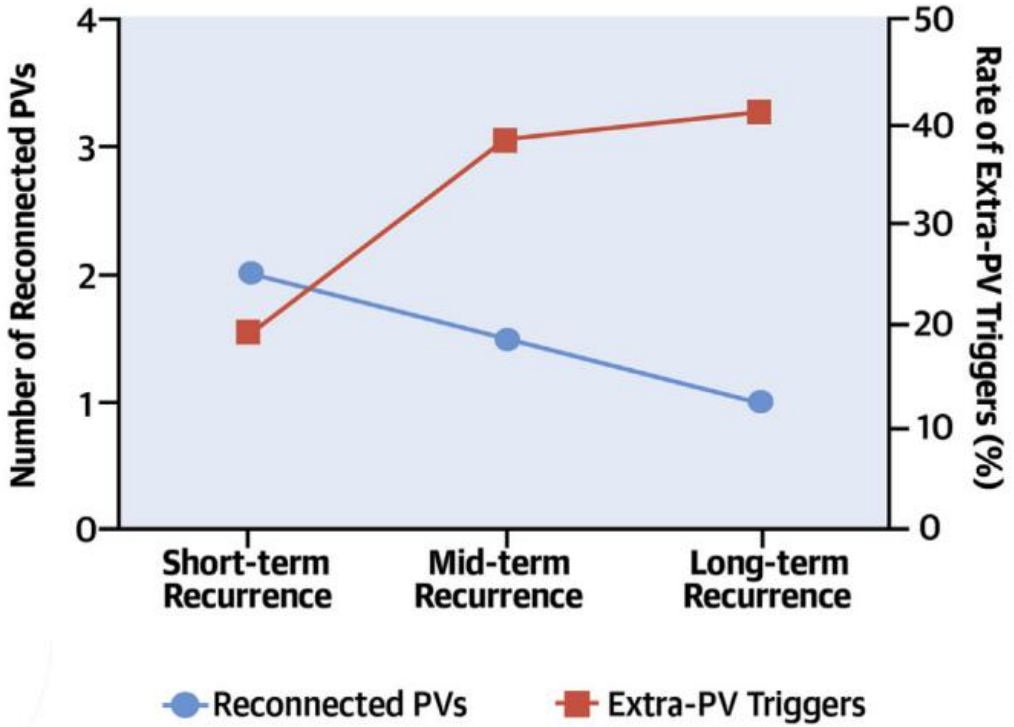


1 What if the number of PVI gaps differs?

Jin Ze, et al. Anti-atrial Fibrillation Effects of Pulmonary Vein Isolation With or Without Ablation Gaps: A Computational Modeling Study. Front Physiol. 2022 Mar 17;13:846620

Background – Extrapulmonary vein trigger

The LTR group (recur 3-years after post AFCA) had fewer reconnected PVs, but extra PV triggers were more common than in the STR (3-12 months) and MTR (1-3 years) groups.



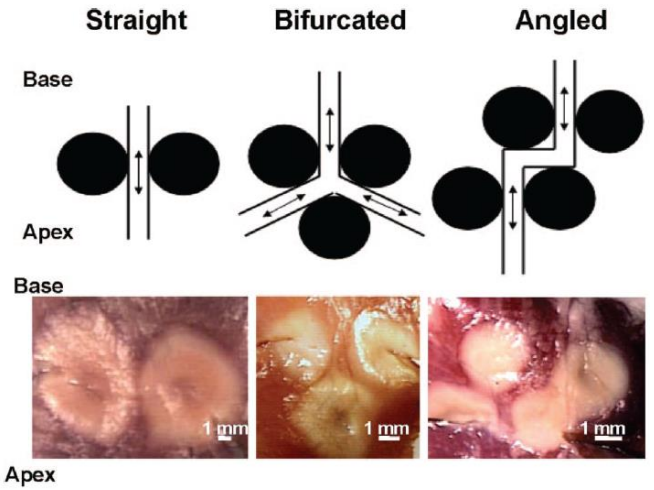
1. What if the number of PVI gaps differs?
2. PVT vs. Ext-PVT in PVI gaps?

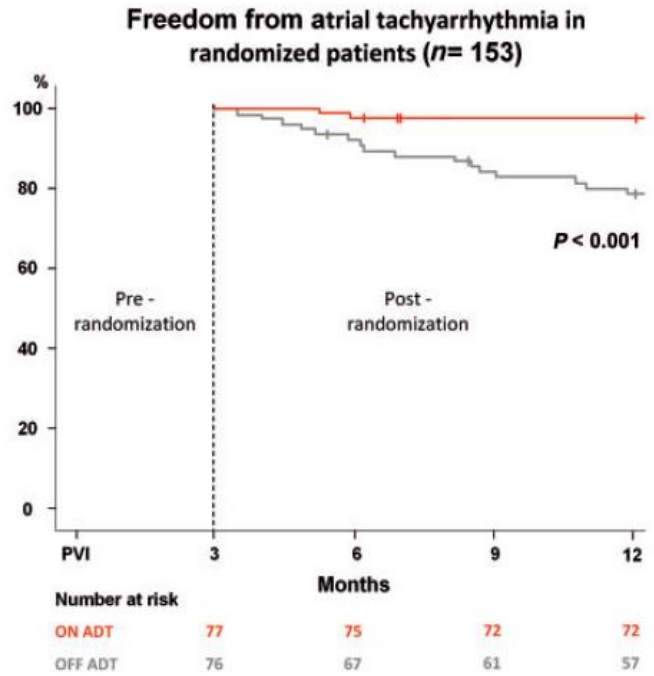
Park JW, et al. Mechanisms of Long-Term Recurrence 3 Years After Catheter Ablation of Atrial Fibrillation. JACC Clin Electrophysiol. 2020 Aug;6(8):999-1007

Background – AAD on PVI gap

AAD can block gap over ablated linear lesions

Patients with continued use of AAD after ablation significantly reduces the recurrence of atrial tachyarrhythmia in the 1st year after PVI.





1. **What if the number of PVI gaps differs?**
2. **PVT vs. Ext-PVT in PVI gaps?**
3. **How does AAD affect PVI gaps?**

Pérez FJ, et al. Effects of gap geometry on conduction through discontinuous radiofrequency lesions. Circulation. 2006 Apr 11;113(14):1723-9.

Duytschaever M, et al. PulmOnary vein isolation With vs. without continued antiarrhythmic Drug trEatment in subjects with Recurrent Atrial Fibrillation (POWDER AF): results from a multicentre randomized trial. Eur Heart J. 2018 Apr 21;39(16):1429-1437.

Background – Hypothesis

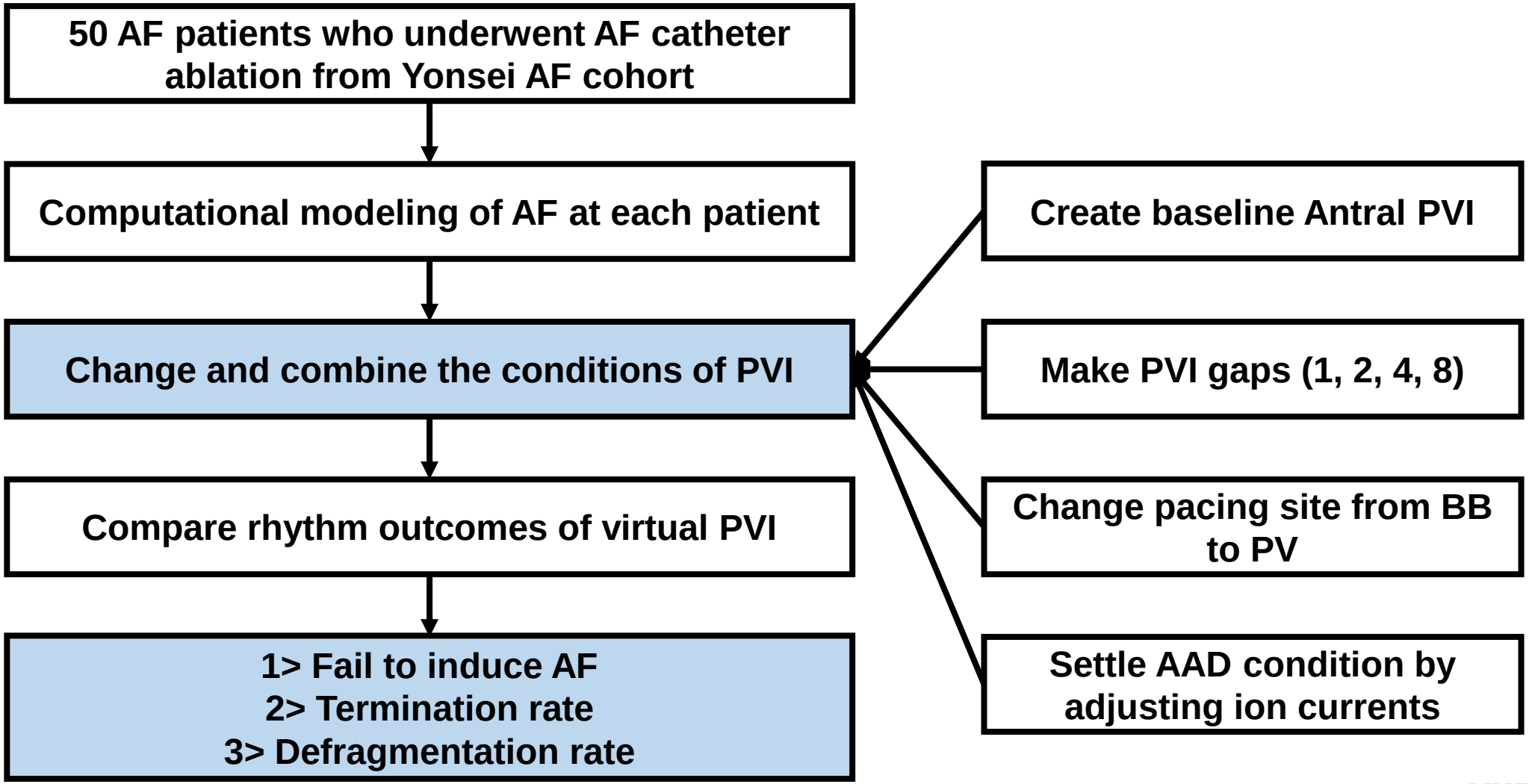
We hypothesized that conditional changes of PVI gap would affect the outcome of the PVI.

However, a quantitative evaluation of the impact of these alterations on PVI gap mentioned above is not possible in human AF.

So, we performed the realistic computational modeling of human AF.

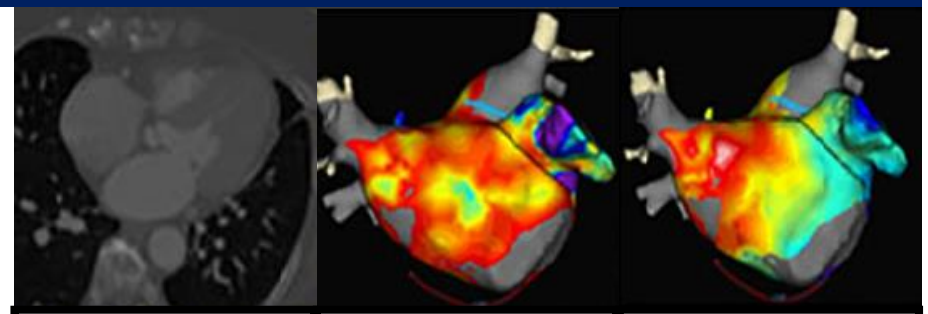
1. What if the number of PVI gaps differs?
2. PVT vs. Ext-PVT in PVI gaps?
3. How does AAD affect PVI gaps?

Methods – Overview



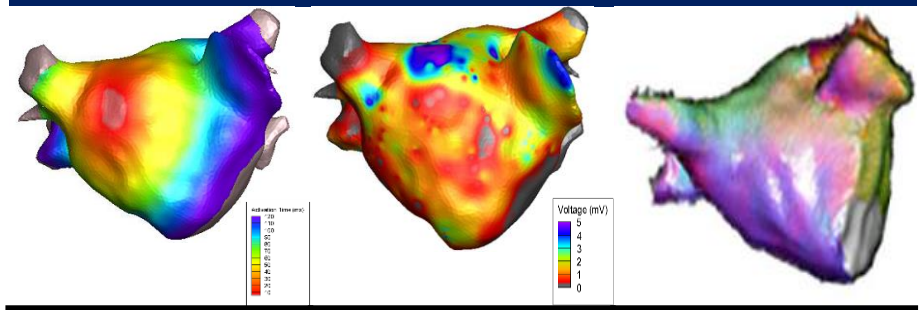
Methods – Computational modeling of AF (1)

A Integrate CT images + EAM



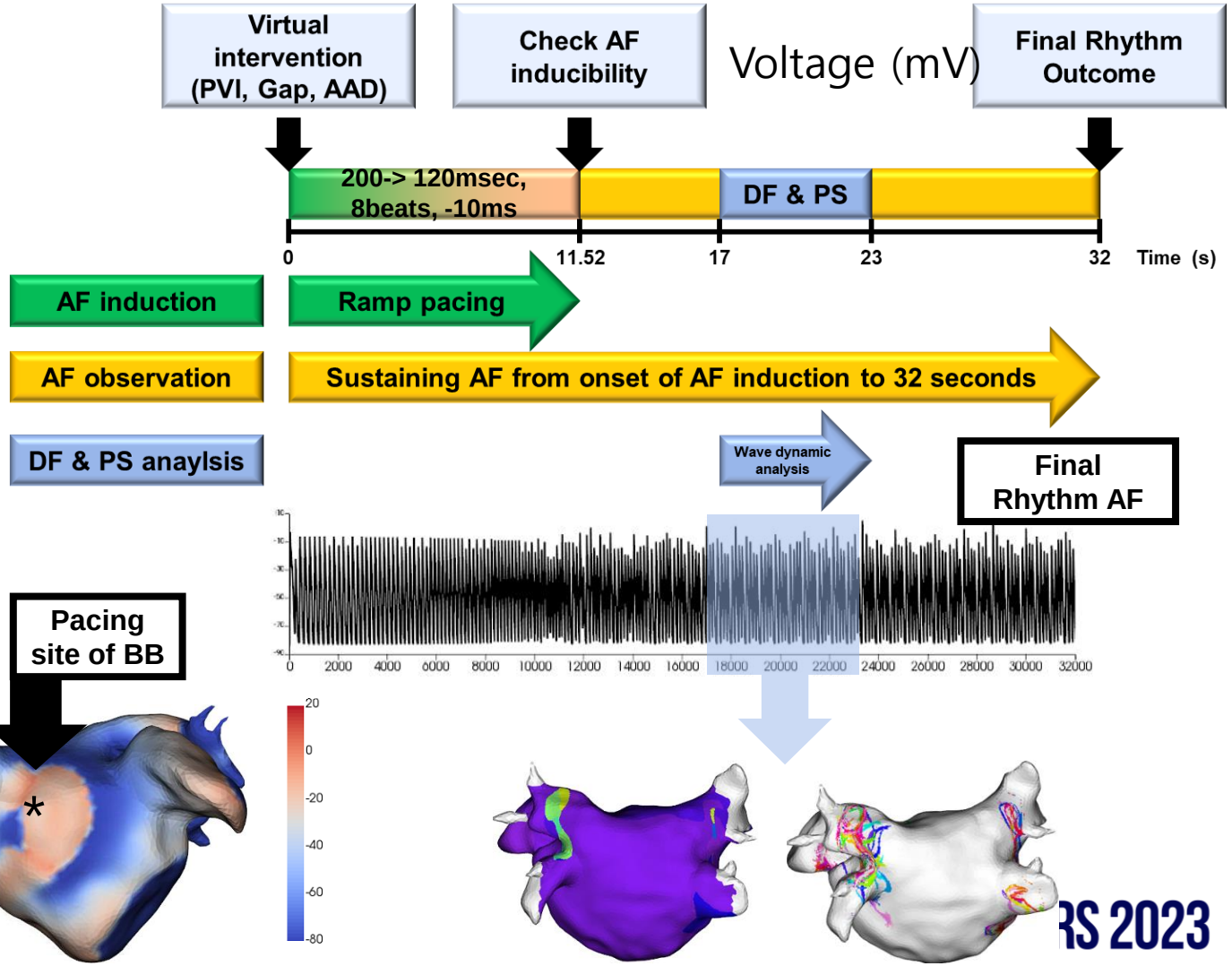
CT map | Voltage map | LAT map

B Create virtual maps of LAT, voltage, fiber orientation, fibrosis



Virtual LATm | Virtual Vm | Fiber orientation map

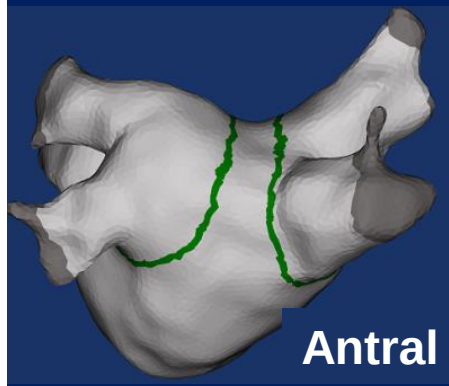
C Induce AF by induction protocol



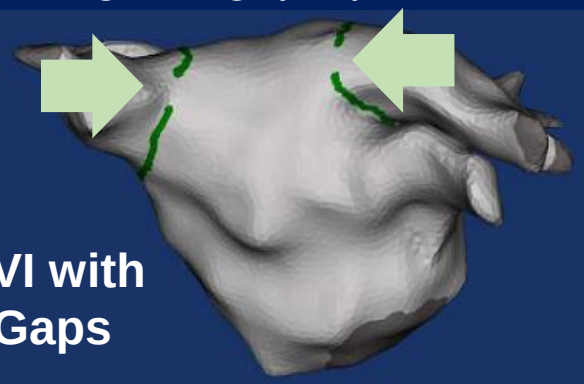
Methods – Computational modeling of AF (2)

D Apply and combine virtual interventions

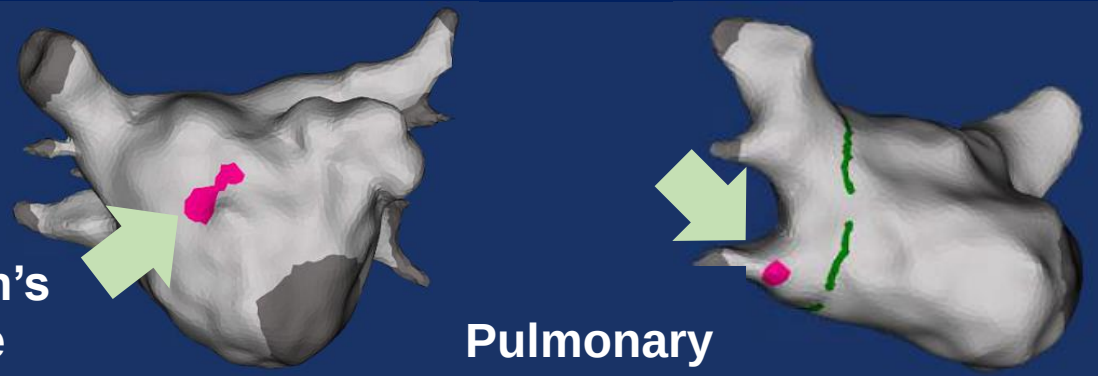
D-1) Create antral CPVI



D-2) Making PVI gaps (1 / 2 / 4 / 8)



D-3) Pacing at different sites (BB vs. PV)

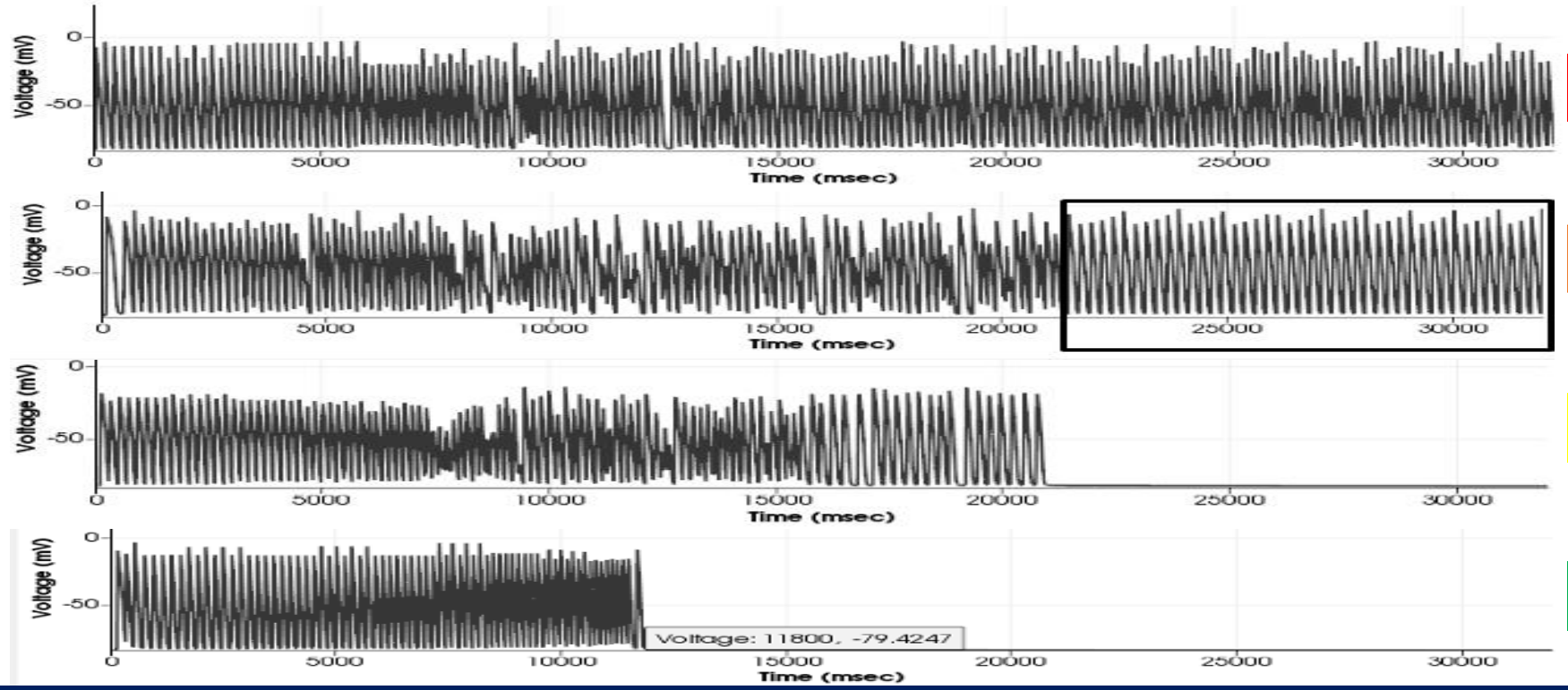


D-4) AMD (10μM) condition in PVI gaps

	SR (%)	AF (%)	AMD 10 uM (%)
gNa	100	90	85
gK1 ↓	100	210	**160**
gto	100	30	30
gKr ↓	100	100	**75**
gCaL	100	30	12
gKur	100	50	50
gKs ↓	100	100	**80**
INaCa (Max)	100	100	100
INaK (Max)	100	100	100
Iup (Max)	100	100	100
Krel	100	100	100
Caup (Max)	100	80	80
Ach ↓	100	100	15

Methods – Rhythm outcomes

E Rhythm outcomes



AF

AT

Termination

Non-inducible AF

Final rhythm at 32 seconds of AF simulation

Failure to induce AF (%) = 4 / Total N

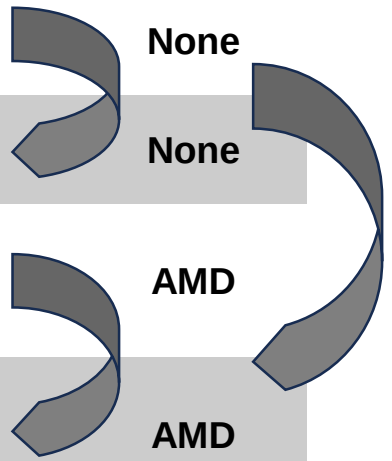
Termination Rate (%) = (4 + 3) / Total N

Defragmentation Rate (%) = (4 + 3 + 2) / Total N

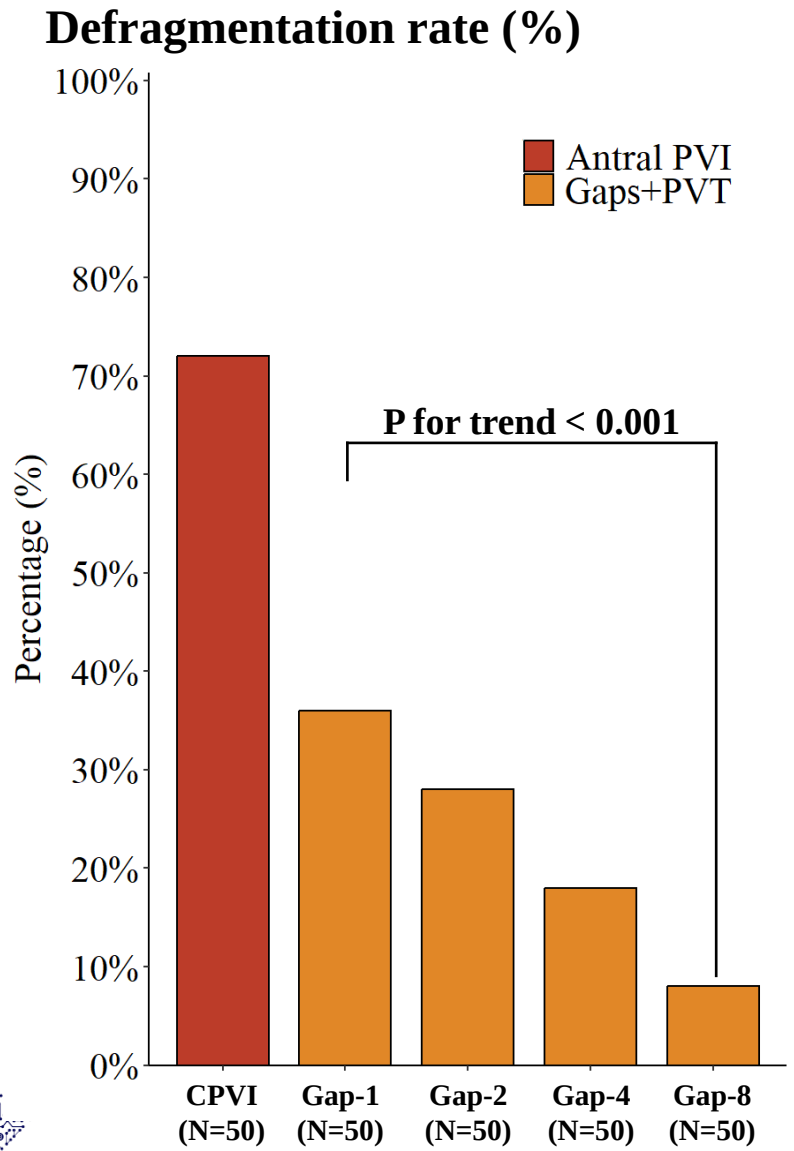
Results – Baseline characteristics

Baseline characteristics (N=50)	
Age, (Years)	61.3±9.4
Male, n (%)	36 (72.0)
Persistent AF, n (%)	38 (76.0)
BMI, (Kg/m^2)	24.4±4.2
CHA_2DS_2-VASc Score	1.6±2.2
Heart failure, n (%)	14 (28.0)
Hypertension, n (%)	24 (48.0)
Diabetes, n (%, n)	8 (16.0)
Stroke/TIA, n (%, n)	11 (22.0)
Echocardiographic Parameters	
LA Dimension, (mm)	44.0±5.3
LA Volume Index, (mL/m^2)	43.9±12.
LVEF (%)	61.5±7.7
E/Em	10.4±3.5

	Number of gaps	Pacing site	AAD
Antral PVI (N=50)	0	BB	None
Gaps + ExtPVT (N=200)	1,2,4,8	BB	None
Gaps + PVT (N=200)	1,2,4,8	PV	None
Gaps + ExtPVT + AAD (N=200)	1,2,4,8	BB	AMD
Gaps + PVT + AAD (N=50)	1	PV	AMD



Results – (1) PVI gap numbers

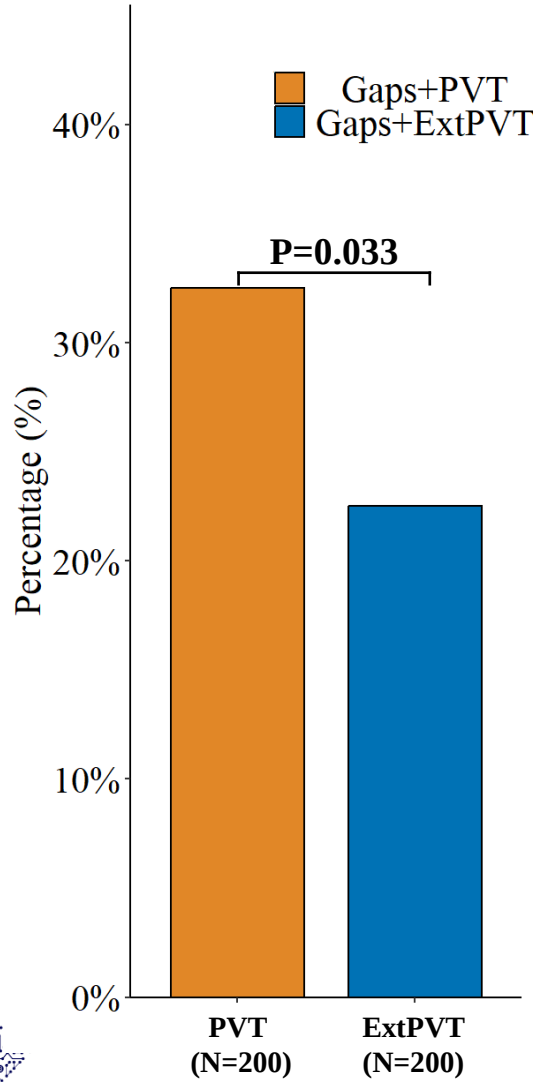


PVT / No AAD	Overall (N=200)	Gap-1 (N=50)	Gap-2 (N=50)	Gap-4 (N=50)	Gap-8 (N=50)	P for trend
Defragmentation Rate (%)	65 (32.5)	29 (58.0)	20 (40.0)	15 (30.0)	1 (2.0)	< 0.001
Termination Rate (%)	26 (13.0)	13 (26.0)	6 (12.0)	7 (14.0)	0 (0)	<0.001
Failure to induce AF (%)	13 (6.5)	7 (14.0)	2 (4.0)	4 (8.0)	0 (0)	0.015

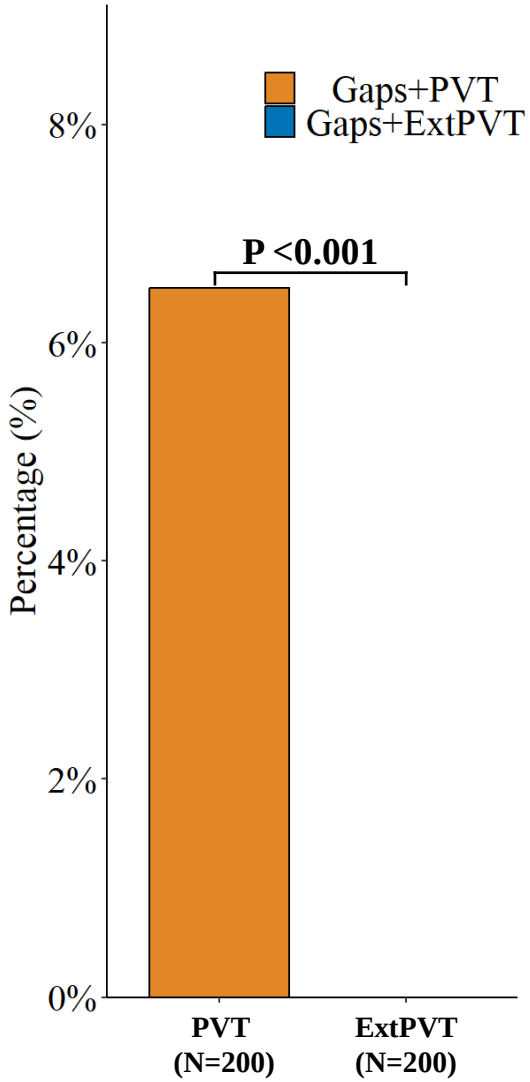
ExtPVT / No AAD	Overall (N=200)	Gap-1 (N=50)	Gap-2 (N=50)	Gap-4 (N=50)	Gap-8 (N=50)	P for trend
Defragmentation Rate (%)	45 (22.5)	18 (36.0)	14 (28.0)	9 (18.0)	4 (8.0)	< 0.001
Termination Rate (%)	18 (9.0)	6 (12.0)	5 (10.0)	4 (8.0)	3 (6.0)	0.269

Results – (2) Trigger site (PVT vs. ExtPVT)

Defragmentation rate (%)



Failure to induce AF (%)



No AAD	PVT (N=200)	ExtPVT (N=200)	P-value
Defragmentation Rate (%)	65 **(32.5)**	45 **(22.5)**	**0.033**
Termination Rate (%)	26 **(13.0)**	18 **(9.0)**	**0.263**
Failure to induce AF (%)	13 **(6.5)**	0 **(0)**	**<0.001**

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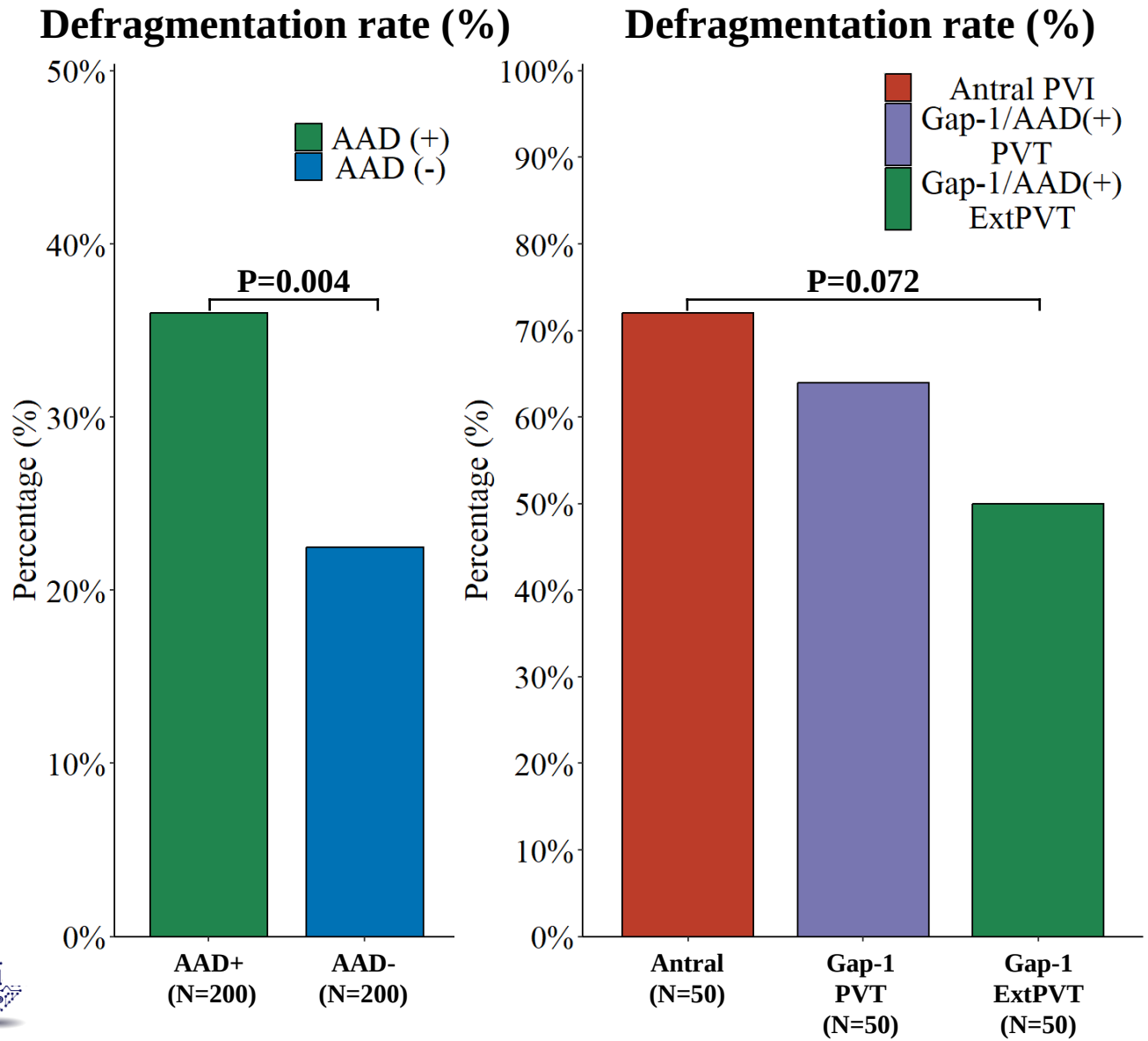
Results – (3) Gaps with AAD



ExtPVT	AAD (N=200)	No AAD (N=200)	P-value
Defragmentation Rate (%)	72 (36.0)	45 (22.5)	0.004
Termination Rate (%)	32 (16.0)	22 (11.0)	0.049

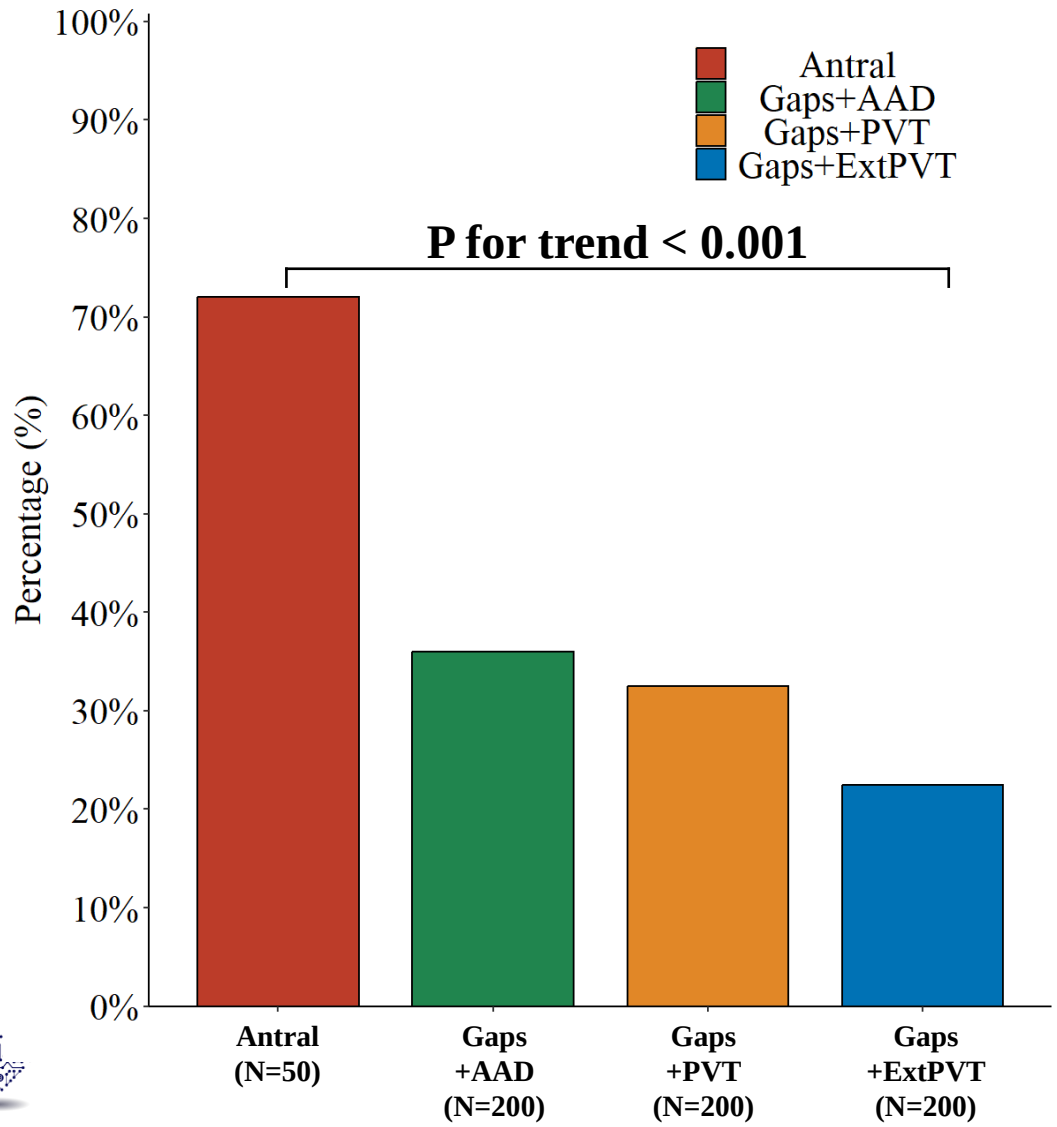
Gap-1 / AAD (+)

	Antral (N=50)	PVT (N=50)	ExtPVT (N=50)	P-value
Defragmentation Rate (%)	36 (72.0)	32 (64.0)	25 (50.0)	0.072
Termination Rate (%)	19 (38.0)	14 (28.0)	16 (32.0)	0.562

(N=50) Antral (N=50) PVT (N=50) ExtPVT

Results – (4) Summary

Defragmentation rate (%)



Summary Table

PVT / No AAD	Antral (N=50)	Gaps +AAD (N=200)	Gaps +PVT (N=200)	Gaps +ExtPVT (N=200)	P for trend
Defragmentation Rate (%)	36 (72.0)	72 (36.0)	65 (32.5)	45 (22.5)	<0.001
Termination Rate (%)	19 (38.0)	32 (16.0)	26 (13.0)	18 (9.0)	<0.001
Failure to induce AF (%)	0 (0)	0 (0)	13 (6.5)	0 (0)	-

Conclusions

1. As the number of PVI gaps increases, the anti-AF effect decreases, and the outcome of PVI tends to worsen.

2. Under the condition of the PVI gaps, the extrapulmonary vein trigger easily induced and maintained AF than the PV trigger.

3. The antiarrhythmic drug improves the anti-AF effects of incomplete PVI, and it would be helpful for patients with few numbers of PVI gaps.

Thank you for your attention