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Medical Congress



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9th to 11th November 2023
Cultural Center,
European University Cyprus

Organized & Supervised by: Professor Dr Ioannis Patrikios

Is Electrophysiology Entering the Era of Selective Highly Precision Medicine?

The case of Pulsed field Ablation for Atrial fibrillation

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1st Cardiac dpt / Electrophysiology dpt,
Henry Dunant Hospital Center, Athens

Presenter Disclosure Information

The presenter has received honoraria for participation in lectures and advisory boards from the following pharmaceutical and biotechnology companies:

- *Abbot*
- *AstraZeneca,*
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- *Bayer Healthcare,*
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- *Bristol-Myers Squibb,*
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- *MSD,*
- *Pfizer,*
- *Sanofi,*
- *Servier,*
- *Unifarma,*
- *Vianex.*

Is Electrophysiology Entering the Era of **Selective Highly Precision Medicine?**

The case of Pulsed field Ablation for Atrial fibrillation





Bing is your AI-powered copilot for the web

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tell me about precision medicine

✓ Searching for: **precision medicine**

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Precision medicine, also known as personalized medicine, is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person^{1 2}. This approach allows doctors and researchers to predict more accurately which treatment and prevention strategies for a particular disease will work in which groups of people¹.

It contrasts with a one-size-fits-all approach, where disease treatment and prevention strategies are developed for the average person, with less consideration for the differences between individuals¹.

Is Electrophysiology Entering the Era of *Selective Highly Precision Medicine?*

The case of **Pulsed field Ablation for Atrial fibrillation**



6 MYTHS ABOUT Atrial Fibrillation



Everyone has palpitations and fluttering

NO! One in four people will develop AF over the age of 64 years and this increases to 50% of people by the age of 80 years old.

MYTH 2

Only old people get atrial fibrillation

People in their 30's, 40's and 50's can develop AF, albeit, it is far less common. The sooner AF is detected, diagnosed, and anticoagulated to prevent AF-related stroke and the AF-treated, the better the outcomes for people with AF.



MYTH 3

If there is no treatment, then there is nothing to worry about

There are several **treatments** including the 'pill in your pocket', regular medication, pacemakers, cardioversion, or ablation.

MYTH 4

All my doctor talks about is stroke, I have an issue with my heart, not my brain!

Your physician will want to reduce your risk of an AF-related stroke caused by a clot forming in your heart and traveling to your brain. Therefore an approach to do so will be the first thing your doctor will want to discuss with you regarding anticoagulation therapy.



MYTH 5

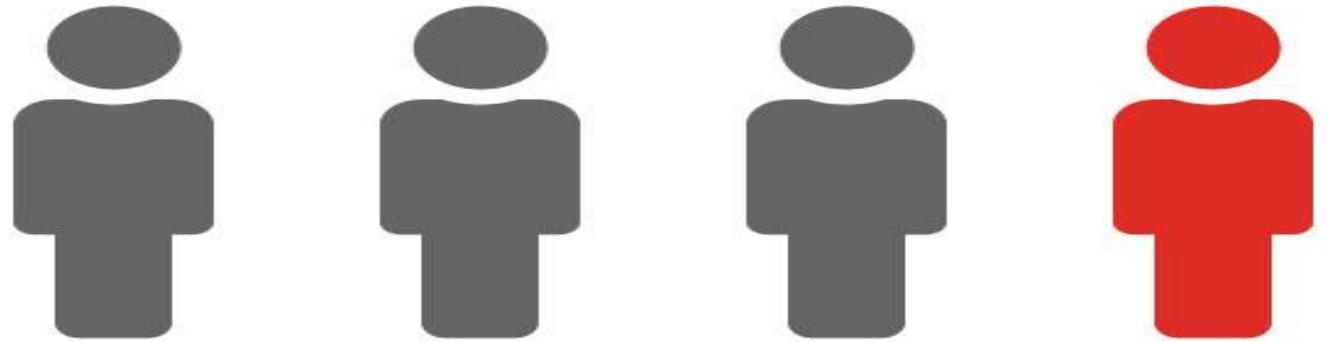
Breathlessness and exhaustion are an indicator of old age

NO! AF can cause you to feel breathless. The heart has four chambers that beat in rhythm. However with AF, the chambers instead of being in rhythm, quiver and prevent a steady flow of blood to pass through the heart – causing a feeling of breathlessness and palpitations.

MYTH 6

Blood thinners haven't stopped the palpitations or breathlessness so I don't bother taking them anymore

Anticoagulation medication does not thin the blood as everyone thinks, nor does it treat the symptoms of AF. Instead, it has the important role of preventing clots from forming in the chambers of the heart due to the quivering and irregular rhythm. It is important to prevent clots as they can travel to the brain causing an AF-related stroke.



By 2050, AFib is expected to affect **72 Million people**,^{5,6}

That's more than twice as many AFib patients as Europe and North America combined.

For healthcare systems across APAC, every 10 years there is a **1.8-5.6x** increase in healthcare costs due to Afib.^{7,8,9,10,11}

For healthcare systems across APAC, every 10 years there is a **1.8-5.6x** increase in healthcare costs due to Afib.^{7,8,9,10,11}

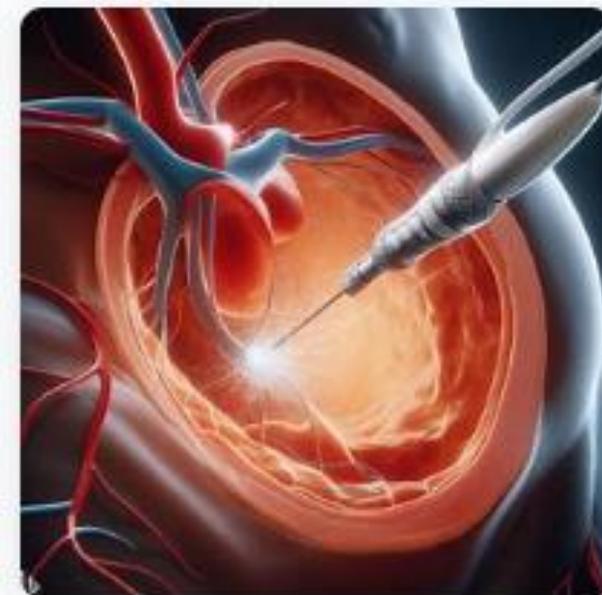
WHY SHOULD WE KNOW ANYTHING ABOUT ABLATION FOR ATRIAL FIBRILLATION?

- **ANTIARRHYTHMIC DRUGS HAVE MODEST EFFICACY**
- **(RANGING FROM 20-45% TO PREVENT AF IN ONE YEAR)**

- **ANTIARRHYTHMIC DRUGS HAVE SIGNIFICANT SAFETY ISSUES**
- **(1% PROARRHYTHMIA)**

Artificial Intelligence can do everything

Can you draw a picture for
point by point atrial
fibrillation ablation?

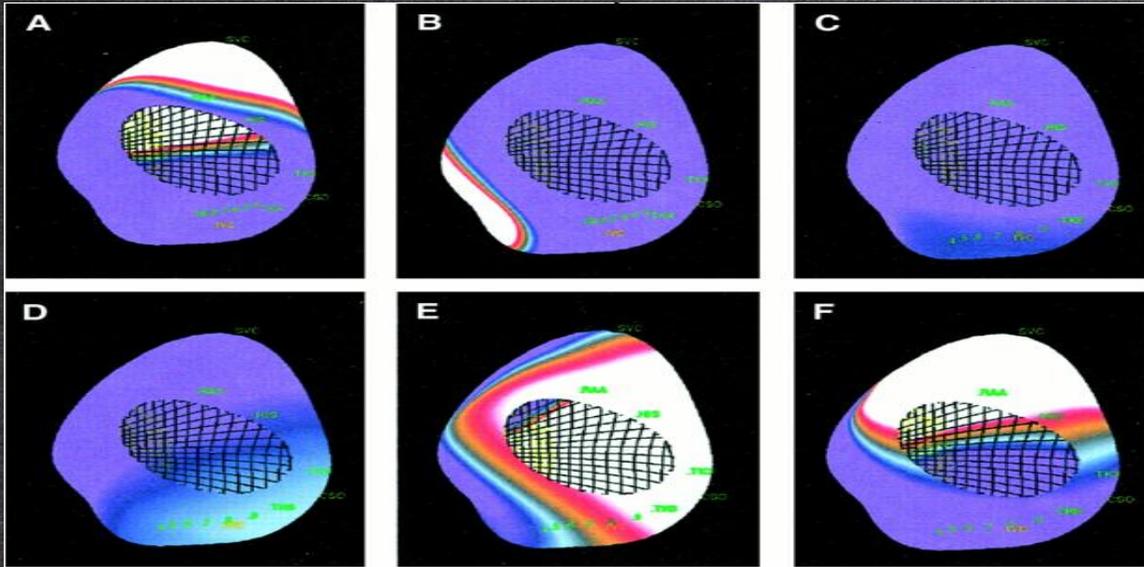


"Point by point atrial fibrillation ablation"

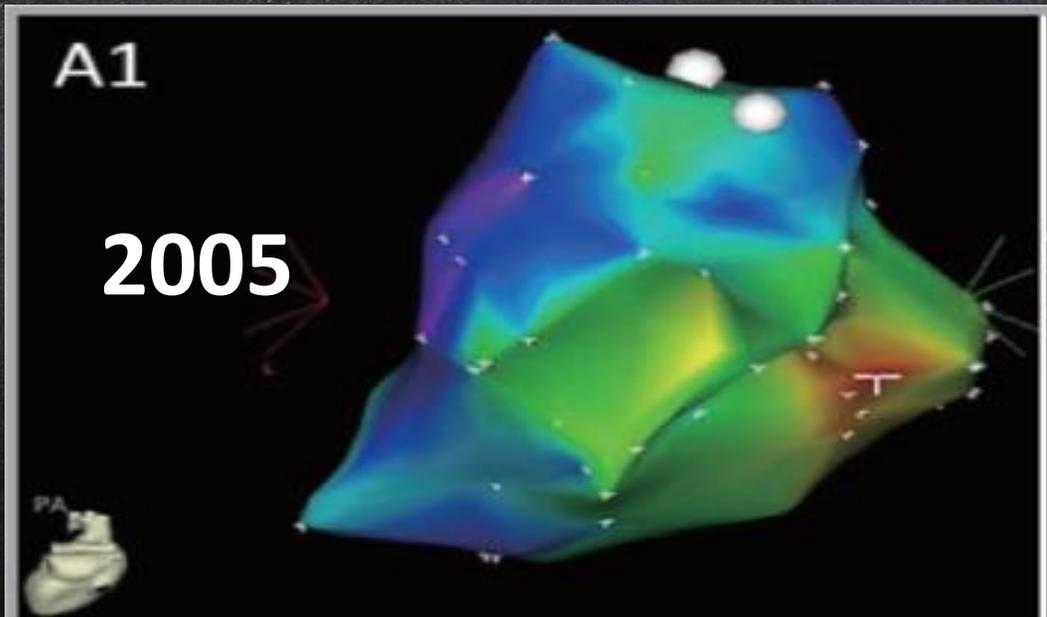
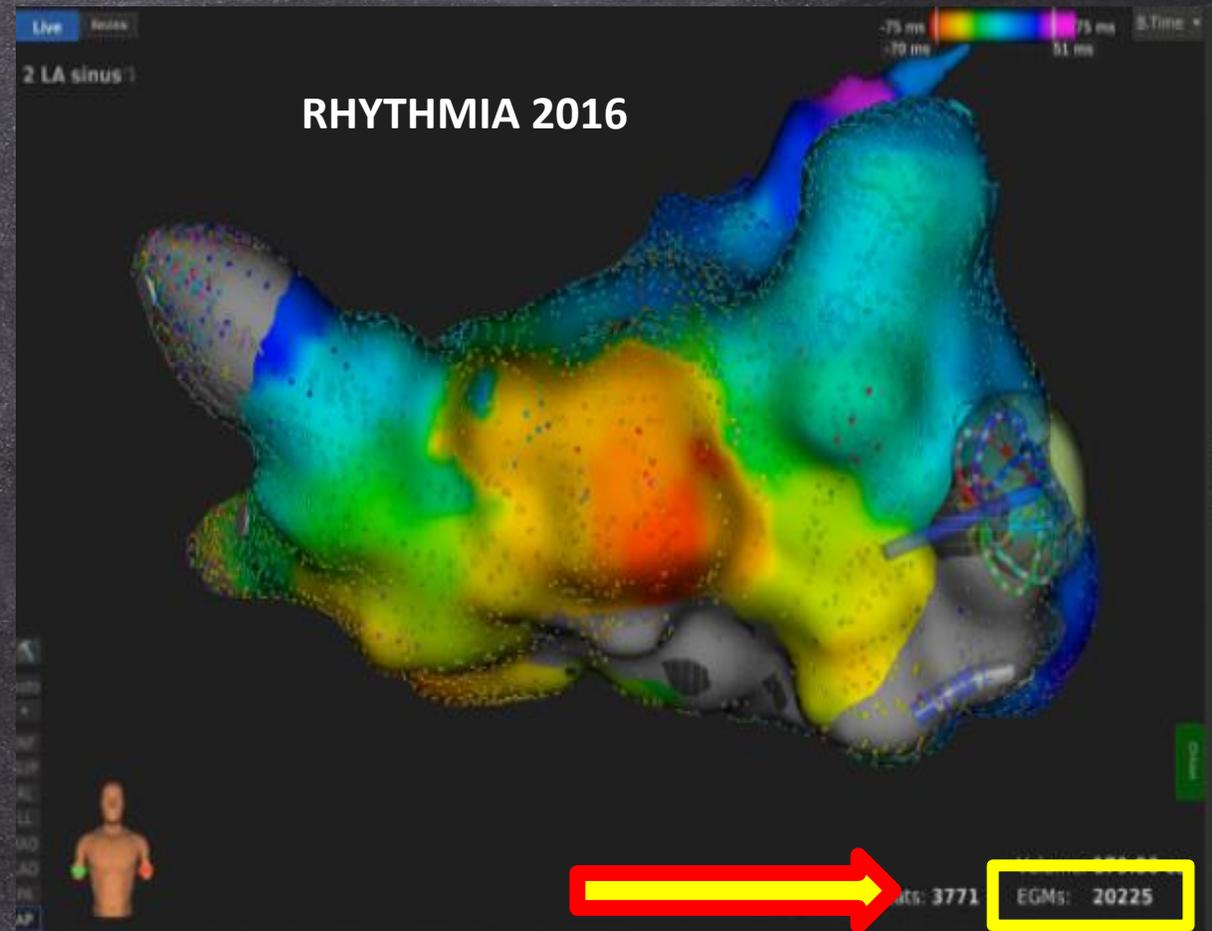
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ENSITE 1999

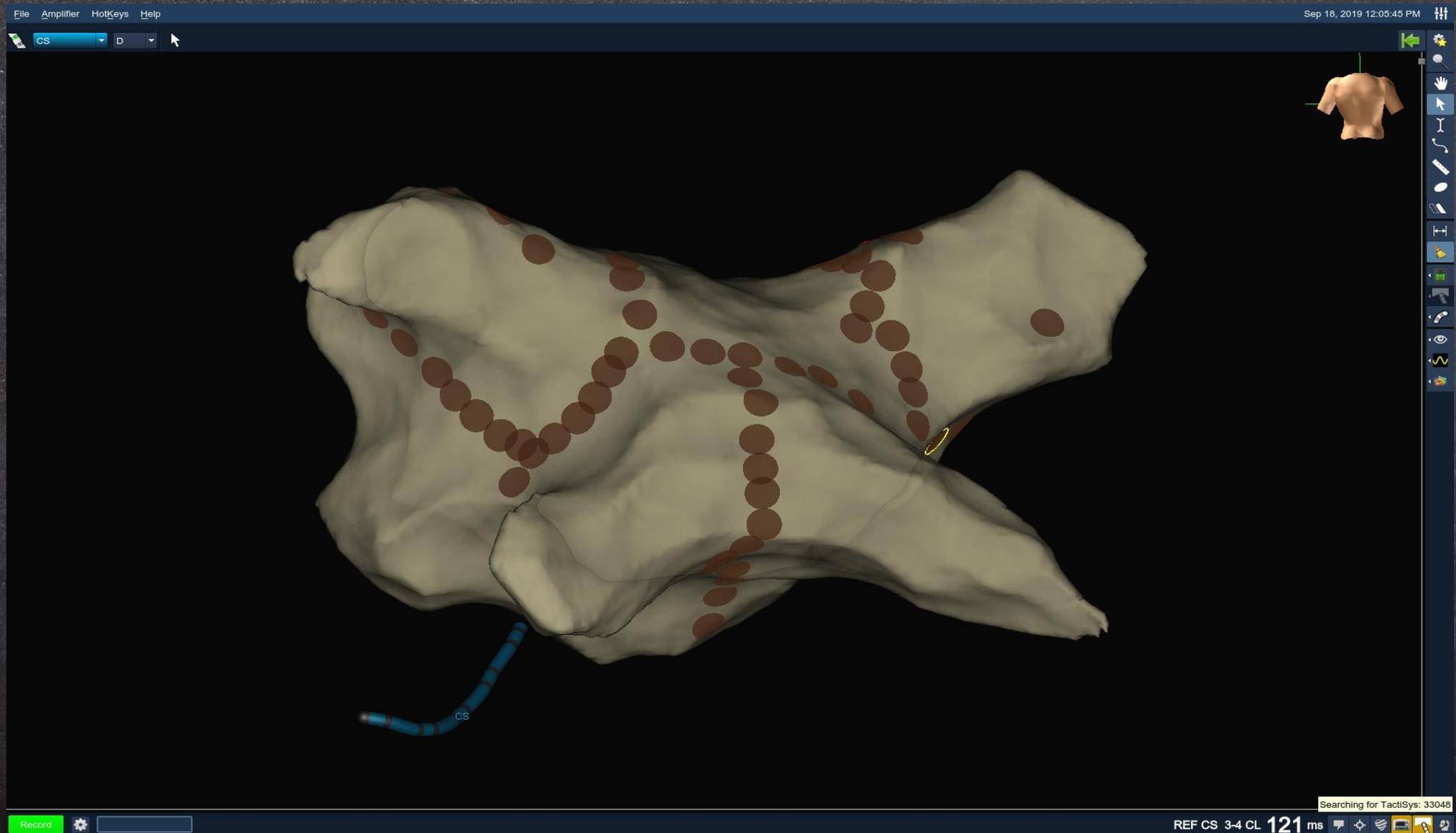


Thomas Paul et al. *Circulation*. 2001;103:2266-2271

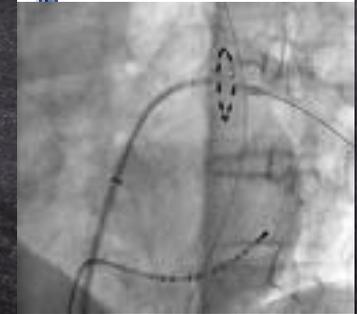
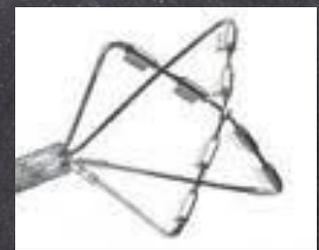
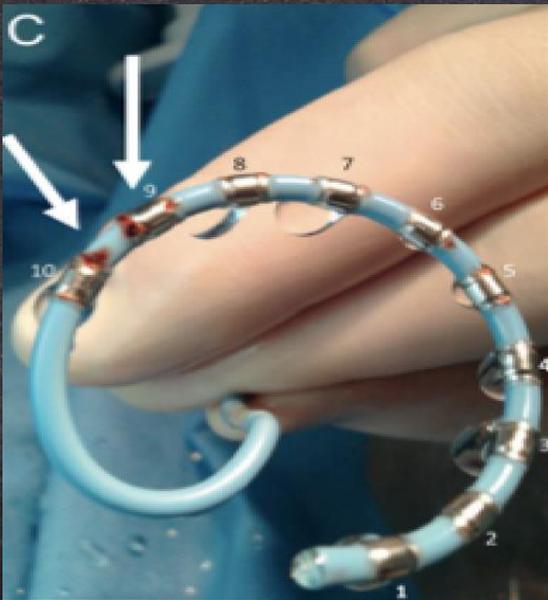
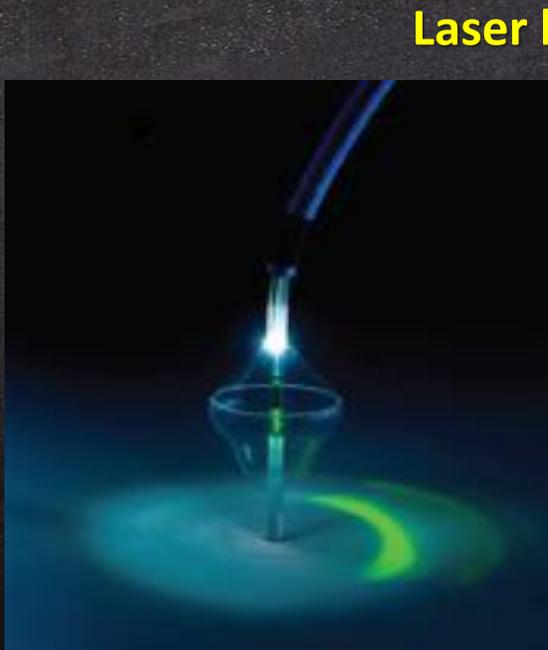
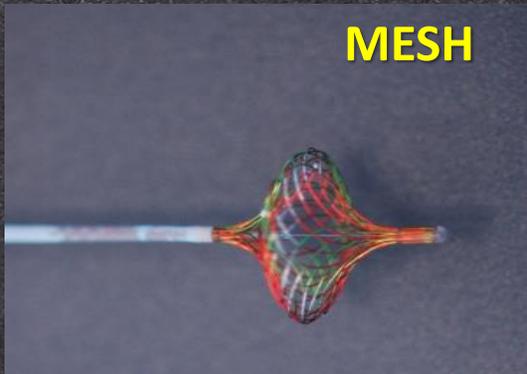


2. ΑΣΘΕΝΗΣ ΜΕ ΙΔΙΑΙΤΕΡΗ ΑΝΑΤΟΜΙΑ

A. Δυνατότητα αλλαγής πλάνου – Ασθενής προγραμματισμένος για Cryoablation



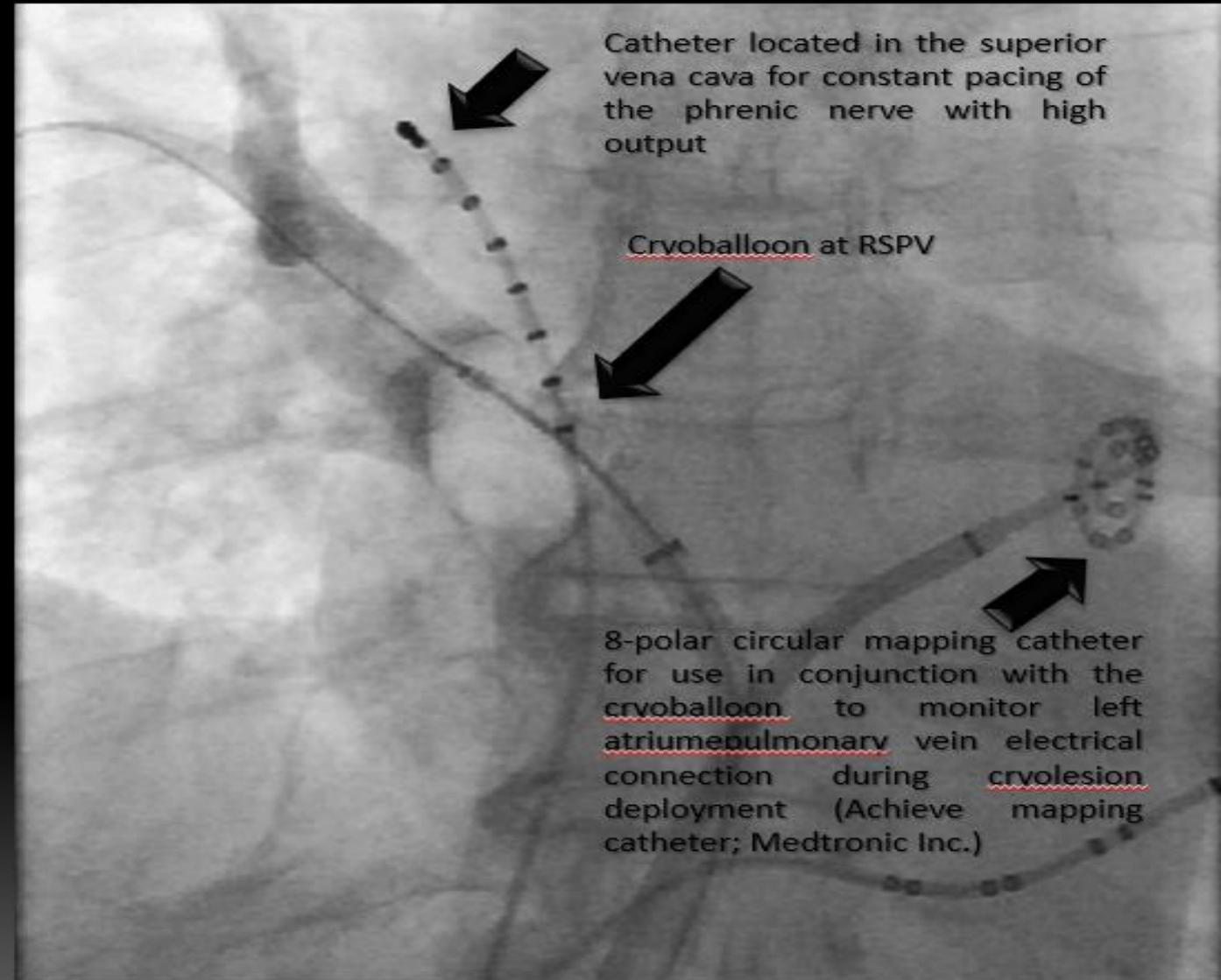
One for ALL and ... all for one purpose?



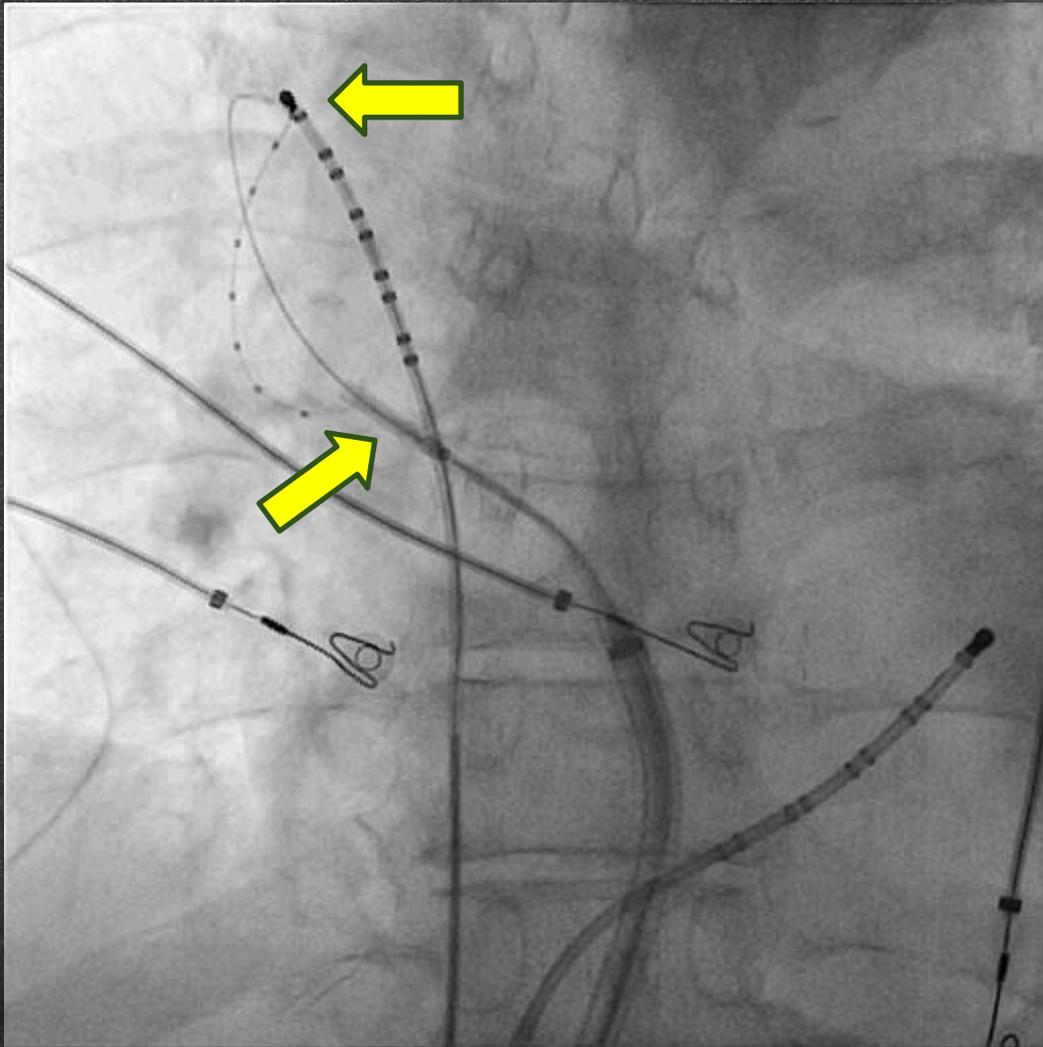
Invasive therapy for atrial fibrillation: recent developments in ablation, navigation and mapping technology

Ablation of the right superior pulmonary vein with the use of the cryoballoon system

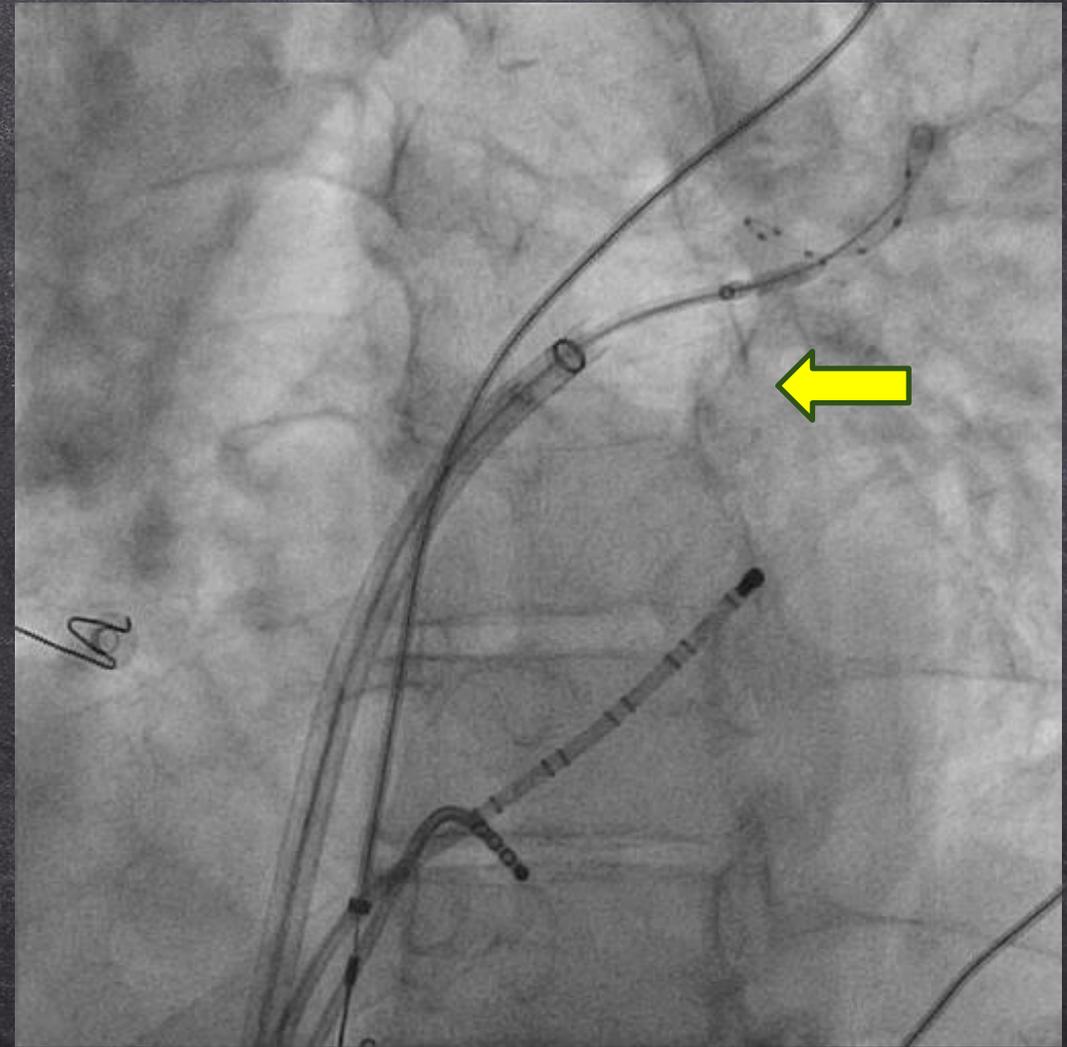
1. Chun KR, Schmidt B, Metzner A, et al. The 'single big cryoballoon' technique for acute pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a prospective observational single centre study. Eur Heart J 2009;30:699e709
2. Linhart M, Bellmann B, Mittmann-Braun E, et al. Comparison of cryoballoon and radiofrequency ablation of pulmonary veins in 40 patients with paroxysmal atrial fibrillation: a casecontrol study. J Cardiovasc Electrophysiol 2009;20:1343e8.
3. 20. Klein G, Oswald H, Gardiwal A, et al. Efficacy of pulmonary vein isolation by cryoballoon ablation in patients with paroxysmal atrial fibrillation. Heart Rhythm 2008;5:802e6.



Απομόνωση πνευμονικών φλεβών με Cryoballoon



Δεξιά άνω πνευμονική φλέβα

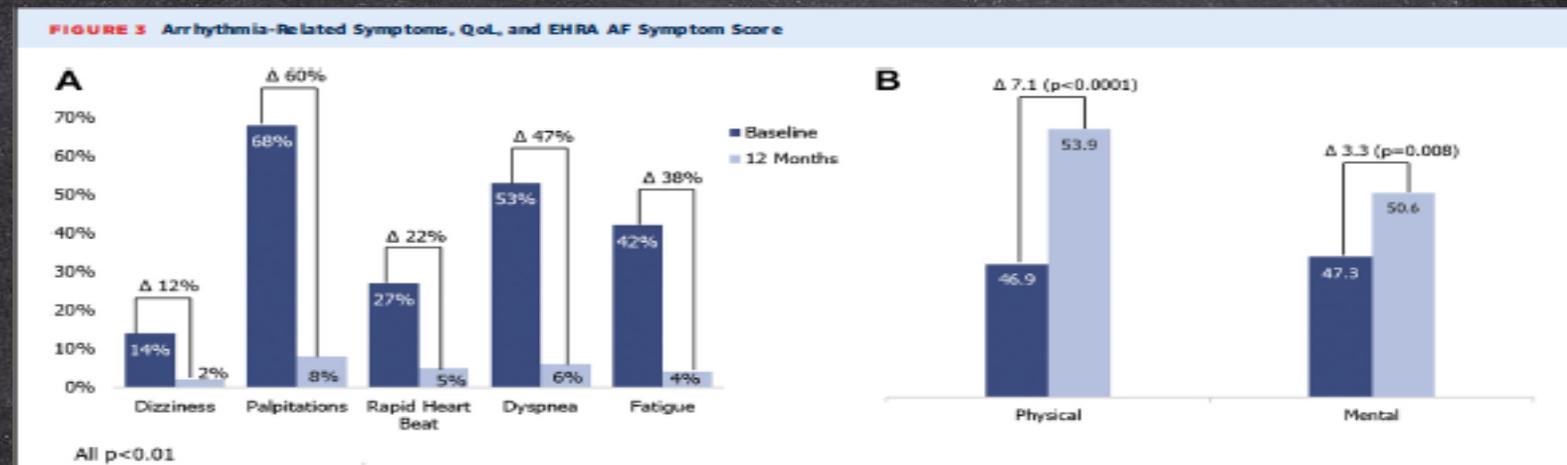
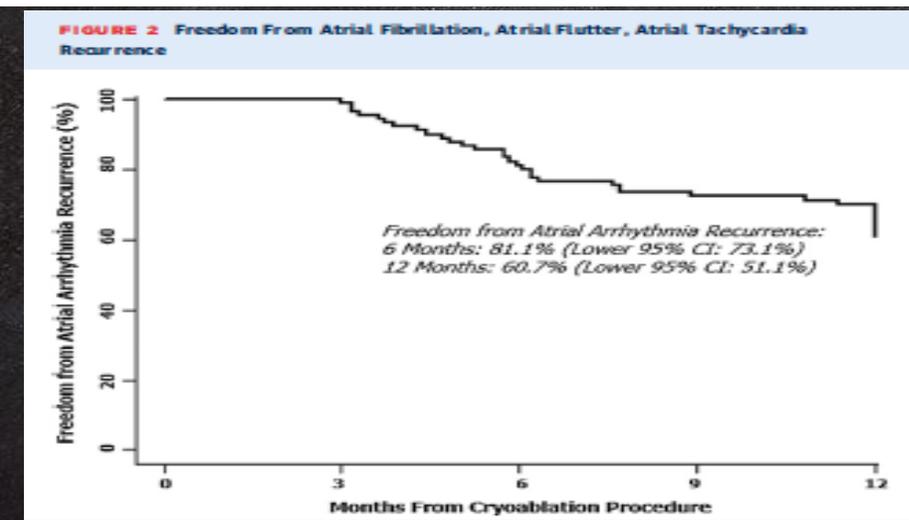


Αριστερή άνω πνευμονική φλέβα

Single-Procedure Outcomes and Quality-of-Life Improvement 12 Months Post-Cryoballoon Ablation in Persistent Atrial Fibrillation

Results From the Multicenter CRYO4PERSISTENT AF Trial

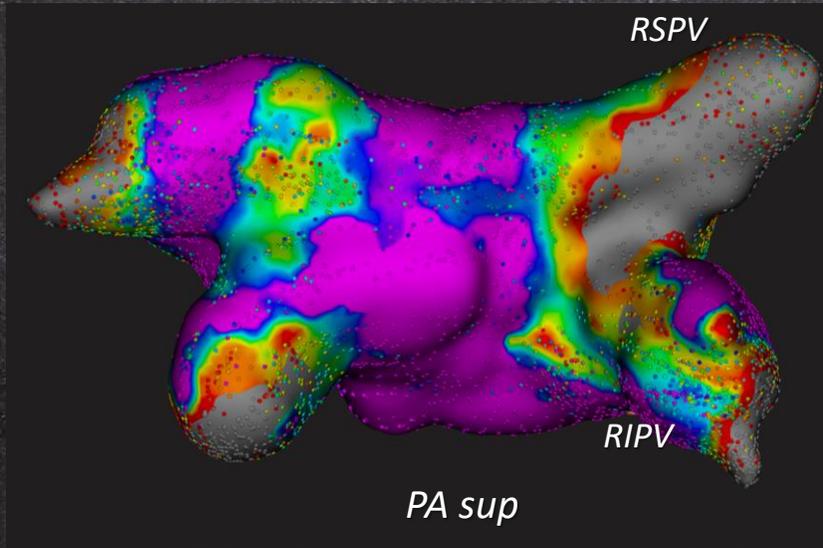
Serge Boveda, MD,^a Andreas Metzner, MD,^b Dinh Q. Nguyen, MD,^c K.R. Julian Chun, MD,^d Konrad Goehl, MD,^e George Noelker, MD,^f Jean-Claude Deharo, MD,^g George Andrikopoulos, MD,^h Tillman Dahme, MD,ⁱ Nicolas Lellouche, MD,^j Pascal Defaye, MD^k (JACC Electrophysiology in press 2018)



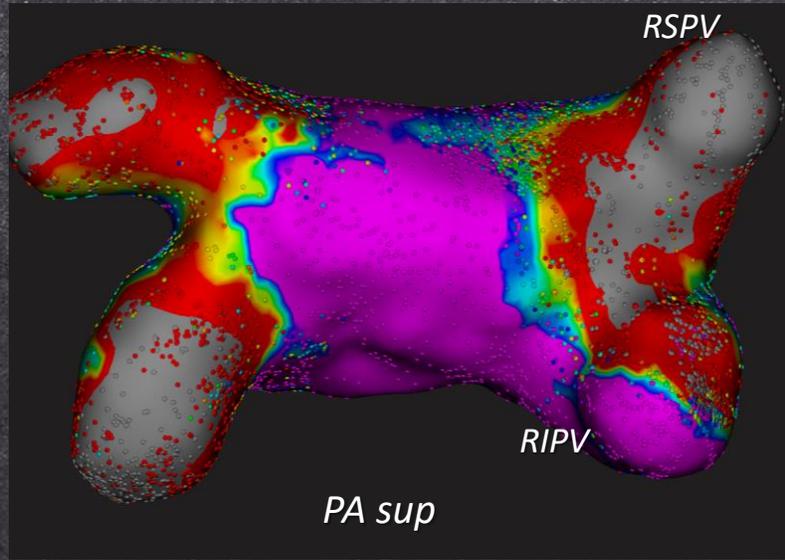
CONCLUSIONS Cryoballoon ablation for treatment of PerAF demonstrated 61% single-procedure success at 12 months post-ablation in addition to significant reduction in arrhythmia-related symptoms and improved quality of life. (Cryoballoon Ablation for Early Persistent Atrial Fibrillation [Cryo4 Persistent AF]; NCT02213731). (J Am Coll Cardiol EP 2018; ■:■-■) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

33-year old patient with long-standing AF 3/2022 Cryoablation - 7/2022 RF ablation

Left Atria 4 months after
Cryo ablation

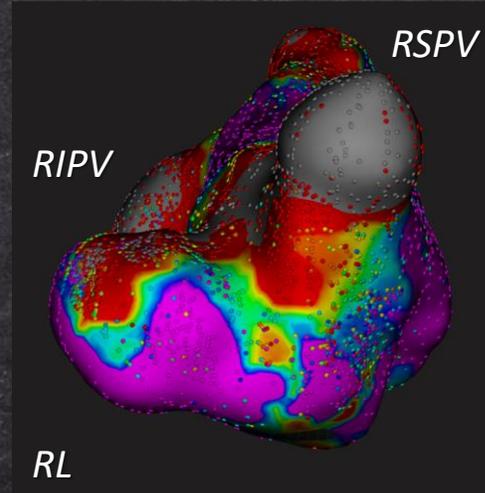
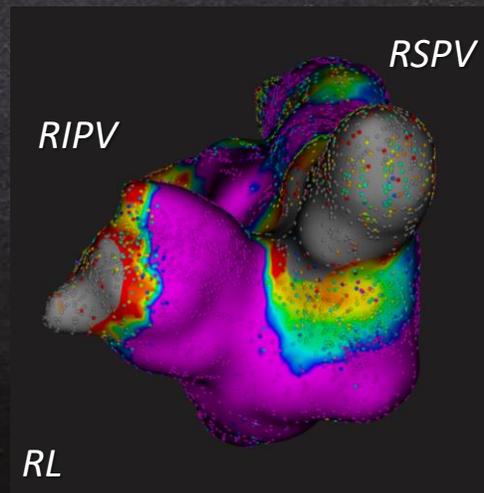


Left Atria 8 months after
RF ablation



Electrophysiologically
Active myocardium

Low voltage areas



Electrophysiologically
Inactive myocardium

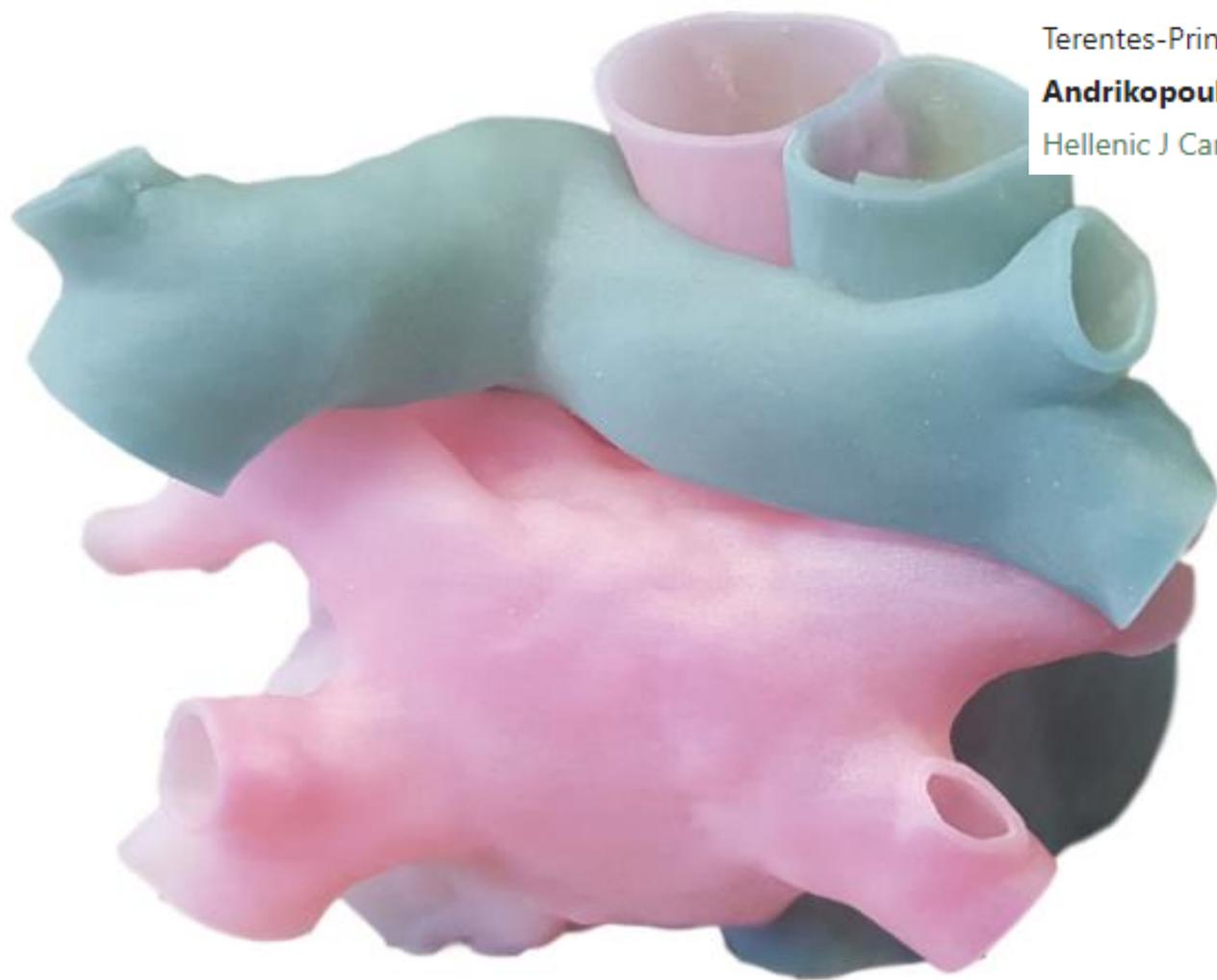
3D Printed atria before AF ablation (The 3-D GALA study)

3D printing for ablation planning in patients undergoing atrial fibrillation ablation: Preliminary results of the pilot randomized 3D GALA trial.

Terentes-Printzios D, Xydis P, Gourgouli I, Tampakis K, Pastromas S, Sikiotis A, Antonopoulos A,

Andrikopoulos G, Tsioufis K, Vlachopoulos C.

Hellenic J Cardiol. 2023 May-Jun;71:64-66. doi: 10.1016/j.hjc.2022.12.004. Epub 2022 Dec 9.





Correspondence

3D printing for ablation planning in patients undergoing atrial fibrillation ablation: Preliminary results of the pilot randomized 3D GALA trial

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Hellenic J Cardiol. 2022 Dec 9;S1109-9666(22)00178-6. doi: 10.1016/j.hjc.2022.12.004. Online ahead of

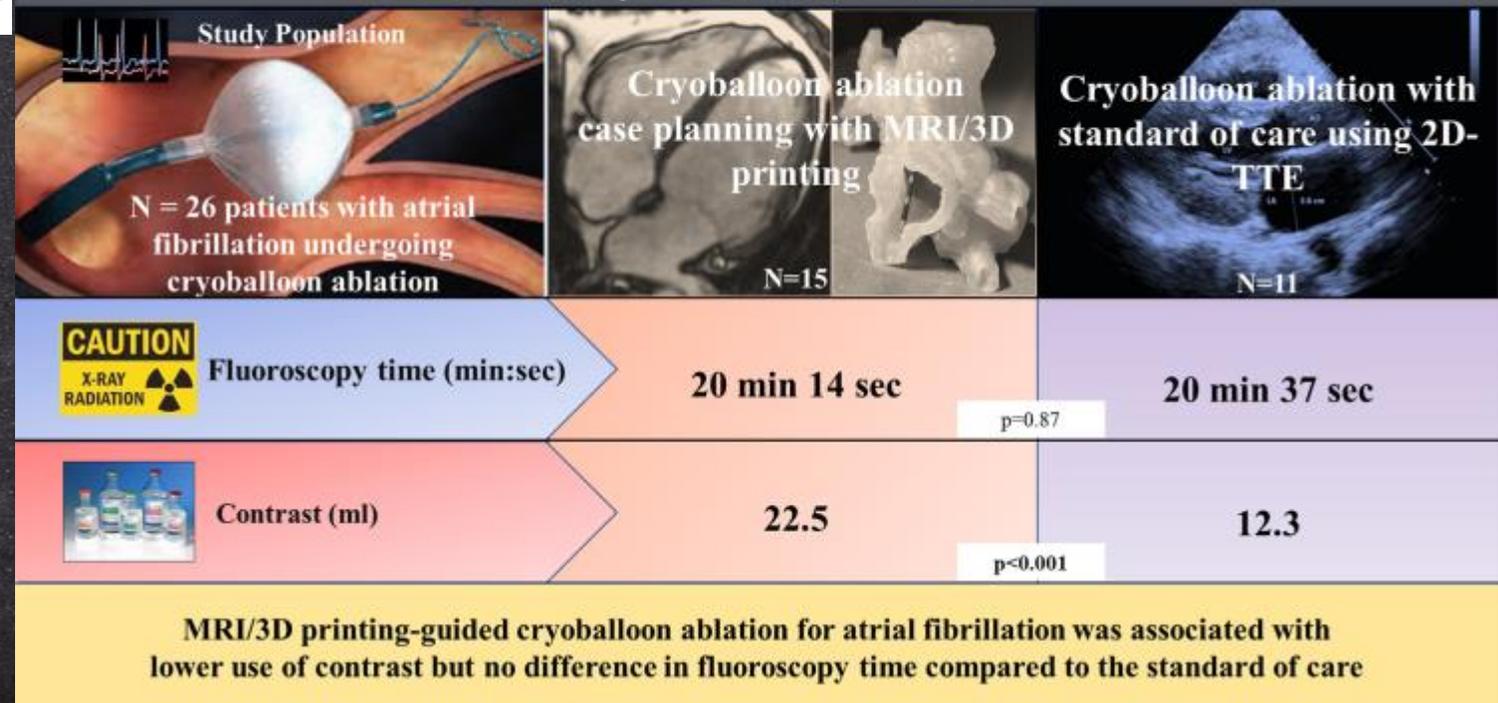
Table 1

Baseline characteristics and procedural results and variables reflecting relative procedural efficiency between case planning with combined MRI/3D printing versus standard of care using 2D-TTE.

Variables	No preprocedural imaging n = 11	MRI+3D model n = 15	p value
Age (years)	61.4 (13.3)	58.2 (13.4)	0.56
Gender, male	7 (64)	11 (73)	0.60
Weight (kg)	77.5 (13.4)	86.2 (12.4)	0.10
Height (cm)	172.6 (9.8)	176.7 (8.6)	0.28
Obesity, n (%)	4 (36)	4 (27)	0.60
Diabetes, n (%)	4 (36)	3 (20)	0.37
Hypertension, n (%)	5 (45)	6 (40)	0.78
Smoking, n (%)	6 (55)	2 (13)	0.024
History of CAD, n (%)	4 (36)	1 (7)	0.06
Persistent AF, n (%)	2 (18)	3 (20)	0.91
LVEF (%)	56.3 (4.9)	55.6 (11.1)	0.85
Left atrium size (mm)	38.6 (4.0)	40.6 (4.1)	0.23
Presence of MR, n	3 (27)	3 (20)	0.66
Presence of TR, n	2 (18)	1 (7)	0.36
<i>Primary and secondary procedural outcomes</i>			
Fluoroscopy time (min:sec)	20:14 (05:58)	20:37 (05:07)	0.87
Contrast (ml)	22.5 (6.5)	12.3 (4.7)	<0.001
Air Kerma (mGy)	495.1 (142.8)	483.4 (198.9)	0.87
Cryoballoon applications, n	4.7 (0.8)	5 (0.7)	0.36

3D-printing for Ablation Planning in Patients Undergoing Atrial Fibrillation Ablation (3D-GALA trial)

Pilot, randomized, open-label, controlled, multicentre, clinical trial

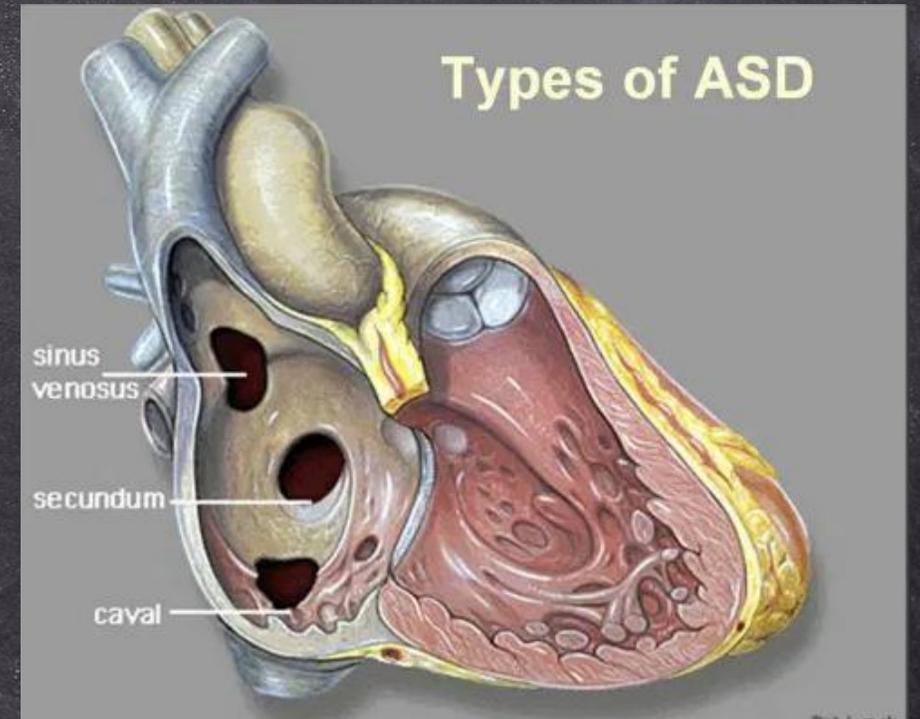


36-year old patient
Right superior vein drainages in Superior vena cava

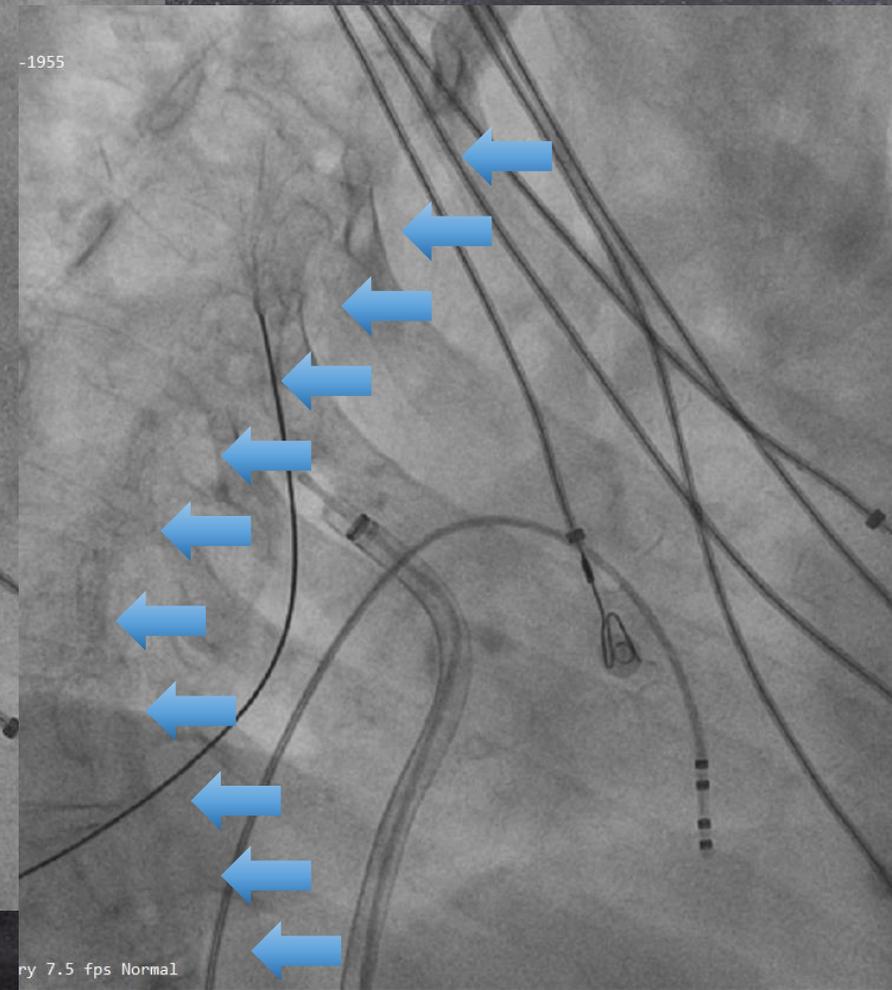
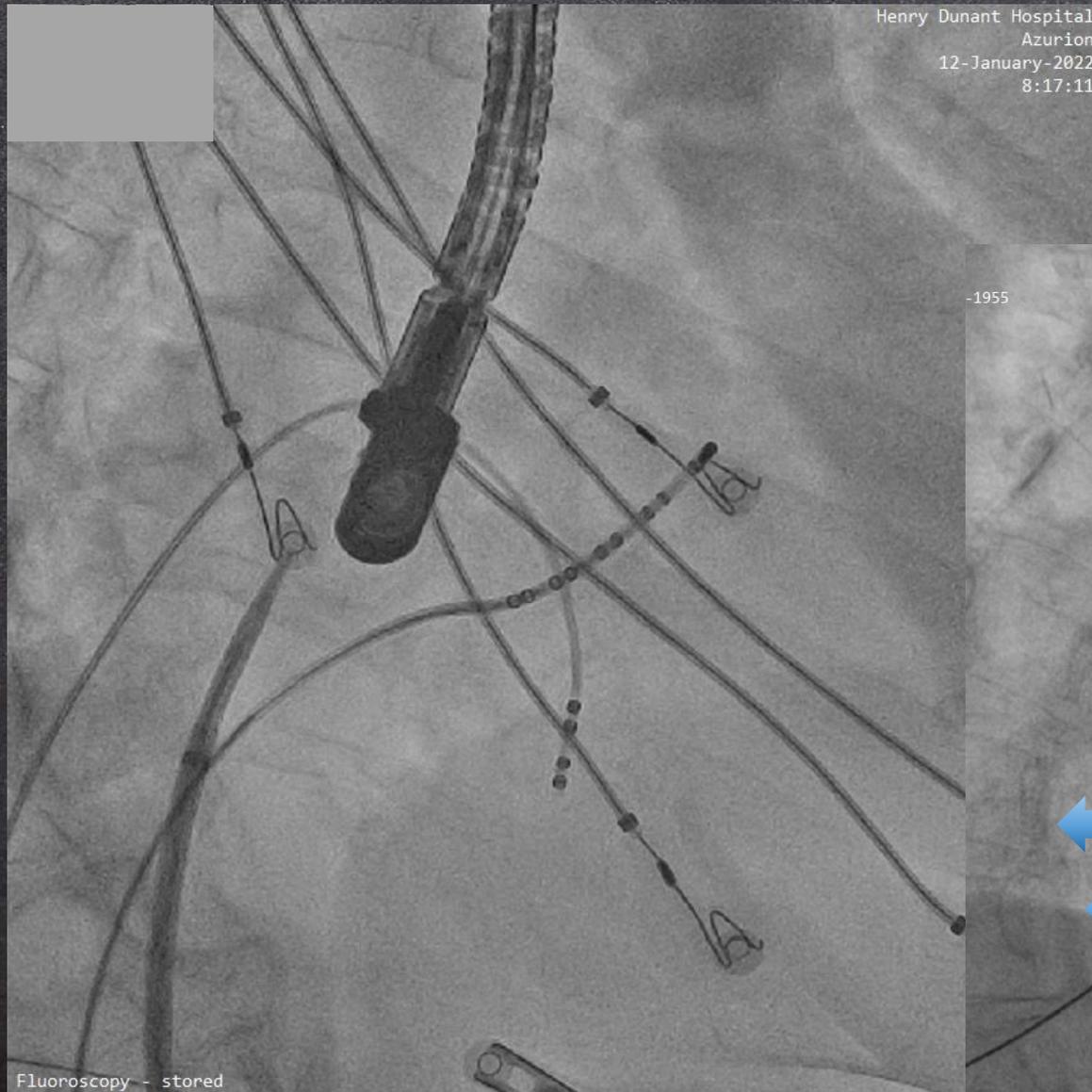


Cardiac MRI multiplanar reconstruction

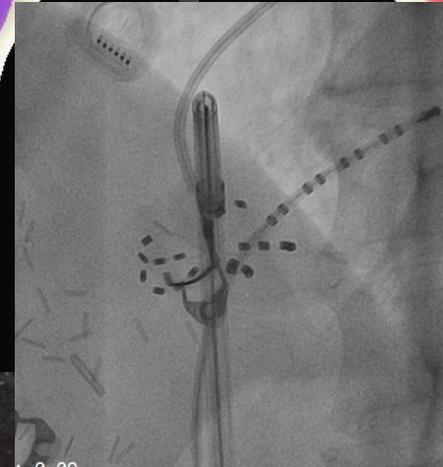
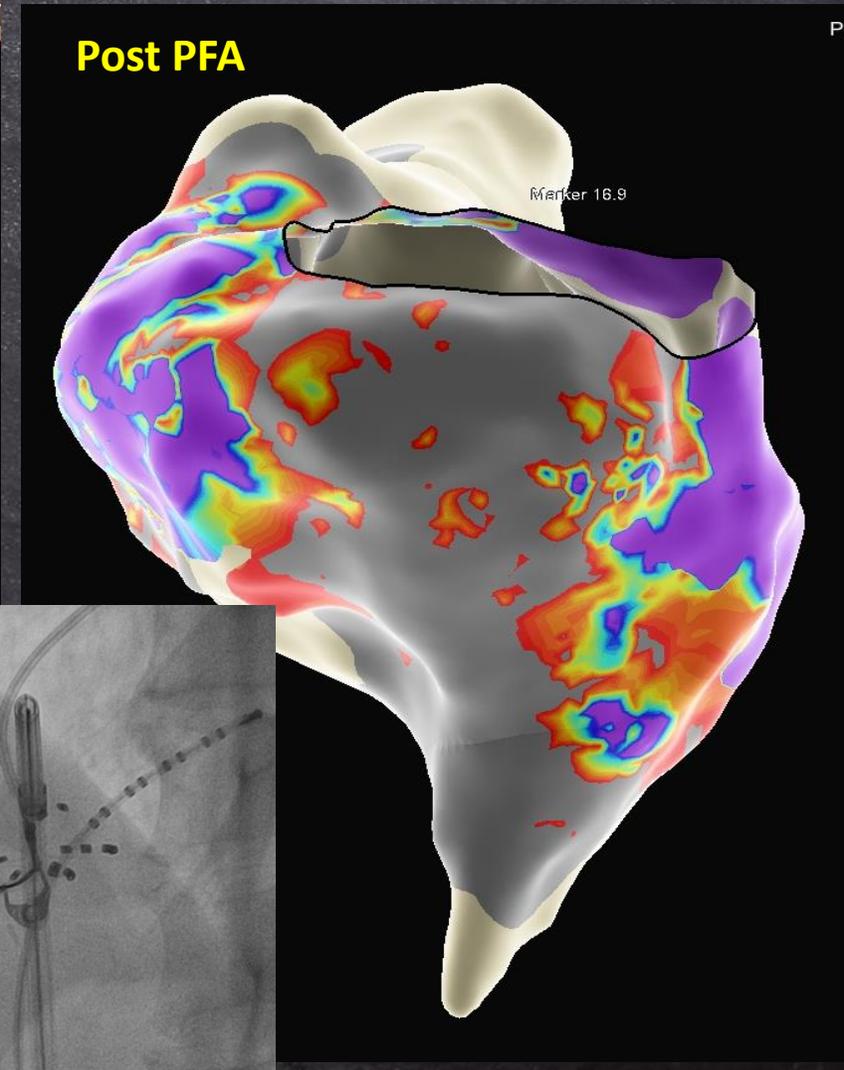
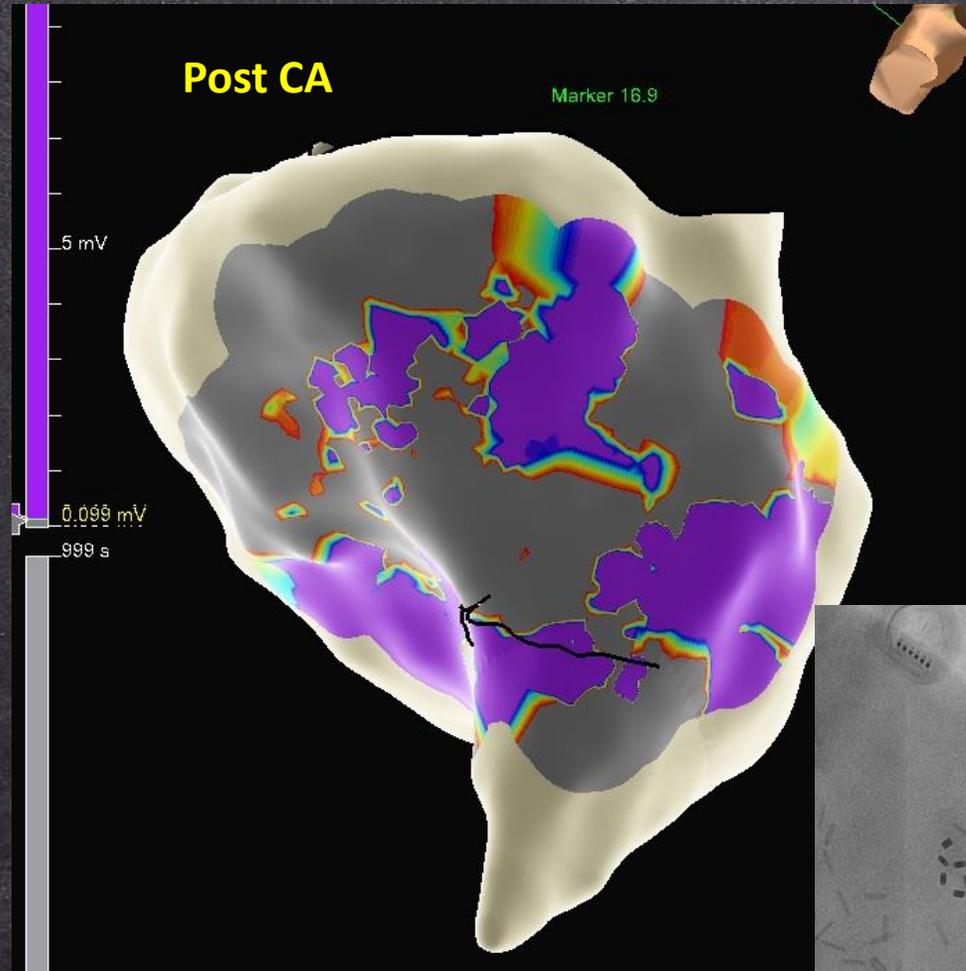
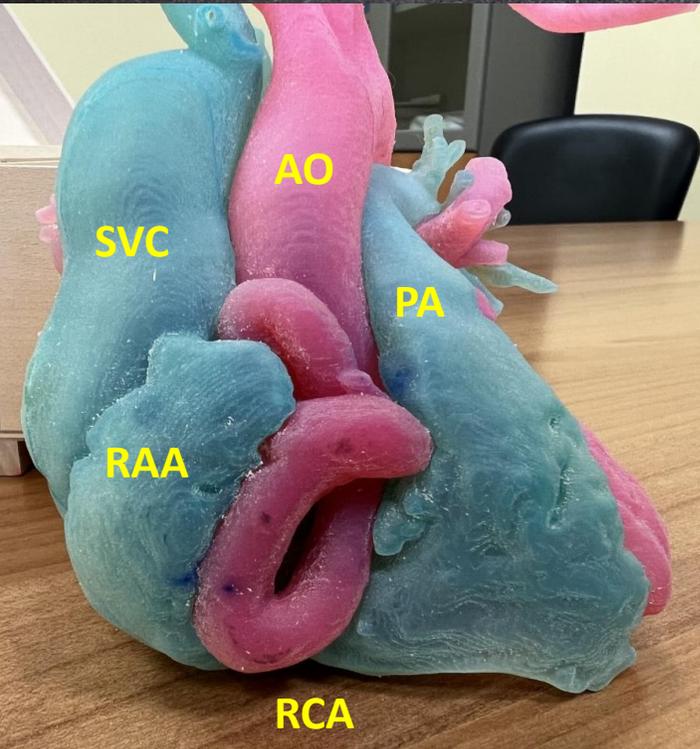
Arrow: right upper pulmonary vein draining into superior vena cava



Scoliosis deforms cardiac anatomy



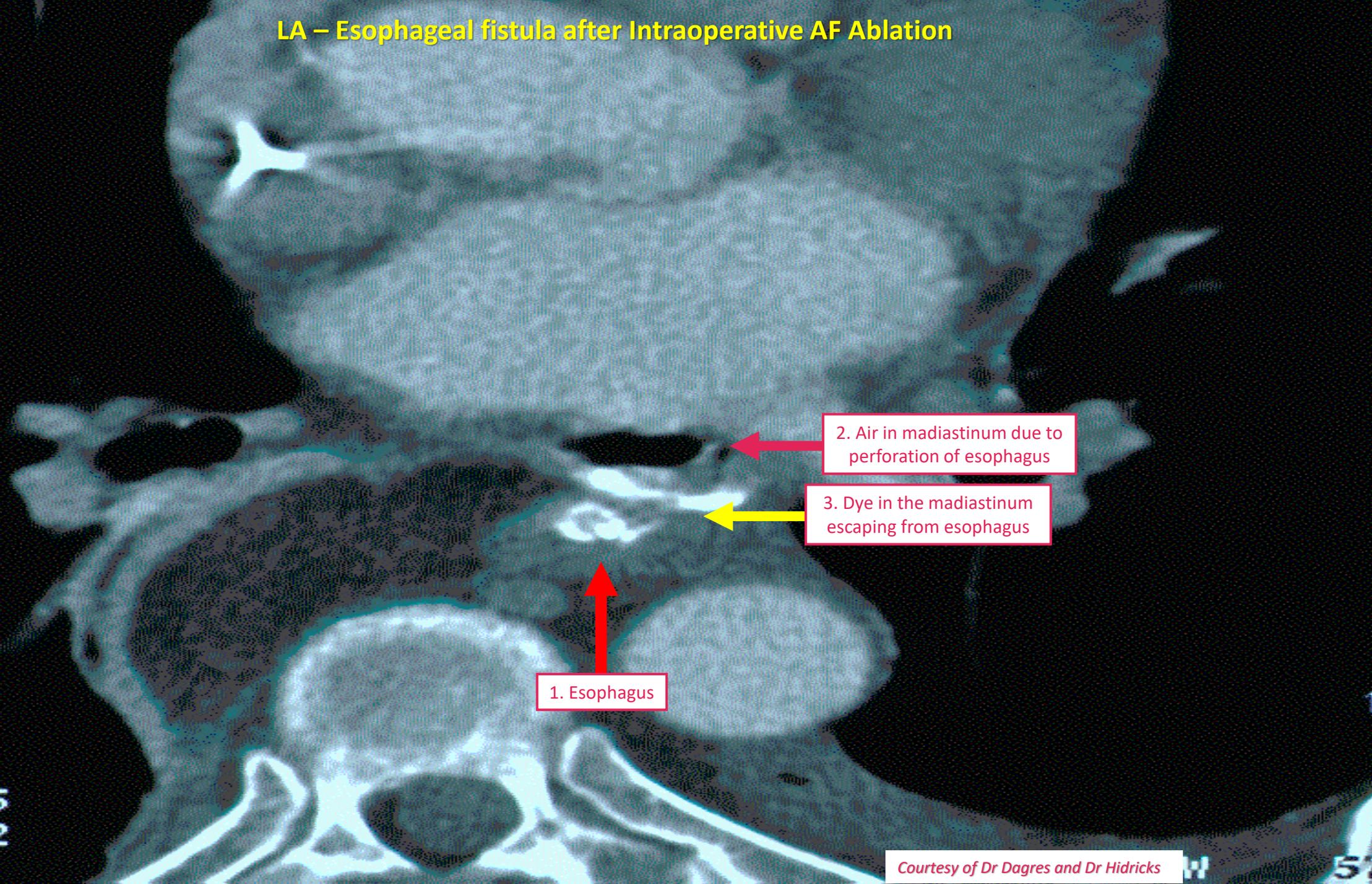
Fluoroscopy guided PF CTI ablation in a patient with peculiar anatomy (CTI bidirectional block NOT feasible with irrigated catheter and electroanatomic mapping)



LA – Esophageal fistula after Intraoperative AF Ablation

299.0
171
5

140
146
1.00
0.0
3.0/4.5
-6/-32
0 L0



1. Esophagus

2. Air in mediastinum due to perforation of esophagus

3. Dye in the mediastinum escaping from esophagus

Farapulse gains CE mark for its pulsed field ablation system

29th January 2021 1630



Farapulse announced that it has received the CE mark for its pulsed field ablation (PFA) system for the treatment of paroxysmal atrial fibrillation (AF). The approval will allow the company to commercialise the cardiac PFA system and permits marketing of the system across the European Union and other CE mark geographies.

Farapulse said in a press release that it will partner with a select number of physicians prior to a broader rollout of the device.

"Farapulse PFA has garnered a high level of interest at scientific symposia in the past several years, making it abundantly clear that the medical community is primed to adopt our technology into routine use. The clinical results and unparalleled volume of data chronicled through investigator-authored abstracts and manuscripts have been exceedingly well received," said Allan Zingeler, president and CEO of Farapulse. "Europe's modern and progressive electrophysiology market represents a unique opportunity for Farapulse to showcase our PFA system's powerful yet incredibly safe ability to lead in the treatment of AF."

Circulation: Arrhythmia and Electrophysiology

ORIGINAL ARTICLE



Pulsed Field Ablation Versus Radiofrequency Ablation

Esophageal Injury in a Novel Porcine Model

Jacob S. Koruth, MD; Kenji Kuroki, MD; Iwanari Kawamura, MD; Richard Brose, MS; Raju Viswanathan, PhD; Eric D. Buck, MS; Elina Donskoy, MD, PhD; Petr Neuzil, MD, PhD; Srinivas R. Dukkipati, MD; Vivek Y. Reddy, MD

BACKGROUND: Pulsed field ablation (PFA) can be myocardium selective, potentially sparing the esophagus during left atrial ablation. In an in vivo porcine esophageal injury model, we compared the effects of newer biphasic PFA with radiofrequency ablation (RFA).

METHODS: In 10 animals, under general anesthesia, the lower esophagus was deflected toward the inferior vena cava using an esophageal deviation balloon, and ablation was performed from within the inferior vena cava at areas of esophageal contact. Four discrete esophageal sites were targeted in each animal: 6 animals received 8 PFA applications/site (2 kV, multispline catheter), and 4 animals received 6 clusters of irrigated RFA applications (30 Wx30 seconds, 3.5 mm catheter). All animals were survived to 25 days, sacrificed, and the esophagus submitted for pathological examination, including 10 discrete histological sections/esophagus.

RESULTS: The animals weight increased by $13.7 \pm 6.2\%$ and $6.8 \pm 6.3\%$ ($P=0.343$) in the PFA and RFA cohorts, respectively. No PFA animals (0 of 6, 0%) developed abnormal in-life observations, but 1 of 4 RFA animals (25%) developed fever and dyspnea. On necropsy, no PFA animals (0 of 6, 0%) demonstrated esophageal lesions. In contrast, esophageal injury occurred in all RFA animals (4 of 4, 100%; $P=0.005$): a mean of 1.5 mucosal lesions/animal (length, -21.8 ± 8.9 mm; width, -4.9 ± 1.4 mm) were observed, including one esophago-pulmonary fistula and deep esophageal ulcers in the other animals. Histological examination demonstrated tissue necrosis surrounded by acute and chronic inflammation and fibrosis. The necrotic RFA lesions involved multiple esophageal tissue layers with evidence of arteriolar medial thickening and fibrosis of periesophageal nerves. Abscess formation and full-thickness esophageal wall disruptions were seen in areas of perforation/fistula.

CONCLUSIONS: In this novel porcine model of esophageal injury, biphasic PFA induced no chronic histopathologic esophageal changes, while RFA demonstrated a spectrum of esophageal lesions including fistula and deep esophageal ulcers and abscesses.

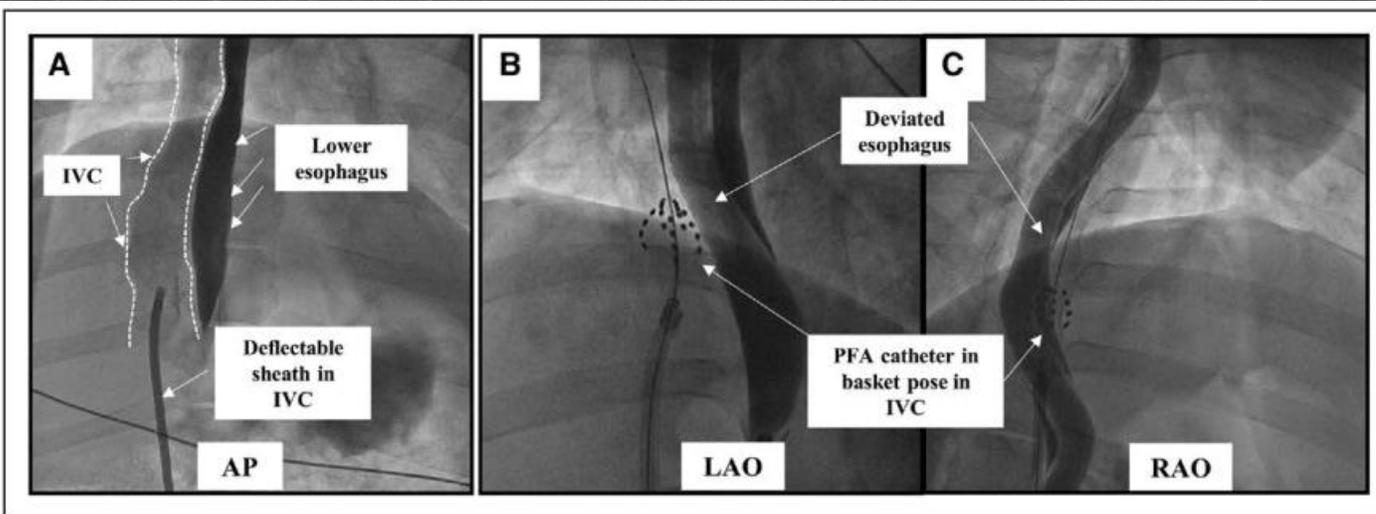
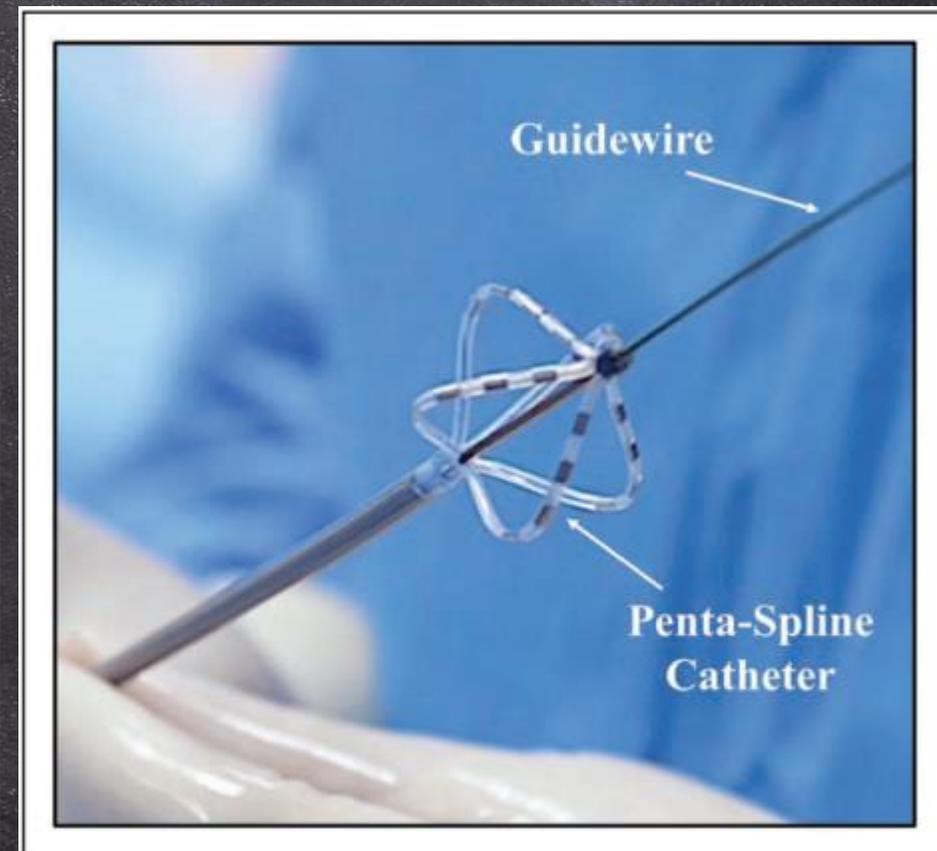


Figure 2. Fluoroscopic view of the esophageal injury mode: pulsed field ablation (PFA) cohort.

A, Contrast angiography was performed using a long deflectable sheath placed in the inferior vena cava (IVC; outlined). In the anteroposterior (AP) view, the IVC is seen rightward of the contrast filled esophagus. **B** and **C**, Left and right anterior oblique (LAO and RAO) projections demonstrate the PFA catheter in basket pose forcefully pushed against the deviated esophagus. The PFA catheter is shown here ablating 2 different esophageal locations.

Figure 1. Pulsed field ablation (PFA) catheter: pentaspline over-the-wire PFA catheter in basket pose.

Theory of Electroporation of Planar Bilayer Membranes: Predictions of the Aqueous Area, Change in Capacitance, and Pore-Pore Separation

Scott A. Freeman,* Michele A. Wang,* and James C. Weaver[†]

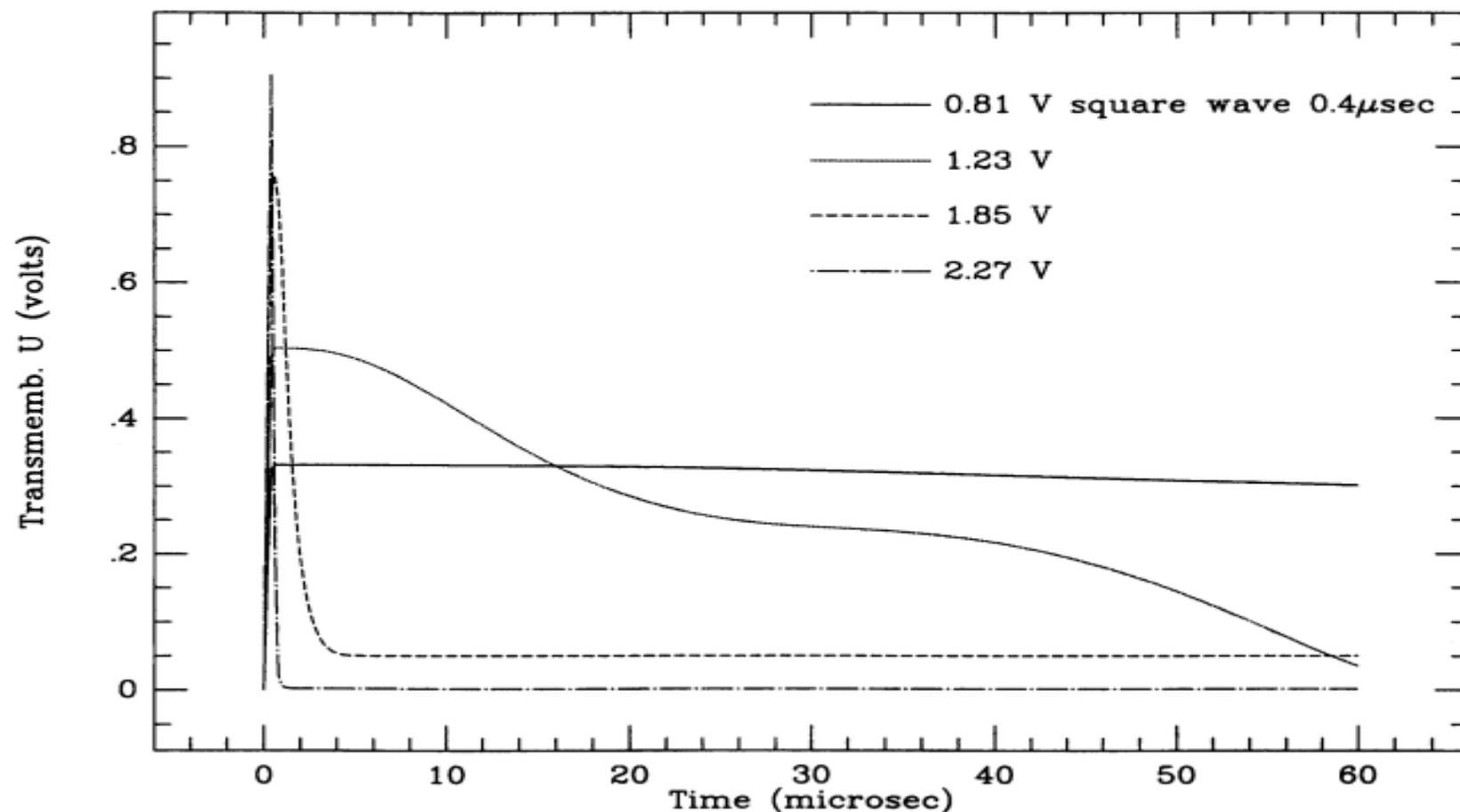
*Department of Physics and [†]Harvard-M.I.T. Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139 USA

Freeman et al.

Change in Capacitance and Pore-Pore Separation

45

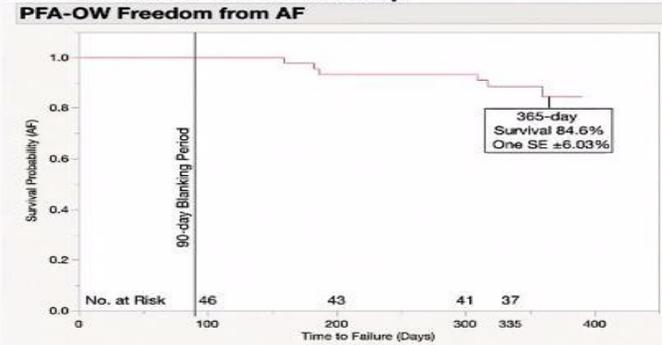
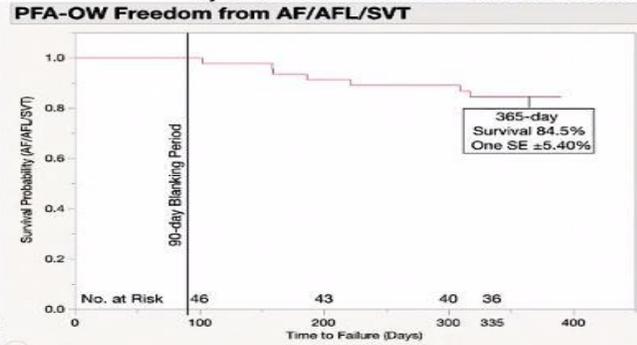
FIGURE 2 Predicted square pulse behavior of the transmembrane voltage, $U(t)$, due to a single 0.4- μ s pulse of the indicated amplitudes. As found previously, four distinguishable outcomes are possible: (1) simple charging of the membrane capacitance (smallest pulse; here 0.81 V), (2) rupture of the membrane (larger pulse; here 1.23 V), (3) incomplete reversible electrical breakdown (still larger pulse; here 1.85 V), (4) reversible electrical breakdown (REB) (largest pulse; here 2.27 V). The electrical behavior predicted by a recent transient aqueous pore model (Barnett and Weaver, 1991) agrees reasonably, but not exactly, with experimental observations of these outcomes (Benz et al., 1979).



PVI in PAF pts

1-Year Clinical Recurrence

- **97 pts reached 1 year of follow-up**
- Optiwave cohort
 - 86% per-week (TTM) and 98% per-monitor (Holter) compliance
 - 85±5% freedom from atrial arrhythmia
 - 6/7 recurrences demonstrated durable PVI at remap



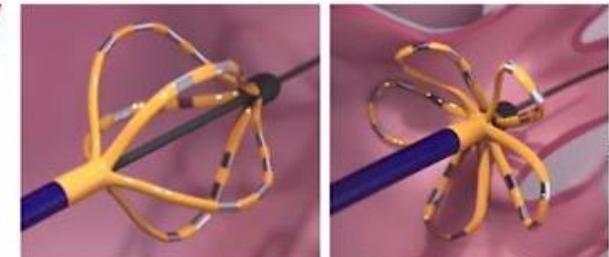
PVI in PAF pts

Remap Results

110 pts returned for prospective remaps at 93±30 days

Cohort	n	Durable PVI (% PVs)	Durable PVI (% pts)
Monophasic	11	45%	18%
Biphasic (Early/Other)	55	84%	58%
Optiwave (Optimized Biphasic)	44	96%	84%

- 4 paired applications / PV @ 1.8-2.0kV
 - 2 pairs in "Flower"
 - 2 pairs in "Basket"



EHRA 2021

As presented by Vivek Reddy

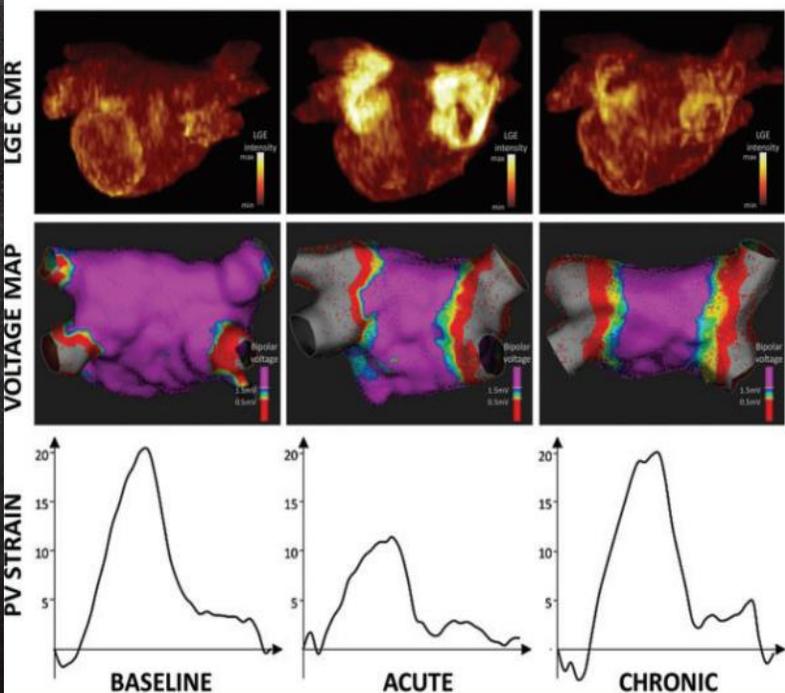


Pulsed field ablation prevents chronic atrial fibrotic changes and restrictive mechanics after catheter ablation for atrial fibrillation

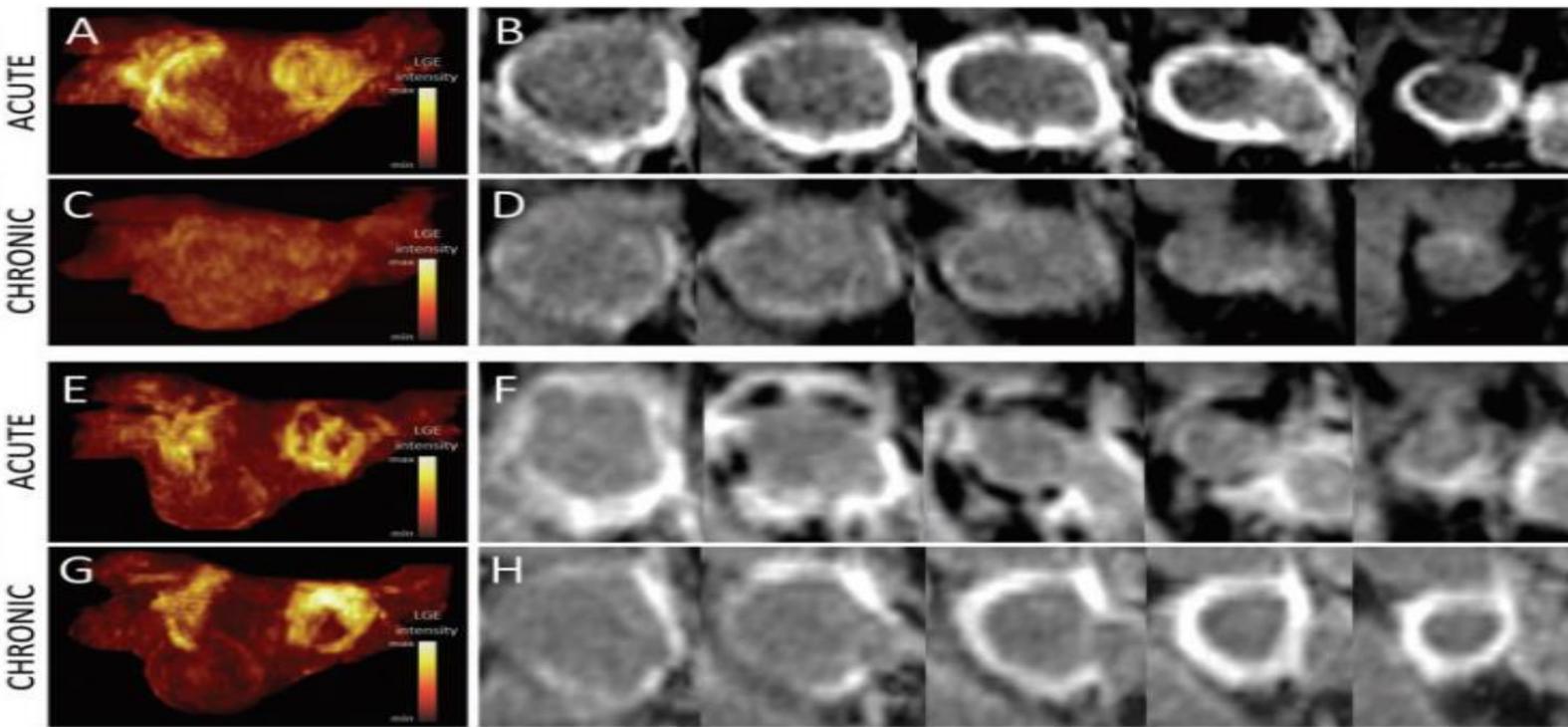
Methods and results

Cardiac magnetic resonance was performed pre-ablation, acutely (<3 h), and 3 months post-ablation in 41 patients with paroxysmal atrial fibrillation (AF) undergoing pulmonary vein (PV) isolation with PFA ($n = 18$) or thermal ablation ($n = 23$, 16 radiofrequency ablations, 7 cryoablations). Late gadolinium enhancement (LGE), T2-weighted, and cine images were analysed. In the acute stage, LGE volume was 60% larger after PFA vs. thermal ablation

Pulsed Field Ablation (PFA)



PULSED FIELD ABLATION



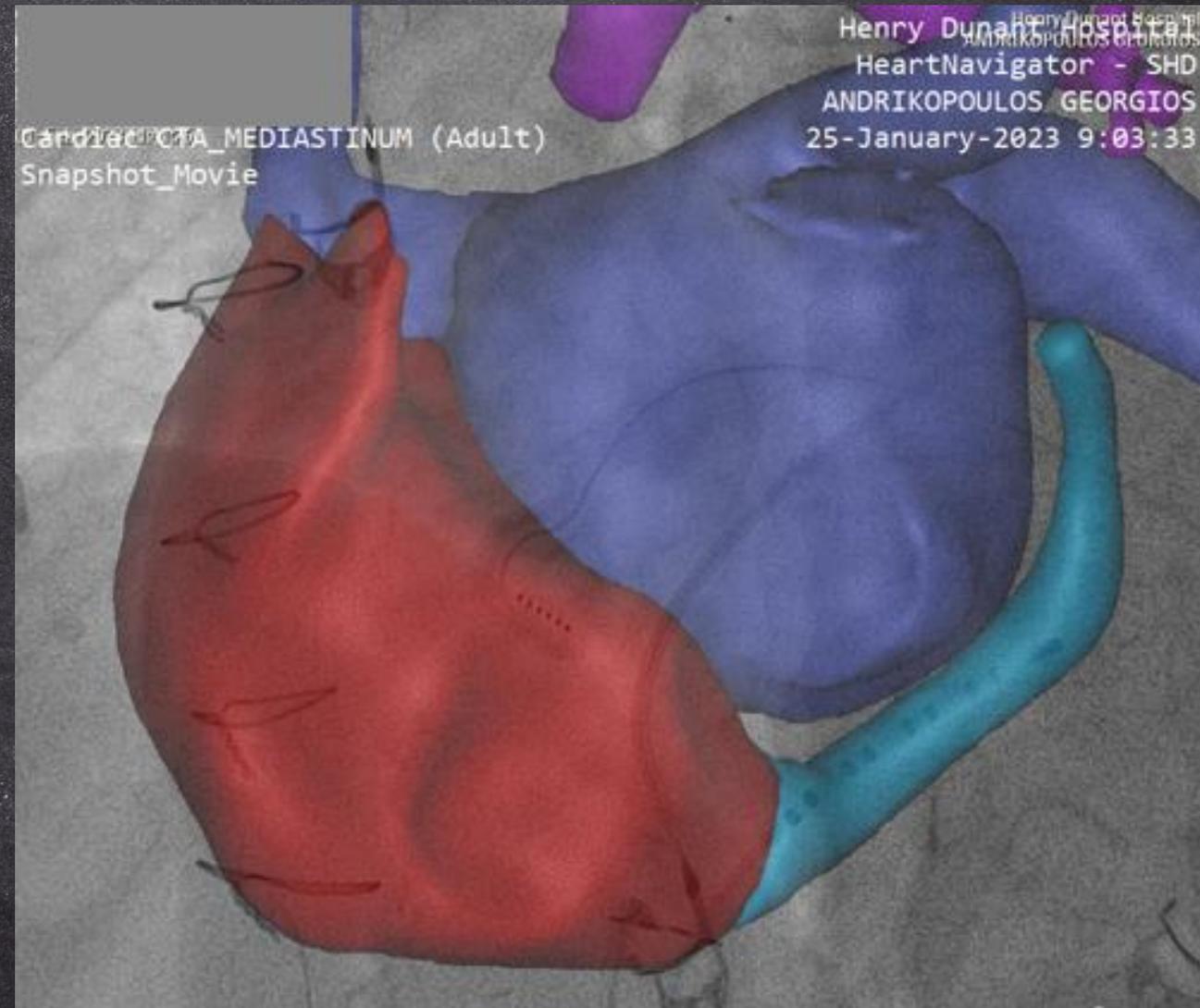
Conclusion

Pulsed field ablation induces large acute LGE without microvascular damage or intramural haemorrhage. Most LGE lesions disappear in the chronic stage, suggesting a specific reparative process involving less chronic fibrosis. This process may contribute to a preserved tissue compliance and LA reservoir and booster pump functions.

CT imaging integrated into Fluoroscopy during PFA ablation

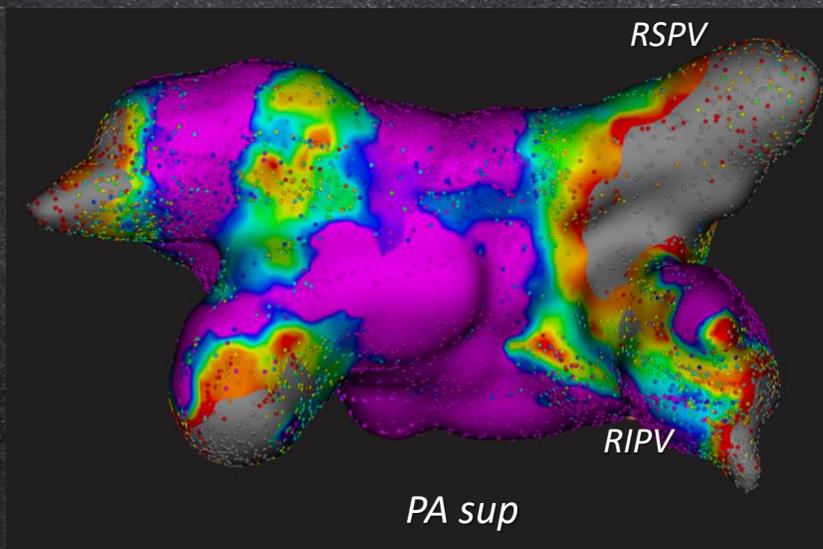


CT imaging integrated into Fluoroscopy

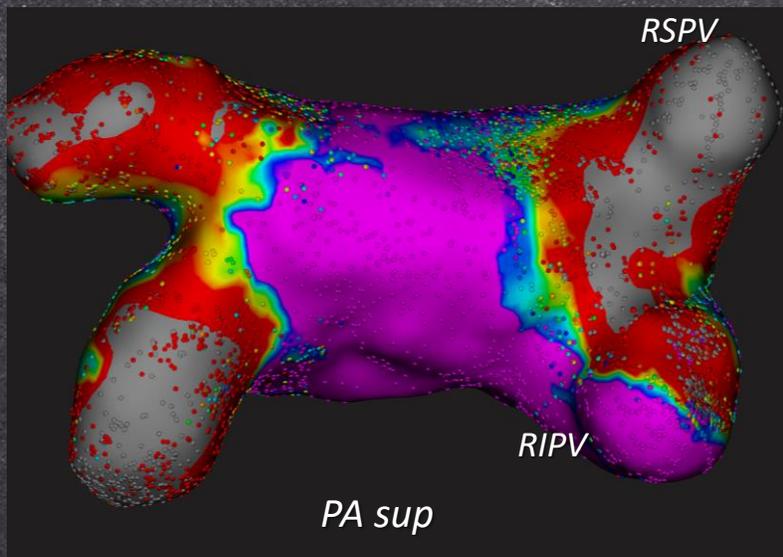


33-year old patient with long-standing AF 3/2022 Cryoablation - 7/2022 RF ablation

Left Atria 4 months after
Cryo ablation

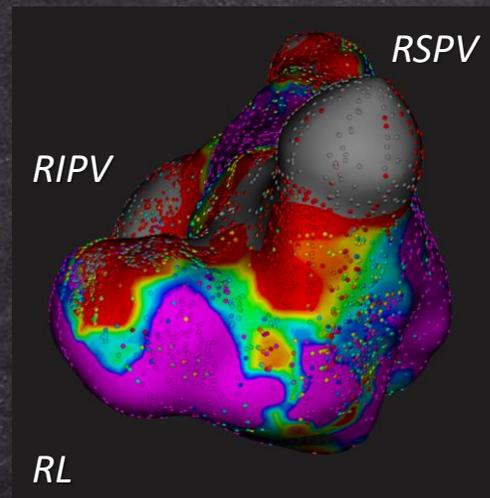
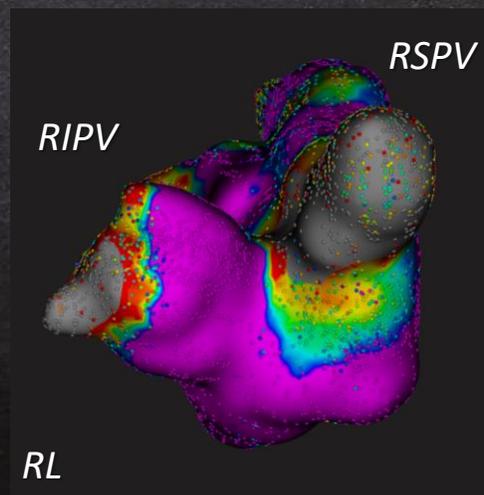


Left Atria 8 months after
RF ablation



Electrophysiologically
Active myocardium

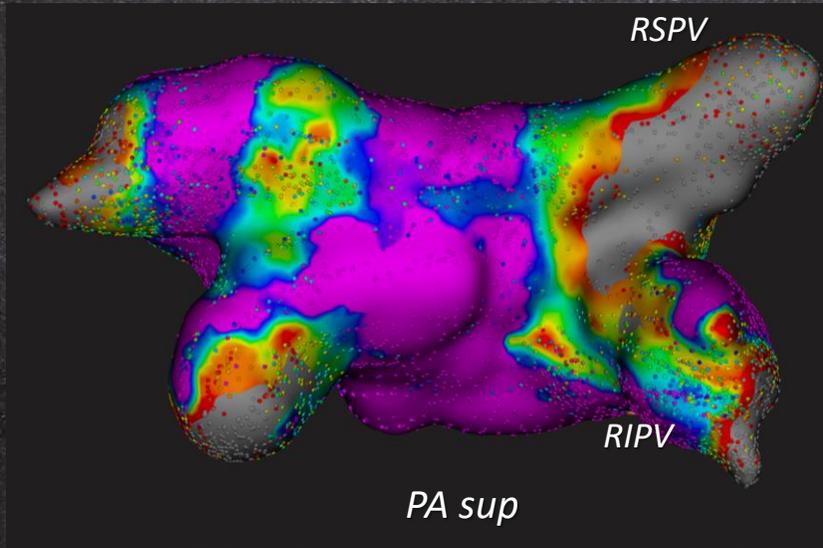
Low voltage areas



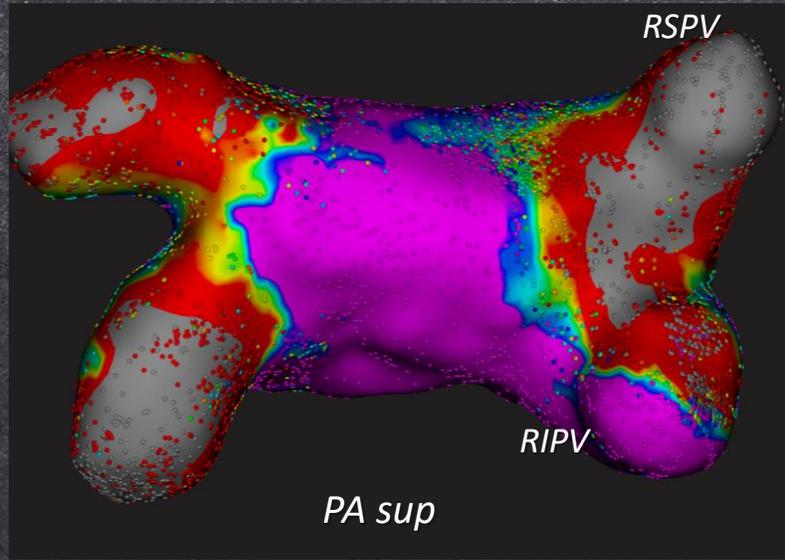
Electrophysiologically
Inactive myocardium

33-year old patient with long-standing AF 3/2022 Cryoablation - 7/2022 RF ablation

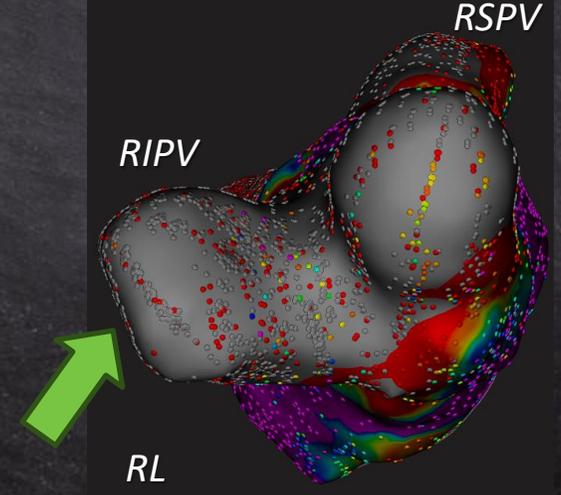
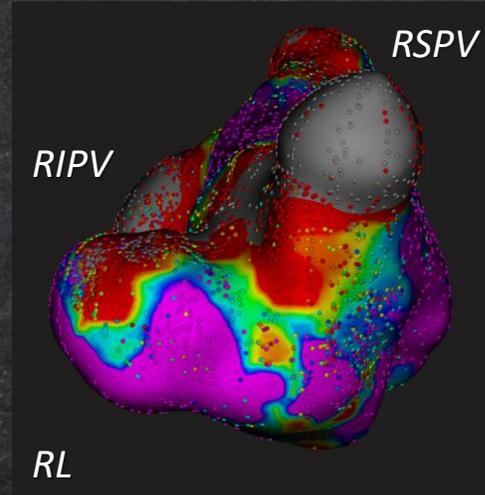
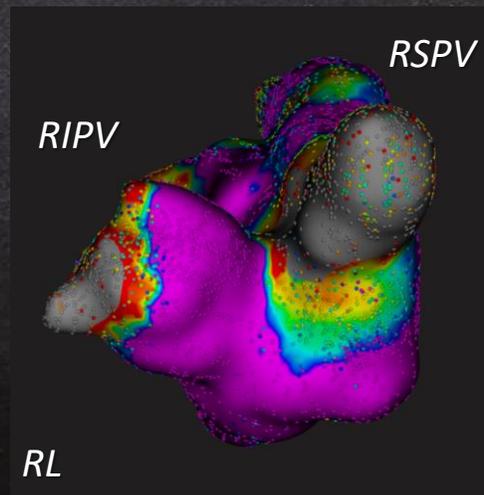
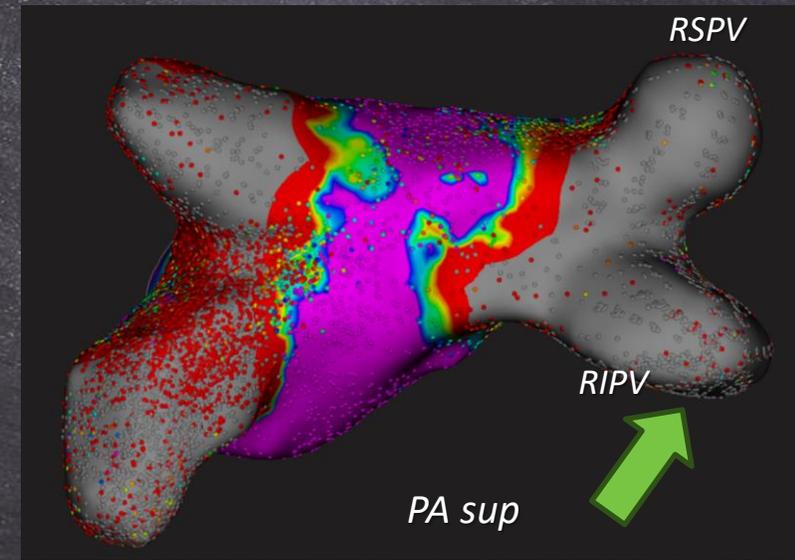
Left Atria 4 months after
Cryo ablation



Left Atria 8 months after
RF ablation



Left Atria after
PFA ablation



Review

Persistent Atrial Fibrillation: The Role of Left Atrial Posterior Wall Isolation and Ablation Strategies

Riyaz A. Kaba ^{1,2,*}, Aziz Momin ^{1,2} and John Camm ¹ 

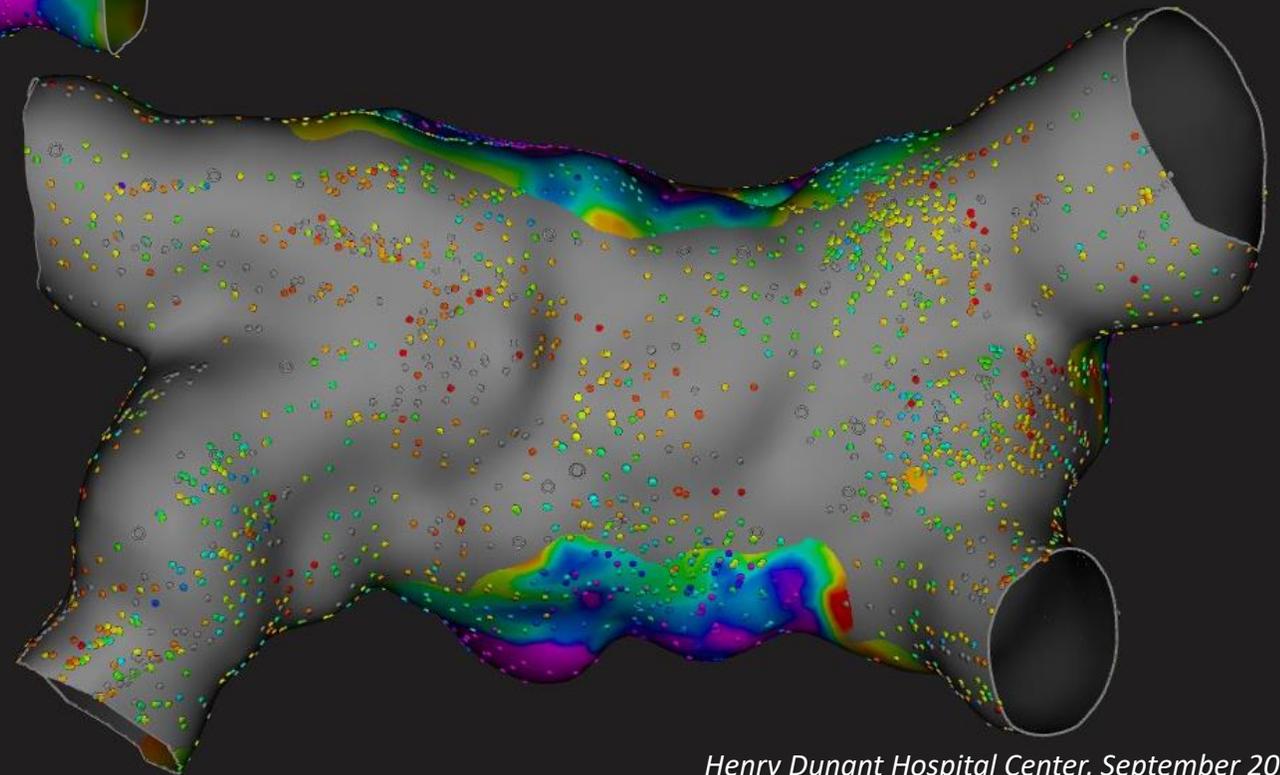
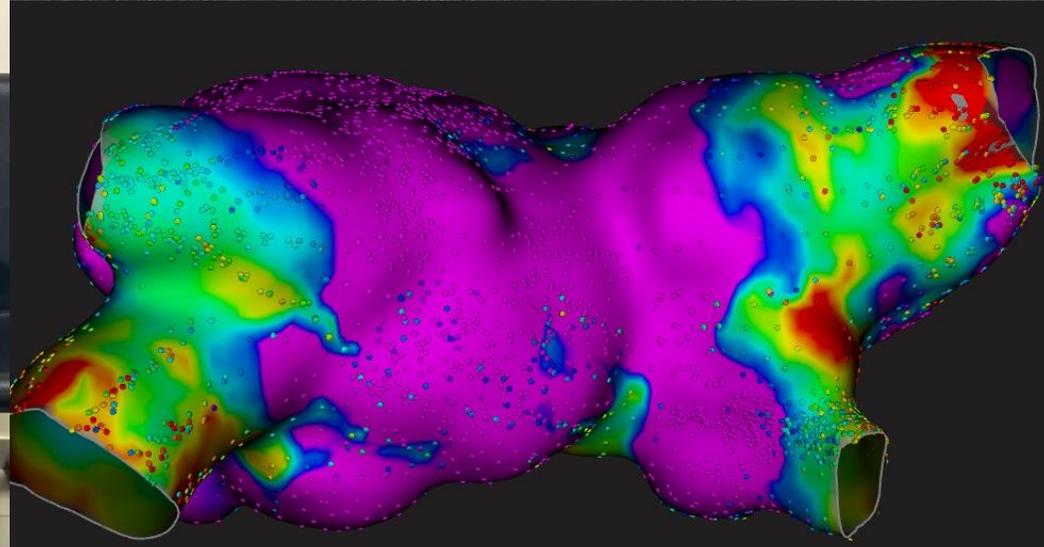
Table 2. Posterior wall (PW) connection rates in studies comparing pulmonary vein isolation (PVI) to PVI + PW isolation.

Study	Posterior Wall Strategy	Follow-Up Time	Population Evaluated for Reconnection	Reconnection Rates in PW Ablation Group
Bai et al. 2016	Debulking with RF	3-months	All patients	37.5% ¹
Lee et al. 2015	Linear ablation with RF	16.2 ± 8.8 months	Recurrent patients	50%
Tamborero et al. 2009	Linear ablation with RF	9.8 ± 4.3 months	Recurrent patients	67%
Tokioka et al. 2020	Linear ablation with RF	1–6 months	Recurrent patients	65.2%

¹ Includes pulmonary vein and PW reconnections; PVI: pulmonary vein isolation; PW: posterior wall; RF: radiofrequency.

“Evidence of endocardial–epicardial dissociation in atrial fibrillation may also limit the effectiveness of endocardial posterior wall isolation, especially when considered in the context of suboptimal transmural. Endocardial–epicardial dissociation, as evidenced by asynchronous activation of the epicardial and endocardial surfaces, was initially demonstrated in animal [50] and computational models [51]. More recently, real-time mapping has shown there may be up to 50–55% asynchronous activation between the epicardial and endocardial surfaces in patients with AF”

Posterior Wall Isolation – NOW FEASIBLE



Transient conduction disturbances acutely after pulsed-field cavotricuspid isthmus ablation: a case report

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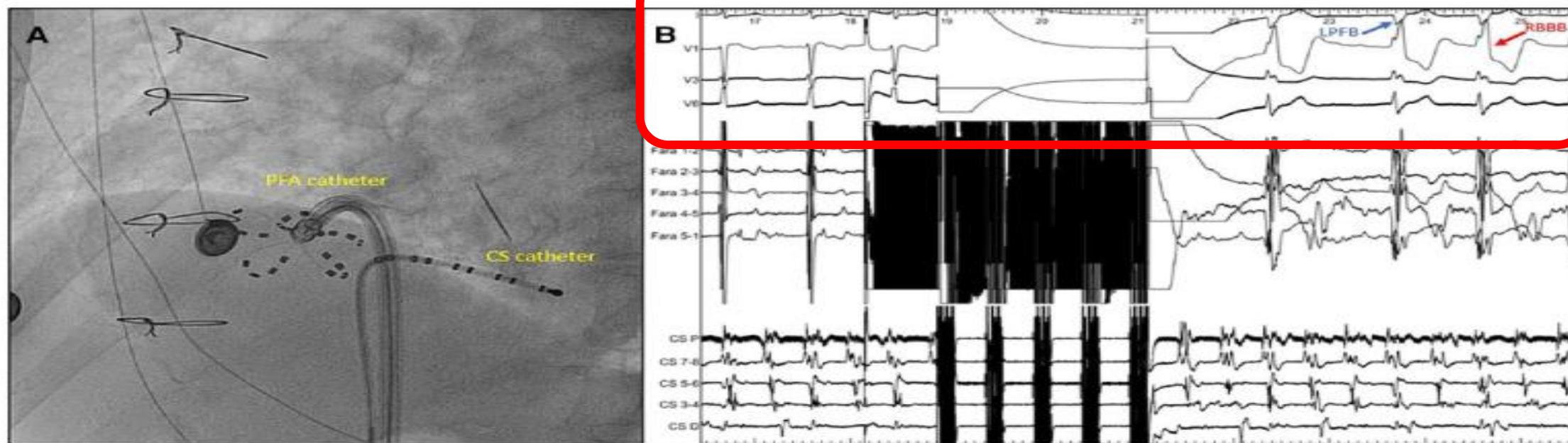
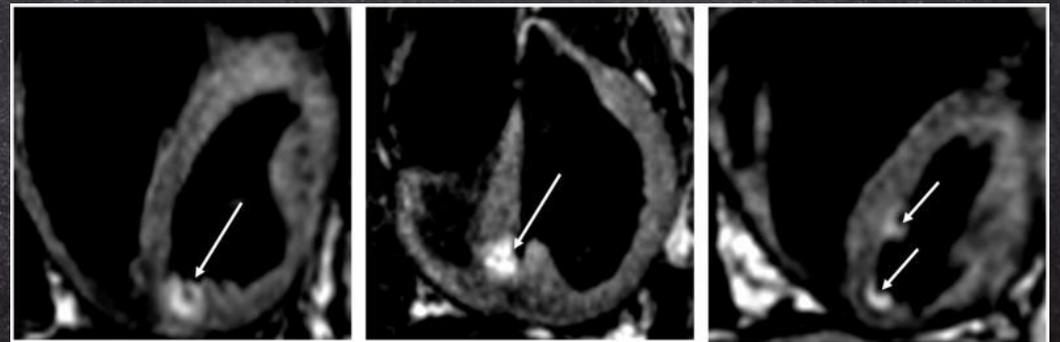
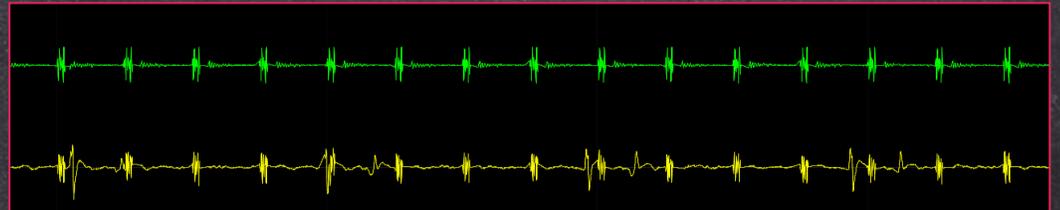
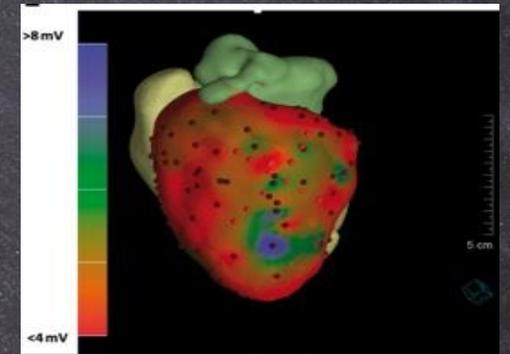
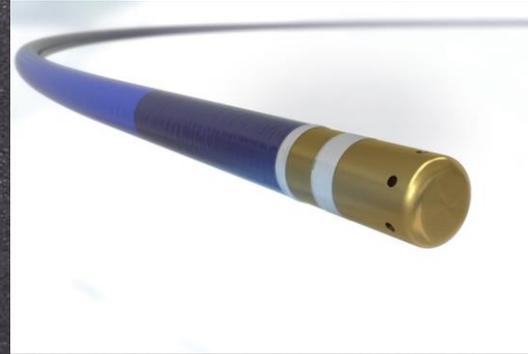


Figure 2 (A) After administration of 2 mg of intravenous nitroglycerine, a single pulsed-field application (with a peak voltage of 2.0 kV), in flower configuration, was delivered at the lateral annular portion of the cavotricuspid isthmus. (B) Acute occurrence of RBBB and LPFB without flutter termination. CS, coronary sinus; PFA, pulsed-field ablation; RBBB, right bundle branch block; LPFB, left posterior fascicular block.

Real-time cardiovascular magnetic resonance-guided radiofrequency ablation: A comprehensive review

Konstantinos Tampakis, Sokratis Pastromas, Alexandros Sykiotis, Stamatina Kampanarou, Georgios Kourgiannidis, Chrysa Pырpiri, Maria Bousoula, Dimitrios Rozakis, George Andrikopoulos



Cost-effectiveness of atrial fibrillation catheter ablation

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Radiofrequency catheter ablation has become an established treatment option for the management of patients with atrial fibrillation (AF). Although the concept of a rhythm control strategy devoid of the adverse events related to antiarrhythmic treatment seems highly attractive, further steps are needed in order to improve our understanding and increase our therapeutic efficacy. Furthermore, the increased number of candidates also mandates the evaluation of this invasive treatment. In this paper, we recapitulate the existing evidence pertaining to cost-effectiveness of AF catheter ablation and present a cost-to-benefit analysis of such a cost-to-benefit analysis.

**The VALUE OF
INNOVATION issue**

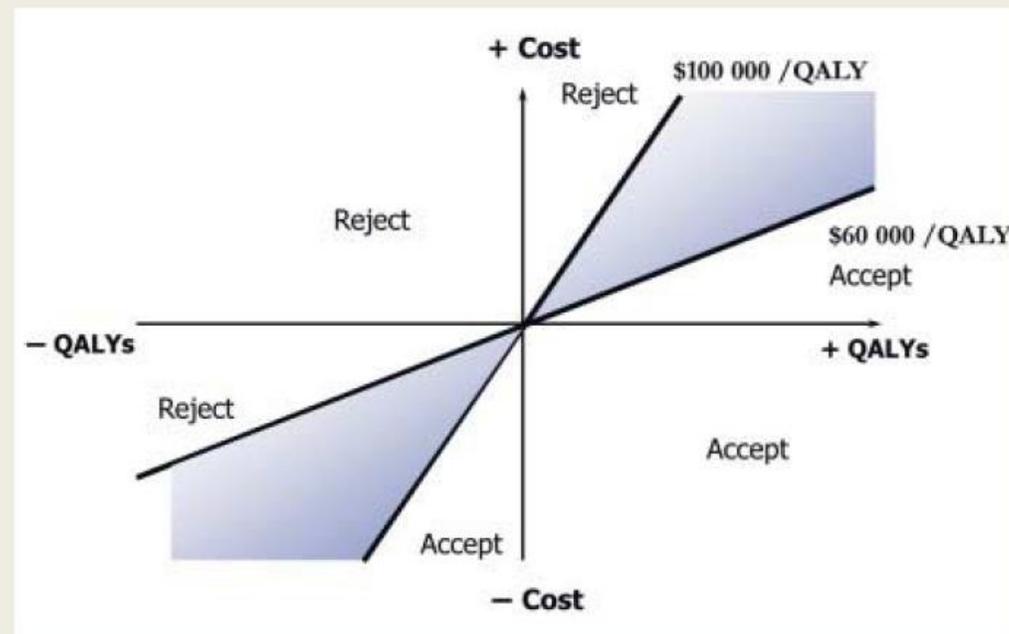


Figure 1 The cost-effectiveness plane.

9^ο
WORKSHOP

Αρρυθμιών & Βηματοδότησης

- Ενδιαφέροντα ηλεκτροκαρδιογραφήματα
- Αντιπαραθέσεις
- Ενδιαφέροντα περιστατικά
- Εξελίξεις στην αντιμετώπιση των αρρυθμιών

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9^ο Workshop Αρρυθμιών & Βηματοδότησης

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