

Fibrozis ile ablasyon stratejileri belirleme

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Kardiyoloji Anabilim Dalı

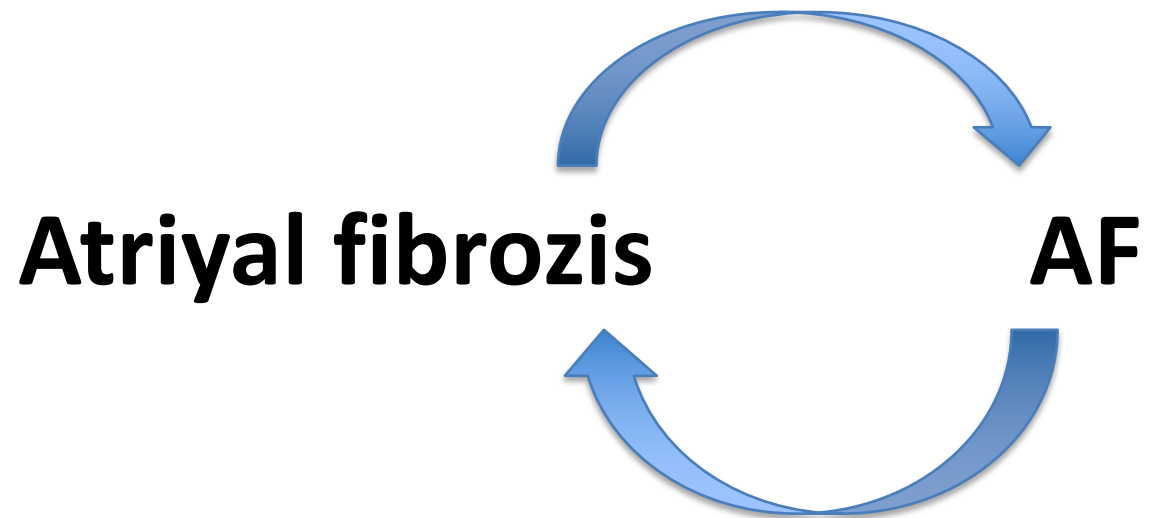
Giriş

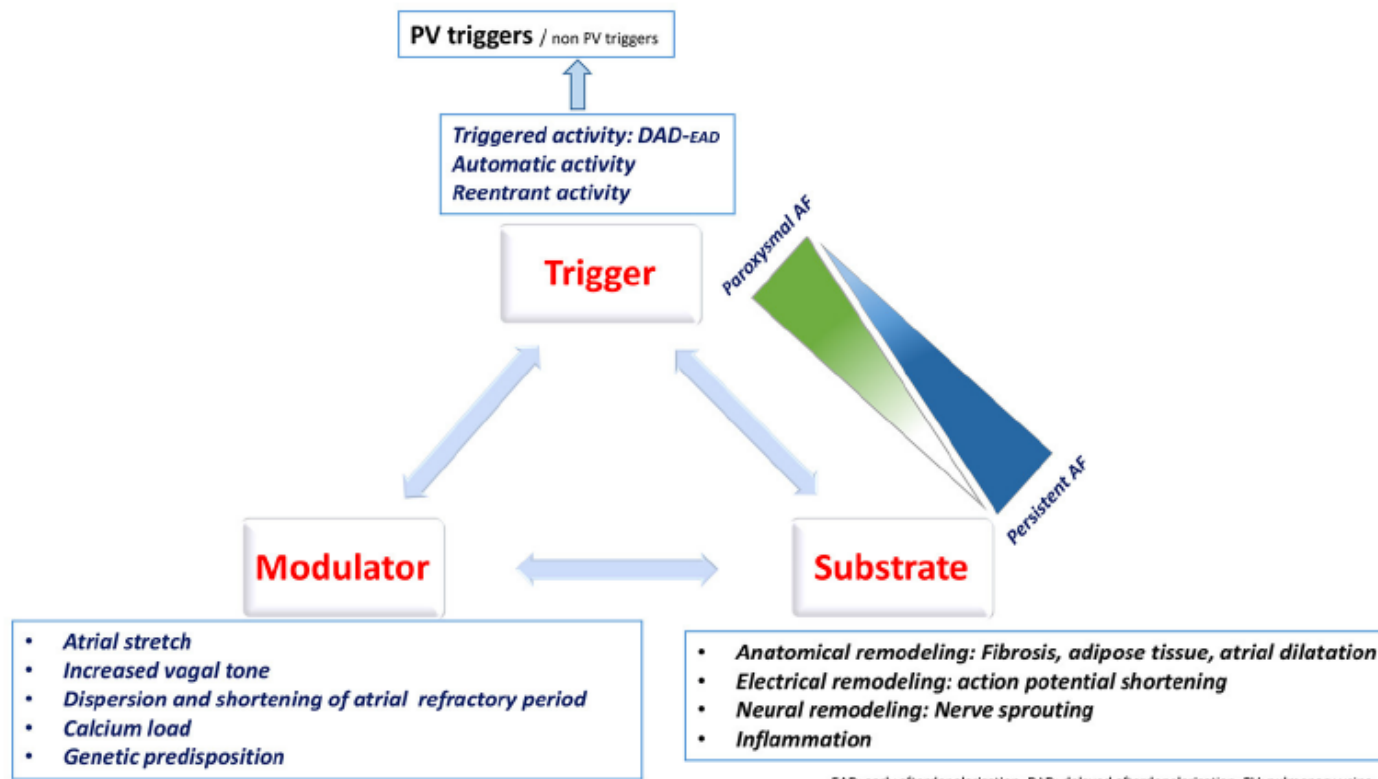
- AF'de kateter ablasyon antiaritmik tedaviden daha üstündür.
- Ancak optimum ablasyon stratejisi hala tartışmalıdır.
- PVI temel ablasyon yöntemidir.

- Atriyal fibrozis ve AF yakından ilişkilidir.
- Atriyal fibrotik değişiklikler ile AF ilişkisi postmortem histolojik çalışmalarda ve cerrahi sırasında alınan biyopsilerde gösterilmiştir.
- Atriyal fibrozis hakkında görüntüleme yöntemleri ve voltaj haritalama ile fikir elde edilebilir.

- AF oluşmasında ve süreklilik kazanmasında atriyal fibrozis önemli rol oynar
- Atriyal fibrozis anormal otomatisite, tetiklenmiş aktivite ve reentri ile aritmiye yol açar
- Atriyal fibrozis uyarı iletim hızında yavaşlamaya yol açar (reentri)

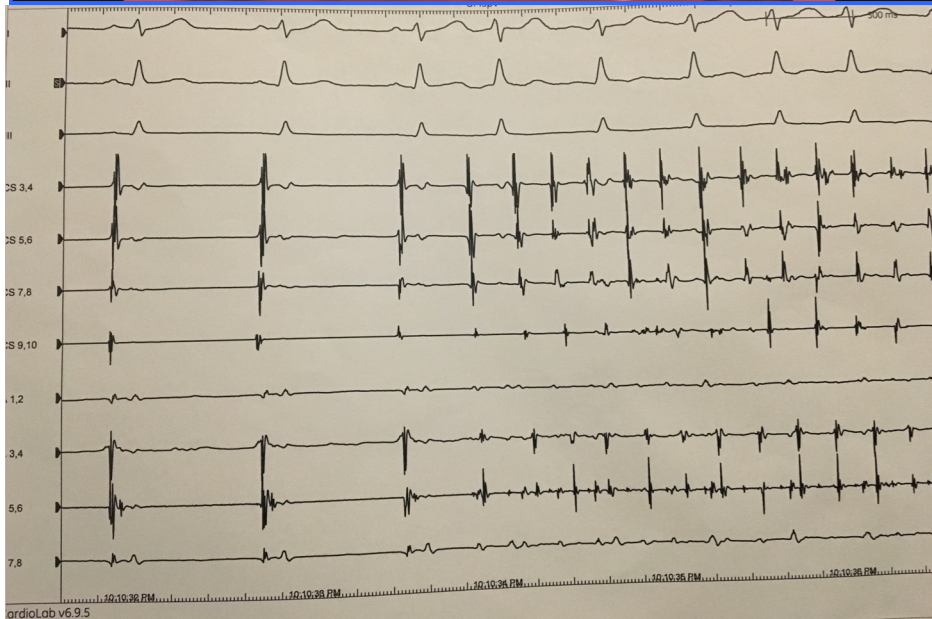
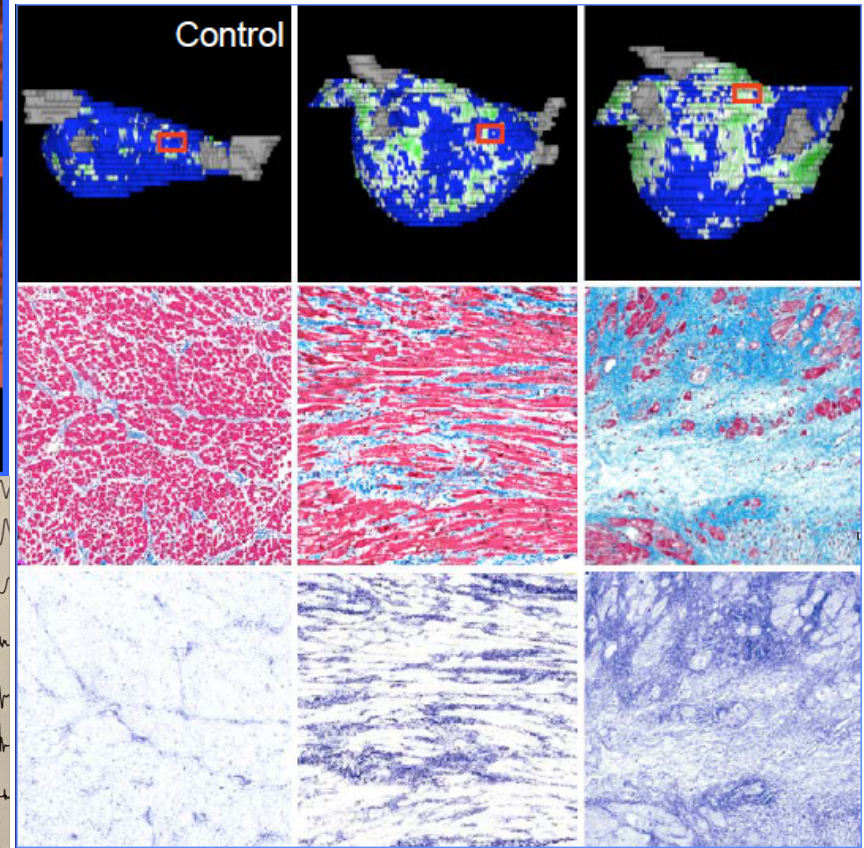
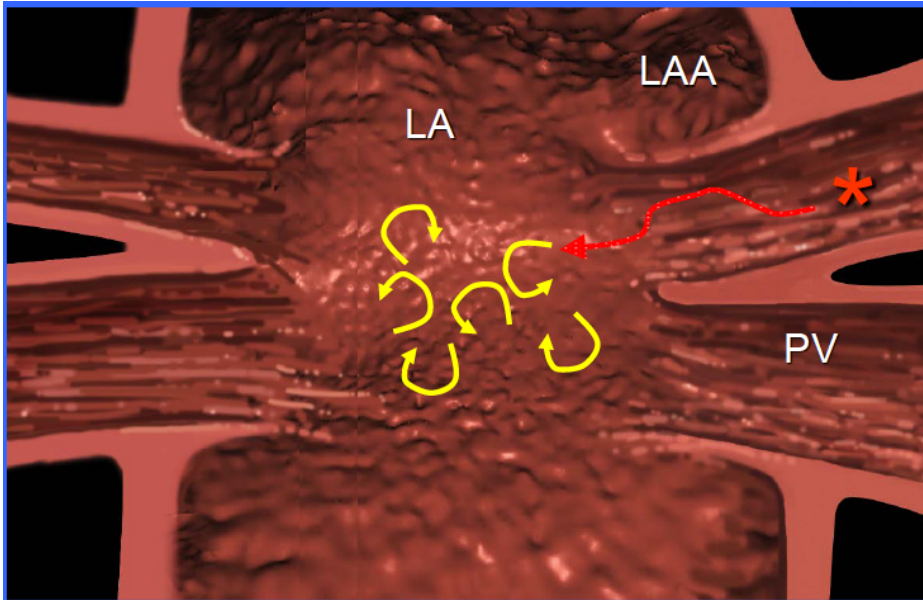
- Reparative fibrozis (ölü kardiyomiyositlerin yerinde gelişen fibrozis)
- Elektriksel iletiyi yavaşlatır
- Anisotropik ilettime neden olur
- Persistan AF'de PVI uzun dönem sonuçları suboptimal ($\approx$ %50)

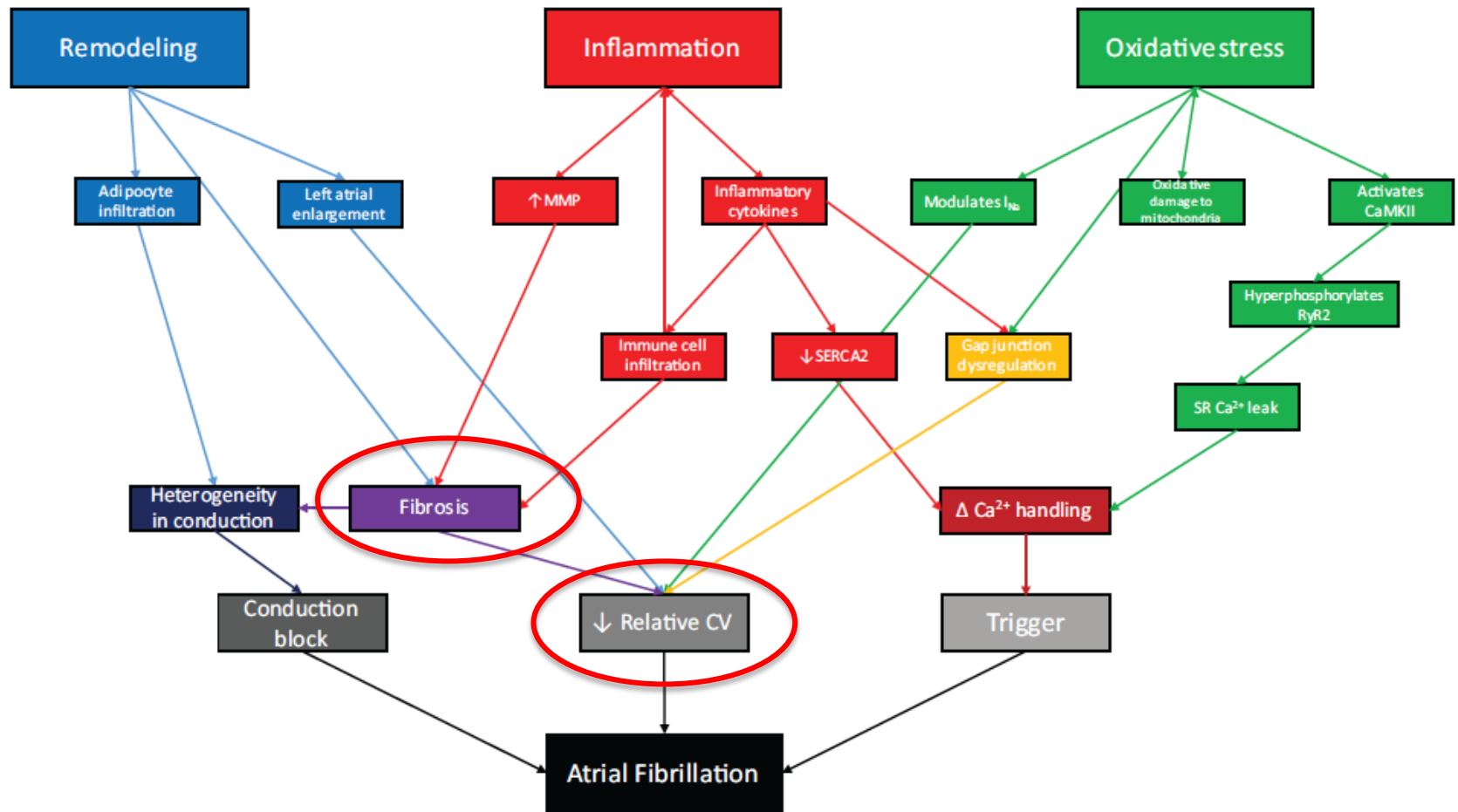




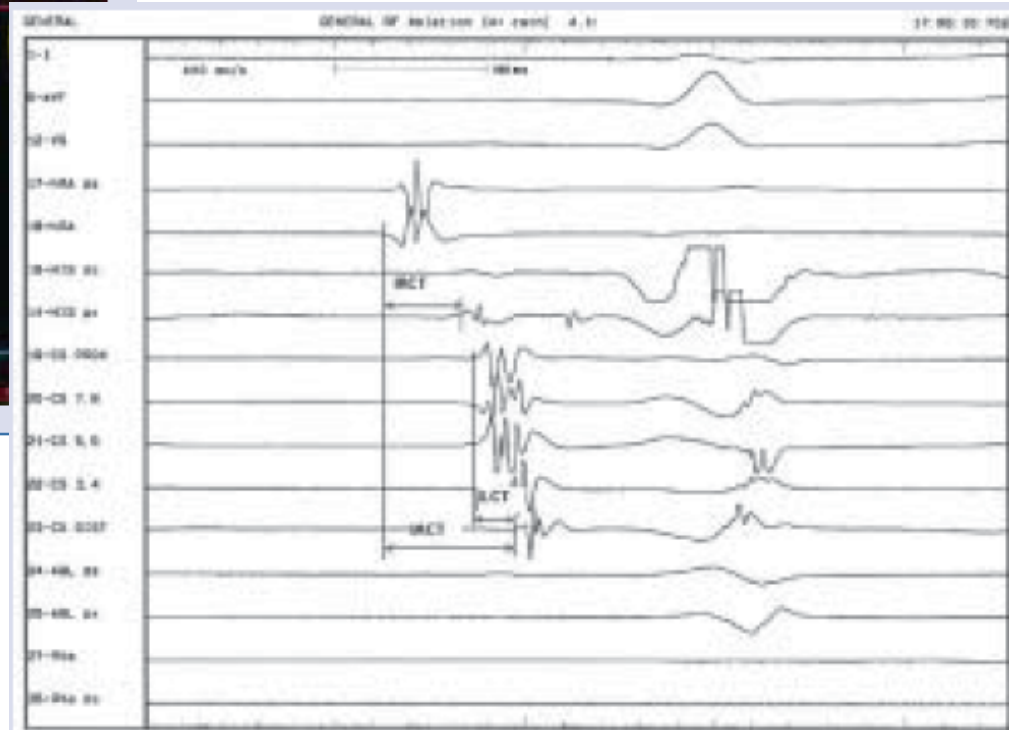
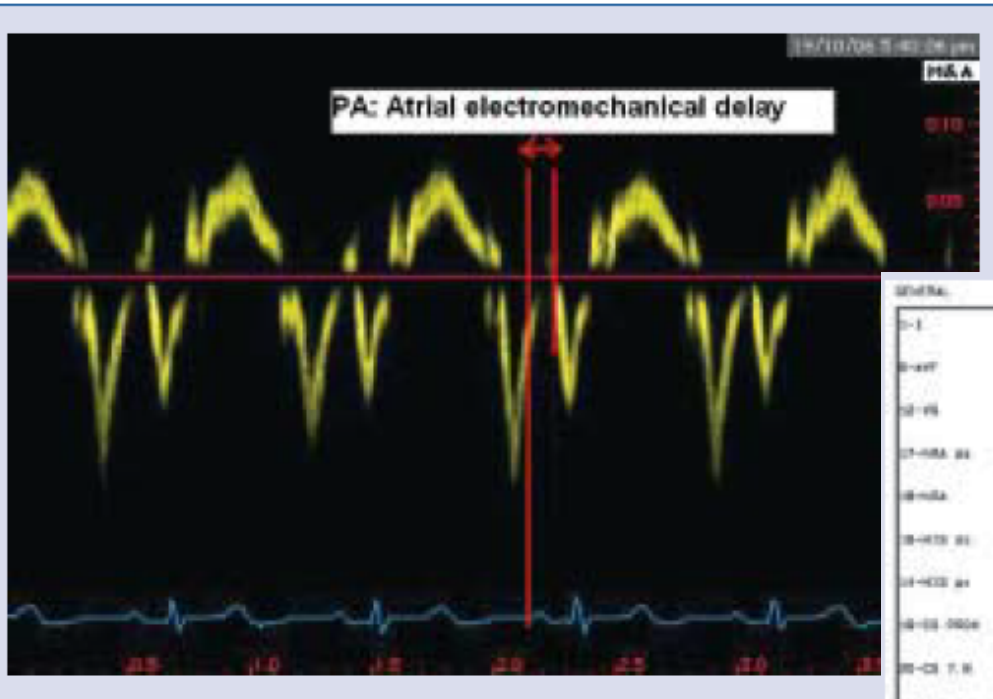
EAD: early afterdepolarization, DAD: delayed afterdepolarization, PV: pulmonary veins

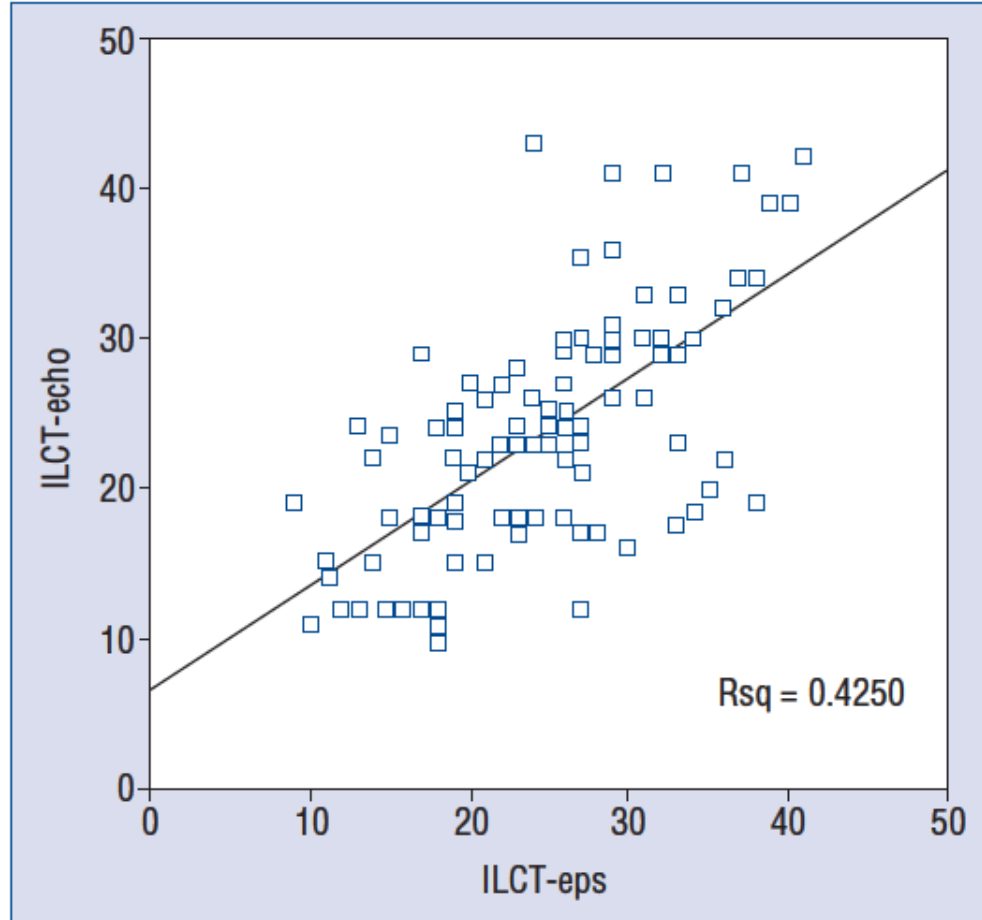
FIGURE 1 | Coulmel triangle summarizing the different contributors to AF.



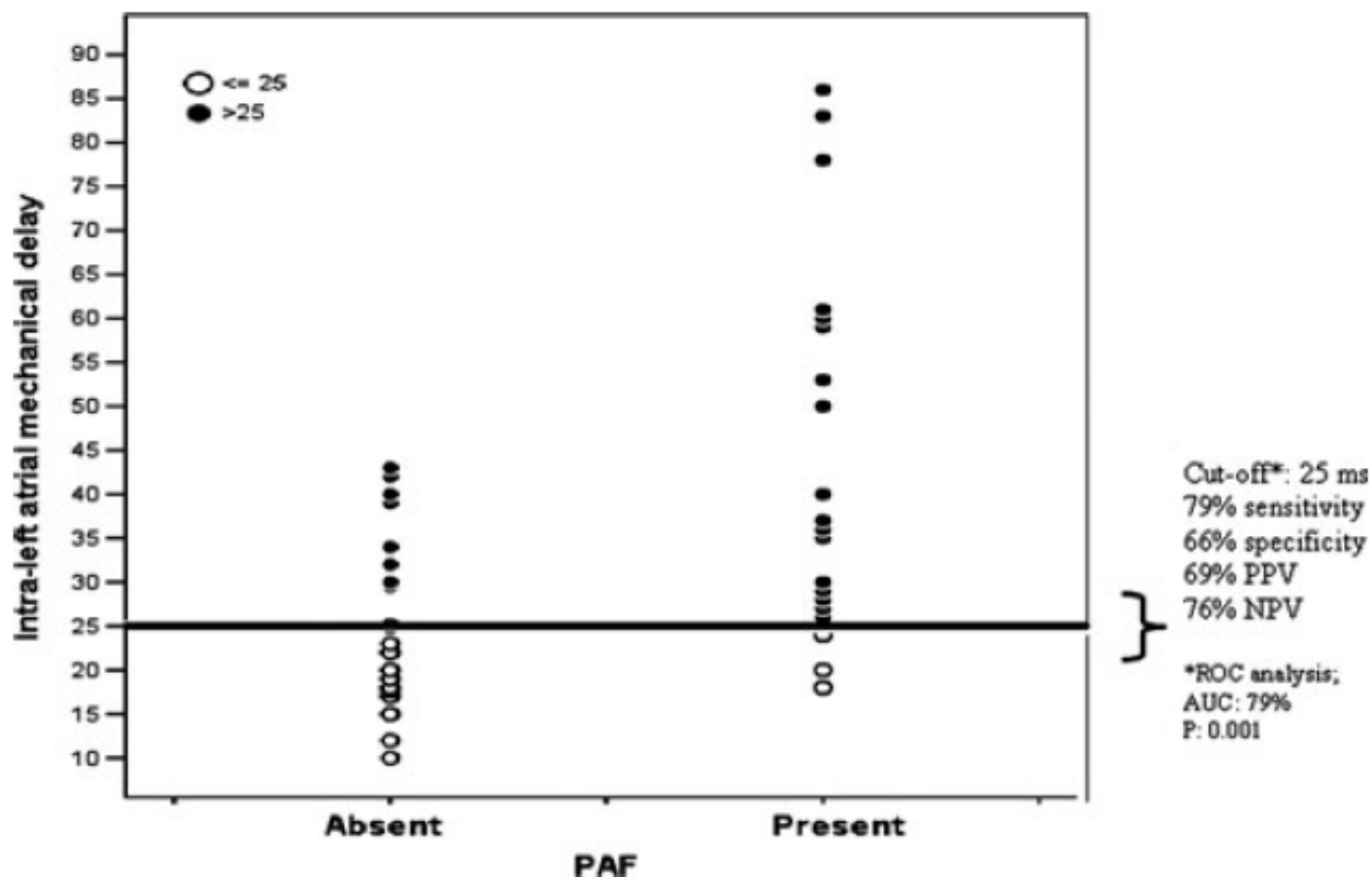


Tissue Doppler echocardiography can be a useful technique to evaluate atrial conduction time





Intra-Left Atrial Mechanical Delay Detected by Tissue Doppler Echocardiography Can Be a Useful Marker for Paroxysmal Atrial Fibrillation



Conduction characteristics in atrial fibrillation

Predictive value of tissue Doppler echocardiography

Tab. 3 Odds ratios of P wave dispersion, ILCT-echo, and IACT-eps for the inducibility of AF during electrophysiological study

	Odds ratio	95% CI	p
P wave dispersion	1.063	1.023–1.103	0.002
ILCT-echo	1.136	1.046–1.234	0.003
IACT-eps	1.054	1.001–1.111	0.047

IACT interatrial conduction delay, *ILCT* intra-left atrial conduction delay, *IRCT* intra-right atrial conduction delay, *CI* confidence interval

Tab. 1 Baseline clinical, ECG, and echocardiographic parameters of patients with (+) and without (–) AF

	AF (–) (n=43)	AF (+) (n=43)	p
Sex (male/female)	14/29	12/31	0.810
Age (years)	36±12	46±13	<0.001
Body mass index (kg/m ²)	24.2±5.6	27.5±4.8	0.005
Hypertension (n)	3	10	0.068
Hyperlipidemia (n)	0	4	0.116
Diabetes (n)	0	5	0.055
Smoking history (n)	2	4	0.676
Coronary artery disease (n)	0	1	1.000
Blood urea nitrogen (mg/dl)	20±6	23±6	0.282
Creatinine (mg/dl)	0.62±0.11	0.73±0.13	0.151
Maximum P wave duration (ms)	90±14	97±18	0.037
Minimum P wave duration (ms)	63±16	51±15	<0.001
P wave dispersion (ms)	27±18	46±19	<0.001
Electrocardiographic left atrial anomaly (n)	6	7	1.000
Left atrial diameter (mm)	29±5	33±4	<0.001
Left atrial volume (ml)	21.5±7.2	27.1±7.0	<0.001
Right atrium (mm)	29±4	28±5	0.586
Left ventricular end diastolic diameter (mm)	44±5	43±4	0.651
Left ventricular end systolic diameter (mm)	28±4	29±4	0.470
Left ventricular ejection fraction (%)	65±3	64±3	0.161
Left ventricular mass (g)	162±52	170±41	0.444
Mitral inflow E/A ratio	1.2±0.3	1.1±0.3	0.045
Mitral inflow E wave deceleration time (ms)	179±36	167±39	0.158
Isovolumic relaxation time (ms)	82±14	88±19	0.054

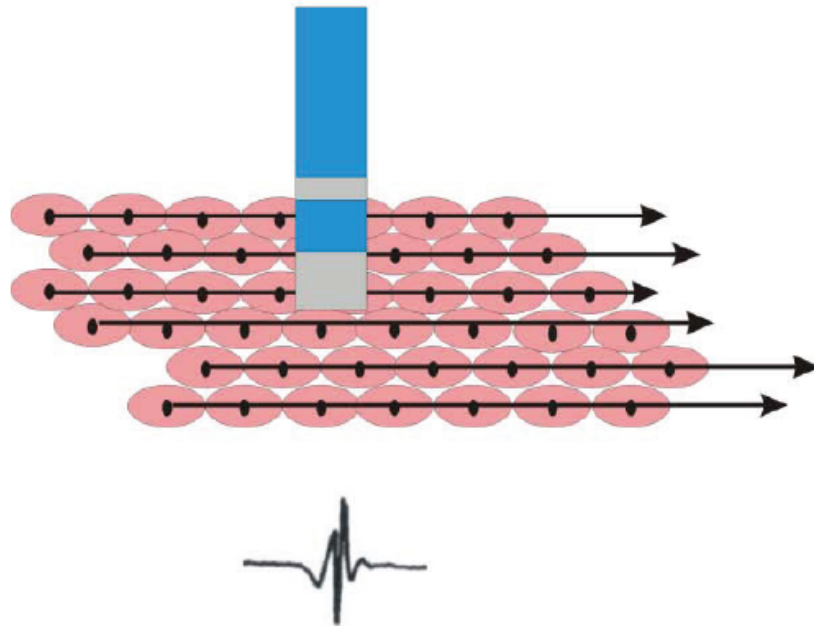
Fibrozis

$$\lambda = \text{ERP} \times \text{iletim hızı}$$

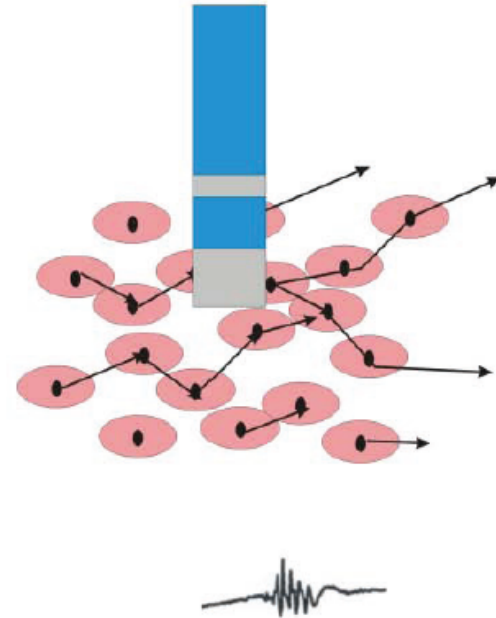
- Dalga boyu reentri dinamikleriyle ilişkili
- Uzamış dalga boyu aritmi kompleksliğini azaltır

CFAE

A



B

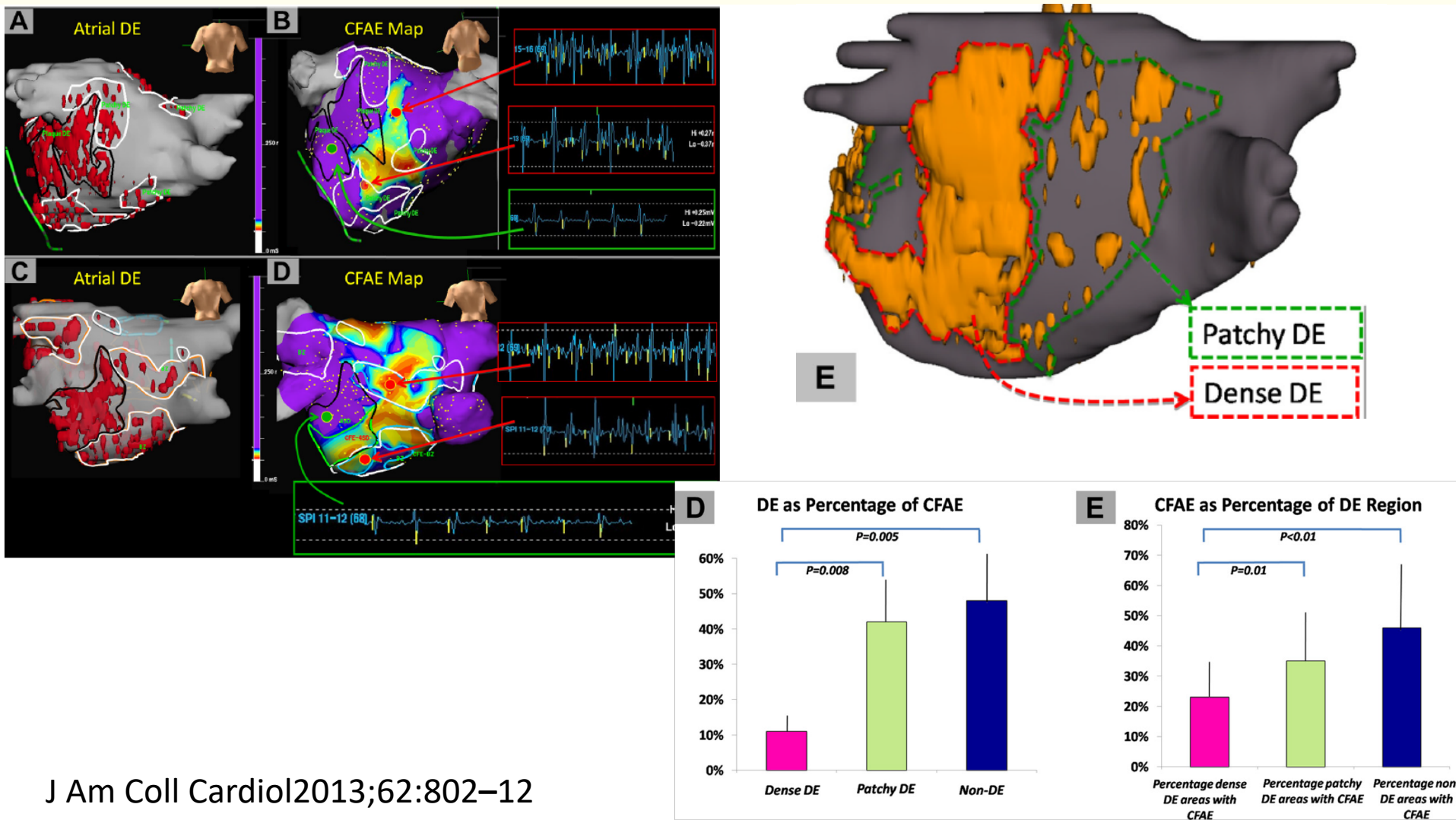


CFAE=fibrozis??

- CFAE artefaktlardan ve uygunsuz filtrelemelerden kaynaklanabilir.
- CFAE farfield sinyaller tarafından etkilenebilir (double counting).
- CFAE pasif olabilir.
- Elektrot boyutu, elektrotlar arası mesafe, temas etkiler
- Aktivasyon hızı ve yerine göre fragmente sinyallerin dağılımı değişebilir.
- CFAE dalga çarpışmasından kaynaklanabilir.

Inverse Relationship Between Fractionated Electrograms and Atrial Fibrosis in Persistent Atrial Fibrillation

Combined Magnetic Resonance Imaging and High-Density Mapping



ORIGINAL ARTICLE

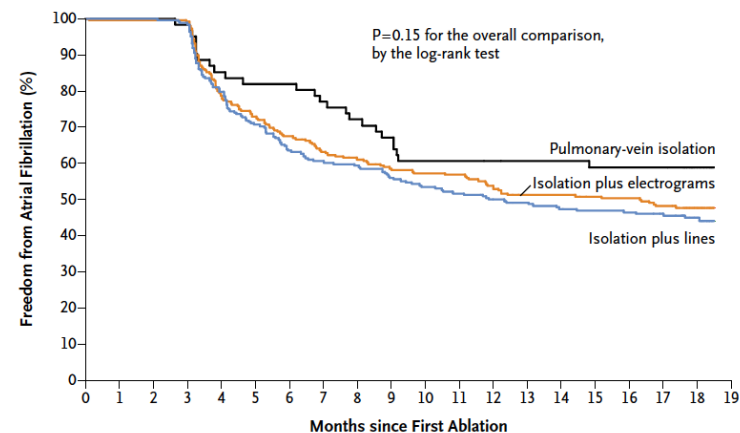
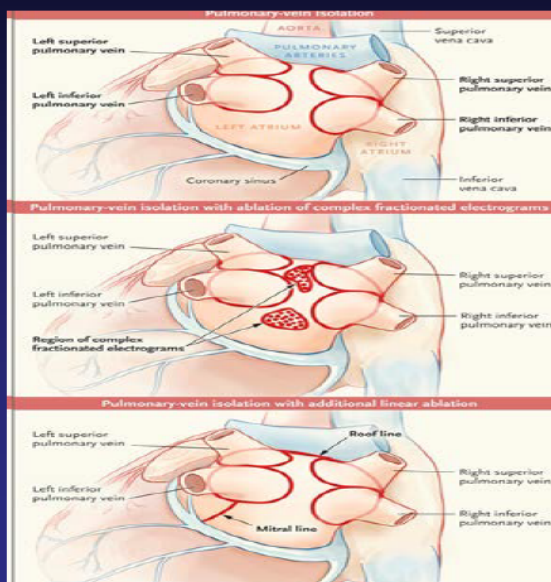
Approaches to Catheter Ablation for Persistent Atrial Fibrillation

PVI

Complex Fractionated Electrograms



Linear Ablation



No. at Risk

	61	60	50	41	36	23
Pulmonary-vein isolation	244	242	161	137	124	72
Isolation plus electrograms	244	240	152	133	115	57

Düşük voltaj/skar/fibrozis

- Düşük voltaj amplitüdü miyokardiyal fibrozis ile eş anlamlı değil
 - Aktivasyon vektörü
 - Angle of incidence (kateterin dokuya göre oryantasyonu)
 - Elektrot boyutu (küçük elektrot küçük dokudan daha düşük sinyalleri kaydeder, küçük elektrotlarla kaydedilen düşük amplitüdlü sinyaller daha büyük elektrotlarla ölçülemeyebilir)
 - Elektrotlar arası mesafe (azaldıkça düşük amplitüdlü sinyaller kaydedilir, elektrotlar arası mesafe azaldıkça düşük voltaj alanlarındaki canlı miyositleri daha iyi gösterilir)
 - Doku teması
 - Filtreleme (filtre değerlerine bağlı olarak peak-to-peak sinyal amplitüdü azalabilir)
 - Haritalama yoğunluğu (yoğunluk azaldıkça interpolasyon artar)
 - Haritalama çözünürlüğü (küçük elektrot, düşük elektrotlar arası mesafe)

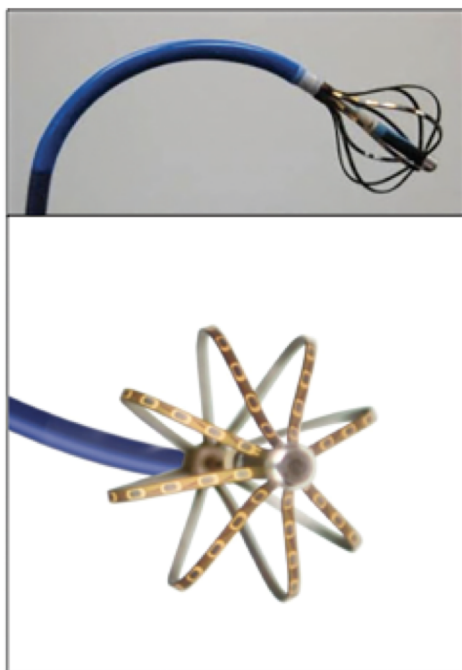
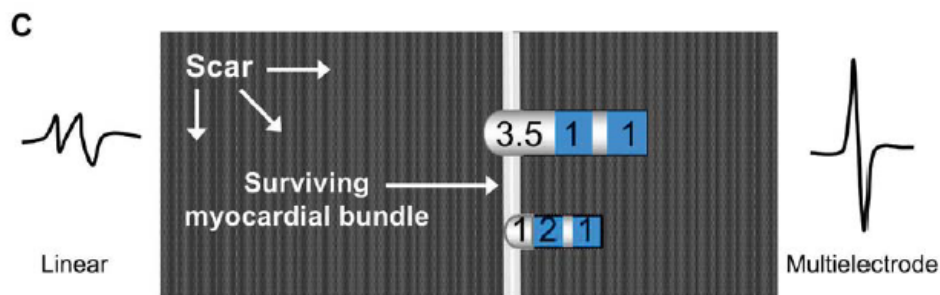
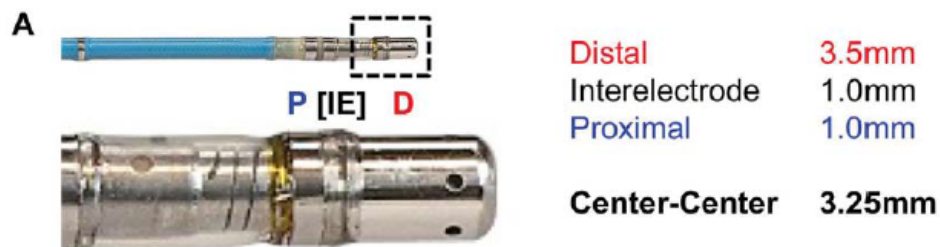
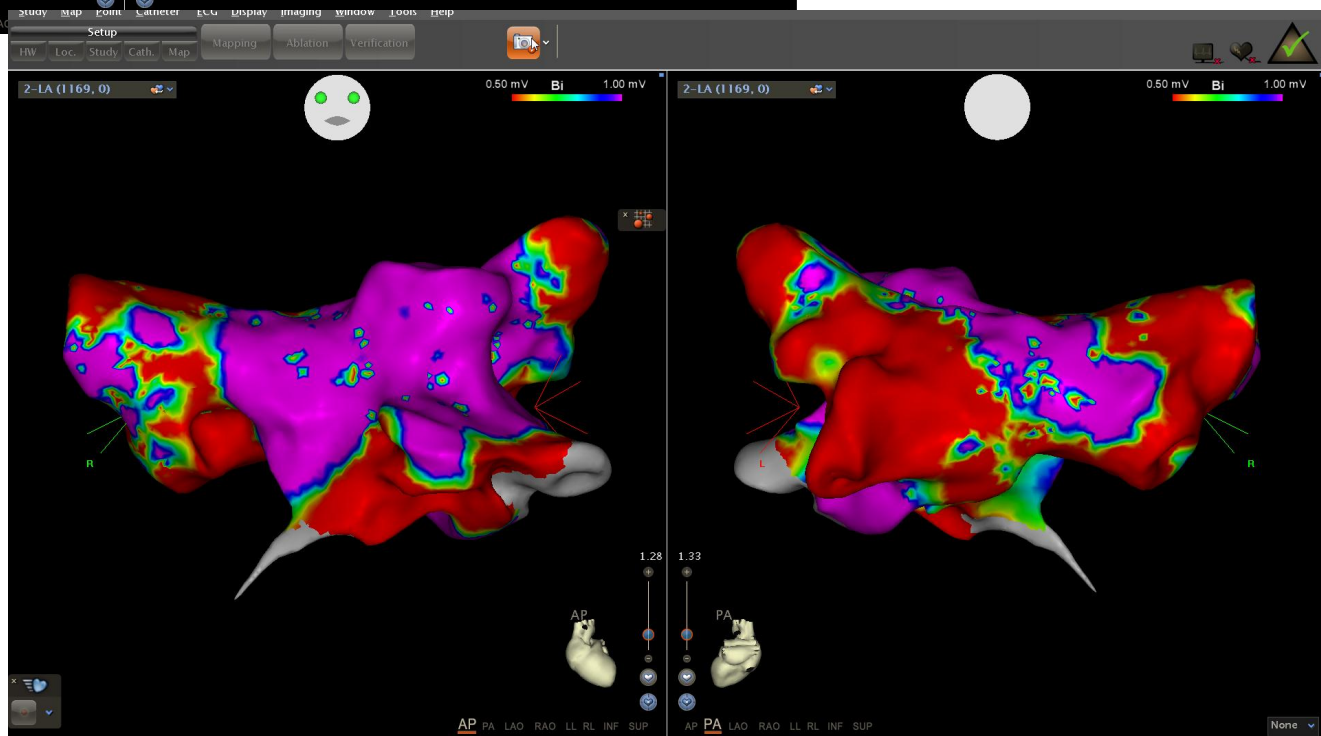
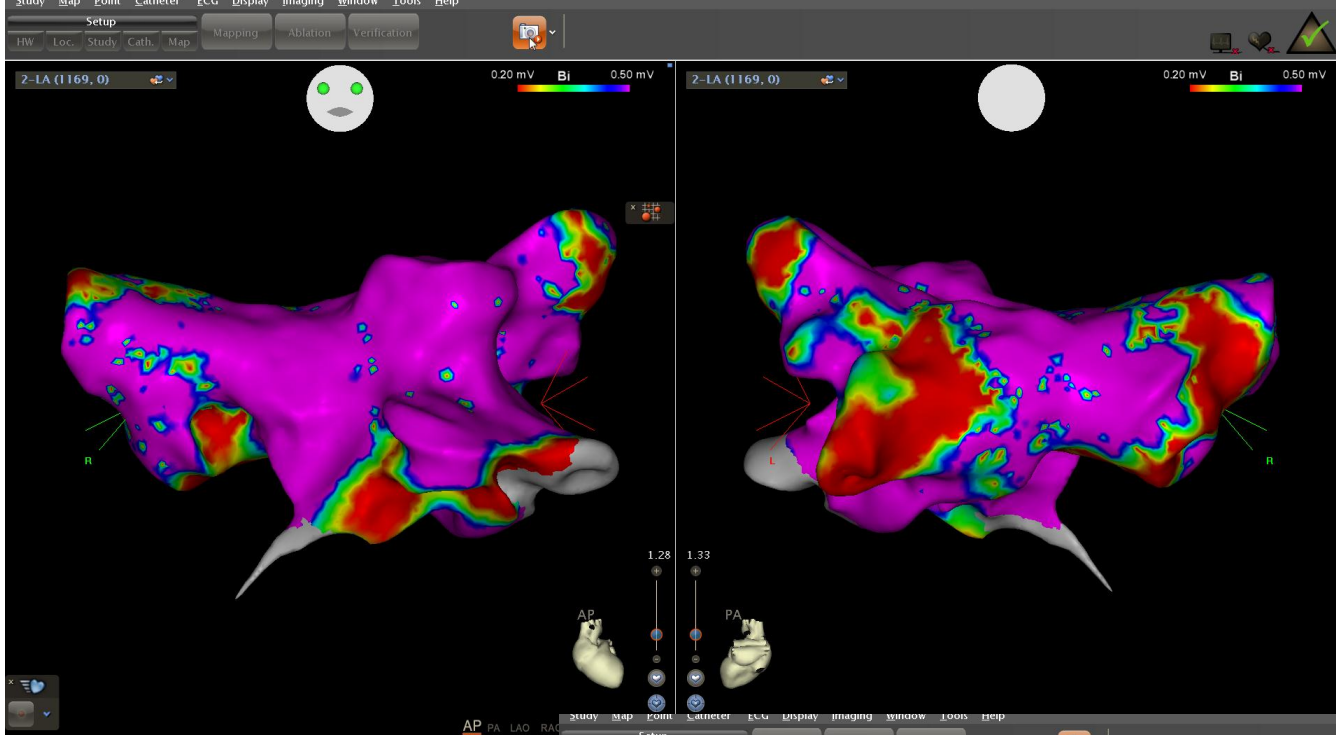
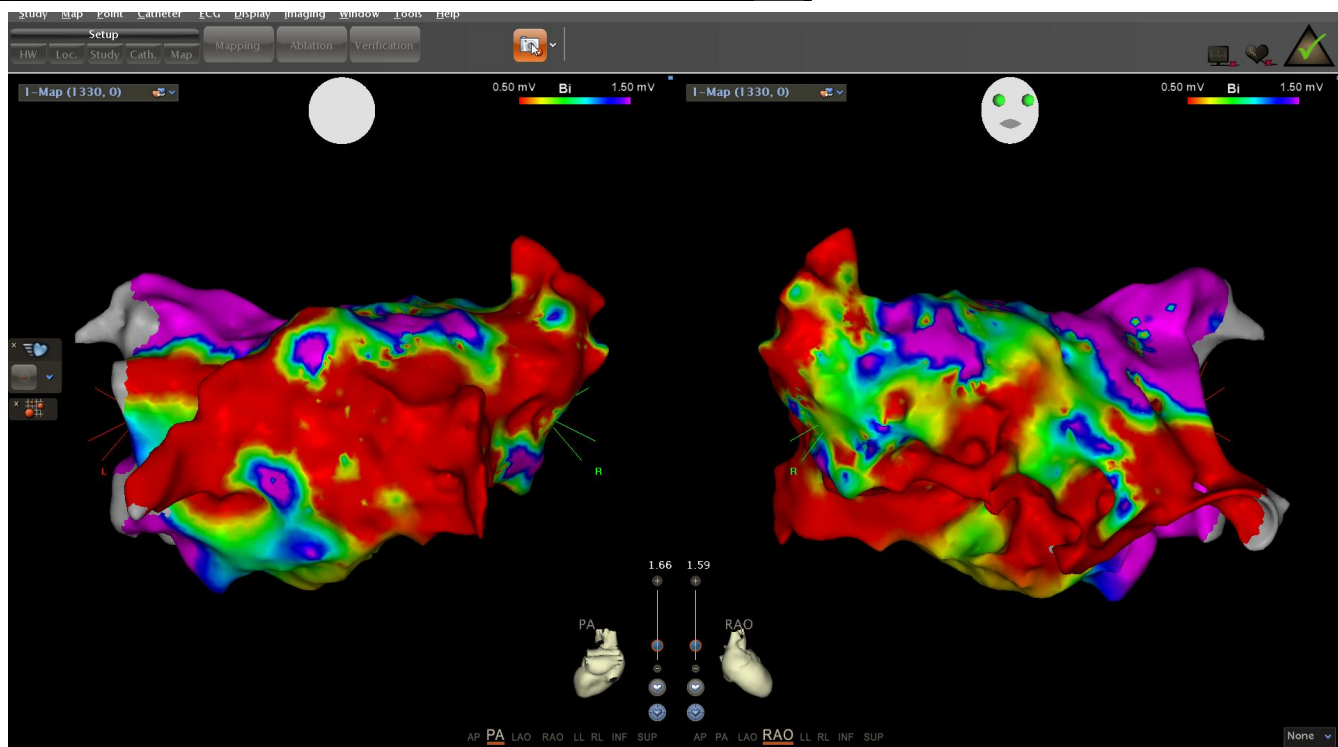
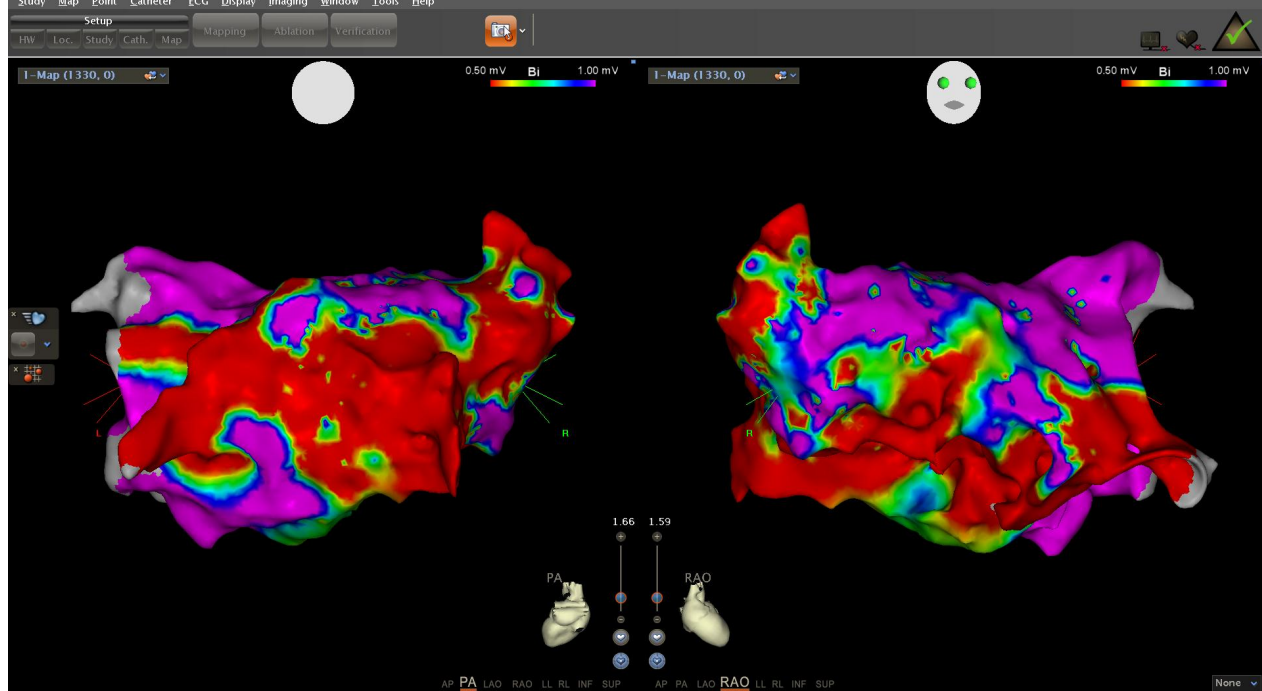


Figure 1: The IntellaMap Orion™ High Resolution Mapping Catheter (Boston Scientific) has 64 imprinted electrodes with 2.5 mm inter-electrode spacing on 8 nitinol splines. The catheter is 8.5 Fr with bidirectional deflection and a variable mini-basket diameter (3-22 mm) that can be adjusted based upon the local anatomy. (Image is provided courtesy of Boston Scientific.)

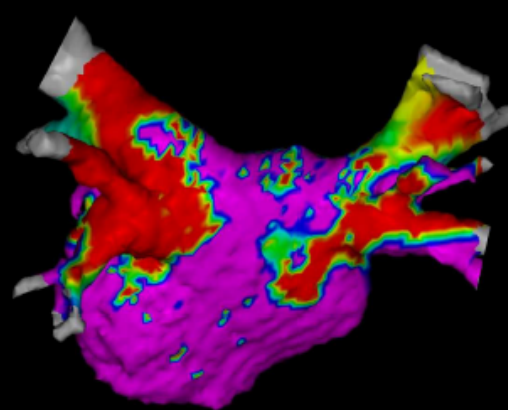
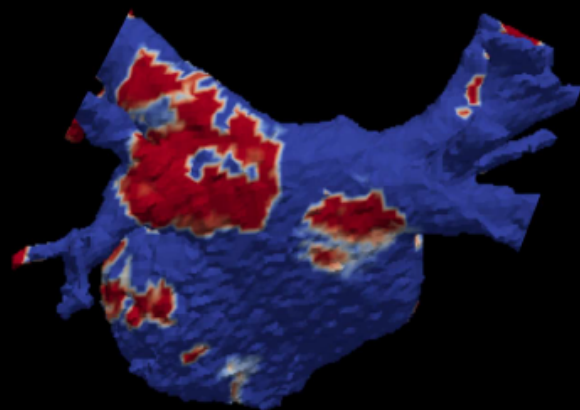






LGE-CMR

EAM



A

● Normal myocardium
● LGE-enhanced myocardium

B

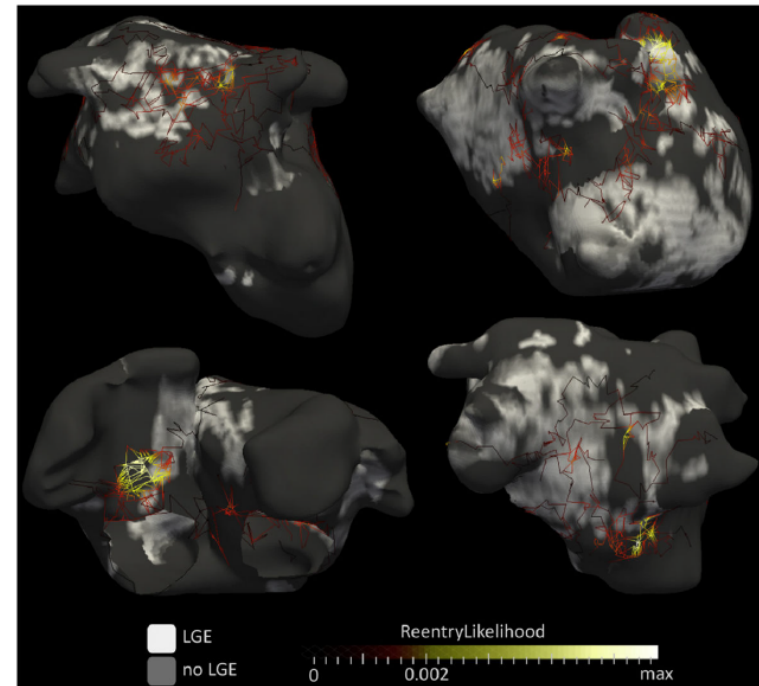
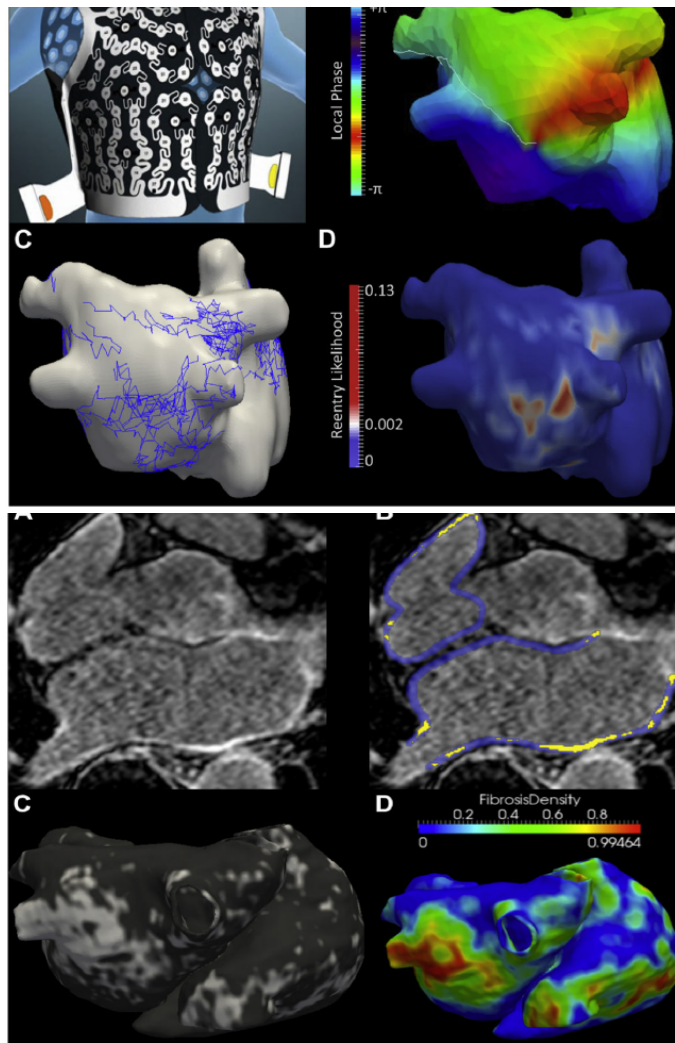
0.20 mV Bi 0.50 mV

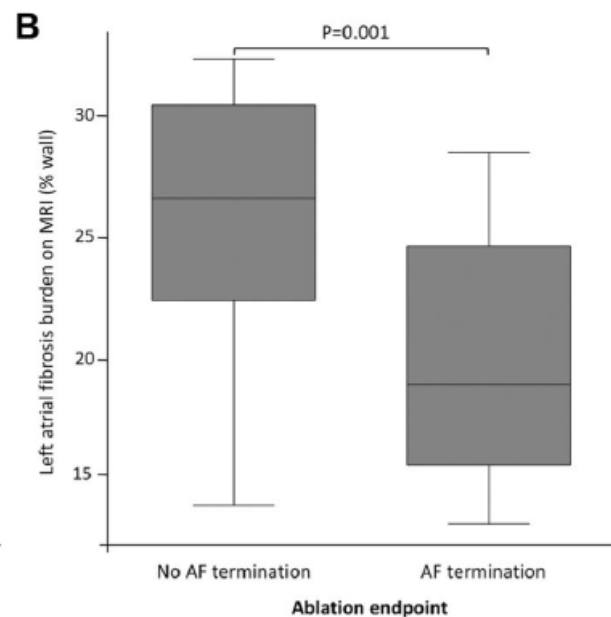
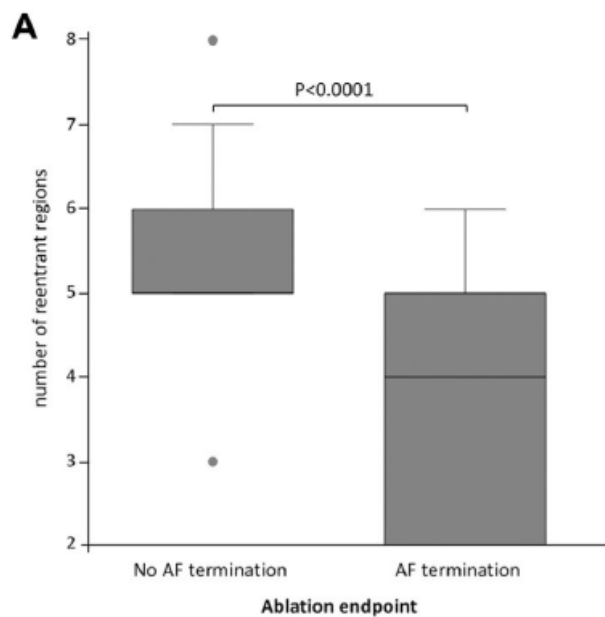
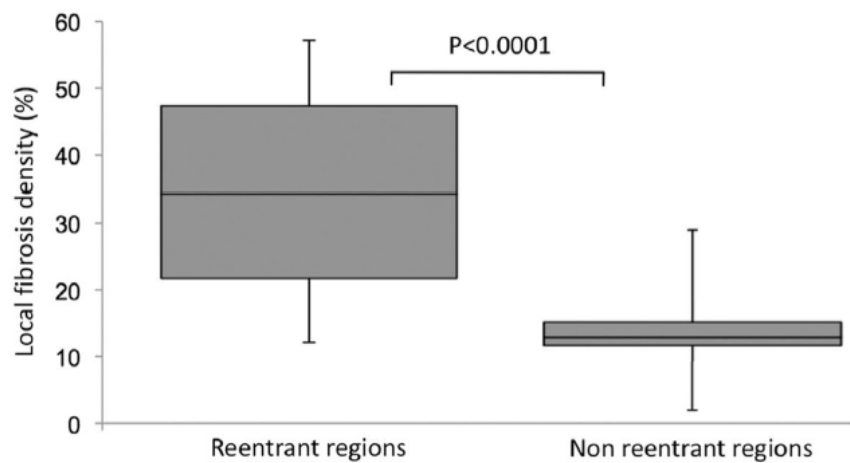
Kardiyak MR

- CMR miyokardın yapısal ve fonksiyonel değerlendirilmesinde kullanılan girişimsel olmayan bir yöntemdir.
- Gadolinium ekstraselüler alanda tutulan kontrast ajandır.
- Gadolinium klirensinde gecikme anormal kardiyak doku göstergesidir (geç gadolinium tutulumu=LGE).
- Fibrotik dokuda LGE normal miyokarda göre daha fazladır.
- LGE olan atriyal dokuda uyarı iletim hızının azaldığı gösterilmiştir.

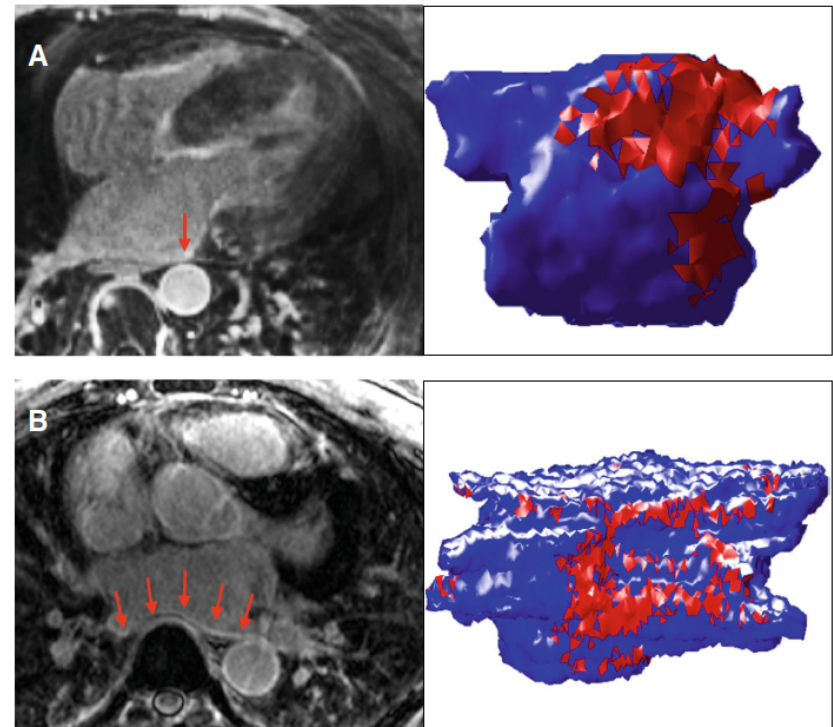
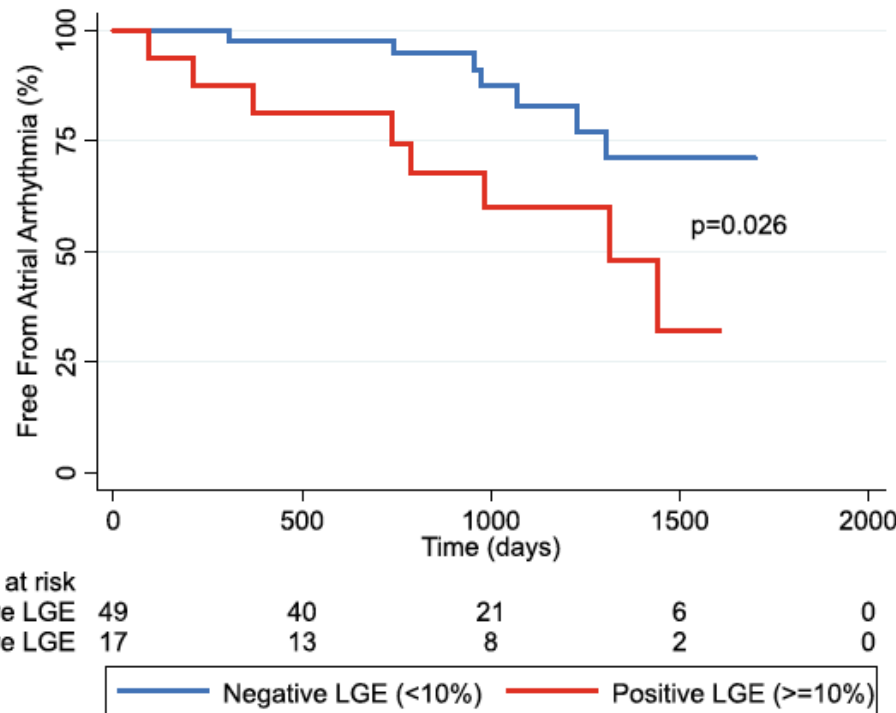
- LGE-CMR görüntüleme atriyal fibrosis tanısında yoğun olarak çalışılmaktadır
- Atriyumun ince duvarlı oluşu CMR'ın suboptimal olmasına yol açar
- CMR→doku fibrosisi için kısıtlı uzaysal çözünürlük, aritmi, kontraktilite ve solunumsal hareketlere bağlı kısıtlılıklar, komşuluktaki kanın neden olduğu yüksek sinyalin skar ile karışması

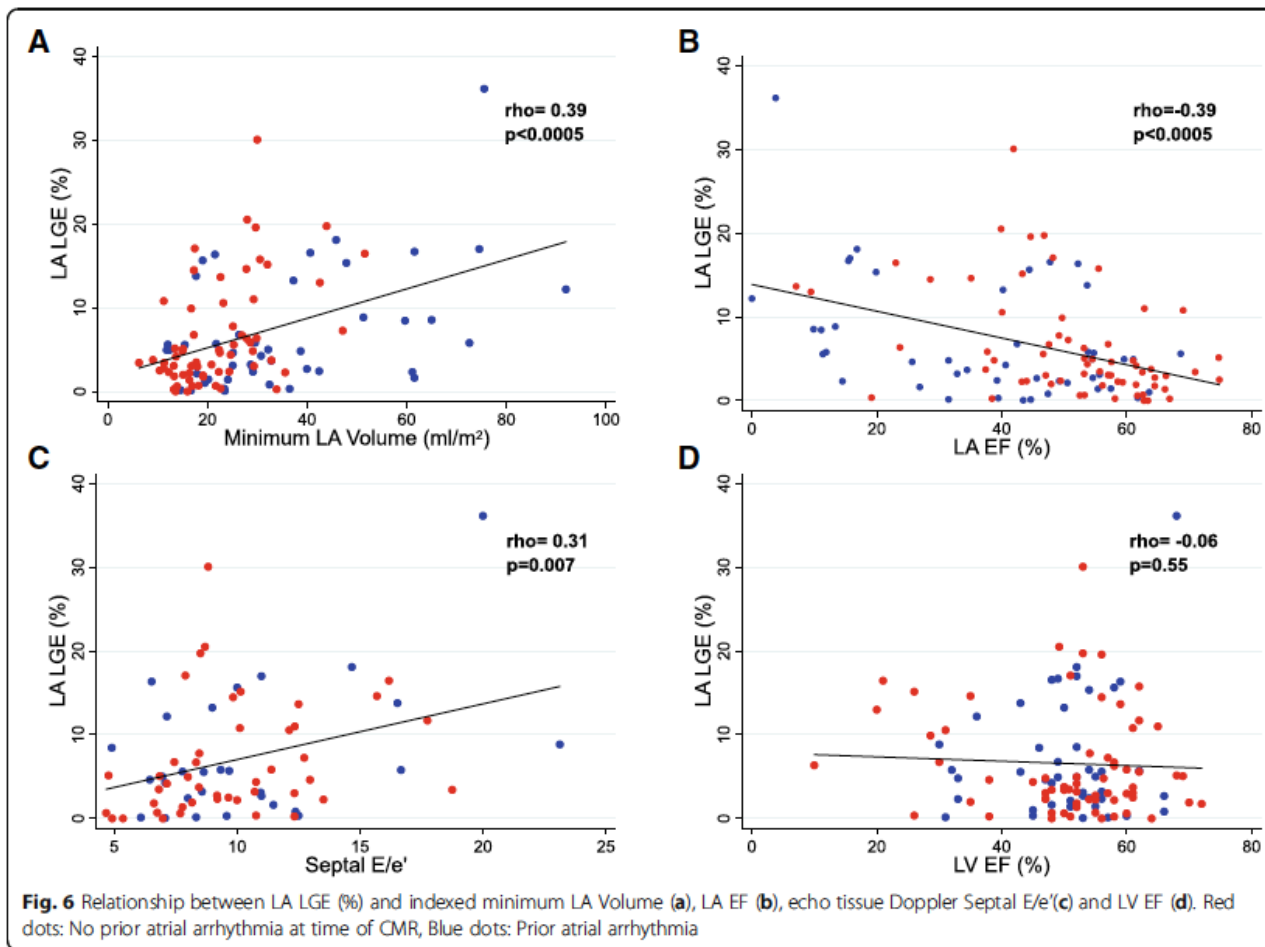
Relationship Between Fibrosis Detected on Late Gadolinium-Enhanced Cardiac Magnetic Resonance and Re-Entrant Activity Assessed With Electrocardiographic Imaging in Human Persistent Atrial Fibrillation





Prognostic and functional implications of left atrial late gadolinium enhancement cardiovascular magnetic resonance





Detection and Quantification of Left Atrial Structural Remodeling With Delayed-Enhancement Magnetic Resonance Imaging in Patients With Atrial Fibrillation

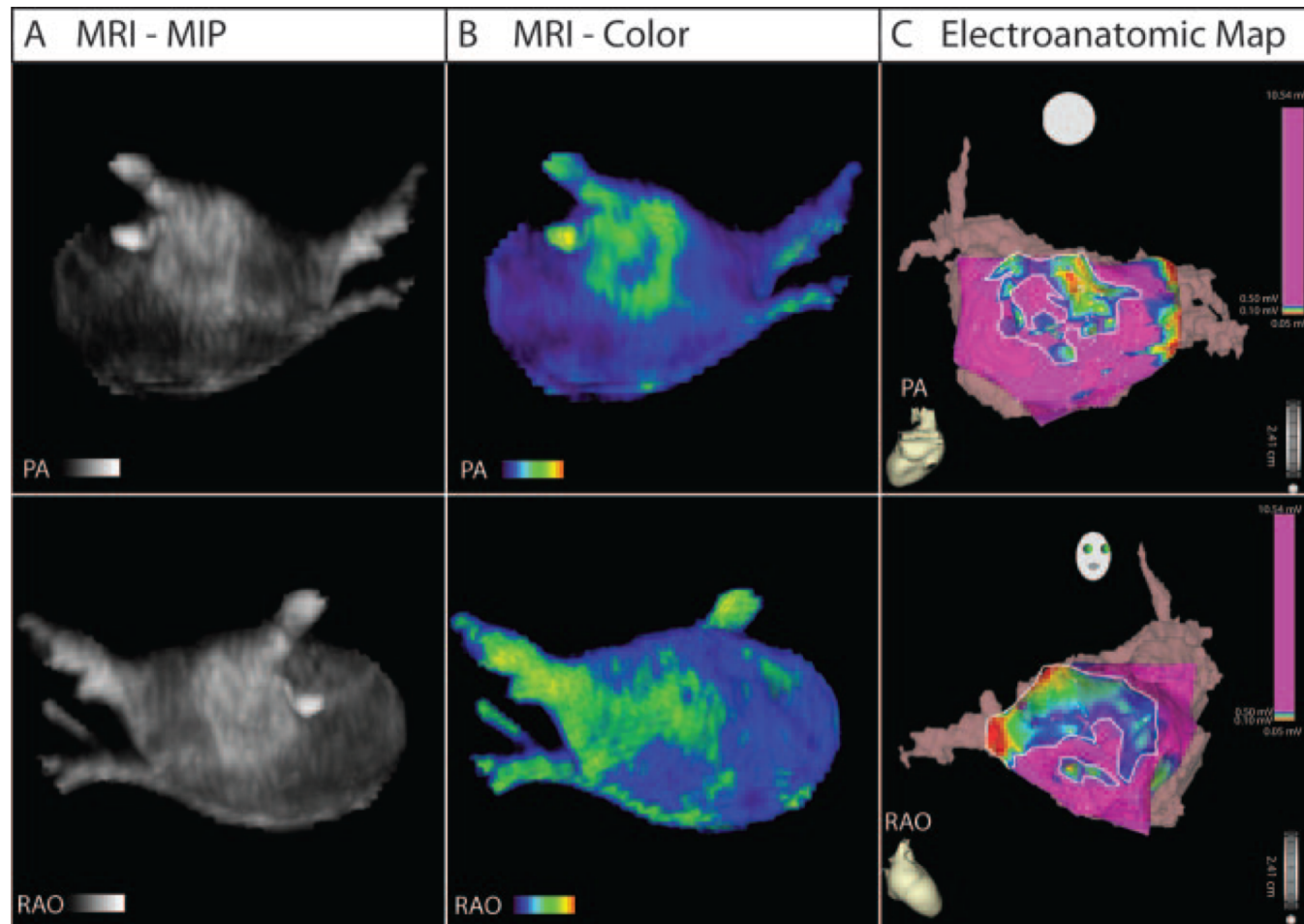
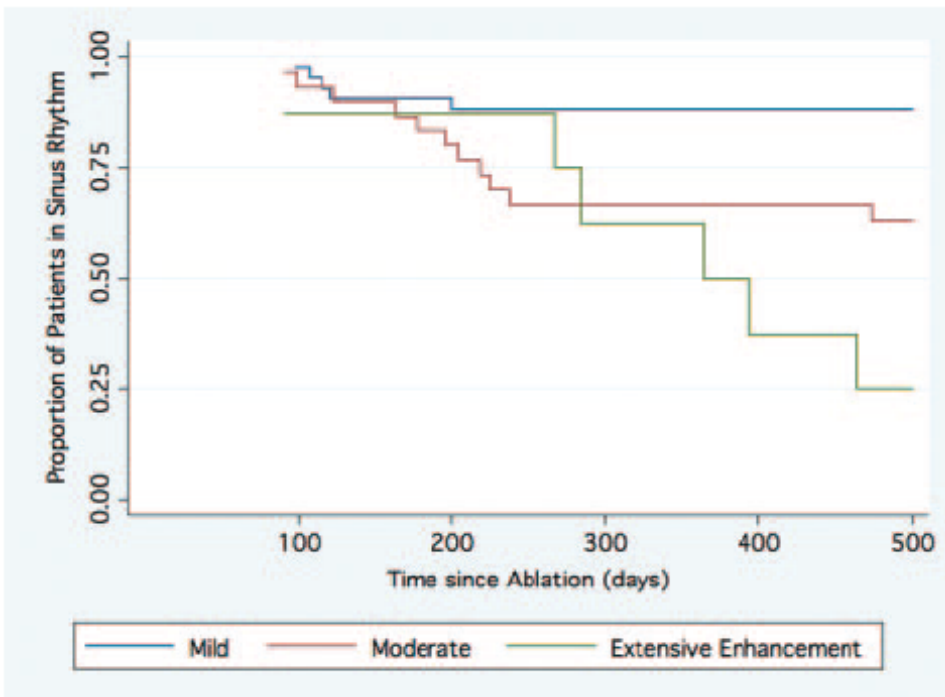
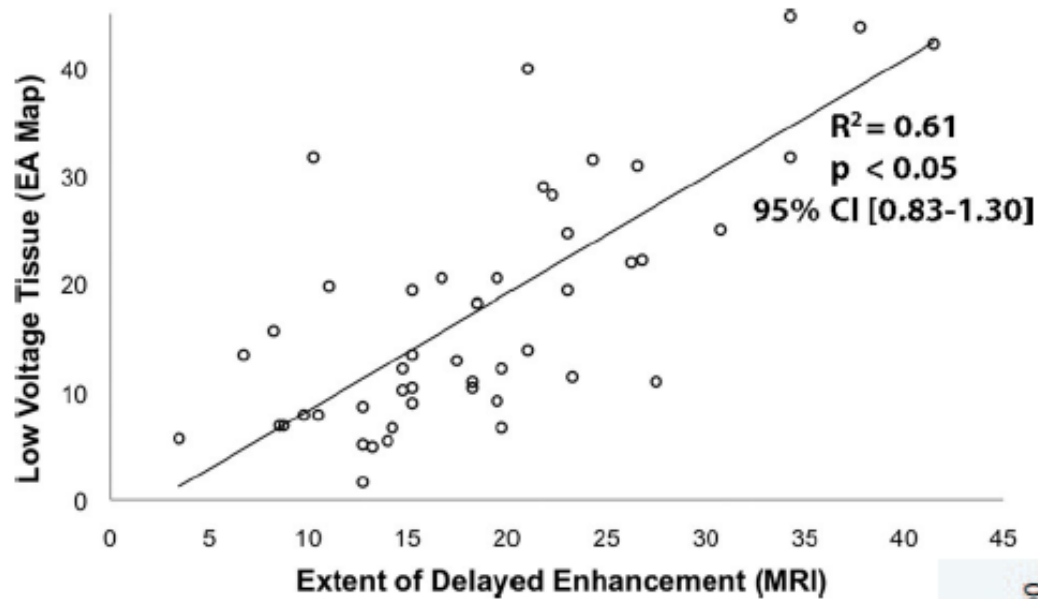


Table 1. Patient Population Characteristics

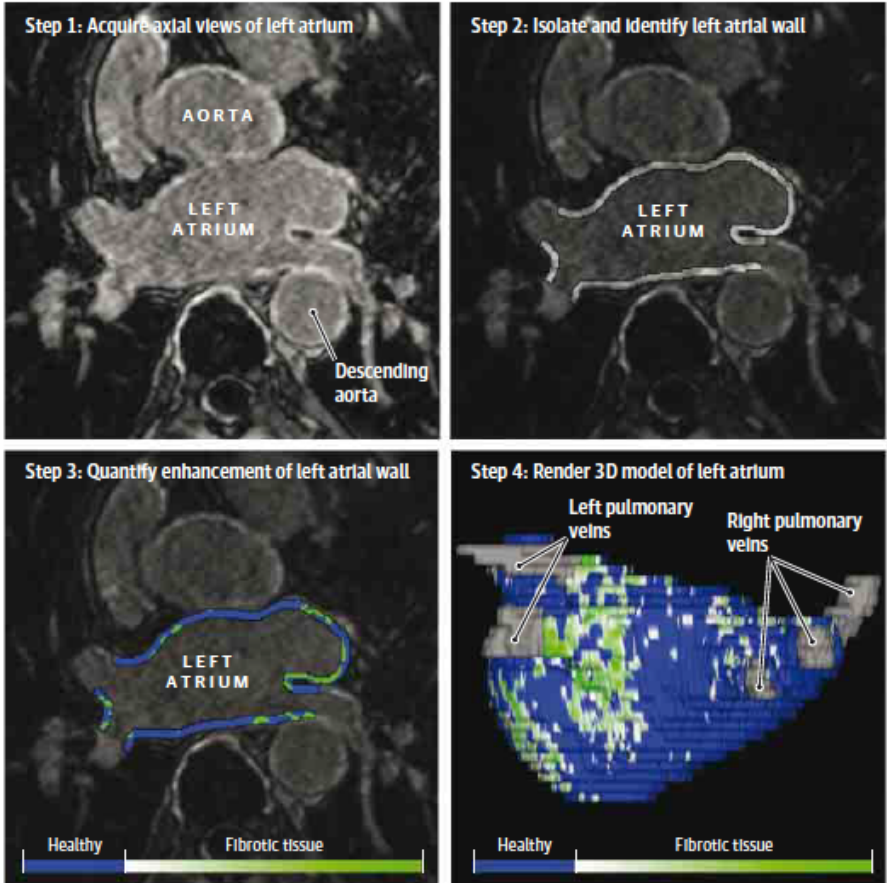
	Total	Mild Enhancement (n=43)	Moderate Enhancement (n=30)	Extensive Enhancement (n=8)	<i>P</i> *
Age, y	63.6±12.0	63.3±12.3	62.2±12.5	70.1±6.0	0.25
Left ventricle ejection fraction, %	52.3±9.8	53.3±10.3	52.4±8.8	46.4±9.0	0.23
Left atrium volume, preprocedure, cm ³	94.3±41.3	83.7±29.4	98.5±48.3	142.1±36.9	<0.001
Gender, n (%)					
Female	29 (35.8)	13 (30.2)	12 (40.0)	4 (50.0)	0.49
Male	52 (64.2)	30 (69.8)	18 (60.0)	4 (50.0)	
Hypertension, n (%)	42 (51.9)	25 (58.1)	13 (43.3)	4 (50.0)	0.49
Diabetes mellitus, n (%)	10 (12.3)	4 (9.3)	4 (13.3)	2 (25.0)	0.36
Coronary artery disease, n (%)	9 (11.1)	5 (11.6)	3 (10.0)	1 (12.5)	1.00
History of smoking, n (%)	9 (11.1)	6 (14.0)	1 (3.3)	2 (25.0)	0.16
Valve surgery, n (%)	3 (3.7)	...	1 (3.3)	2 (25.0)	0.01
Myocardial infarct, n (%)	2 (2.5)	2 (4.7)	...	...	0.60
Medications at the time of ablation, n (%)†					
Antiarrhythmic medications	22 (27.2)	9 (20.9)	11 (36.6)	2 (25.0)	0.15
Amiodarone	15 (18.5)	8 (18.6)	4 (13.3)	3 (37.5)	0.31
Digoxin	12 (14.8)	6 (14.0)	5 (16.7)	1 (12.5)	0.90
β-Blockers	42 (51.8)	23 (53.4)	15 (50.0)	4 (50.0)	0.87
Calcium channel blockers	10 (12.3)	5 (11.6)	3 (10.0)	2 (25.0)	0.52
Response to antiarrhythmic medications, n (%)					
Failed ≥1 medications	32 (39.5)	14 (32.6)	12 (40.0)	6 (75.0)	0.080



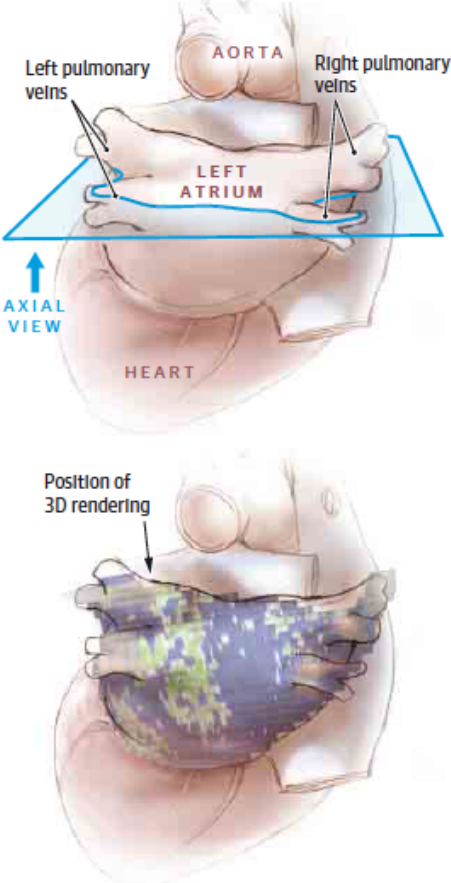
Association of Atrial Tissue Fibrosis Identified by Delayed Enhancement MRI and Atrial Fibrillation Catheter Ablation

The DECAAF Study

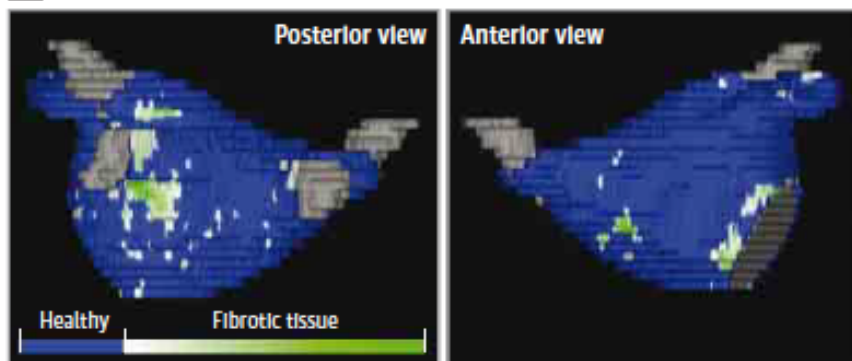
A Delayed enhancement magnetic resonance imaging analysis



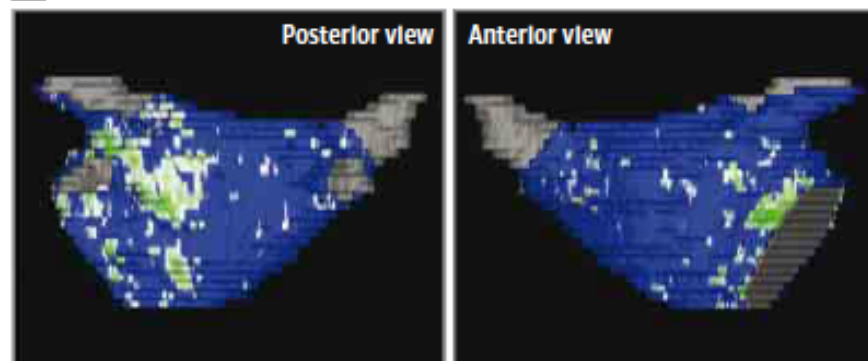
B Schematic posterior view of left atrium



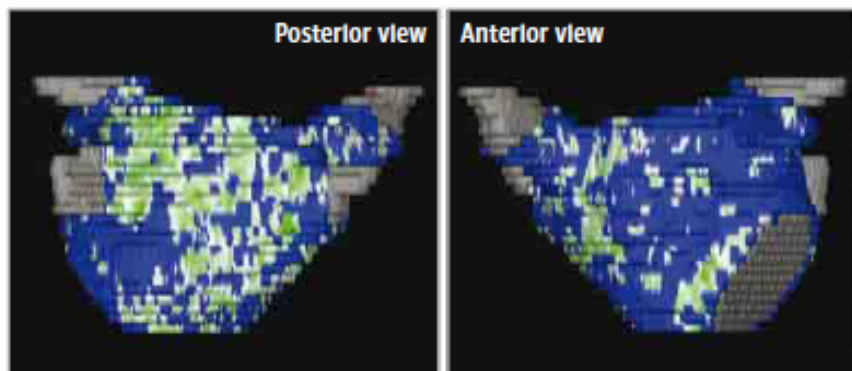
A Stage 1 (<10% of atrial wall)



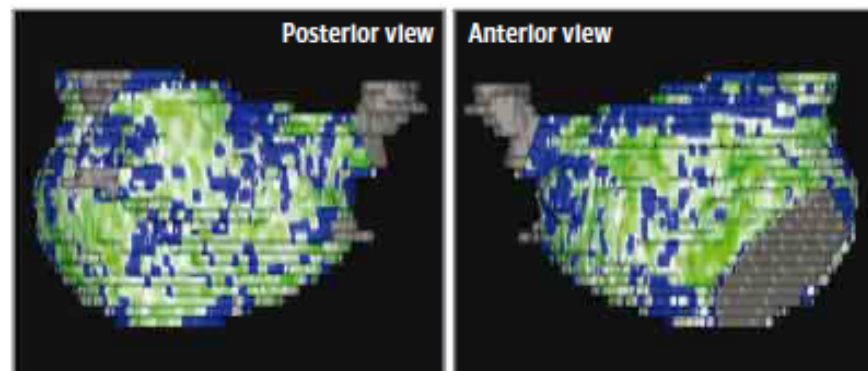
B Stage 2 ($\geq 10\%$ -<20% of atrial wall)

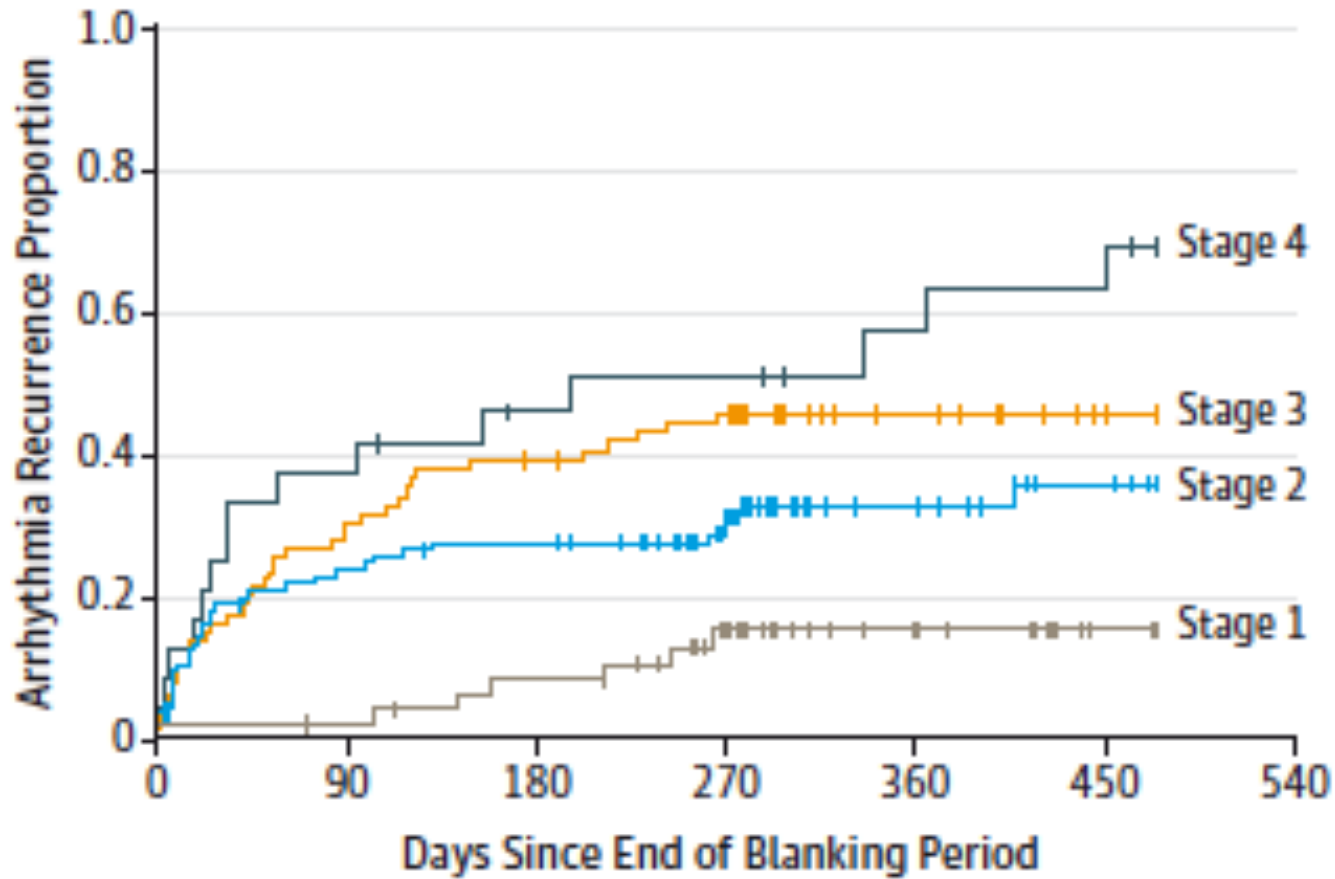


C Stage 3 ($\geq 20\%$ -<30% of atrial wall)



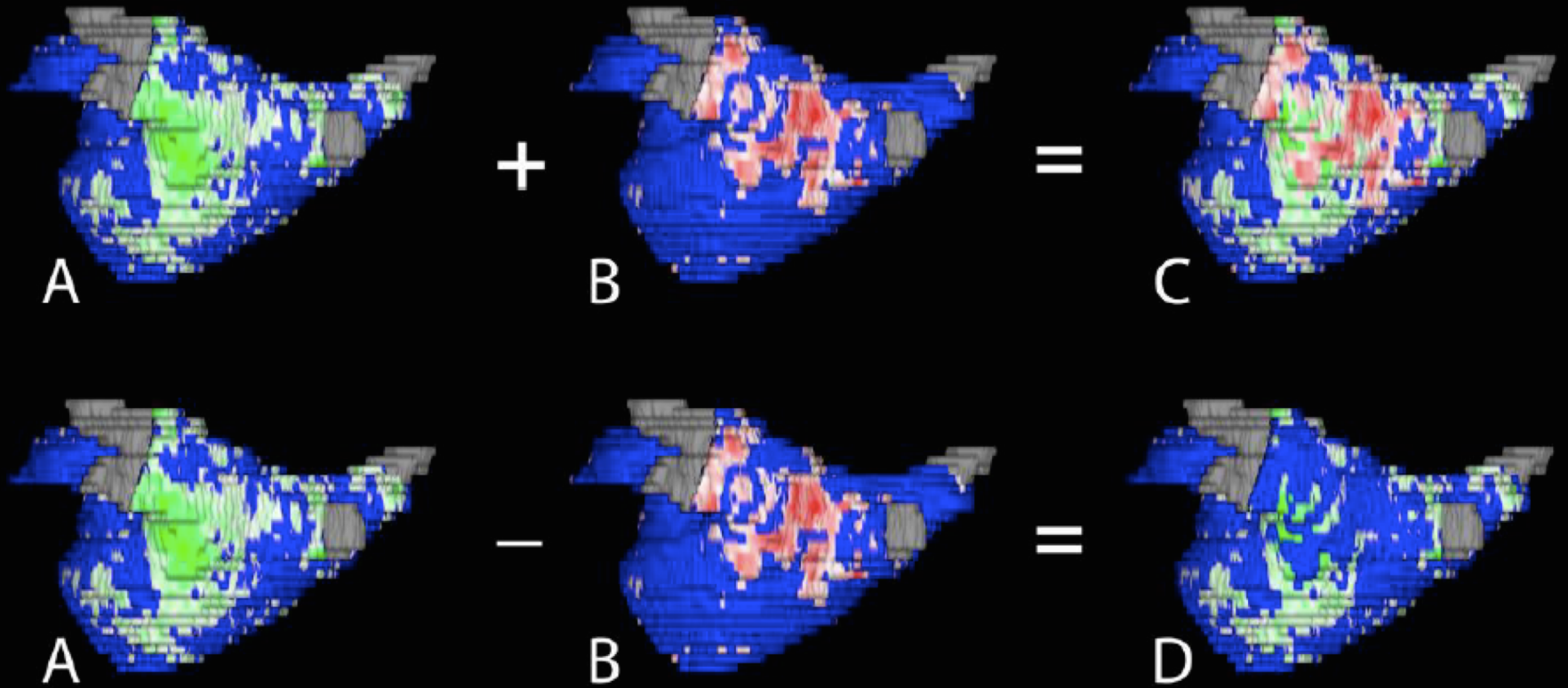
D Stage 4 ($\geq 30\%$ of atrial wall)

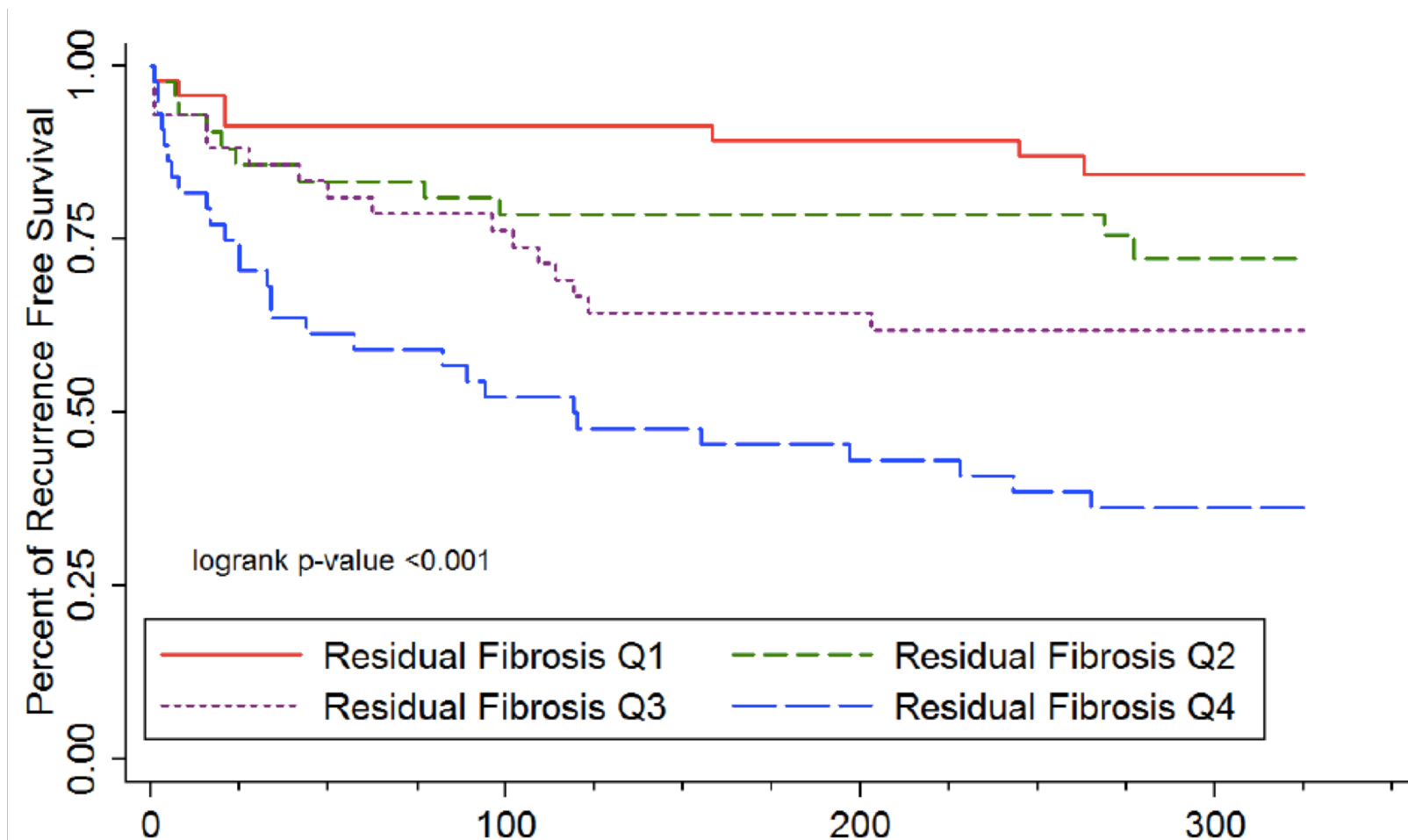




Atrial fibrosisdeki %1'lik artış kateter ablasyon sonrası rekürren atriyal aritmi riskinde %6 artışa neden olur

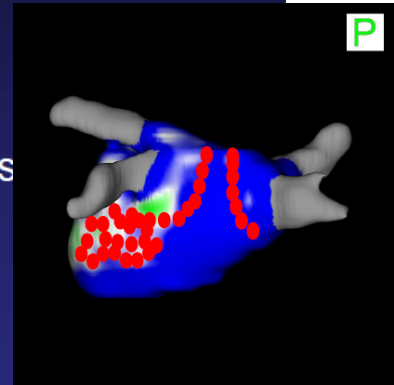
MRI Assessment of Ablation-Induced Scarring in Atrial Fibrillation: Analysis from the DECAAF Study





- Ablasyon öncesi LGE-CMR optimal ablasyon stratejisini belirlemede yararlı olabilir.
- LGE yükü fazla olan hastalarda PVI dışında daha geniş ablasyon stratejilerinin yararlı olabileceği bildirilmiştir.
- LGE olan bölgelere yönelik substrat modifikasyonu persistan AF'li hastalarda yararlı olabilir.

Efficacy of DE-MRI-Guided Fibrosis Ablation vs. Conventional Catheter Ablation of Atrial Fibrillation

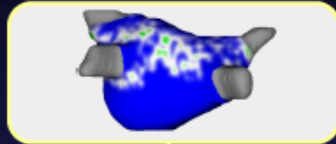


Management of AF guided by fibrosis imaging

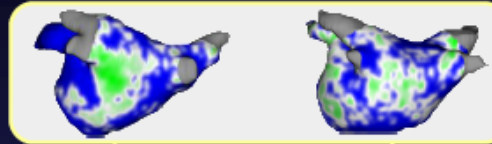
Fibrosis <10%



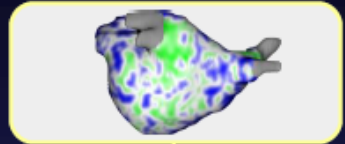
Fibrosis ≥10%-<20%



Fibrosis ≥20%-<30%



Fibrosis ≥30%



Localized
fibrosis

Scattered
fibrosis

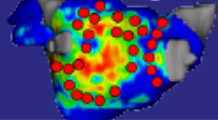
PVI ± Homogenization of scar

Non-ablative management or
homogenization of fibrosis
(awaiting DECAAF II)

Post-ablation recurrence

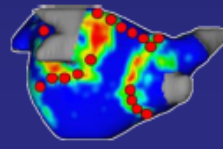
No fibrosis progression

Extensive post-ablation
scarring



? Connection and
homogenization
of existing scar

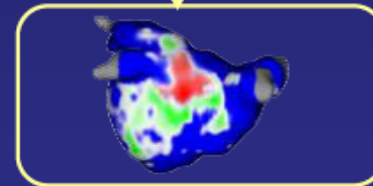
Post PVI scarring



? Re-isolation of PVs
+ connection of ablation scar
+ flutter line

Depth of ablation scar
2.5mm
1.25mm
0mm

Extensive postablation
progression of fibrosis

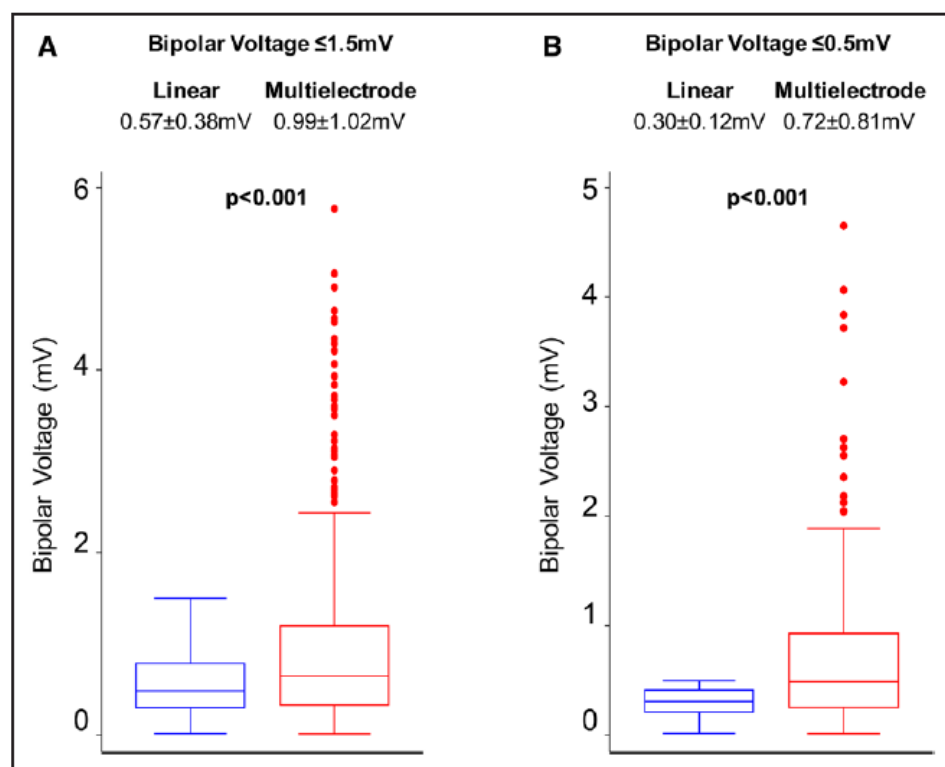
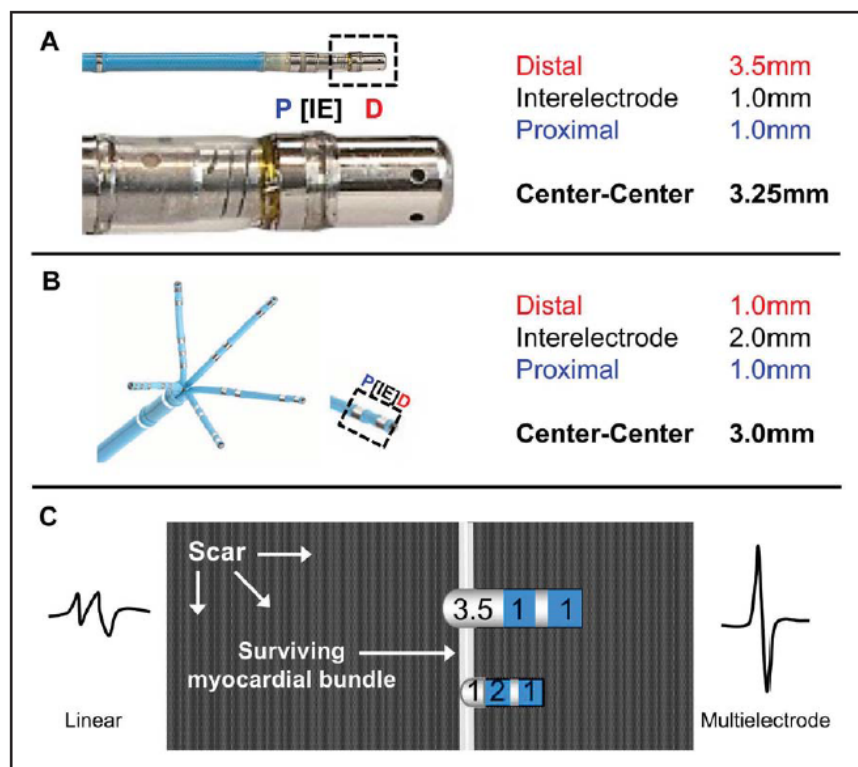


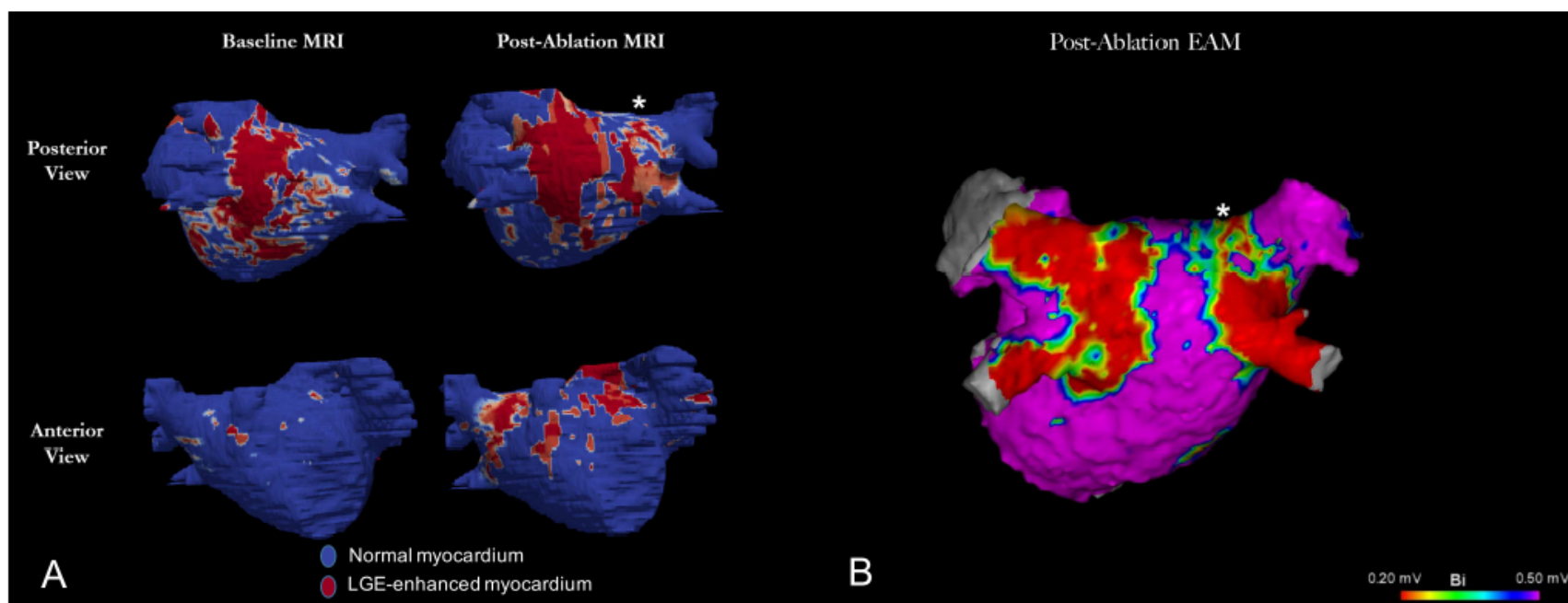
Ablation scar

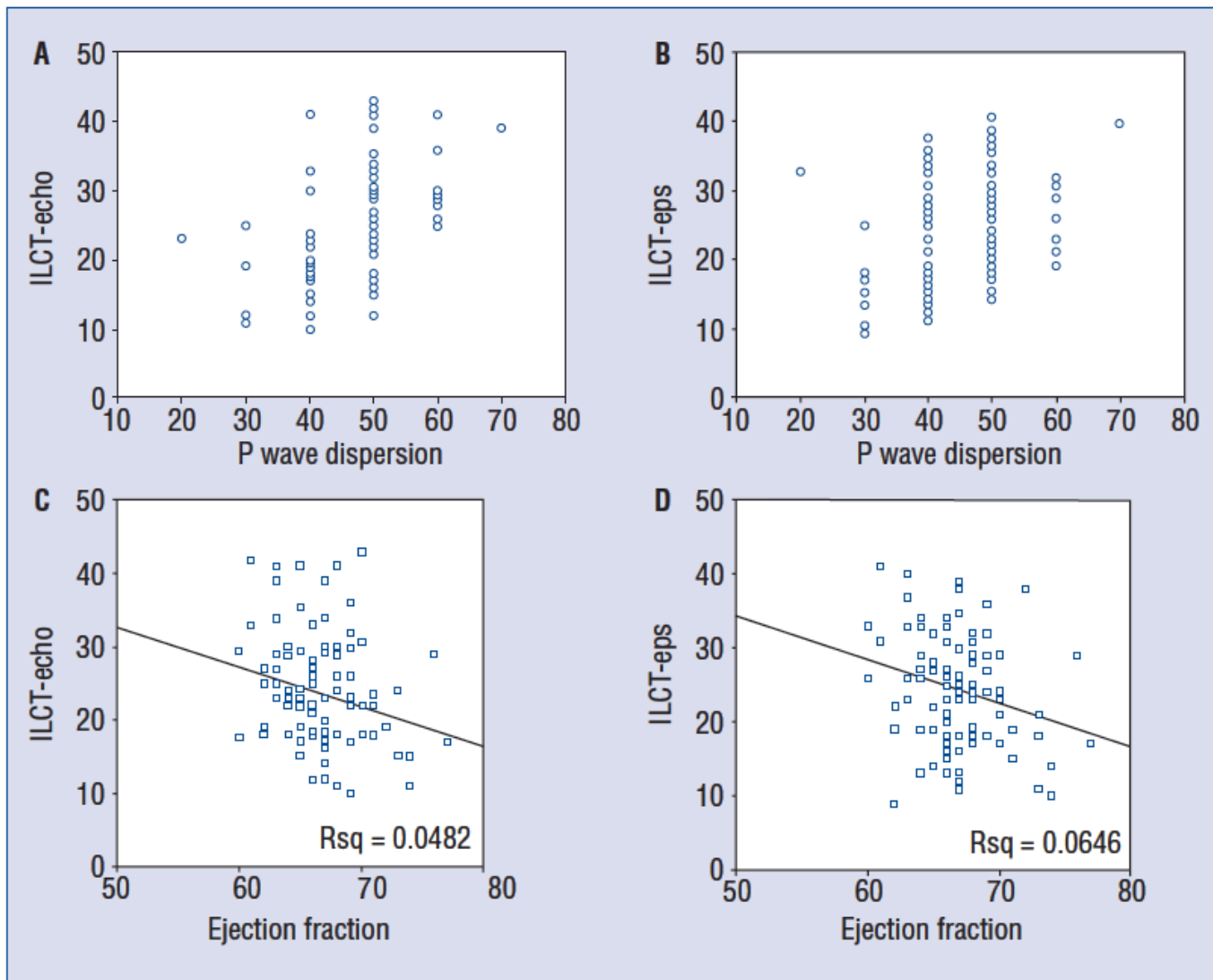
Teşekkürler

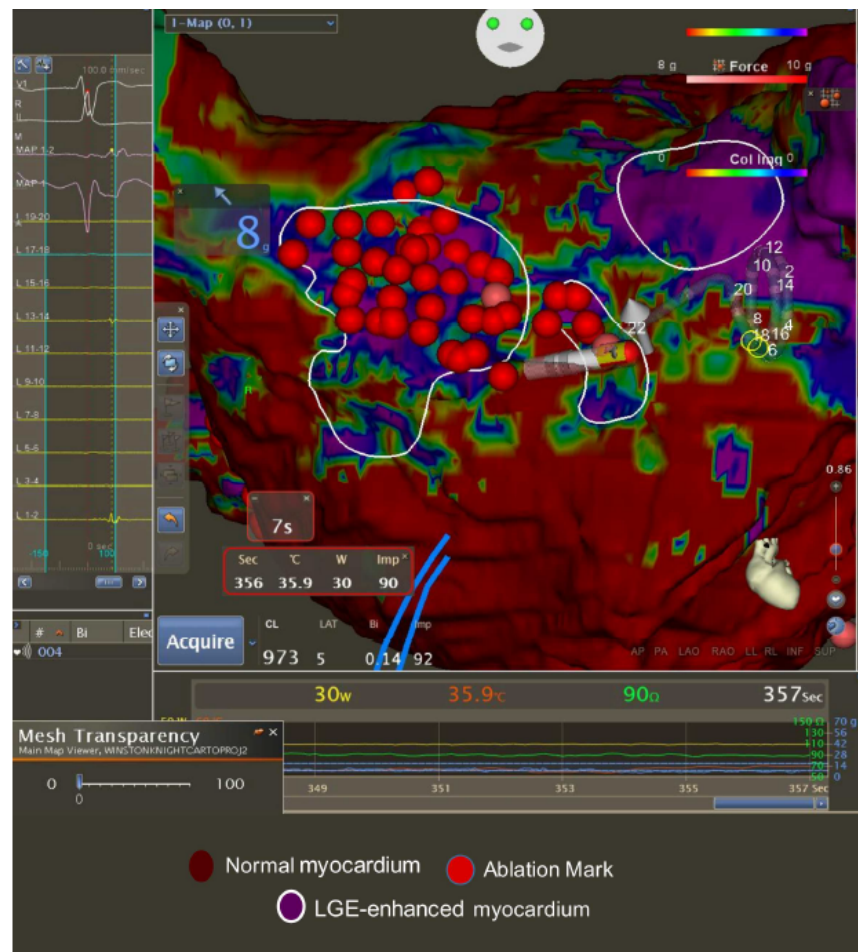
High-Resolution Mapping of Ventricular Scar

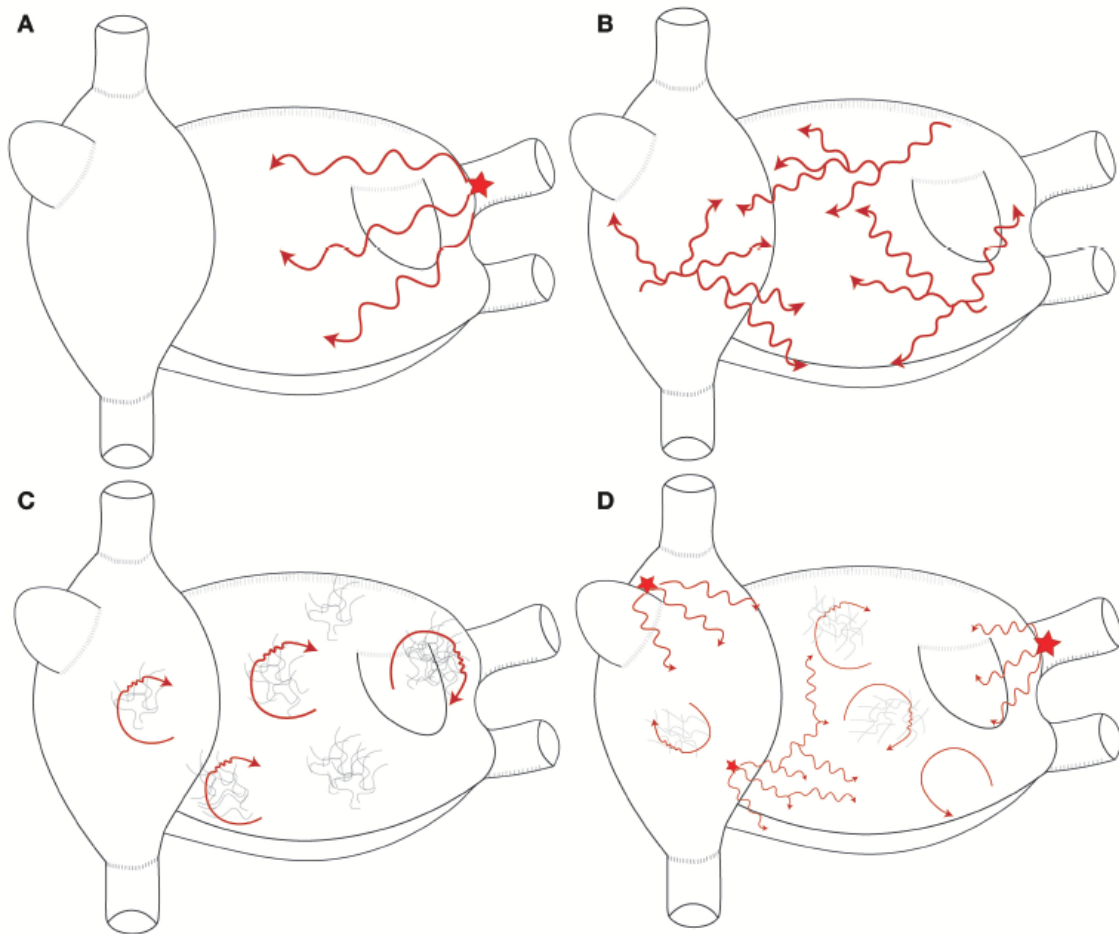
Comparison Between Single and Multielectrode Catheters











- Despite the different techniques, CPVI remains the
- cornerstone of the treatment of AF, regardless of the AF
- form and of the AF duration (Voskoboinik et al., 2017). No
- strategy consistently demonstrated superiority to CPVI in
- preventing long term recurrences of atrial arrhythmias.

- Catheter ablation is superior to antiarrhythmic drugs in
- preventing AF recurrence (Hazard ratio = 0.53) as reported
- in the CABANA trial. However, the best strategy is still to be
- identified.

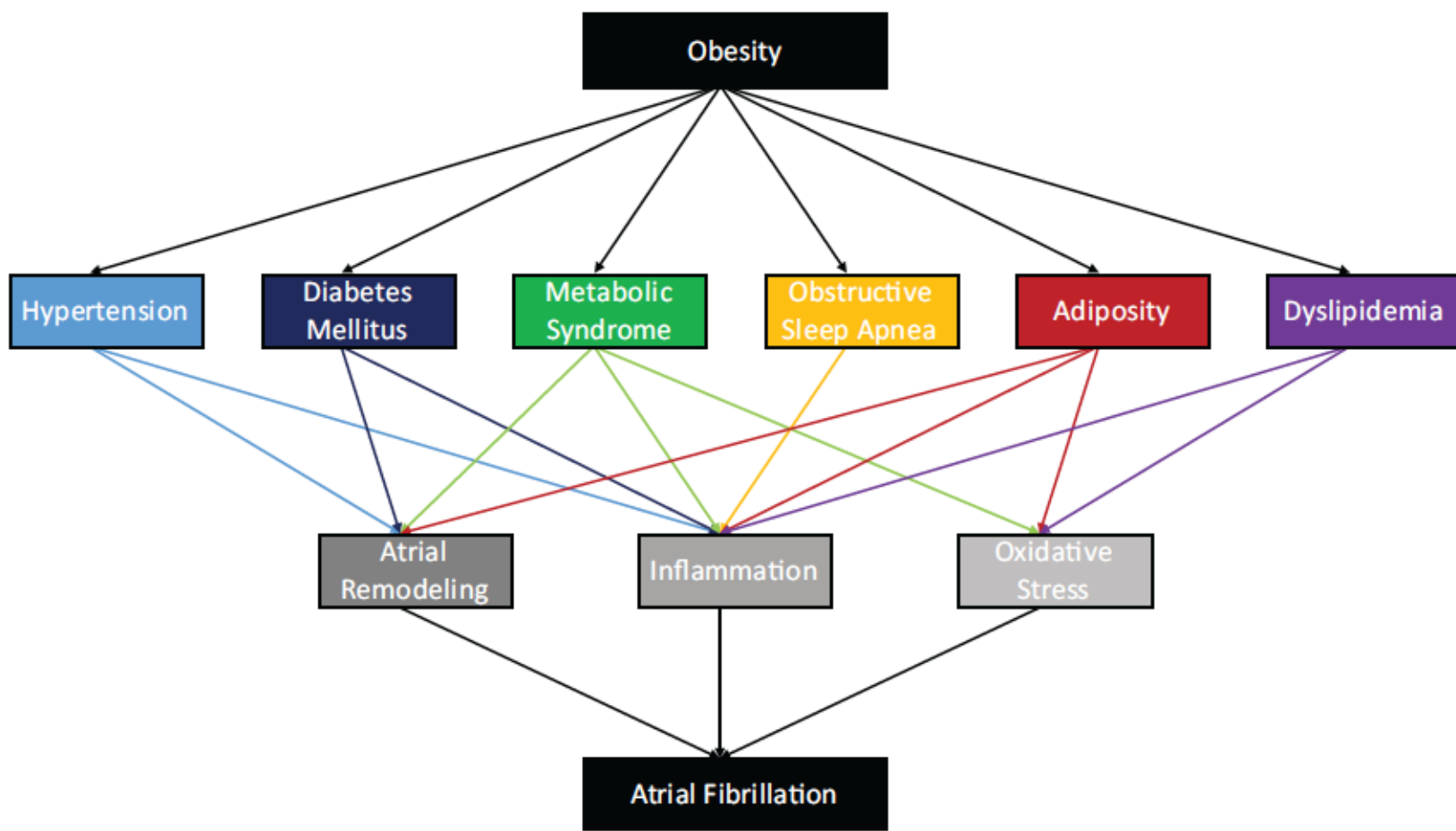
- Long term rates of persistent AF suppression after PVI remain suboptimal (~50%)⁶⁵
- and may be resultant from extensive arrhythmogenic fibrosis not targeted by PVI.

- CE-MDCT→ iskeminin neden olduğu fokal değişiklikleri gösterir, ancak ventriküldeki diffüz miyokardiyal fibrosisi göstermekte yetersiz, daha ince duvarlı atriyumda fibrosisi göstermede yetersiz

- One such approach pertains to the concept that atrial fibrosis, detected on pre-ablation
- LGE-CMR, may serve as a potential target for substrate modification during catheter ablation of
- persistent AF. Figure 6 illustrates intra-procedural targeting of pre-ablation myocardial substrate
- (mapped on LGE-CMR) in a patient with long-standing persistent AF. The hypothesis that LGE
- substrate modification in addition to PVI will enhance AF control in patients with myocardial
- remodeling is being studied in the ongoing DECAAF II trial (Clinicaltrials.gov ID: NCT02529319).

- Pre-ablation LGE-CMR may also be beneficial in determining the
- optimal ablation strategy. It has been suggested that in patients with higher LGE burden, a more
- expansive ablation strategy beyond pulmonary vein isolation may be necessary to neutralize the
- arrhythmogenic substrate driving AF.^{41–43} Current studies are underway to evaluate this paradigm
- before its adoption in clinical practice.

- Electrograms at the areas with fibrosis were analyzed by Jadidi
- et al. (2013) in a group of patients undergoing ablation for
- persistent and long-lasting PsAF. Atrial fibrosis was associated
- with lower amplitude and a slower and more organized activity.
- However, complex fractionated atrial electrograms were recorded
- outside the areas of fibrosis in 90% of the cases.



- Oakes and colleagues who examined left atrial LGE in 81 patients
- with symptomatic AF and demonstrated a strong association between low-voltage areas on electroanatomical
- mapping (EAM) and LGE.¹⁴ The extent of pre-existing LA scar has been categorized by
- the Utah group as: Group I with <5%, Group II with 5-20%, Group III with 20-35%, and Group
- IV with >35% LGE (with bearings on outcomes as discussed below). These results were
- corroborated on LA biopsy in 10 patients undergoing surgery (9 with AF and 1 without AF) such
- that myocardial fibrosis matched with regions of LGE on CMR,

- Fukumoto et al. have demonstrated that increased local LGE within LA myocardium is associated
- with lower conduction velocity, potentially increasing its arrhythmogenicity.¹¹
- Burstein B, Nattel S. Atrial Fibrosis: Mechanisms and Clinical Relevance in Atrial Fibrillation.
- J Am Coll Cardiol. 2008;51(8):802-809.
doi:10.1016/j.jacc.2007.09.064.

- It has been reported that fibrosis analysis on LGE was not
- possible in up to 20% of CMRs due to significant artifact, primarily due to presence of AF at time of
- acquisition.³⁷
- Thus, rhythm control strategy using pharmacotherapy or electric cardioversion prior to
- image acquisition may improve image quality.

- One of the largest to date is the DECAAF study, spearheaded by the Utah
- group.⁴⁰ In this multicenter prospective cohort study of 260 participants with paroxysmal and
- persistent AF, LGE-MRI was acquired up to 30 days before the first ablation and were followed for
- AF recurrence. The extent of atrial fibrosis was directly associated with AF recurrence such that
- cumulative incidence of recurrent arrhythmia by end of follow-up was 15.3% for fibrosis stage I,
- 35.8% for stage II, 45.9% for stage III, and 69.4% for stage IV.

- Haissaguerre et al. (2016) analyzed the presence of fibrosis
- and its density within each 2.5mm spherical atrial volume in
- 13 patients undergoing CMR. The borders of the fibrotic areas
- hosted the majority of the reentrant activities. In fact, 80% of the
- reentrant activities were located in areas with a fibrotic density
- >70%. Conversely, only 10% of the non-driver region harbored
- such a high fibrotic density.