Curative treatment of AF:

Too far to reach?

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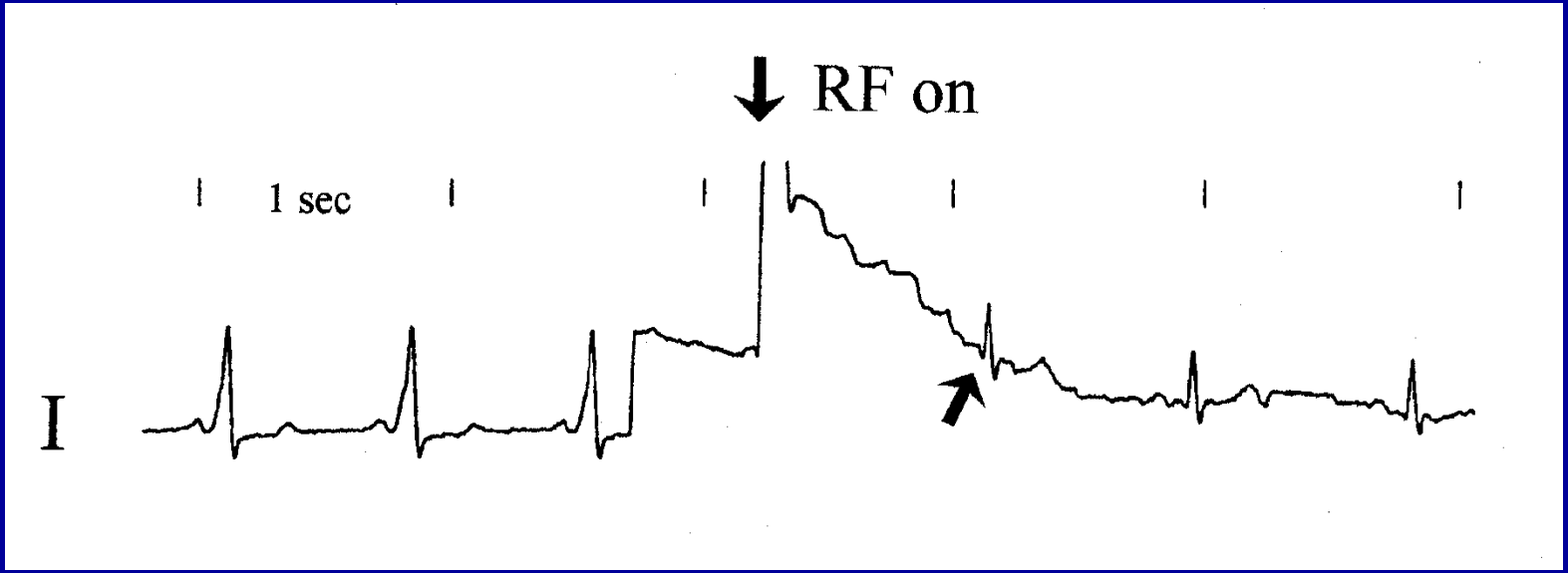
Presenter Disclosure Information

Gerhard Hindricks has received honoraria for lectures from Biosense, St. Jude Medical, Biotronik, Medtronic, Boehringer Ingelheim

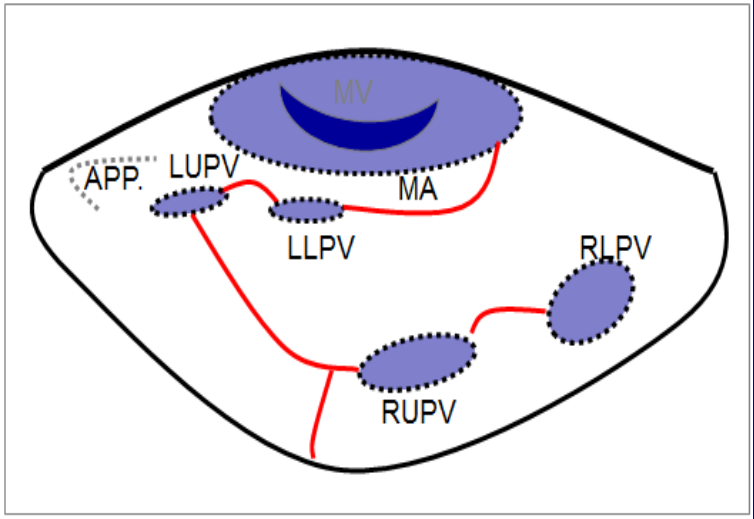
Gerhard Hindricks has received research grants from St. Jude Medical, Biotronik, Biosense

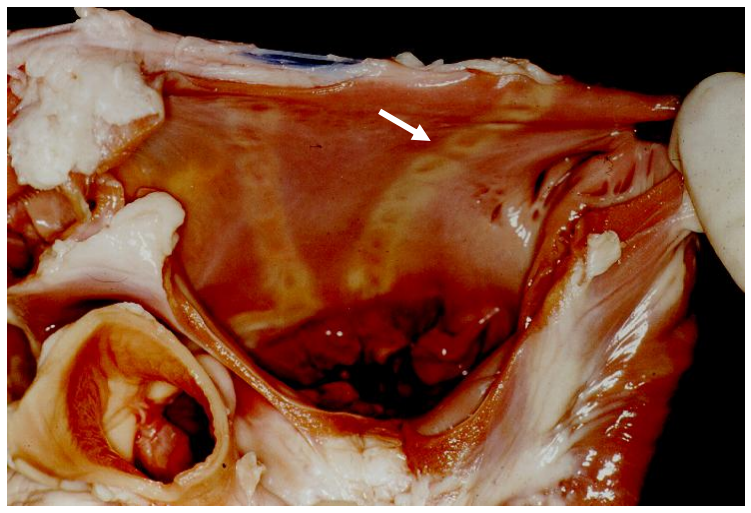
Gerhard Hindricks is a member of the Advisory Board / consultant for Biosense, St. Jude Medical, Biotronik, Stereotaxis,

The beauty of catheter ablation…

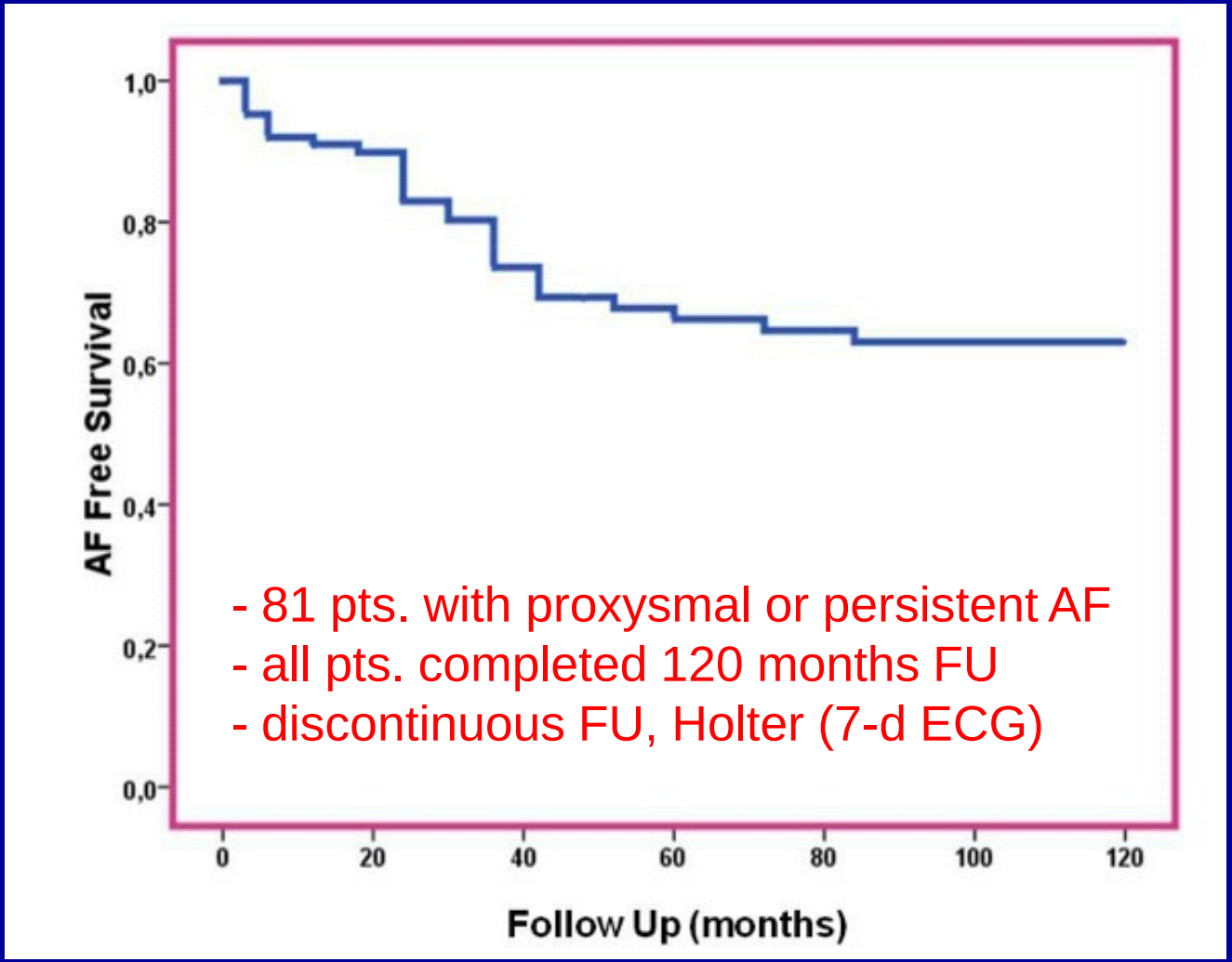


Intraoperative ablation of AF – 10 yr. FU



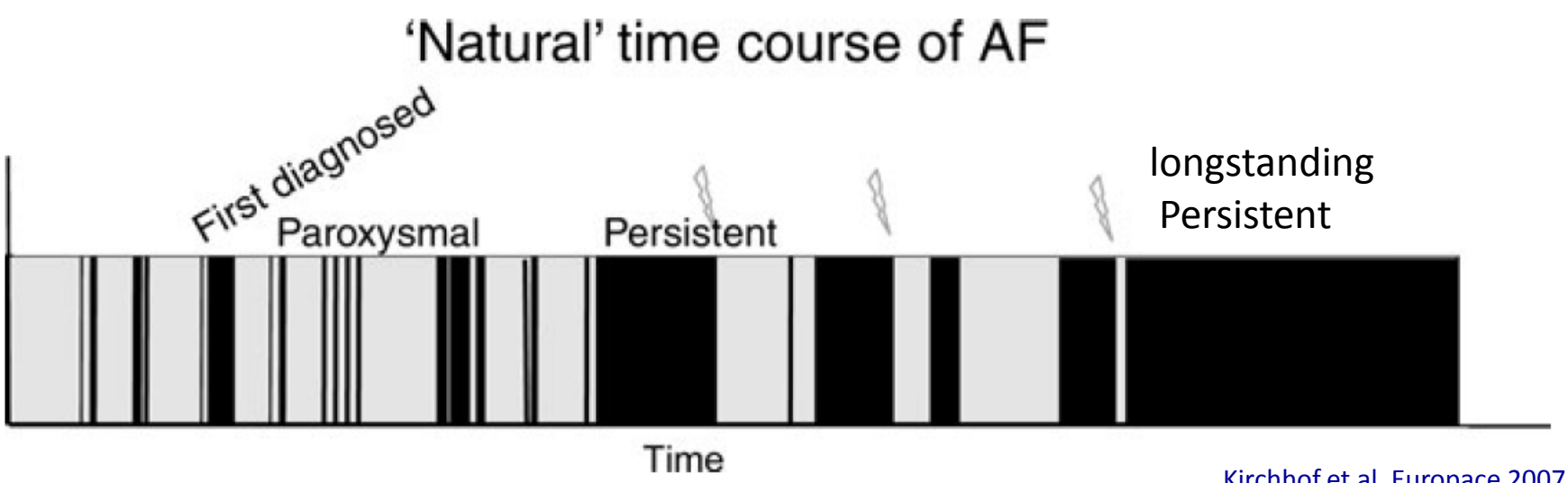


Intraoperative ablation of AF: 10 yr follow-up



Progression of atrial fibrillation

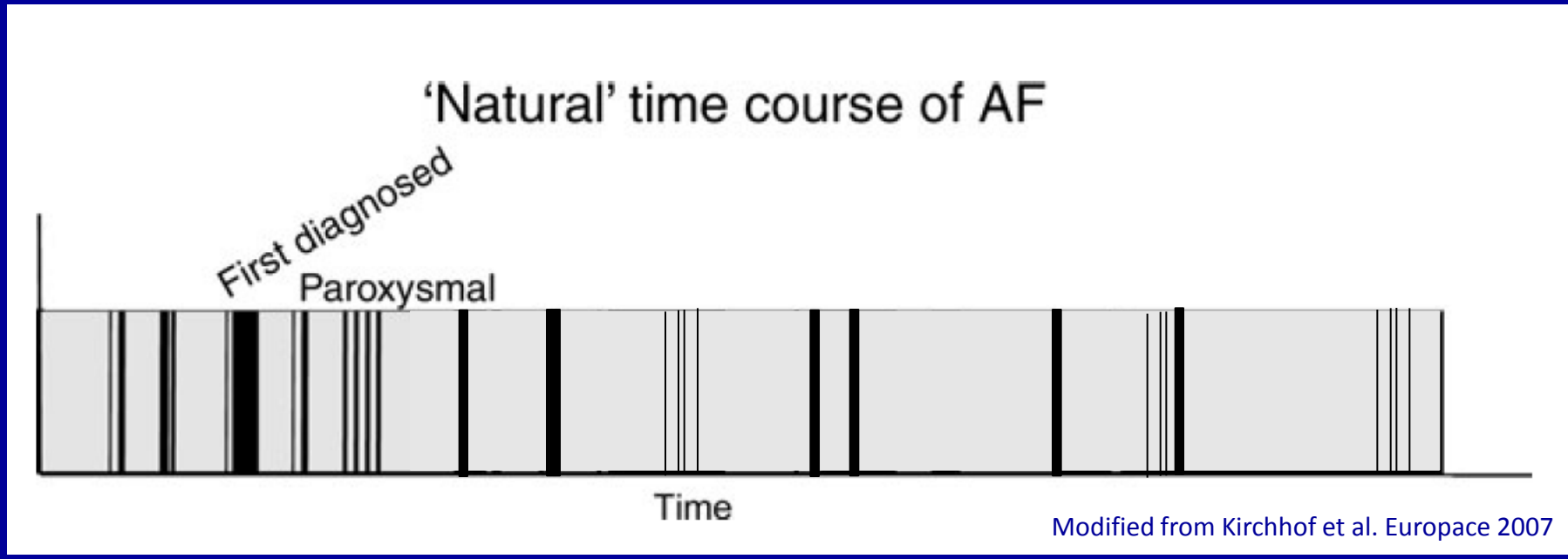
- Why does AF progress?
- What are the (main) drivers promoting AF progression?
- Can these drivers be modulated by catheter ablation?



Kirchhof et al. Europace 2007

Progression of atrial fibrillation

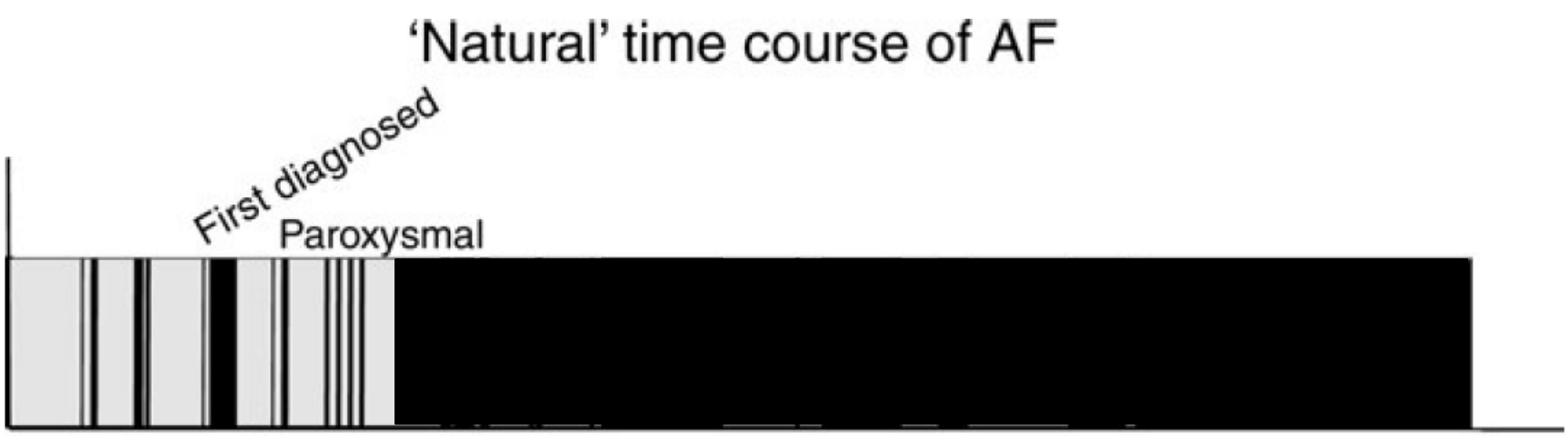
- Which mechanisms / factors govern the dynamics of AF progression?
- Are mechanisms / factors the same in all AF patients?



Modified from Kirchhof et al. Europace 2007

Progression of atrial fibrillation

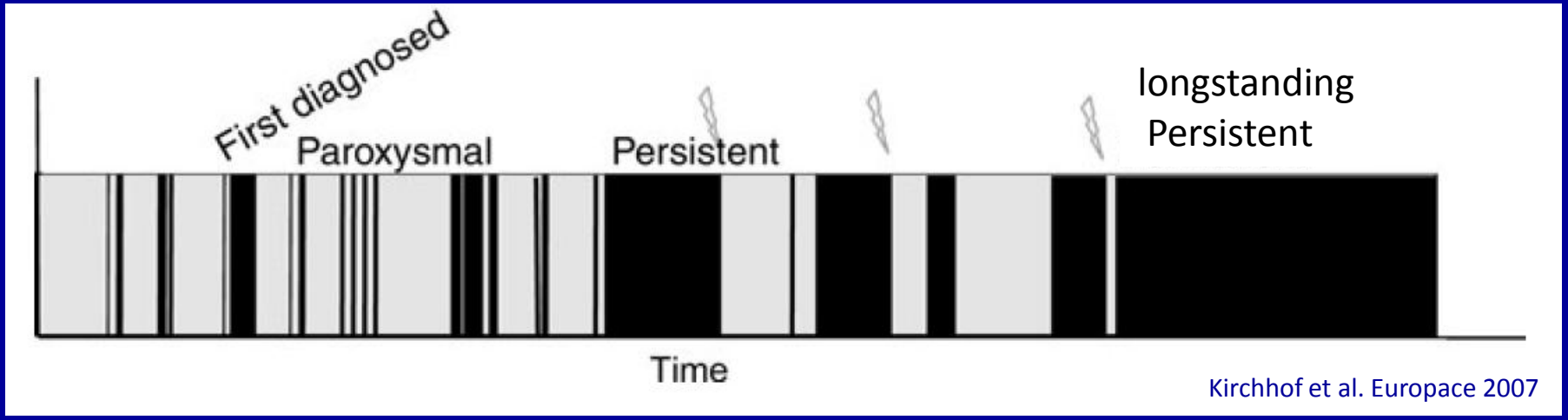
- Which mechanisms / factors govern the dynamics of AF progression?
- Are mechanisms / factors the same in all AF patients?
- Is there a point of no return to SR?



Modified from Kirchhof et al. Europace 2007

Progression of atrial fibrillation: the concept

- AF begets AF
- AF induced re-modeling
  - electrophysiological properties
  - structural re-modeling
  - atrial fibrosis
- “The more you have… the more you get!”



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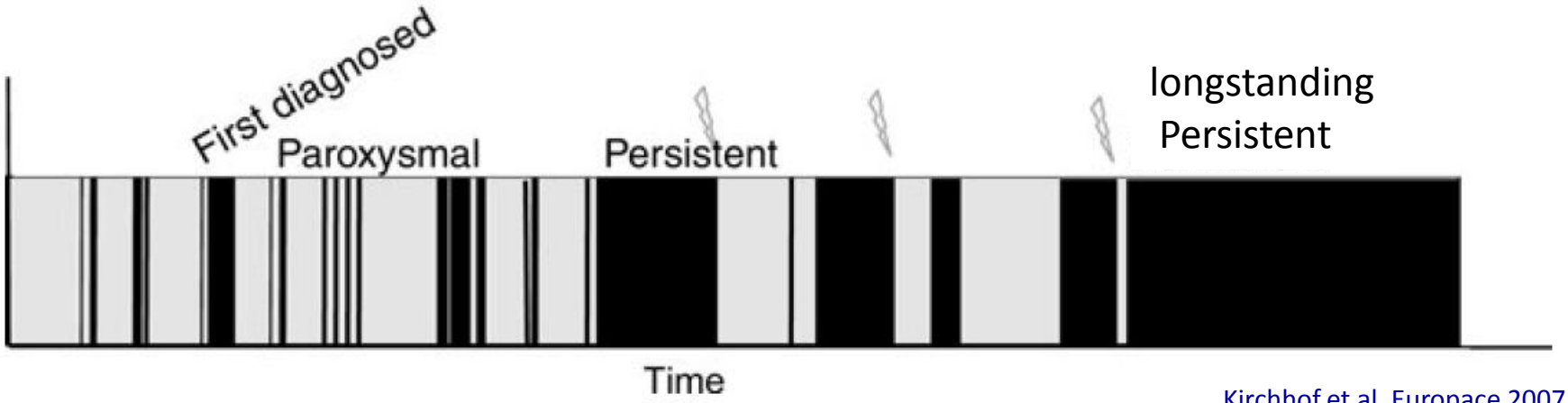
hypertension

age **LVEF**

valvular HD



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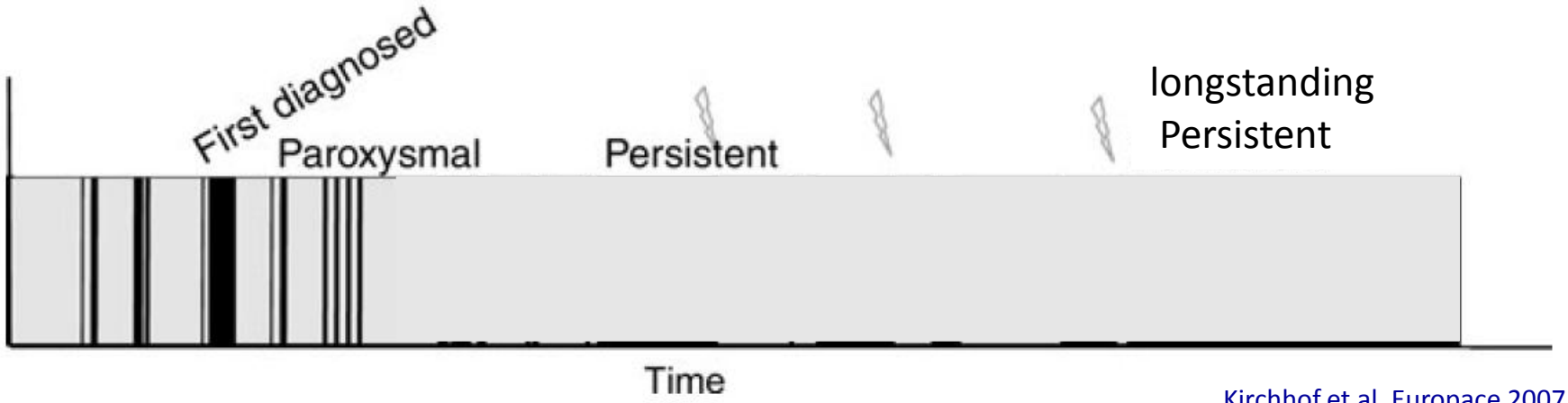

Kirchhof et al. Europace 2007

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- AF begets AF

CURE?

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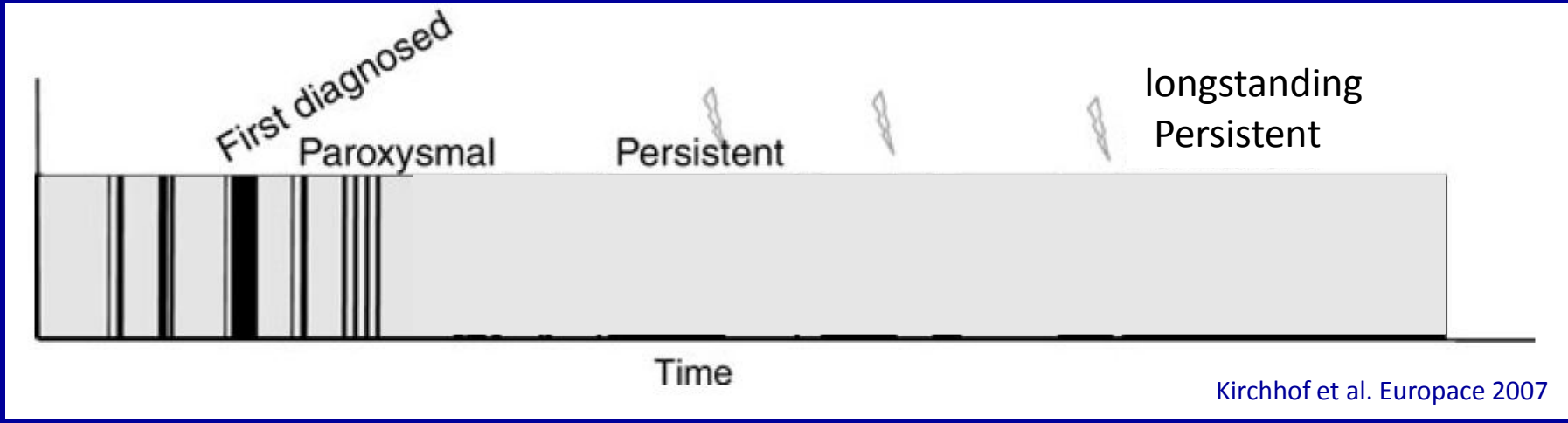


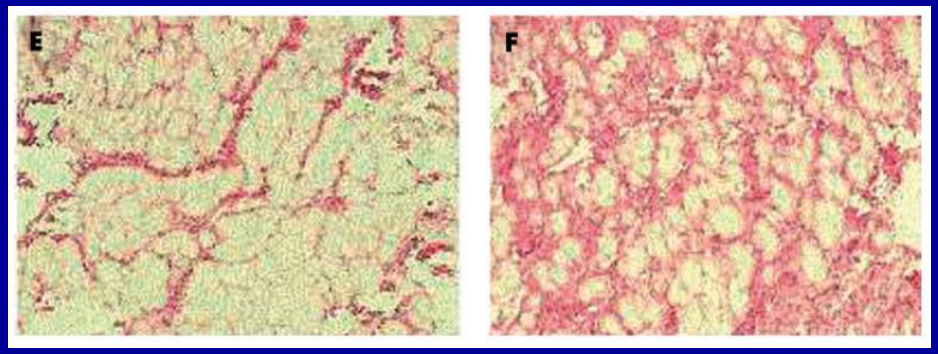
Kirchhof et al. Europace 2007

Thoughts about “AF begets AF”

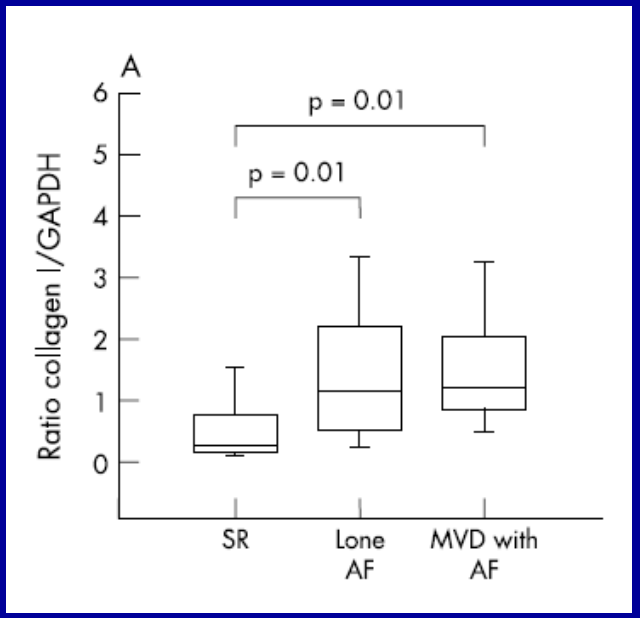
- The concept is based on animal experimental studies performed in healthy goats driven to AF by high frequency stimulation.
- The relevance for human AF is not fully established.
- Is atrial re-modeling a consequence of AF…..or is AF a consequence of re-modeling?
- What do we know about the substrate of human AF?
  - data from pathology, imaging, and electrophysiologial studies.

The substrate of human AF: pathology

- Expression of major extracellular matrix (collagen I and III, fibronectin protein) in patients with SR, lone AF, and AF plus MVD.
- Left atrial tissue from 118 patients undergoing cardiac surgery.



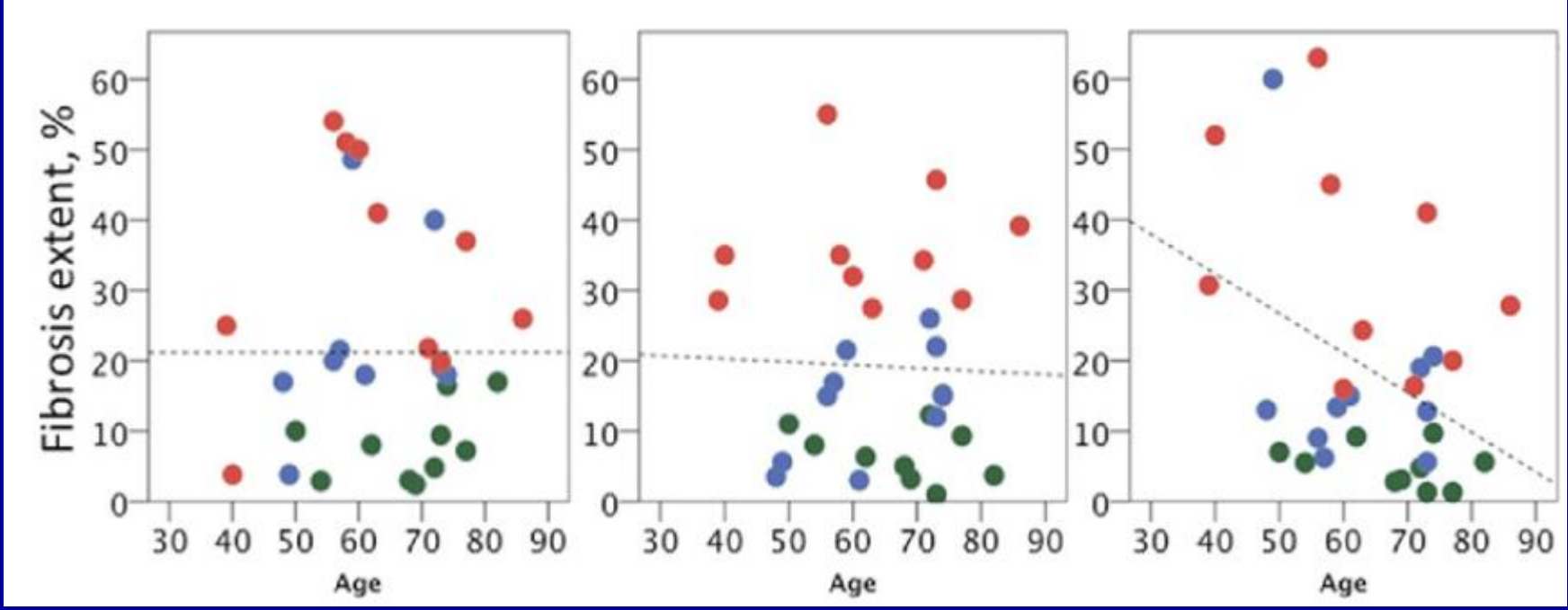
SR AF



Boldt et al, Heart 2004

The substrate of human AF: pathology

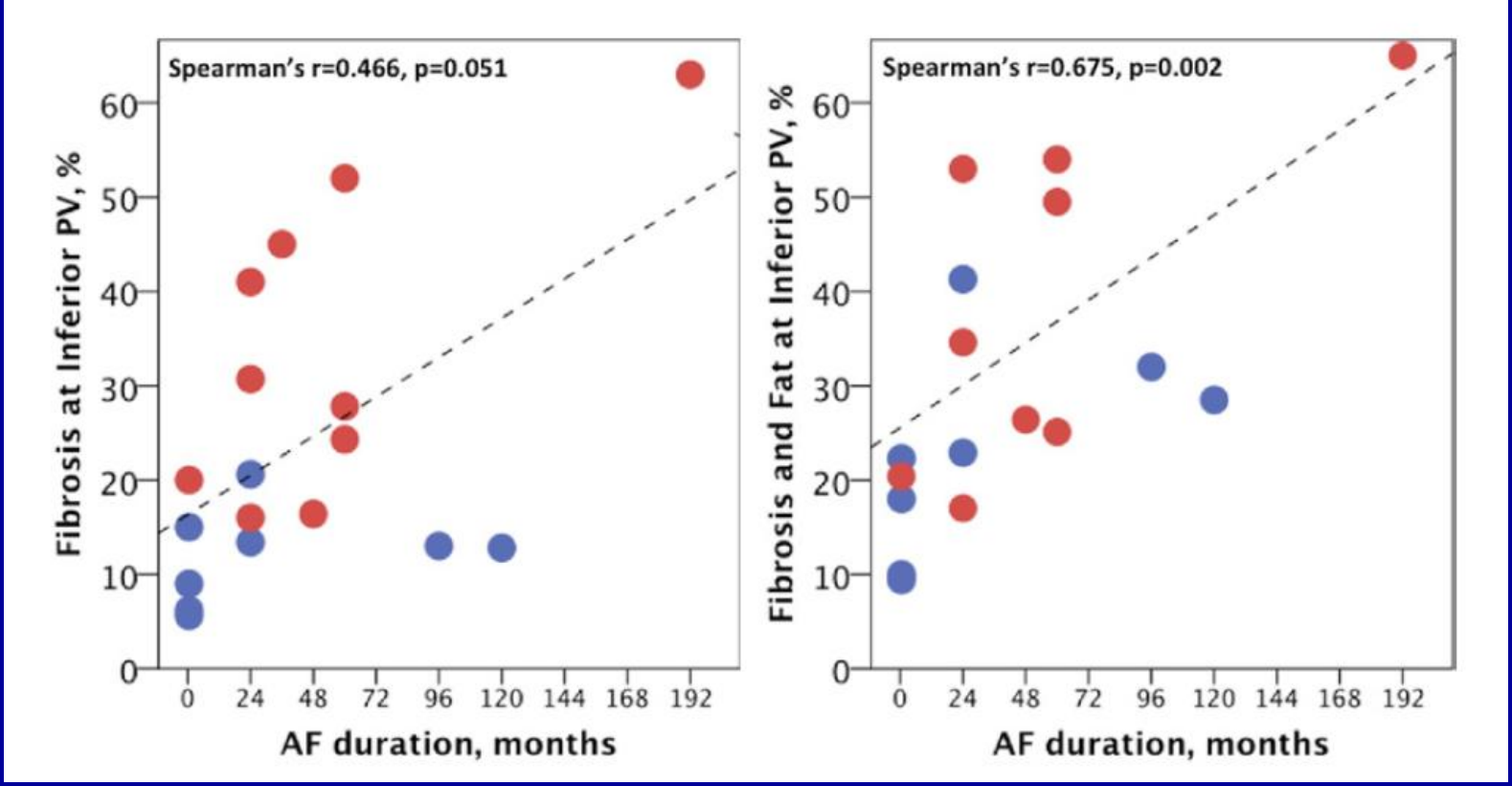
- post mortem analysis of fibrosis
- no AF, PAF, permanent AF
- correlation with age



Platonov & Ho, JACC 2011

The substrate of human AF: pathology

- Fibrosis and AF type (PAF, permanent AF)



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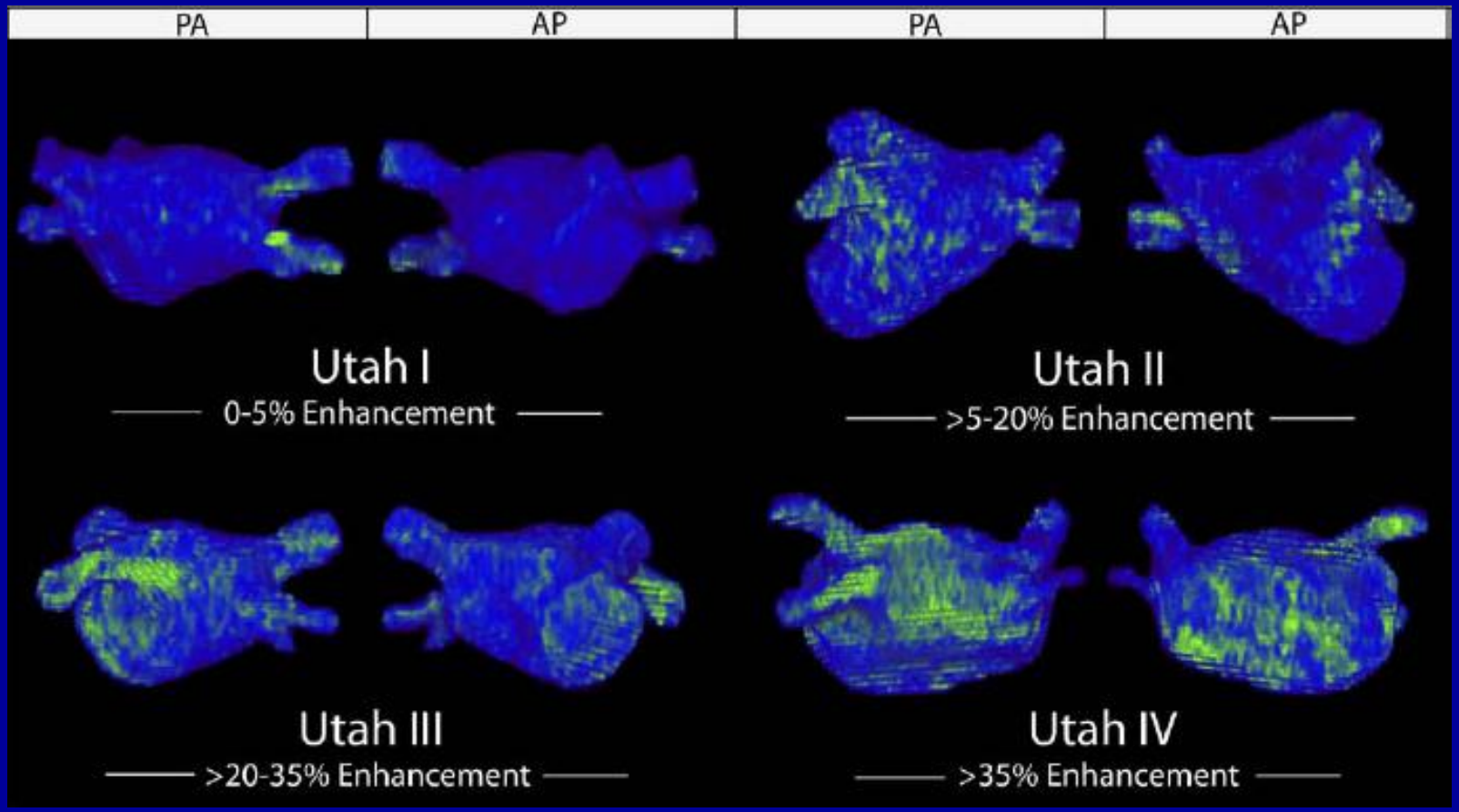
Substrate of human AF

- Significant structural re-modeling, i.e. extensive atrial fibrosis, has been found in lone AF, paroxysmal and persistent AF. However, there seem to be only weak correlations between AF duration and extent of fibrosis.
- Age does not correlate with fibrosis.

Visualisation of fibrosis with DE MRI



Mahnkopf et al., Heart Rhythm 2010

Visualisation of fibrosis with DE MRI

Table 3 Distribution in Utah I to IV

	Total (n = 333)	Lone AF (n = 40)	Non–lone AF (n = 293)	*P* value
Utah I, n (%)	21	4 (10)	17 (5.8)	.298
Utah II, n (%)	141	26 (65)	187 (63.82)	.884
Utah III, n (%)	148	9 (22.5)	67 (22.87)	.959
Utah IV, n (%)	23	1 (2.5)	22 (7.51)	.334

Mahnkopf et al., Heart Rhythm 2010

Visualisation of fibrosis with DE MRI

CONCLUSION—The degree of LA structural remodeling as detected using DE-MRI is independent of AF type and associated comorbidities. Selecting appropriate treatment candidates based on the quality and quantity of atrial fibrosis using DE-MRI would improve procedural outcome and avoid unnecessary intervention.

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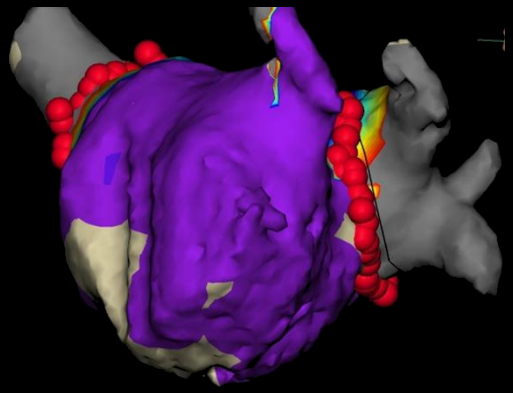
- DE MRI: the extent of fibrosis does not correlate with type of AF and co-morbidities.

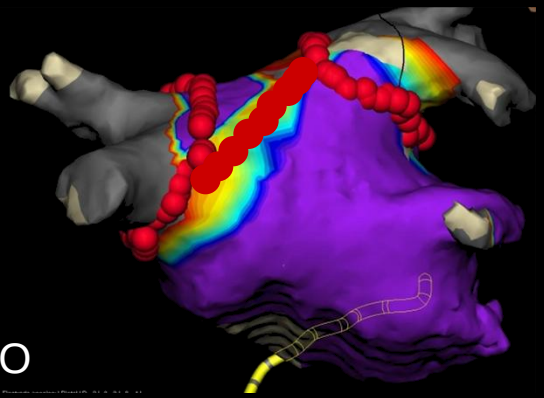
Substrate analysis: generation of voltage maps

Individualized lesion deployment according to fibrosis

Case II

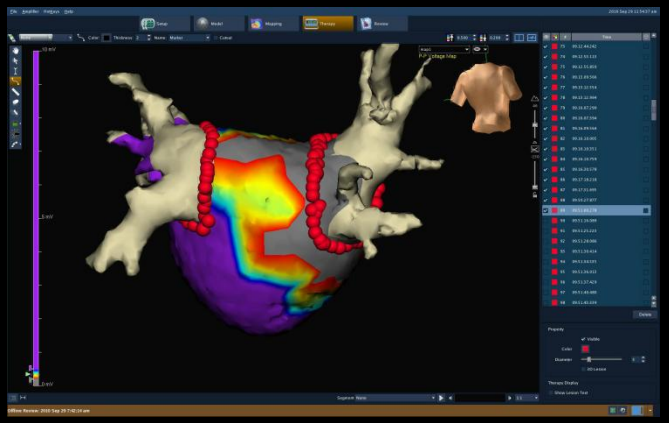


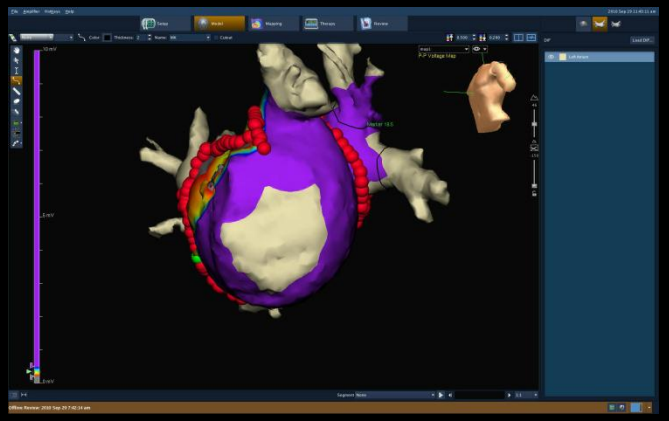
LAO

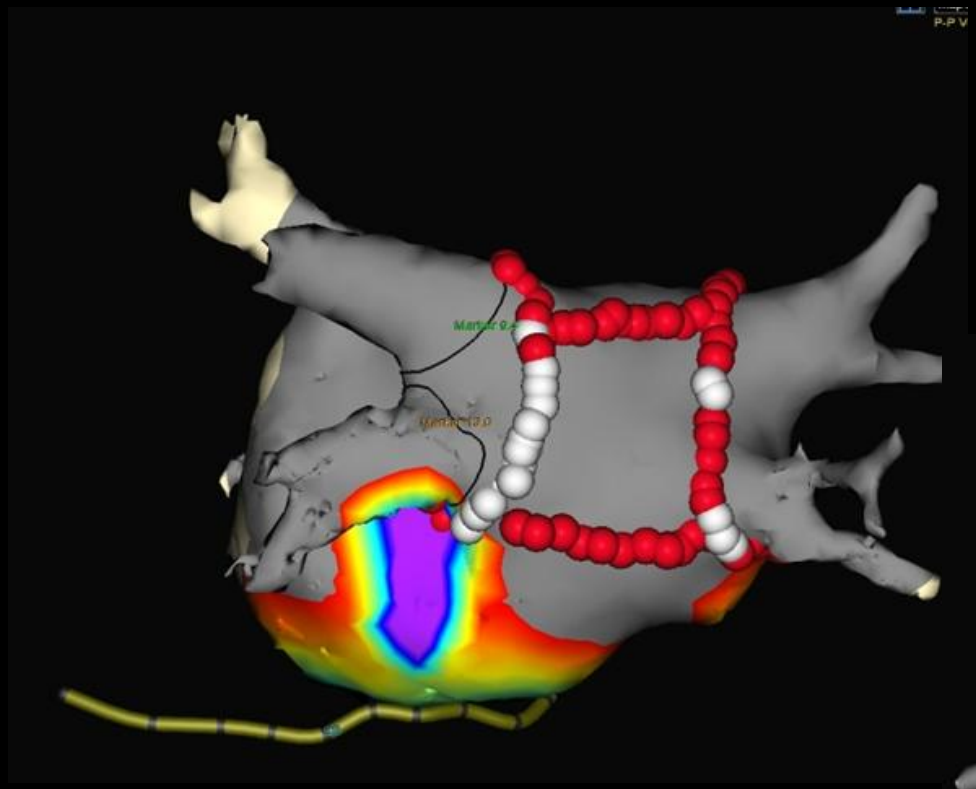


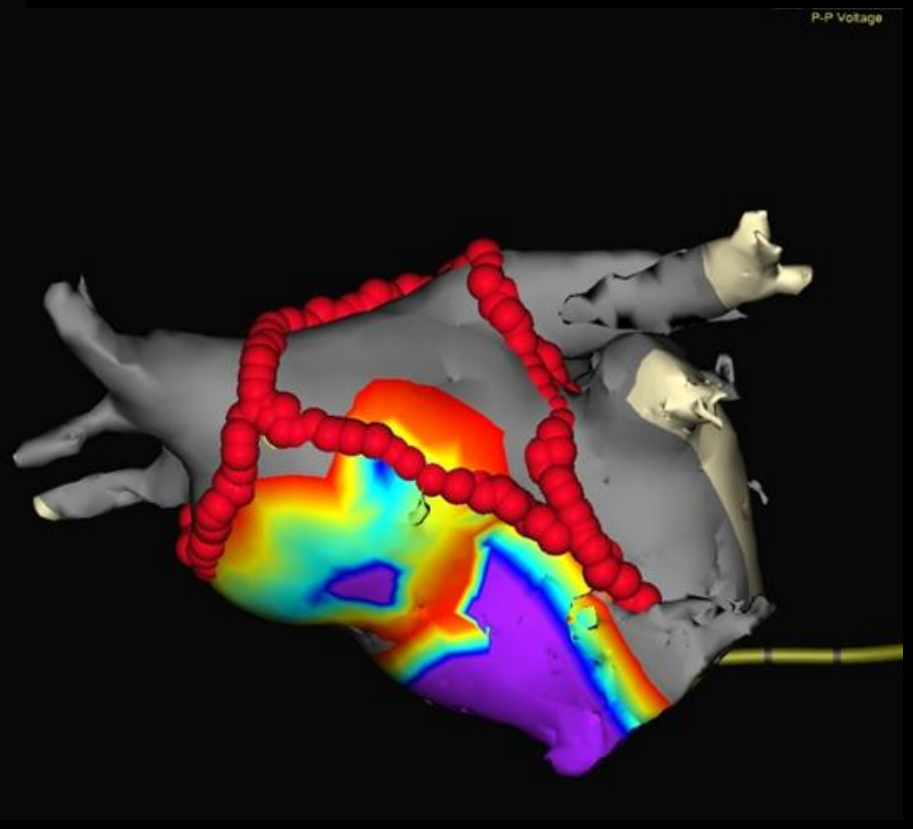
RAO

Case III



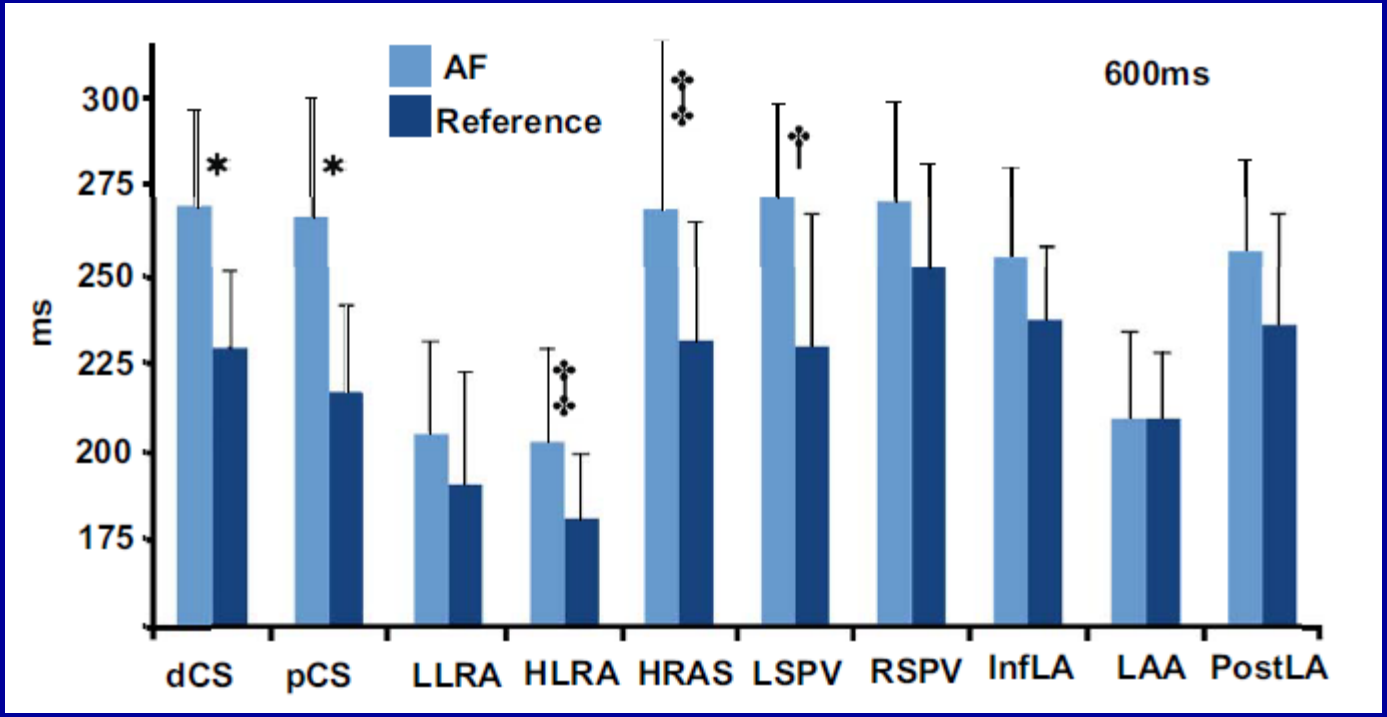





P-P Voltage

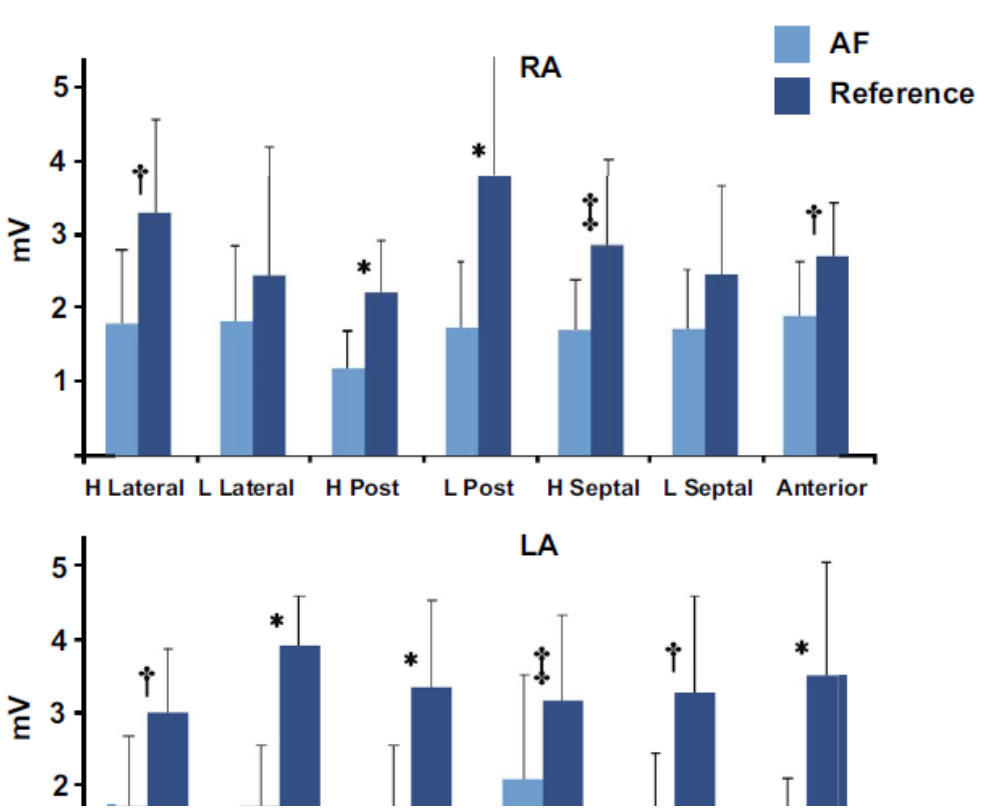
Electrophysiological studies in lone AF

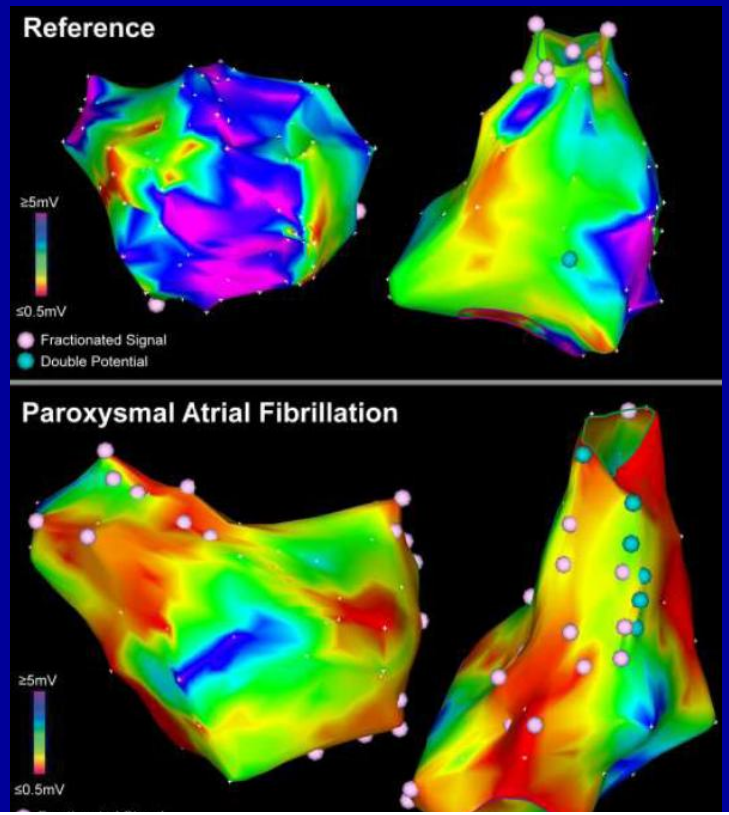
- 25 pts. with lone AF ***without*** arrhythmia in the week prior
- compared to 25 patients without AF
- conduction time & velocity, refractory periods, voltage



Stiles et al, JACC 2011

Electrophysiological studies in lone AF





Conclusions

Patients with paroxysmal lone AF, remote from arrhythmia, demonstrate bi-atrial abnormalities characterized by structural change, conduction abnormalities, and sinus node dysfunction. These factors are likely contributors to the "second factor" that predisposes to the development and progression of AF. (J Am Coll Cardiol 2009;53: 1182–91) © 2009 by the American College of Cardiology Foundation

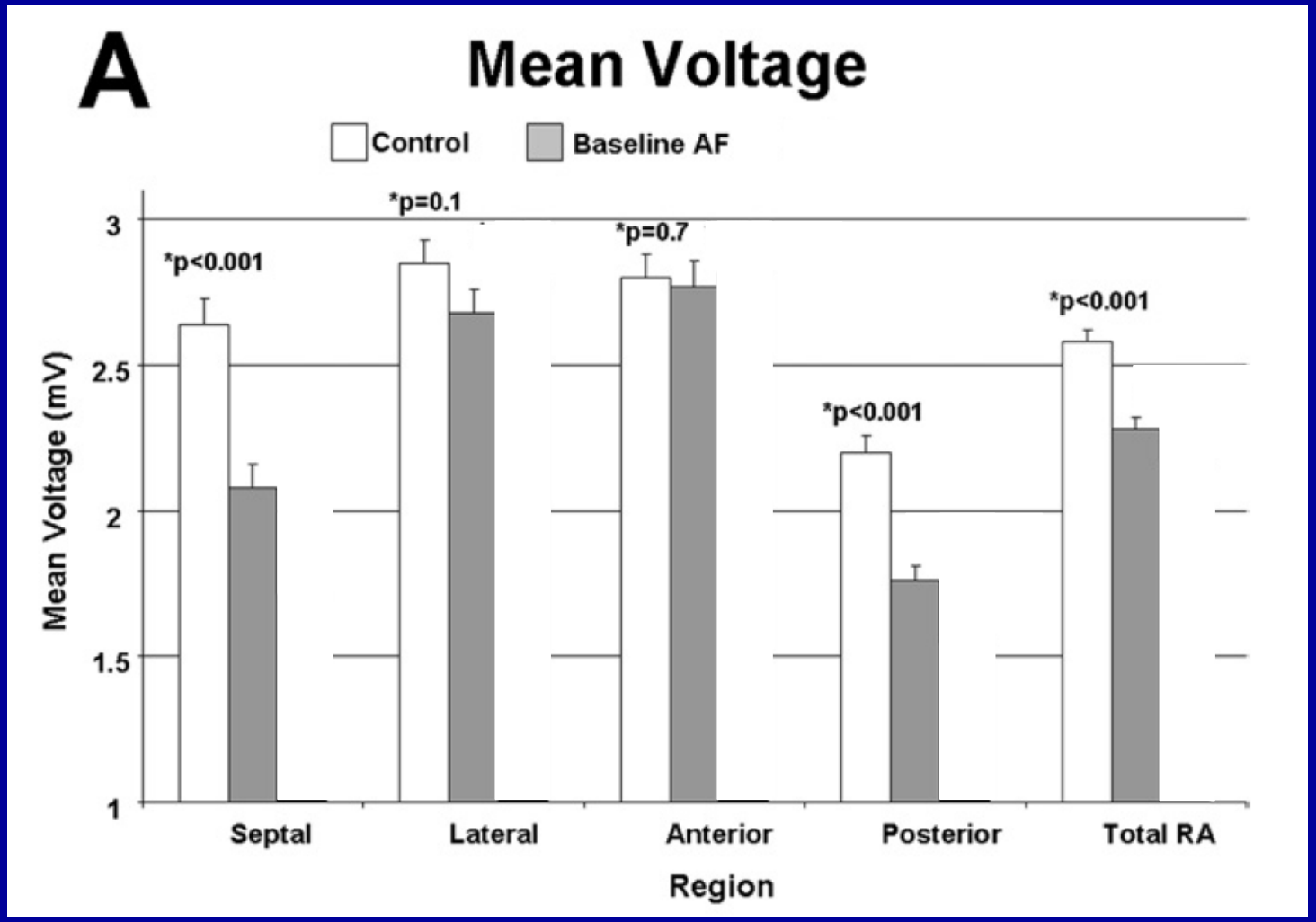
Stiles et al, JACC 2011

Is there reversed remodeling after catheter ablation?

- 11 pts. with AF and no apparent structural heart disease were compared to 11 control patients
- Detailed right atrial voltage maps, conduction properties, refractory periods were assesed at baseline and > 6 months after successful AF ablation.
- Mean FU at re-study was 10±13 months

Teh et al, Heart Rhythm 2012

Is there reversed remodeling after catheter ablation?



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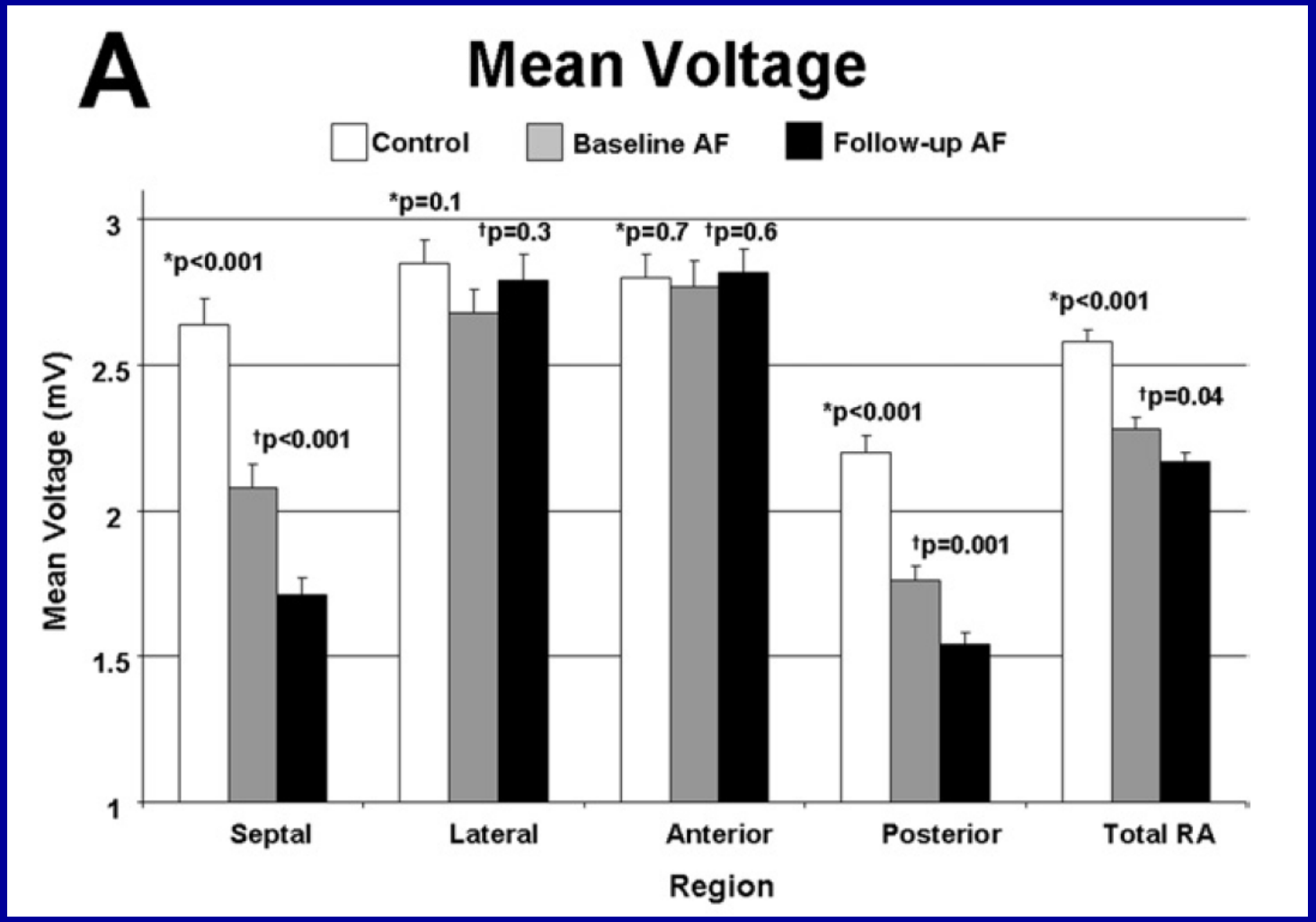

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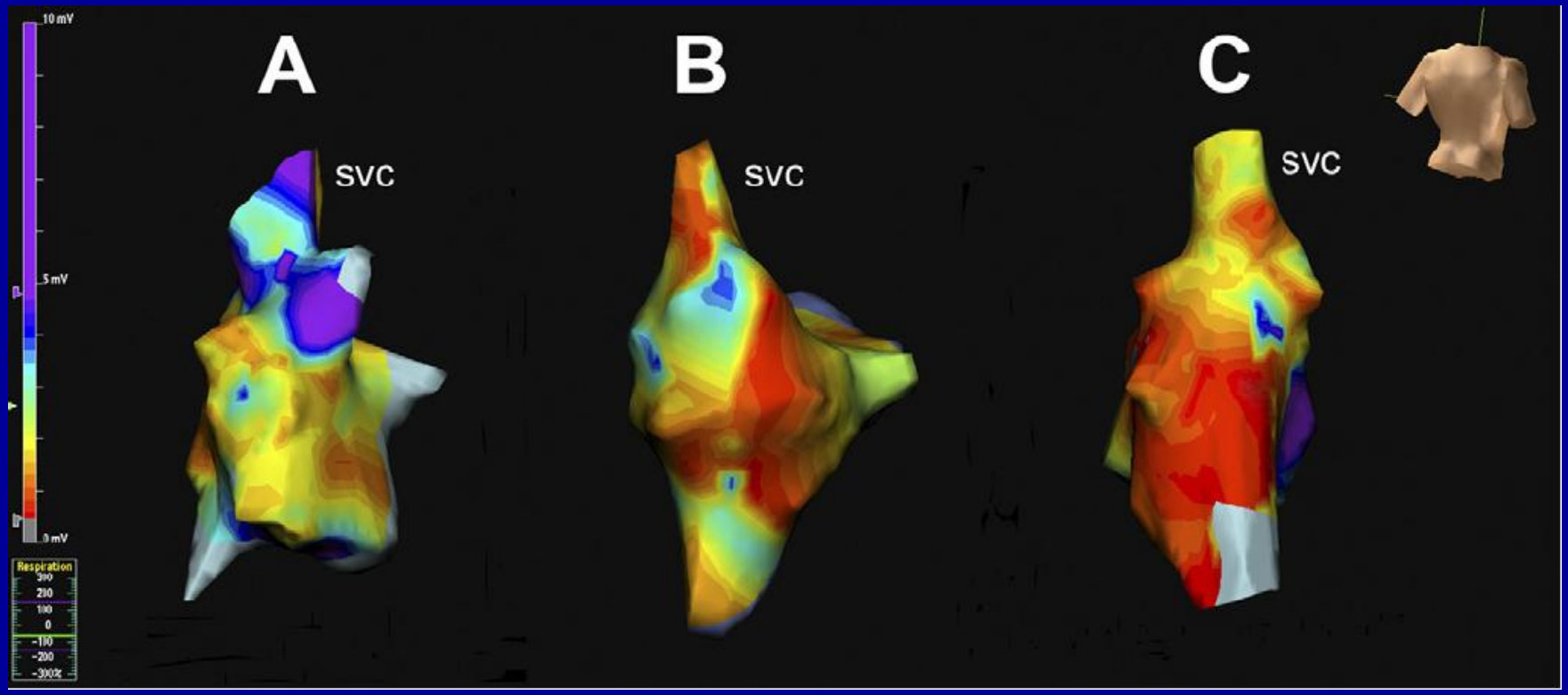

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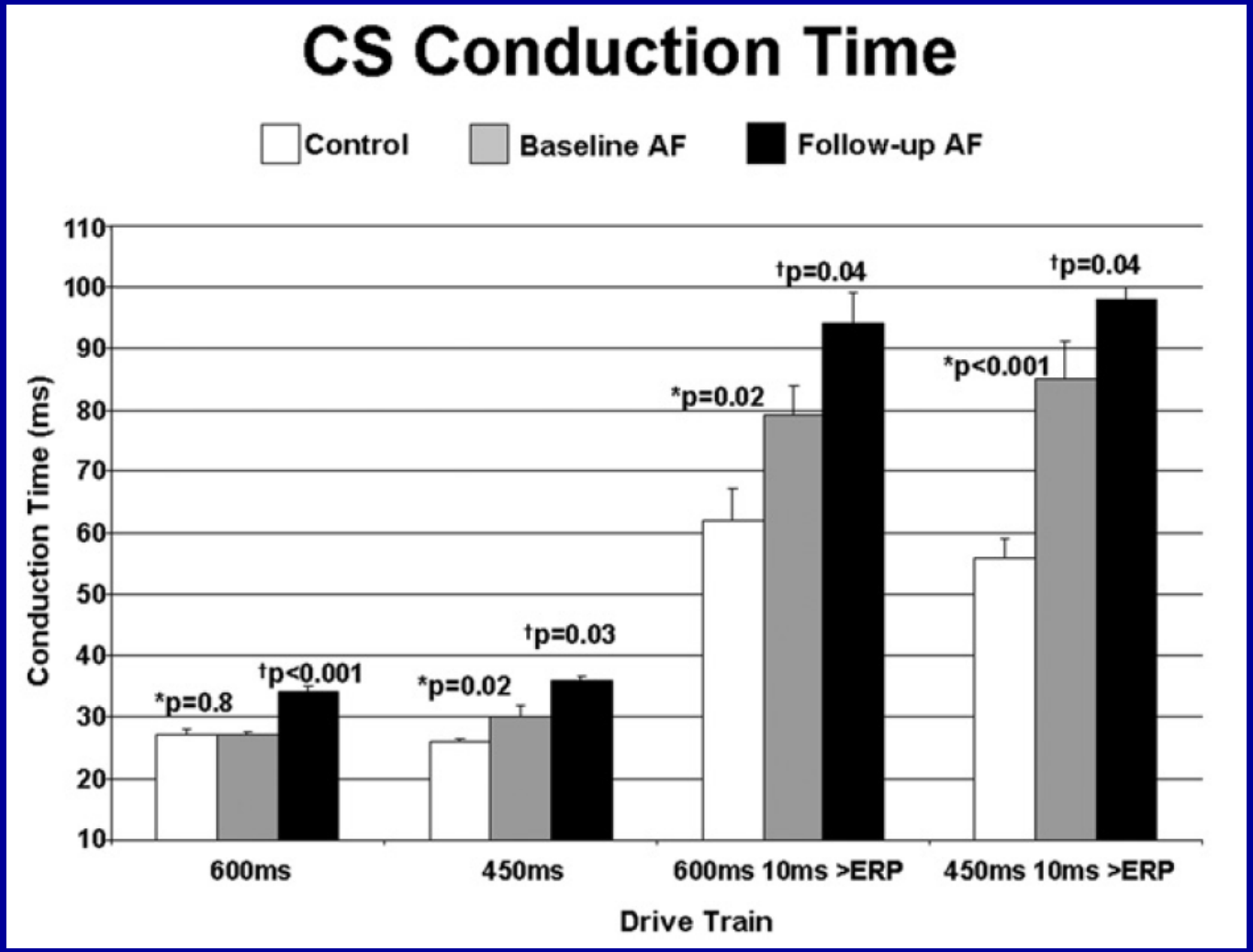

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- Significant structural re-modeling, i.e. extensive atrial fibrosis, has been found in lone AF, paroxysmal and persistent AF. However, there seem to be only weak correlations between AF duration and extent of fibrosis.
- Age does not correlate with fibrosis.
- DE MRI: the extent of fibrosis does not correlate with type of AF and co-morbidities.
- Human EP studies in patients with lone AF clearly show a significant electrophysiolocial re-modeling even in “early” stage of AF.
- This re-modeling may be irreversible. Moreover, it seems possible that there is substrate progression despite successful ablation.

Final thoughts

- There is growing evidence that the concept of “AF begets AF” may not be fully applicable in human AF.
- Even in early stages of (lone) AF significant re-modeling can be observed.
- It seems to be likely that “second factors”, e.g. fibrosis that promotes AF, are operative in the progression of AF.
- Atrial re-modeling may be irreversible – this should give rise to consider early intervention. However, it is unknown at present whether progression of AF is affected by successful ablation in
  - all patients
  - selected patient populations
  -…or not at all.

Future perspective

- Longitudinal studies are needed to better understand the "natural" progression of AF in different subset of patients – I believe they are not all the same.
- Non-invasive imaging using MRI seems to be the best approach to systematically generate such data.
- Genetic studies on potential "second factors" may further improve our understanding of AF progression.
- Invasive substrate-based treatment of AF in an MRI environment seems desirable…..and feasible in the near future.