



# Welchen Vorteil bietet die Cryoablation bei Vorhofflimmern?

**B. Keweloh**

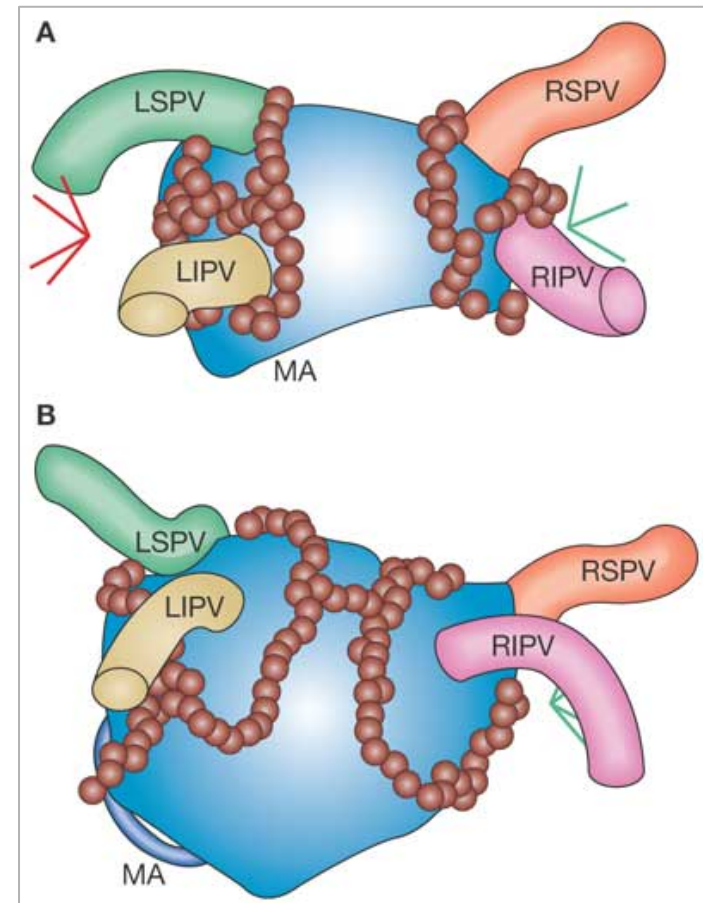
**Unfallkrankenhaus Berlin**

Kardiologie heute  
Berlin 20.11.2010



# Standards of Radio Frequency Ablation of Atrial Fibrillation

1. Pulmonary vein isolation
2. Additional substrate modification of LA:
  - Linear Lesions
  - CAFE Ablation
  - Ganglionated Plexus Ablation





## Complications RF-PV Isolation

Pulmonary vein stenosis	1,3	%
Esophageal injury	0,25	%
Coronary artery injury	0,25	%
Cardiac tamponade	2,4	%
Phrenic nerve injury	0,5	%

\*\* Pooled data from n>50 published studies using RF Ablation:

Pappone et al	JACC 2003:42,185-197
Nademanee K et al	JACC 2004:43,2044-53
Kottkamp H et al	JACC 2004:44:869-877
Haissaguerre M et al	JCE 2005:16:1125-1137
Lim et Al	PCE 2006:29:374-379

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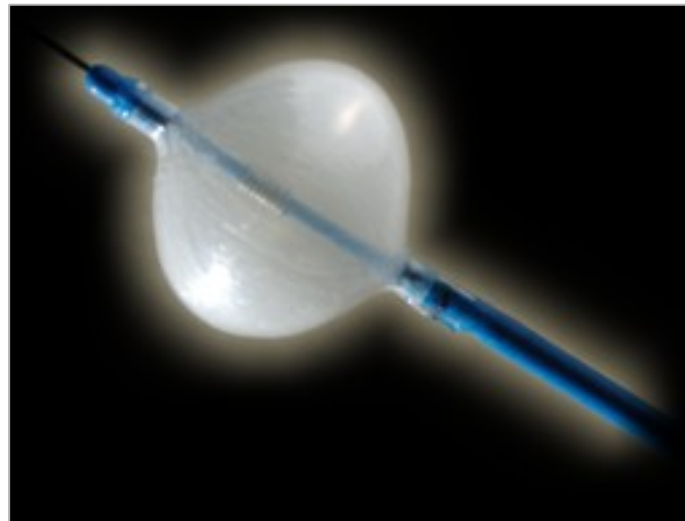


# Alternative Energy Sources to Radio Frequency

- Ultrasound
- Laser
- Freezing / Cryo Technique



# Medtronic / CryoCath Ablation Technology



Arctic Front Balloon



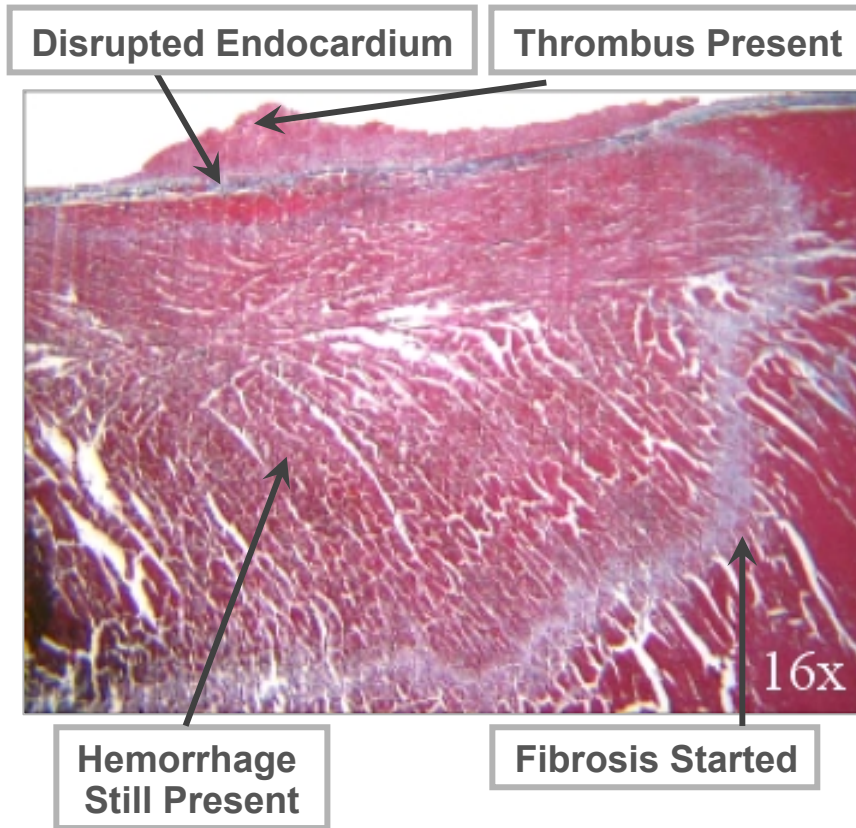
Focal Cryo Ablation Catheters



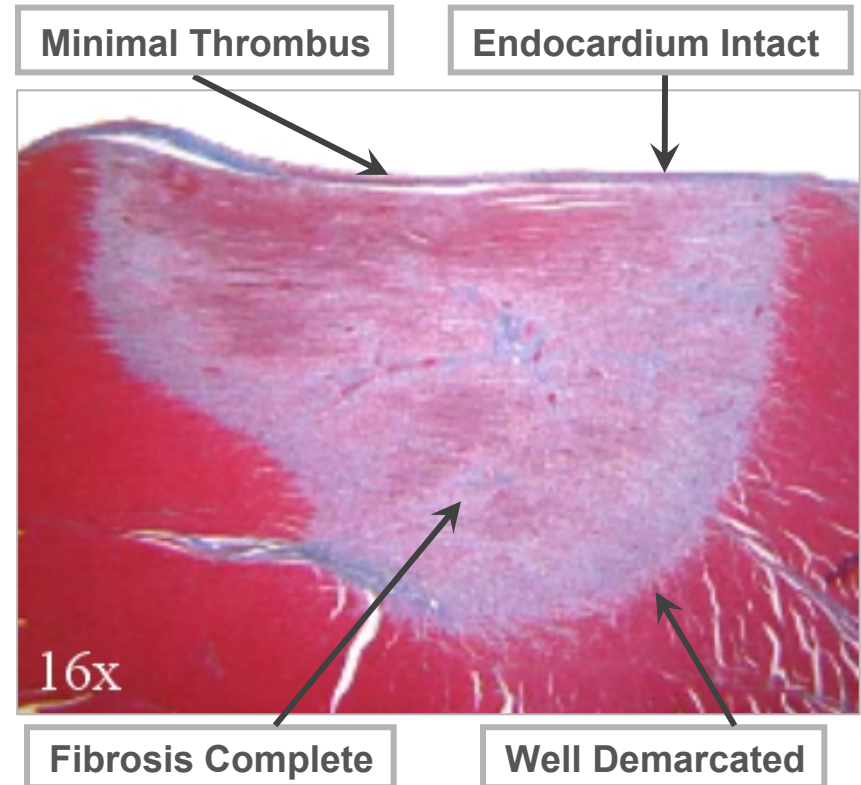
Steerable transseptal Sheath



# Effect on the Connective Tissue Matrix



RF Lesion at 1 Week (canine model)  
+70° C • 50 W • 60 seconds



Cryolesion at 1 Week (canine model)  
-75° C • 1 x 4 minutes

Khairy P, et al. *Circulation*. 2003;107:2045-2050.



# Paroxysmal atrial fibrillation, case report 1

- Male patient, 46 years
- Paroxysmal atrial fibrillation since 2 years
- Takes  $\beta$ -blocker, one episode in 14 days, usually terminated by flecainide as pill in the pocket concept
- Echo and Exercise ECG normal
- LA not enlarged
- No structural heart disease



## Small balloon, single freeze Cryo-PVI approach (ukb)

Symptomatic PAF despite  $\beta$ -blockers, normal LA size, veins < 20mm

- One quadripolar catheter in RVA / SVC
- Single transseptal puncture
- PV angiography
- Occlusion by Cryoballoon, 1 x 300s freezing per vein
- If Occlusiongrade 3 or 4 no Lasso Measurements
- Cardioversion if necessary





# Occlusion Grade

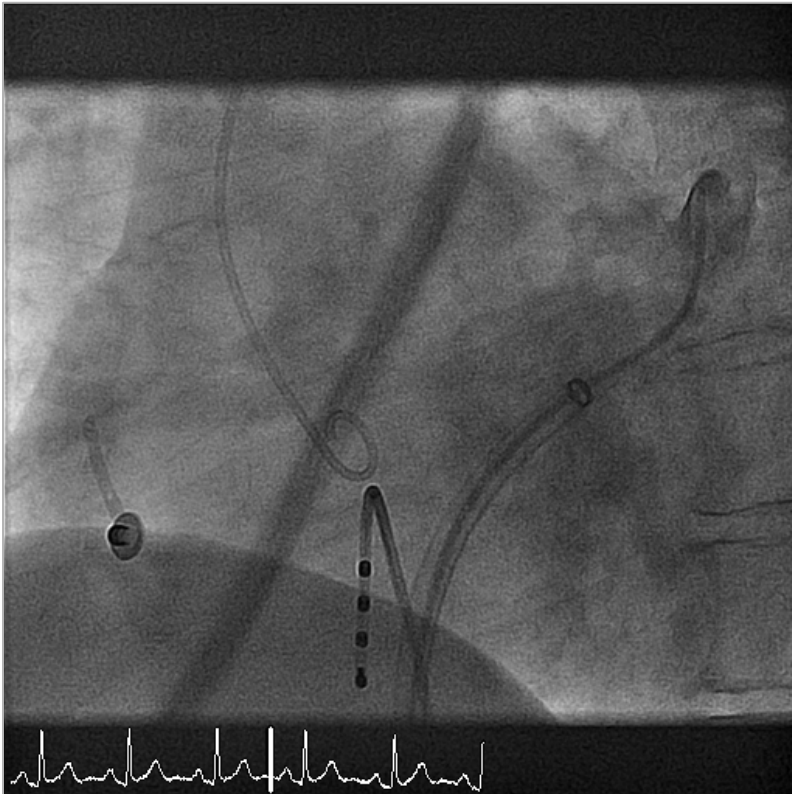
- 1 - no occlusion
- 2 - incomplete occlusion with big contrast leak to LA
- 3 - subtotal occlusion with small leak to LA
- 4 - total occlusion

Neumann, Vogt, Schumacher et al,  
JACC 2008, Vol 52, No 4, 273-78

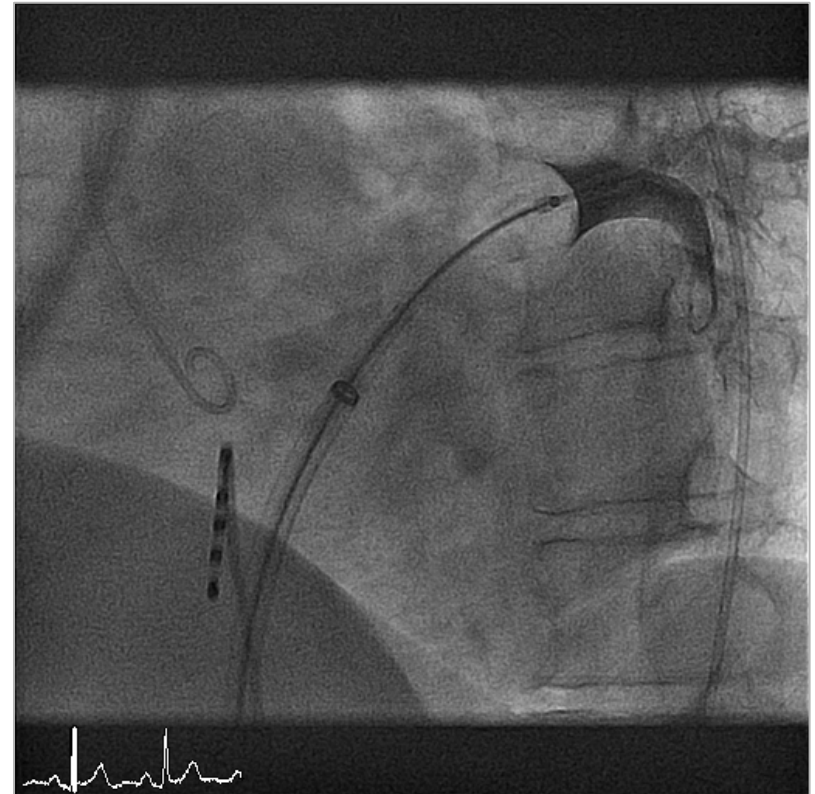


# LSPV

Angiography



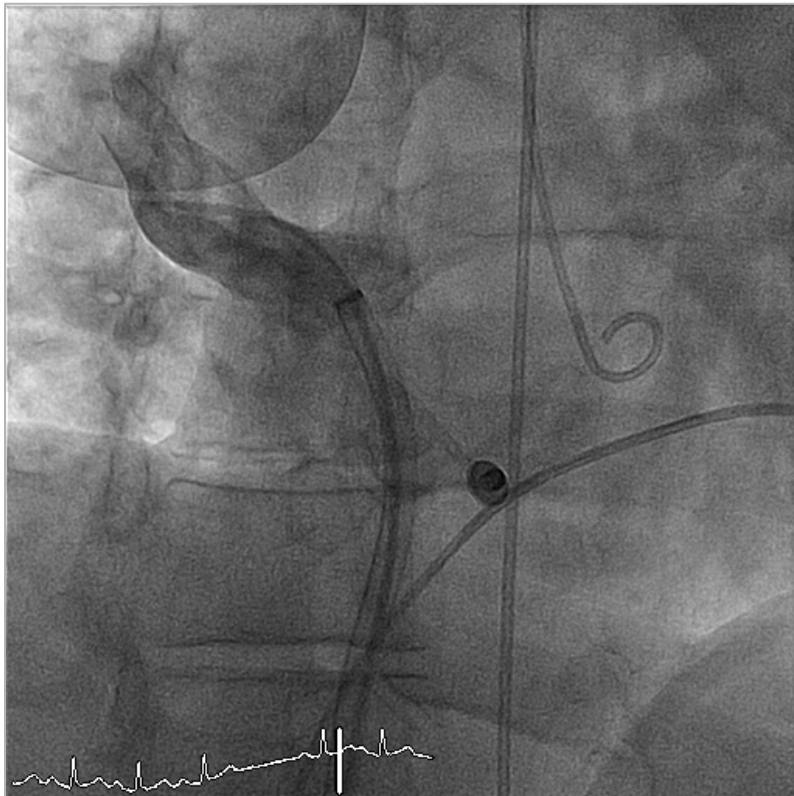
Ablation



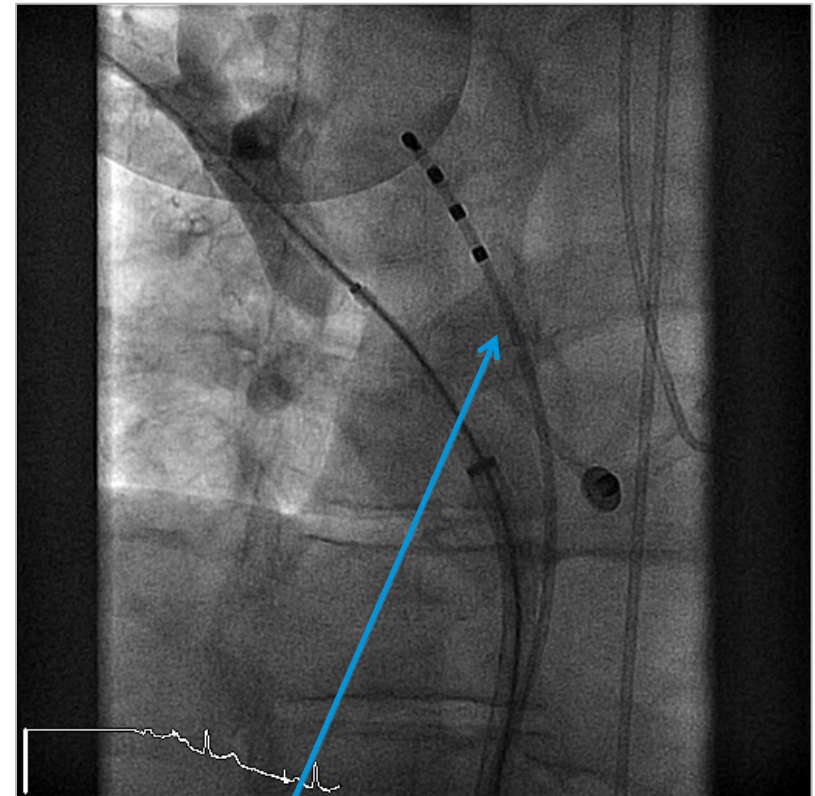


# RSPV

## Angiography



## Ablation

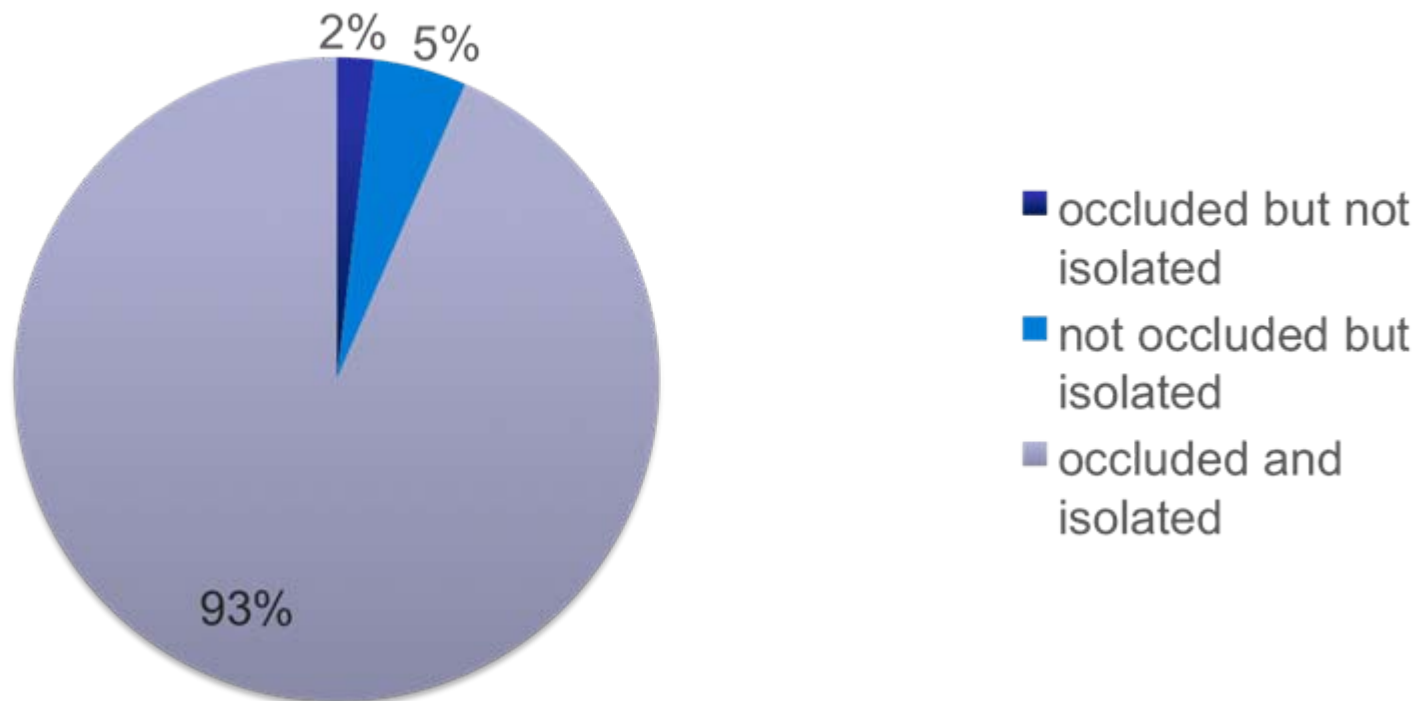


Stimulation catheter in SVC for pacing of right phrenical nerve



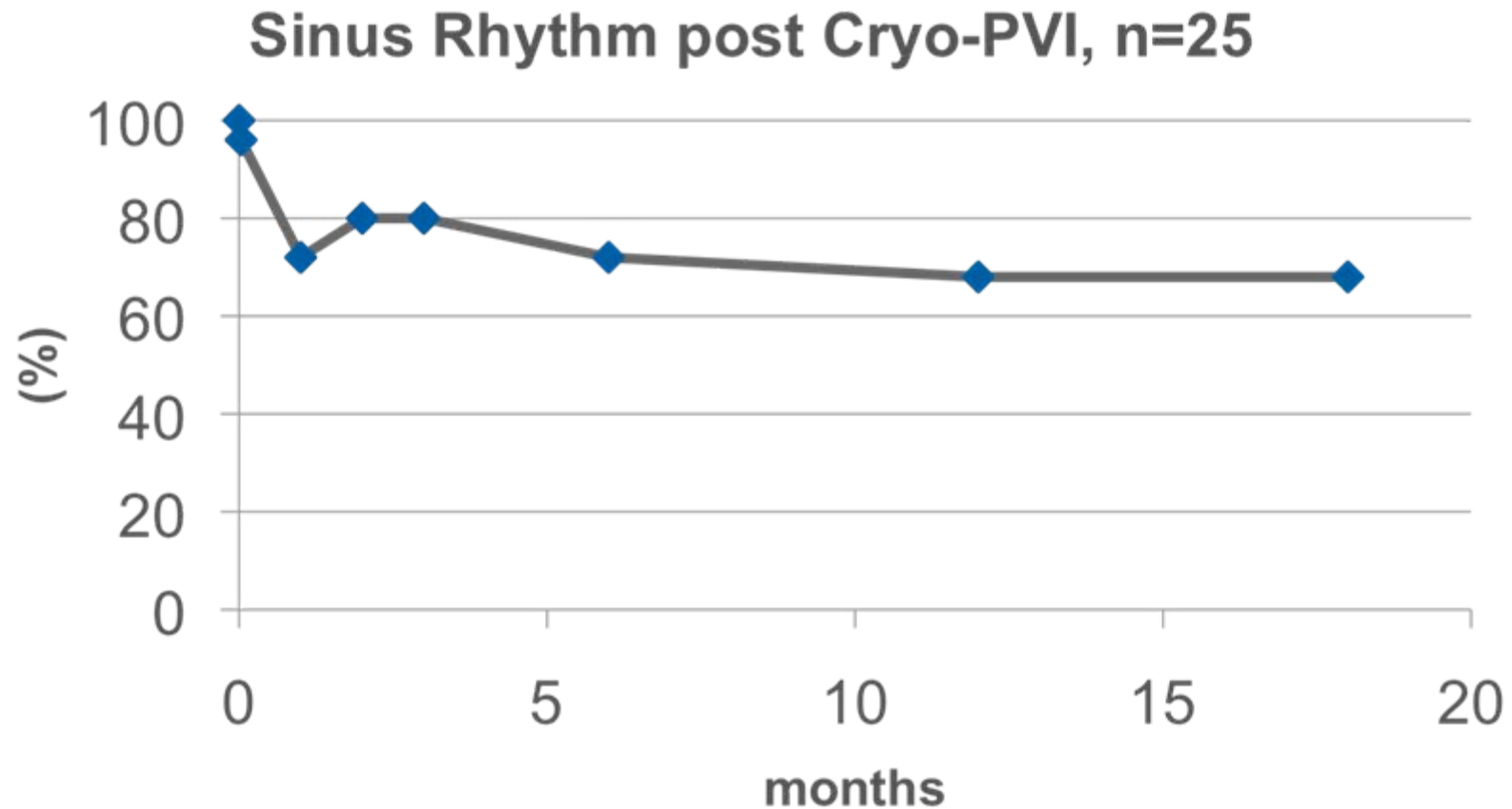
## PV Isolation rate, ukb

Angiographic Occlusion and Electrical Isolation,  
n = 107 treated Veins, 98% isolated





# Small Ballon -Single Freeze - Approach, ukb



Keweloh B, Winterhalter M, Siaplaouras S et al.

CRT 2/2009 Washington, DGK 4/2009 Mannheim, ESC 9/2009 Barcelona, DGK 4/2010 Mannheim, ESC 2010 Stockholm



## PVI Complications ukb, n=70

Pericardial effusion	2/70
Transient ST segment elevation	1/70
Thrombembolic events	0/70
PV Stenosis	0/70
Esophageal injury	0/70
Coronary artery injury	0/70
Left atrial flutter	2/70
Right phrenic nerve palsy, trans.	10/70



# Persistent atrial fibrillation, case report

- Female patient, 57 years
- Hypertension
- EF normal, LA enlarged
- PsAF since 1/2010, before 2 years of PAF
- After cardioversion only 1 week in SR
- Dronedarone efficient but stopped because of QT Prolongation



## Best fitting balloon, standard Cryo-PVI approach

Symptomatic PsAF despite AA, enlarged LA, all vein sizes

- Quadripolar catheter in RVA / SVC
- Transseptal puncture
- PV angiography
- Biggest PV > 20mm = 28mm Balloon  
Biggest PV < 20mm = 23mm Balloon
- 2 x 300-360 s freezing per vein
- CS catheter, Lasso catheter: proof of isolation
- Touch up with Balloon or focal catheter



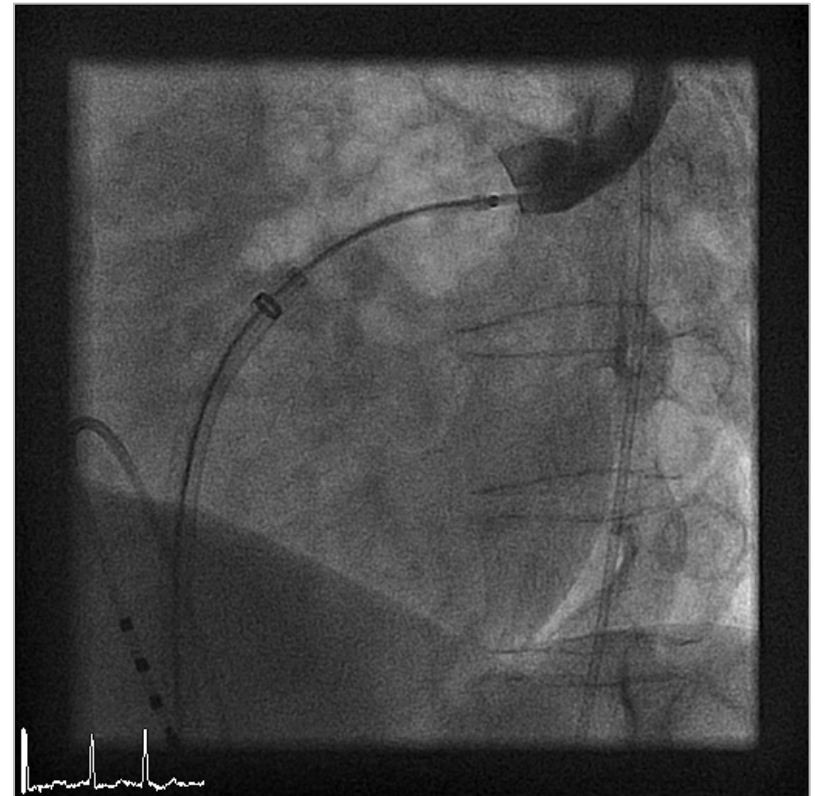
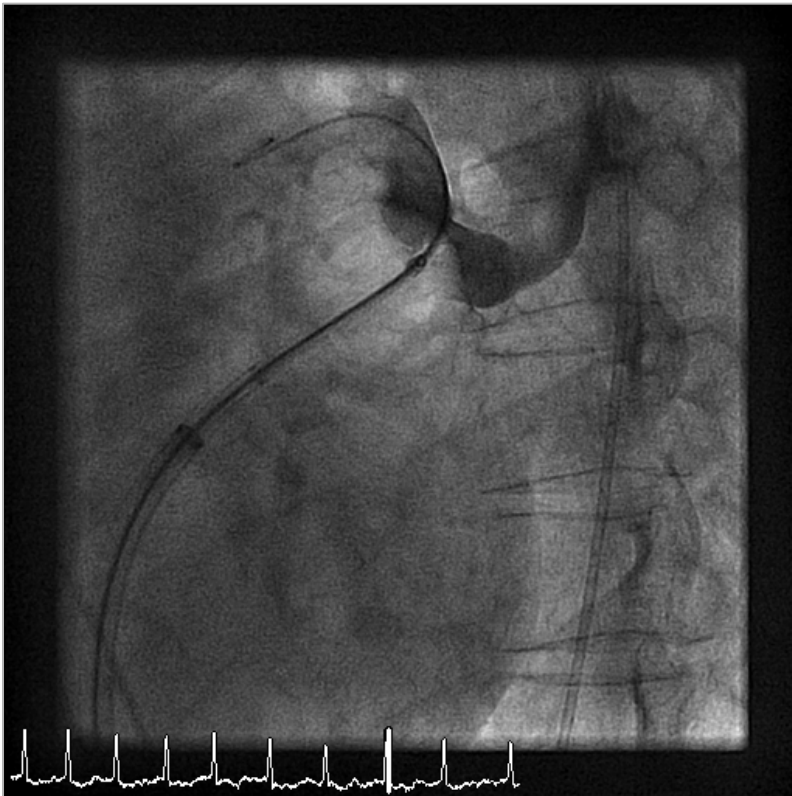


# LSPV

## Ablation

Guide wire in **upper** branch

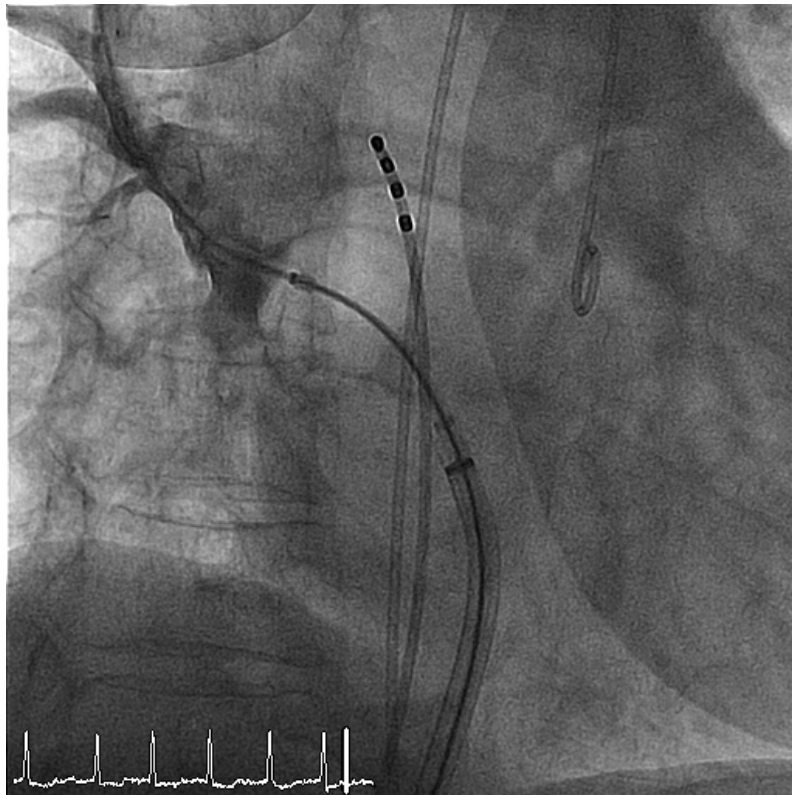
Guide wire in **lower** branch





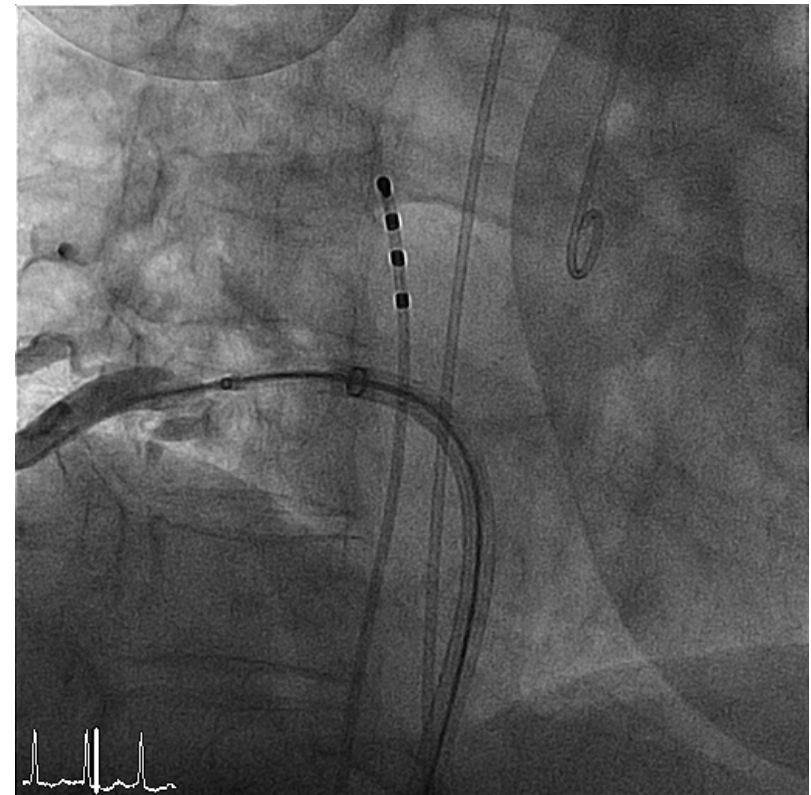
# RSPV

Ablation



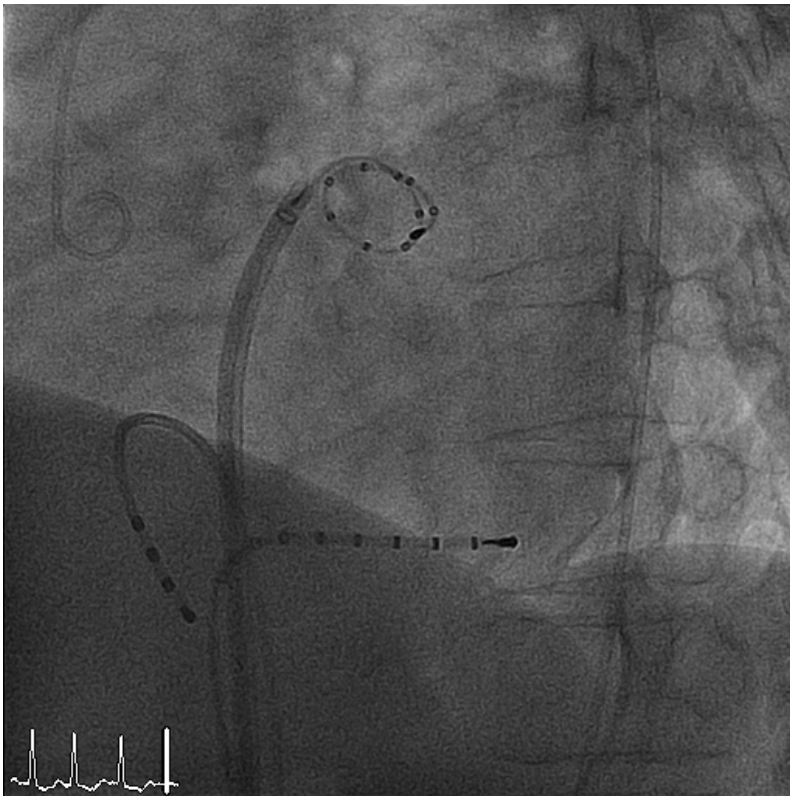
# RIPV

Ablation





# Proof of PV isolation

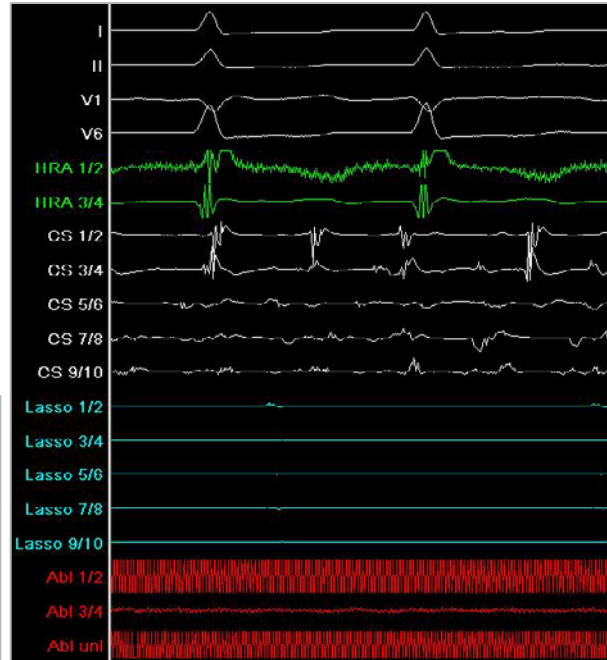
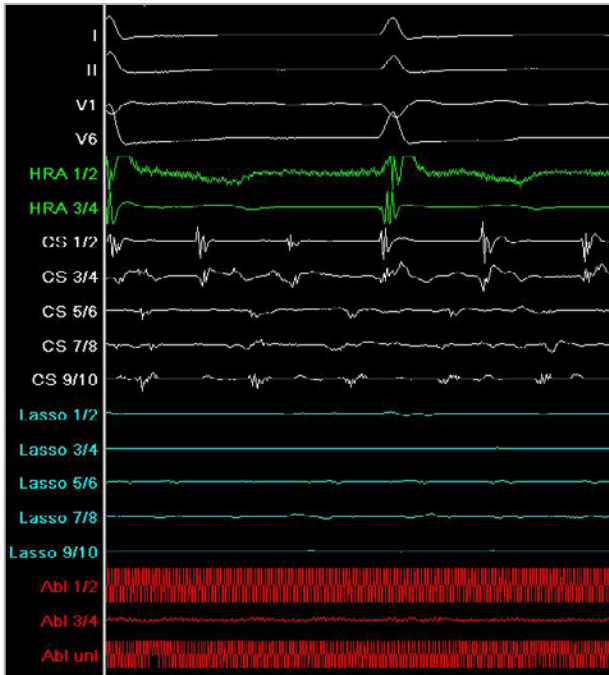


Sizeable  
Lasso catheter

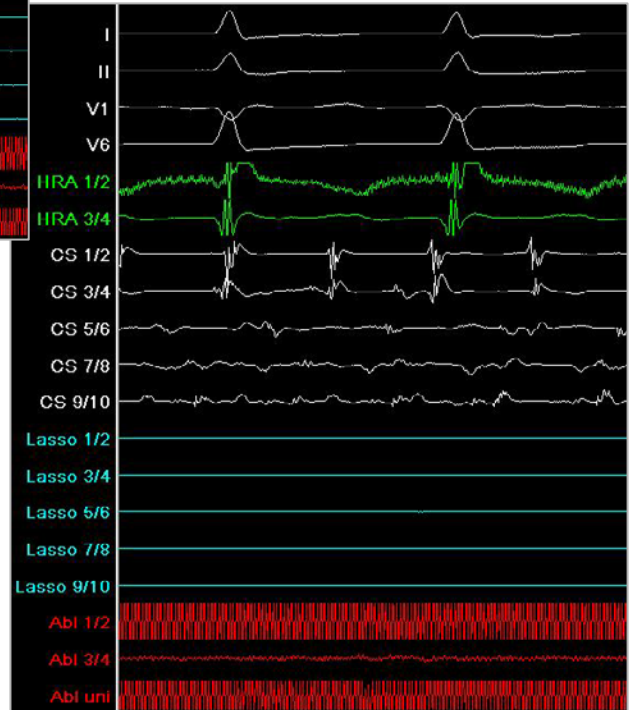
CS catheter



# LSPV OCG 4



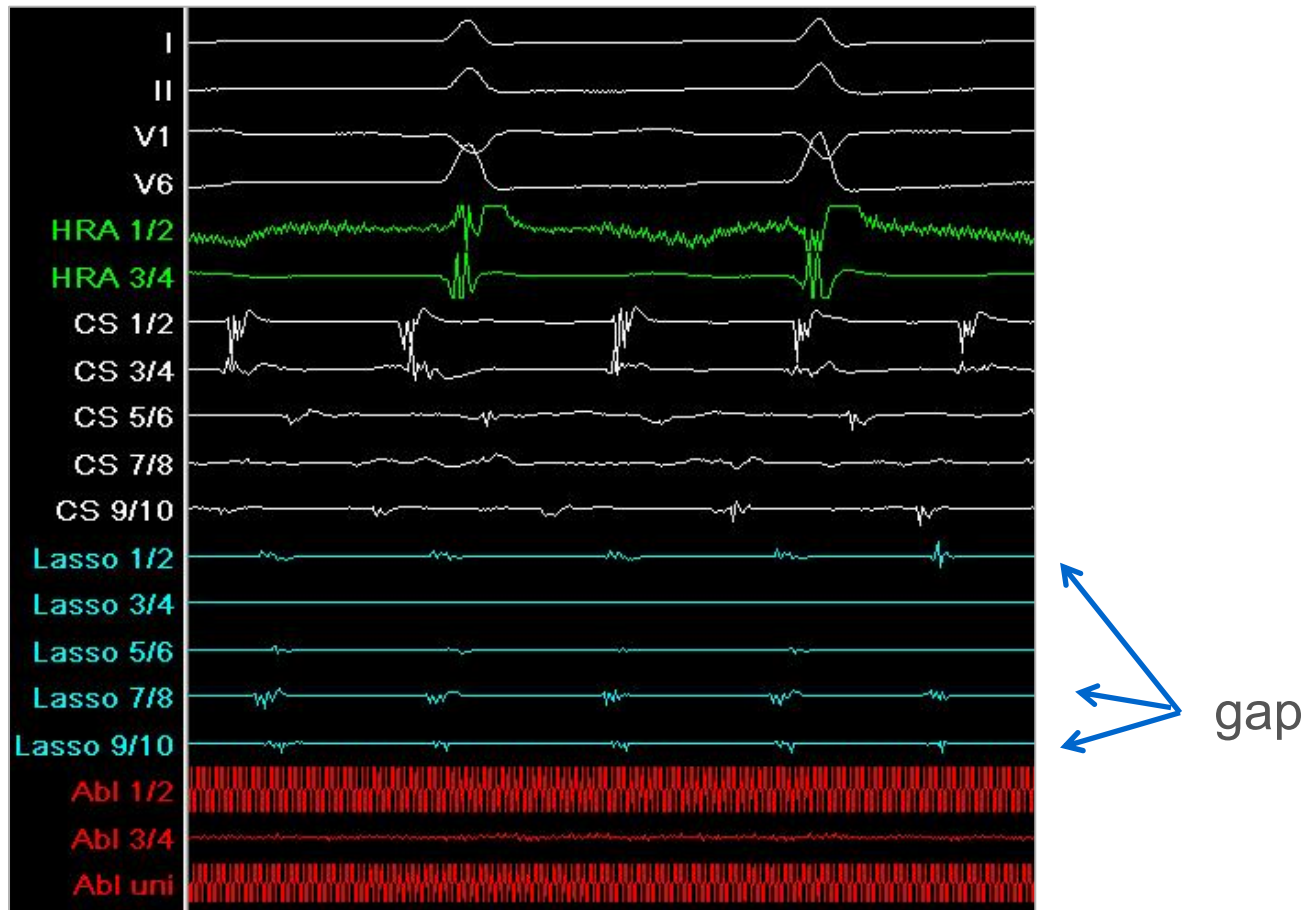
# RSPV OCG 4



# RIPV OCG 3

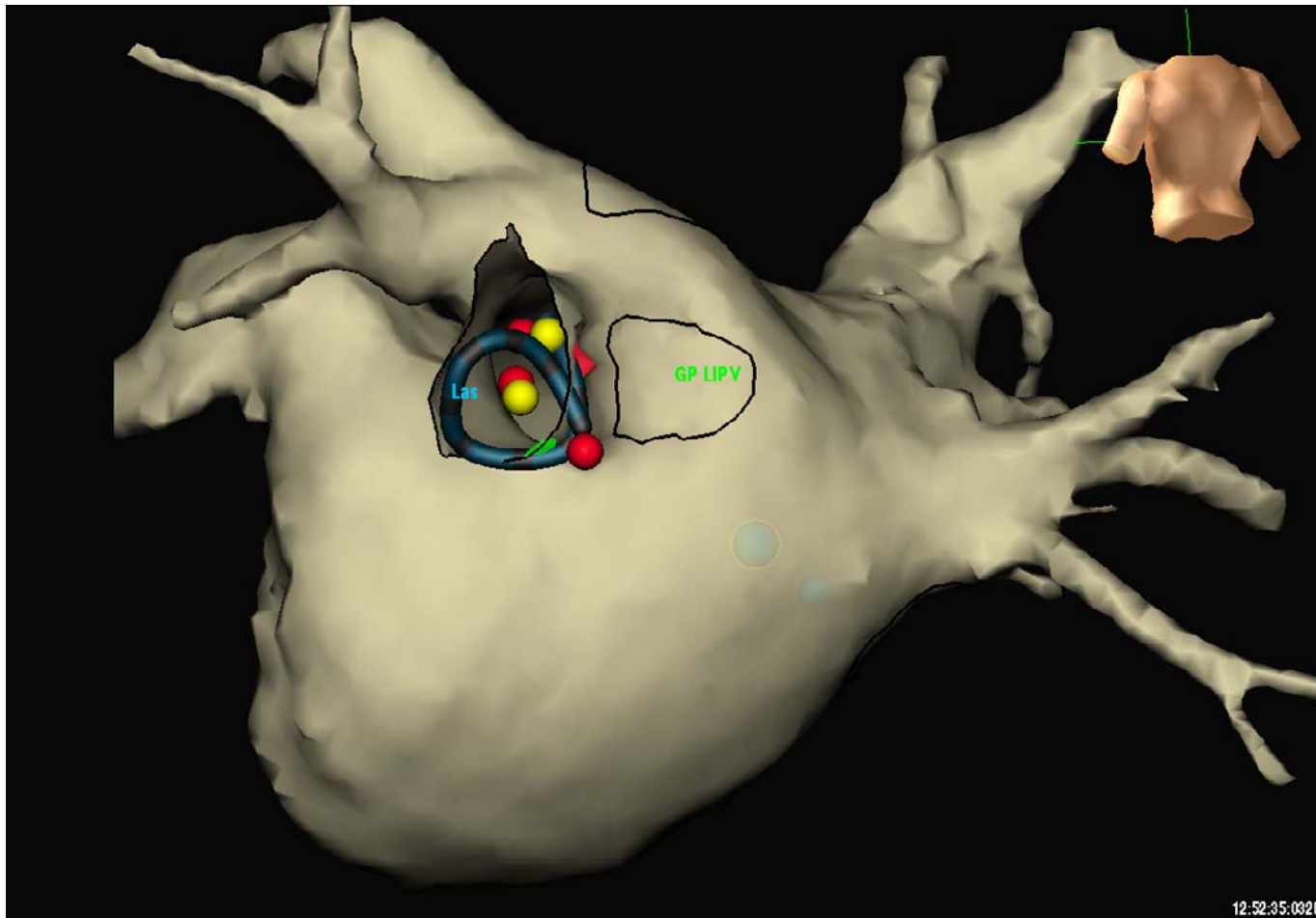


# LIPV post Ablation, Occlusion Grade 3



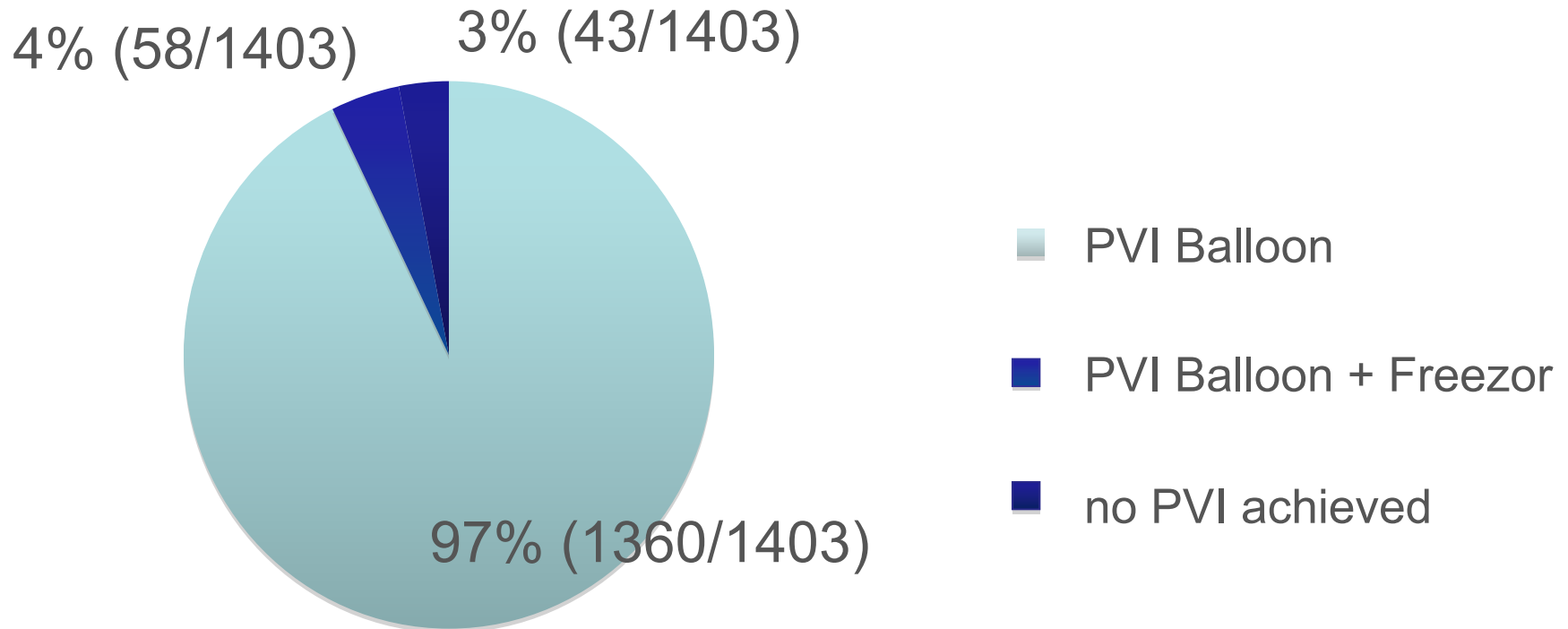


# Closing the Gaps of LIPV





## Acute PV Isolation rate n = 1403



Neumann, Vogt, Schumacher et al,  
JACC 2008, Vol 52, No 4, 273-78



# Success Rate PV Isolation Radio Frequency vs Cryo Technology

	Radio Frequency (%) **	CryoCath (%) *
Paroxysmal Atrial Fibrillation	38-78%	74%
Permanent Atrial fibrillation	35%	38%

\*\* Pooled data from n>50 published studies using RF Ablation:

Pappone et al	JACC 2003:42,185-197
Nademanee K et al	JACC 2004:43,2044-53
Kottkamp H et al	JACC 2004:44:869-877
Haissaguerre M et al	JCE 2005:16:1125-1137
Lim et Al	PCE 2006:29:374-379

....

\* Neumann, Vogt, Schumacher et al, JACC 2008,52,4,273-78





## Complications PV Isolation, n = 346 pts.

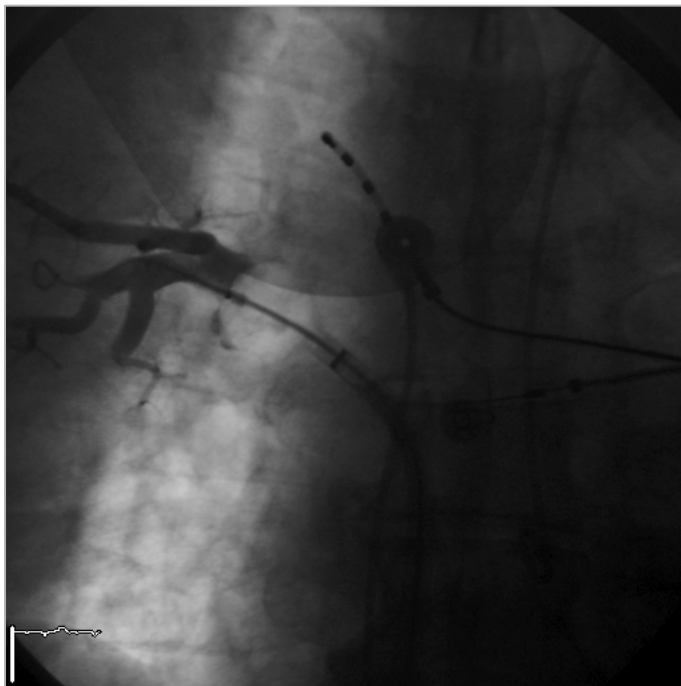
	RF (%)	CryoCath (%)
Pulmonary vein stenosis	1,3	0
Esophageal injury	0,25	0
Coronary artery injury	0,25	0 (0,5 transient ST elevation)
Cardiac tamponade	2,4	0 (0,5 Pericardial effusion)
Phrenic nerve injury	0,5	7,5 (0 one yr follow up)

Neumann, Vogt, Schumacher et al,  
JACC 2008, Vol 52, No 4, 273-78

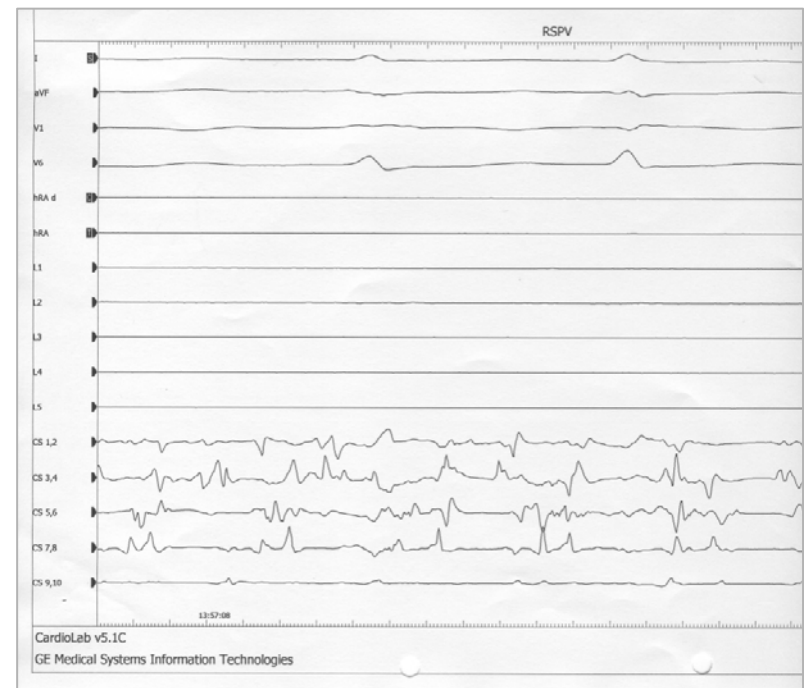


# Ablation RSPV, phrenicus paresis

PP after 140 seconds of cryo application, application immediately stopped, PP transient, no PP at the end of the procedure



Occlusion grade 4

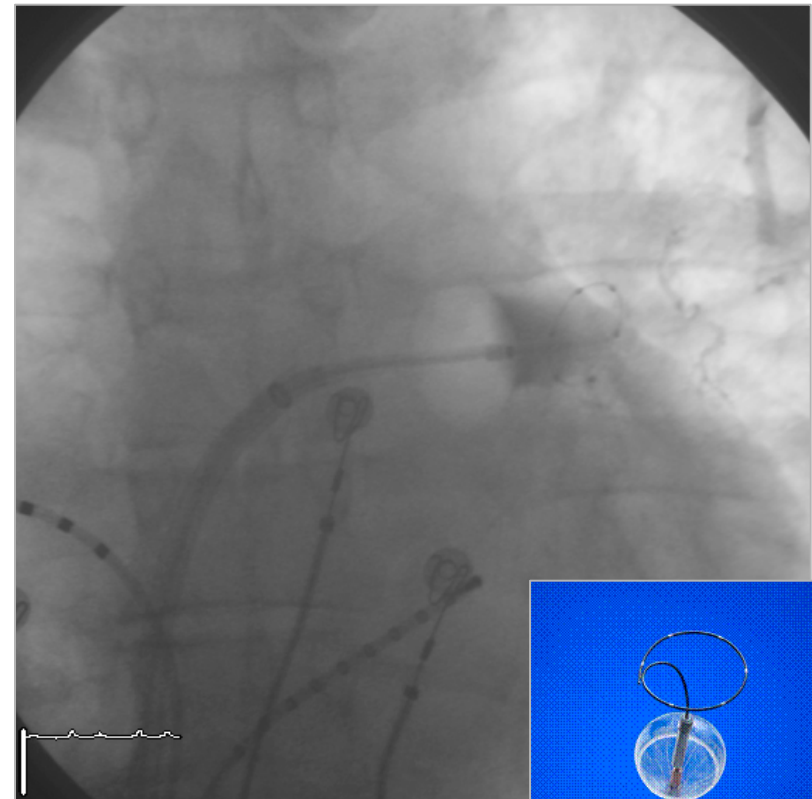
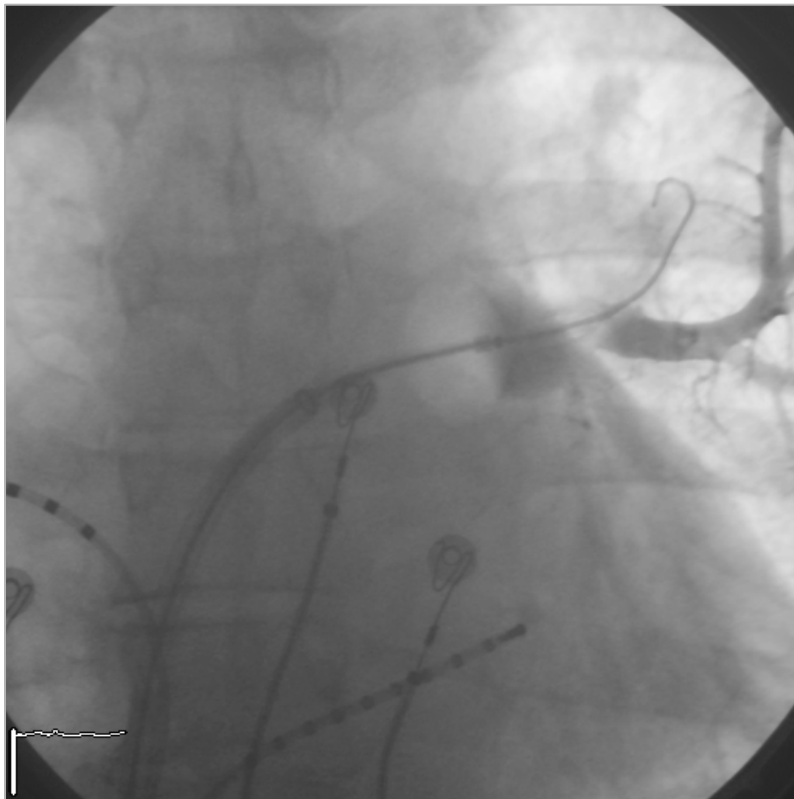


RSPV post ablation



# Ablation LI

## Straight guide wire / Promap Lasso guide wire



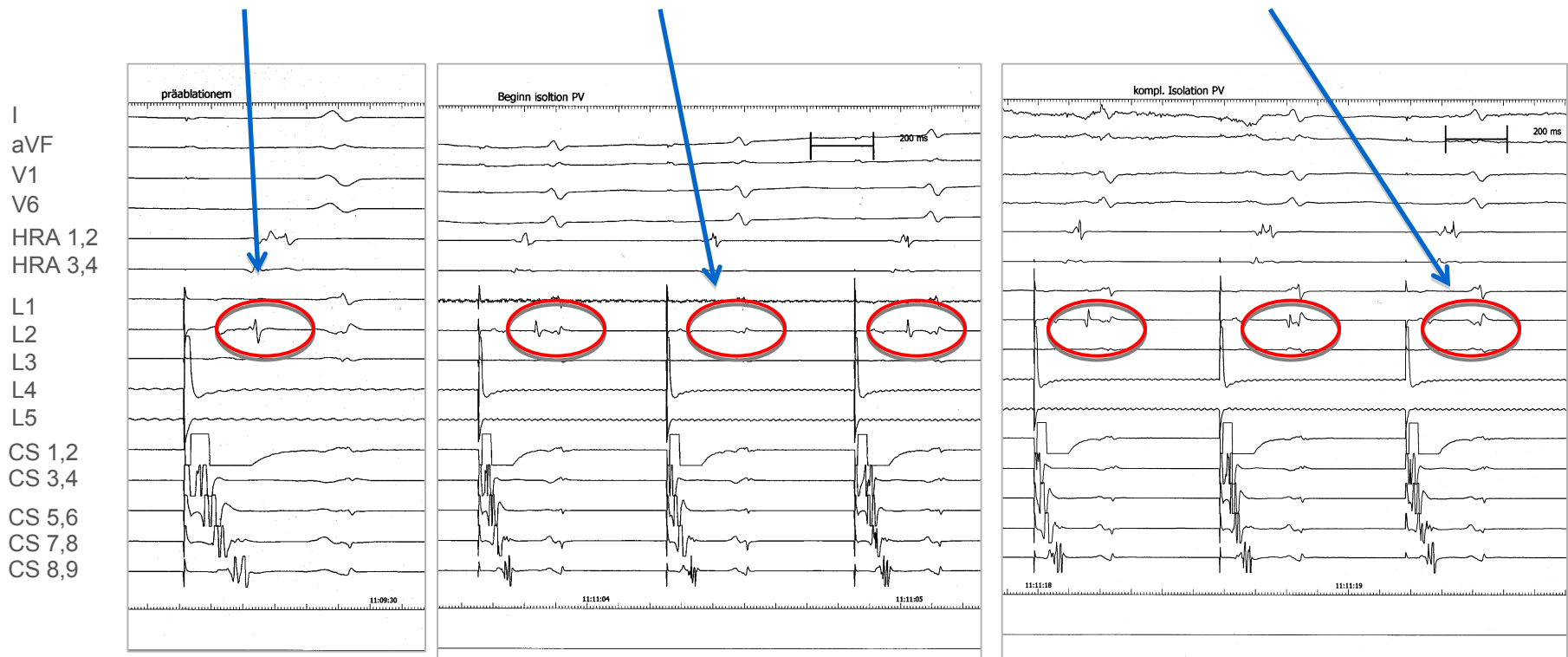


# PV-Isolation, pot. recorded during ablation with ProMAP

Before ablation

First degree block

Complete block after 47 sec





## Time to Block

- 80 Cryo-PVI pts, measurements of time to block by Pro MAP Lasso wire:

Time to Block < 82 sec  
= no PV reconnection  
= no AF reoccurrence  
(spec & sens of 95%)

- good occlusion, short freezing time to block, no reoccurrence of AF



## Cryoballon PVI, first conclusions

- in PAF with normal LA efficient and fast method, very safe, no PV potential measuring necessary if vein totally occluded, single freeze, small balloon approach possible
- bigger veins need bigger balloons, best fitting balloon approach including PV measurements and touch up freezing for all other cases recommended
- in PsAF outcome to poor, additional substrate modification is needed, so far no approach published with cryo

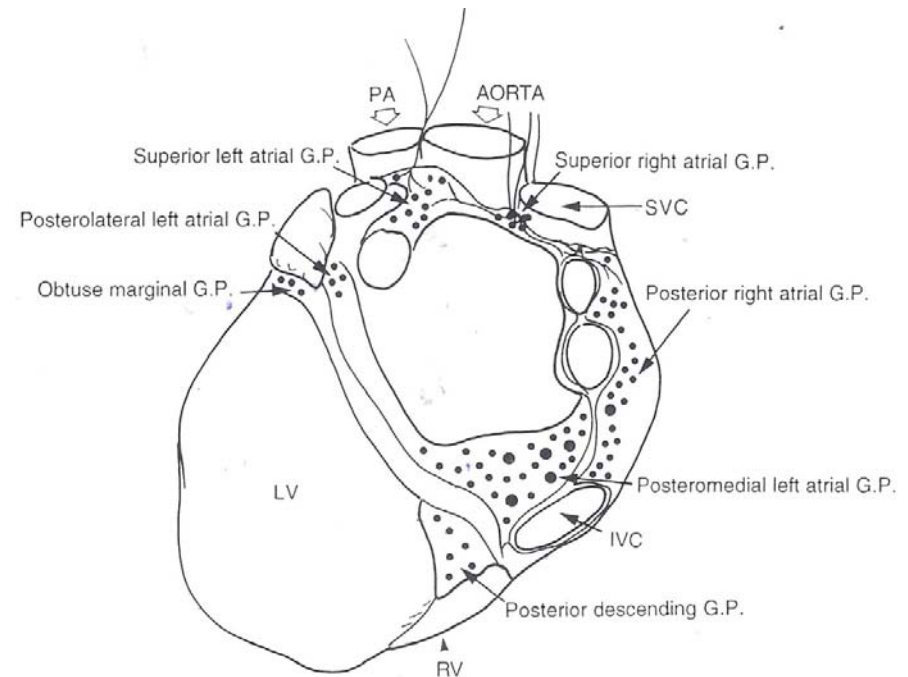
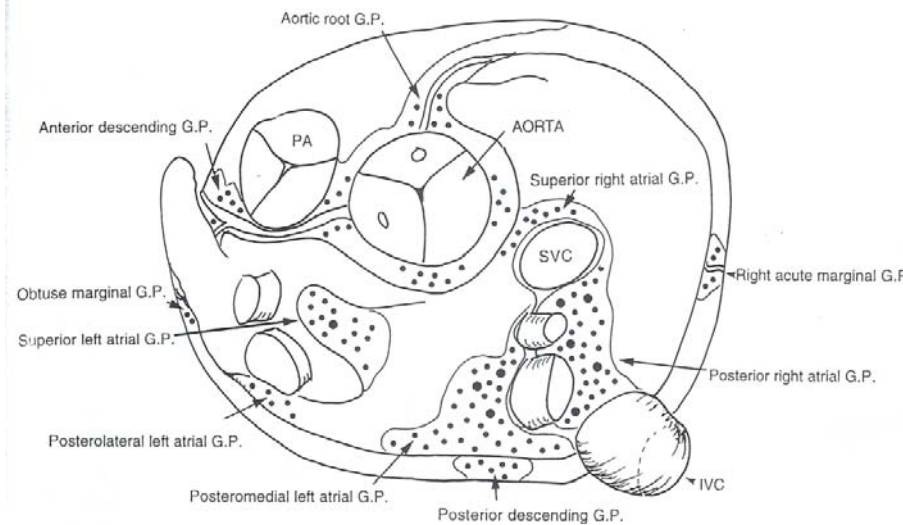


# Which LA substrate modifications (additional to pulmonary vein isolation) is possible with the Cryo Technique?

1. Linear Lesions
2. Complex Atrial Fractionated Electrograms (CAFE) ablation
3. Ganglionated Plexus Ablation



# Human intrinsic cardiac nervous system, location of ganglionated plexus



Gross and Microscopic Anatomy of the Human Intrinsic Cardiac Nervous system,  
J.A.Armour et al

The Anatomical Record 247:289-298 (1997)



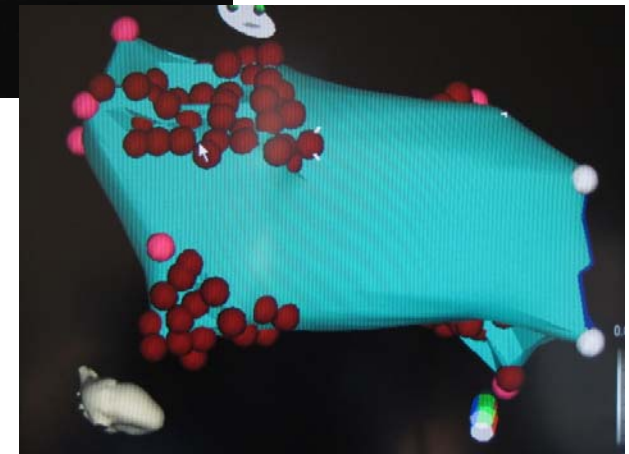
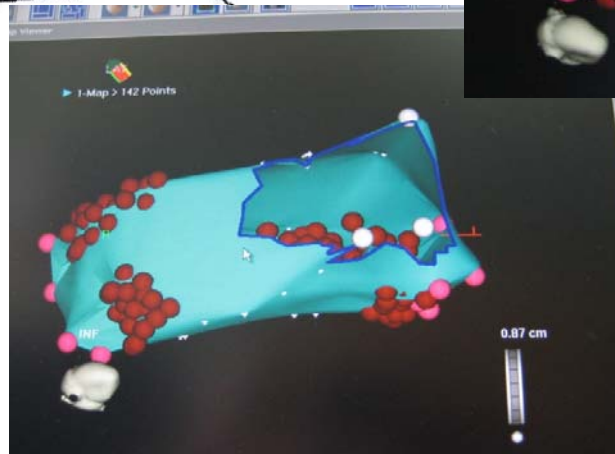
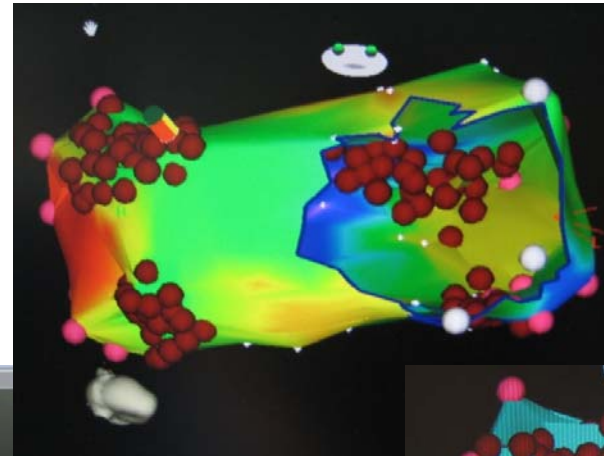
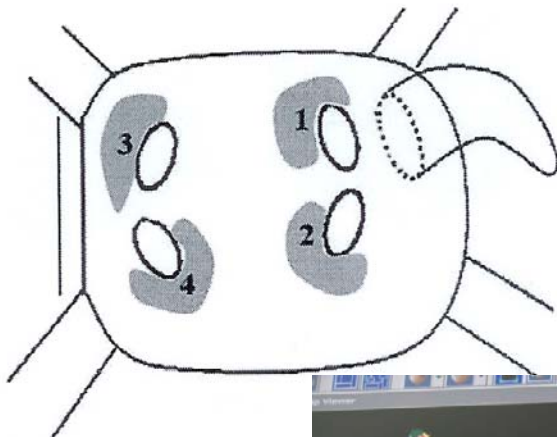


## Basic science, ganglionated plexus ablation

- High frequency stimulation of GP leads to atrial fibrillation
- Neurotransmitter from GP (acetylcholine, epinephrine) shorten atrial refractory period
- GP ablation transiently decreases heart rate variability
- Cardiac GP have a low anatomic location variation



# Catheter Ablation of Left Atrial Ganglionated Plexi for Atrial Fibrillation, targeted GP Areas



Pokushalov E et al, Heart Rhythm. 2009 Sep;6(9):1257-64



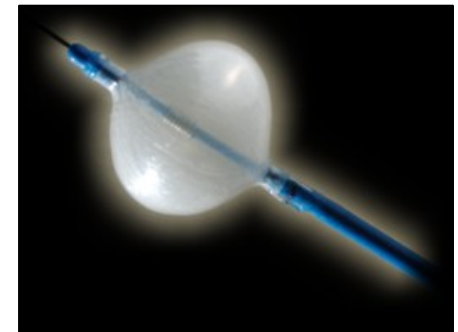
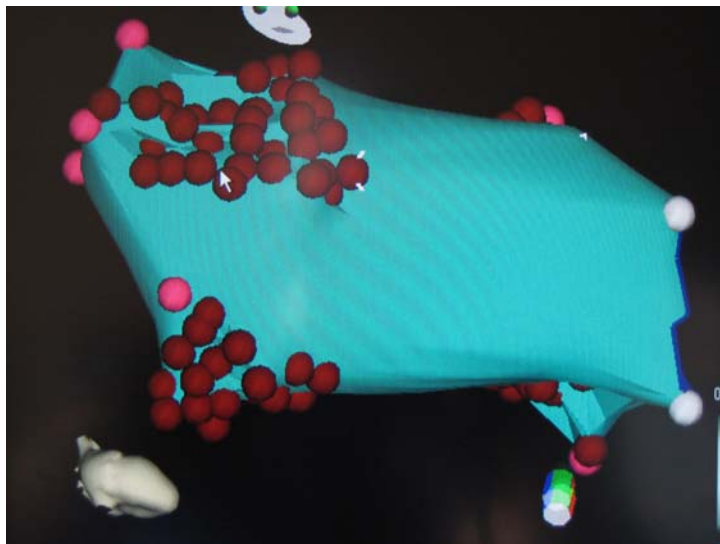
## GPA for treating Atrial fibrillation

- N=58 Patienten, 41-67 Jahre  
(21 permanent/22 persistierend/15 paroxysmal)
- Vorhofgröße 93.1+- 6.1 ml
- Ganglien Plexus Ablation, 4 Regionen des linken Vorhofes
- Keine circumferentielle Pulmonalvenenisolation
- Vorhofflimmern terminierte in 94.1%
- 7 Monats Erfolgsrate: 86% SR



# Cryo-Ganglionated Plexus Ablation ?

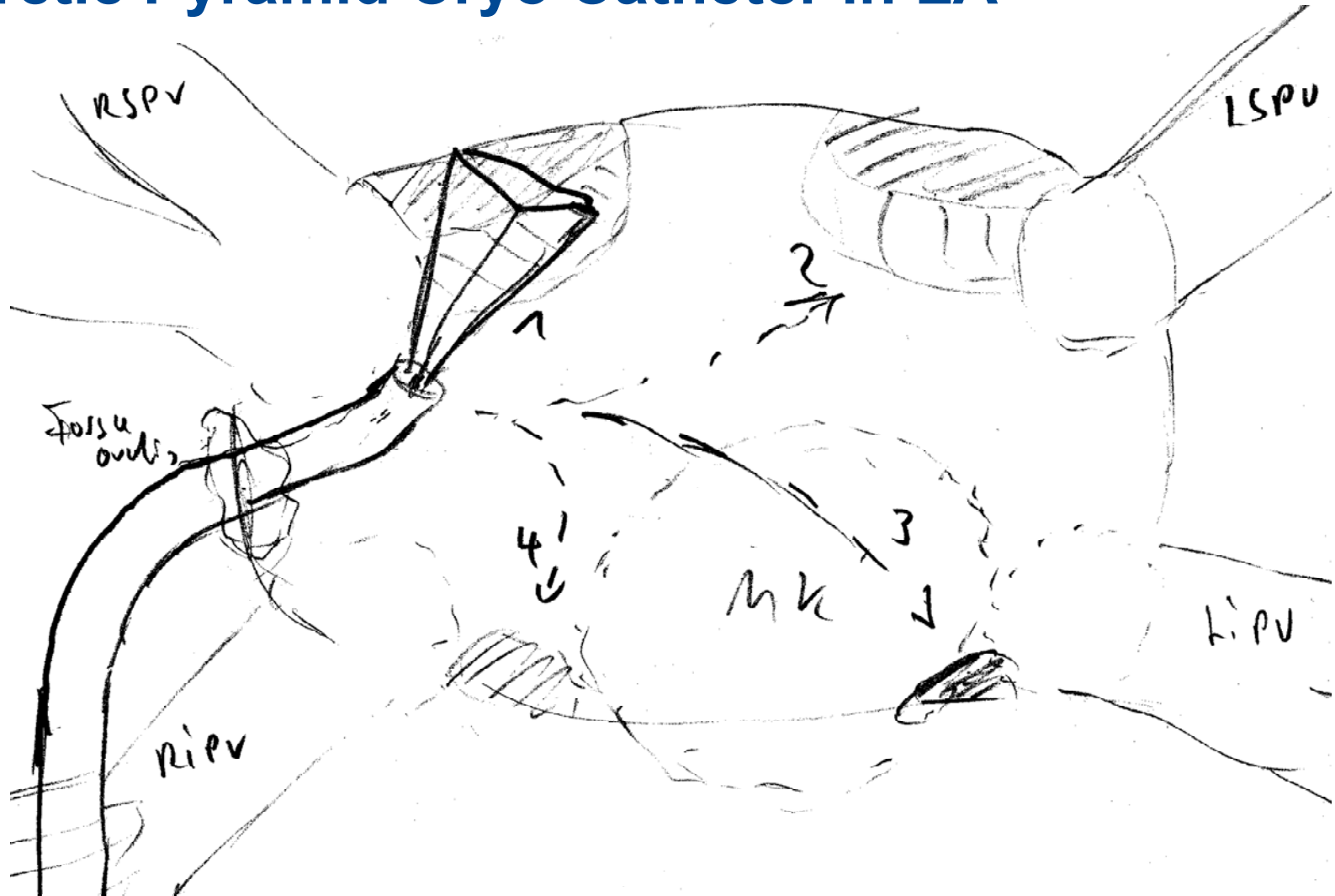
- Idea: Combining the efficacy of the anatomical guided GP ablation approach with the safety of the Cryo technology



Problems:  
Focal cryo ablation to slow  
balloon does not hit all of the GP target areas

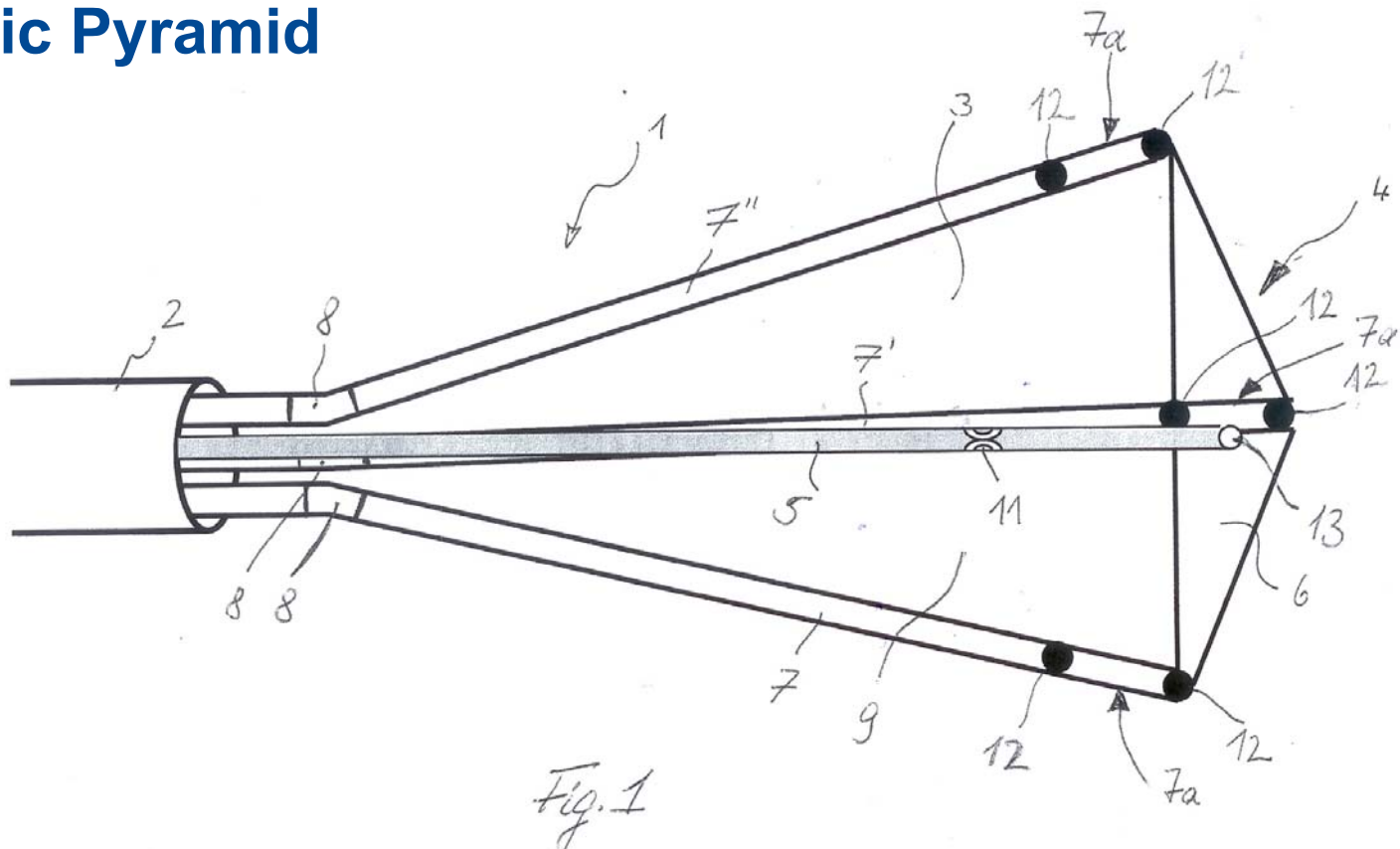


# Arctic Pyramid Cryo Catheter in LA





# Arctic Pyramid

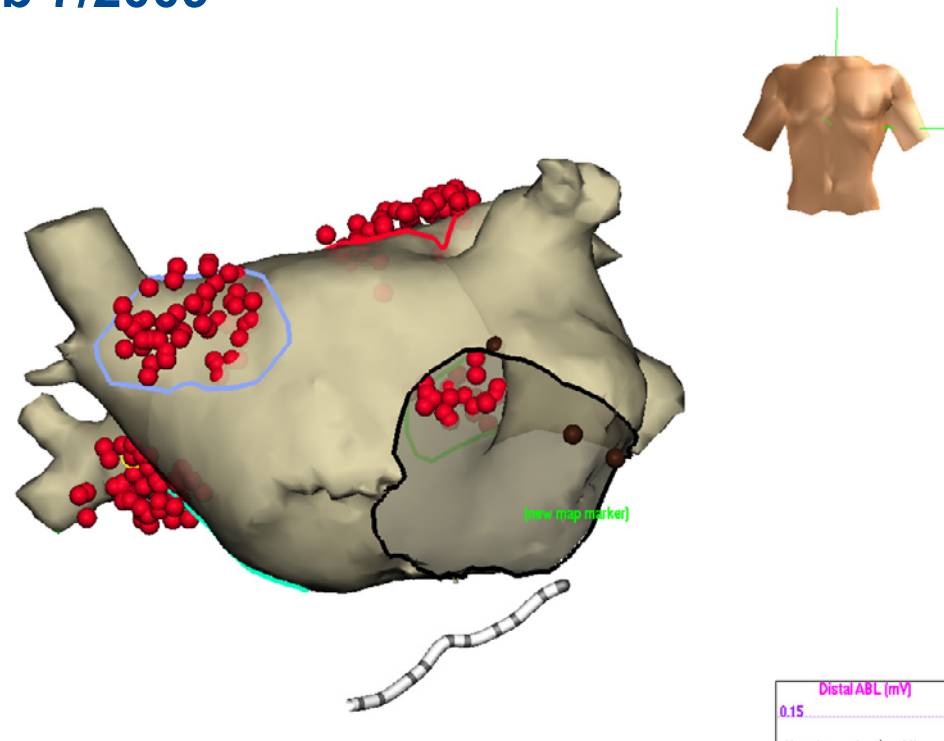


Patentanmeldung, Deutsches Patent- und Markenamt München, 29.05.2009, KEW090501GDE-5/CS



# RF Ganglionated plexus ablation

first two cases ukb 7/2009



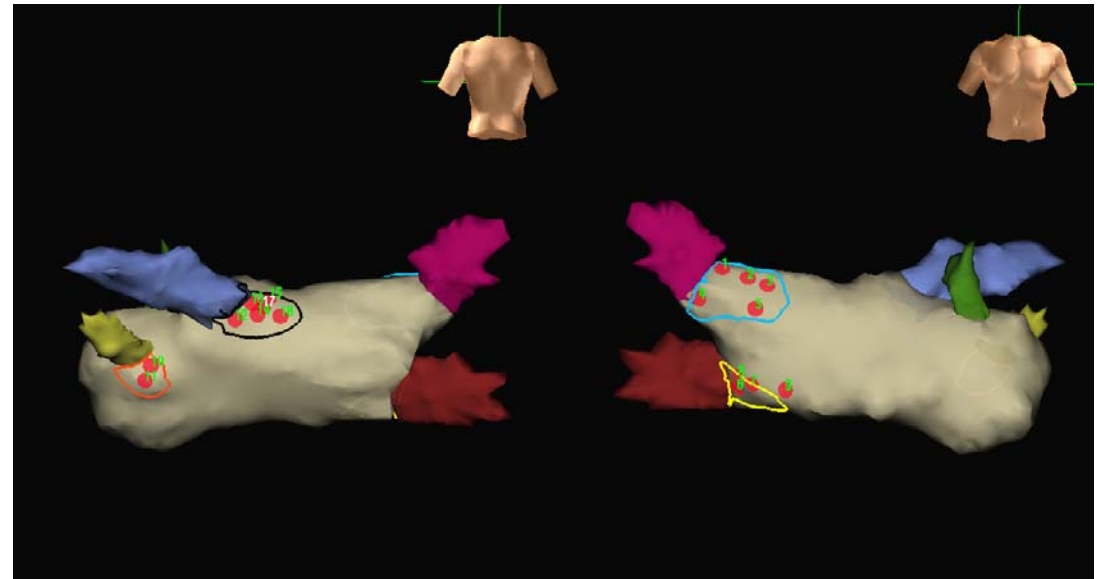
3D EnSite NavX Map combined with CT scan



# Cryo ganglionated plexus ablation 20 cases since 7/2009

## Technique:

- CS catheter
- Single transseptal puncture steerable Agilis Sheath
- Freezor Extra focal Cryo catheter
- Ensite NavX 3D Map of LA
- Anatomical GPA, 4 areas, 3 minutes freezing per point, 30-40 points, additional lesions from RA

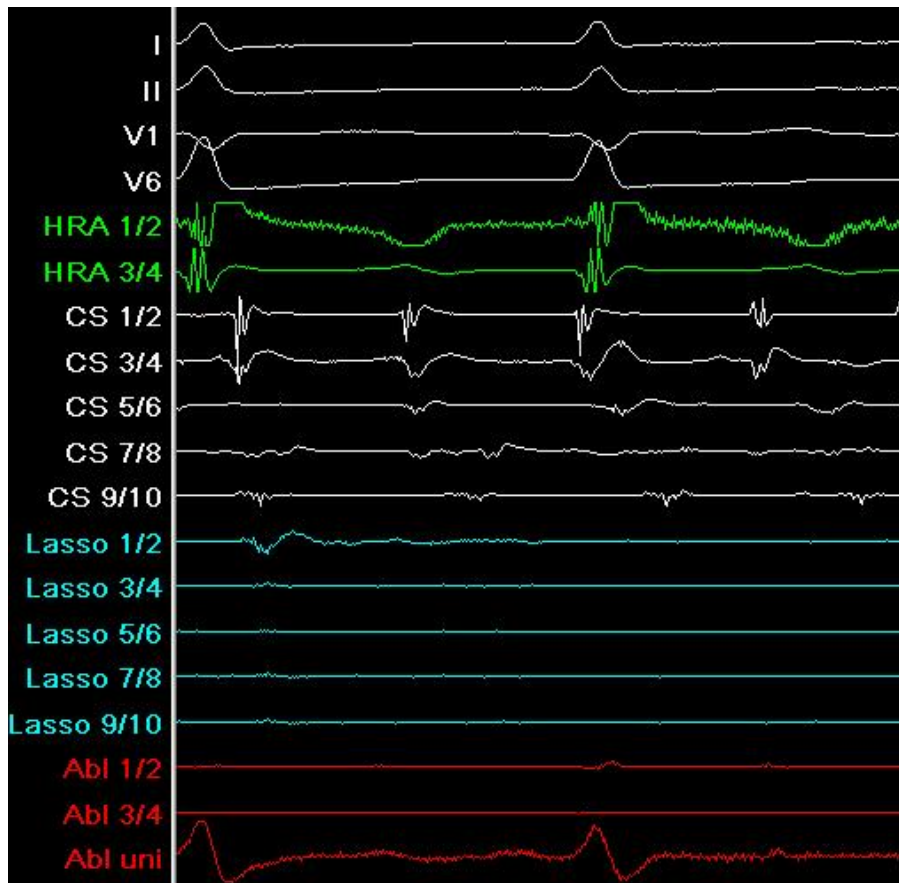




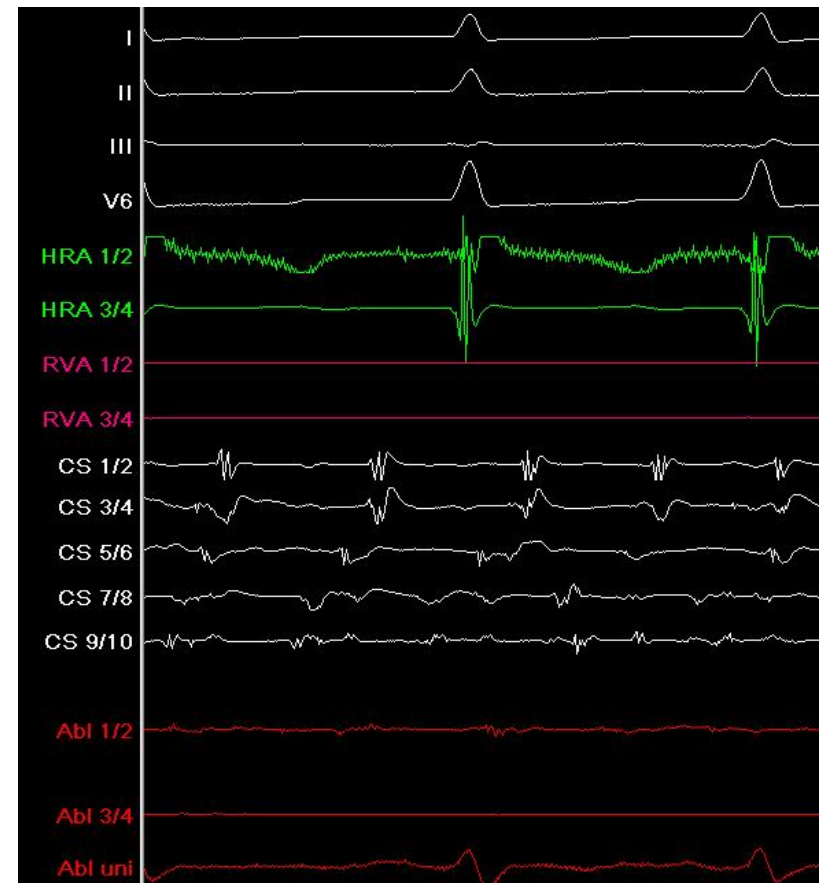


# Voltage Mapping, GP target Areas

LI GP Area



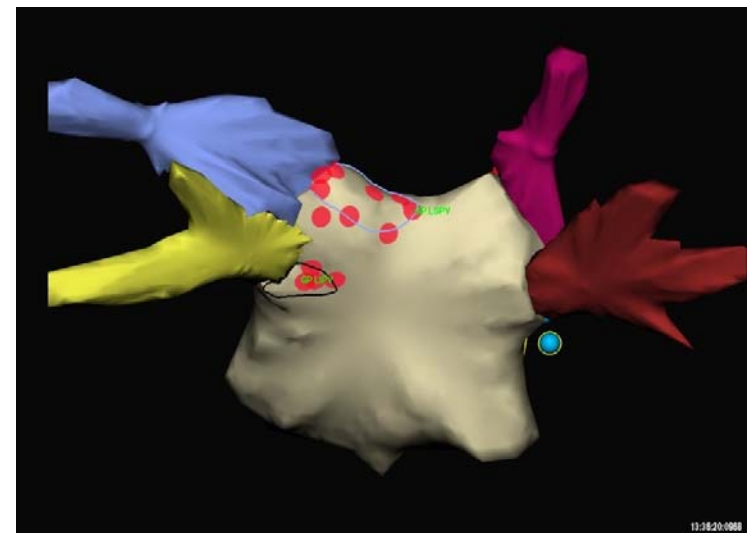
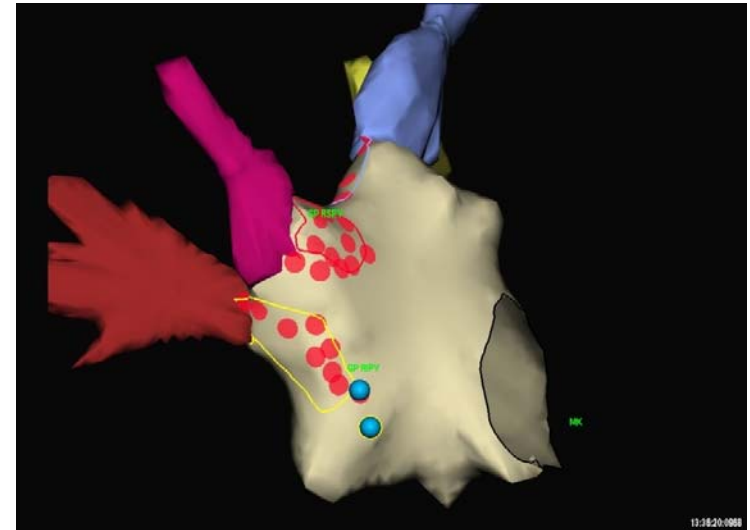
LS GP Area





# Cryo GPA

- Male pat, 67 years
- non significant coronary heart disease
- CTI ablation 2009
- No more Aflut but highly symptomatic episodes of PAF
- Normal LA size
- 32 lesions in 4 regions including from RA
- 3months follow up 72h ECG: 10h PAF, symptoms better, fewer episodes





# Cryo GPA, results & conclusions

- 20 pts. so far:
- 8 pts Cryo GPA in PAF, 2 pt Cryo GPA in PsAF
- 5 pts Cryo PVI + GPA in PsAF, 5 pts Cryo PVI + GPA in LsAF
- Cryo GPA technically possible
- The cryoballoons ablate big parts of the GP target areas (28 > 23mm balloon) if GPA is used additional to PVI
- Stand alone Cryo GPA with focal cryo catheter is possible but takes very long (4h)
- Wall potentials reduced, transmuralitY unknown, efficiency unknown
- Success rate so far not known

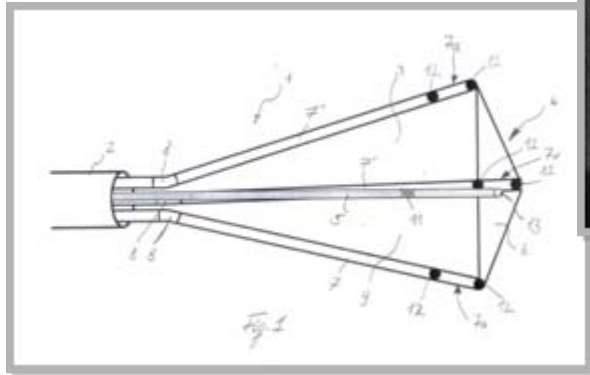
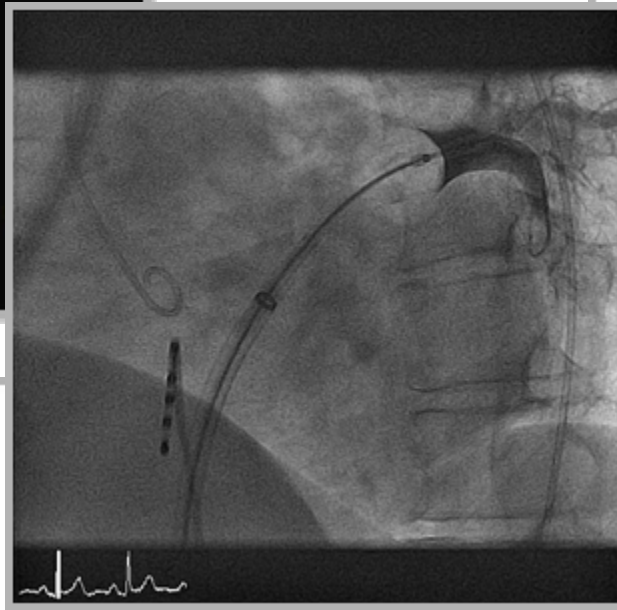
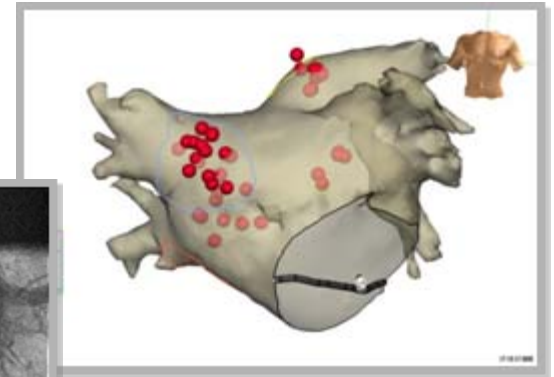
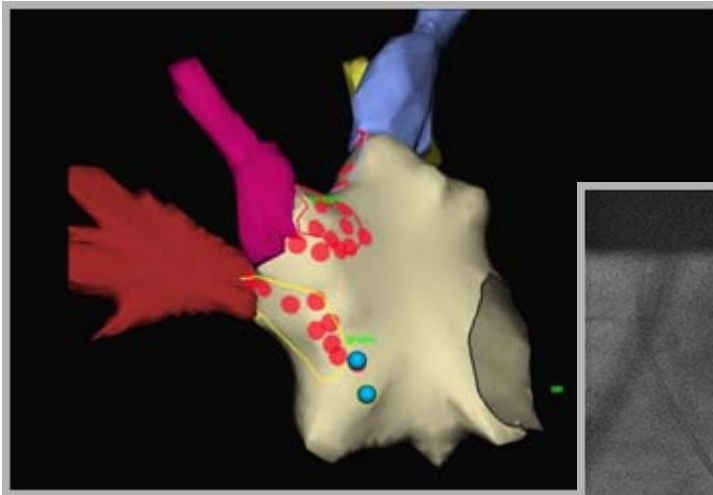


## Which advantages does the cryo technique offer?

- Cryoballoon technically easy, very standardized, short procedure
- Very good success rates in Paroxysmal AF
- Success rates yet low in PsAF and LsAF, as with RF ablation, but we are working on it...
- Very safe technology



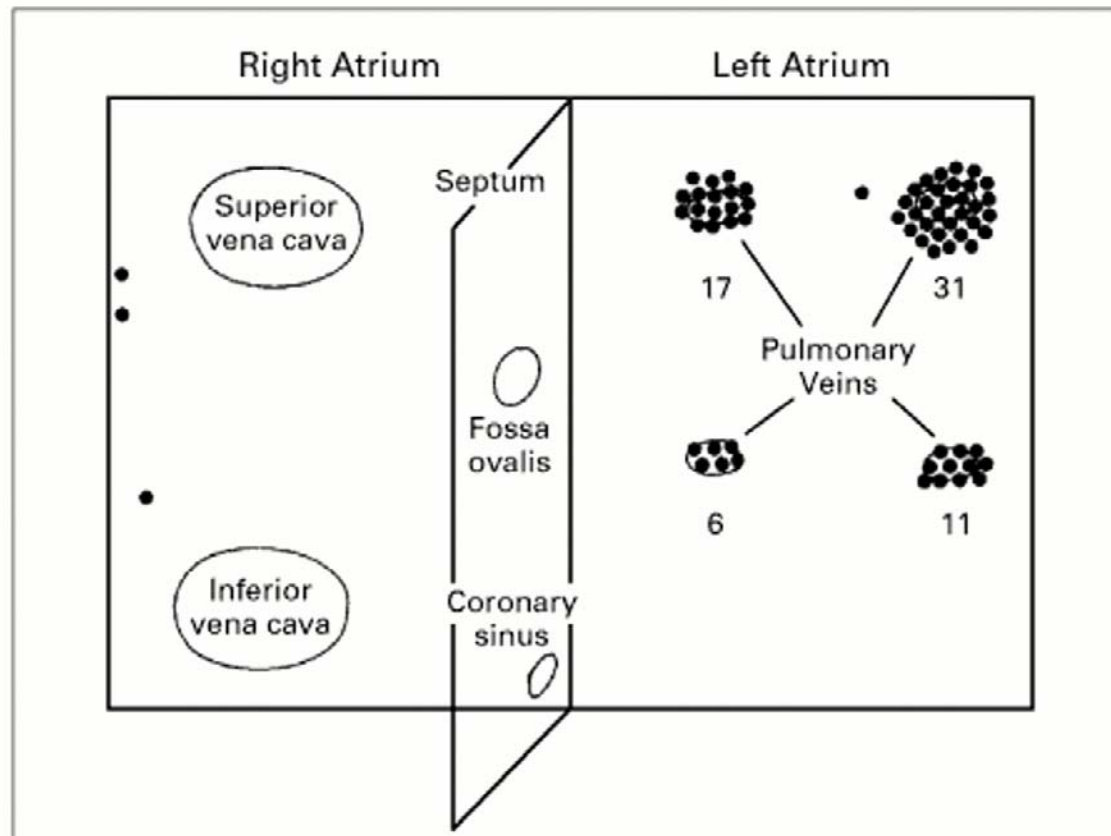
# Vielen Dank für Ihre Aufmerksamkeit !







# Diagram of the Sites of 69 Foci Triggering Atrial Fibrillation in 45 Patients



Haissaguerre M et al. N Engl J Med 1998;339:659-666



## Cryoballoon PVI with real time recordings from the pulmonary veins

- 18 pts, 39 of 72 PV's = 54% real time ProMap recording during PVI
- 46% without recording: no PVI, distal position ProMap, isolation with regular guide wire
- Time to block shorter in PV with sustained isolation > 30 minutes

Chun, Kuck et al, J Cardiovasc Electrophysiology 2009 Nov;20(11):1203-10

- 23 pts, 51% ProMap, feasibility study

Tang, Gerds-Li et al, J Cardiovasc Electrophysiology 2010 Jun 1;21(6):626-31





# Long-term clinical outcome after GP - ablation for atrial fibrillation: anatomical approach versus selective approach

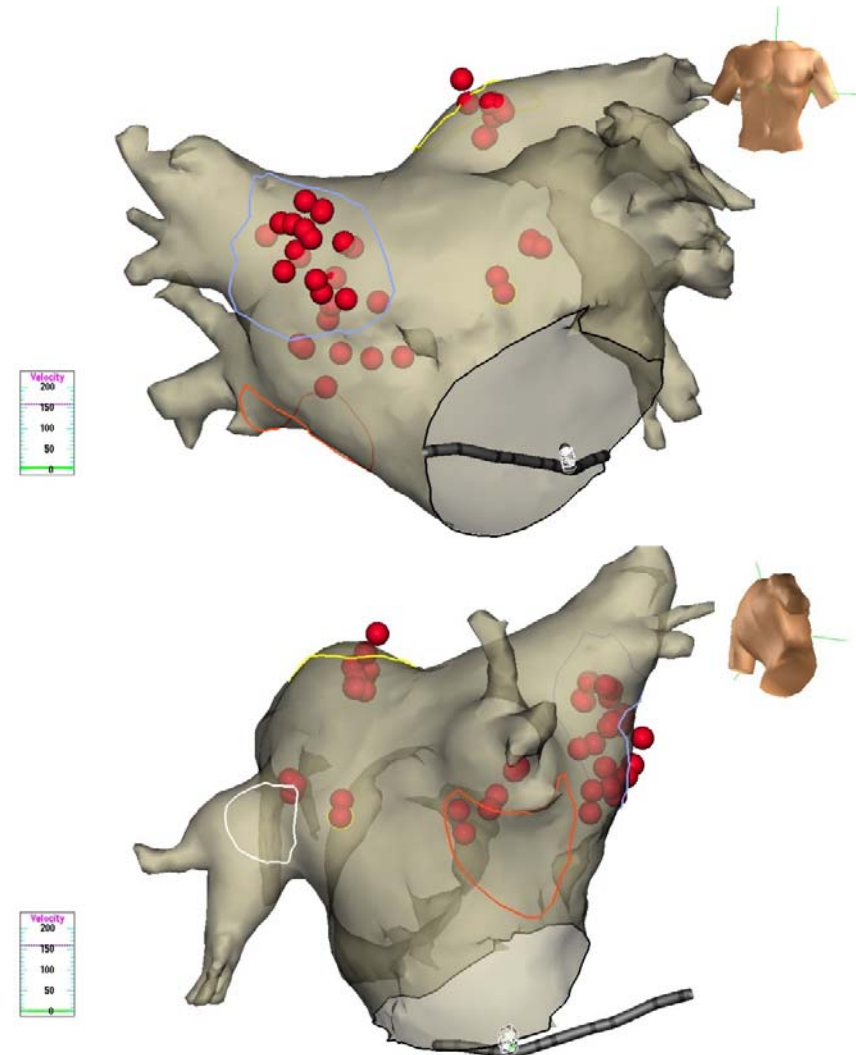
80 patients. Two groups. At 12 months, 42.5% of patients who underwent SGPA and 82.5% of patients who underwent AGPA were free of symptomatic PAF. Parasympathetic denervation was more prominent in patients free of AF compared to these with AF recurrence.

*Pokushalov et al Europace Journal ( 2009 ) 11 ( S6 ), Abstract 91*



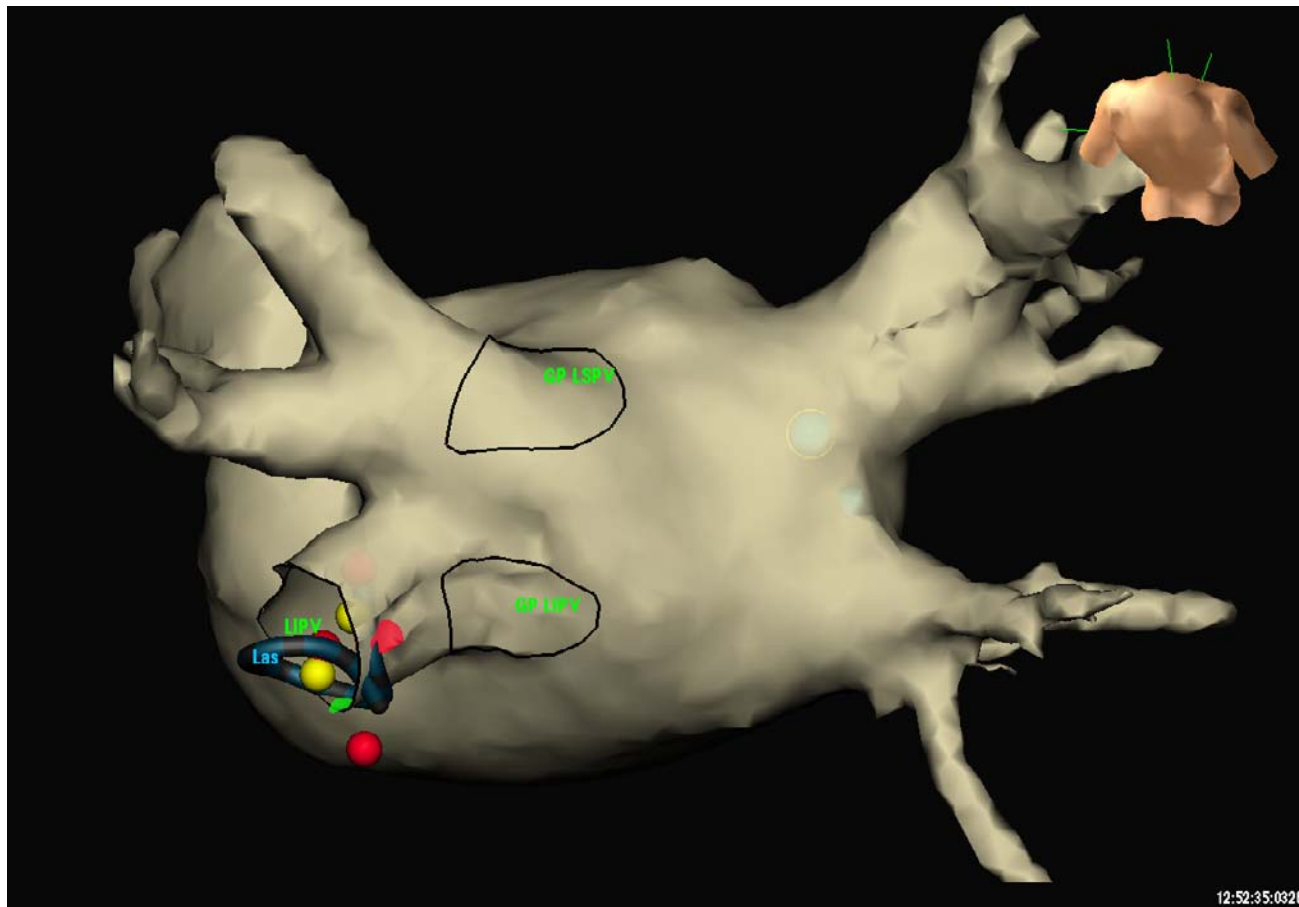
# Cryo GPA

- Male pat, 80 years
- PAF since 1 year
- 2 symptomatic episodes per week
- 19 lesions in 4 regions
- 3 months follow up:
- Sinusrhythm





# After Cryo-PVI additional Cryo-GPA as Substrate Modification





## **Cryoballon PVI temporarily modulates the intrinsic cardiac autonomic nervous system**

- 14 pts, PAF, Cryoballon PVI, acute HR changes, heart rate variability during holter at 1 week, 1, and 3 months
- 36% bradycardia during PVI, HRV decreased at 1 week and 1 months, normalised at 3 months

Oswald, Klein et al, J Interv Card Electrophysiology 2010 Oct;29(1):57-62