Arytmogenní kardiomyopatie pravé komory
Terapie

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Stratifikace a léčba ARVC

Subgroups	Risk markers	Recommendations	Follow-up	ICD indication
Definite ARVD High risk	Aborted SCD Sustained VT Unexplained syncope	Reduce physical exercise Avoid competitive sport β-blockers	Annually including: Electrocardiography Cardiac imaging (echocardiography vs. CMR) Holter Exercise stress testing	Recommended
Definite ARVD Moderate risk	Extensive disease (severe RV dysfunction, large LV involvement) Nonsustained VT	Reduce physical exercise Avoid competitive sport β-blockers	Annually including: Electrocardiography Cardiac imaging (echocardiography vs. CMR) Holter Exercise stress testing	Consider
Definite ARVD Low risk	Remaining patients with definite diagnosis of ARVD	Reduce physical exercise Avoid competitive sport β-blockers	Annually including: Electrocardiography Cardiac imaging (echocardiography vs. CMR) Holter Exercise stress testing	Not recommended
Asymptomatic mutation carriers	Asymptomatic mutation-carrying relatives of ARVD	Reduce physical exercise Avoid competitive sport	Annually including: Electrocardiography Cardiac imaging (echocardiography vs. CMR) Holter Exercise stress testing	Not recommended

ARVD: Arrhythmogenic right ventricular dysplasia; CMR: Cardiac magnetic resonance; LF: left ventricle; RV: right ventricle; SCD: Sudden cardiac death; VT: ventricular tachycardia

Brugada J et al. ESC 2012

Omezení sportovních aktivit

- Při zátěži dochází díky defektu desmosomů k oddělení jednotlivých myocytů a buněčné smrti → zánět a nahrazení fibrózou
- Sportování aktivity u pacientů s ARVC
  - Zvýšení rizika NSS (5x)
  - Progresi onemocnění
- Zákaz závodních sportů
- Omezení v rekreačních sportech:
  - Kuželky, golf, jízda na koni, bruslení, chůze, fitness

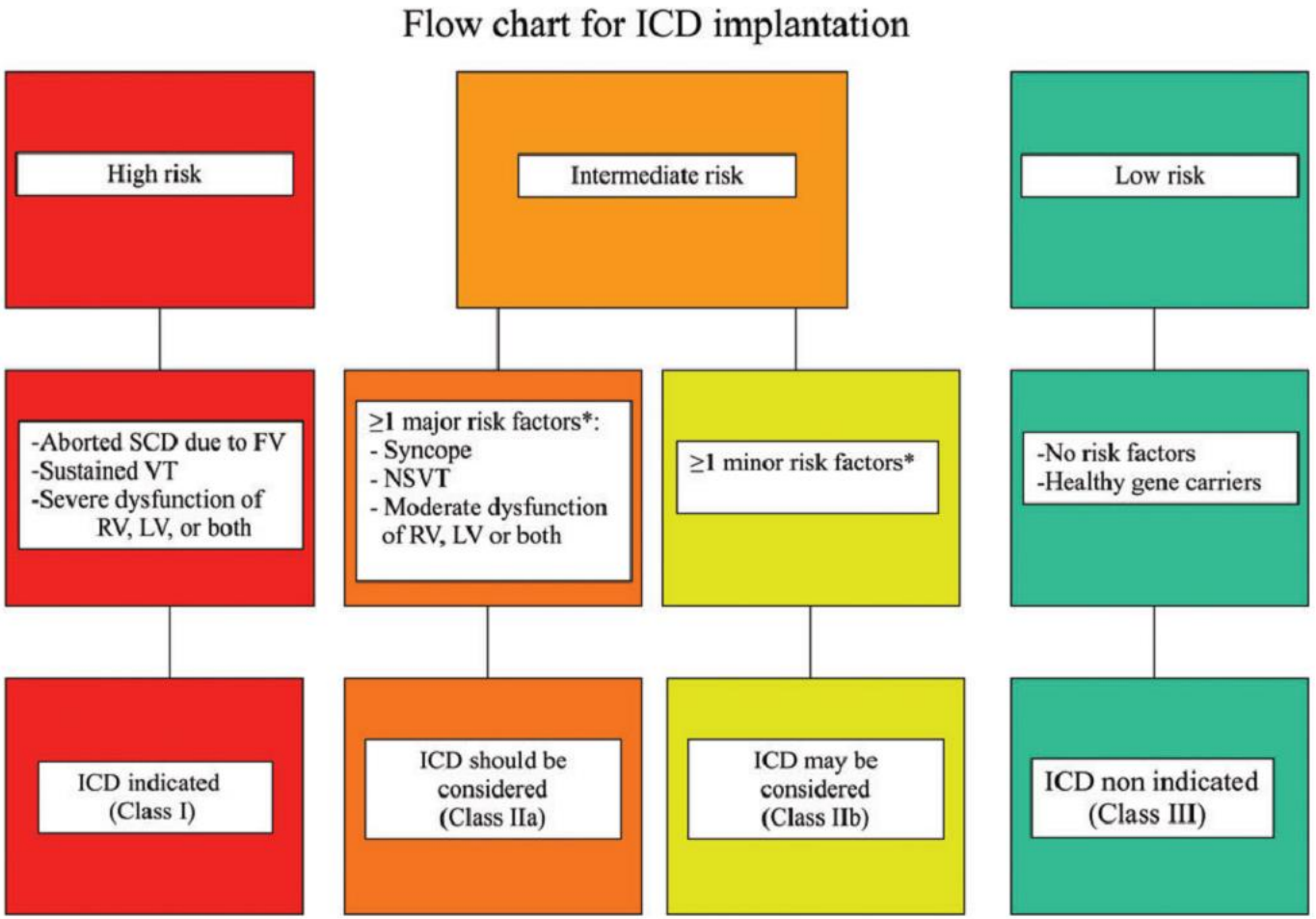
Maron B Circulation 2004

Antiarytmická léčba

- Adjuvantní k prevenci terapií ICD
- Betablokátory, sotalol, amiodaron
- Ve starších studiích sotalol vysoce účinný v prevenci arytmií (testování AA PSK)#
- **GM Marcus *JACC* 2009;54(7):609.**
  - Srovnání efektivity AA medikace u 95 pacientů s prokázanou ARVC
  - Pouze léčba amiodaronem snížila intervence ICD,
  - Sotalol zvýšil (průměrná dávka 240mg/den)

#Wichter T Circulation 1992

Indikace k implantaci ICD



Corrado EHJ 2015

Riziková stratifikace ARVC

Risk factor	Definition	Patients, *n*	Study end point	HR/OR
Cardiac arrest	Aborted SCD due to VF	132	ICD interventions on rapid VT/VF	79
Unstable sustained VT	Sustained (>30 s) VT causing syncope or haemodynamic collapse		ICD interventions on rapid VT/VF	14
Sustained VT or VF	VT lasting >30 s or VF	108	Any appropriate ICD intervention	N/A
	VT lasting >30 s or VF	50	Cardiac death (SCD in 67% and heart failure in 33%)	22.97
Syncope	Syncopal episodes unrelated to extracardiac causes and occurring in the absence of documented ventricular arrhythmias and/or circumstances clearly leading to reflex-mediated changes in vascular tone or heart rate	132	ICD interventions on rapid VT/VF	7.5
	Idem	106	Any appropriate ICD intervention	2.94
			ICD interventions on rapid VT/VF	3.16
	N/A	50	Cardiac death (SCD in 67% and heart failure in 33%)	10.73
Non-sustained VT	≥3 consecutive ventricular beats with a rate >100 beats/min, lasting <30 s, documented during exercise testing or 24-h Holter	84	Any appropriate ICD intervention	10.5
	Idem	106	Any appropriate ICD intervention	1.62
LV dysfunction	Angiographic LV EF <55%	132	ICD interventions on rapid VT/VF	0.94
	Angiographic LV EF <40%	130	Cardiac death (SCD in 33% and heart failure in 67%)	10.9
	Angiographic LV EF <55%	60	Any appropriate ICD intervention	1.94
	Echocardiographic LV EF <50%	61	Cardiac death and heart transplantation (SCD in 53%, heart failure death in 13%, heart transplantation in 34%)	N/A
	Angiographic LV EF <55%	313	Sudden cardiac death	14.8
RV dysfunction	Angiographic RV EF <45%	60	Any appropriate ICD intervention	2.09
	FAC % per unit decrease	70	Composite (death in 0%, heart transplantation in 7%, ventricular fibrillation in 10%, sustained ventricular tachycardia in 36%, arrhythmic syncope in 4%).	1.08
RV dilation	RV end-diastolic area, cm^2, per unit increase	70	As above	1.05
Right-atrial dilation	Right atrium, short axis, mm, per unit increase	70	As above	1.03
Biventricular dysfunction	Echocardiographic RV and LV dysfunction (EF <50%)	96	Cardiac death and heart transplantation (SCD in 30%, heart failure death in 30%, death of unknown cause in 5%, heart transplantation in 35%)	6.3
Heart failure	Clinical signs of RV heart failure	130	Cardiac death (SCD in 33% and heart failure in 67%)	13.7
	Clinical signs or symptoms of congestive heart failure	61	Cardiac death and heart transplantation (SCD in 53%, heart failure death in 13%, heart transplantation in 34%)	N/A
Young age	Per 5 yr increment	132	ICD interventions on rapid VT/VF	0.77
	Per 1 yr increment	108	ICD interventions on rapid VT/VF	N/A
Male gender		215	Composite (cardiac arrest in 9%, ICD intervention in 22%, sustained VT in 69%)	1.8
		134	Composite (SCD in 5%, cardiac arrest 27%, sustained VT 64%, ICD shock 5%)	2.76
Complex genotype	Compound or digenic heterozygosisity	134	Composite (SCD in 5%, cardiac arrest 27%, sustained VT 64%, ICD shock 5%)	3.71
Proband status	First family member affected by the genetic defect who seeks medical attention because of the occurrence of clinical manifestations	215	Composite (cardiac arrest in 9%, ICD intervention in 22%, sustained VT in 69%)	7.7
Inducible VT/VF	VT or VF that lasted >30 s or required termination because of haemodynamic compromise	84	Any appropriate ICD intervention	4.5
	N/A	60	Any appropriate ICD intervention	2.16
	N/A		ICD intervention on fast VT/VF	N/A
	VT that lasted >30 s or required termination because of haemodynamic compromise. Induction of VF not considered	62	Composite (cardiac death in 13%, heart transplantation in 10%, unstable VT/VF in 70%, syncope in 7%).	2.5
Extent of electroanatomic scar on RV endocardial voltage mapping	low-voltage (<0.5 mV) areas on bipolar electroanatomic voltage mapping. Per 5% increment.	69	Composite arrhythmic (SCD in 5%, ICD intervention in 37%, sustained VT in 58%)	1.6
Fragmented electrograms on RV endocardial voltage mapping	Multiple (>3) discrete deflections, amplitude <1.5 mV, and duration >100 ms	95	Any appropriate ICD intervention	21.2
T-wave inversion in inferior leads	Negative T-waves in leads II, III, aVF	108	Any appropriate ICD intervention	N/A
	Inverted T waves in 2 of 3 inferior leads	111	Composite (6% cardiac death; 8% heart transplantation; 16% VF; 67% sustained VT; 3% arrhythmic syncope)	2.4
Extent of T-wave inversion	Inverted T waves in ≥3 precordial leads	215	Composite arrhythmic (cardiac arrest in 9%, ICD intervention in 22%, sustained VT in 69%)	4.2

Corrado EHJ 2015

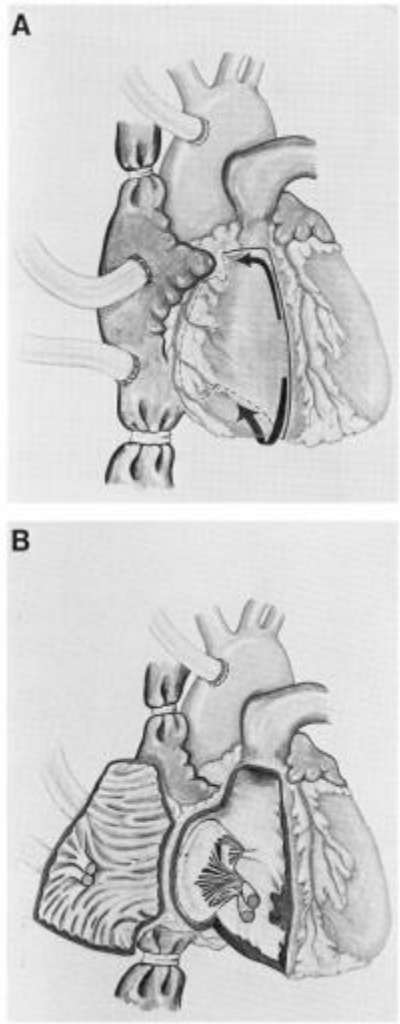
ICD u pacientů s ARVC

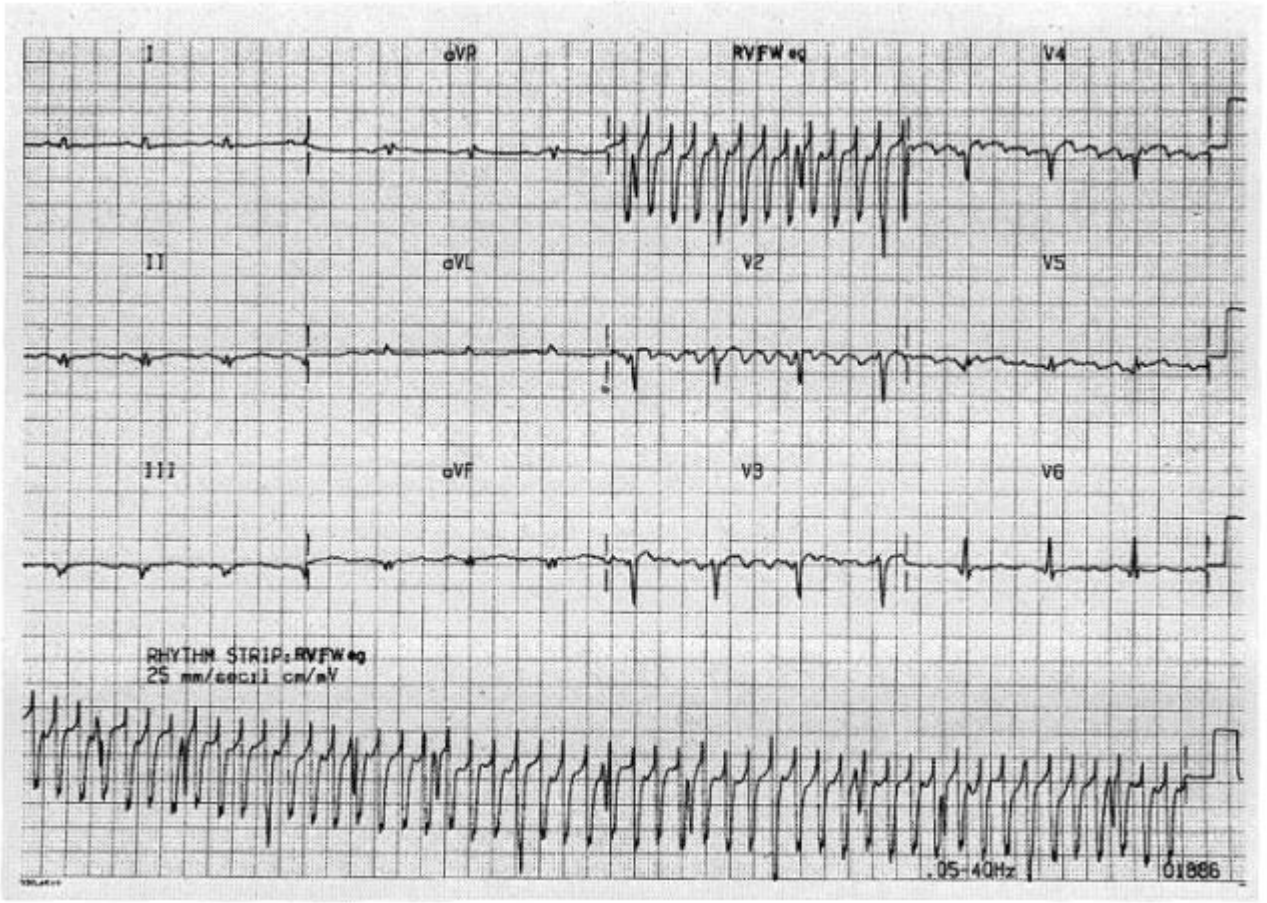
- Doporučovaný 1D ICD (Subkutánní-ICD?)
- Riziko komplikací ICD
  - Nepřiměřené terapie 4.4%/rok (sin. tachy, SVT)
  - Porucha elektrody 3.7%/rok
- U 4% pacient s ARVC je třeba pro poruchu sensingu RV eletrody implantace další elektrody na RV septum

Corrado EHJ 2015

Nefarmakologická léčba
KT u ARVC

Total Disconnection of the Right Ventricular Free Wall: Surgical Treatment of Right Ventricular Tachycardia Associated with Right Ventricular Dysplasia



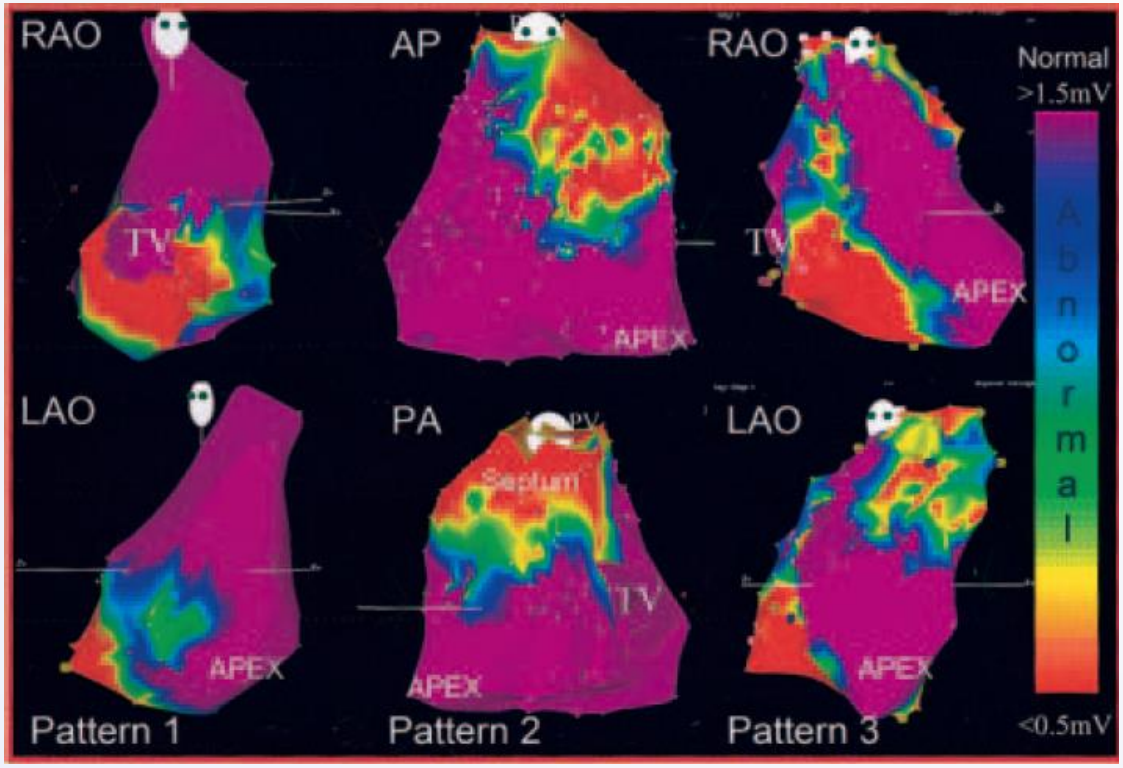


Report on two patients
Follow up 3 and 4 months

Guiraudon GM, Circulation 1983

Katetrizační ablace KT

Charakteristické postižení

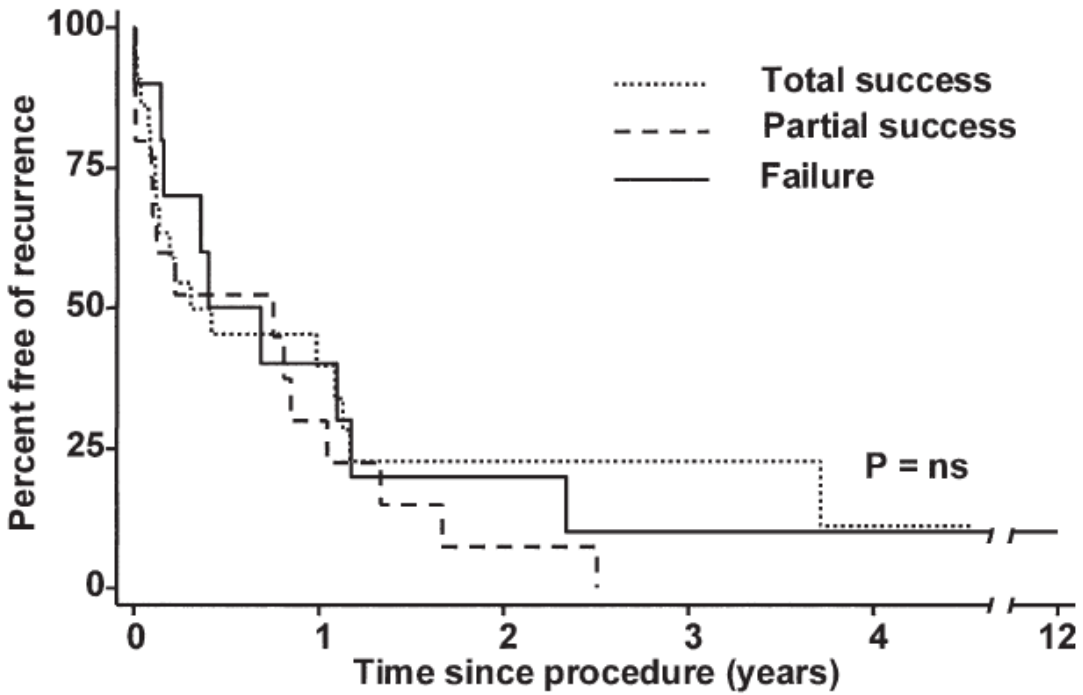


21 ARVD pts, 55 of 66 VTs originated in perivalvular region
no VT recurred after ablation in 17 pts (89%) during 27±22 months

Marchlinski FE, et al. Circulation 2004;110:2293-98

Catheter ablation of ARVC

Long Term Outcome…



	Events/At risk				
Total success	13/22	3/7	0/2	1/2	0/1
Partial success	10/15	3/4	1/1	-	-
Failure	6/10	2/4	1/2	0/1	0/1

24 pts (age 36±9 y)
John Hopkins
ablation registry
FU 32±36 months

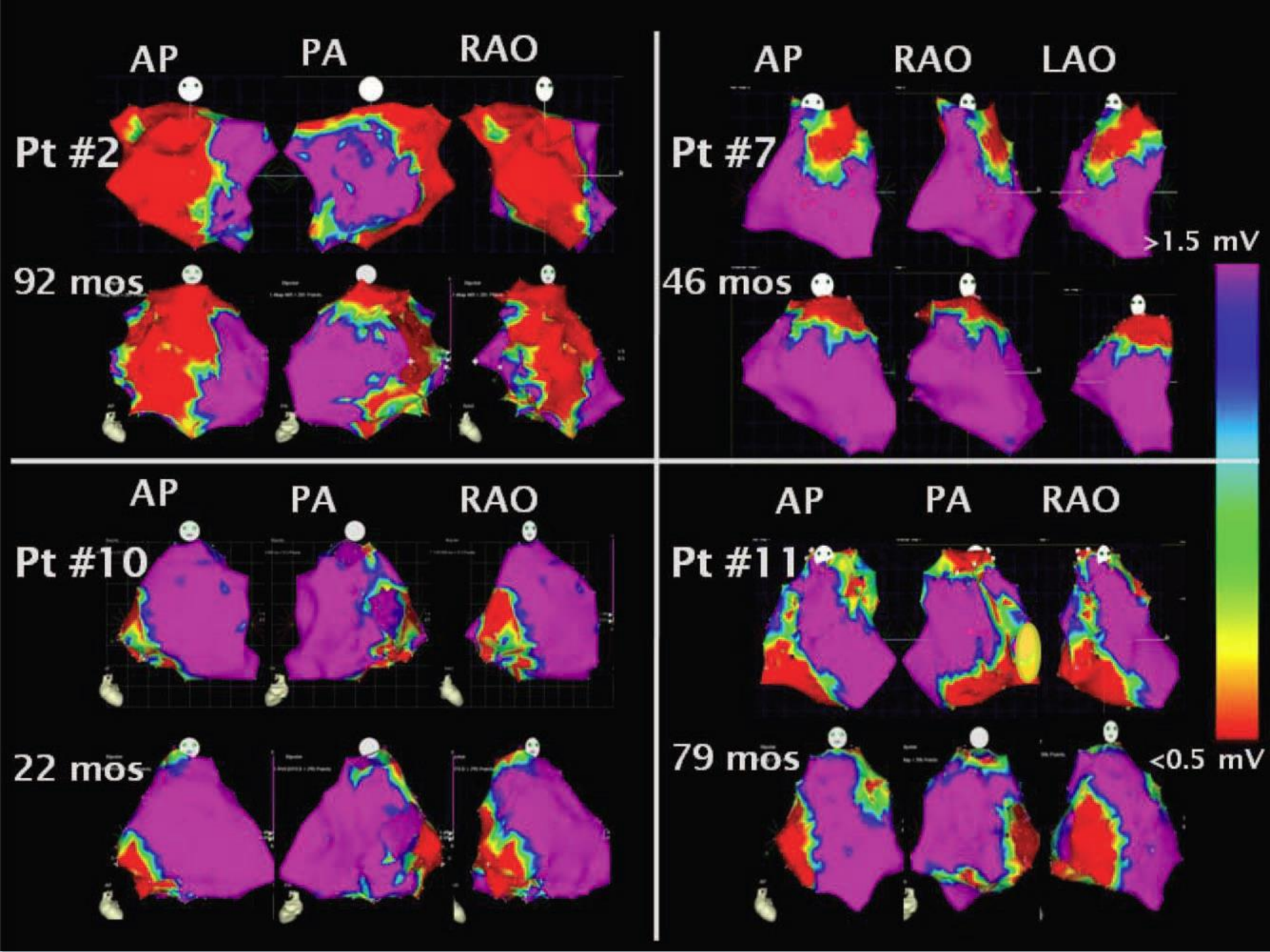
48 RF procedures
(10 w. EAN mapping)

85 % recurrence rate

Calkins H, et al. JACC 2007;50:432-40

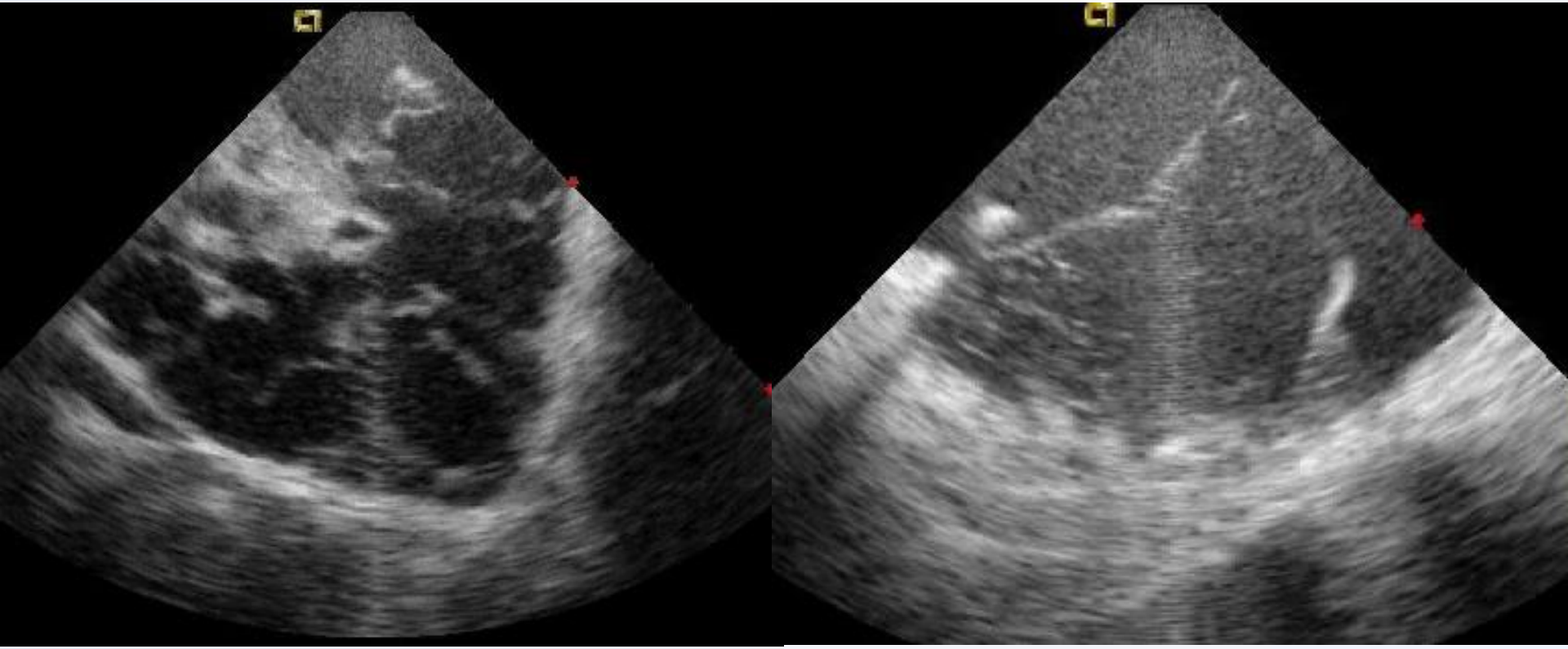
Reasons for Recurrences?

- Disease progression
- Difficult substrate for ablation – fissures, trabeculae…
- Predominant epicardial location (at least in earlier stages – ie in young patients)

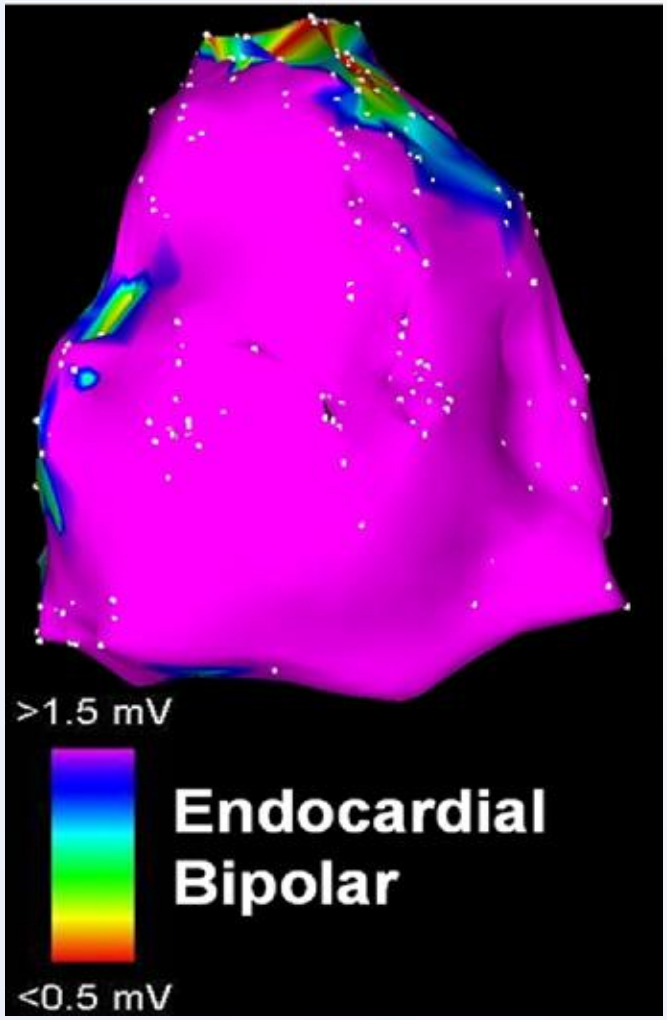

AP
PA
RAO
Pt #2
92 mos
AP
RAO
LAO
Pt #7
46 mos
>1.5 mV
<0.5 mV
AP
PA
RAO
Pt #10
22 mos
AP
PA
RAO
Pt #11
79 mos

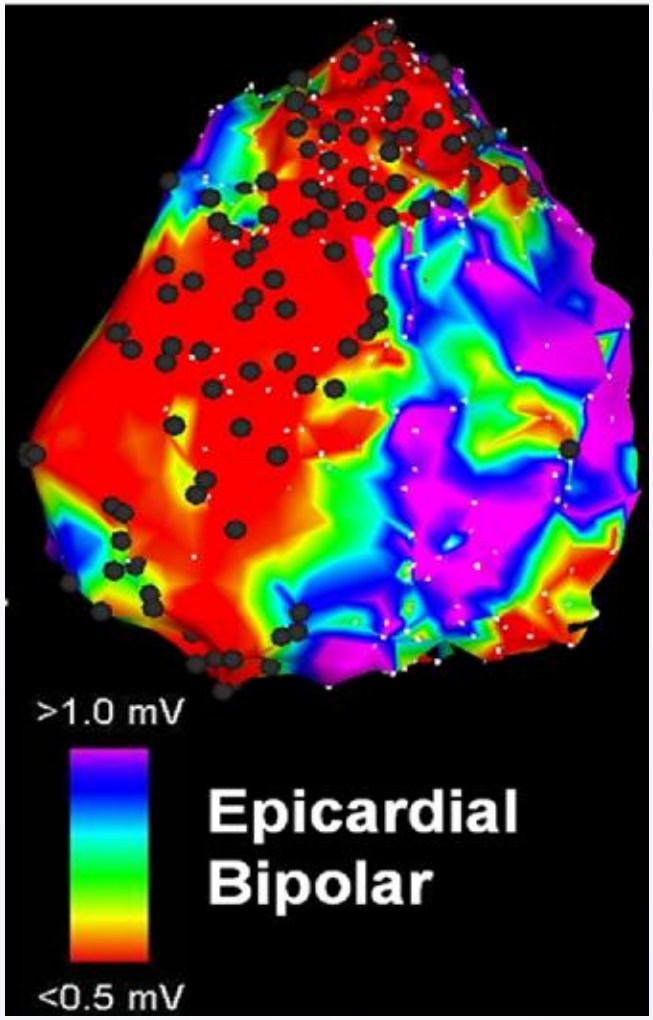
Technique of ablation matters…

Monitoring catheter in microaneurysms by intracardiac echocardiography



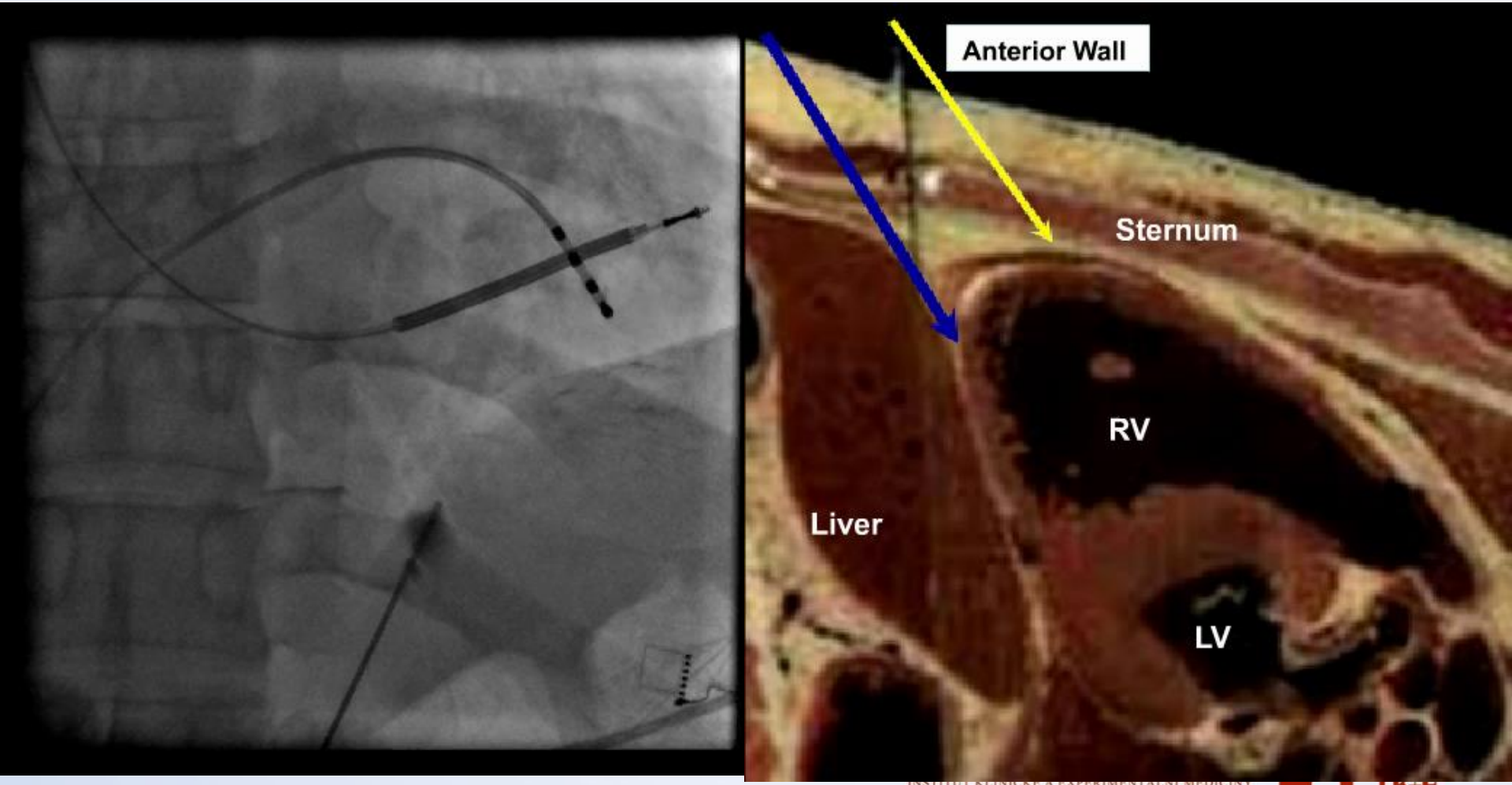
Predominant Epi Location



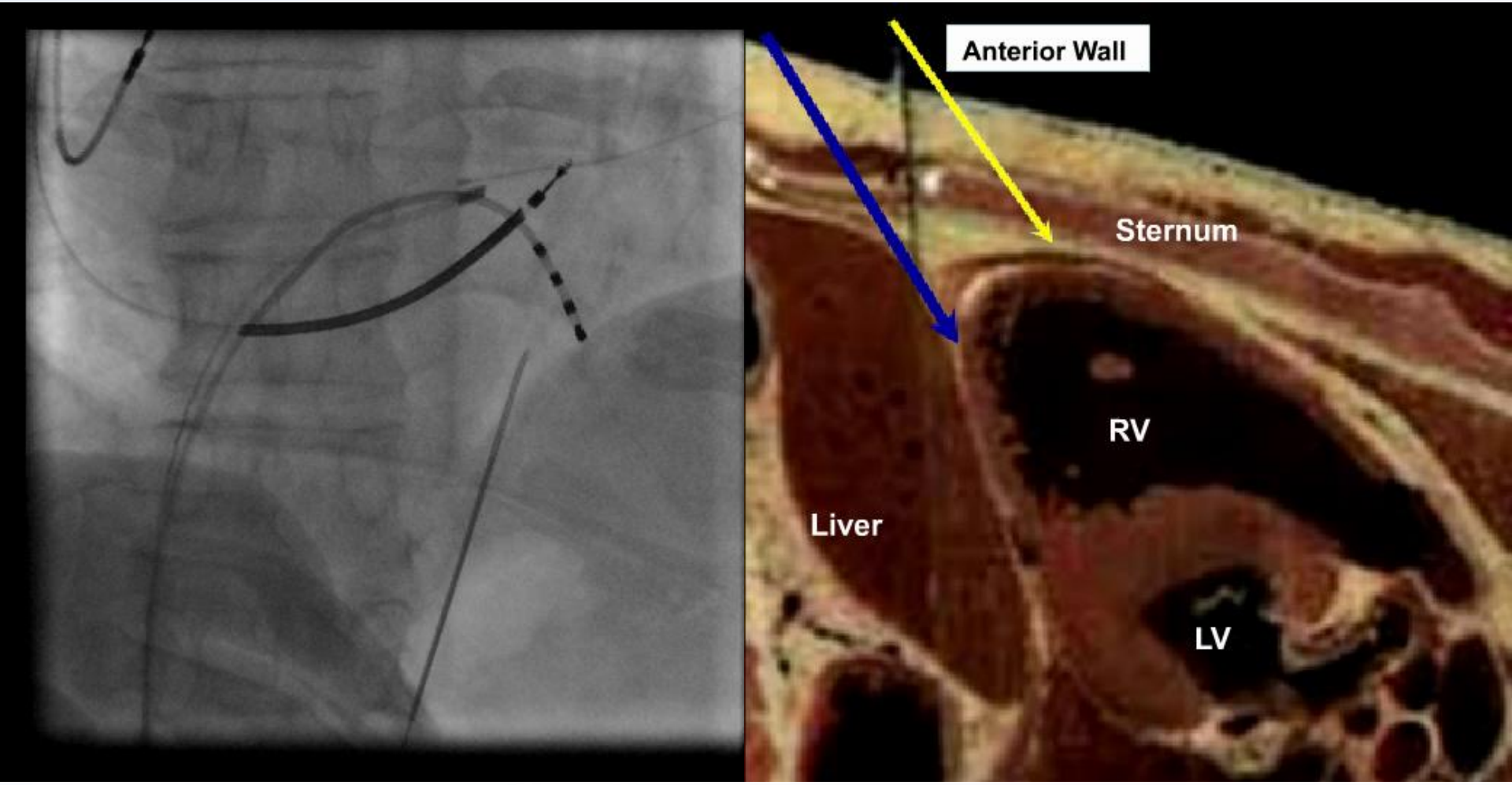


Polin GM, et al. Heart Rhythm 2011;8:76-83

Epicardial approach

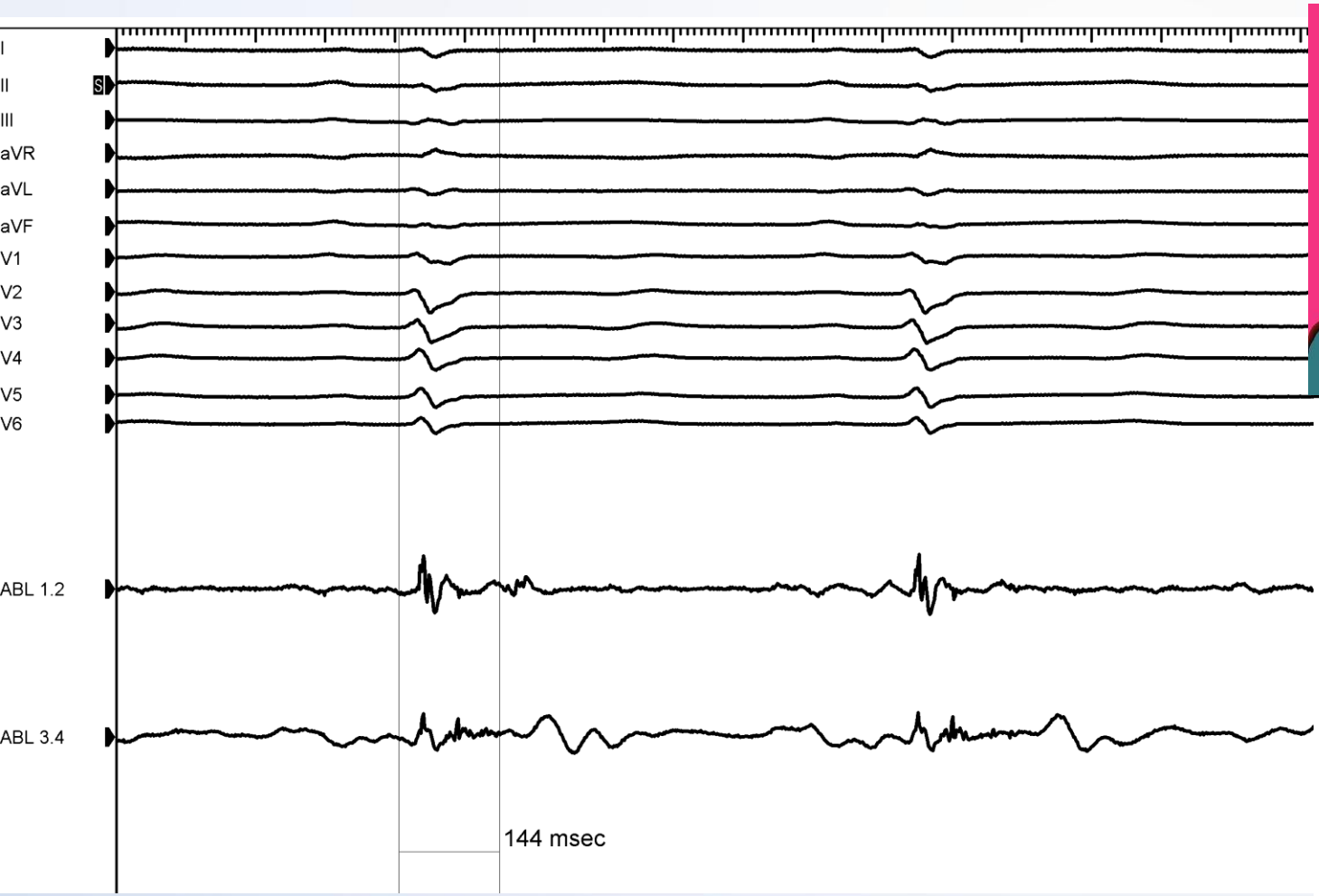


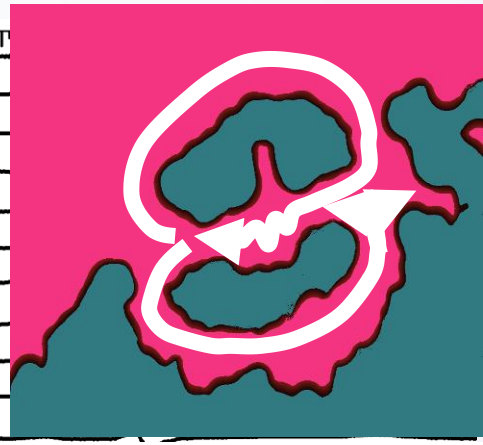
Epicardial approach

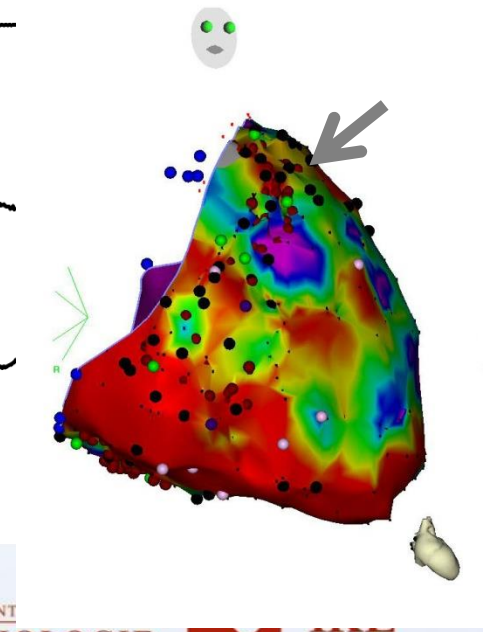


Mapování substrátu

Pozdní potenciály

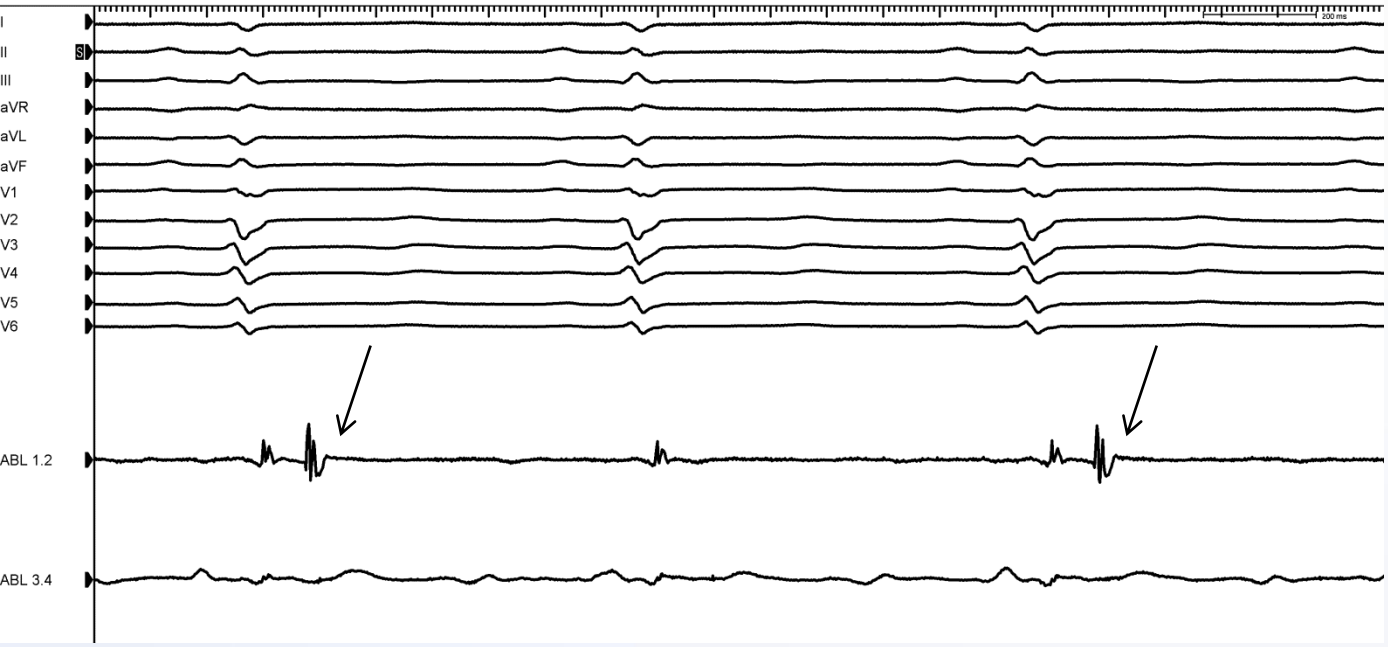


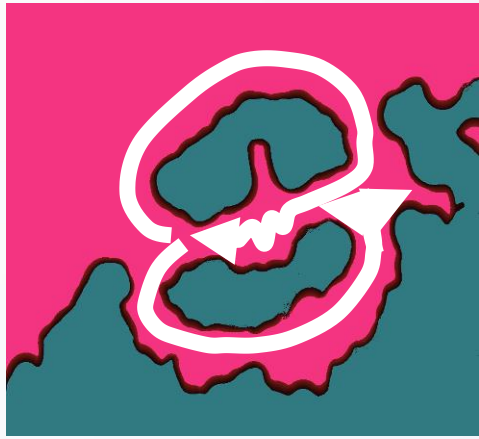


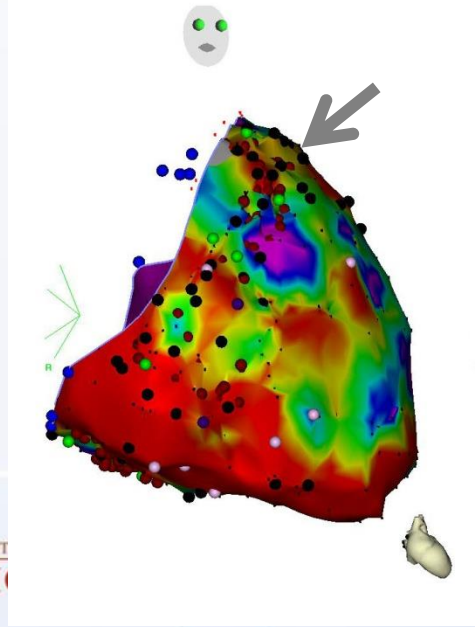


Mapování substrátu

Odstranění pozdních potenciálů ablací





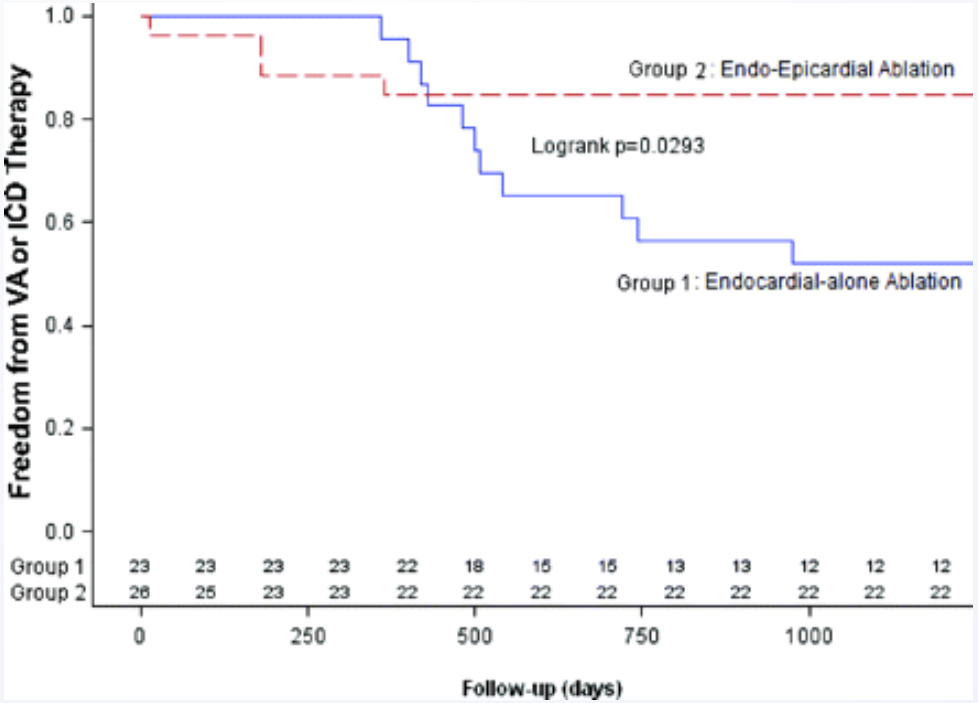


- Zpomalení vedení pomalým kanálem do jizvy po katetrizační ablaci
- Na konci výkonu došlo k úplnému vymizení pozdních potenciálů v oblasti RVOT

Ablation of substrate in ARVC

Role of epicardial ablation

- 49 pts with ARVC and ICD
  - Group 1 (23pts) – only endocardial ablation
  - Group 2 (26pts) – endo-epi ablation
- Lower recurrence rate of ICD therapy for epicardial ablation.



Bai R, Circ EP 2011;4:478-485

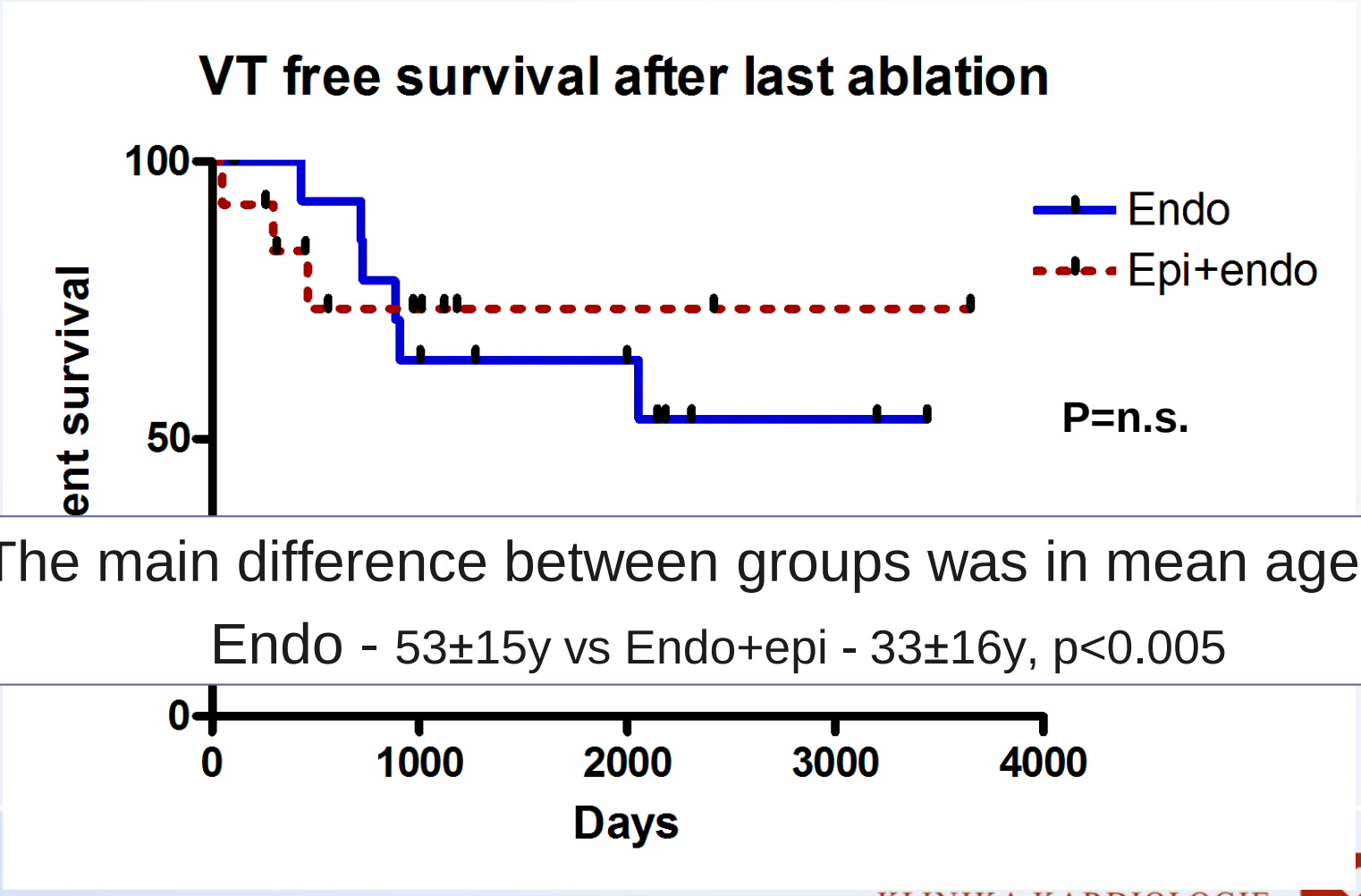
Ablation for ARVC

IKEM experience

- 2001-2016
- 33 ARVC pts, 8F, mean age 45±18y
- 1.8±1.3 ablations/patient (range 1-5)
  - 13 endo-epicardial (repeated epi in 2pts)
  - 20 only endocardial ablation

Ablation for ARVC

IKEM experience



The main difference between groups was in mean age!!

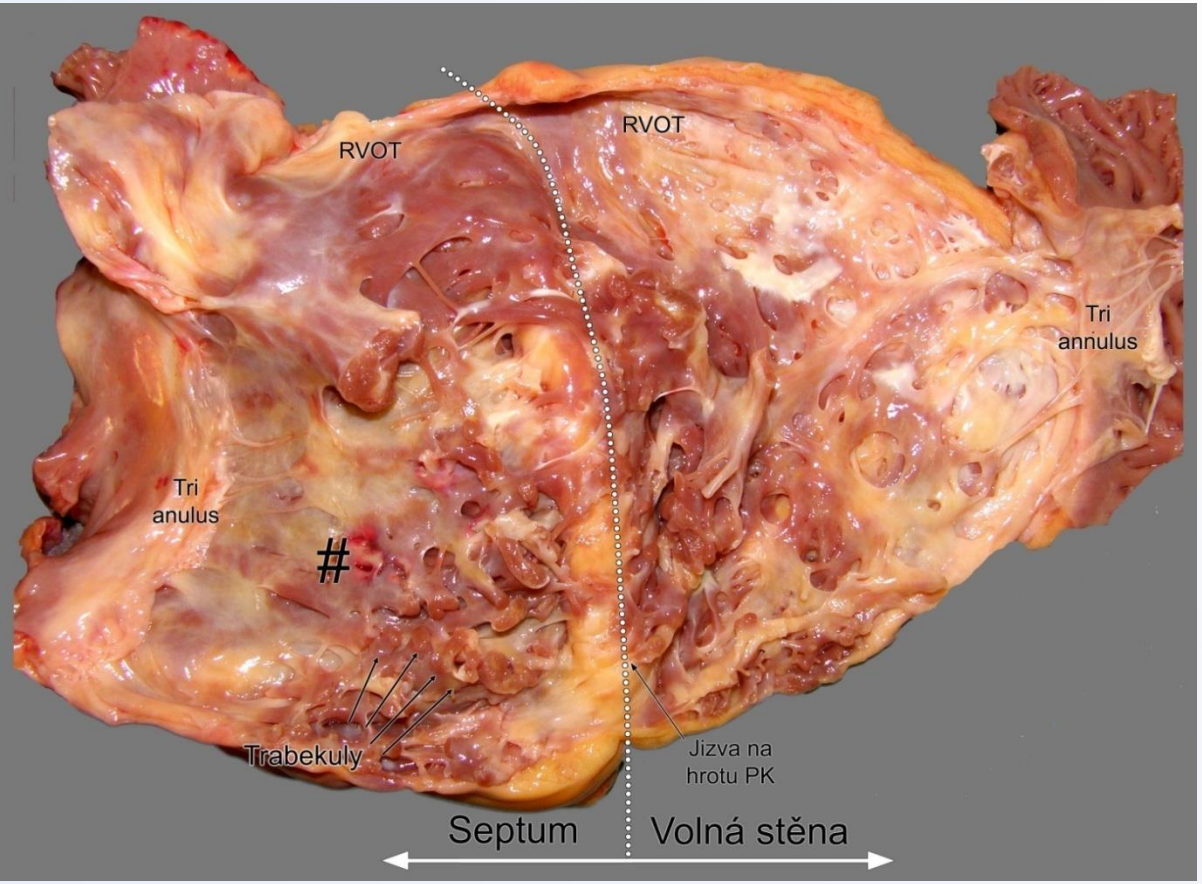
Endo - 53±15y vs Endo+epi - 33±16y, p<0.005

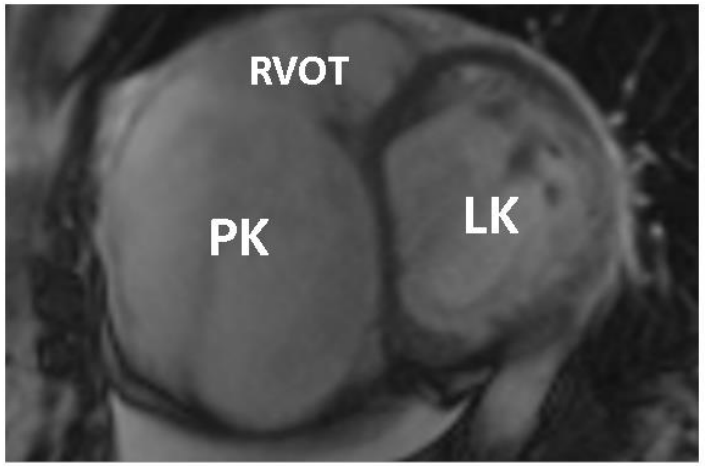
Závěry

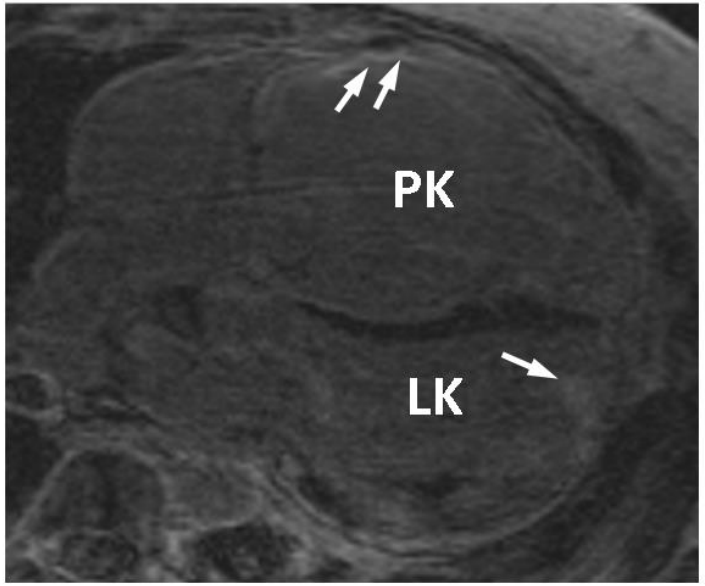
- **Omezení sportovních** aktivit platí pro všechny pacienty s ARVC
- **Implantace ICD** je indikována v sekundární prevenci NSS, kritéria primárně preventivní indikace nejsou jednoznačně stanovena
- **Z antiarytmik** je nejúčinnější amiodaron
- **Katetrizační ablace endo/epi** je přítupem volby, **především v mladém věku**

Pokročilá ARVC

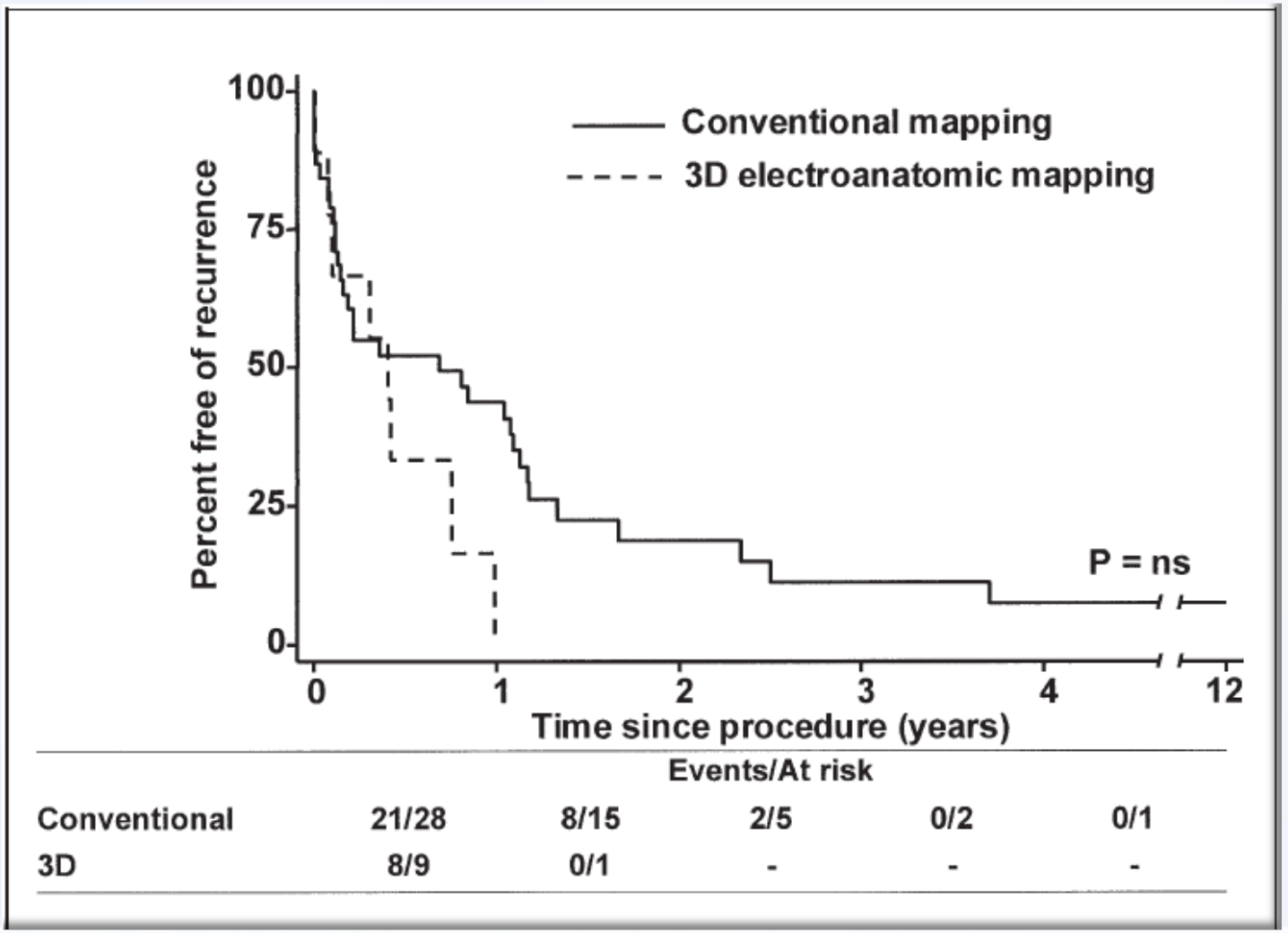
nález při Tx srdce







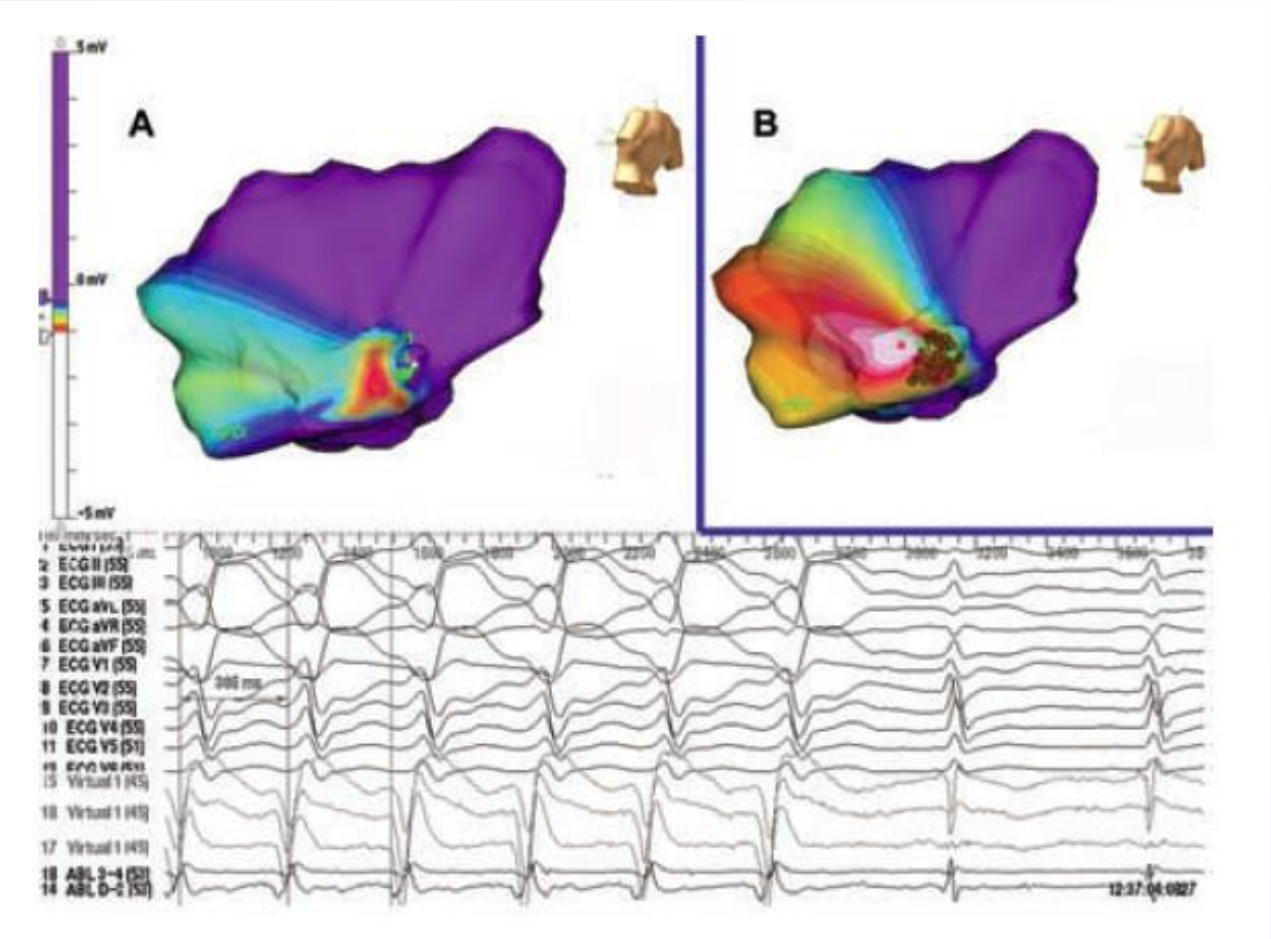
Long Term Outcome?



	Events/At risk				
Conventional	21/28	8/15	2/5	0/2	0/1
3D	8/9	0/1	-	-	-

Calkins H, et al. JACC 2007;50:432-40

NonContact Mapping



32 ARVD pts (6F, 37.2±13.8 y)

67 VTs, EnSite mapping of earliest V activation site, regional ablation

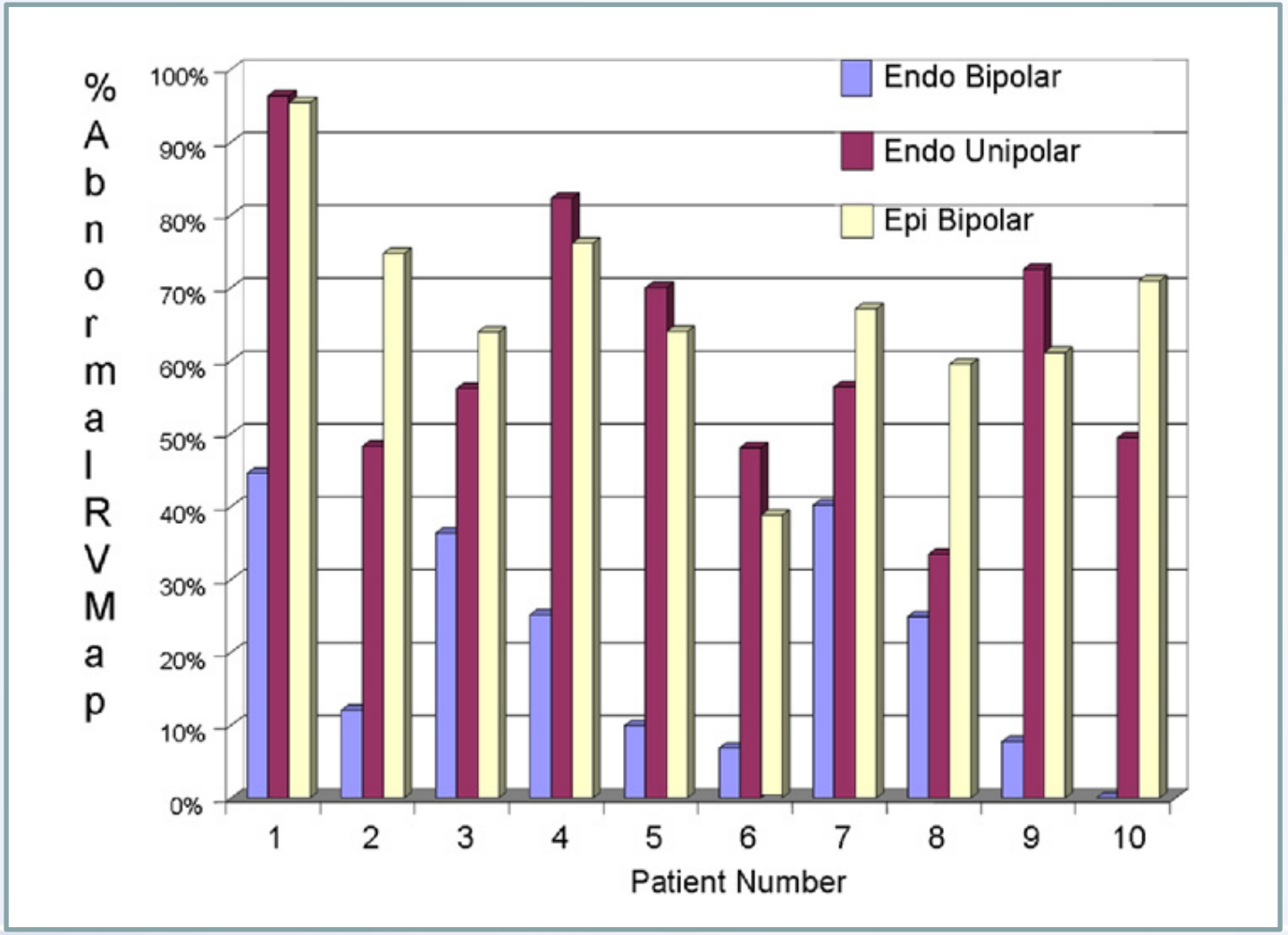
Acute success 84.4%
Significant improvement in 15.6%

FU 28.6±16 months, 81.3 % free of VT and AA incl delayed success in some pts (3)

Yao Y, et al. PACE 2007;30:526-33

Why There Are Such Differences?

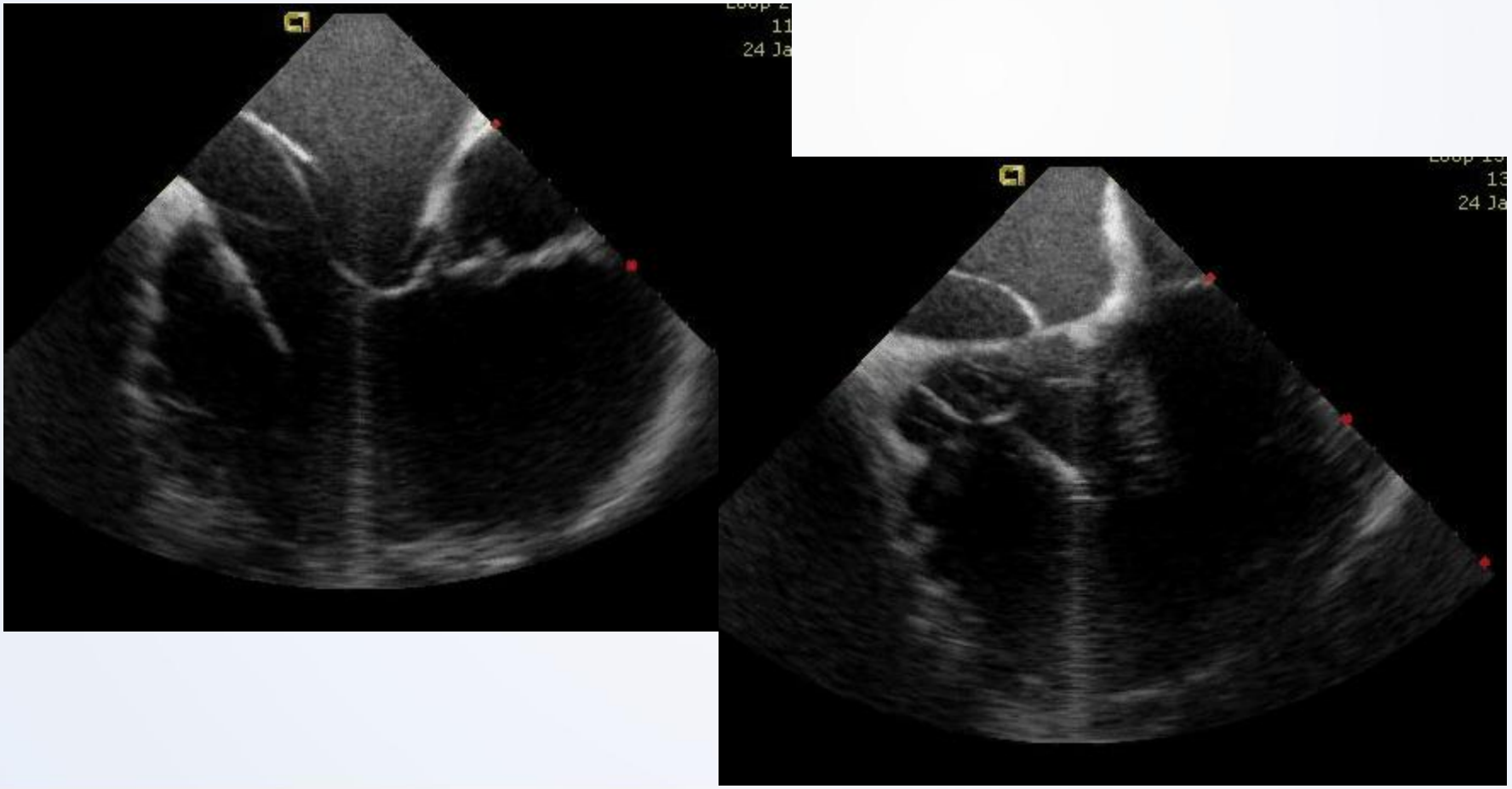
Predominant Epi Location



Polin GM, et al. Heart Rhythm 2011;8:76-83

Fissures and Trabeculae

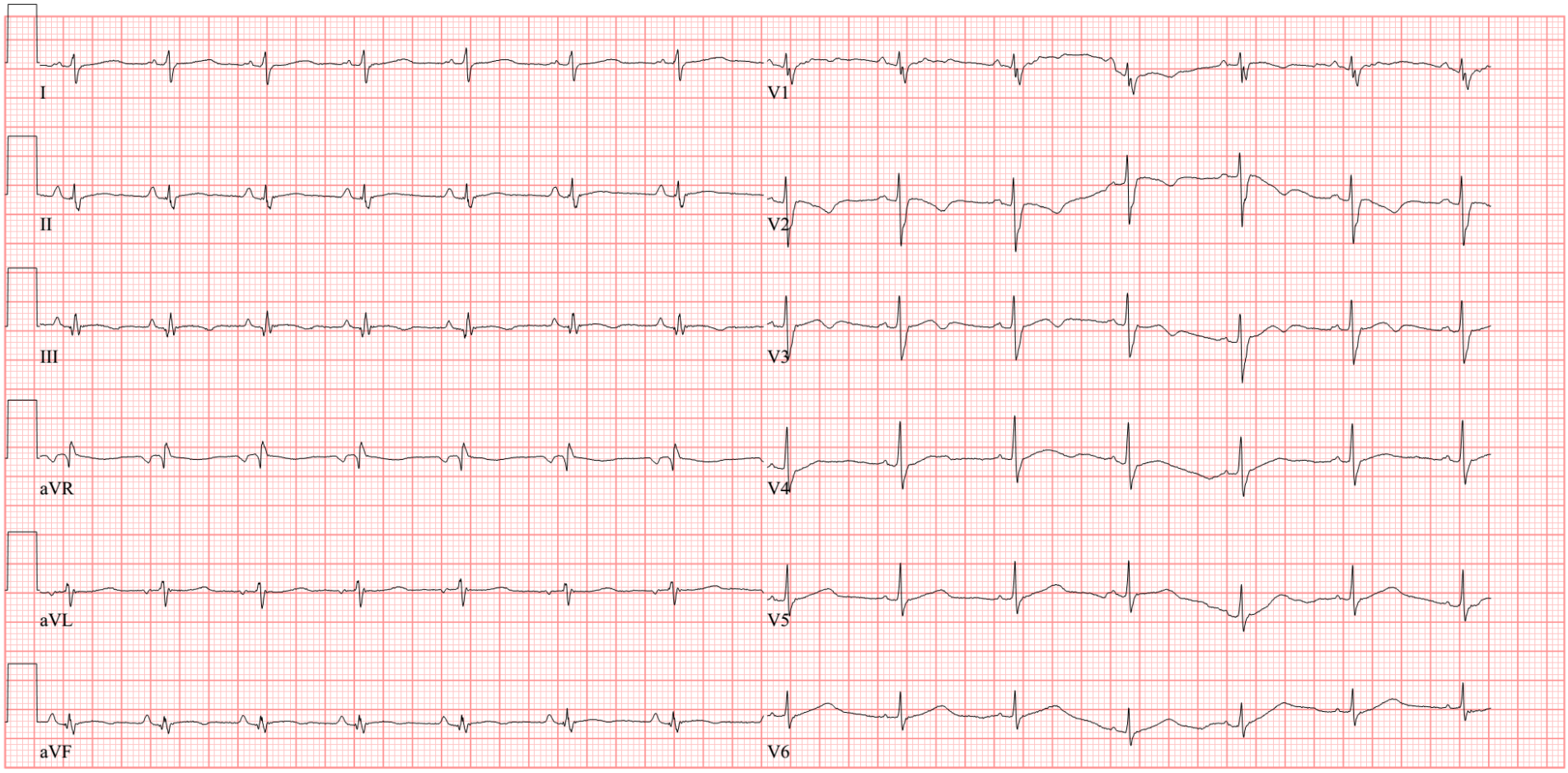
Monitoring of Catheter Position and Contact



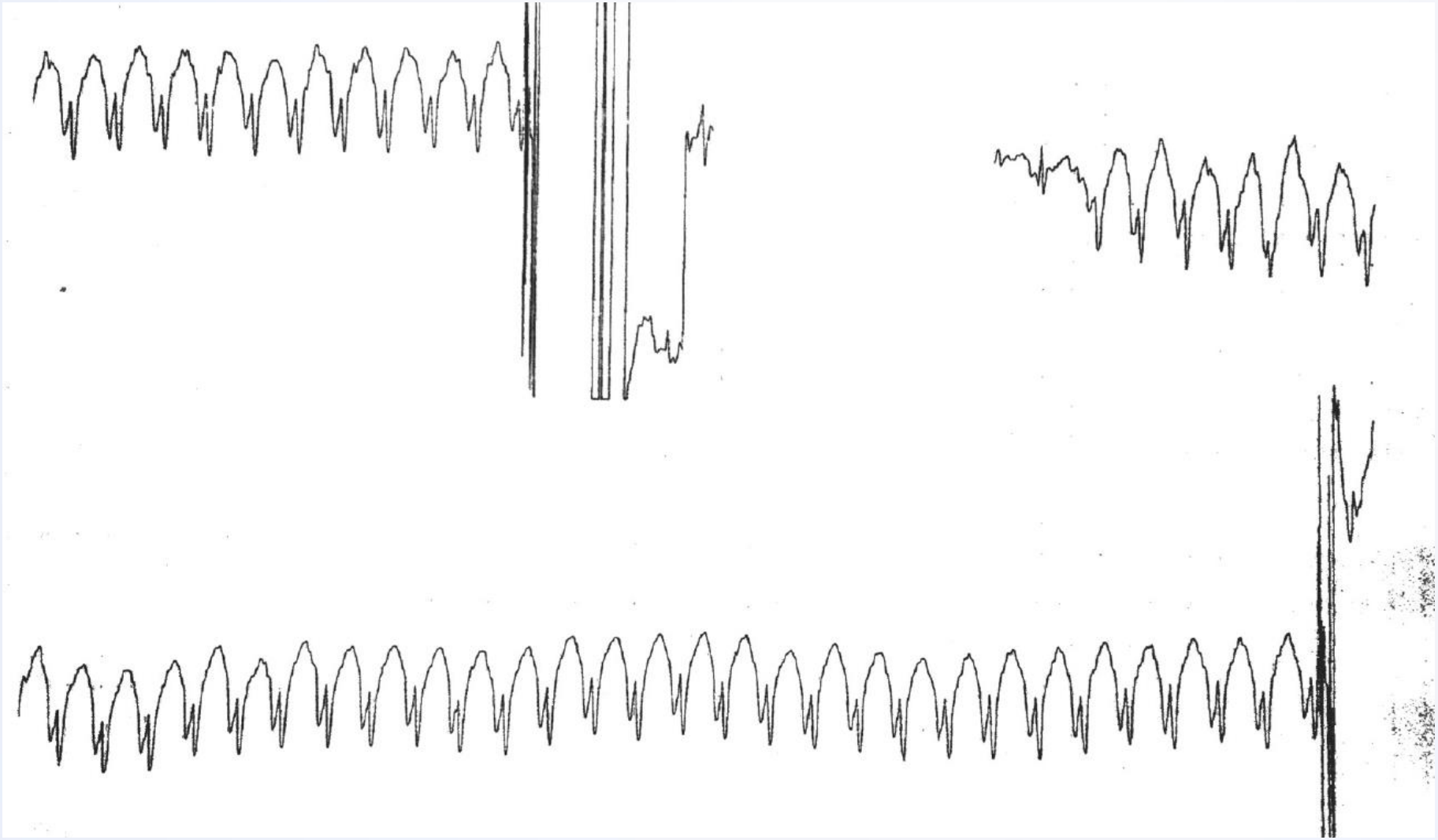
Komentář

- Naše případy-ICE guidance k posouzení přesné lokalizace katetru, zejména u trikuspidálního ústí nebo v oblasti trabekul
- Epikardiální ablace je je nutná u mladých pacientů s relativně málo vyvinutým substrátem, kdy převaha změn vždy epikardiálně
- U starších pacientů s rozsáhlým postižením pravé komory a hemodynamicky tolerovanými tachykardiemi lze provést ablaci úspěšně z endokardiálního přístupu
- U většiny nemocných je nutná opakovaná ablace, která dokáže zabránit dalším recidivám KT

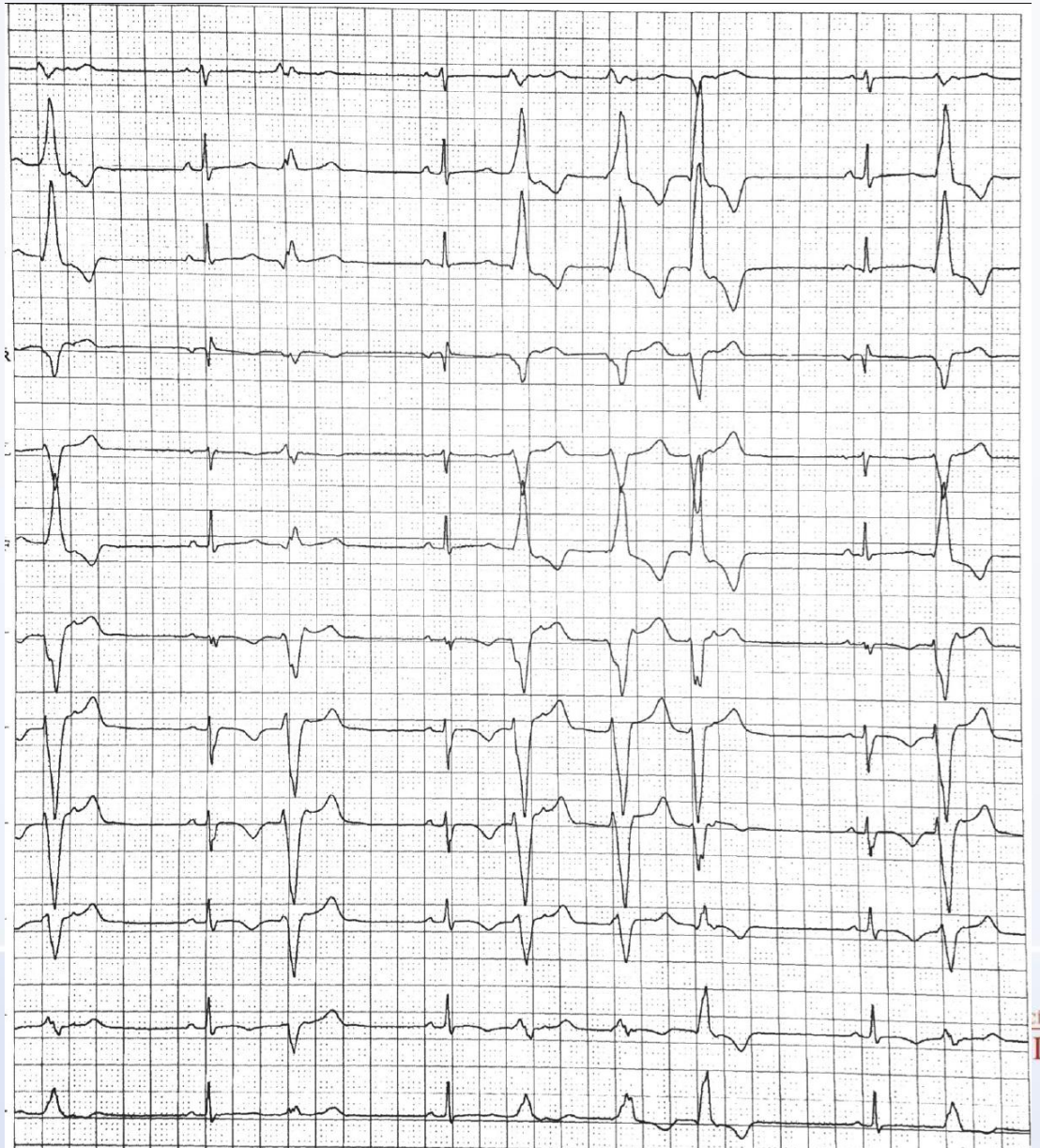
23-letý pacient



25mm/s 10mm/mV 150Hz 8.0.1 12SL 237 CID: 7 EID:16 EDT: 06:41 11-NOV-2014 ORDER:



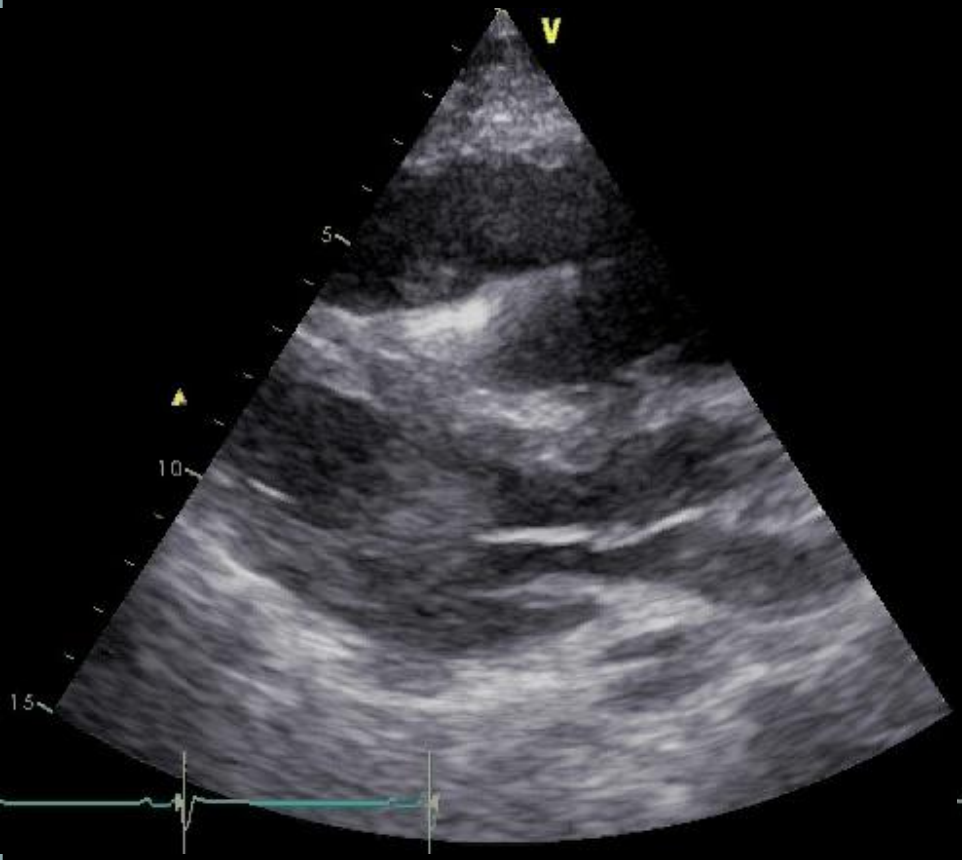
Jaká je možná etiologie?



Anamnéza

- 23-letý pacient
- 2007 KPCR pro KT
- Dle echo dysfunkce PK, MRI s nálezem susp. z arytmogenní kardiomyopathie pravé komory
- Při EFV vyvolatelná pouze nsKT
- Implantace 1D ICD
- Chronická medikace: Sotalol 80 1-1-1
- Následně opakované adekvátní výboje ICD
- 04/2014 reimplantace ICD

ECHO



Anamnéza

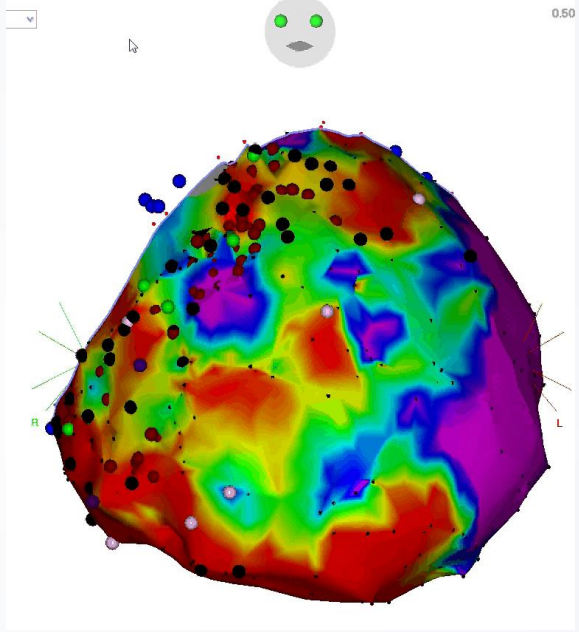
- 6.11.2014 arytmická bouře pro KT 200/min – 44 výbojů z toho 42 neúčinných
  - Zevní EKV vedoucí k resetu ICD
- Incesantní KT i přes max. farmakoterapii (BB+amio+mesocain), následně UPV
- Při pokusu o odtlumení četná komorová ektopie
- Nízký sensing na PK elektrodě

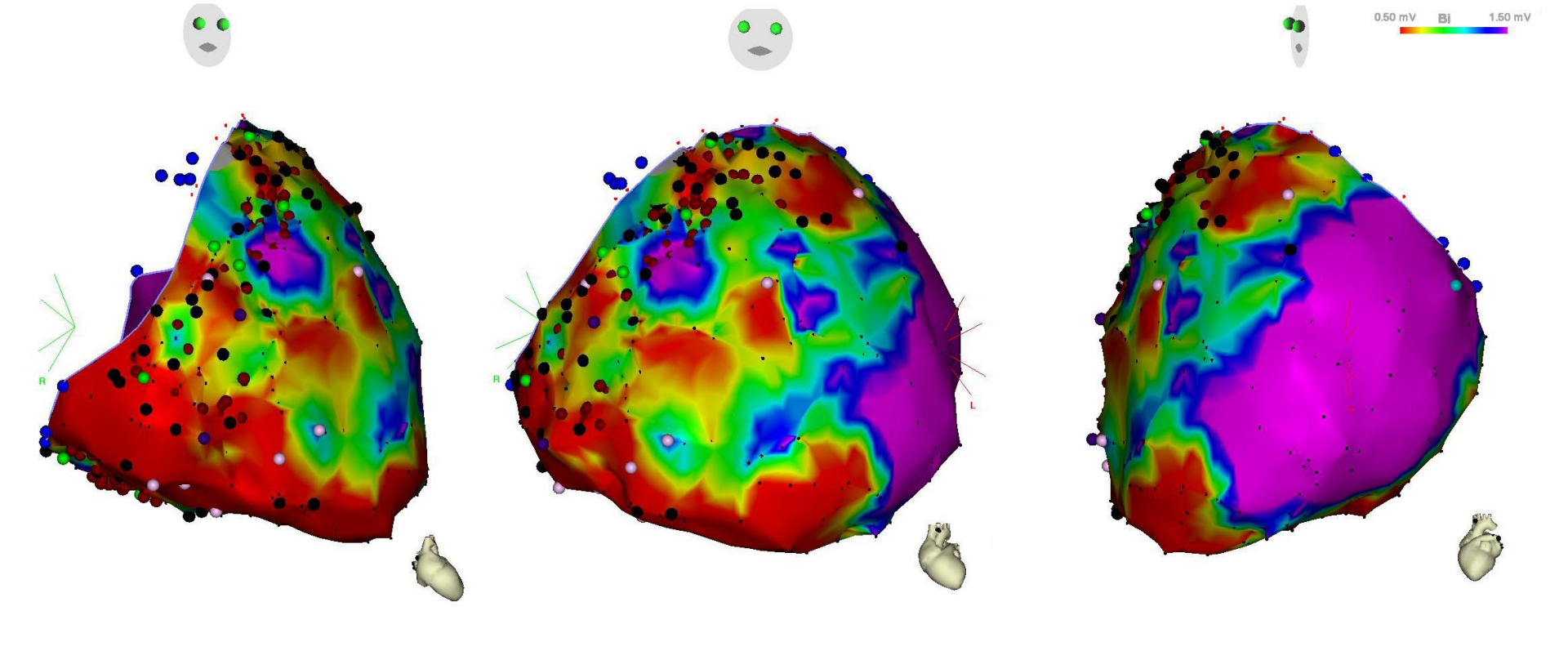
Jaký další postup?

A. Pokračovat v extubaci
B. Sycení amiodaronem
C. Provedení katetrizační ablace
D. Revize ICD systému
E. Jiná/kombinace výše uvedeného

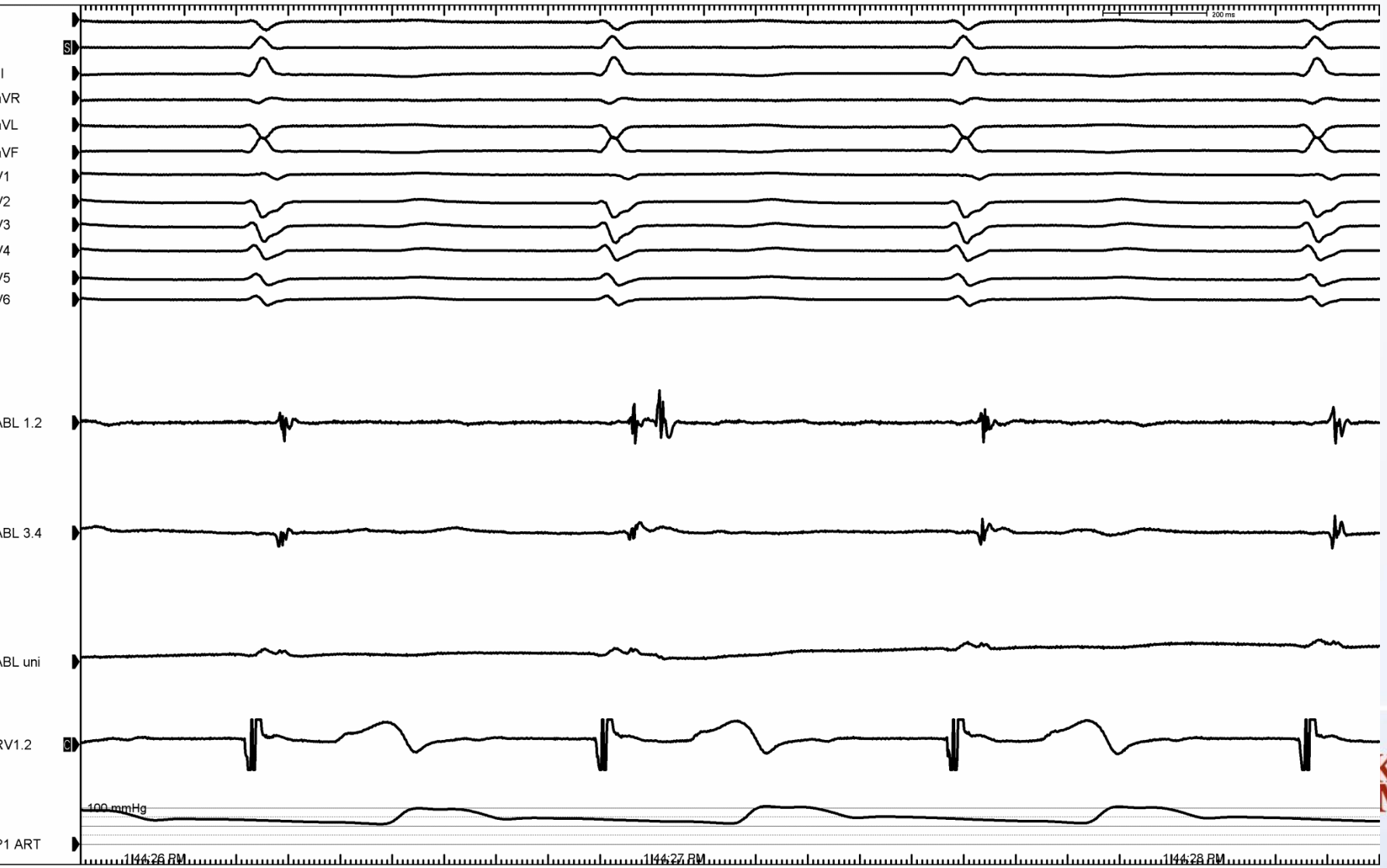
Elektroanatomické mapování povrcu srdce

- V oblasti výtokového traktu PK a inferolaterálně rozsáhlé oblasti jizevnaté tkáně

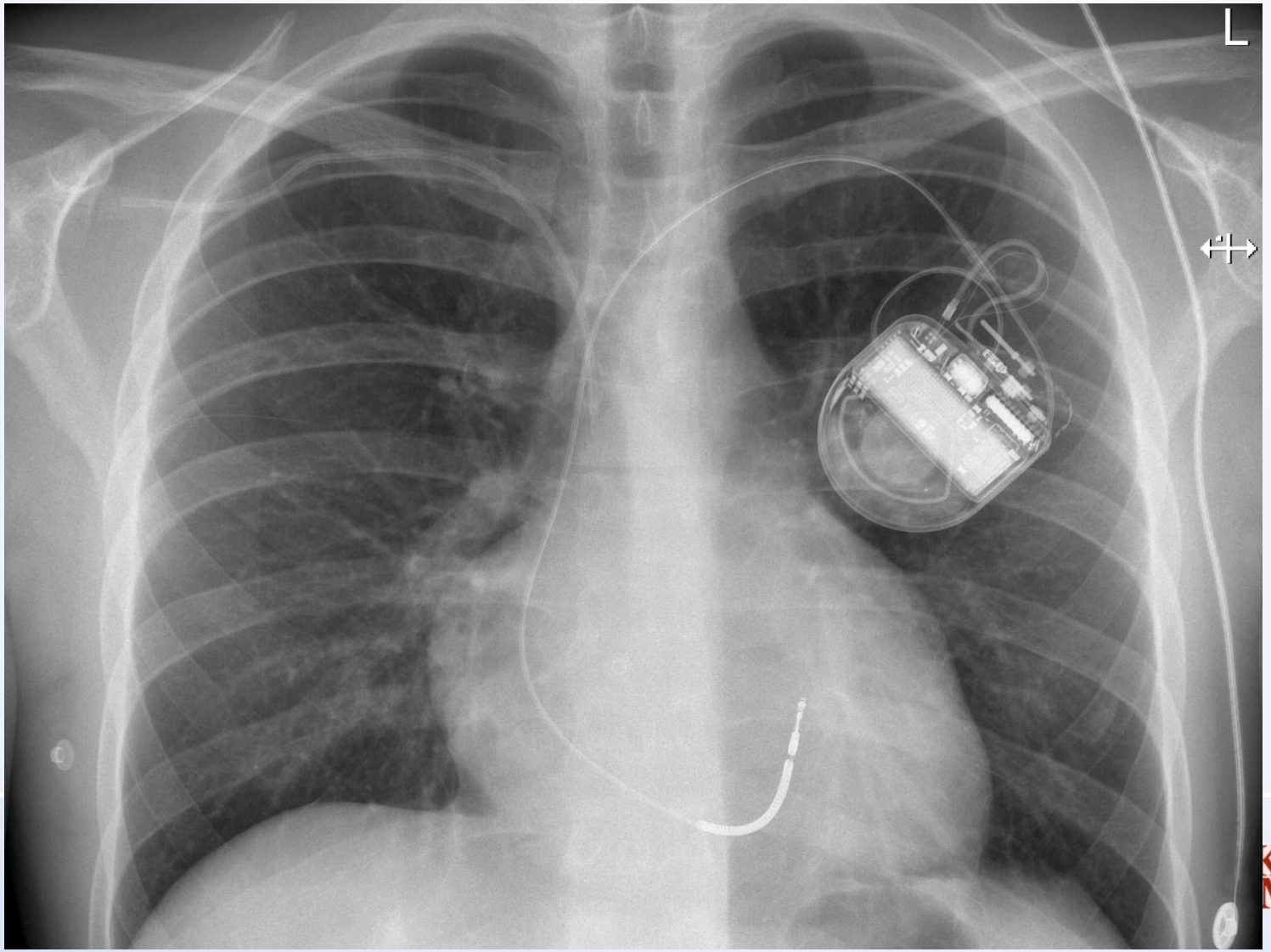




Dissociated LP



Jak dále s ICD?

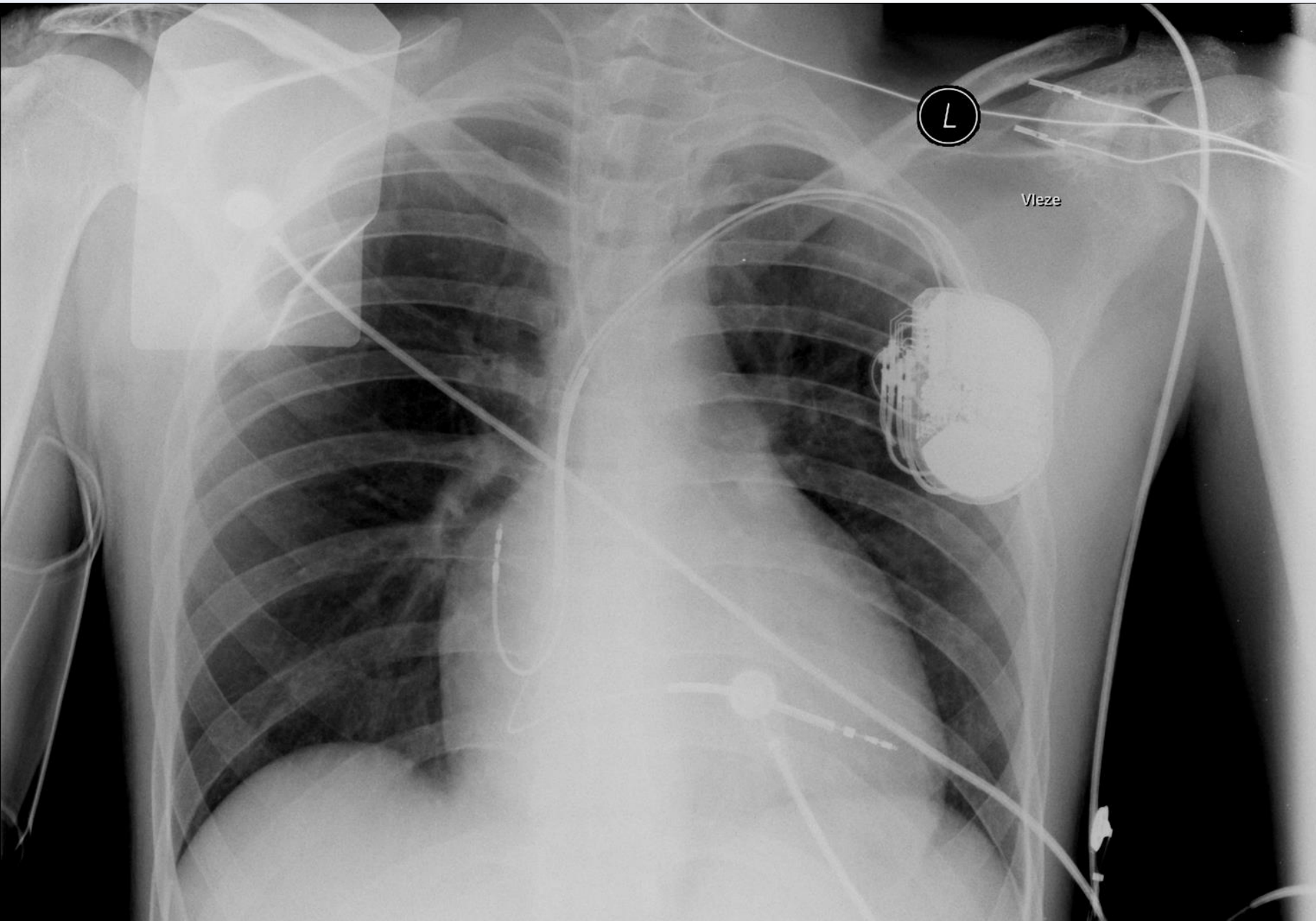


Jak dále s ICD?

- Ponechání původního ICD?
- Zachování/extrakce původní defibrilační elektrody ?
- Ponechání septální polohy elektrody/umístění do hrotu ?

Revize ICD systému

- Extrakce defibrilační elektrody (systém Evolution)
- Implantace nového DDD ICD
  - Defibrilační elektroda umístěna do hrotu PK
- Testování ICD – 15J přerušuje indukovanou FiK

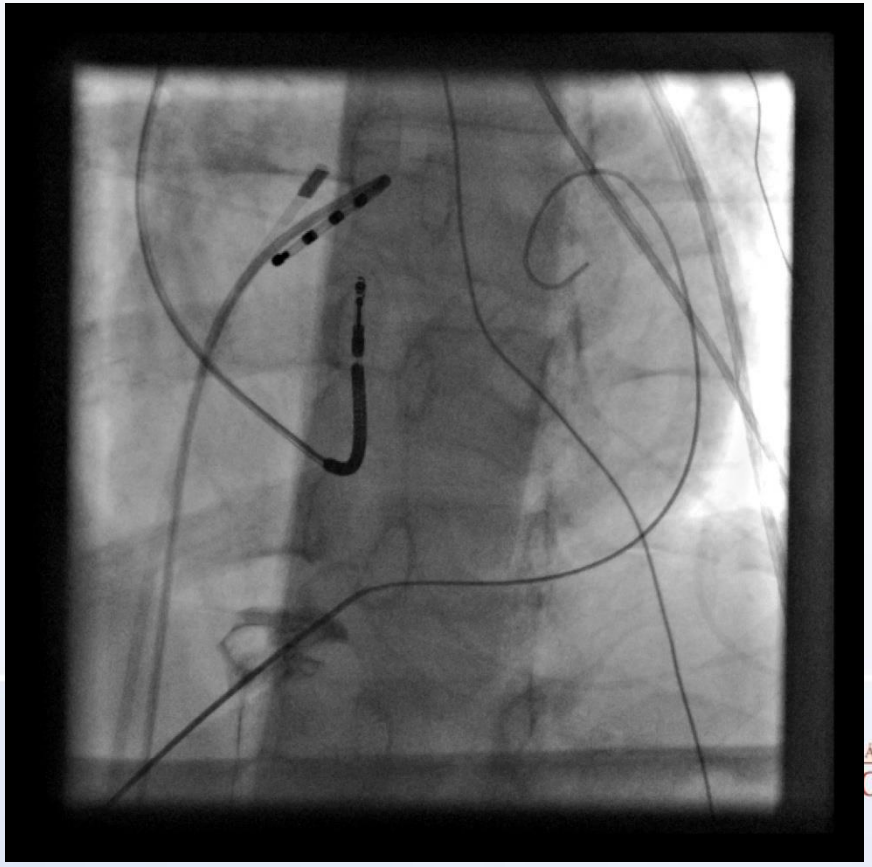

L
Vieze

Follow up

- Od ablace/revize bez recidivy arytmie
- Poslední kontrola 05/2015
- Terapie: Sotalol 80 1-1-1
- Parametry PK elektrody:
  - Senzing 9.3mV, práh 0.6V/0.4ms, imp 519Ohm

Katetrizační ablace 11.6.2014

- Nelze vyvolat žádnou setrvalou KT při programované stimulaci komor
- Provedena modifikace arytmogenního substrátu epikardiálním přístupem
-



Komentář ARVC

- Rozdíl v úspěšnosti ablací (někteří jako Calkins tvrdí, že nemá cenu ablaci dělat pro vysoké rekurence)
- Existuje několik důvodů pro rozdíly – většinou se to svádí na progresi, ale Penn group ukázala, že progrese substrátu není moc velká v čase
- Dále epi lokalizace – u nás vždy u mladých (nebylo popsáno)
- Dále substrát v PK je horší než v LK, vyžaduje zobrazení (ICE)
- Technika ablace vyžaduje optimálně EA mapping systém a kontrolu ICE

Outcomes of RFA in Literature

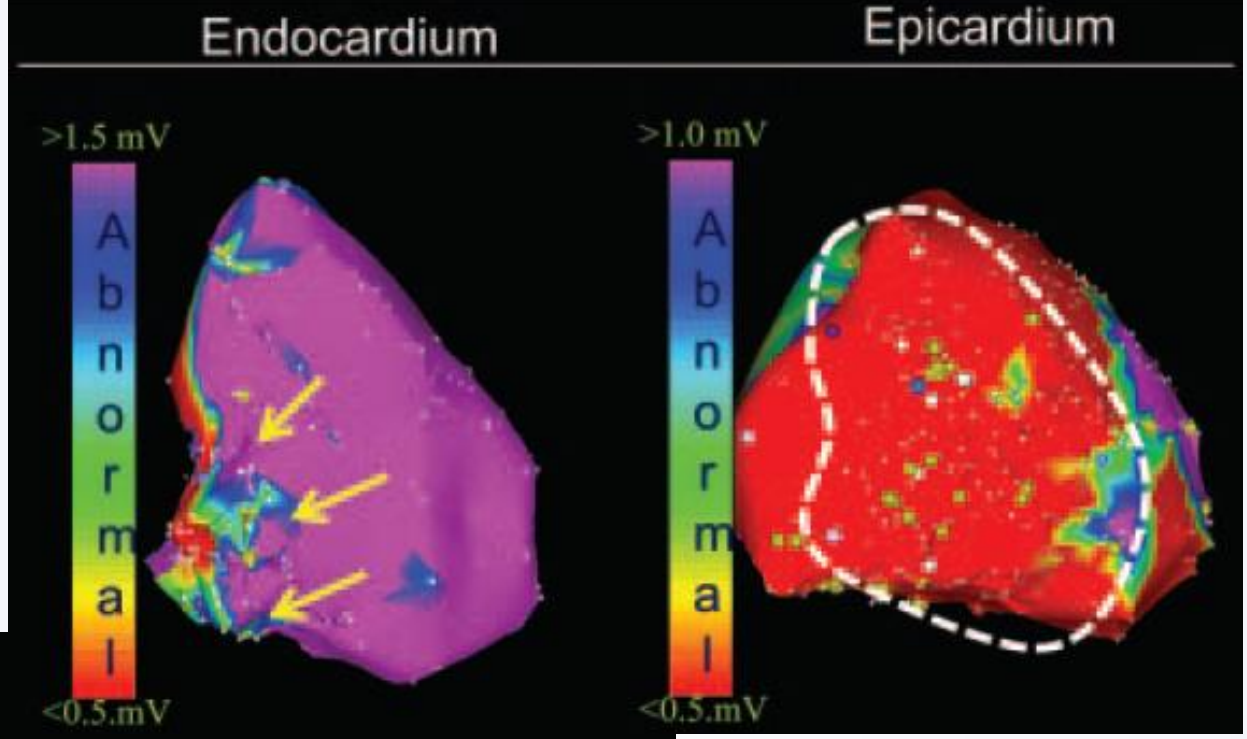
Outcomes of Radiofrequency Catheter Ablation of VT in ARVD

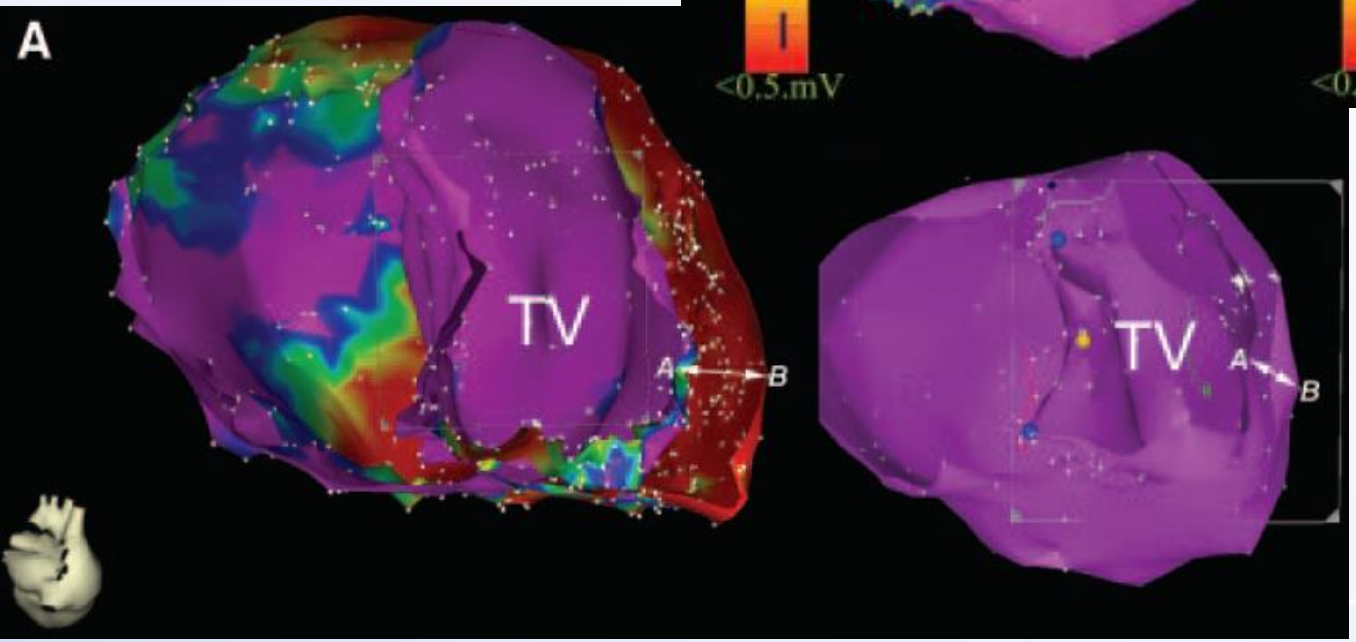
Author	Number of Patients	Number of VTs	Acute Success	Complications	ICD Implanted	Follow-Up (months)	Events at Follow-Up
Ellison *et al.*[55]	5	19	8/19 VTs 2/5 pts[*]	None	1	17 (11 to 24)	No episodes (3 pts on amiodarone)
Reithman *et al.*[71]	5	-	4/5 pts	None	4	7 ± 3	No. of ICD therapies reduced[†] (3 pts on amiodarone) 3 pts no ICD therapy 1 pt w/o ICD recurred
Van der Burg *et al.*[106]	32	-	28 pts	3 pts	-	34 ± 11 (1–57)	5 pts had VT recurrence (4 with a different VT morphology)
Wicther *et al.*[63]	30	-	22/30 pts	None	-	52 ± 37	2 sudden cardiac arrests 16 pts VT recurrence 2 pts syncope
Marchlinski *et al.*[64]	19[‡]	66	14/19 pts[§]	None	-	27 ± 22 (2 to 67)	2 pts had VT recurrence (≤1 VT episode / 3 mo)
Zou *et al.*[88]	3	5	3/3 pts 5/5 VTs[□]	None	-	8.6 (6 to 12)	None
Miljoen *et al.*[34]	11	12	9/12 VTs	None	4	36 (9 to 50)	1 death (non cardiac) No ICD events Non-inducible VT in 5/7 pts without ICD
Verma *et al.*[74]	22	3 ± 2 VT / pt	18/22 pts[#]	Cardiac tamponade (1 pt)[¶]	22	37 (25 to 44)	8 pts with VT recurrence[**] (6 pts on amiodarone, 11 pts on sotalol, 3 pts on mexiletine and 4 on flecainide)
Satomi *et al.*[72]	17	26	23/26 VTs 15/17 pts	-	2	26 ± 15 (6 to 46)	2 pts had VT recurrence[††] (9 pts on AAD)
Dalal *et al.*[92]	24[‡‡]	-	37/48 procedures	Death (1 pt)[§§]	19	32 ± 36 (1 day to 12 years)	40/48 procedures recurred (14 pts on class I or III AAD and 7 pts on beta-blockers)
Yao *et al.*[89]	32	67	27/32 pts[□□]	None	2	28.6 ± 16 (9–12)	4 pts had VT recurrence (9 pts on ADD)
Marchlinski *et al.*[65]	30	-	29/30 pts[¶¶]	-	-	34 ± 28	9 pts had VT recurrence (13 pts on class I or III AAD)
Garcia *et al.*[94]	13[##]	27	10/13 pts	-	-	18.3 ± 12.7	1 pt transplantation (after acute failure) 2 pts with a single VT episode (3 pts on AAD–none with amiodarone)

AAD = antiarrhythmic drug; ATP = antitachycardia pacing; VT = ventricular tachycardia; pt = patient. [*]Faster VT induced at the end of the procedure in one patient; [†]P <0.05; [‡]Second procedure needed in 13 patients; §Polymorphic or rapid (<300 ms) VT was induced in the other 5 patients and were not targeted; [□]A non-clinical VT was induced in 1 patient that was not targeted; ¶Pericardiocentesis was performed and no surgery was needed; [#]A second succesful procedure was perfomed in 3 of 4 patients with initial failure; [**]Second procedure in 3 patients that were initially successful and had recurrence of 1 pt at follow-up; [††]Responsive to previously failed antiarrhythmic therapy; [‡‡]A total of 48 procedures were needed; §§A highly unstable VT was induced during a third procedure for incessant VT. Hypotension developed and surgery was performed for fear of perforation, with unfavourable outcome (postoperative pulmonary complications); [□□]Second procedure performed in 10 patients. ¶¶Second procedure performed in 21 pts. [##]Consecutive patients with prior failed endocardial ablation.

Arbelo E, Josephson ME. JCE 2010;21:473-86

Epicardial Ablation in ARVC



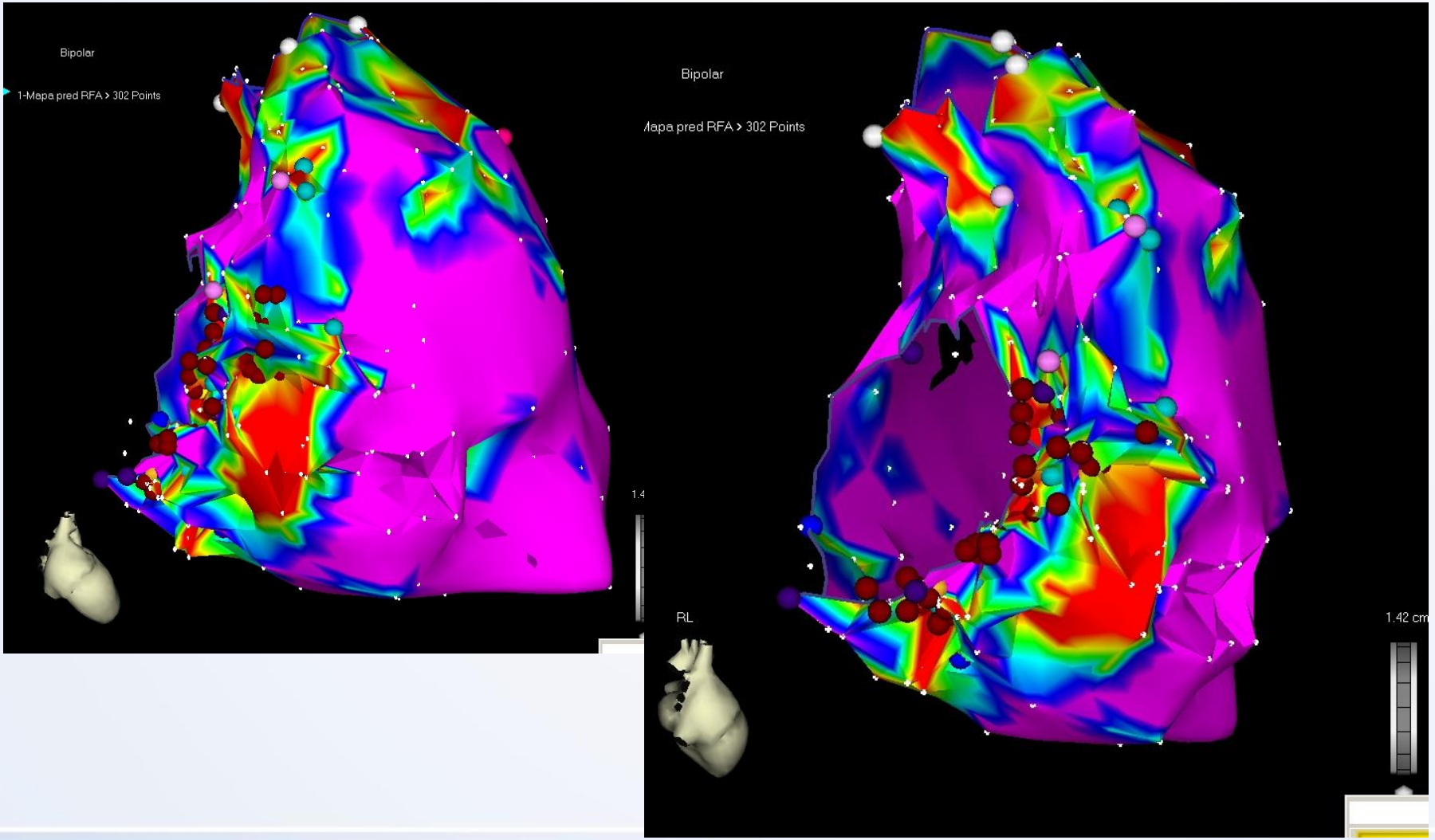


13 pts (17-70 years) failed endo VT ablation

epi sites opposite ineffective endo sites in 11 pts (85 %)
77% VT free in 18±13 mths

Garcia FT, et al. Circulation 2009;120:366-375

Technique of Ablation



Mapování substrátu

Dlouhý stimulus-to-QRS interval