GENOTYPE, PHENOTYPE AND OUTCOMES OF ATIENTS WITH HYPERTROPHIC ARDIOMYOPATHY REFERRED FOR VT ABLATION

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EPIDEMIOLOGY

- Prevalence of unexplained hypertrophy is estimated to be 1/500 adults
- Equal distribution per sex
- HCM presents AD inheritance with variable expressivity

Table 1. Prior Estimates of HCM Prevalence With Echocardiography in 6 Populations

First Author (Ref. #)	Year	N	Age (yrs)	% Male	Maximal LV Thickness (mm)	Reported Prevalence (%)	Study Subjects
Maron et al. (4)	1995	4,111	25–35	71	17 ± 2	0.17	Random sampling from urban general population (CARDIA study)
Hada et al. (6)	1987	1,584	47*	76	17 ± 3	0.17	Annual health examinations
Maron et al. (8)	1999	15,137	57*	48	21 ± 4	0.19	Mobile echocardiography in rural communities
Maron et al. (9)	2004	3,501	60	50	21 ± 3	0.23	American Indian tribal communities†
Zou et al. (5)	2004	8,080	52	69	17 ± 6	0.16	Random sample from 9 communities in China
Maro et al. (10)	2006	6,680	55	68	21 ± 0.4	0.19	East African (Tanzanian) district regional hospital

emsarian C, Ingles J, Maron MS, Maron BJ. New perspectives on the prevalence of hypertrophic cardiomyopathy. J Am Coll Cardiol. 2015

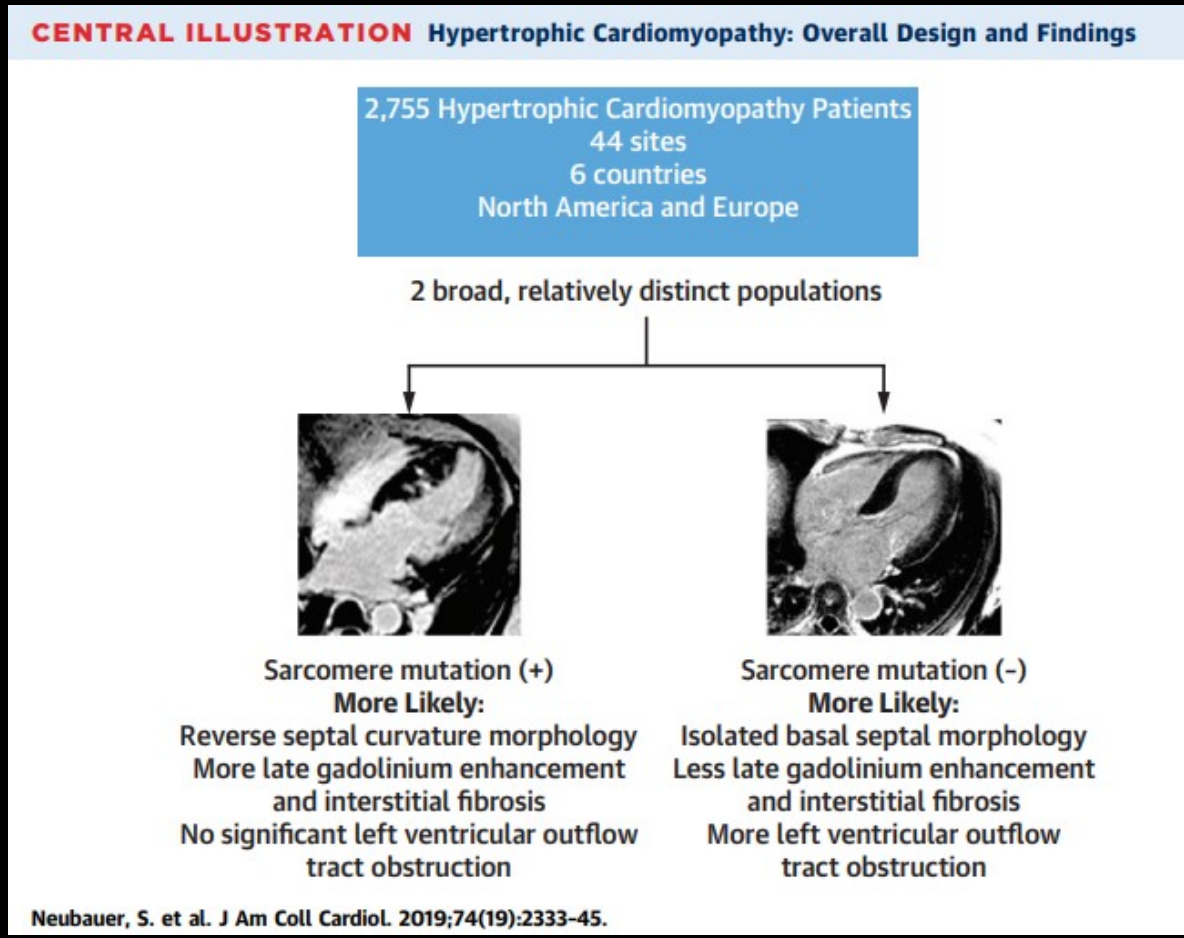
DIAGNOSTIC CRITERIA

- Adults → LV WT ≥ 15 mm, anywhere in the ventricle, no apparent cause for hypertrophy *
- Children → Actual ≥ 2 - Z-score deviation in LV WT *
- Class IV/V mutation carriers
  - No phenotype → patient at risk for development

024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy, JACC. 2024 Jun

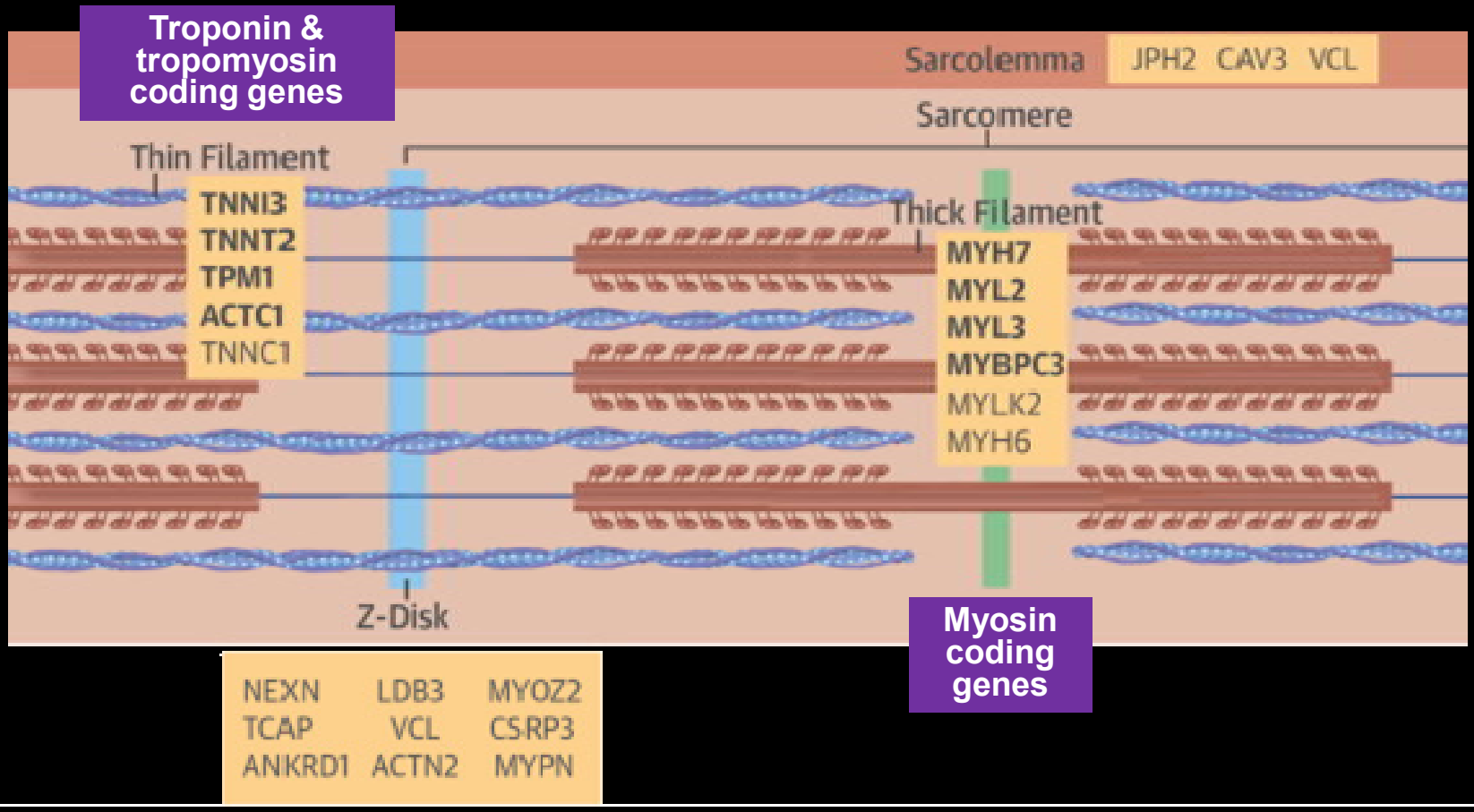
GENETICS

- 30-60% patients have identified LP/P mutation
- Most frequent genetic mutations are Sarcomeric mutations
- Incomplete penetrance



eubauer S, K, et al. Distinct Subgroups in Hypertrophic Cardiomyopathy in the NHLBI HCM Registry. J Am Coll Cardiol. 2019

SARCOMERIC PROTEIN CODING GENES

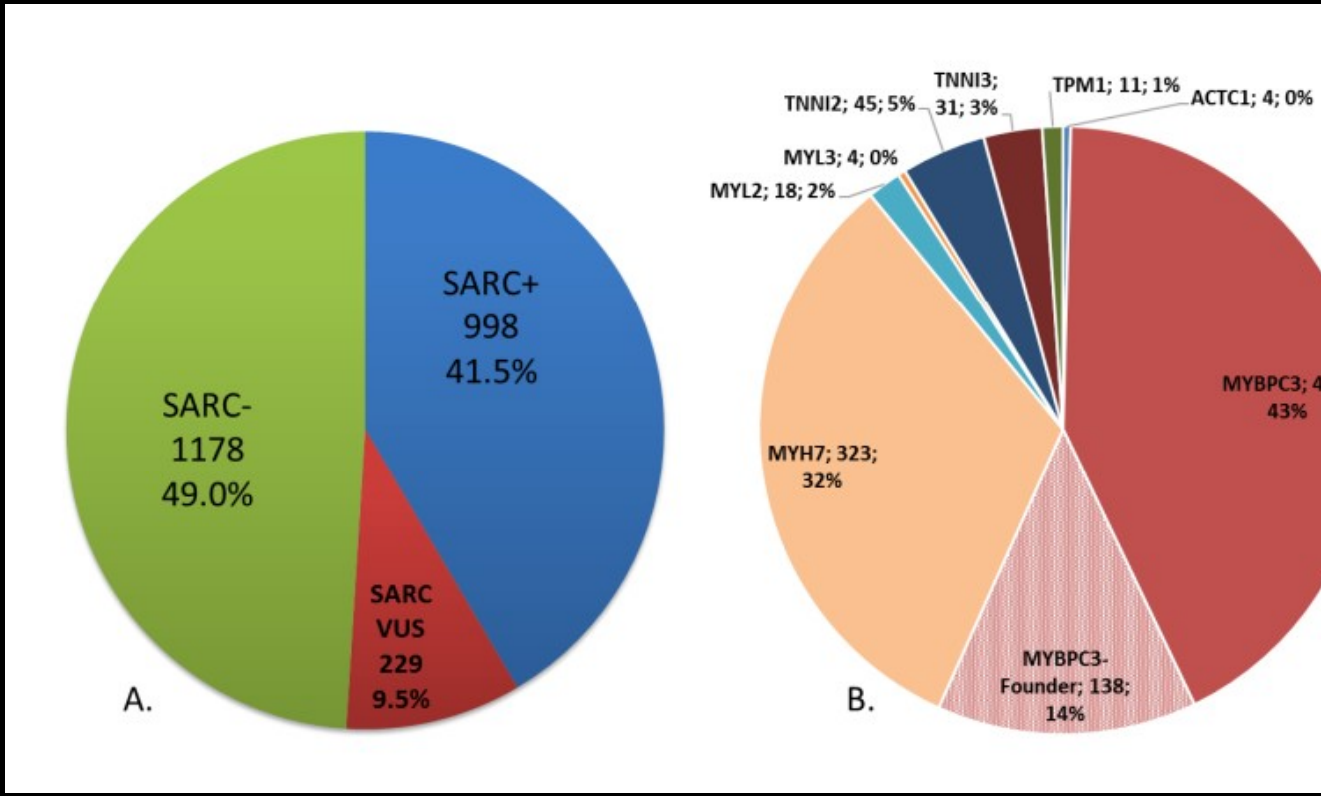


rke MA, Cook SA, Seidman JG, Seidman CE. Clinical and Mechanistic Insights Into the Genetics of Cardiomyopathy. J Am Coll Cardiol. 2016

GENETICS

SHaRe registry

- 2763/4519 patients genotyped → 1279 had a Sarcomeric mutation
- MYBPC3 43% (+ 14% with founder mutations)
- MYH7 32%



o CY, et al. Genotype and Lifetime Burden of Disease in Hypertrophic Cardiomyopathy: Insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe). irculation. 2018

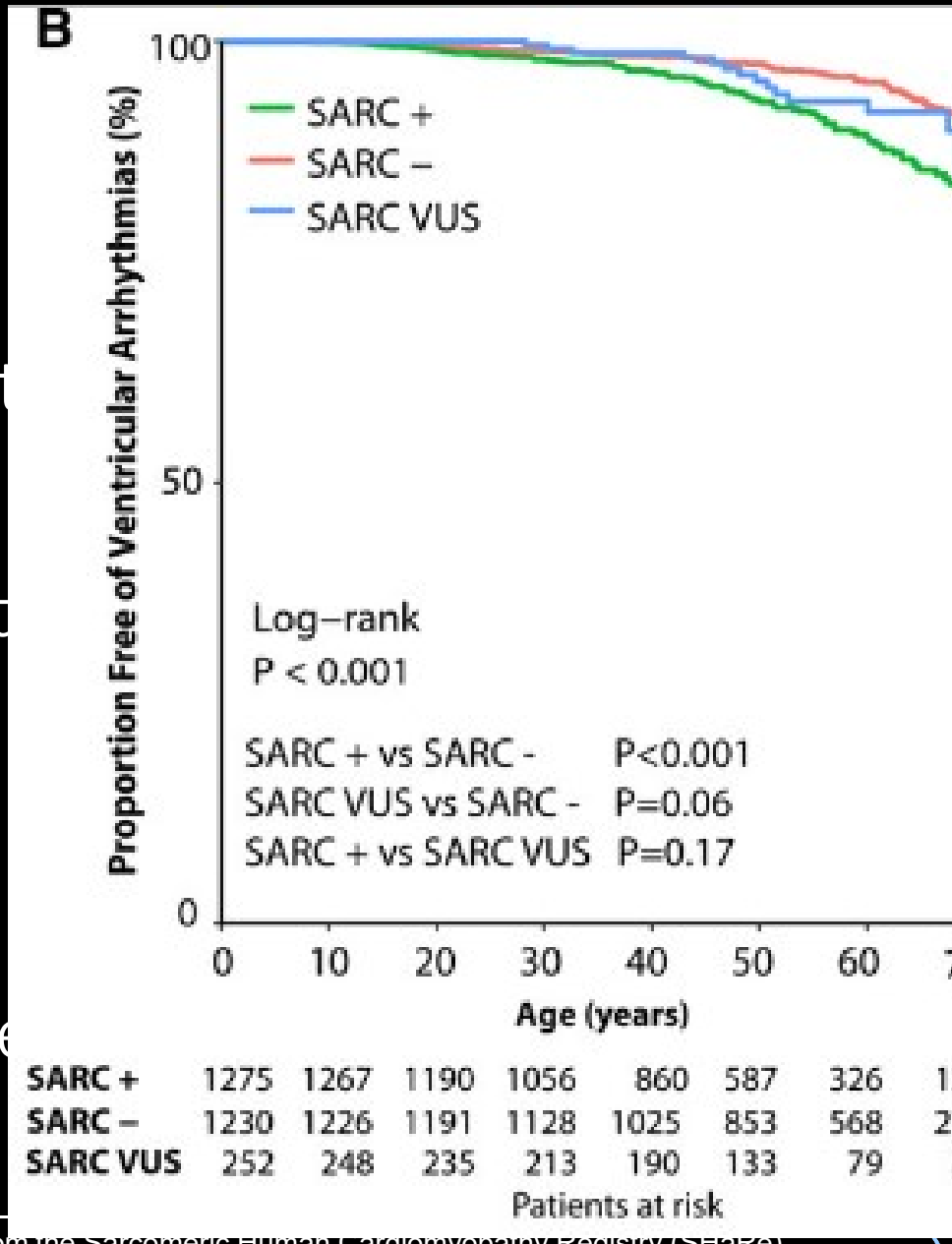
VA INCIDENCE

- Recent large population studies report SCD 1.2-1.5%/yr
- Risk assessment for SCD should be lead by periodical re-evaluation in patients care
- Current risk scores don’t account for new markers
  - Moreover, no consensus on best LGE quantification method

rrish G, Ding T, et al. Development of a novel risk prediction model for sudden cardiac death in childhood hypertrophic cardiomyopathy (HCM Risk-Kids). JAMA rdiol 2019;

VA INCIDENCE

- EPS induced VA is non-specific and not
- No RCT on AAD to prevent SCD
- Historical belief → SCD in HCM is relat
- In patients w/ ICD
  - SMVT is the MOST COMMON VA
  - ATP is successful in ~ 70% episodes
- RFCA in patients w/ recurrence despite



o CY, et al. Genotype and Lifetime Burden of Disease in Hypertrophic Cardiomyopathy: Insights from the Sarcomeric Human Cardiomyopathy Registry (SHaRe). irculation. 2018

OUR DATA

METHODS

- Consecutive patients from the Leiden VT registry referred for RFCA for VA
- Baseline: index VT ablation

- From 2011 up to 2023 → 1063 patients referred for VT ablation
  - 9 ♂ patients presented HCM phenotype

METHODS

- Medical records, family history, AAD, ECG, ICD registries
- Multimodal imaging evaluation
  - Echocardiographic evaluation
  - MS Contrast enhanced Cardiac CT analysis
  - Contrast enhanced MRI
- Electroanatomic map, VT ablation procedures and bail out strategies

RESULTS

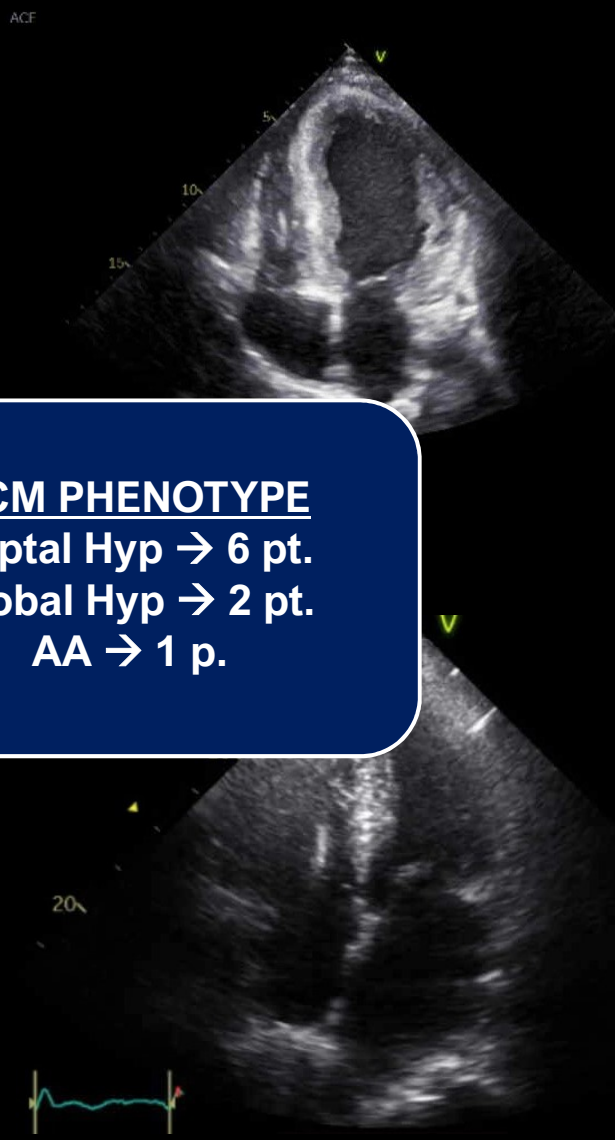
BASELINE CHARACTERISTICS

Population	
Age at ablation	59 (IQR 45-61) years
Age at HCM diagnosis	40 (IQR 27-53) years
Family history HCM	4 (44.4%)
Family history SCD	4 (44.4%)
Prior Syncope	5 (55.5%)
OHCA	3 (33.3%)
Betablocker	8 (88.8%)
Failed Amiodarone	6 (66.6%)
Failed Sotalol	4 (44.4%)
Failed Amio + class I	4 (44.4%)
Device at ablation	8/9 (88.8%)
1ary prevention	4/9 (44.4%)
S-ICD	2/9 (22.2%)
Dual-chamber ICD	6/9 (66.6%)
Pre Ablation ATP (6M)	8986 therapies (IQR 9-17.962)
Pre Ablation Shocks (6M)	8 shocks (IQR 6-9)
VT episodes (6M)	20 episodes (IQR 2-900)

54 CMP genes tested i
all patients:
6/9 patients with Class
mutation
all in MYBPC3

TTE

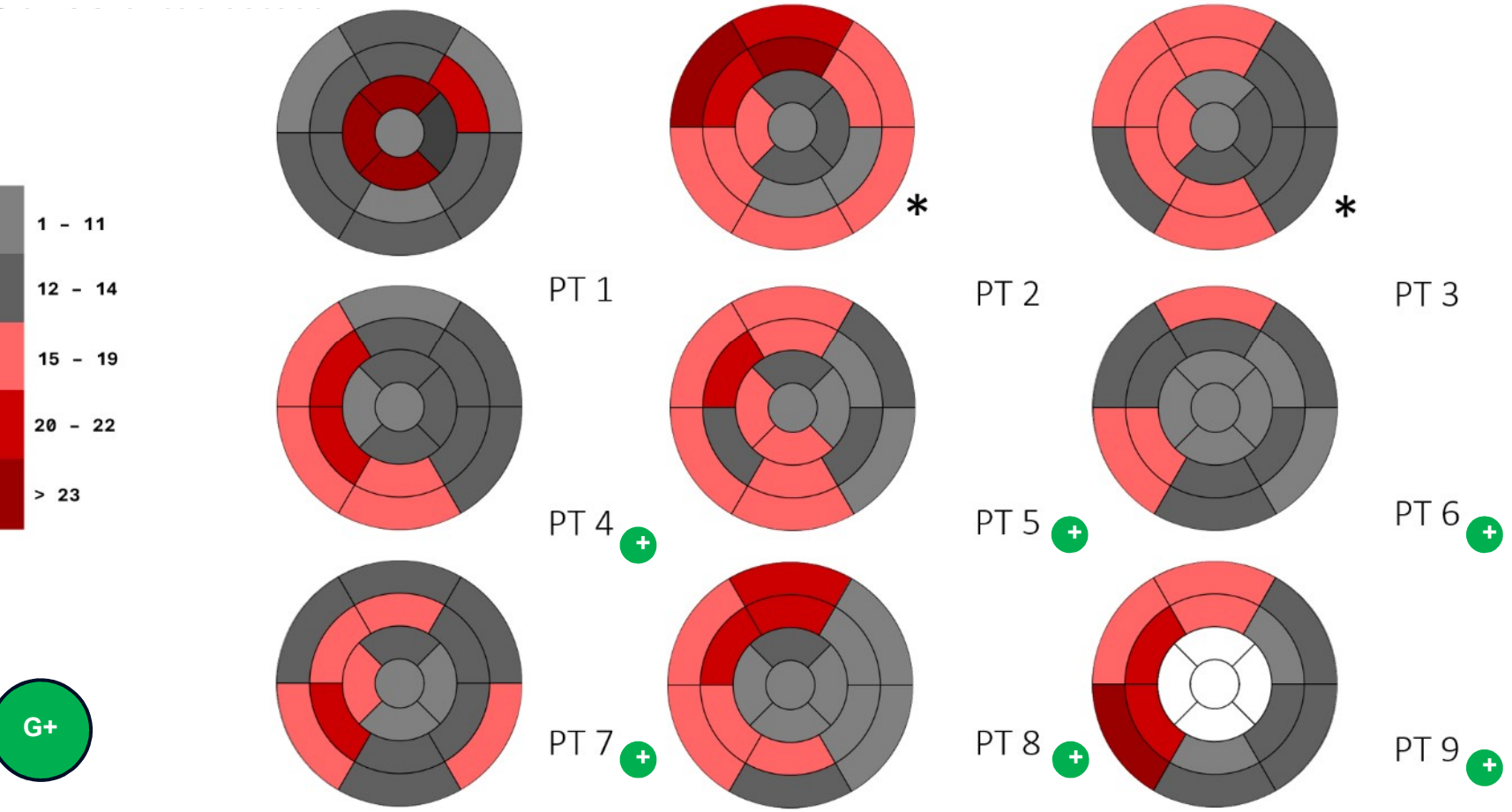
- Median EF → 42% (IQR 35-52%)
- LV mass index → 253 g/m^2 (IQR 217 – 281)
- Septal WT → 20 mm (IQR 16,5 – 22,1)
- Posterior WT → 12,2 mm (IQR 10 – 15)
- LAVI → 44,4 ml/m2 (IQR 38,3 – 48,4)
- LV GLS → 7,5% (IQR 6-13.4)
- No LVOT > 50 mmHg at baseline

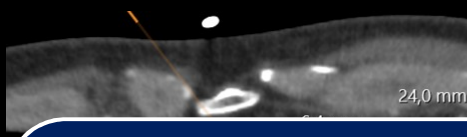


HCM PHENOTYPE
Septal Hyp → 6 pt.
Global Hyp → 2 pt.
AA → 1 p.

CE MSCT

Median segmental WT in mm



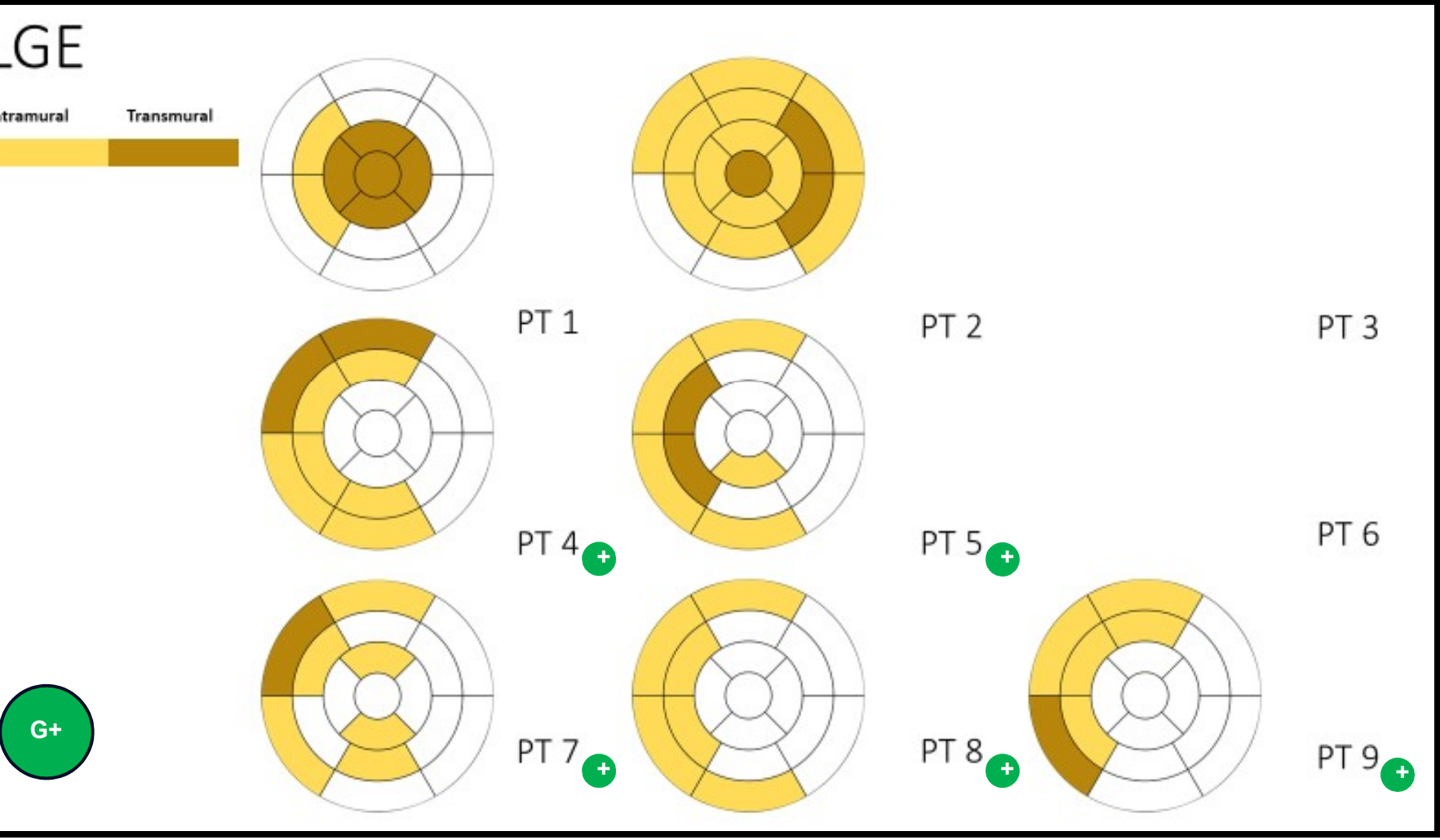


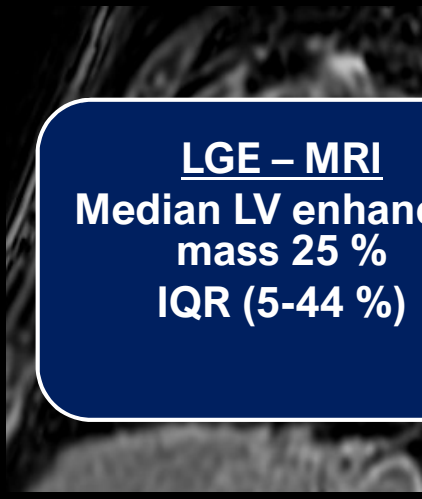
CT WT

All patients with at le
1 segment ≥ 17 mm

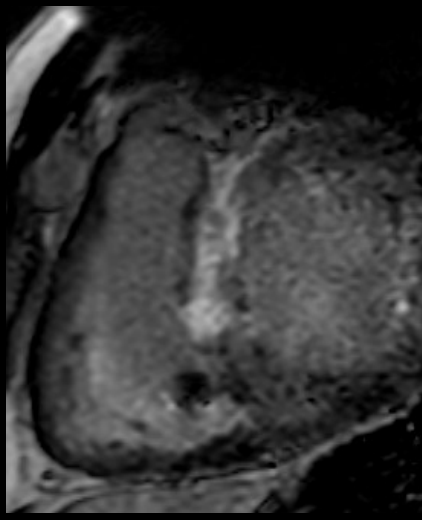
Thickest segment w
mid ventricular
anteroseptum

LGE DISTRIBUTION



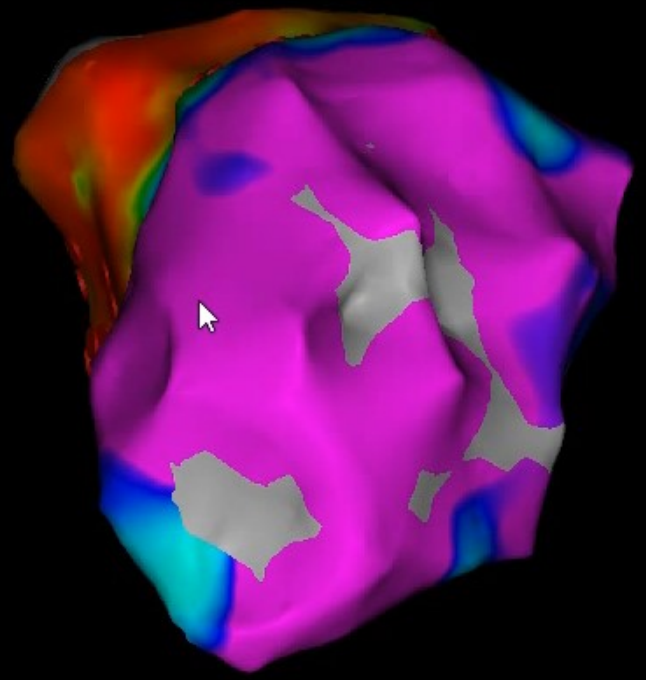


LGE – MRI
Median LV enhan
mass 25 %
IQR (5-44 %)



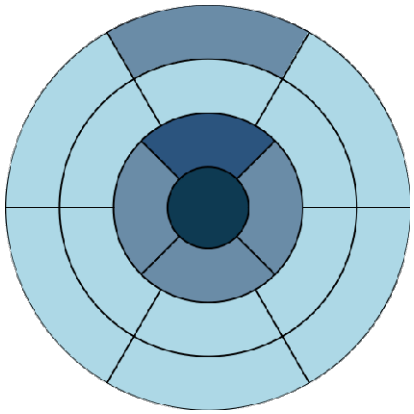
NDEX VT ABLATION

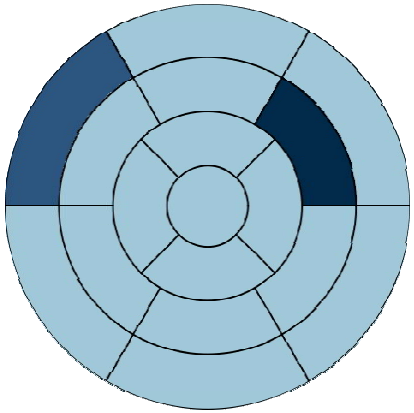
- 8/9 patients inducible for SMVT
  - Median procedural VTs 4 (IQR 3-5)
- Median procedural time 302 min
- VT substrate IVS intramural in 7
- Median RF applications 22 (IQR 11-66)
- Median RF time 769 sec
- Epicardial map in 2/9 patients



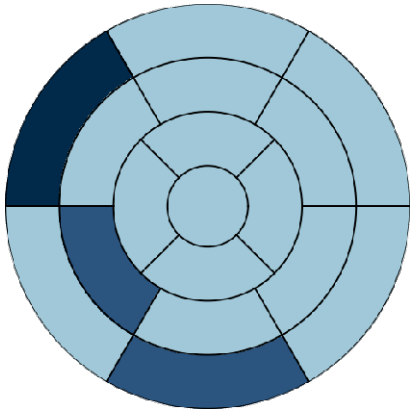
AM BV

0.5 mV 1.5 mV



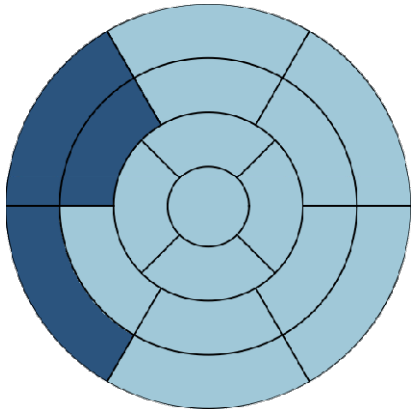


PT 1

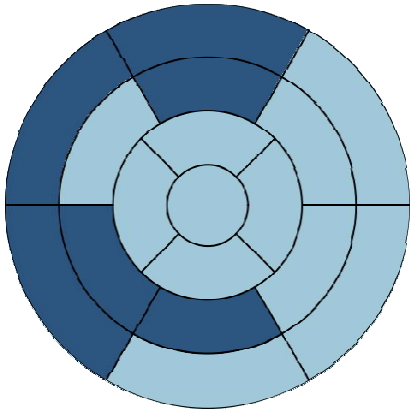


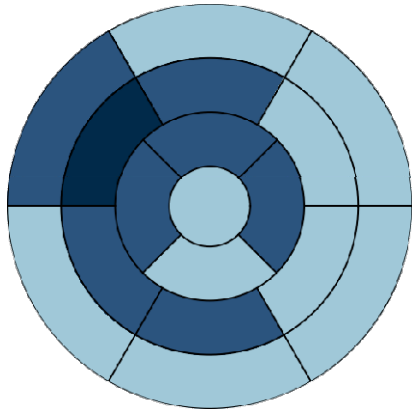
PT 2

PT



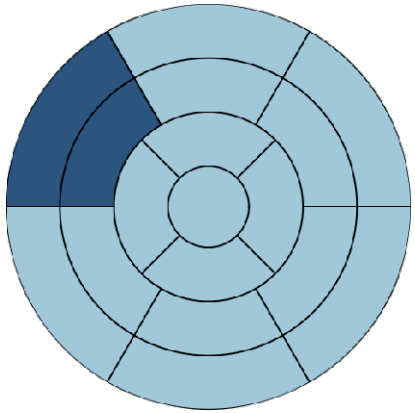
PT 4



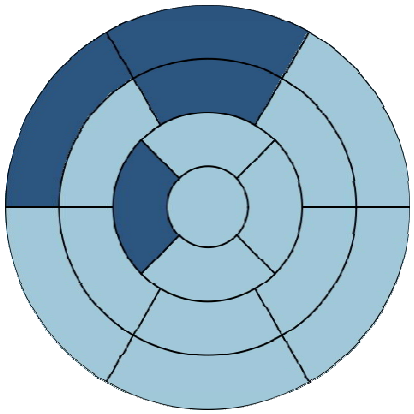


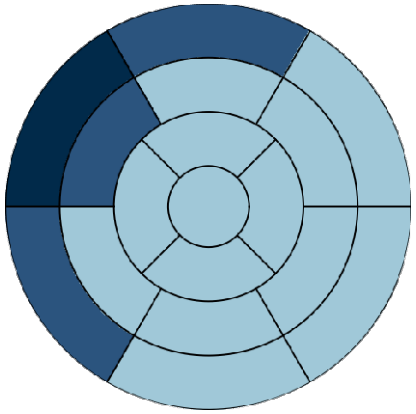
PT 5

PT



PT 7





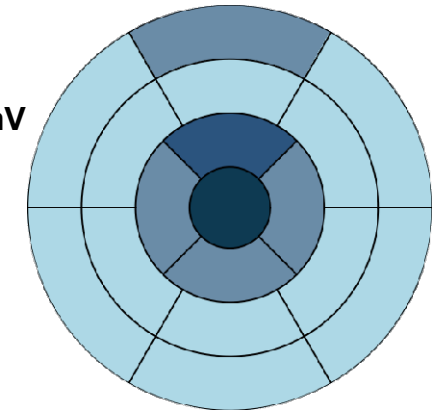
PT 8

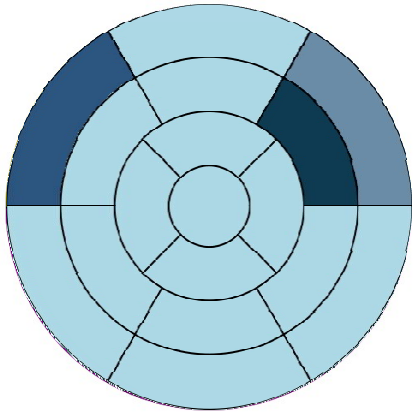
PT

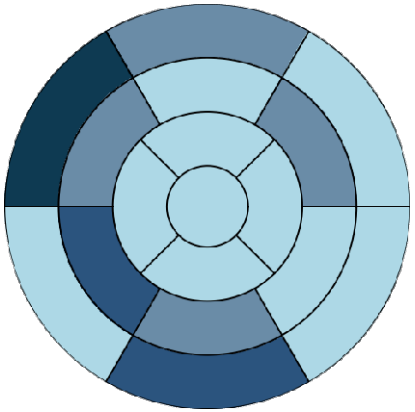
G+

AM BV

•1.5 mV •> 3.0 mV



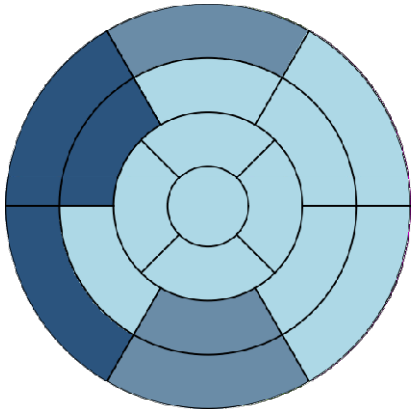


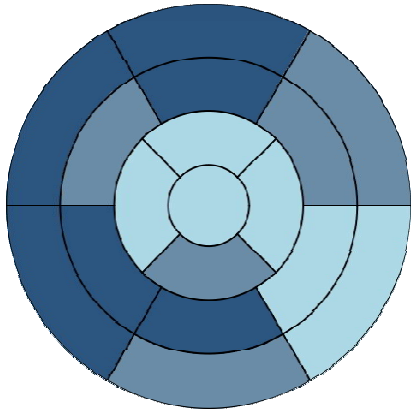


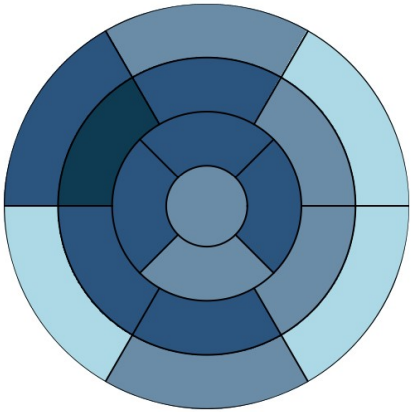
PT 1

PT 2

PT





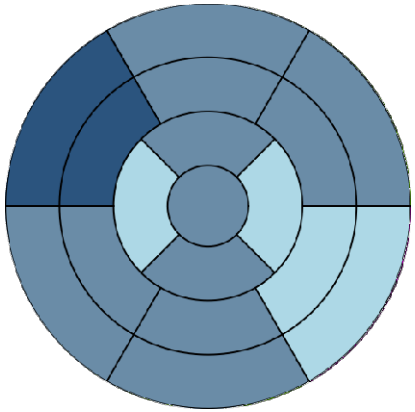


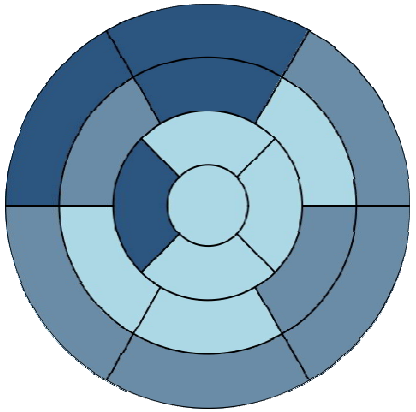
PT 4

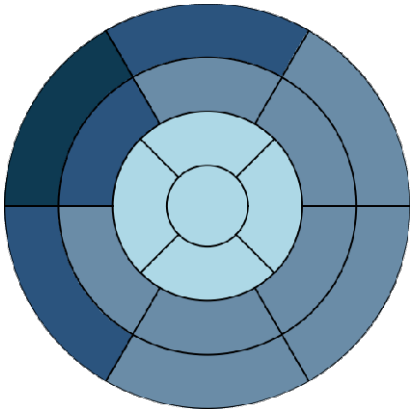
PT 5

PT

G+







PT 7

PT 8

PT

APP

•1.5 mV •> 3.0 mV

– 4

– 9

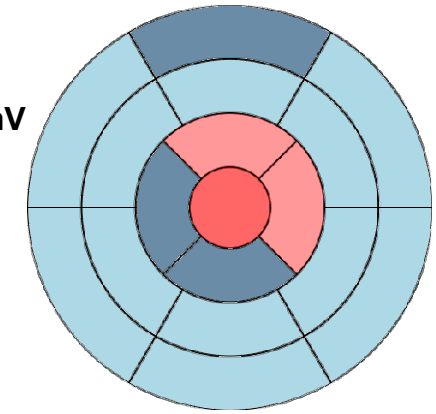
– 14

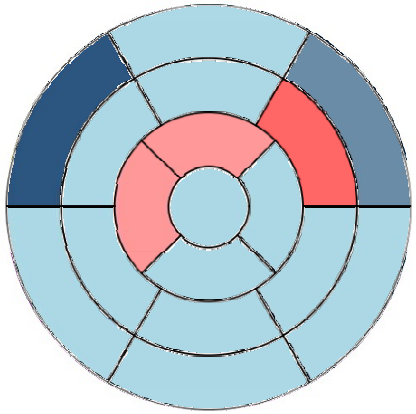
– 19

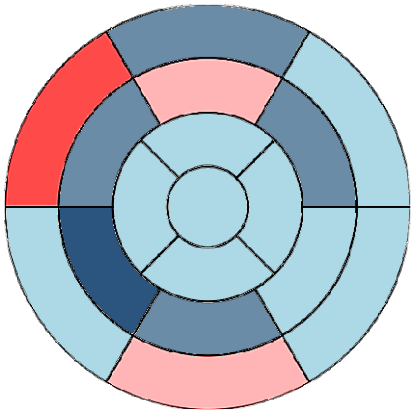
– 24

25

G+



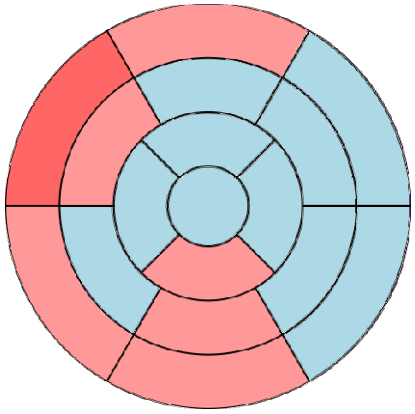


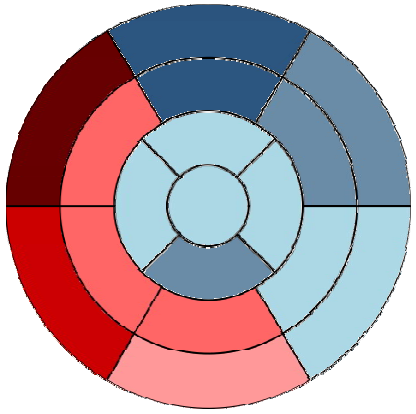


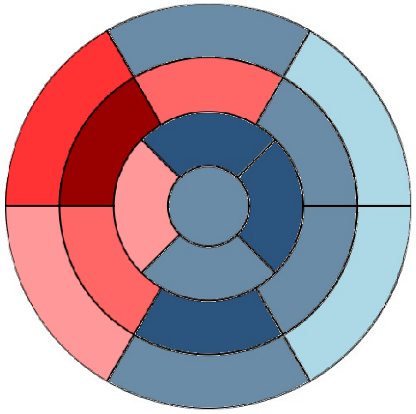
PT 1

PT 2

PT



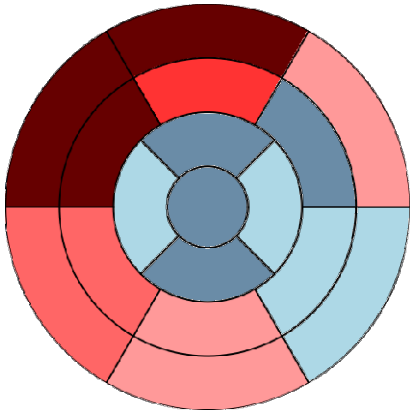


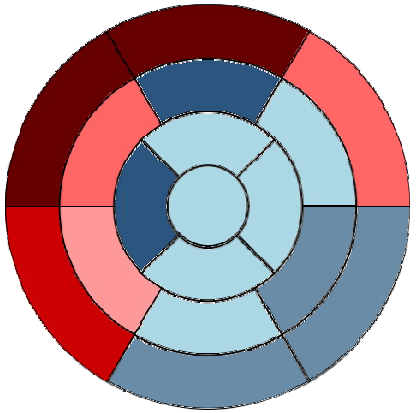


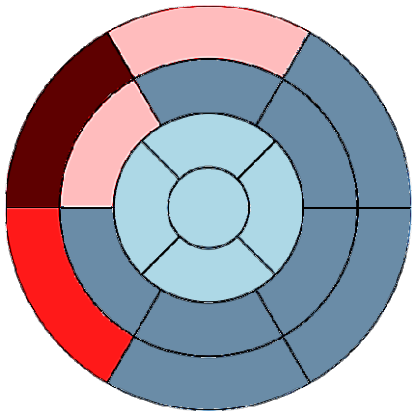
PT 4

PT 5

PT



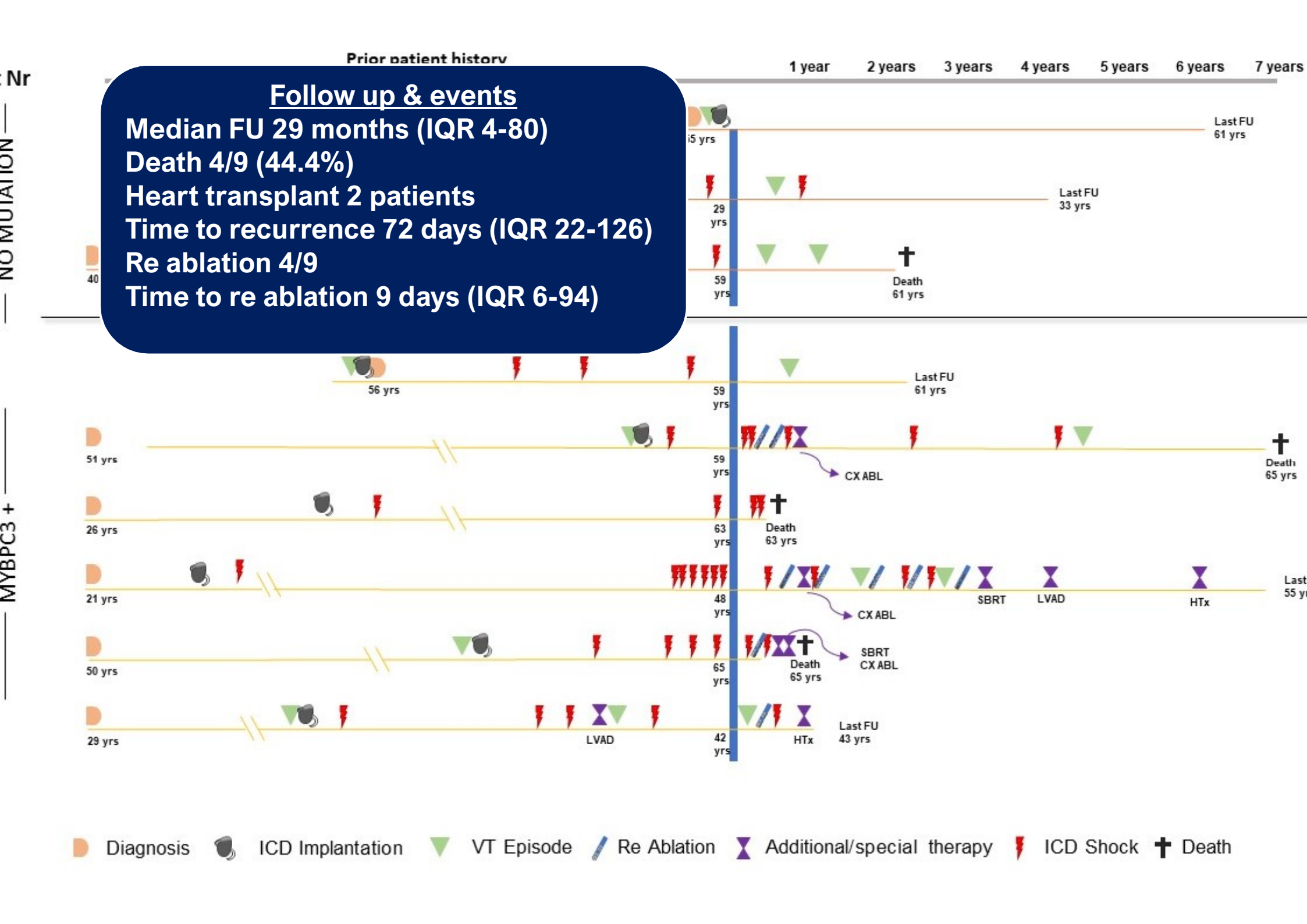




PT 7

PT 8

PT


Follow up & events
Median FU 29 months (IQR 4-80)
Death 4/9 (44.4%)
Heart transplant 2 patients
Time to recurrence 72 days (IQR 22-126)
Re ablation 4/9
Time to re ablation 9 days (IQR 6-94)
Prior patient history
1 year
2 years
3 years
4 years
5 years
6 years
7 years
Nr
NO MUTATION
MYBPC3 +
Last FU 61 yrs
Last FU 33 yrs
29 yrs
59 yrs
Death 61 yrs
56 yrs
59 yrs
Last FU 61 yrs
51 yrs
59 yrs
CX ABL
Death 65 yrs
26 yrs
63 yrs
Death 63 yrs
21 yrs
48 yrs
SBRT
LVAD
HTx
CX ABL
50 yrs
65 yrs
Death 65 yrs
SBRT CX ABL
29 yrs
LVAD
42 yrs
HTx
Last FU 43 yrs
Diagnosis
ICD Implantation
VT Episode
Re Ablation
Additional/special therapy
ICD Shock
Death

BAIL OUT STRATEGIES (MYBPC3+)

- Ablation with half saline in 4/9 index VT ablations (+ 3 re ablations)
- TCEA attempted in 3 patients Bipolar ablation
- Ablation with ECMO hemodynamic support
- SGB in 2 patients
- SBRT in 2 patients
- Surgical substrate resection in 2 patients

CONCLUSIONS

CONCLUSIONS

- 1 % of patients referred for CA of SMVT to a high-volume center had a HCM phenotype
- MYBPC3 variant was identified in 67% with predominant septal compromise
- VT free survival appears to be particularly poor in MYBPC3 variant carriers despite all treatment modalities
- Early screening for advanced heart failure management including heart transplantation is important.

THANK YOU

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