Substrate Mapping in CAD Implications for Ablation of Unstable VT

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Dr. Josephson has the following Potential Conflicts of Interest:
Consultant/honoraria for Medtronic and Biotronik
Advisory board for Biowatch, Vicor, NewCardio, Rhythmia Medical
none of which is relevant to the material in this presentation

PATHOPHYSIOLOGIC SUBSTRATE OF VT DUE TO CAD

HYPOTHESIS

PATIENTS WITH VT DUE TO CAD SHOULD HAVE AN ELECTROPHYSIOLOGIC SUBSTRATE CHARACTERIZED BY:

- Slow conduction
  - amplitude and duration of endocardial electrograms
  - late potentials
- Potential pathways of conduction, bounded by anatomic or functional boundaries
- Depressed excitability
- Dispersion of refractoriness
- Dispersion of "total" recovery (activation plus refractoriness)
- Adjacent areas of delayed activation and short refractory periods

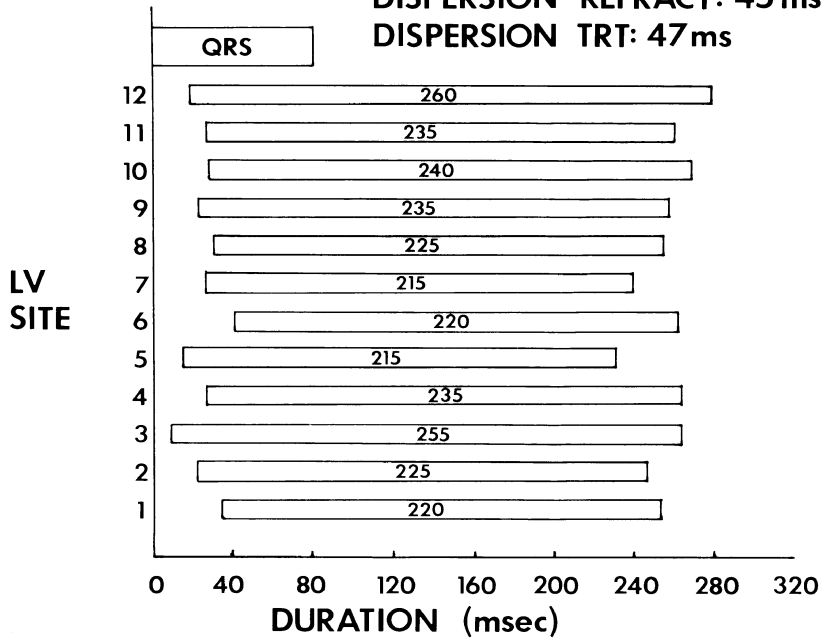
Destruction or isolation of this substrate could prevent VT

Josephson, Cassidy, Vassallo, Kienzle, Wit et al 1977-1986

RELATIONSHIP OF HETEROGENEITY OF ACTIVATION, REFRACTORINESS, TOTAL RECOVERY AND INDUCIBILITY

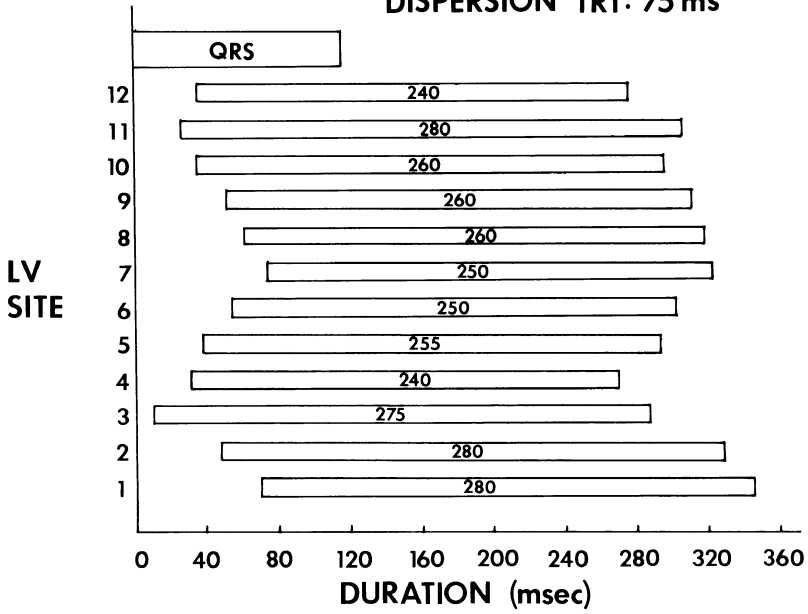
Normal

ENDOCARDIAL ACT: 32 ms
DISPERSION REFRACT: 45 ms
DISPERSION TRT: 47 ms



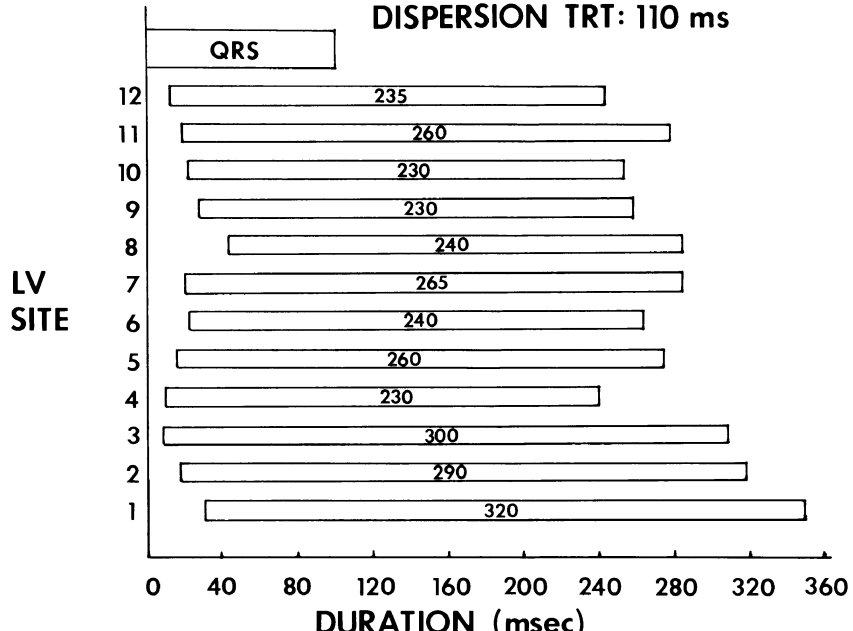
CAD VT

ENDOCARDIAL ACT: 64 ms
DISPERSION REFRACT: 40 ms
DISPERSION TRT: 75 ms



Long QT

ENDOCARDIAL ACT: 38 ms
DISPERSION REFRACT: 90 ms
DISPERSION TRT: 110 ms



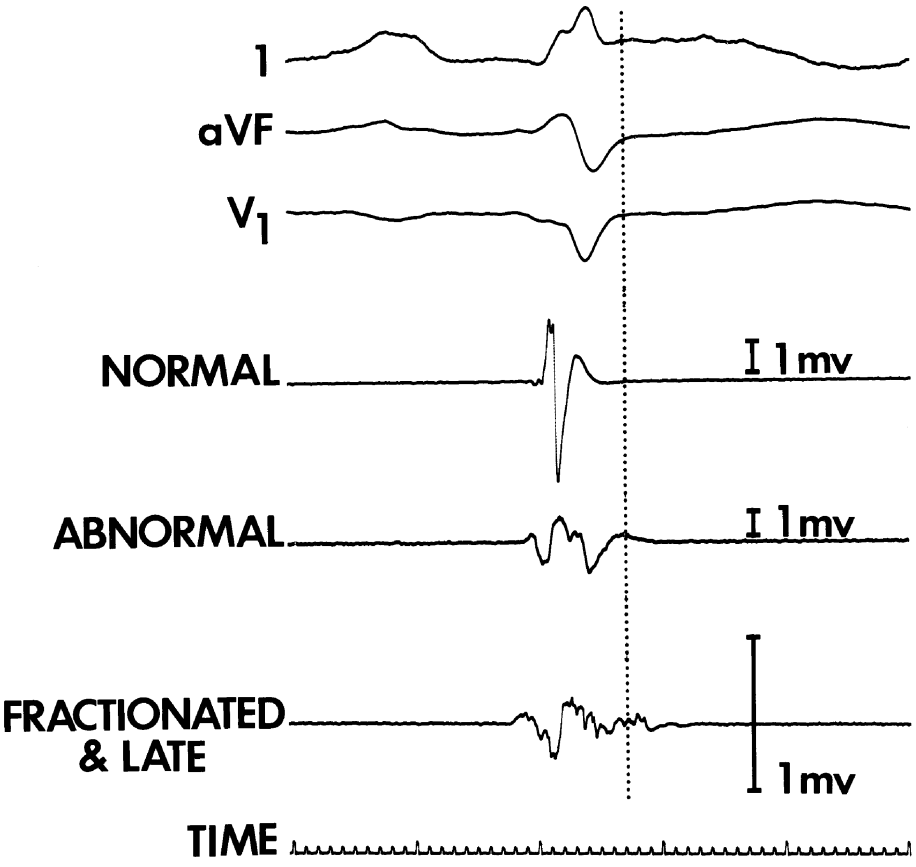
PATHOPHYSIOLOGIC SUBSTRATE OF VT DUE TO CAD

These findings suggest:

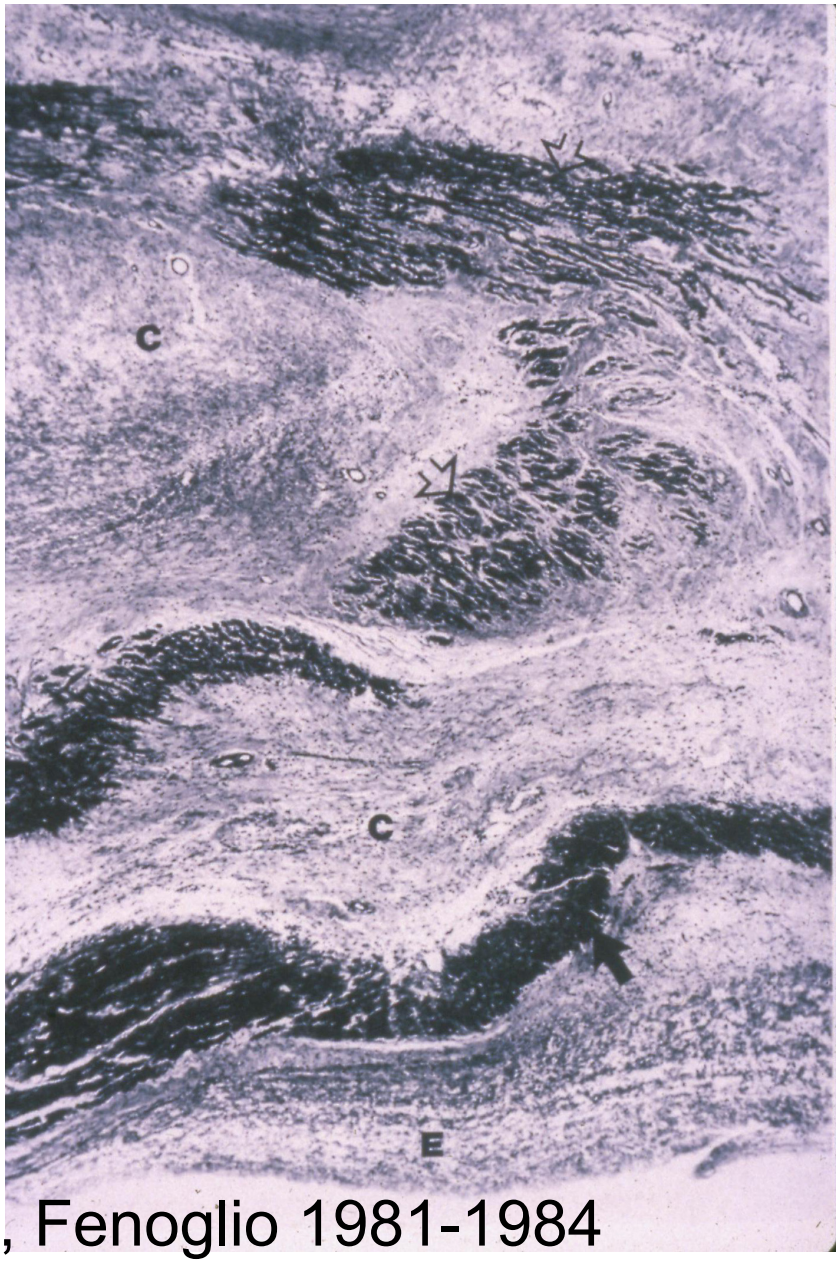
Slow conduction and depressed excitability are the primary features of scar related reentrant arrhythmias following myocardial infarction.

Josephson, Cassidy, Vassallo, Kienzle, Wit et al 1977-1986

Elecrograms from Patients with Myocardial Infarction



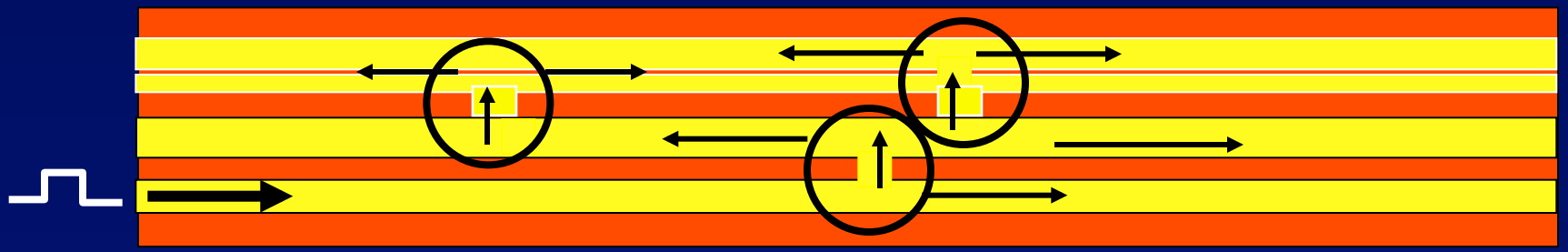
Anatomic Substrate for Fractionated EGM in CAD



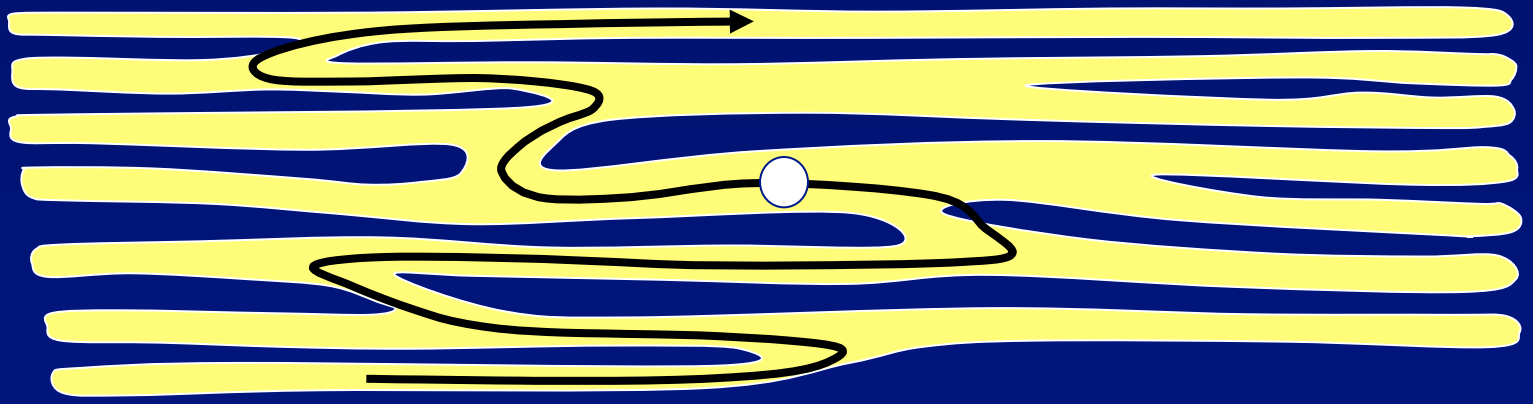
Josephson, Cassidy,Wit, Fenoglio 1981-1984

Fibrosis and fractionated electrograms

Asynchronous conduction



Electrode

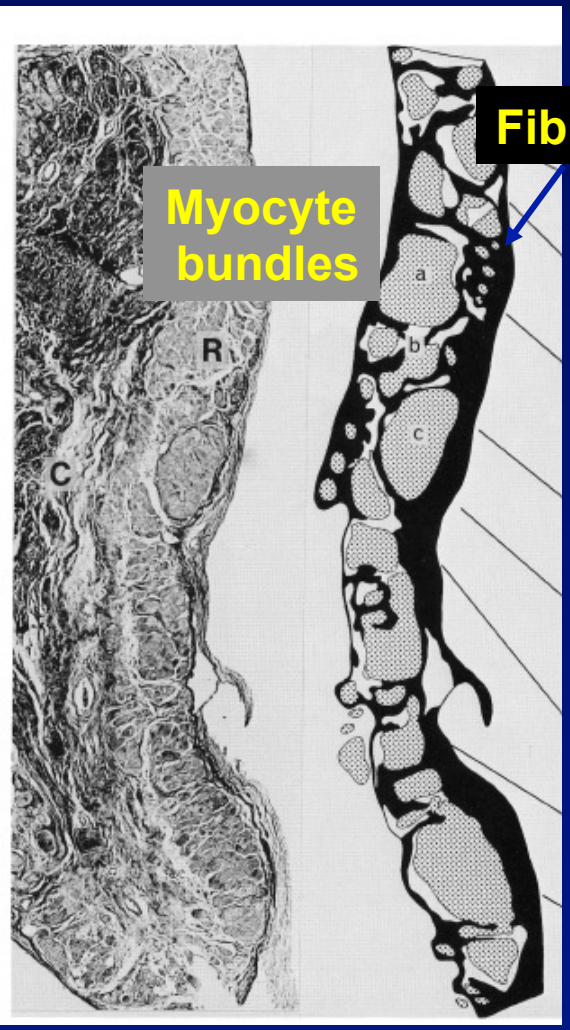


fibrosis
myocardium

Fractionated electrogram

Courtesy of J de Bakker

The Link between Ventricular Scar and VT



De Bakker, et al. Circulation 1993;88:915.

Structure / Geometry

Conduction Slowing

Conduction Block

Reentry

SUBSTRATE OF VENTRICULAR ARRHYTHMIAS IN CAD

LV MAP	NSVT	CA	VT
NL (%)	63±26	57±27	42±19
Abnl (%)	35±23	37±23	48±17
Fractionated (%)	2±4	6±12	10±10
Late (%)	11±11	8±12	15±16
Endo Activation (ms)	54±23	60±28	73±32
Duration Longest EG	102±12	112±34	129±43

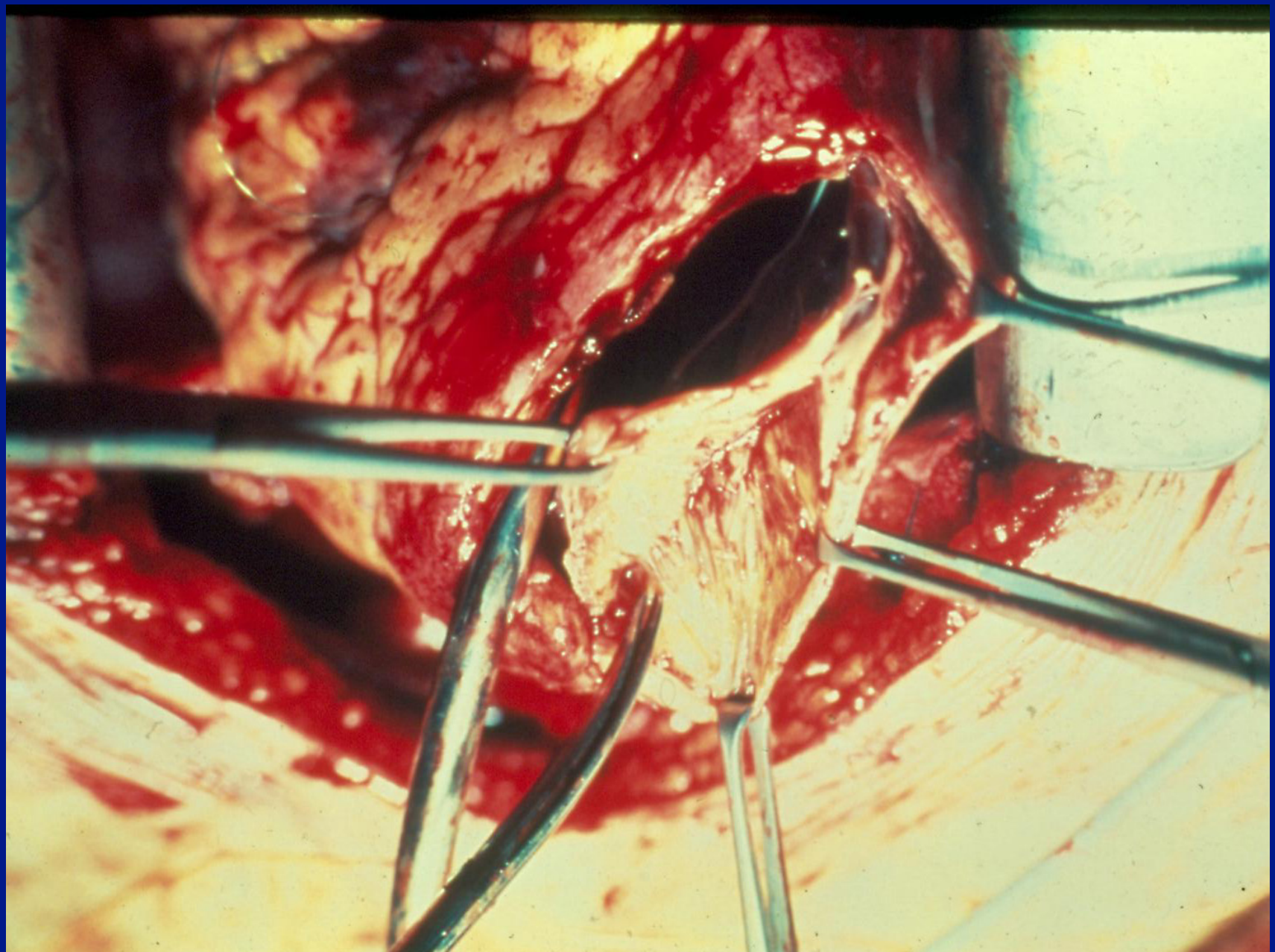
RELATIONSHIP OF SINUS RHYTHM ELECTROGRAM AND VT ORIGIN

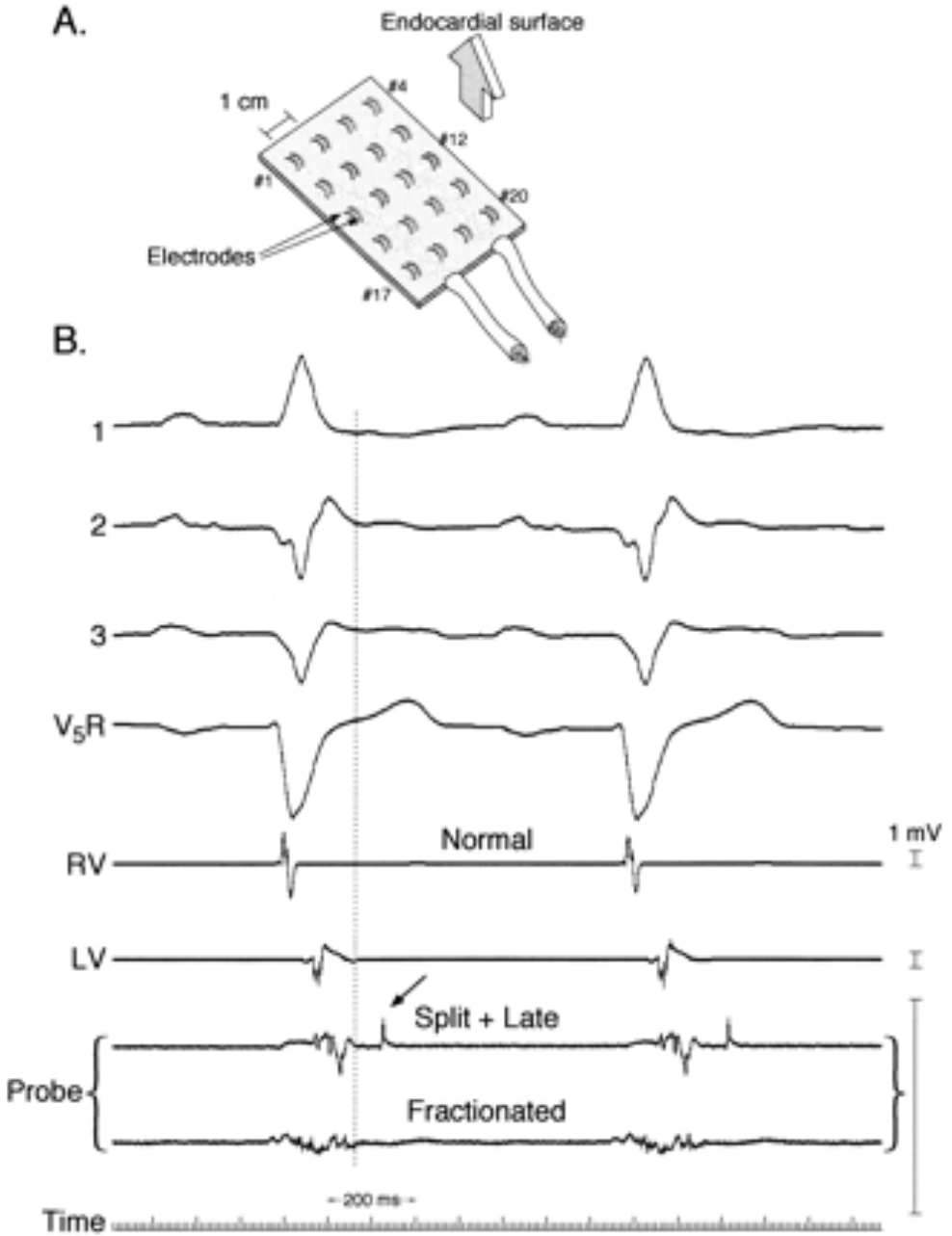
102 VTs in 52 patients

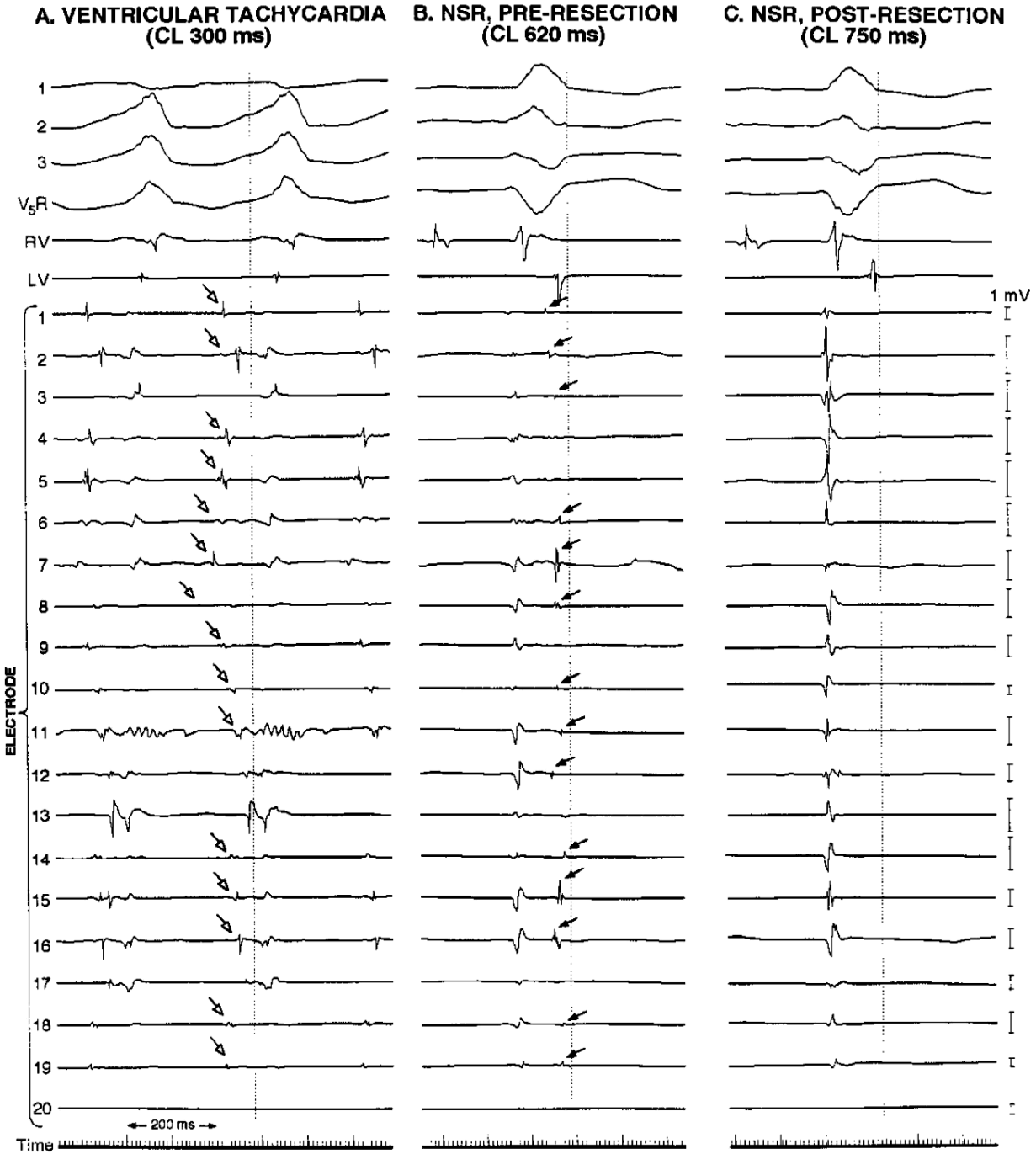
Electrogram type	Sensitivity	Specificity	PPV
Normal	14/102 (14%)	224/444 (49%)	14/234 (6%)
Abnormal	88/102 (86%)	220/444 (48%)	88/312 (29%)
Fractionated	10/102 (10%)	407/444 (92%)	10/47 (21%)
Abnl late	26/102 (26%)	390/444 (88%)	26/80 (33%)
Fx late	8/102 (8%)	426/444 (96%)	8/26 (31%)
Longest	11/102 (11%)	408/444 (92%)	16/52 (31%)

Cassidy et al Circ 1984

WHAT DID WE LEARN FROM VT SURGERY?




A.
Endocardial surface
1 cm
#4
#12
#1
#20
Electrodes
#17
B.
1
2
3
V5R
Normal
1 mV
RV
LV
Split + Late
Probe
Fractionated
200 ms
Time


A. VENTRICULAR TACHYCARDIA
(CL 300 ms)
B. NSR, PRE-RESECTION
(CL 620 ms)
C. NSR, POST-RESECTION
(CL 750 ms)
1
2
3
V5R
RV
LV
ELECTRODE
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
1 mV
200 ms
Time

Conclusions fro Intraoperative Studies

- Split potentials, late potentials, and fractionated activity are present in areas of the infarct critical to VT.
- These areas are in or near the subendocardium (1-3mm) and could be amenable to catheter ablation

VT ablation in healed CAD

- **Conventional VT ablation:**
  ~ 85 - 90% successful in inducible well tolerated VT

- **Mappable VT (10-25% of patients with VT)**
  - Inducible
  - Hemodynamically tolerated
  - Stable in response to pacing, catheter manipulation
  - Of 78 patients referred for ablation of mappable VT, 32 initial procedures were unsuccessful (no tolerated VT, failed RF)

Most patients with recurrent VT have unmappable VTs

Callans DJ: AJC 1998

Before VT Ablation

Most patients referred for scar-based VT ablation have ICD in place with multiple shocks/ATPs as indication

- Significant comorbidities/features impact your procedure
  - Heart failure
  - Residual ischemia (coronary arteriography first?)
  - Peripheral vascular disease (access)
  - Pulmonary disease
  - Left ventricular thrombus
  - Medications (antiarrhythmic drugs, warfarin, insulin, etc.)

These factors may limit what you can accomplish

- Goal of therapy generally to decrease shocks, not cure

This may limit what you want to accomplish

MAPPING AND ABLATION OF UNSTABLE VT

POTENTIAL OBSTACLES

- Hemodynamic instability precludes detailed point by point mapping and evaluation of the response of VT to pacing (I.e. entrainment mapping)
- A substrate based approach is required
- A different substrate, in terms of extent of abnormalities of conduction and area and depth of scar, appears to be present in VT producing cardiac arrest when compared to stable monomorphic VT

Difficulty with Ablation of Untolerated Scar Related VTs

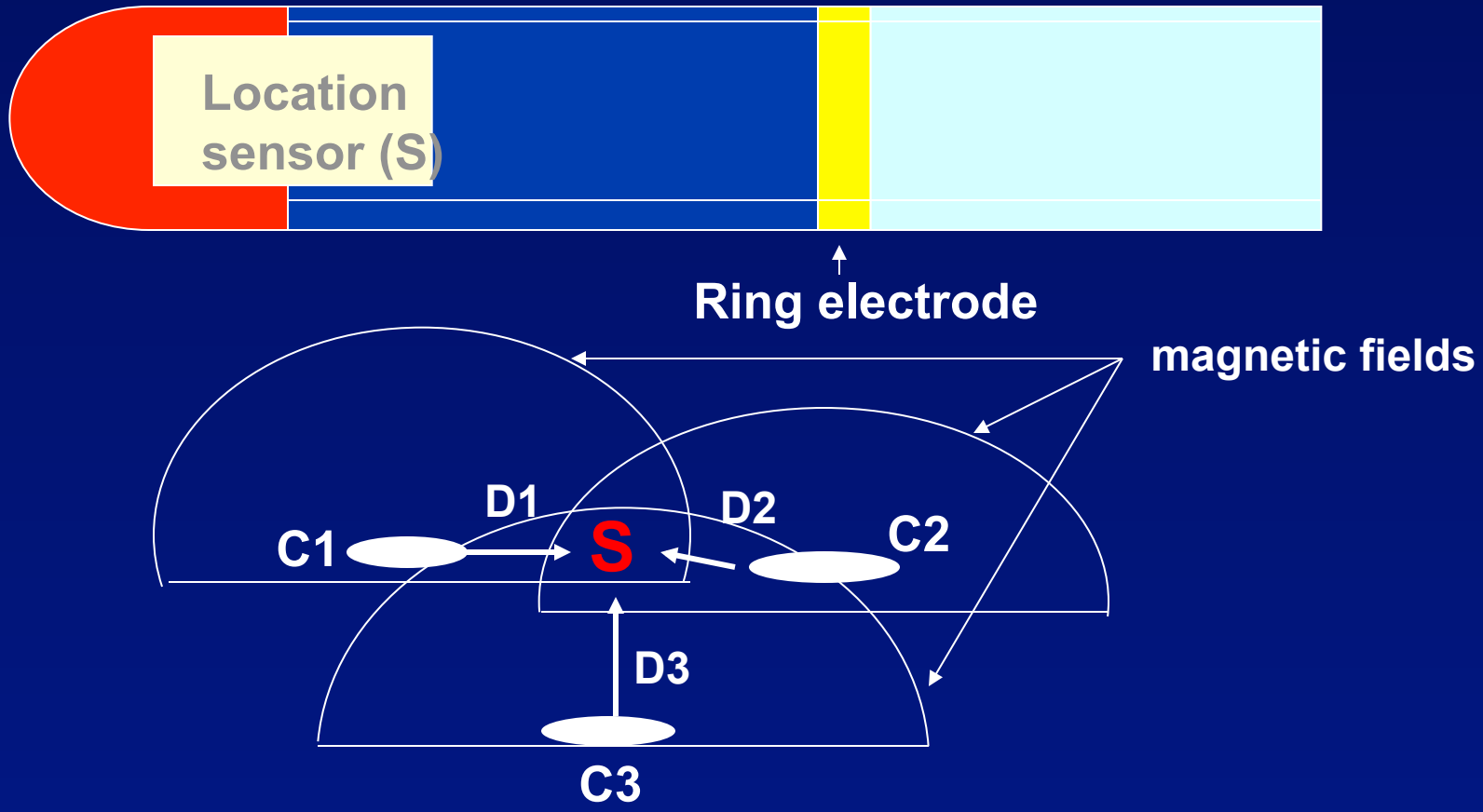
Multiple Potential Circuits

LIMITATIONS OF INTIAL ENDOCARDIAL MAPPING STUDIES

- Only 12 endocardial regions were evaluated with variable density of mapping sites
- No online analysis or automated display
- No method of defining exact site from which recordings were made; internal points could not be edited
- Manual measurement of voltage required

SOLUTION: Electrical-Anatomic Mapping

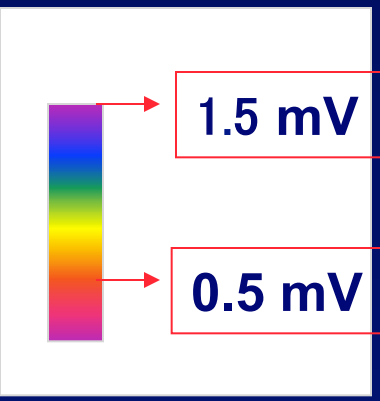
Electroanatomic Mapping (CARTO™)

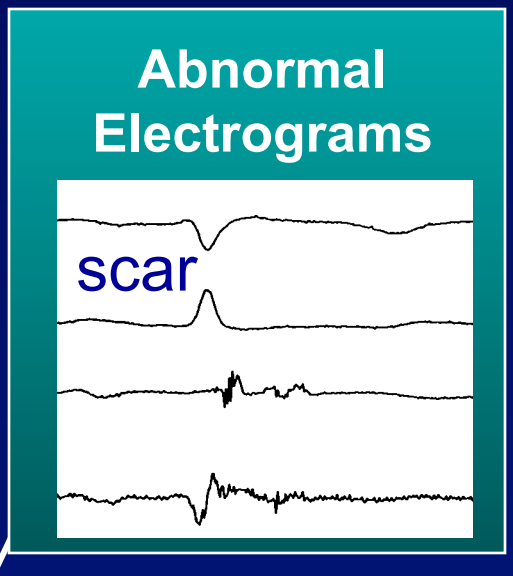


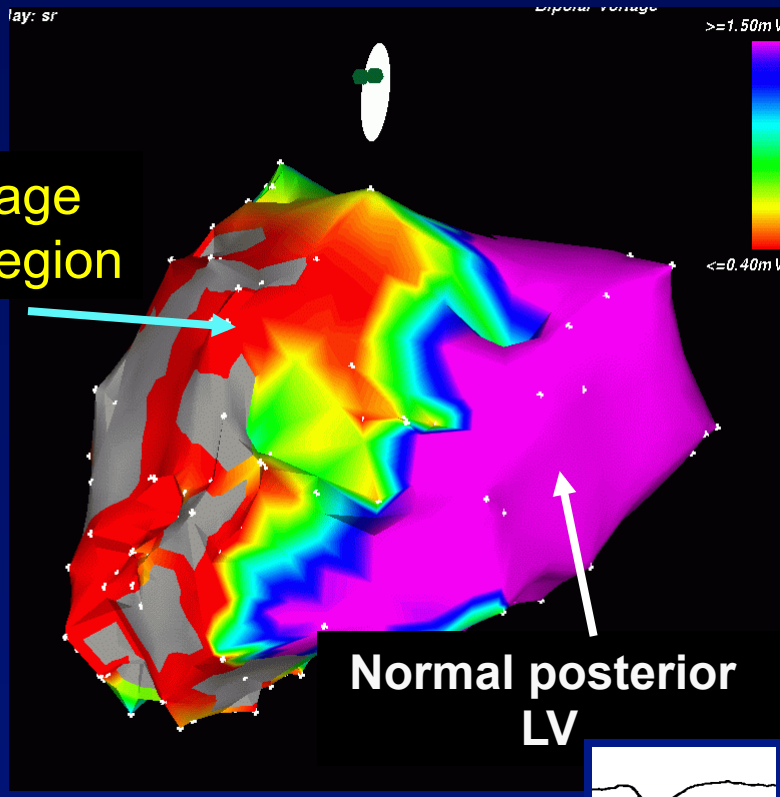
C1, C2, C3 represent coils which generate magnetic fields
D1, D2, D3 represent the distances from the sensor to the coils

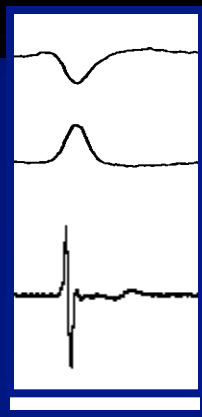
Gepstein, L. et al. Circulation 1995:6, 1612

VOLTAGE MAPPING









- **Low amplitude region correlates well the infarct region in animal models** Gepstein, et al. Circ 1998. 98: 2055. Kornowski, et al. Circ 1998. 98:1116. Callans, et al. Circ 1999. 100: 1744.
- **95% of normal LV electrograms > 1.55 mV**

(bipolar 4 mm tip to 2 mm ring electrode, filtered at 10 to 400 Hz)
Marchlinski et al Circ 2000;101:1288; Reddy *JACC* 2003;41:2228

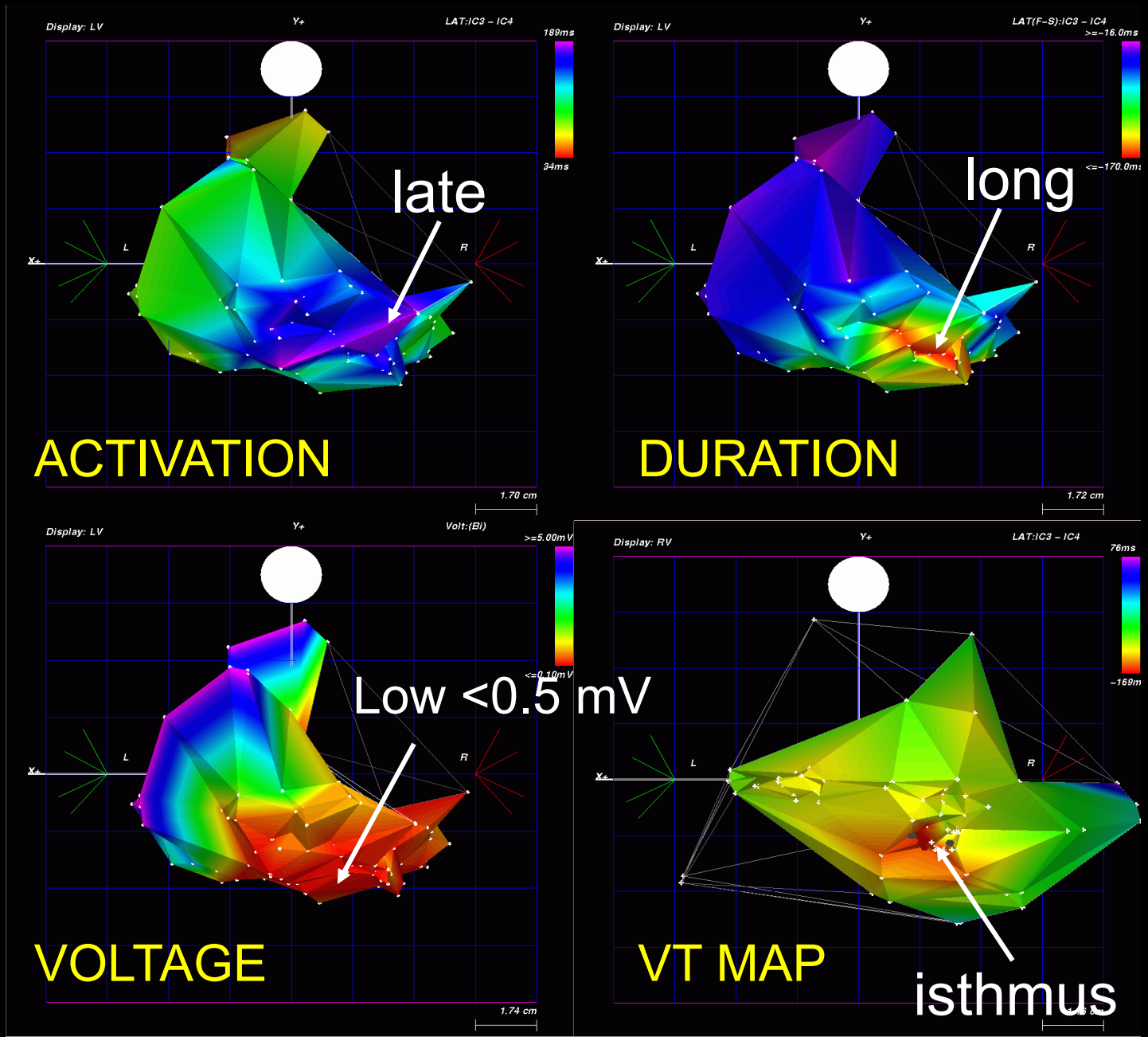
Identification of Arrhythmogenic Substrate to Guide Ablation

Perform detailed endocardial map (>200 points) in NSR or RV pacing

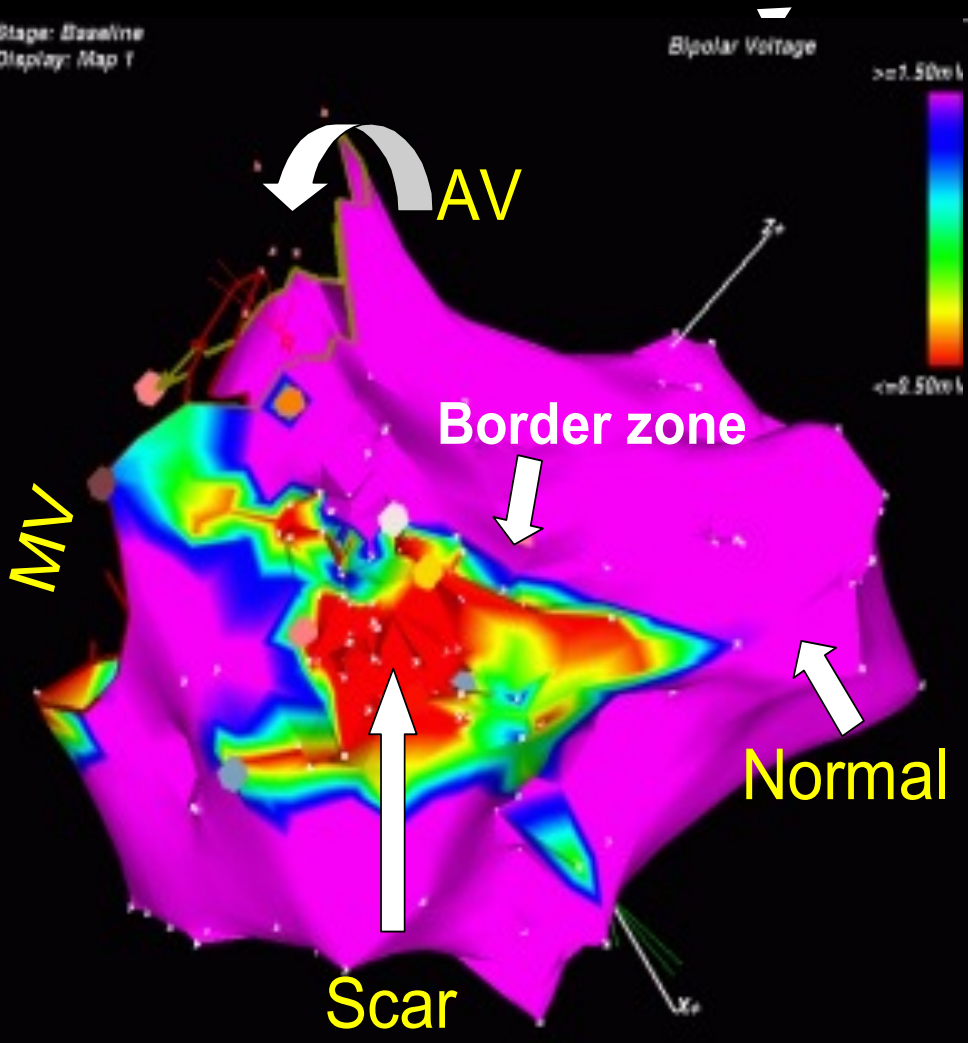
Record EGM voltage, activation, late and split potentials, and fractionated

EGMs (long duration).Note adjacent sites of early and late activation in NSR

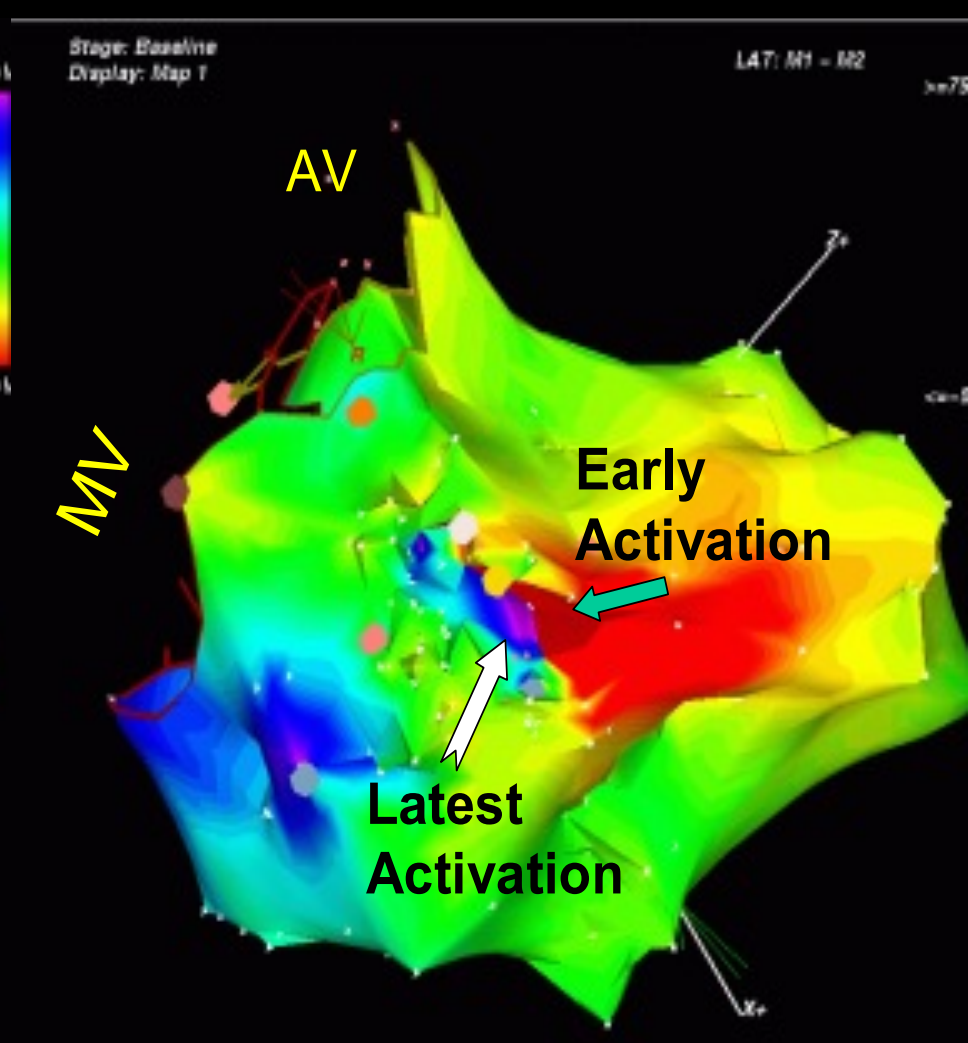
RELATIONSHIP OF ABNORMAL EGMS TO VT ORIGIN



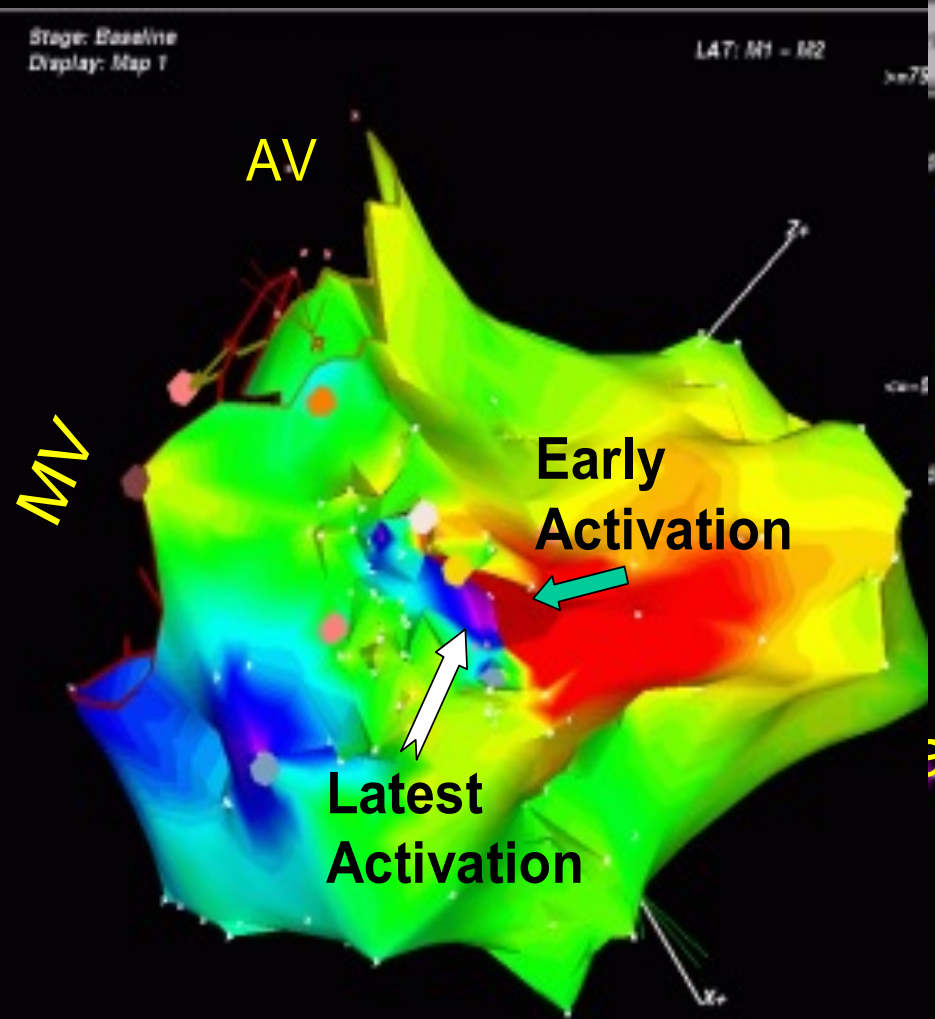
NSR VOLTAGE MAP INFEROSEPTAL MI

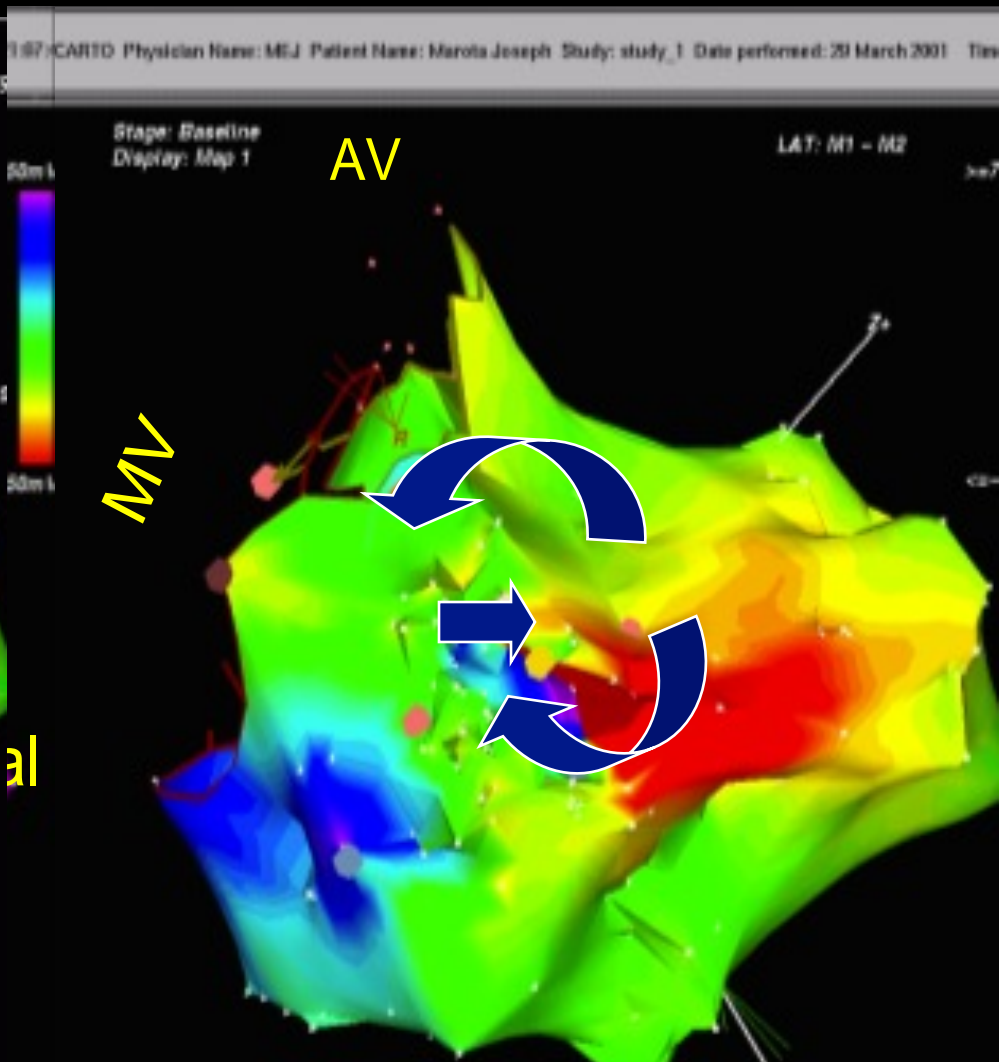


NSR ACTIVATION INFEROSEPTAL MI



NSR ACTIVATION INFEROSEPTAL MI → REENTRANT VT





IDENTIFICATION OF DENSE SCAR

1984

- Fractionated, low amplitude EGMs (5-10 mm interelectrode distance, 2 of 3 parameters)
  - Amplitude ≤ 3mV
  - Duration ≥133 msec
  - Amplitude/duration ≤ 0.005
  - Amplitude < 0.1mV considered dense scar
    - » Cassidy et al Circ 1984

2001

- Very low voltage:
  - < 0.5 mV bipolar Carto (95% normal ~ 1.5mV)
    - » Marchlinski et al Circ 2000
  - < 0.1 mV bipolar Carto – thin wall aneurysm (echo, MRI)
    - » Josephson BIDMC 2001
- Depressed excitability (high pacing threshold)
  - Excitability directly related to presence of scar and EGM duration. Fragmented EGM < .1 mV low excitability; strength interval curve shifted up and to right
    - » Kienzle et al AJC 1986
  - No capture by unipolar stimulation at 10 mA
    - » Soejima et al Circ 2002

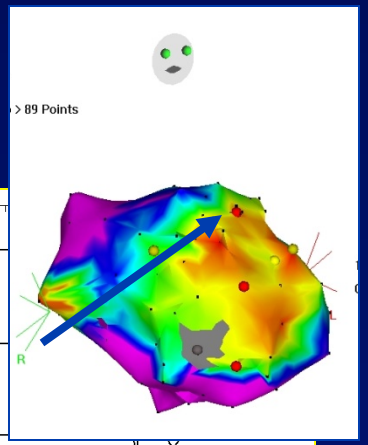
Methods to Define Potential Channels which Could form Isthmuses

- Pace-mapping at Border Zone to Identify Exits Sites and Isthmuses
- Redefine voltage windows to find potential channel with scar initially defined by 0.5 mV.
- Pacing (unipolar/bipolar) to define inexcitable tissue
- Identification of split potentials to define barriers to an isthmus
- Identify late potentials to identify critical isthmus sites leading to isolated mid-diastolic potentisls during VT

Defining Isthmus and Exit Sites by Voltage and Pace-mapping

- Define endocardial surface with detailed mapping in the area of abnormal signals (>100 sites)
- Define areas with voltage $\geq$1.5 mV, < 0.5 mV, and $\leq$ 0.1 mV, and all late potentials
- Induce VT
- If untolerated VT(s) induced, pace along 1.5 mV border to find site with best pace map and define area between that site and sites within the scar with similar pace maps and longer stimulus-QRS
- Make linear lesion from border to dense scar with line perpendicular at border

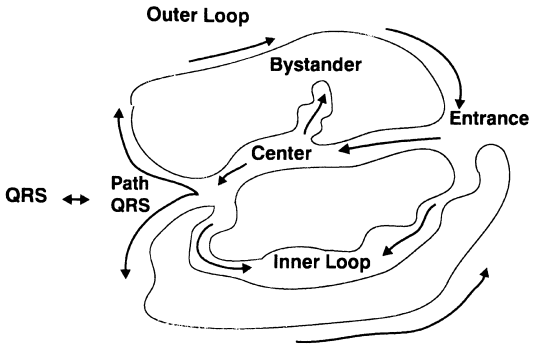
Pace-map: Exits suggested by QRS match with short S-QRS at border zone sites



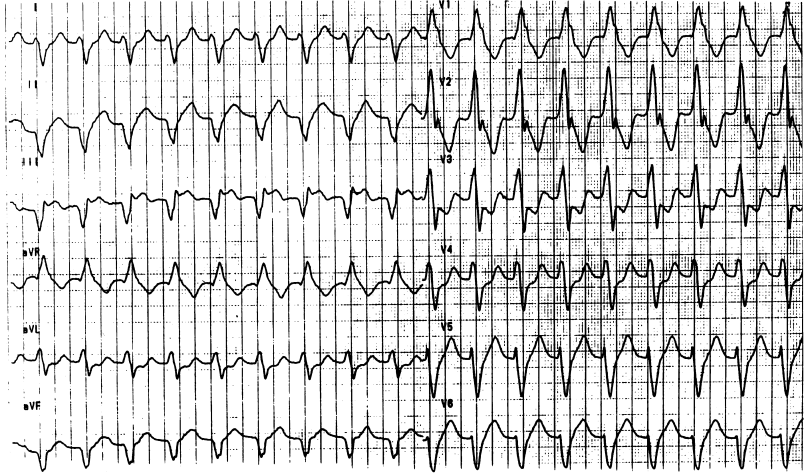
Limitations of Pace-mapping at Border Zone to Identify Exits Sites and Isthmuses

- **False negative:**
  - pacing in isthmus produces different QRS than VT due to bidirectional activation of isthmus
  - Isthmus formed by functional barriers not present in NSR resulting in paced QRS different than VT
  - Different QRS due to excessive current activating tissue outside isthmus.
- **False positive:**
  - Pacing dead end pathway attached to isthmus
  - Pacing near exit, but outside circuit

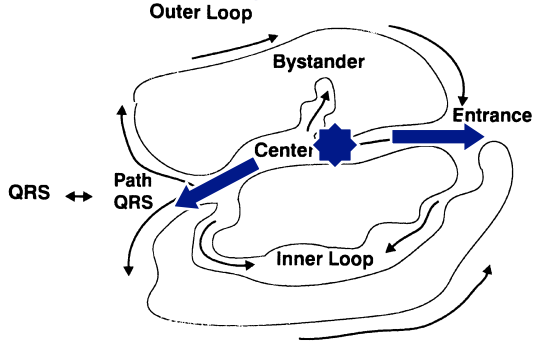
VT



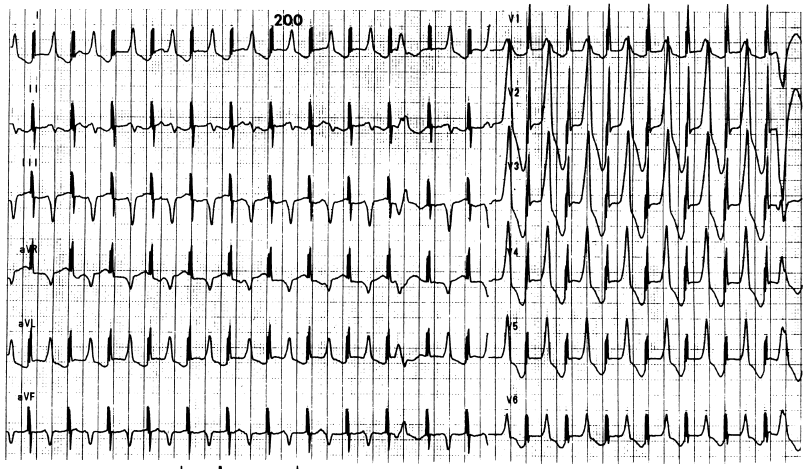
A



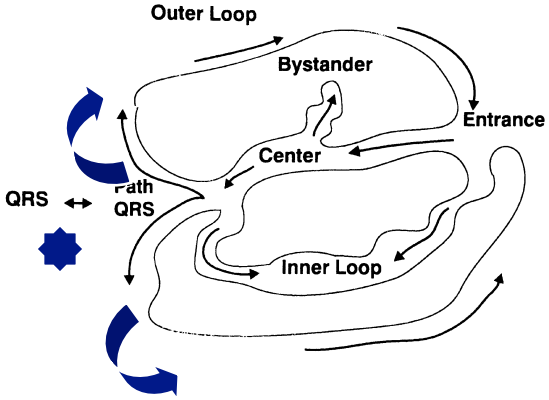
False negative in isthmus



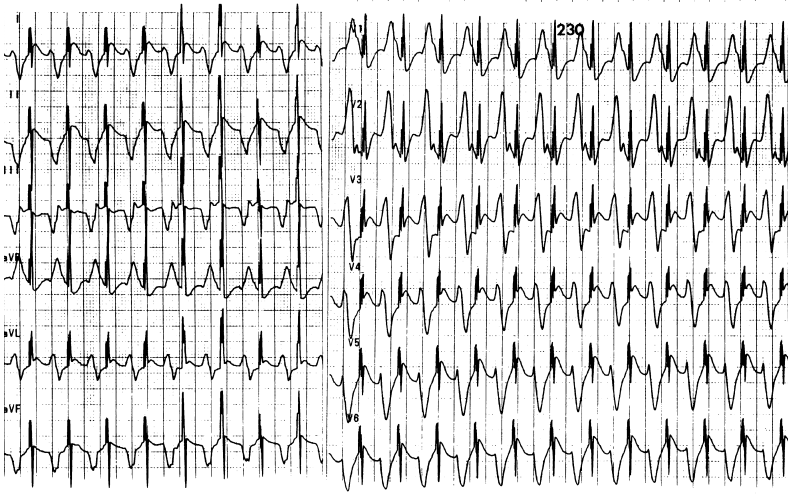
B



False positive near exit



C



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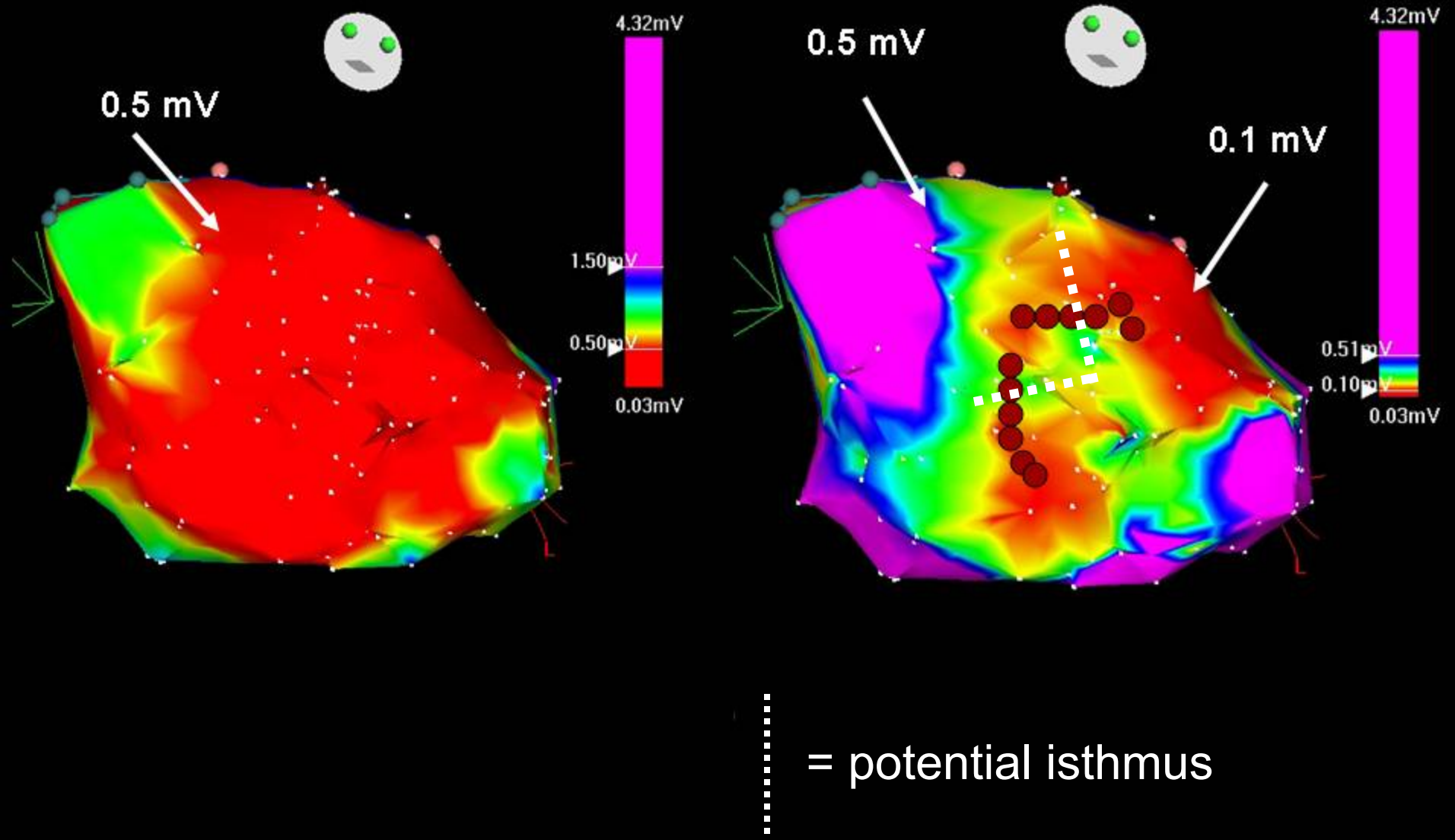
Detection of Potential Isthmus by Changing Voltage Criteria for Scar



Limitations to Adjustment of Voltage Limits tp 0.1mv – 0.5 mV to Identify Channels of Viable Tissue in Scar that Could form Isthmuses

- Some channels are very small and may not be detected if insufficient sampling is done.
- Some viable fibers give rise to signals less than 0.1 mV which are interpreted as scar.
- Some small channels may be obscured by adjacent high voltage signals and would not be seen (misclassified as “normal”).
- This hypothesis is based on maps of tolerated VT- may be different for untolerated VT

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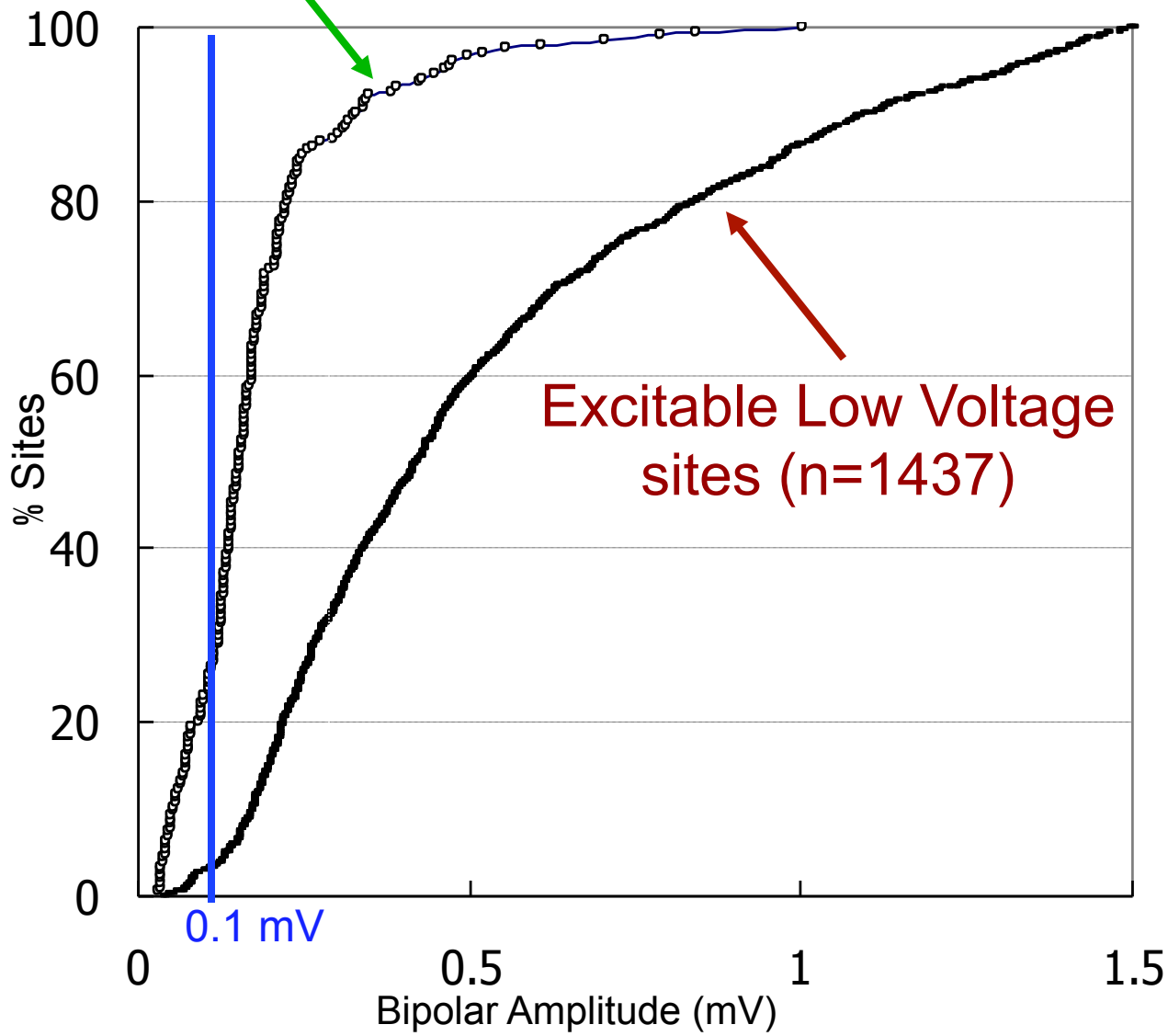
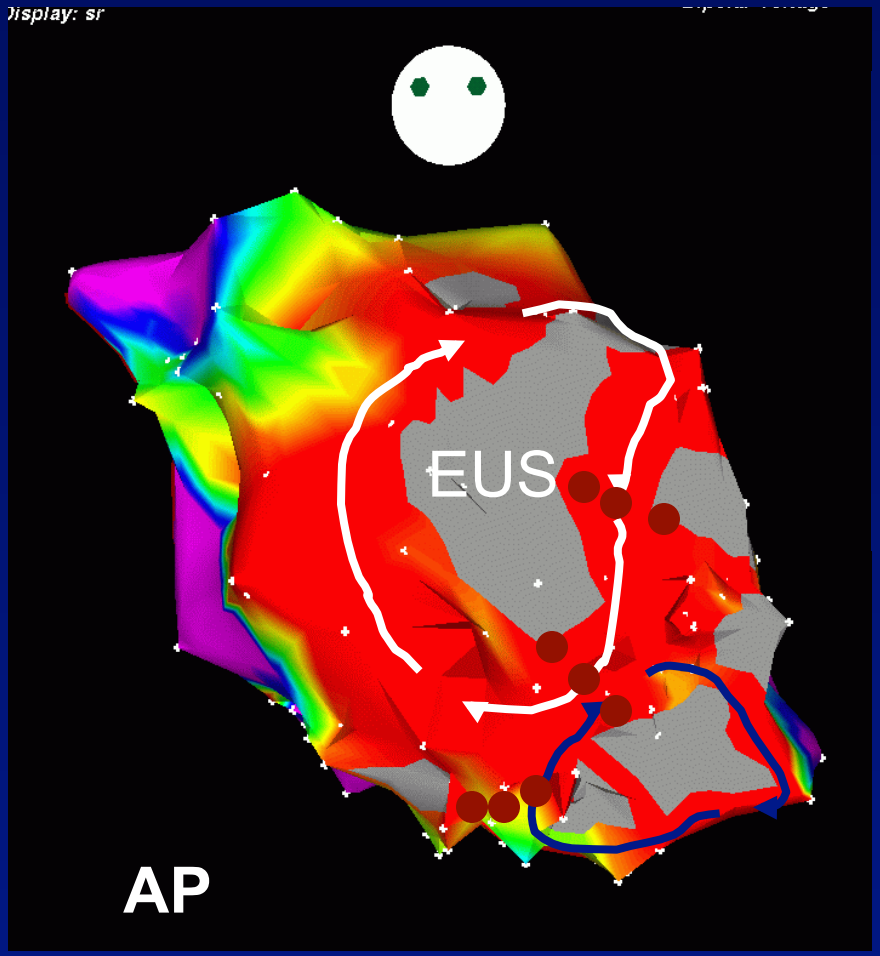
    - » **Marchlinski et al Circ 2000**
  - **< 0.1 mV bipolar Carto – thin walled aneurysm (echo, MRI)**
    - » **Josephson BIDMC 2001**
- **High pacing threshold**
  - **Excitability directly related to presence of scar and EGM duration**
    - » **Kienzle et al AJC 1986**
  - **No capture by unipolar stimulation at 10 mA**
    - » **Soejima et al Circ 2002**

EUS: electrically unexcitable scar
unipolar pacing threshold >10 mA (n=204)



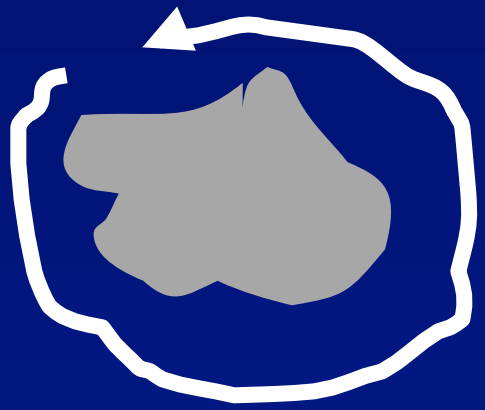
Soejima et al Circulation 2002

SUBSTRATE-GUIDED ABLATION
Connecting Inexcitable Scar



Electrically inexcitable scar (EUS):

unipolar pacing threshold > 10 ma at pulse width 2 ms



Soejima et al 2002

Limitations of Pacing to Identify Inexcitable Tissue

- No proof of accuracy to detect anatomic barrier, particularly since fibers may be tiny (<0.1 mm and catheter tip is 3.5-4 mm)
- Pacing can overcall excitable tissue because the virtual electrode encorporates normal/viable and excitable tissue.

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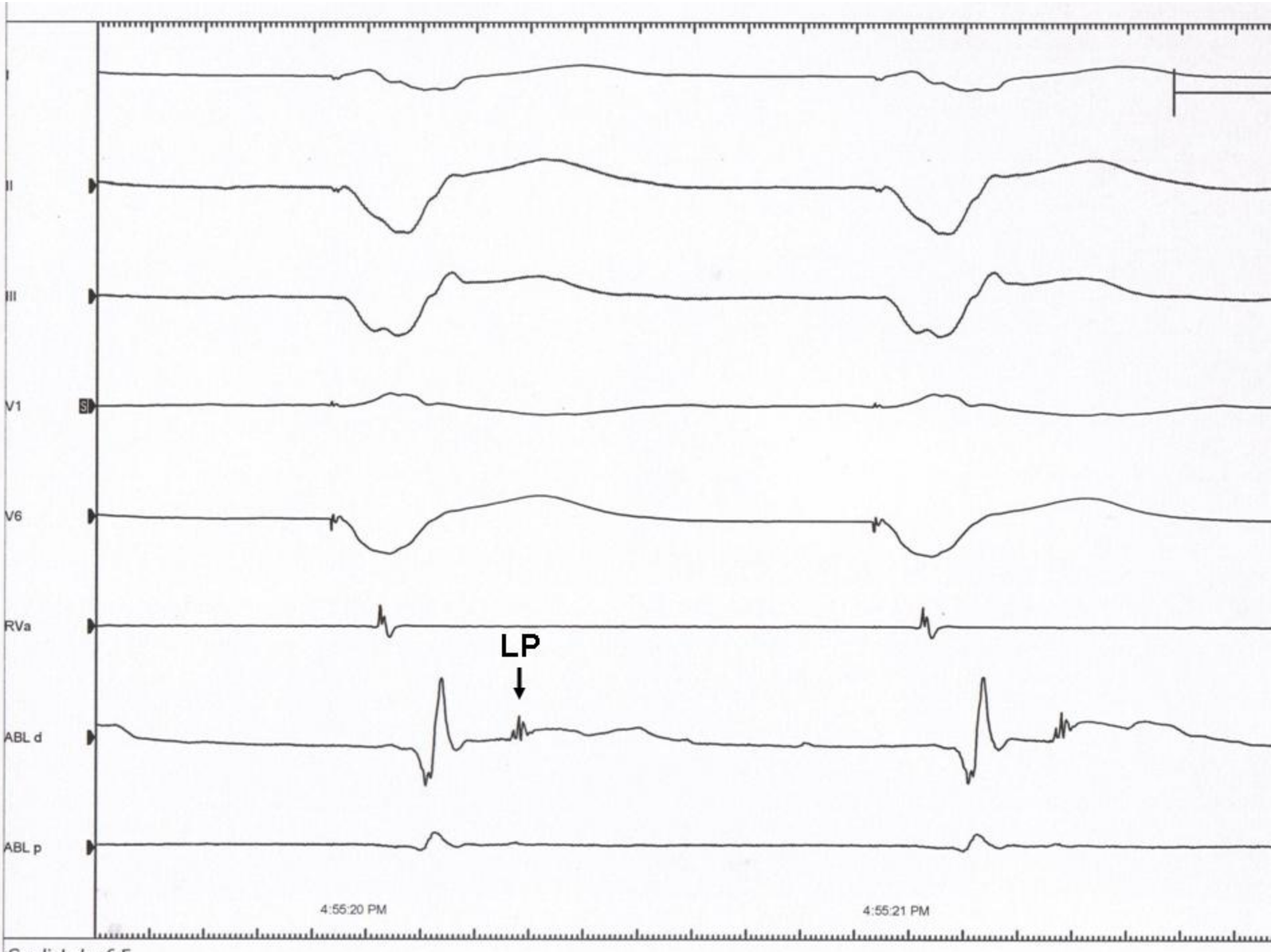
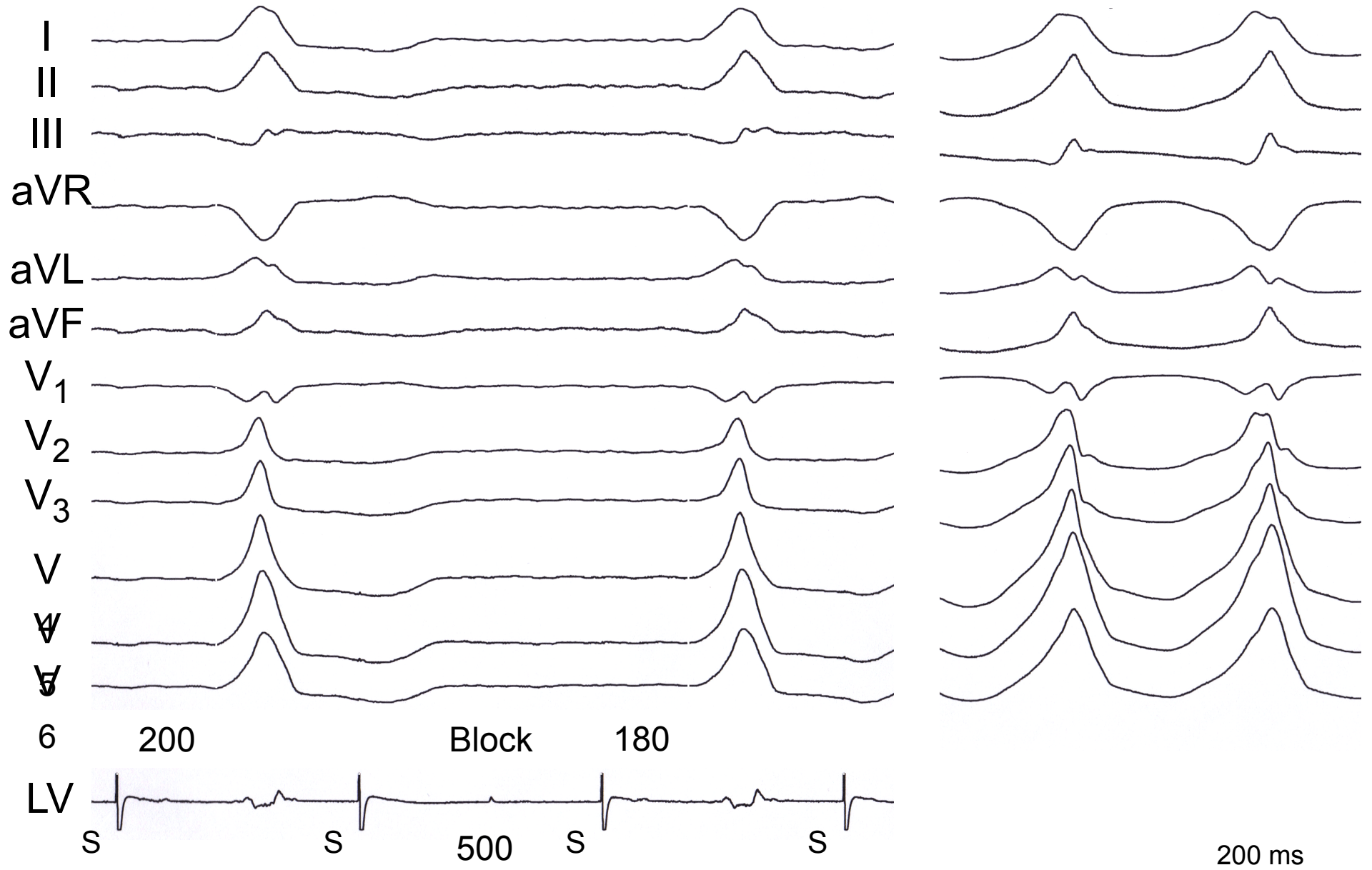
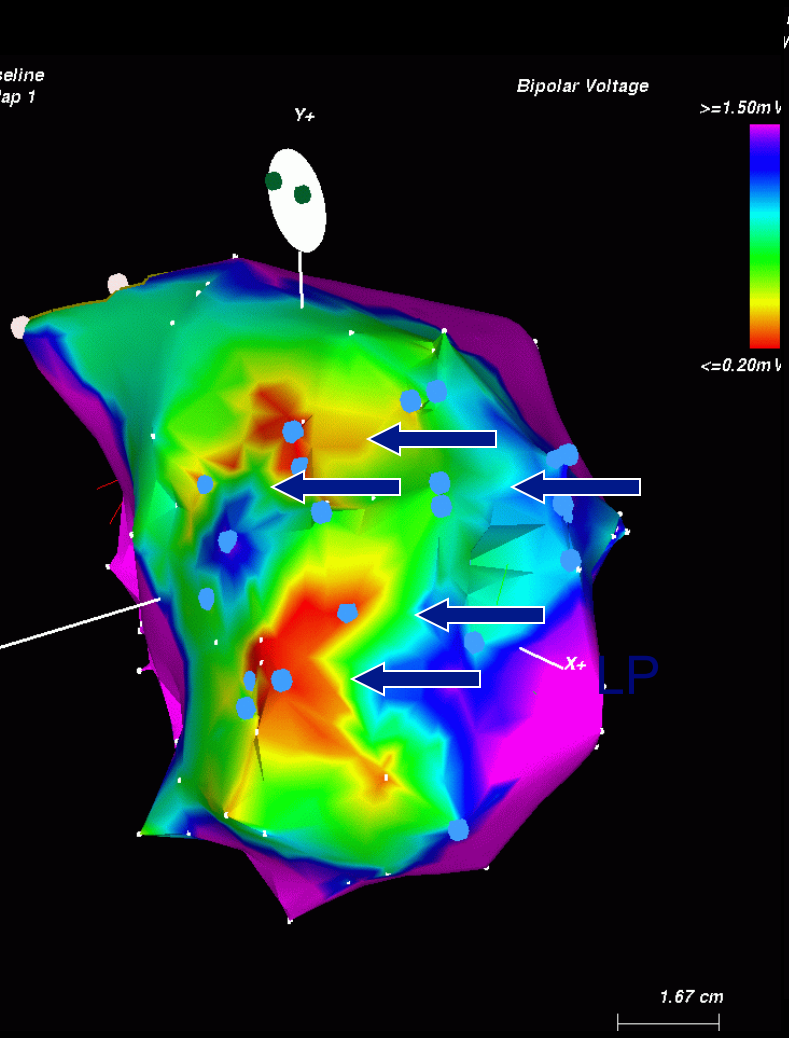
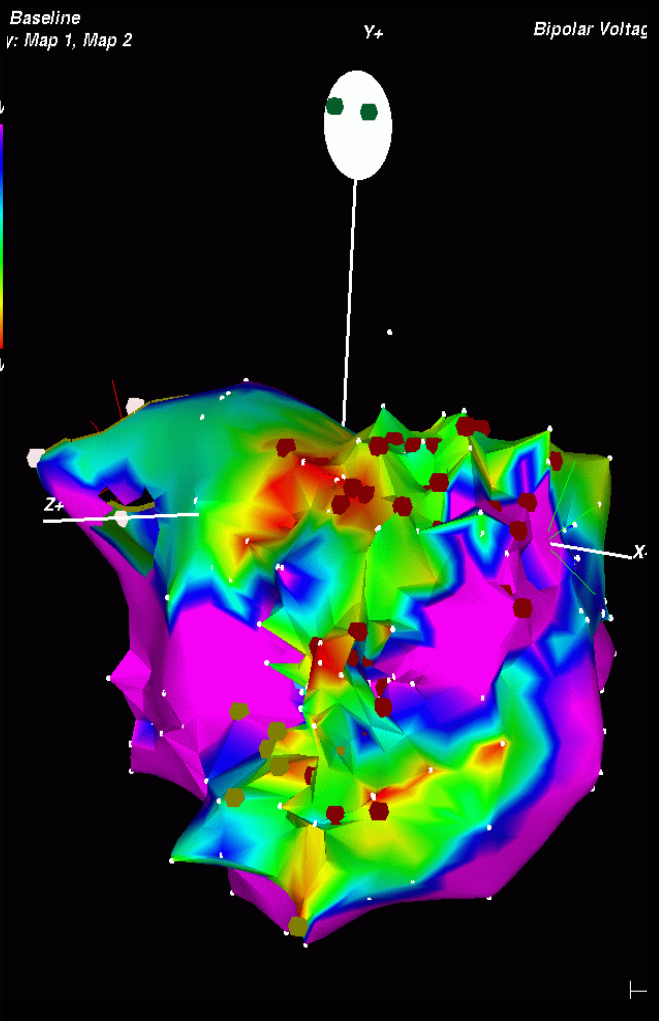

I
II
III
V1
V6
RVa
LP
ABL d
ABL p
4:55:20 PM
4:55:21 PM

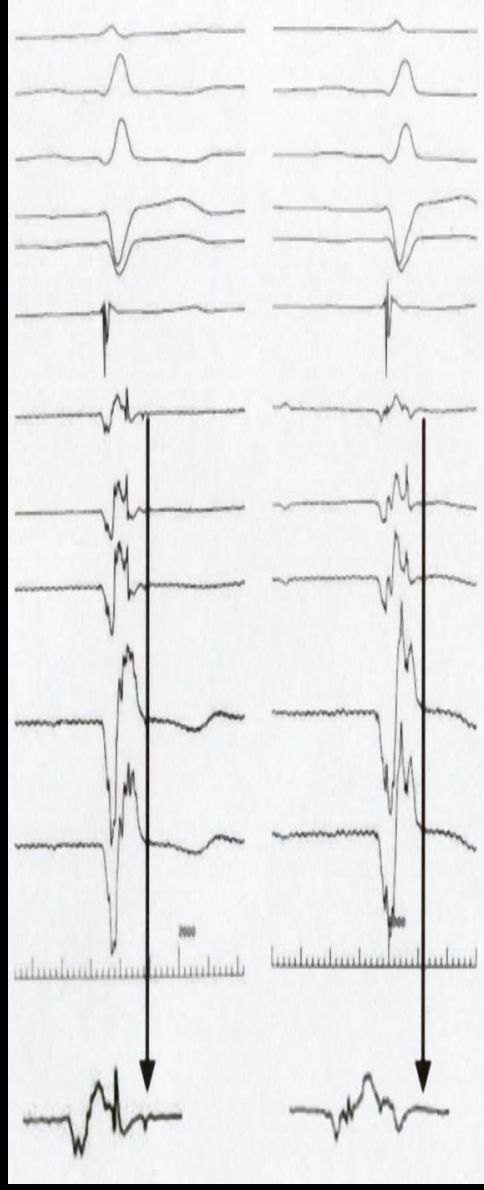
Pacing at LV ILP

VT









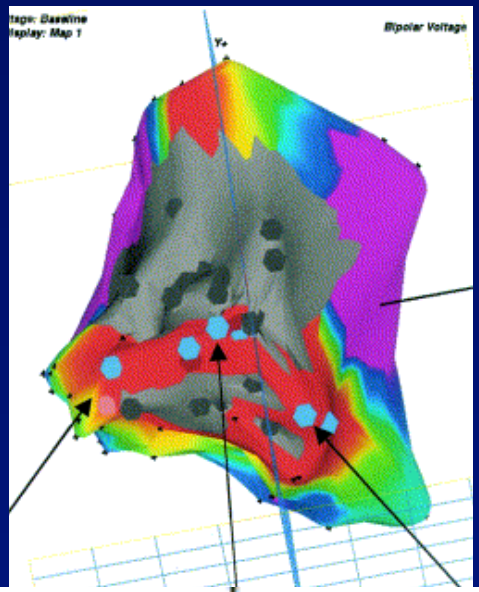
VOLTAGE AND LATE POTENTIAL MAP

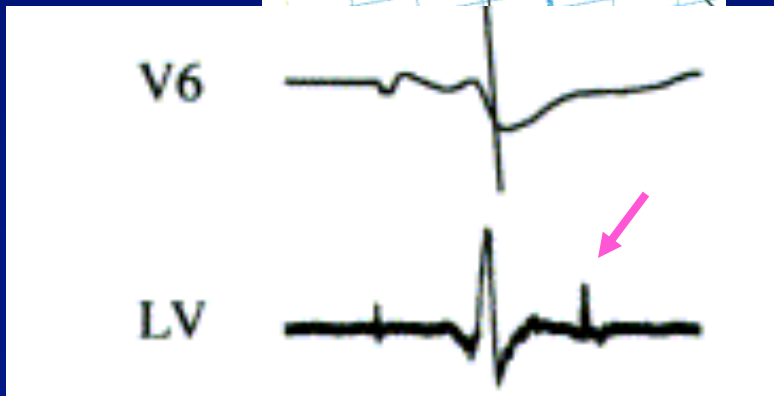
ABLATION OF ALL LATE POTENTIALS

Ablation of electrograms with an isolated, delayed component for unmappable VT

Arenal et al. JACC 2003, 42: 81

- 18 patients (15 ischemic CM) with unstable VTs
- RF ablation (1 – 39 lesions) targeting isolated potentials in low Voltage regions identified during sinus rhythm or RV pacing
- Follow-up: 4 – 19 months
  - 13 / 18 patients with no VT

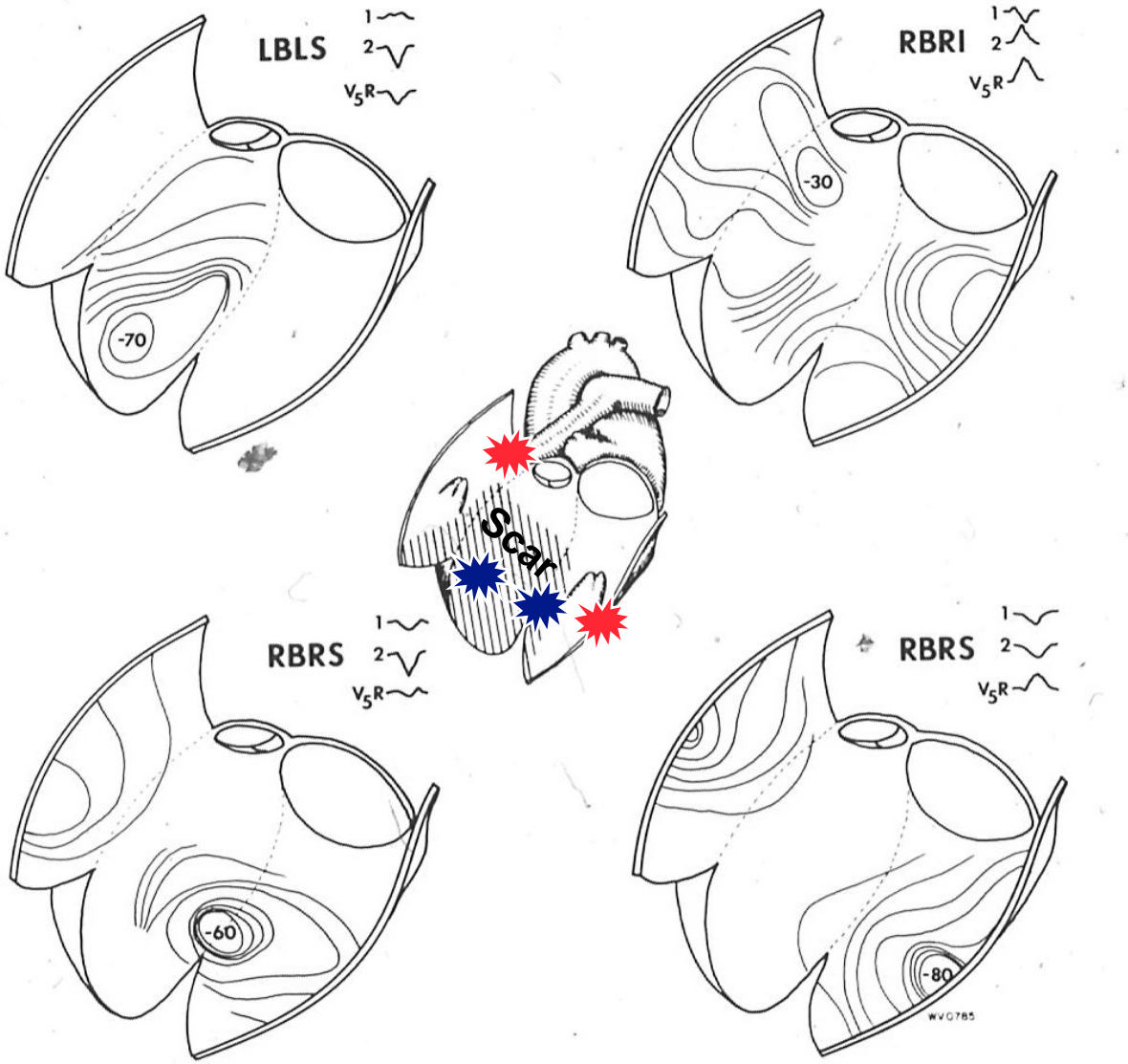




Limitations of Use of Late/Split Potentials to Define Isthmuses

- However split potentials don't necessarily mean block and/or they may be functional and dependent on the direction of the wavefront of activation.
- Late potentials are widespread and not only at arrhythmogenic sites.
- Late potentials may represent dead end pathways
- Late potentials may require the development of functional block and are not seen in sinus or during VT
- Late potentials may be very small (i.e. <0.1 mV) and may be missed,
- The density of mapped sites must be very high to record all late potential.

NOT ALL VTs ARISE FROM VISIBLE OR ELECTRICALLY IDENTIFIABLE ENDOCARDIAL SCAR



? ROLE OF EPICARDIAL MAPPING

CONCLUSIONS

- Although substrate can be identified, ablation using multiple parameters will be necessary to eliminate all VT
- Unknown whether one needs to eliminate all inducible VT; i.e. successful surgery did not require removal of all scar.
- What about VF or non-inducible arrhythmia in someone with clinical VF?

Despite these questions a small, randomized trial (SMASH VT) demonstrated a 70% reduction of all therapies in patients with implanted ICDs.

ICD Shocks
30-50% are inappropriate

- ↓ Quality of life/ ↓ physical capacity after ICD shocks – especially if multiple shocks
- ↑ Hospitalizations and mortality related to appropriate shocks
- DINAMIT – increase in non-sudden mortality borne by pts with shock; in 1 yr, 40% mortality
- SCD-HeFT – 4.85 HR for all cause mortality
- Madit II – 31% all shocks were inappropriate, 11% of all patients with ICD, increased mortality

Dorian P: Circulation 2004 abstract
Poole J: Heart Rhythm 2006 abstract

SMASH-VT: Results

- **Duration of Follow-Up: 24 months**
  - **Appropriate ICD therapy (shocks + ATP):**
    - » **Control** **20 (31.3%)** **p=0.03***
    - » **Ablation** **9 (14.5%)**
  - **Appropriate ICD shocks:**
    - » **Control:** **16 (24%)** **p=0.02***
    - » **Ablation:** **5 (8.1%)**
- **Mortality:**
    - » **Control:** **11 (17.2%)** **p=0.18***
    - » **Ablation:** **5 (8.1%)**

(*Using the Fisher's exact test with 2-sided p-value)

MAPPING APPROACHES FOR ABLATION OF SCAR RELATED VTs

Initiate VT

Stable VT

Entrainment mapping
identify isthmus

Unstable/Unmappable VT

Regional Approach
voltage map
LP map
excitability map
pace-map

? Prevention of VF