Role of Pre-procedure Imaging Before VT Ablation – Just Pretty Pictures or Critical Information to Guide Ablation?

- 7th Annual California Heart Rhythm Symposium-

Timm Dickfeld, MD, PhD
Professor of Medicine, University of Maryland
MACIG (Maryland Arrhythmia and Cardiac Imaging Group)
www.umm.edu/heart/macig

Disclosure-of-Relationship

- Research Grants – Biosense-Webster, General Electric

Unlabeled Indications

- Use of Gadolinium for MRI Scar Imaging

Clinical Challenge

- 249 ischemic VT pts
- 3.9% adverse events
- ICD shock: 81.2% vs 26.8%
- 38% sustained VT recurrence at 6 months

Marchlinski et al. JACC 2016;67:674-83

Clinical Challenge

- Possible Causes: Non-inducibility, hemodynamic instability, protected foci, inefficient lesion creation
- Question: Can pre-procedural imaging improve ablation outcomes?
- Targets for Pre-procedural Imaging
- Imaging Techniques
- Role and Evidence for Its Use
Anatomic Evaluation
- Cardica Anatomy -

Chamber Anatomy

Anatomic Evaluation
- Endocavitary Structures -

- Underappreciated entity
- 190 VT RFA
- 24% ECS affecting case
  - 67% mapping (n=31)
  - 33% RF target (n=15)

8% of all cohort
- 30% papillary muscle
- 47% moderator band
- 23% false tendon

Good et al., Heart Rhythm. 2008;:1530; Tian et al. Circulation 2008; 118:S690

Anatomic Evaluation
- Myocardial Structures: VSD patch and Pledgets -

56 yo pt, 6 weeks post IMI with LV wall rupture and LV patch

Anatomic Evaluation
- Epicardial Structures: CA, Epicardial Fat -

- Coronary Arteries
  - 5-10mm safety distance; thermal injury with abrupt thrombosis or delayed SMC hypertrophy
- Epicardial Fat
  - Mapping: decreased voltage with ≥ 2.8mm
  - RF delivery not effective with 3.5-7.3mm
- Phrenic Nerve

Adapted from Stevenson et al. Circulation. 1993;88:1647

Scar Imaging
Anatomic Substrate of Reentrant VT

Inner Loop

Outer Loop

Isthmus

Exit

Blind Alley

Scar And MACE

• 195 likely CAD pts. (EF 54±14%) with 16m F/U
• Threshold effect with HR of >7 with 1.4% LGE

HR for MACE for % LGE/LV and WMS%

Kwong R. et al. Circulation. 2006;113:2733

4.3g myocardium = 1.4% LV mass

Computed Tomography
**Computed Tomography**

Advances in Multi-detector CT
- ≥ 256 slices; <0.4s gantry rotation
- submillimeter resolution; <1mSv radiation

• **Anatomic Evaluation**
  - Wall thickness, calcifications

• **Dynamic Evaluation**
  - Wall motion, wall thickening

• **Perfusion Evaluation**
  - First-pass hypoperfusion, delayed enhancement

> Comprehensive Scar Characterization; n=11

---

**Anatomic Evaluation**

- **Calcification**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>HU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>0</td>
</tr>
<tr>
<td>Bone</td>
<td>1000</td>
</tr>
<tr>
<td>Air</td>
<td>-1000</td>
</tr>
<tr>
<td>Ca++</td>
<td>&gt;200</td>
</tr>
</tbody>
</table>

**Fatty Replacement**

- Intramyocardial remodelling with hypoattenuation
- 22 post-MI patients undergoing VT ablation
- 50% of VT circuits in close proximity to fat deposits

Sasaki et al. Heart Rhythm 2015;12:1508

**Wall Thickness**

- 2D-CT WT Contouring
- Segm. WT Analysis
- Segm. Volt. Analysis
- WT Projection

Tian et al. Circ Arrhythm Electrophysiol 2010;3:496
Dynamic Evaluation: Comparison with LV Voltage Map

CT Image                17-Seg Analysis           Voltage Map

Tian et al. Circ Arrhythm Electrophysiol 2010;3:496

Comparison of Anatomic/Dynamic Parameters between Voltage-Defined Abnormal and Normal Segments

Normal segments (>1.5mV): 43 segments
Abnormal segments (<1.5mV): 28 segments (5 scar, 3 BZ, 20 scar/BZ)

Prediction of Abnormal Voltage Segments with Anatomic and Dynamic Parameters

- Regression Model:
  - ESWT and WT with best prediction value
  - correctly classifies 82% segments
  - AUC= 0.85±0.05

Perfusion

- 1st pass Hypoperfusion -

Computed Tomography
- Perfusion Characteristics: 1st pass Hypoperfusion -

Transmural Scar  Endocardial Scar

Correlation of Hypoperfusion and Voltage

- LV Scar Burden
  - Perfusion CT: 33.3±8.5%
  - Voltage <1.5mV: 37.4±11.4%
  - **r=0.77, P=0.006**

- 82% of successful RF sites in border zone
- 18% in scar center

Tian et al. Circ Arrhythm Electrophysiol 2010;3:496

Delayed Contrast Enhancement

- Viable Myocardium
- Acute Myocardial Infarction
- Chronically Infarcted Myocardium

- Normal Cell Membranes
- Ruptured Cell Membranes
- Collagen Matrix

- Tissue Volume predominantly intracellular (75%)
- Increased volume of distribution
- Myocyte replacement, increased interstitial space/VoD

Kim RJ, et al.: Lippincott Williams and Wilkins, 2010

First Pass and Late Enhancement

- First Pass “Black”
- Late Enhancement “White”

- 37 patients (16 acute, 21 chronic MI)

Gerber BL. Circulation 2006; 113:823
Computed Tomography
- Perfusion Characteristics: Delayed Enhancement -

Pre-contrast
Post-contrast

Anatomic Evaluation
- Comparison with EAM -

13 post-MI patients
CT wall thickness <5mm ~ endocardial <1.5mV
LAVA: 87% within WT<5mm; rest within 23mm

Komatsu Y et al. Circ Arrhythm Electrophysiol. 2013;6:342

Anatomic Evaluation
-Wall Thickness in Non-Ischemic CM -

- Very limited data on NICM
- 3/3 pts with wall thinning <5mm (1/3 with LGE)
- 63 ± 21% overlap with <1.5mV

Cochet H et al. JCE 2013:24:419

Magnetic Resonance Imaging
MRI: Near-Cellular Substrate Resolution

- LAD ligation
- Rat-infarct model
- LGE ex-vivo 7T MRI
- Voxel: 50x50x50μm
- MRI/histology correlation ($R^2=0.96$)
- Ability to detect clefts 2-4 myocytes thick

Schelbert et al. Circ Cardiovasc Imaging 2010;3;743

Correlation: MRI and Voltage

DE MRI

Voltage Map

Correlation of Scar Transmurality and Voltage

Dickfeld et al. Circ Arrhythm Electrophysiol. 2011;4:172

CMR: MRI Scar and Voltage Scar

15 post-MI pts

Wijnmaalen et al. Eur Heart J. 2011;32:104
**MRI Scar and Voltage Mapping**

- **Best voltage cut-off for MRI scar:**
  - Bipolar voltage: 1.0-1.54mV
  - Unipolar voltage: 4.46-6.52mV

- **Comparison MRI and Voltage Scar Area:**
  - MRI scar ~ <0.5mV scar area
  - MRI scar ~ <1.5mV scar+border zone area
  - MRI scar slightly larger than 1.5mV area

- **Significant Mismatch:** 1/3 of patients

---

**Mismatch: MRI Scar > Voltage Scar**

Endocardial layer of ~2mm normal myocardium masks intramural scar (predominantly in septal location)

- **Mismatch:** MRI Scar > Voltage Scar

---

**Mismatch: Voltage Scar > MRI Scar**

- **Suboptimal Catheter Contact:**
  - Frequently basal "pseudoscar"

- **Decreased MRI Sensitivity to detect patchy scar**

- **Limited Mapping Density:** incorrect low voltage extrapolation
Image-Guided VT Ablation

MRI-Guided Ablation: Border Zone

Pacemapping Guided by MRI Scar
Pacemap Match
Dickfeld et al. Circ Arrhythm Electrophysiol. 2011;4:172

MRI-Guided Ablation: Abnormal Substrate

Surviving Pap. Muscle
Substrate-Guided Mapping
PM Match
Dickfeld et al. Circ Arrhythm Electrophysiol. 2011;4:172

MRI-Guided Ablation
- Successful Ablation Site Characteristics -

Reprojection of PM Site
80-Sector Segmentation
Transmurality Display
**MRI-Guided Ablation: Midmyocardial Scar**

LV Voltage Map

VT

**Mid- and Epicardial Scar with Preserved Endocardial Voltage**

Dickfeld et al. Circ Arrhythm Electrophysiol. 2011;4:172

---

**Successful RF Site Characteristics**

- Bipolar Voltage: 0.60-0.72mV (SD≤0.9)
- Unipolar Voltage: 1.9-2.20mV (SD≤2.1)
- Fractionated Signals: 32-62%
- Diastolic Potentials: 23-66%
- Transmurality: 60-68% (SD≤38%)
- Infarct core 17-71%
- Grey zone/periphery 29-83%
- **MRI LGE: 100%**

Desjardins et al. Heart Rhythm 2009;6:644
Perez-David E et al. J Am Coll Cardiol 2011;57:184
Wijnmaalen et al. Eur Heart J. 2011;32:104
Dickfeld et al. Circ Arrhythm Electrophysiol. 2011;4:172

---

**Commercial Image Integration Software**

A. Align short/long axis

B. Histogram-based Definition of Scar (pink) and Border Zone (blue).

C. Bipolar Voltage Map

D. Registered MRI, Scar (red), GZ (blue)

E. Procedural Guidance
• Frequency shift with complete ("signal void") and partial dephasing ("white halo")
• Affecting 54±21% of LV myocardium

Metal Artifact of MRI


ICD Artifact Suppression

• Artifact reduction 48±18% to 12±10% (p<0.001) in RV and 62±26% to 10±7% (p<0.001) in LV.

ICD Artifact Suppression

• Further refinement of binary concept (DE+/-)
• Introduction of MRI scar core and periphery
• Analogous to voltage-defined border zone

‘Gray Zone’
- Mixture of Scar and Normal Myocardium -

De Bakker JM. Circ Arrhythm Electrophysiol 2010; 3:204
‘Gray Zone’
- Mixture of Scar and Normal Myocardium -

- Gray zone correlated in ischemic patients with all-cause mortality, inducibility of MMVT and appropriate ICD shocks
  - Roes S. Circ Cardiovasc Imaging 2009;2:183

- Three different definitions:
  - Scar (>3SD), Gray Zone (2-3 SD)
  - Scar (>50% max SI), Gray Zone (>peak remote/<50% max SI)
  - Scar (>50% max SI), Gray Zone (35-50% max SI)

Gray Zone – Human Studies

- 10 patients with ischemic CMP and VT RFA
- Voltage as gold standard
- Best MRI match with FWHM 60% and subendocardial half-wall thickness (scar \( r^2 = 0.81; p < 0.001 \) and BZ: \( r^2 = 0.49; p = 0.025 \))
- Identified 81% of voltage-defined channels

Comparison of Three Gray Zone Algorithms

- FWHM
- NSD
- Mod. FWHM

Resolution-Dependency of Gray Zone (Partial Volume Effect)

- LAD-occlusion model in rats (n=8)
- 7T MRI with voxel size of 50x50x50 \( \mu \text{m} \)
- Gray zone increase from 7 to 14% (p<0.01)

Schelbert et al. Circ Cardiovasc Imaging 2010;3;743
Positron Emission Tomography

FDG PET/CT Imaging: Molecular Imaging

PET CT

PET/CT Fusion

3D Volume Rendering: Visualization of Epicardium and Endocardium

PET: Detection of Falsely-Low Voltage Recordings
4±2% of LV Mapping Points

**PET/Voltage Scar Correlation**

- **Registration Accuracy:** 3.7±0.7mm
- **Scar Burden:**
  - Voltage: 21.4±37.2%
  - PET: 20.1±38.9%
  - \( r = 0.88; \ p < 0.05 \)
- **PET Scar (p<0.05):**
  - ↓ bi/unipolar voltage
  - ↑ latency/fractionation

Dickfeld et al. JACC CV IM;1:73:2008

**Metabolic VT Substrate**

PET: Detection of Metabolically Alive Myocardium within Scar

Dickfeld et al. JACC CV IM;1:73:2008

**Metabolic VT Substrate**

PET: Detection of Scar within Normal Myocardium

Dickfeld et al. JACC CV IM;1:73:2008

**Metabolic Properties of Scar/BZ**

- Scar: 7%
- Border Zone: 5%
- Normal: 88%

\( p<0.05 \)

Tian et al. JCE 2008;20:597
**PET/CT: Substrate Characterization**

### 3D Scar Characterization

- **Voltage Map**
- **PET Scar**
- **PET Scar/BZ**

*Tian et al. JCE 2008;20:597*

**PET/EAM Correlations**

- 19 post-MI VT RFA
- 50% FDG-PET scar threshold (68.6±49.2 cm²)
- 0.9mV best correlation (70.4±49.3 cm²)

- 7 ischemic VT patients
- Voltage areas of <0.5V, 0.5-1V and 1-1.5V correlated with FDG PET uptake of 43.1%, 49.5% and 60.1%

*Fahmy T et al. Heart Rhythm 2008;5:1538*

### Metabolic Evaluation

*Tian et al. JCE 2008;20:597*

**SPECT**

- Thallium-201 imaging widely available

- Ten patients with ischemic VT: Scar (49±29%), Border zone (57±21%) and healthy myocardium (77±14%)

*Polar Map: Thallium/Bipolar Voltage*  

*68-segment model*

*Ten patients with ischemic VT: Scar (49±29%), Border zone (57±21%) and healthy myocardium (77±14%)*


- ROC-curve: 70% cut-off with AUC of 0.79±0.03
- SPECT scar (18.8±5.2%) best approximated <1.5mV area (20.8±15.7%) vs. <0.5mV (5.8±5.8%).
- All 14 successful RF sites within the SPECT-defined scar/border zone

*Registered SPECT Scar*  

**Cardiac Innervation**

- **I-123-metaiodobenzylguanidine (MIBG):**
  - Norepinephrine analog
  - Similar transport and storage
  - Cardiac sympathetic activity
  - Regional efferent adrenergic neuronal function

- Previous studies: only global cardiac MIBG uptake
- Predictive in chronic heart failure: cardiac mortality, ventricular arrhythmias, SCD and HF progression

**SPECT Innervation Imaging**

- I-123-metaiodobenzylguanidine
- MIBG: norepinephrine analog
- Similar transport and storage
- Cardiac sympathetic activity
- Regional efferent adrenergic neuronal function

- Previous studies: only global cardiac MIBG uptake
- Predictive in chronic heart failure: cardiac mortality, ventricular arrhythmias, SCD and HF progression

**Planar Imaging ~ Global Innervation**

- **Heart-to-mediastinum ratio (HMR):**
  - Abnormal < 1.7 – 2.2

- **Washout rate:****
  \[
  \frac{([H] - [M]_{early} - ([H] - [M]_{late}) \times 100}{([H] - [M]_{early}}
  \]
  - Abnormal > 27%

**SPECT MIBG: Regional Innervation**

- Mapping system
- 3D Reconstruction
- Voltage Map

<table>
<thead>
<tr>
<th>% MIBG defect</th>
<th>% voltage scar</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>27±10</td>
<td>11±9</td>
<td>0.001</td>
</tr>
</tbody>
</table>
**Feasibility Trial (n=15):** 36% of successful ablations with >1.5mV voltage, but all innervation defect

Klein et al. Circ Arrhythm Electrophysiol. 2015 8(3):583-91

**Moving Beyond - Multi-Modality Assessment**

- 13 patients with ICM and triple data sets: CMR, MIBG, EP map

Kiddy et al. Submitted.

**Moving Beyond - Multi-Modality Assessment**

- All 11 VT channels in denervated CMR scar
- Fibrosis + Denervation: Proarrhythmic Region?

Kiddy et al. Submitted.

Reithman C. Clin Res Cardiol 2016

**CMR Guidance for Endo/Epicardial Ablation**
**Effect of Imaging on VT Ablation Procedure**

- 116 VT RFA pts (67 ICM; 30 NICM; 19 ARVC)
- MDCT 91%; CMR 30%; both 22%)
- Imaging identified 89% of VT isthmi
- Motivated additional mapping and epicardial access in 57% and 33%
- CA/phrenic nerve integration modified epicardial RF strategy in 43%

---

**Effect of Imaging on VT Ablation Outcomes**

- 125 post-MI VT patients from 2009-2013
- Image Integration in 38% (CMR 39%, CT 93%)
- MV analysis: reduced VT recurrence: LAVA elimination (RR=0.52) image integration (RR=0.49), use of multipolar catheters (RR 0.75)

---

**Effect on VT Ablation**

- Not randomized, more imaging in later years with better RFA technology, sicker patient (e.g. VT storm)=less imaging?
- 3D Mapping used in only 51% of non-image guided VT ablations
- More LAVA with image integration
- Longer procedure time

---

**CMR Guidance for Endo/epicardial Ablation**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Epi only (4) or predominant epi (12)</th>
<th>Endo (9): success:2 Epi (7): success 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reithman et al Clin Res Card 2016</td>
<td>44 NICM pts</td>
<td>Epi only (4) or predominant epi (12)</td>
<td>Endo (9): success:2 Epi (7): success 7</td>
</tr>
<tr>
<td>Njeim et al JCE 2016</td>
<td>12 NICM, 8 ICM pts</td>
<td>Epi LGE (9), endo- or septal LGE or artifact (11)</td>
<td>Epi LGE–EPI VT: 9</td>
</tr>
<tr>
<td>Andreu et al Eur Heart J 2014</td>
<td>80 NICM pts</td>
<td>Subepi LGE (14.3% of pts) with 84.6/100% sensitivity/specificity for Epi VT</td>
<td>Epi (11): success:11</td>
</tr>
<tr>
<td>Piers et al Circ A&amp;E 2013</td>
<td>19 NICM pts</td>
<td>Basal anteroseptal scar (42%), inferolateral scar (47%)</td>
<td>63% of inferolateral scar needed epi access</td>
</tr>
</tbody>
</table>

---

Yamashita S. JCE 2016;27:699
PET – Metabolic Border Zone

- 35 patients with ischemic (69%) and non-ischemic (31%) CMP following after VT ablation (EF 27±10%)
- Mortality of 31% after 18 months (IQR 12-48)
- Segmental analysis:
  - 19% PET scar (<50%)
  - 28% PET BZ (50-70%)
  - 53% normal (>70%)

Conclusion

- Imaging reported mostly as single center feasibility trials
- No prospective studies or multi-center trials of value of image integration
- Established track record for anatomic and scar imaging
- Emerging evidence to guide epicardial RFA
- Possibly improved procedural outcome
- Current Challenges: Variable ablation strategies, commercial image integration capabilities just emerging

Thanks

- Jean Jeudy
- Vasken Dilsizian
- Mark Smith
- Wengen Chen
- Steve Shorofsky
- Tas Saliaris
- Vincent See
- Seth Kligerman
- Jing Tian
- Ben Remo
- Ghada Ahmad
- Hasan Imanli

- Kiddy Umi
- Emi Bob-Manuel
- Alejandro Jimenez
- Oluotimi Mesubi
- Tom Klein
- Shaun Bhatti
- Mohammed Abdulghani
- Ayman Hussein
- Ramazan Asoglu
- Taehoon Shin
- Hiroko Beck
- Mussaber Ahmad

www.umm.edu/heart/maci