Imaging Technologies for Stereotactic Ablative Radiotherapy (SABR) of Cardiac Ventricular Tachycardia

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Background

- Ventricular Tachycardia (VT) is a major cause of sudden cardiac death
- Invasive catheter ablation has become a primary therapy, but with a moderate success rate for patients with structural heart disease (SHD)
- Early preliminary studies have shown promising outcome of Stereotactic Ablative Radiotherapy (SABR) as non-invasive treatment option for refractory VT
Reentrant Ventricular Tachycardia

Ablation requires accurate substrate mapping

https://www.hunterheart.com.au

Muser et al. Current Cardiology Review V15. 2019
RF Catheter Ablation

• Point-by-point ablation (invasive and time-consuming)

• Common failures:
  • Inadequate heating at desired target
  • Arrhythmia substrate location is inaccessible
  • Missing the critical central isthmus

Mahida et al. Circulation V136. 2017
Spartalis M et al. World J of Cardiology, V10, 2018
Catheter ablation strategies

Radiation ablation: possible to ablate entire scar or multiple scars simultaneously

- Accurate target localization is still critical
- Too small – missing the isthmus
- Too large - normal tissue toxicity
- Respiration and cardiac motion

Arrhythmia target mapping technologies

• Electrophysiological based:
  • 12-lead ECG
  • Cardiac Electroanatomic Mapping (EAM)
  • Electrocardiographic Imaging (ECGI)

• Non-invasive cardiac imaging – Structure or functional
  • Cardiac MRI (CMR)
  • Multi-detector Cardiac CT (MDCT) or Angiograph
  • Nuclear imaging (SPECT/PET)
• 12-lead ECG provides location info of the exit site of the circuit (~1cm away from isthmus)
• Remains as a guide to further mapping, rather than pinpointing the actual site
Electrophysiological Mapping

• Catheter-mounted intra-cardiac electrodes
  • Unipolar or Bipolar
  • Various mapping techniques
    • Activation mapping
    • Entrainment mapping
    • Pacing mapping
    • Substrate mapping
  • Area of low amplitude voltage is associated with surviving myocardia tissues

Electroanatomic Mapping (EAM)

- Combine the electrical information from catheter-mounted electrode and 3D spatial information
- Real-time guidance for ablation with minimal use of fluoroscopy
- Large uncertainties due to:
  - Inconsistencies in catheter contact
  - Sparse sampling and extrapolation
- Invasive, time consuming
- Data not compatible to RT planning

Spartalis M et al. World J of Cardiology, V10,2018
Electrocardiographic imaging (ECGI)

- Vest of 250 ECG electrodes over patient’s torso
- Body surface potential map generated to derive substrate exit and entrance site
- Projected on patient’s CT
- Non-invasive mapping
- Not widely available, requires active stimulation of VT

Cardiac MR Imaging (CMR)

- Late gadolinium enhancement (LGE) CMR: clinical gold standard for characterization of myocardial fibrotic tissue
- Well validated in histopathologic studies and correlated with electrophysiological mapping

Zeppenfeld et al. JACC Clin Electrophysiology v4. 2018
Njeim et al. JACC Cardiovascular Imaging. v9 2016
LGE-CMR

- Safety concerns in patients with ICD and pacemaker implants (tissue heating, device malfunction)

- Device-induced image artifacts: void or hyperintensity

Courtesy of Dr. Peng Hu, UCLA
Hyperintensity artifacts can be eliminated by a wide-bandwidth RF inversion pulse, enabling diagnostic scar imaging…
Wideband LGE-CMR

Figure 2

standard wideband standard wideband

ICD

Rashid, Hu et al. Radiology v270, 2014
Wideband LGE vs EAM

Stevens, Hu et al. Heart Rhythm, v11, 2014
Wideband LGE for SABR target localization
Cardiac CT

- High spatial resolution (<1mm)
- Lower contrast-to-noise ratio
- Imaging characteristics for scar:
  - Wall thinning, adipose metaplasia, Hypoperfusion
- Delineate detailed cardiac anatomy
  - Coronary arteries, valve apparatus, phrenic nerves…

Esposito et al. JACC Cardiovascular Imaging. v9 2016
Nuclear Imaging (SPECT, PET)

- Provide complementary functional information to EAM defined scar
- Mapping of metabolically active surviving tissue or perfusion defects
- Do not provide sufficient anatomic information
- Intrinsic low spatial resolution

Zei et al. Curr Cardiol Rep 19, 2017
<table>
<thead>
<tr>
<th>Modality</th>
<th>Mechanism</th>
<th>Advantage</th>
<th>Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAM (EP)</td>
<td>catheter-mounted contact electrode + 3D spatial info</td>
<td>real-time electrophysiological info</td>
<td>invasive; sparse sampling and extrapolation; data not compatible with RT planning</td>
</tr>
<tr>
<td>ECGI (EP)</td>
<td>EGM map derived from high density ECG jacket</td>
<td>non-invasive ECG mapping; 3D combined with CT</td>
<td>only mapping exit/entrance site; not widely available; reliability and accuracy to be proved</td>
</tr>
<tr>
<td>LGE-CMR (Structural)</td>
<td>contrast demarcates extracellular space as surrogate of dense fiber</td>
<td>high CNR allowing 3D scar characterization (size, border zone, heterogeneity)</td>
<td>MR safety concerns &amp; Image artifact; non-axial images; low resolution in slice thickness; renal function for contrast</td>
</tr>
<tr>
<td>Cardiac CT (Structural)</td>
<td>imaging of wall thinning, hypoperfusion</td>
<td>axial images with detailed cardiac anatomy; high spatial resolution</td>
<td>low CNR and sensitivity; renal function for contrast; imaging radiation exposure</td>
</tr>
<tr>
<td>PET/SPECT (Functional)</td>
<td>mapping of metabolically active surviving tissue or perfusion defects</td>
<td>axial images; distinguish NICM etiologies with inflammation</td>
<td>no anatomy info; low spatial resolution (PET)</td>
</tr>
</tbody>
</table>
Multi-modality target delineation

Electrophysiological (ECG, EAM, ECGI)

Functional (SPECT, PET)

Structural (Cardiac MRI, CT)

Mahida et al. Circulation. 2017
### Table 1: Registration Methods and Accuracy

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Author</th>
<th>Publication Year</th>
<th>Registration Error (mm)</th>
<th>Registration Method</th>
<th>Landmarks (if Applicable)</th>
<th>Registration Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>Codrea et al.</td>
<td>2008</td>
<td>N/R</td>
<td>LM</td>
<td>Aorta, LV apex, MA</td>
<td>offline</td>
</tr>
<tr>
<td></td>
<td>Desjardins et al.</td>
<td>2009</td>
<td>4.3</td>
<td>LM + SURF</td>
<td>Aorta, LV apex, MA</td>
<td>offline</td>
</tr>
<tr>
<td></td>
<td>Bogun et al.</td>
<td>2009</td>
<td>4.8</td>
<td>LM + SURF</td>
<td>Aorta, LV apex, MA</td>
<td>online</td>
</tr>
<tr>
<td></td>
<td>Ilg et al.</td>
<td>2010</td>
<td>3.5</td>
<td>LM + SURF</td>
<td>N/R</td>
<td>online</td>
</tr>
<tr>
<td></td>
<td>Andreu et al.</td>
<td>2011</td>
<td>3.4</td>
<td>LM + SURF</td>
<td>Aorta, LV apex, MA, RV</td>
<td>online</td>
</tr>
<tr>
<td></td>
<td>Wijnmaalen et al.</td>
<td>2011</td>
<td>3.8</td>
<td>LM + SURF</td>
<td>Left main</td>
<td>online</td>
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<tr>
<td></td>
<td>Dickfeld et al.</td>
<td>2011</td>
<td>3.9</td>
<td>VA</td>
<td>NA</td>
<td>online</td>
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<tr>
<td></td>
<td>Perez-Devid et al.</td>
<td>2011</td>
<td>N/R</td>
<td>LM</td>
<td>LV apex and MA</td>
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<tr>
<td></td>
<td>Tao et al.</td>
<td>2012</td>
<td>4.3</td>
<td>SURF</td>
<td>NA</td>
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<tr>
<td></td>
<td>Gupta et al.</td>
<td>2012</td>
<td>3.8</td>
<td>LM + SURF</td>
<td>Aorta, LV apex, MA</td>
<td>online</td>
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<tr>
<td></td>
<td>Fiers et al.</td>
<td>2012</td>
<td>3.2</td>
<td>LM + VA</td>
<td>Left main</td>
<td>online</td>
</tr>
<tr>
<td></td>
<td>Speers et al.</td>
<td>2012</td>
<td>3.6</td>
<td>LM + SURF</td>
<td>Aorta, LV apex, MA or His</td>
<td>offline</td>
</tr>
<tr>
<td></td>
<td>Cochet et al.*</td>
<td>2013</td>
<td>N/R</td>
<td>LM + SURF</td>
<td>Aorta, CS, left atrium, MA</td>
<td>online</td>
</tr>
<tr>
<td></td>
<td>Sasaki et al.</td>
<td>2012</td>
<td>2.8</td>
<td>LM + SURF</td>
<td>Aorta, LV apex, MA, RV septal insertions</td>
<td>offline</td>
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<tr>
<td>MDCT</td>
<td>Desjardins et al.</td>
<td>2010</td>
<td>3.0</td>
<td>LM + SURF</td>
<td>Epicardial apex, most lateral tricuspid and MA</td>
<td>offline</td>
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<tr>
<td></td>
<td>Tian et al.</td>
<td>2010</td>
<td>3.3</td>
<td>VA + SURF</td>
<td>NA</td>
<td>online</td>
</tr>
<tr>
<td></td>
<td>v Huis v Taxis et al.</td>
<td>2013</td>
<td>2.8</td>
<td>LM + SURF</td>
<td>Left main</td>
<td>online</td>
</tr>
<tr>
<td></td>
<td>Piers et al.</td>
<td>2012</td>
<td>2.0</td>
<td>LM + SURF</td>
<td>Left main</td>
<td>online</td>
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<tr>
<td></td>
<td>Komatsu et al.</td>
<td>2013</td>
<td>N/R</td>
<td>LM + SURF</td>
<td>CS, aortic root, LV apex and MA</td>
<td>online</td>
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<tr>
<td>PET/CT</td>
<td>Fahmy et al.</td>
<td>2008</td>
<td>5.1</td>
<td>LM + SURF</td>
<td>Coronary ostia, cusps, apex</td>
<td>online**</td>
</tr>
<tr>
<td></td>
<td>Dickfeld et al.</td>
<td>2008</td>
<td>3.7</td>
<td>VA</td>
<td>NA</td>
<td>online</td>
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<tr>
<td></td>
<td>Tian et al.</td>
<td>2009</td>
<td>4.3</td>
<td>VA + SURF</td>
<td>NA</td>
<td>online</td>
</tr>
<tr>
<td>SPECT</td>
<td>Tian et al.</td>
<td>2012</td>
<td>4.4</td>
<td>LM + SURF</td>
<td>MA</td>
<td>offline</td>
</tr>
</tbody>
</table>

2-5 mm registration error between EAM and non-invasive imaging
MUSIC integration platform

- MUSIC: MUltimodality platform for Specific Imaging in Cardiology

https://team.inria.fr/epione/en/software/music/
Motion management

• Complex respiration and cardiac motions

• Cardiac motion primarily as twist contraction with reduced magnitude in patients with chronic cardiomyopathy

• Respiration motion: 4DCT + IVT or Dynamic tracking/gating of fiducials

• Assessment of cardiac motion and compensation strategies remain challenges to be addressed

Roujol et al. PLoS One, 8(11) 2013
Bertini et al. JACC Cardiovascular Imaging 2(12), 2009
<table>
<thead>
<tr>
<th>Publication</th>
<th>Substrate Assessment Modalities</th>
<th>Treatment Platform</th>
<th>Dose Delivered</th>
<th>Procedure Length</th>
<th>Motion Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loo et al. 2015</td>
<td>Echocardiogram, PET, 12-lead ECG</td>
<td>CyberKnife</td>
<td>25 Gy/1 fraction</td>
<td>90 min</td>
<td>Dynamic tracking (Synchrony) with temporary pacing wire as fiducial for respiratory. Fluoroscopy during transient breath holds for cardiac.</td>
</tr>
<tr>
<td>Neuwirth et al. 2019</td>
<td>Diagnostic CT, EAM studies</td>
<td>CyberKnife</td>
<td>25 Gy/1 fraction</td>
<td>114 min</td>
<td>Dynamic tracking (Synchrony) with LV electrode as fiducial. No additional safety margin.</td>
</tr>
<tr>
<td>Zel et al. 2017</td>
<td>Cardiac CT, CMR, PET, 12-lead ECG, prior EAM studies</td>
<td>CyberKnife</td>
<td>25 Gy/1 fraction</td>
<td>Not reported</td>
<td>Dynamic tracking (Synchrony) with fiducial tracking as available.</td>
</tr>
<tr>
<td>Cuculich et al. 2017</td>
<td>SPECT, CMR, cardiac CT, echocardiogram, ECGi (CardioInsight Noninvasive 3D Mapping System), prior EAM studies</td>
<td>TrueBeam</td>
<td>25 Gy/1 fraction</td>
<td>11–18 min</td>
<td>4D respiratory-gated CT to determine target volume plus cardiac and respiratory motion, plus safety margin of 5 mm.</td>
</tr>
<tr>
<td>Jumeau et al. 2018</td>
<td>Planning CT, CMR, prior EAM studies</td>
<td>CyberKnife</td>
<td>25 Gy/1 fraction</td>
<td>45 min</td>
<td>Dynamic tracking (Synchrony) with RV ICD lead as fiducial. No additional safety margin.</td>
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<tr>
<td>Robinson et al. 2019</td>
<td>SPECT, CMR, cardiac CT, echocardiogram, ECGi (CardioInsight Noninvasive 3D Mapping System), prior EAM studies</td>
<td>TrueBeam</td>
<td>25 Gy/1 fraction</td>
<td>15.3 min</td>
<td>4D respiratory-gated CT to determine target volume plus cardiac and respiratory motion, plus safety margin of 5 mm.</td>
</tr>
<tr>
<td>Haskova et al. 2018</td>
<td>Planning CT, intracardiac echo, prior EAM</td>
<td>CyberKnife</td>
<td>25 Gy/1 fraction</td>
<td>Not reported</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Zeng et al. 2019</td>
<td>Planning CT, 12-lead echocardiogram, prior EAM</td>
<td>CyberKnife</td>
<td>24 Gy/3 fractions</td>
<td>Not reported</td>
<td>Dynamic tracking (Synchrony) with fluoroscopically implanted fiducial (pacemaker lead) for respiratory, fluoroscopy for cardiac.</td>
</tr>
<tr>
<td>Neuwirth et al. 2019</td>
<td>Planning CT, ECG-gated CT, prior endocardial +/- epicardial EAM</td>
<td>CyberKnife</td>
<td>25 Gy/1 fraction</td>
<td>68 min</td>
<td>ECG-gated CT for cardiac motion. Dynamic tracking (Synchrony) with existing ICD leads as surrogate fiducials for respiratory motion. No additional safety margin.</td>
</tr>
</tbody>
</table>
Summary

• SABR has been shown to be a promising non-invasive treatment for refractory cardiac VT

• Success of cardiac SABR relies on accurate target localization and treatment delivery
  
  • Non-invasive imaging for substrate characterization
  
  • Multi-modality image integration and registration
  
  • Motion assessment and compensation
Acknowledgement

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