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

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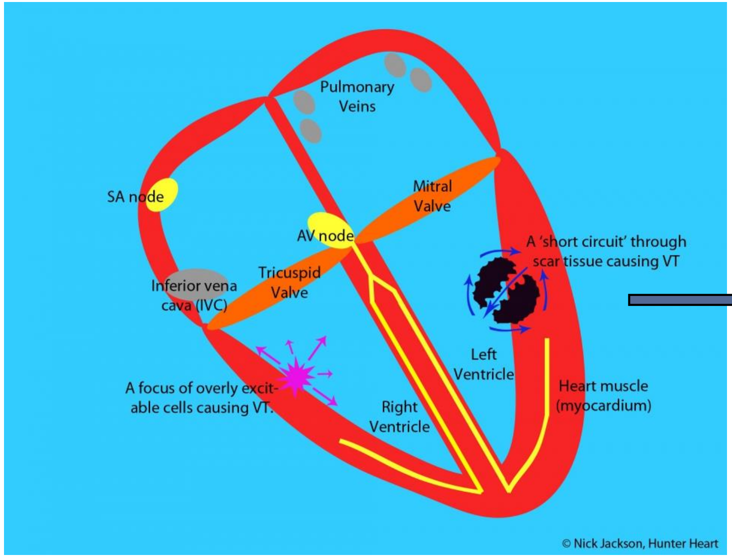
Background

- 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

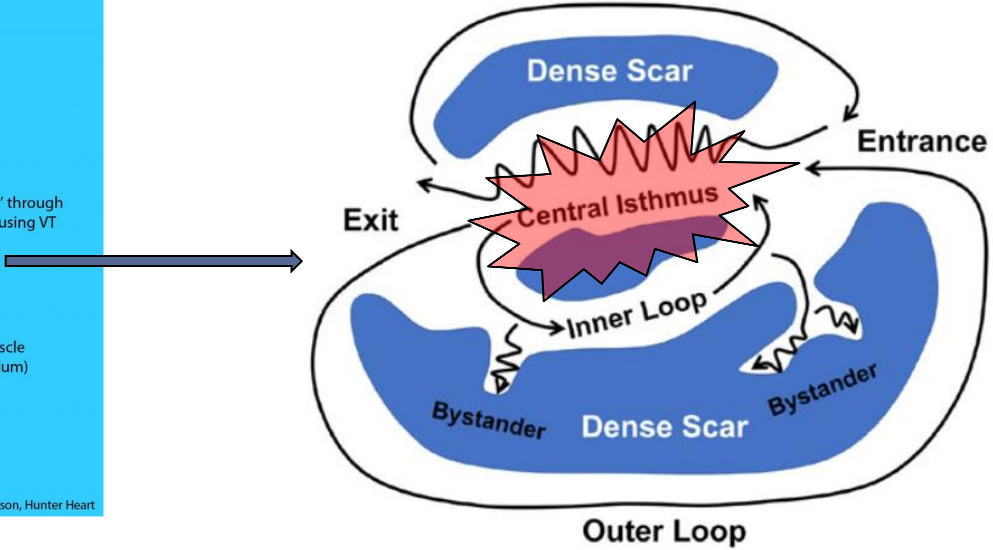
Reentrant Ventricular Tachycardia

Ablation requires accurate substrate mapping



https://www.hunterheart.com.au

Reentrant substrate



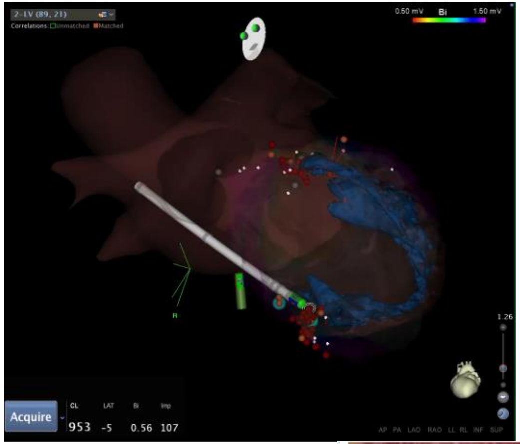
Muser et al. Current Cardiology Review V15. 2019

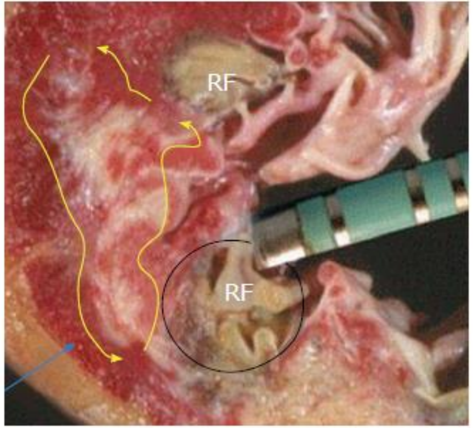
David Geffen School of Medicine

UCLA Health

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

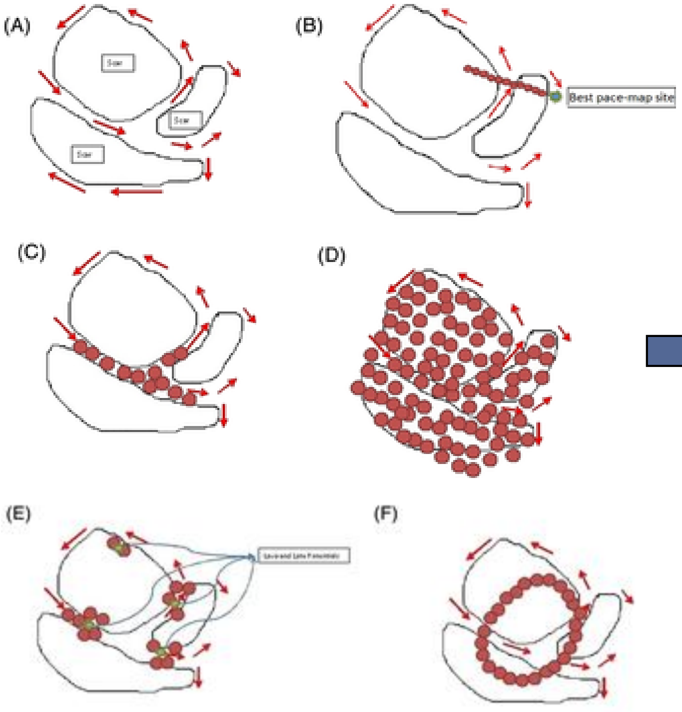




Mahida *et al*. Circulation V136. 2017

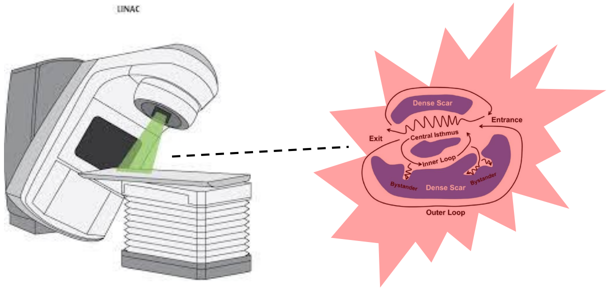
Spartalis M *et al*. World J of Cardiology, V10,2018

Catheter ablation strategies



Pandozi *et al.* Clin. Cardiology,4, 2019

Radiotherapy ablation

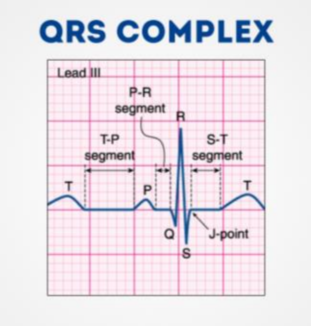


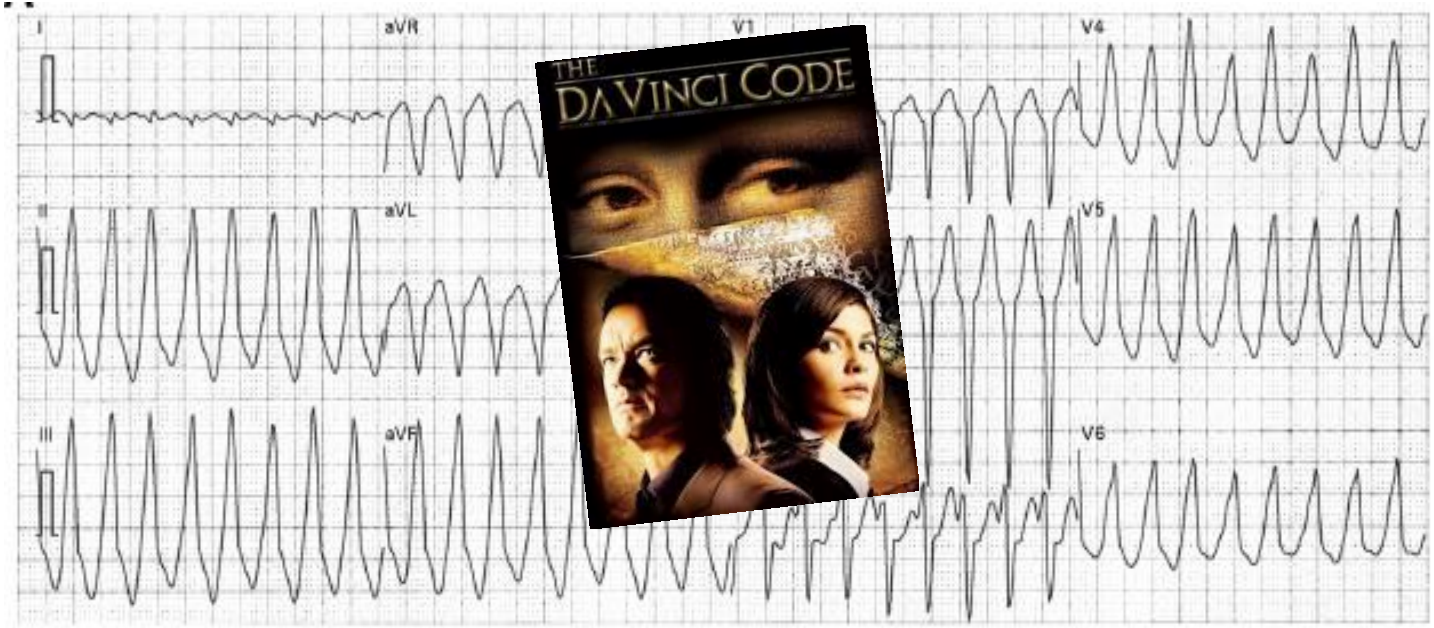
Radiation ablation: possible to ablate entire scar or multiple scars simultaneously

- 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)



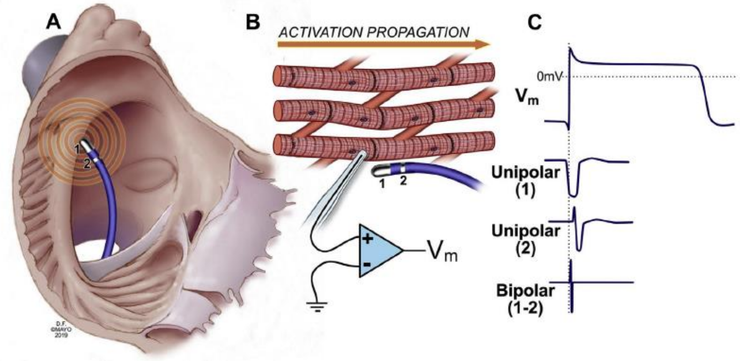


- 12-lead ECG provides location info of the exit site of the circuit (~1cm away from isthmus)
- Remains as a guide to further mapping, rather than pinpointing the actual site

Miller *et al*. Card Electrophysiol Clin 9 (2017)

Electrophysiological Mapping

- Catheter-mounted intra-cardiac electrodes
  - Unipolar or Bipolar
  - Various mapping techniques
    - Activation mapping
    - Entrainment mapping
    - Pacing mapping
    - Substrate mapping

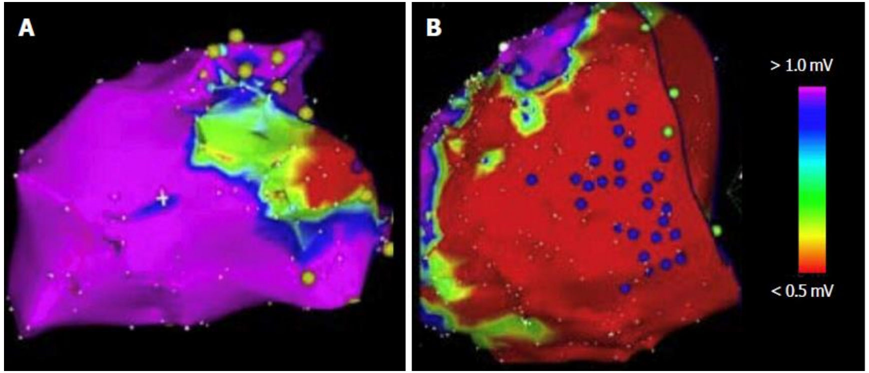


Lada *et al*. Card Electrophysiol Clin 11 (2019)

  - Area of low amplitude voltage is associated with surviving myocardia tissues

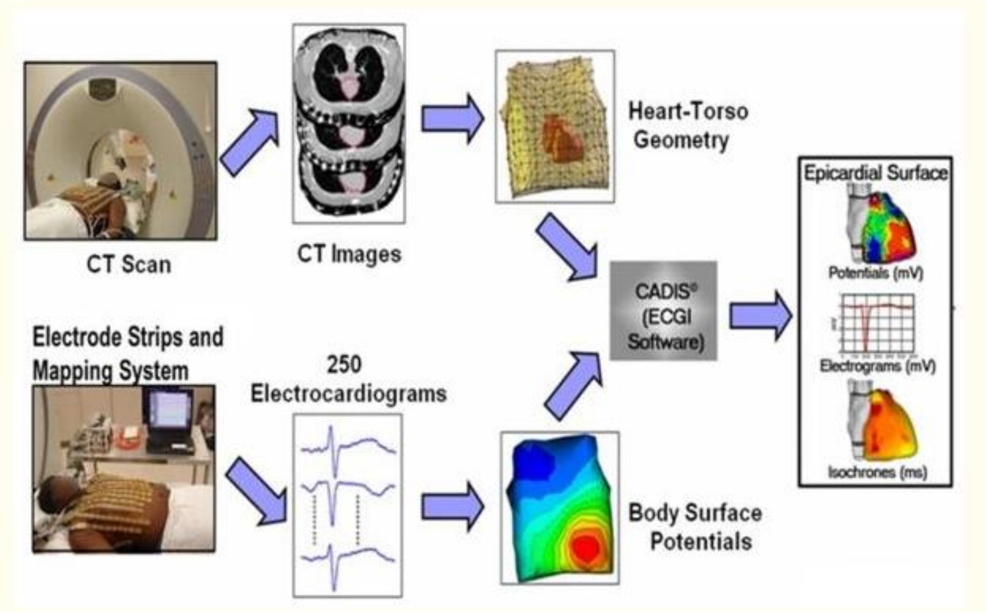
Electroanatomic Mapping (EAM)

- 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)

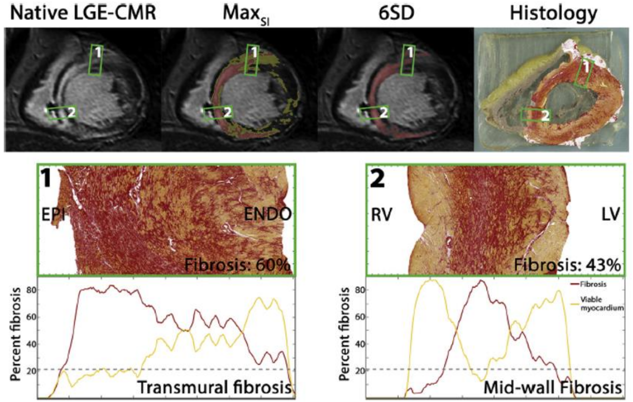


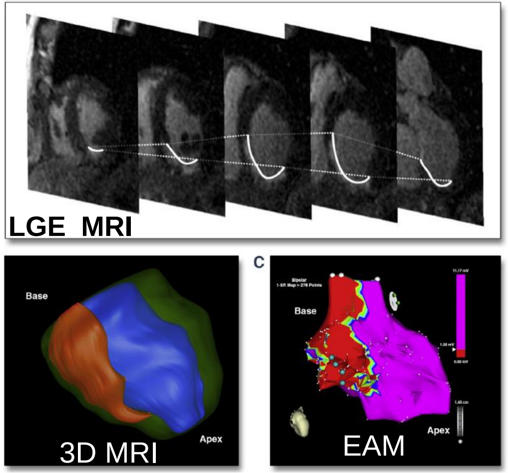
- Vest of 250 ECG electrodes over patient’s torso
- Body surface potential map generated to derive substrate exit and entrance site
- Projected on patient’s CT
- Non-invasive mapping
- Not widely available, requires active stimulation of VT

Rudy. Circ Res 112 (5), 2013

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

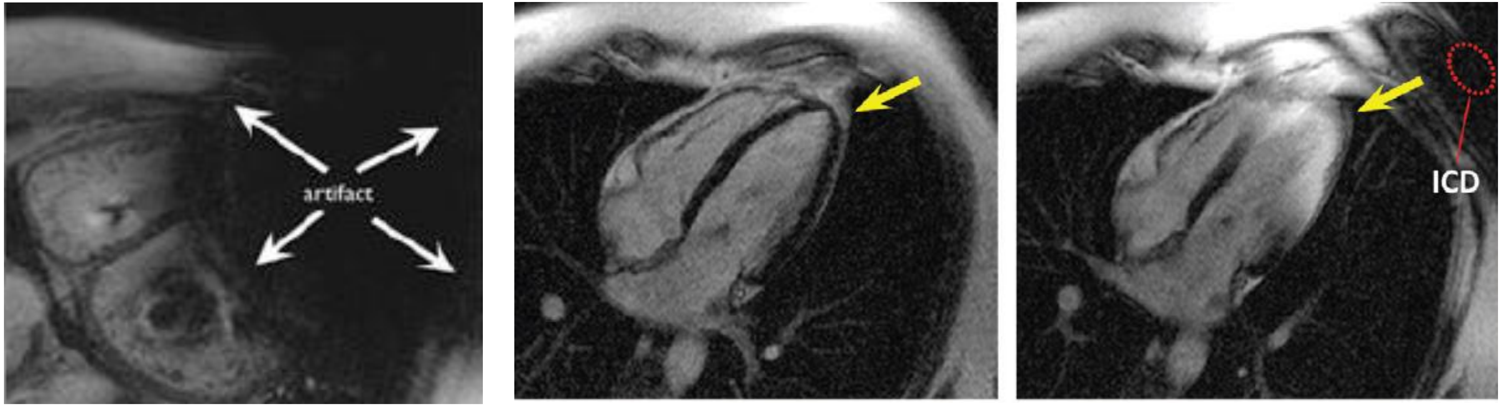




Zeppenfeld et al. JACC Clin Electrophysiology v4. 2018
Njeim et al. JACC Cardiovascular Imaging. v9 2016

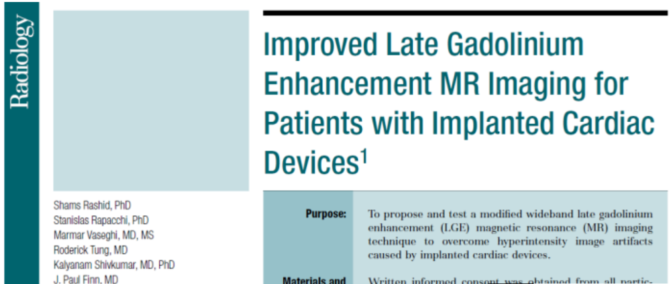
LGE-CMR

- 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

Wideband LGE-CMR



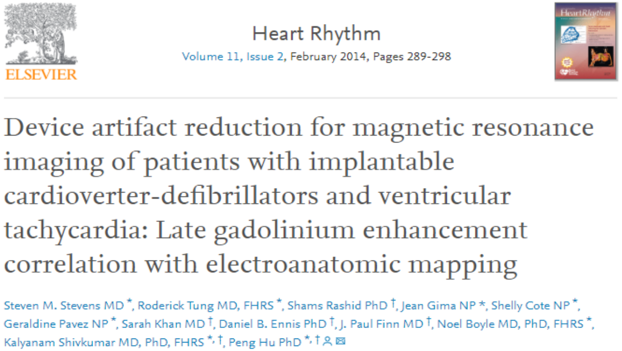
Radiology

Improved Late Gadolinium Enhancement MR Imaging for Patients with Implanted Cardiac Devices[1]

Shams Rashid, PhD
Stanislas Rapacchi, PhD
Marmar Vaseghi, MD, MS
Roderick Tung, MD
Kalyanam Shivkumar, MD, PhD
J. Paul Finn, MD
Peng Hu, PhD

Purpose: To propose and test a modified wideband late gadolinium enhancement (LGE) magnetic resonance (MR) imaging technique to overcome hyperintensity image artifacts caused by implanted cardiac devices.

Materials and Methods: Written informed consent was obtained from all partic- ipants, and the HIPAA-
proved by the institution

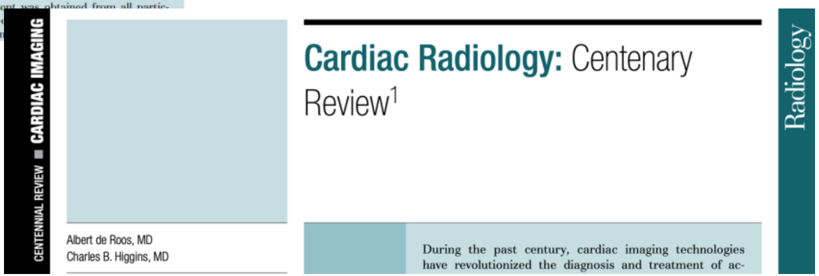


ELSEVIER

Heart Rhythm
Volume 11, Issue 2, February 2014, Pages 289-298

Device artifact reduction for magnetic resonance imaging of patients with implantable cardioverter-defibrillators and ventricular tachycardia: Late gadolinium enhancement correlation with electroanatomic mapping

Steven M. Stevens MD [*], Roderick Tung MD, FHRS [*], Shams Rashid PhD [†], Jean Gima NP [*], Shelly Cote NP [*], Geraldine Pavez NP [*], Sarah Khan MD [†], Daniel B. Ennis PhD [†], J. Paul Finn MD [†], Noel Boyle MD, PhD, FHRS [*], Kalyanam Shivkumar MD, PhD, FHRS [*, †], Peng Hu PhD [*, †]



CENTENNIAL REVIEW ■ CARDIAC IMAGING

Cardiac Radiology: Centenary Review[1]

Albert de Roos, MD
Charles B. Higgins, MD

During the past century, cardiac imaging technologies have revolutionized the diagnosis and treatment of ac-

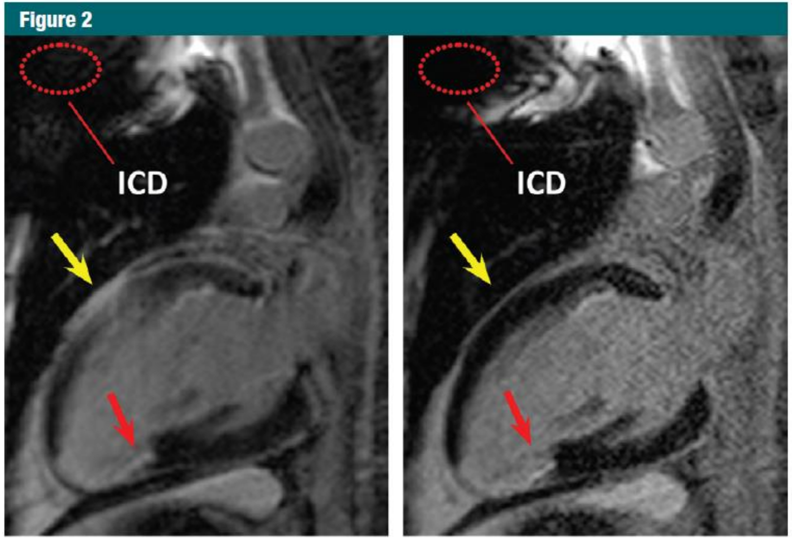
Radiology

- Hyperintensity artifacts can be eliminated by a wide-bandwidth RF inversion pulse, enabling diagnostic scar imaging …

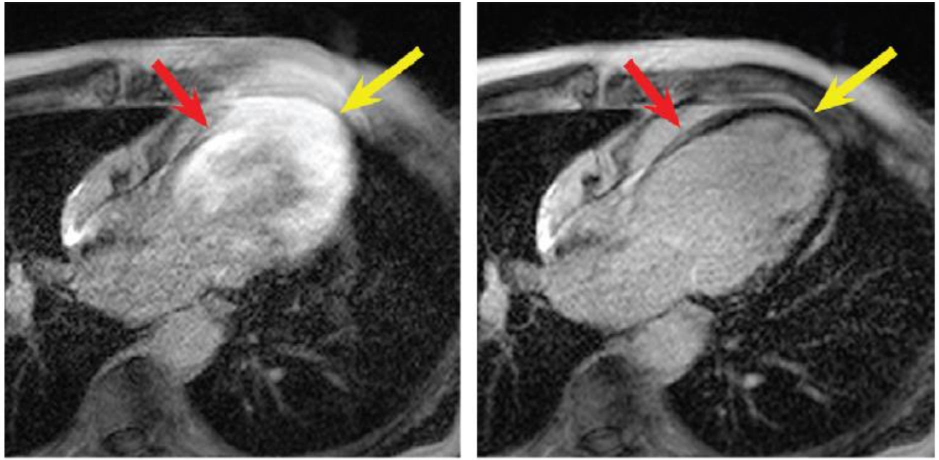
David Geffen
School of Medicine

UCLA Health

Wideband LGE-CMR



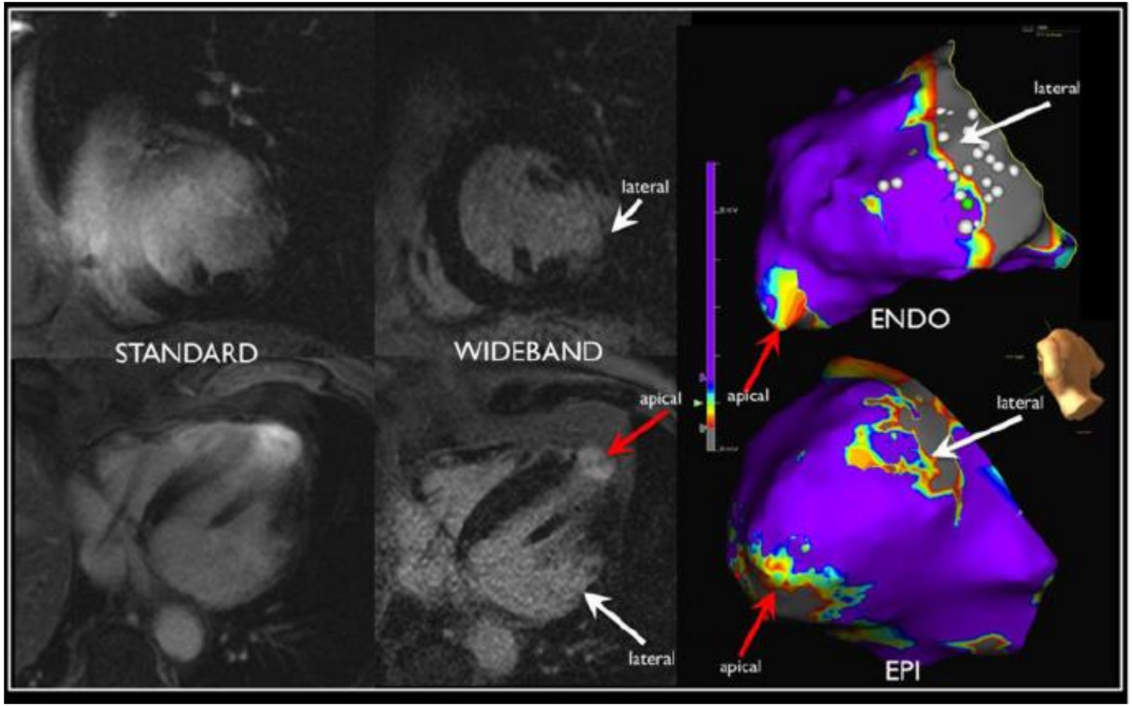
standard wideband



standard wideband

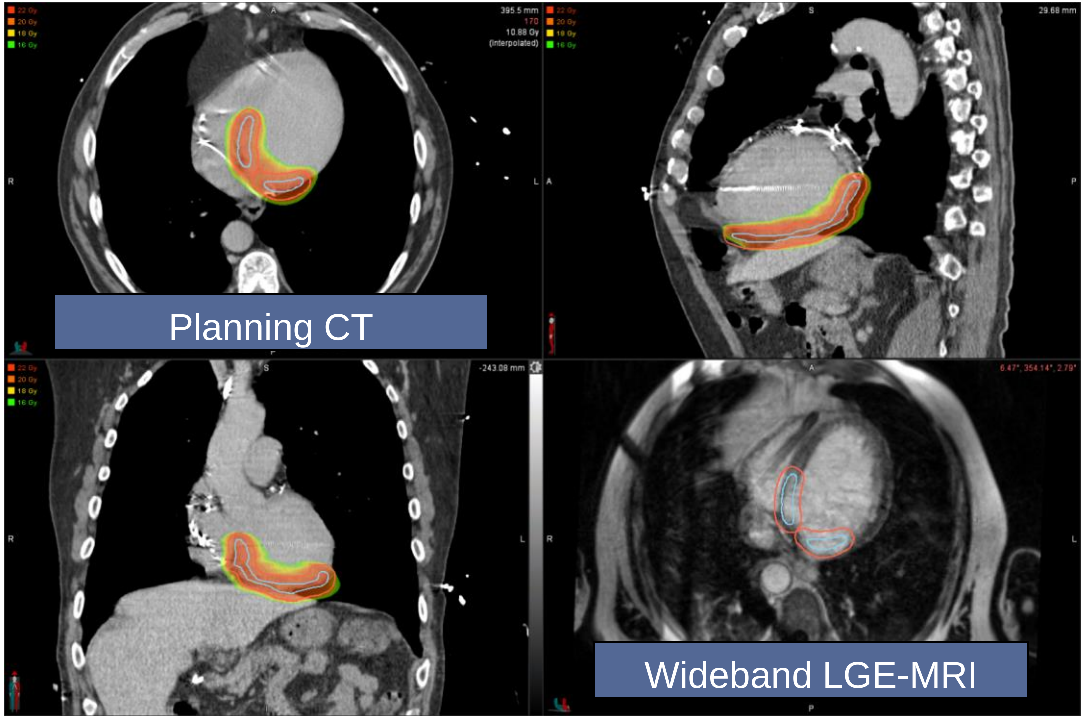
Rashid, Hu *et al*. Radiology v270, 2014

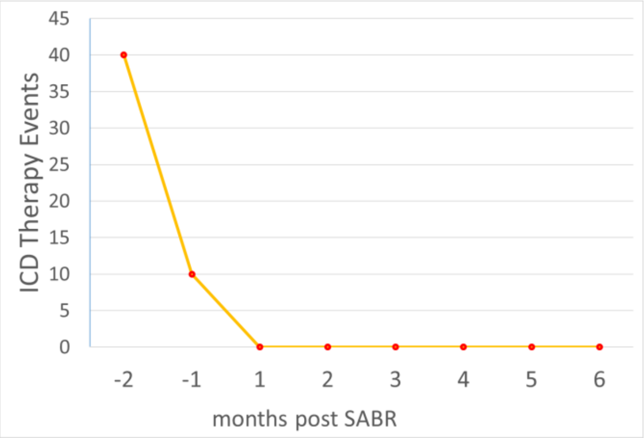
Wideband LGE vs EAM



Stevens, Hu *et al*. Heart Rhythm, v11, 2014

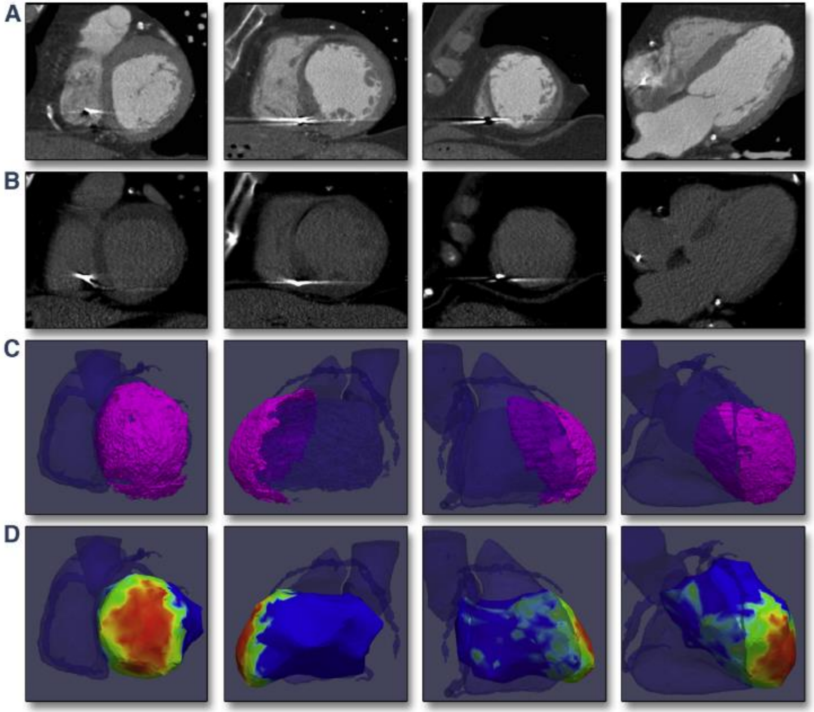
Wideband LGE for SABR target localization





Cardiac CT

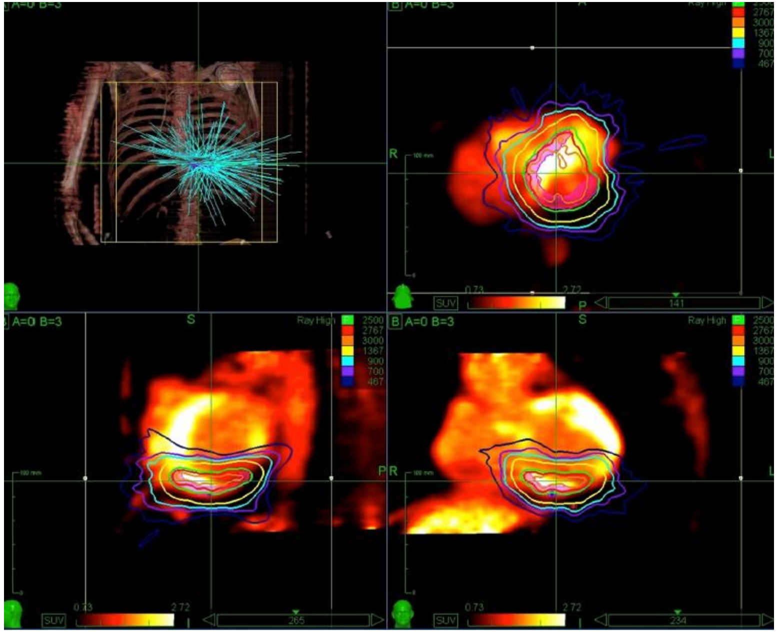
- High spatial resolution (<1mm)
- Lower contrast-to-noise ratio
- Imaging characteristics for scar:
    - Wall thinning, adipose metaplasia, Hypoperfusion
- Delineate detailed cardiac anatomy
    - Coronary arteries, valve apparatus, phrenic nerves…



Esposito et al. JACC Cardiovascular Imaging. v9 2016

Nuclear Imaging (SPECT, PET)

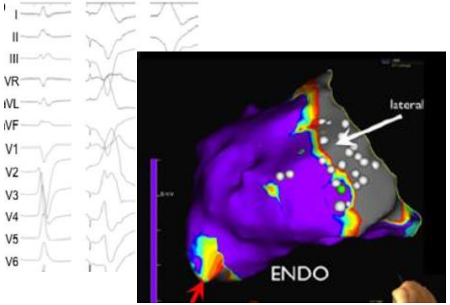
- Provide complementary functional information to EAM defined scar
- Mapping of metabolically active surviving tissue or perfusion defects
- Do not provide sufficient anatomic information
- Intrinsic low spatial resolution



Zei et al. Curr Cardiol Rep 19, 2017

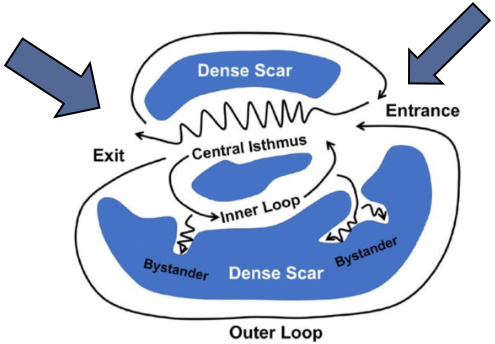
Modality	Mechanism	Advantage	Disadvantage
EAM (EP)	catheter-mounted contact electrode + 3D spatial info	real-time electrophysiological info	invasive; sparse sampling and extrapolation; data not compatible with RT planning
ECGI (EP)	EGM map derived from high density ECG jacket	non-invasive ECG mapping;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

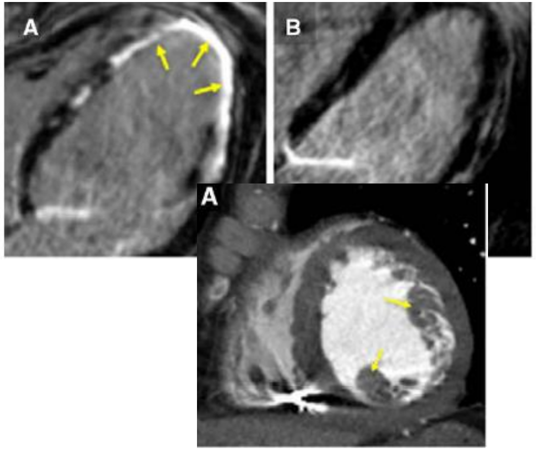
Multi-modality target delineation



Electrophysiological

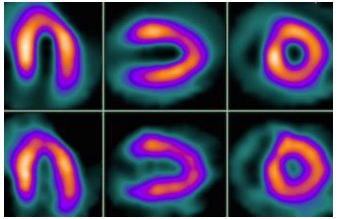
(ECG, EAM, ECGI)





Structural

(Cardiac MRI, CT)



Functional

(SPECT, PET)

Mahida et al. *Circulation.* 2017

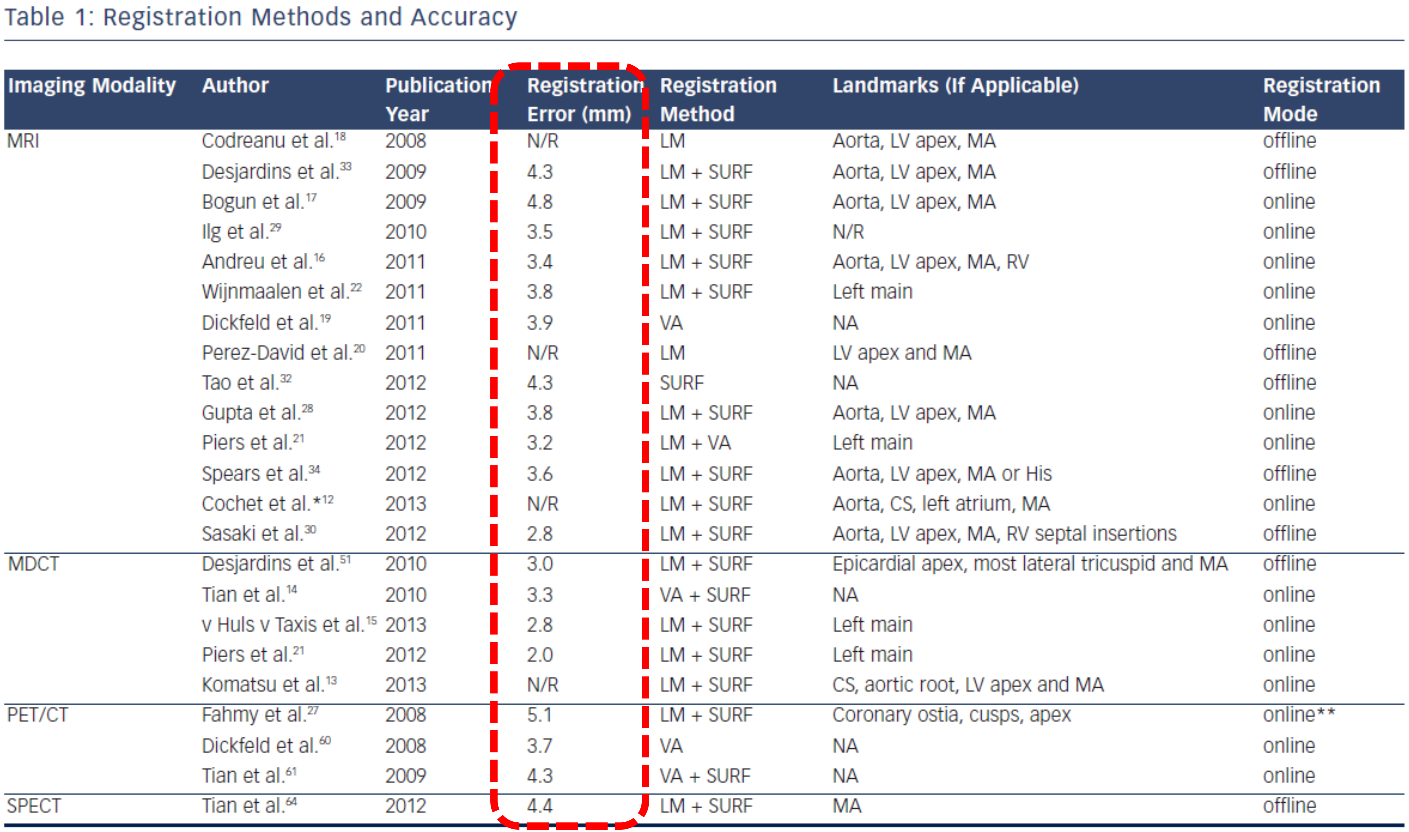


Table 1: Registration Methods and Accuracy

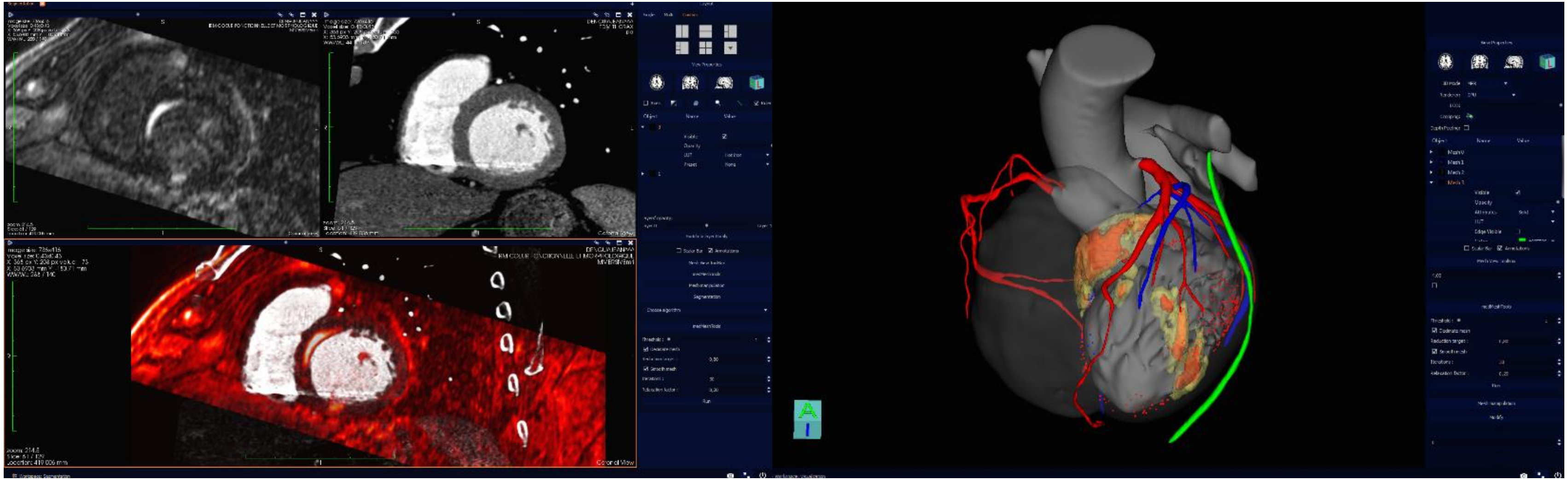
Imaging Modality	Author	Publication Year	Registration Error (mm)	Registration Method	Landmarks (If Applicable)	Registration Mode
MRI	Codreanu et al.[18]	2008	N/R	LM	Aorta, LV apex, MA	offline
	Desjardins et al.[33]	2009	4.3	LM + SURF	Aorta, LV apex, MA	offline
	Bogun et al.[17]	2009	4.8	LM + SURF	Aorta, LV apex, MA	online
	Ilg et al.[29]	2010	3.5	LM + SURF	N/R	online
	Andreu et al.[16]	2011	3.4	LM + SURF	Aorta, LV apex, MA, RV	online
	Wijnmaalen et al.[22]	2011	3.8	LM + SURF	Left main	online
	Dickfeld et al.[19]	2011	3.9	VA	NA	online
	Perez-David et al.[20]	2011	N/R	LM	LV apex and MA	offline
	Tao et al.[32]	2012	4.3	SURF	NA	offline
	Gupta et al.[28]	2012	3.8	LM + SURF	Aorta, LV apex, MA	online
	Piers et al.[21]	2012	3.2	LM + VA	Left main	online
	Spears et al.[34]	2012	3.6	LM + SURF	Aorta, LV apex, MA or His	offline
	Cochet et al.*[12]	2013	N/R	LM + SURF	Aorta, CS, left atrium, MA	online
	Sasaki et al.[30]	2012	2.8	LM + SURF	Aorta, LV apex, MA, RV septal insertions	offline
MDCT	Desjardins et al.[51]	2010	3.0	LM + SURF	Epicardial apex, most lateral tricuspid and MA	offline
	Tian et al.[14]	2010	3.3	VA + SURF	NA	online
	v Huls v Taxis et al.[15]	2013	2.8	LM + SURF	Left main	online
	Piers et al.[21]	2012	2.0	LM + SURF	Left main	online
	Komatsu et al.[13]	2013	N/R	LM + SURF	CS, aortic root, LV apex and MA	online
PET/CT	Fahmy et al.[27]	2008	5.1	LM + SURF	Coronary ostia, cusps, apex	online**
	Dickfeld et al.[60]	2008	3.7	VA	NA	online
	Tian et al.[61]	2009	4.3	VA + SURF	NA	online
SPECT	Tian et al.[64]	2012	4.4	LM + SURF	MA	offline

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

Piers et al. Arrhythmia & Electrophysiology Review 2013

MUSIC integration platform

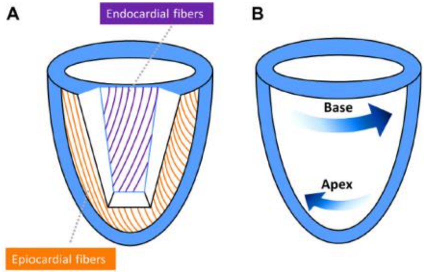
- MUSIC: MUltimodality platform for Specific Imaging in Cardiology

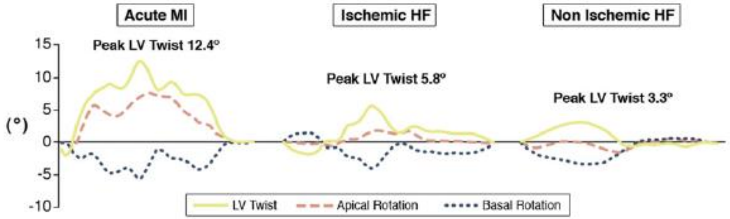


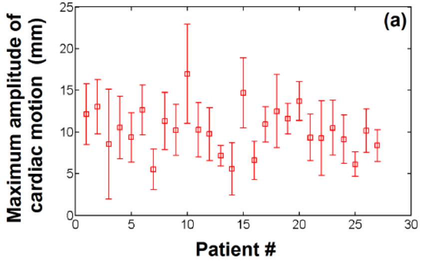
https://team.inria.fr/epione/en/software/music/

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



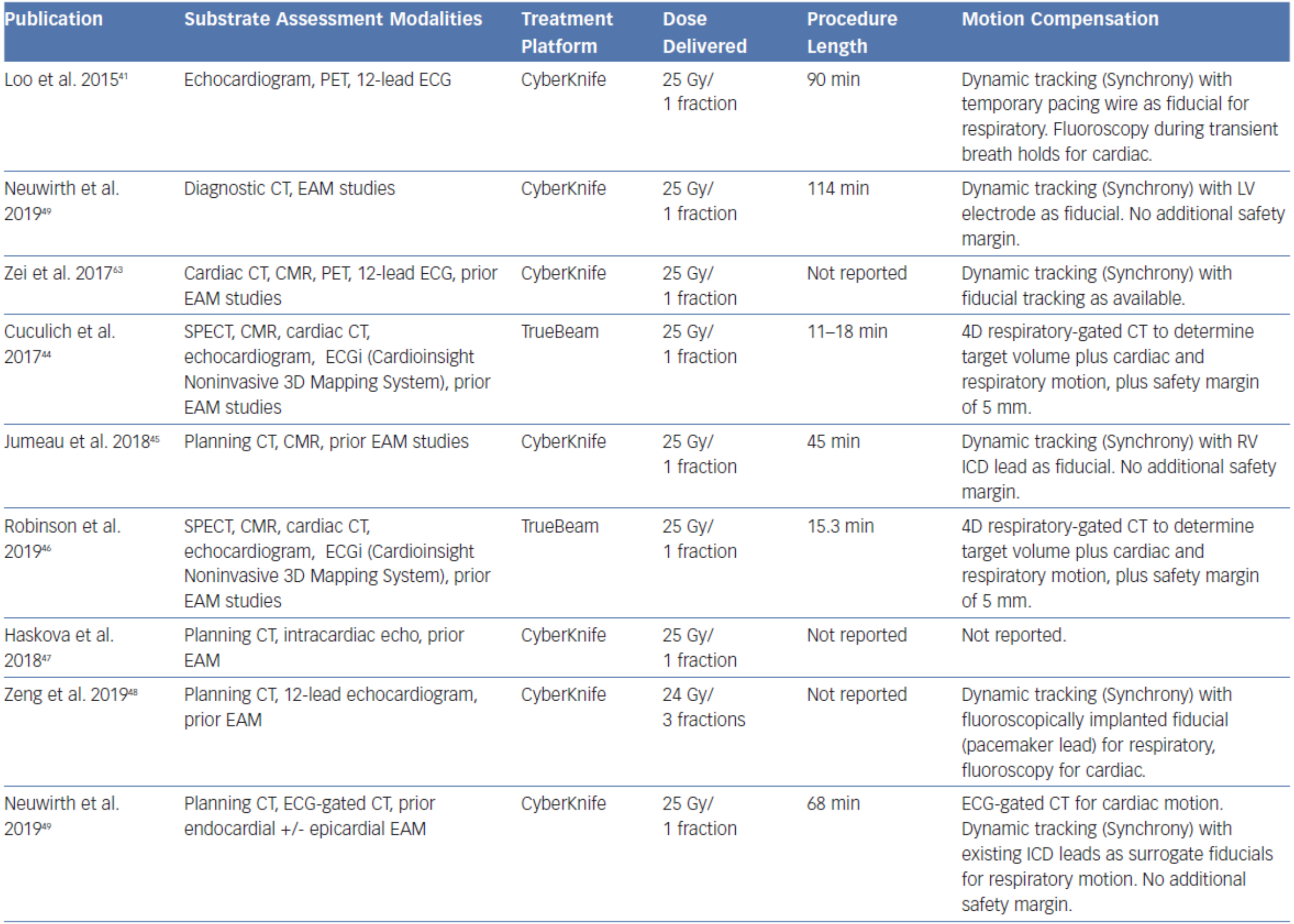




Roujol et al. PLos One, 8(11）2013

Stohr et al. Am J Physiol Heart Circ Physiol, 311(3), 2016

Bertini et al. JACC Cardiovacular Imaging 2(12), 2009



Publication	Substrate Assessment Modalities	Treatment Platform	Dose Delivered	Procedure Length	Motion Compensation
Loo et al. 2015[41]	Echocardiogram, PET, 12-lead ECG	CyberKnife	25 Gy/ 1 fraction	90 min	Dynamic tracking (Synchrony) with temporary pacing wire as fiducial for respiratory. Fluoroscopy during transient breath holds for cardiac.
Neuwirth et al. 2019[49]	Diagnostic CT, EAM studies	CyberKnife	25 Gy/ 1 fraction	114 min	Dynamic tracking (Synchrony) with LV electrode as fiducial. No additional safety margin.
Zei et al. 2017[63]	Cardiac CT, CMR, PET, 12-lead ECG, prior EAM studies	CyberKnife	25 Gy/ 1 fraction	Not reported	Dynamic tracking (Synchrony) with fiducial tracking as available.
Cuculich et al. 2017[44]	SPECT, CMR, cardiac CT, echocardiogram, ECGi (Cardioinsight Noninvasive 3D Mapping System), prior EAM studies	TrueBeam	25 Gy/ 1 fraction	11–18 min	4D respiratory-gated CT to determine target volume plus cardiac and respiratory motion, plus safety margin of 5 mm.
Jumeau et al. 2018[45]	Planning CT, CMR, prior EAM studies	CyberKnife	25 Gy/ 1 fraction	45 min	Dynamic tracking (Synchrony) with RV ICD lead as fiducial. No additional safety margin.
Robinson et al. 2019[46]	SPECT, CMR, cardiac CT, echocardiogram, ECGi (Cardioinsight Noninvasive 3D Mapping System), prior EAM studies	TrueBeam	25 Gy/ 1 fraction	15.3 min	4D respiratory-gated CT to determine target volume plus cardiac and respiratory motion, plus safety margin of 5 mm.
Haskova et al. 2018[47]	Planning CT, intracardiac echo, prior EAM	CyberKnife	25 Gy/ 1 fraction	Not reported	Not reported.
Zeng et al. 2019[48]	Planning CT, 12-lead echocardiogram, prior EAM	CyberKnife	24 Gy/ 3 fractions	Not reported	Dynamic tracking (Synchrony) with fluoroscopically implanted fiducial (pacemaker lead) for respiratory, fluoroscopy for cardiac.
Neuwirth et al. 2019[49]	Planning CT, ECG-gated CT, prior endocardial +/- epicardial EAM	CyberKnife	25 Gy/ 1 fraction	68 min	ECG-gated CT for cardiac motion. Dynamic tracking (Synchrony) with existing ICD leads as surrogate fiducials for respiratory motion. No additional safety margin.

Wei C et al. Arrhythmia & Electrophysiology Review 2019;8(4)

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

Radiation Oncology:

- Robert Chin, MD. PhD
- Yingli Yang, PhD

Radiology:

- Peng Hu, PhD

Cardiac Electrophysiology:

- Jason Bradfield, MD
- Justin Hayase, MD