



Department of
Radiation Oncology



PROTON THERAPY FOR VENTRICULAR TACHYCARDIA

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Lead Proton Dosimetrist

Bret Kazemba, CMD
Proton Dosimetrist

AAMD 51st Annual Meeting
Orlando, FL



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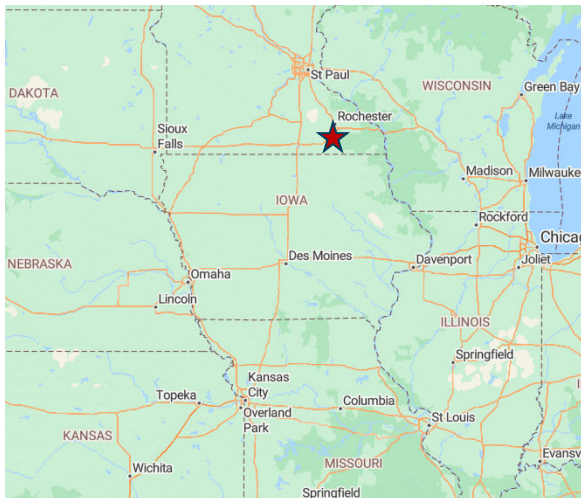
DISCLOSURES

- “We have no disclosures”

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MAYO CLINIC ROCHESTER



- **50+ Radiation Oncologists**

- **48 Dosimetrists**

- 1 Dosimetry Supervisor
- 18 Proton Dosimetrists
- 21 Photon Dosimetrists
- 9 Regional Photon Dosimetrists

- **Protons**

- 4- Proton gantries (180 degrees)
- 2- 360-degree Proton gantries (*coming soon 2027*)

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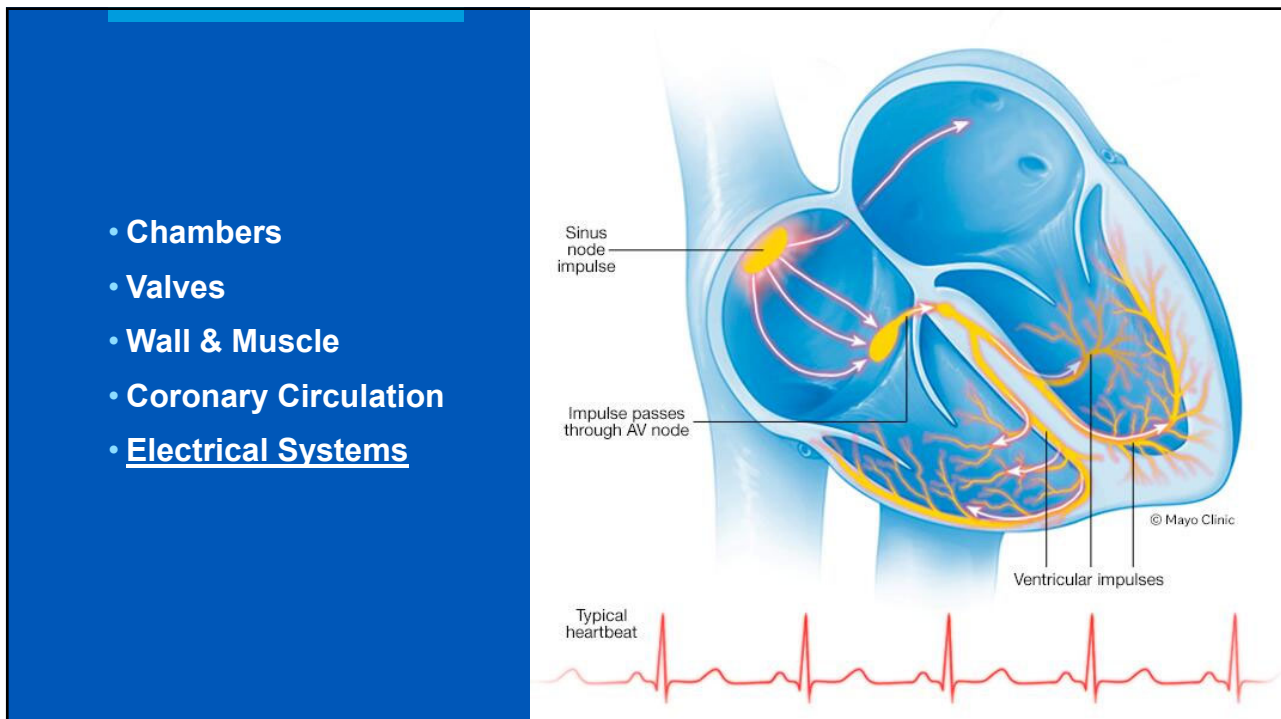


“LEARNING OBJECTIVES”

- Understand ventricular tachycardia (VT)
 - Clinical Presentation & Management Strategies
- Describe the step-by-step workflow developed at Mayo Clinic for proton-based cardiac radioablation.
- Evaluate early clinical outcomes for proton based cardiac radioablation.

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“WHAT HAPPENS WHEN THE HEART’S ELECTRICAL SYSTEM GOES “OUT OF SYNC”?”

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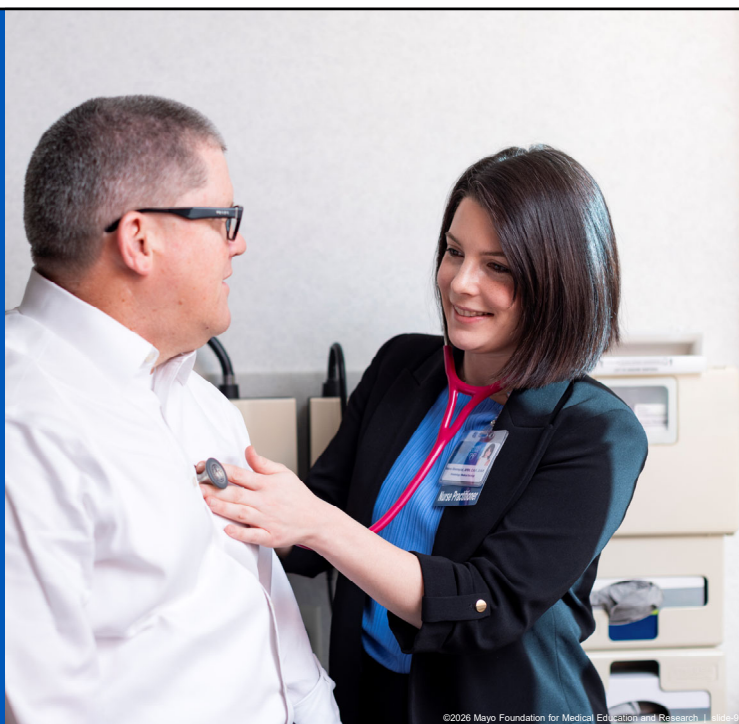
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- Sinus Bradycardia
- Sick Sinus Syndrome
- First-Degree AV Block
- Second-Degree AV Block (Mobitz I & II)
- Third-Degree AV Block (Complete Heart Block)
- Atrial Tachycardia
- Atrial Flutter
- Atrial Fibrillation
- Supraventricular Tachycardia (SVT)
- **Ventricular Tachycardia (VT)**
- Ventricular Fibrillation (VF)
- Premature Atrial Contractions (PACs)
- Premature Ventricular Contractions (PVCs)
- Bundle Branch Block (Right or Left)
- Fascicular Block
- Torsades de Pointes
- Long QT Syndrome
- Brugada Syndrome
- Wolff-Parkinson-White (WPW) Syndrome
-and more

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WHAT IS VENTRICULAR TACHYCARDIA



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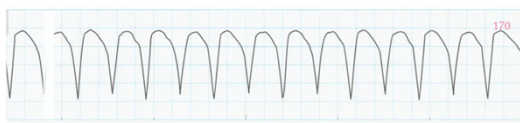
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VENTRICULAR TACHYCARDIA

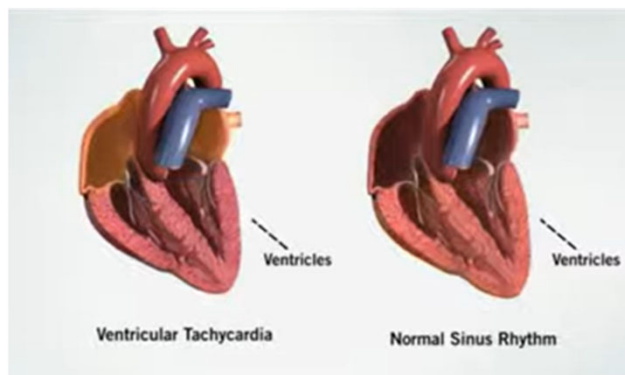
- A rapid heart rhythm that starts in the lower chambers (ventricles), causing the heart to beat too fast and sometimes leading to serious symptoms such as palpitations, dizziness, fainting or cardiac arrest and sudden death.



Typical heart rhythm



VT



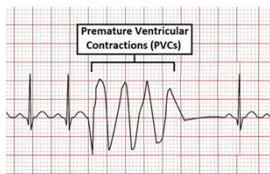
Ventricular Tachycardia

Normal Sinus Rhythm

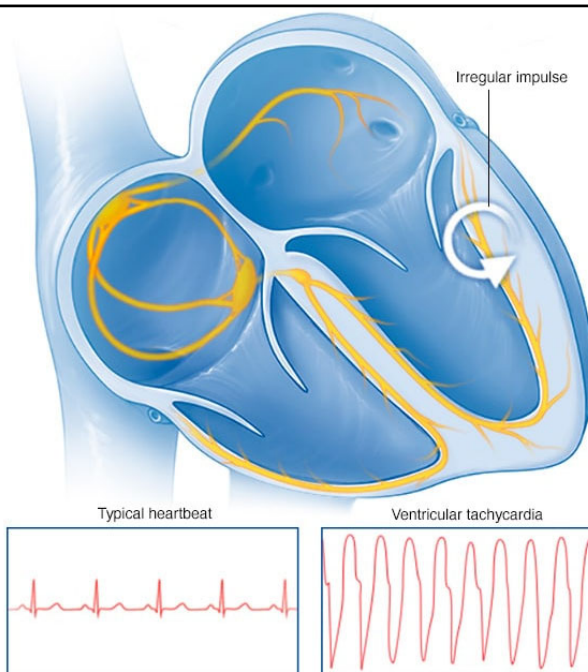
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- Non-sustained: 3 or more beats of ventricular origin with rates over 100 bpm lasting less than 30 seconds



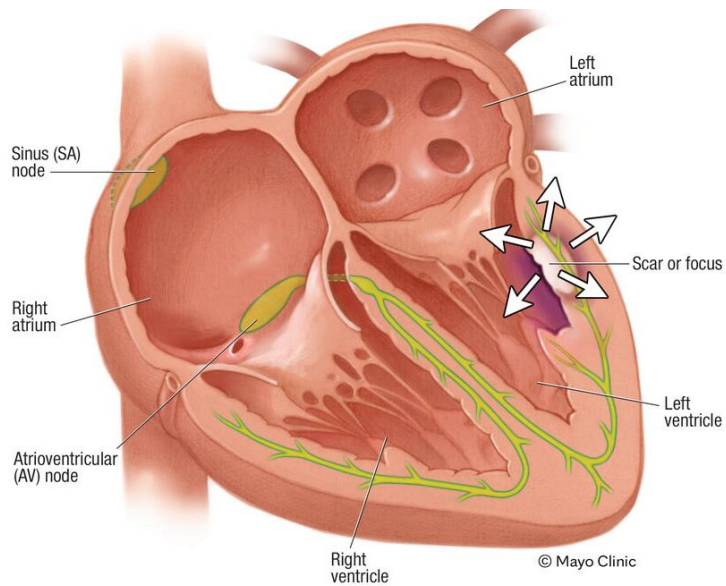
- Sustained: Rhythm lasting longer than 30 seconds or hemodynamic instability occurs
- Impulses become irregular and can create a re-entry impulse
- But Why and what causes this?



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- Structural Heart Disease
 - Myocardial Infarction
 - Coronary Artery Disease
 - Cardiomyopathy
 - Myocarditis
 - Heart Valve Disease
 - Electrical System Disorders
- Reversible Factors
 - Medications
 - Electrolyte imbalances
- Post Surgical
- Genetics
- Unknown Causes



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EPIDEMIOLOGY

- Prevalence Rate 0.2-0.4%
 - Heart disease increases risk by 25-50%
- Sudden cardiac deaths ~300,000 (VT/VF)
- Higher prevalence in men and >60 years of age

References

Mayo Clinic. Ventricular Tachycardia – Overview. <https://www.mayoclinic.org/diseases-conditions/ventricular-tachycardia>

Al-Khatib SM, et al. 2022 AHA/ACC/HRS Guideline for the Management of Ventricular Arrhythmias. *Circulation*. 2022;146:e1–e140

Zipes DP, et al. Sudden Cardiac Death and Ventricular Tachycardia Epidemiology. *Journal of the American College of Cardiology (JACC)*. 2023.

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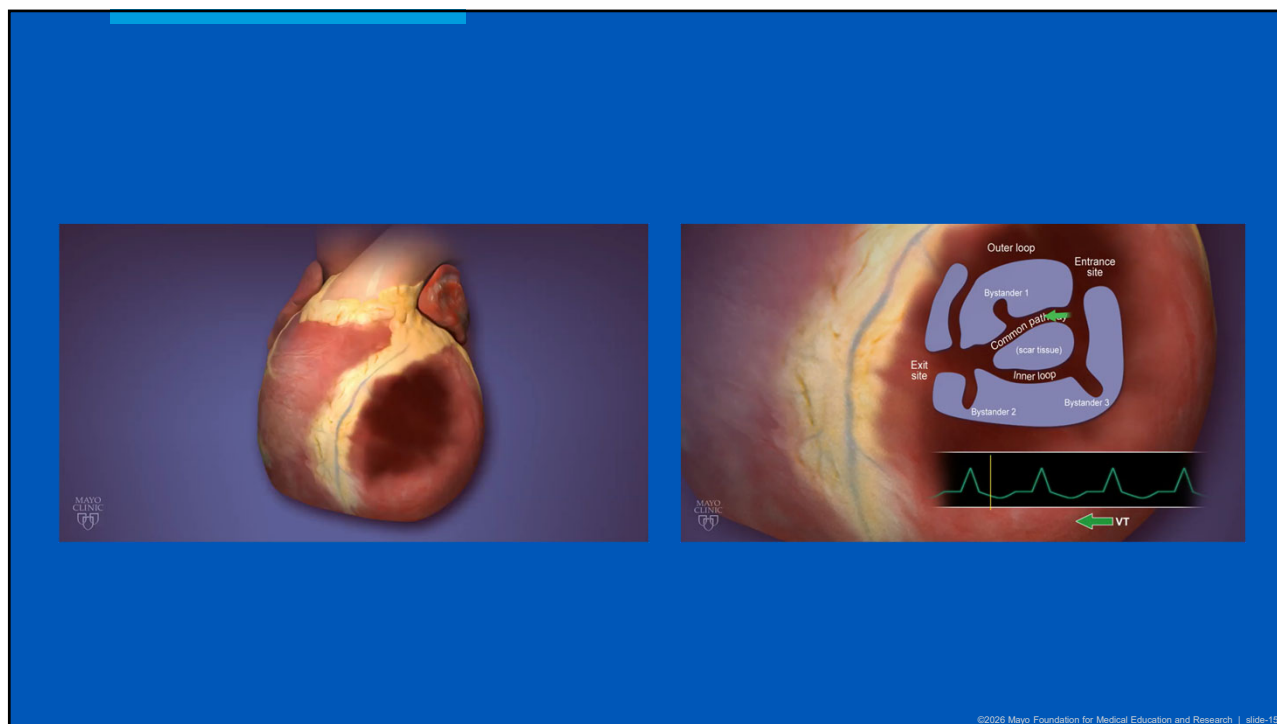
DIAGNOSIS

- 12-lead ECG
- Rhythm strip
- Holter monitor
- Event monitor
- Implantable loop recorder (ILR)
- Echocardiogram
- Chest X-ray/CT/MRI/PET –
 - Assesses heart size and lung status.
 - Detects coronary artery disease.
 - Identifies scar tissue or fibrosis.
 - Detects metabolic or inflammatory changes.
- Electrophysiology (EP) program study



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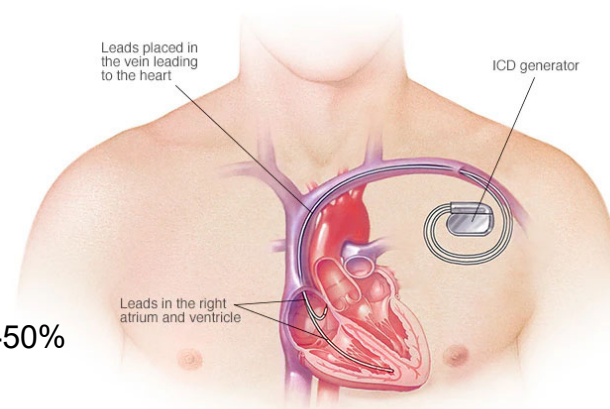


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HISTORICAL TREATMENTS

- ICD
 - 10k/month implanted in US*
- Antiarrhythmic Medications
- Catheter Ablation
 - 70-90% success rate.
 - 0.5% mortality rate
 - Future recurrence or new VT in 25-50%
- Heart Transplant



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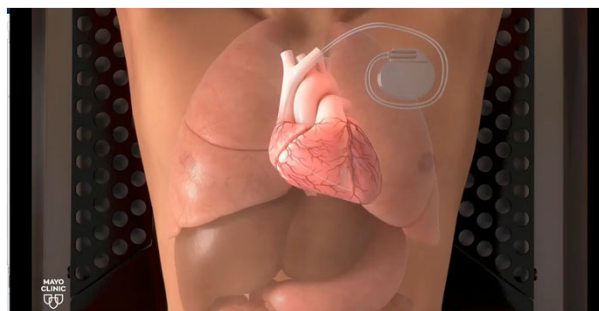
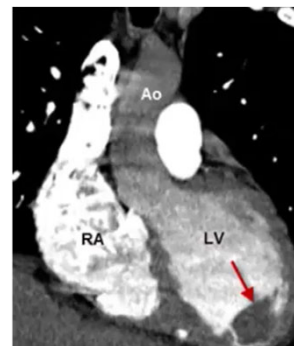
*WRITING GROUP MEMBERS et al. "Heart disease and stroke statistics--2010 update: a report from the American Heart Association." *Circulation* vol. 121.7 (2010): e46-e215. doi:10.1161/CIRCULATIONAHA.109.192667

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NEW & EMERGING TREATMENT

- Pulsed Field Ablation (PFA)
- Biological and Molecular Therapies
- Cardiac Radioablation (CRA)
 - Larger substrates in difficult locations
 - Shorter procedures
 - Mechanical Valves
 - Post catheter ablation failure rates



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THE NEW ENGLAND JOURNAL OF MEDICINE
ORIGINAL ARTICLE

Noninvasive Cardiac Radiation for Ablation of Ventricular Tachycardia

Phillip S. Cuculich, M.D., Matthew R. Schill, M.D., Rojaino Kashani, Ph.D., Sasa Mucic, Ph.D., Adam Lang, M.D., Daniel Cooper, M.D., Mitchell Faddis, M.D., Ph.D., Marye Glover, M.D., Jami Noheria, M.B., B.S., Timothy W. Smith, M.D., D.Phil., Dennis Hallahan, M.D., Yoram Rudy, Ph.D., and Clifford G. Robinson, M.D.

Longer Term Results from a Phase I/II Study of EP-guided Noninvasive Cardiac Radioablation for Treatment of Ventricular Tachycardia (ENCORE-VT)

C.G. Robinson,¹ P. Samson,² K.M.S. Moore,² G.D. Hugo,¹ N. Knutson,¹ S. Mucic,³ S.M. Goddu,¹ D.H. Cooper,² M. Faddis,² A. Noheria,² T.W. Smith,² P.K. Woodard,² R.J. Gropler,² D.E. Hallahan,² Y. Rudy,⁴ and P. Cuculich²; ¹Washington University School of Medicine, Department of Radiation Oncology, St. Louis, MO, ²Washington University School of Medicine, Department of Internal Medicine, Division of Cardiology, St. Louis, MO, ³Washington University School of Medicine, Department of Radiology, St. Louis, MO, ⁴Washington University in St. Louis, Department of Radiation Oncology, St. Louis, MO, ⁵Washington University School of Medicine, Department of Biomedical Engineering, St. Louis, MO

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Radiosurgery for ventricular tachycardia: preclinical and clinical evidence and study design for a German multi-center multi-platform feasibility trial (RAVENTA)

Oliver Blanck¹, Daniel Buegry², Maren Venz^{3,4}, Lina Eidinger^{1,5}, Adrian Zaman⁶, David Krug¹, Boris Rudic⁴, Judit Boda-Heggemann⁷, Frank A. Giordano⁸, Leif-Hendrik Boldt⁹, Felix Mehrhof¹⁰, Volker Budde¹¹, Achim Schweikard¹², Denise Olbrich¹³, Inke R. König¹⁴, Frank-Andre Siebert¹⁵, Reinhard Vonthein¹⁶, Jürgen Dunst¹, Hendrik Bonnemeyer¹⁷

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Stereotactic radiosurgery for ablation of ventricular tachycardia

Radek Neuwirth¹, Jakub Cvek^{2*}, Lukas Knybel², Otakar Jiravsky³, Lukas Molenda², Michal Kodaj², Martin Fiala¹, Petr Peichl⁴, David Feltl⁵, Jaroslav Januska¹, Jan Hecko², and Josef Kautzner⁴

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Long Term Follow-Up of Stereotactic Body Radiation Therapy for Refractory Ventricular Tachycardia in Advanced Heart Failure Patients

John Wight^{1*}, Thomas Bigham², Arielle Schwartz³, Arslan T. Zahid⁴, Neal Bhatia⁵, Soroosh Kiani⁶, Anand Shah⁷, Stacy Westerman⁸, Kistin Higgins⁹ and Michael S. Lloyd¹⁰

¹School of Medicine, Emory University, Atlanta, GA, United States; ²Chicago Medicine, Chicago, IL, United States; ³Section of Cardiac Electrophysiology, Emory University, Atlanta, GA, United States; ⁴Department of Radiation Oncology, Emory University, Atlanta, GA, United States

Radiosurgery for ventricular tachycardia (RAVENTA): interim analysis of a multicenter multiplatform feasibility trial

David Krug¹, Adrian Zaman², Lina Eidinger^{1,2}, Melanie Grehn¹, Judit Boda-Heggemann³, Boris Rudic⁴, Felix Mehrhof⁵, Leif-Hendrik Boldt⁶, Stephan Hohmann⁷, Roland Merten⁸, Daniel Buegry⁹, Jens Fleckenstein¹⁰, Anne Kluge¹¹, Annette Rogge¹², Marcus Both¹³, Dirk Rades¹⁴, Roland Richard Tilz¹⁵, Denise Olbrich¹⁶, Inke R. König¹⁷, Frank-Andre Siebert¹⁸, Achim Schweikard¹⁹, Reinhard Vonthein²⁰, Hendrik Bonnemeyer²¹, Jürgen Dunst¹, Oliver Blanck¹

Received: 27 December 2018; revised version 13 April 2019; accepted 16 April 2019; online publication date 23 May 2019

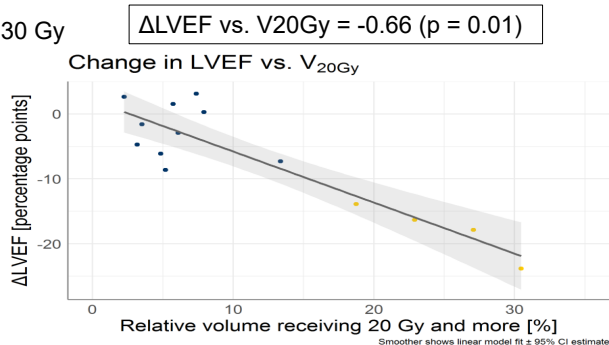
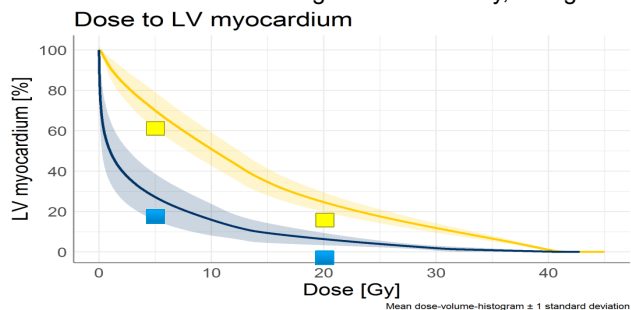
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LEFT VENTRICLE NON-TARGET MYOCARDIUM

Two groups with different LV myocardium doses

- High dose: 3 targets to 40 Gy
- Low dose: 1 target to 30 or 40 Gy, 2 targets to 30 Gy



No relevant LVEF impairment seen with V20Gy up to 5% of LV myocardium,
 Approximately 4 % LVEF decline for every additional 5% increase of V20Gy

Left Ventricle Non-target Myocardium Goal: V20Gy \leq 5%

Slide Courtesy of Amanda Deisher PhD

Hohmann Heart Rhythm 2019

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PHOTON

PROTON

"Practice" plan

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PROTON BEAM THERAPY FOR REFRACTORY VT

FIRST-IN-HUMAN (IDE #G200015) (NCT04392193)

- Phase 1 feasibility and safety study (FDA IDE)
- Inclusion criteria
 - Age \leq 80 yrs; scar-mediated VT; EF $<$ 50%; prior catheter ablation and subsequent ICD shocks or ATPs (\geq 2 episodes)
 - Failure on AAD in last 9 months
- 8 patients enrolled (March 2021 to March 2023)
 - 7 males, mean age 67.5 years
 - 7 treated - 1 withdrew before treatment

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METHODS

PRESCRIBED DOSE

- 30 Gy** prescription dose to target myocardium (single fraction)
- Dose constraints to non-target myocardium
 - \leq 10% volume receiving 30Gy
 - \leq 15% volume receiving 20Gy
 - \leq 20% volume receiving 10Gy
- Dose constraints to non-myocardial OARs according to SBRT lung cancer trials
- Required **30 Gy** to **$>$ 90% of the target volume**

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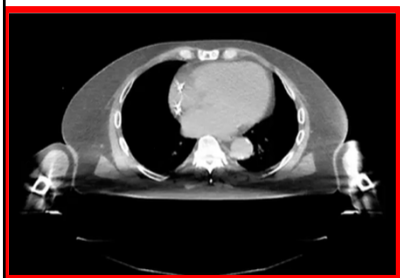
PROTON CARDIAC RADIOABLATION AT MAYO CLINIC



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RADIATION TREATMENT PLANNING WORKFLOW



CT Simulation

- Free Breathing 4DCT
- Non contrast cardiac 4DCT
- Contrast cardiac 4DCT

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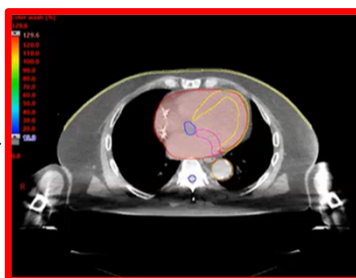
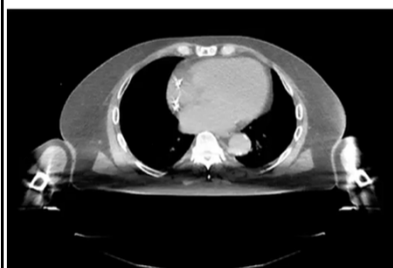
SIMULATION

- NPO
- Arm(s) up preferred: Wing board, upper Vac-Lok
 - Can be simulated one arm up/one arm down, or both arms down if target location allows, or as needed for patient comfort.
 - Arm(s) down, will result in extra CT artifact and reduced separation between the target and ICD.
- 1mm Respiratory 4DCT
- 1mm non-contrast cardiac 4DCT at end expiration – used for 4D dose calculation studies
- 1mm contrast cardiac 4DCT at end of expiration

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RADIATION TREATMENT PLANNING WORKFLOW



CT Simulation

- Free Breathing 4DCT
- Non contrast cardiac 4DCT
- Contrast cardiac 4DCT

Target delineation and normal tissue contouring

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TARGET DELINEATION/CONTOURING

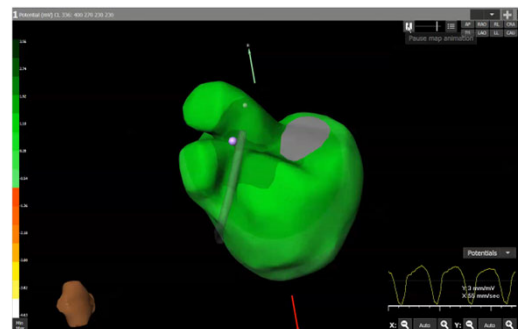
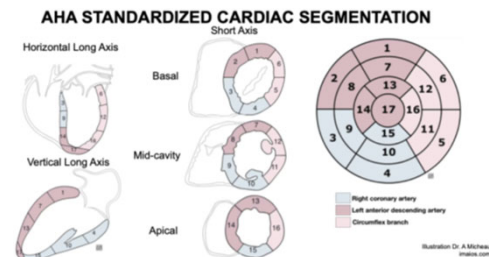
- 70% cardiac contrast phase is prepped for cardiology.
 - Target and cardiac OARs are propagated to other phases of cardiac scan for a combined ITV
- Planning scan = a subset of the respiratory phase gated Avg. scan is prepped with a goal of 2-3mm of motion (a 40% or so, duty cycle)
 - Cardiac contours rigidly transferred to the planning scan.
- A balance of conservative targeting, prioritizing safety due to the unknown myocardial dose tolerance Vs. need for complete coverage.
- EP defined targets that didn't require the whole segment.
- Trade-off: lower collateral dose, potential residual VT.

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MAPPING THE VT SITE

- **12-lead ECG during clinical VT**
- **Non-Invasive Programmed Stimulation (NIPS)**
 - VT induced; 12-lead ECG acquired, followed by pacing to sinus rhythm
- **Additional sources**
 - Prior ablation maps, including scar regions and late potential data
 - Anatomical imaging (MRI, CTA) for scar localization and target refinement
 - Non-invasive cardiac mapping systems (many in use or under development)



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CARDIAC MOTION: HIGH FREQUENCY, LOW AMPLITUDE

Motion type

Respiratory

- High magnitude
- Low frequency

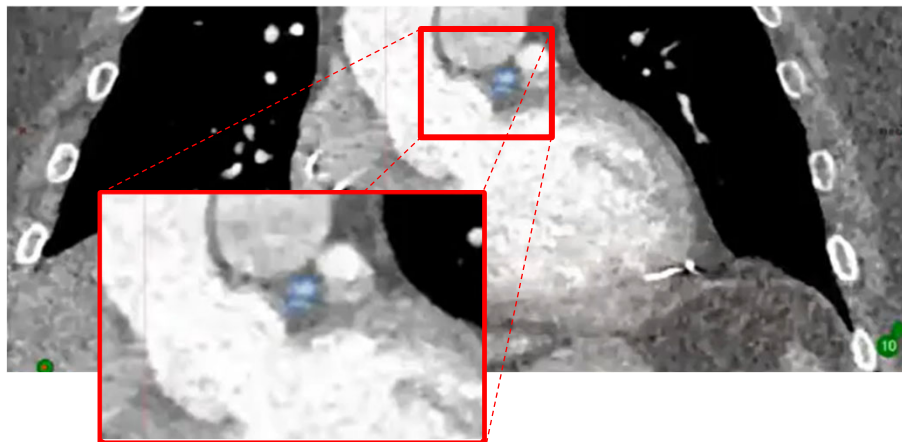


Cardiac

- Low magnitude
- High frequency



Image from Figure 1. Motion management techniques for cardiac and respiratory motion. Adapted from Lydiard S, Blanck O, Hugo G, et al. *Int J Radiat Oncol Biol Phys.* 2021;109(3):783-800.



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CARDIAC MOTION: HIGH FREQUENCY, LOW AMPLITUDE

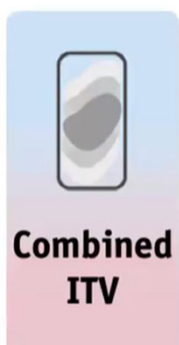
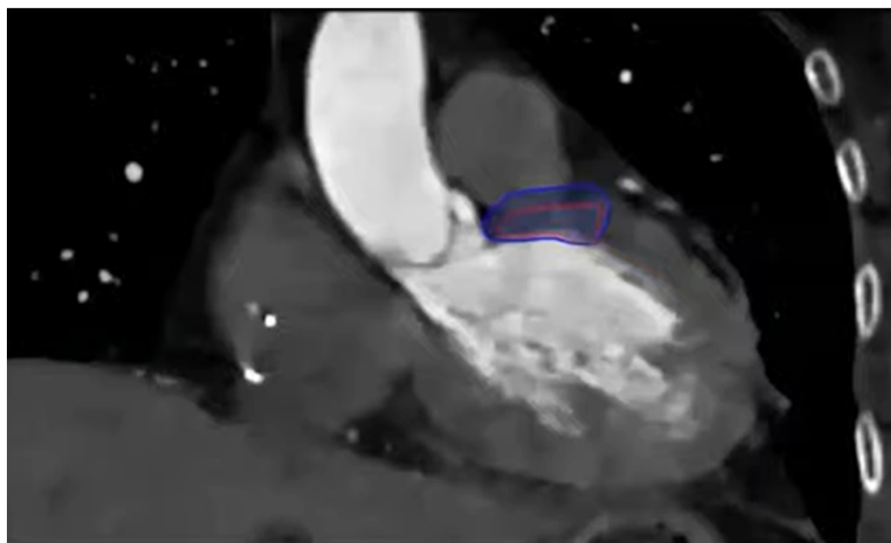


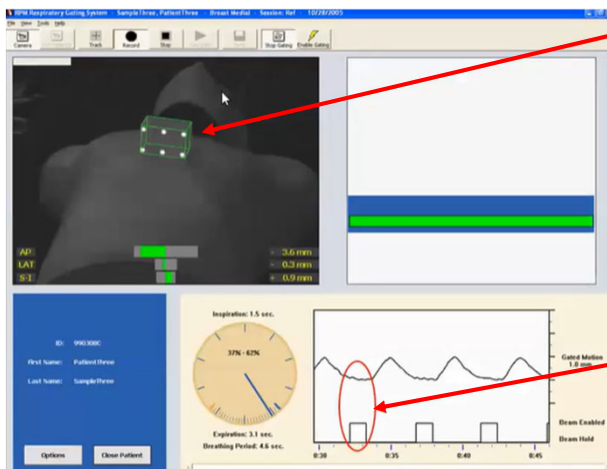
Image from Figure 1. Motion management techniques for cardiac and respiratory motion. Adapted from Lydiard S, Blanck O, Hugo G, et al. *Int J Radiat Oncol Biol Phys.* 2021;109(3):783-800.



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RESPIRATORY MOTION: LOW FREQUENCY, HIGH AMPLITUDE

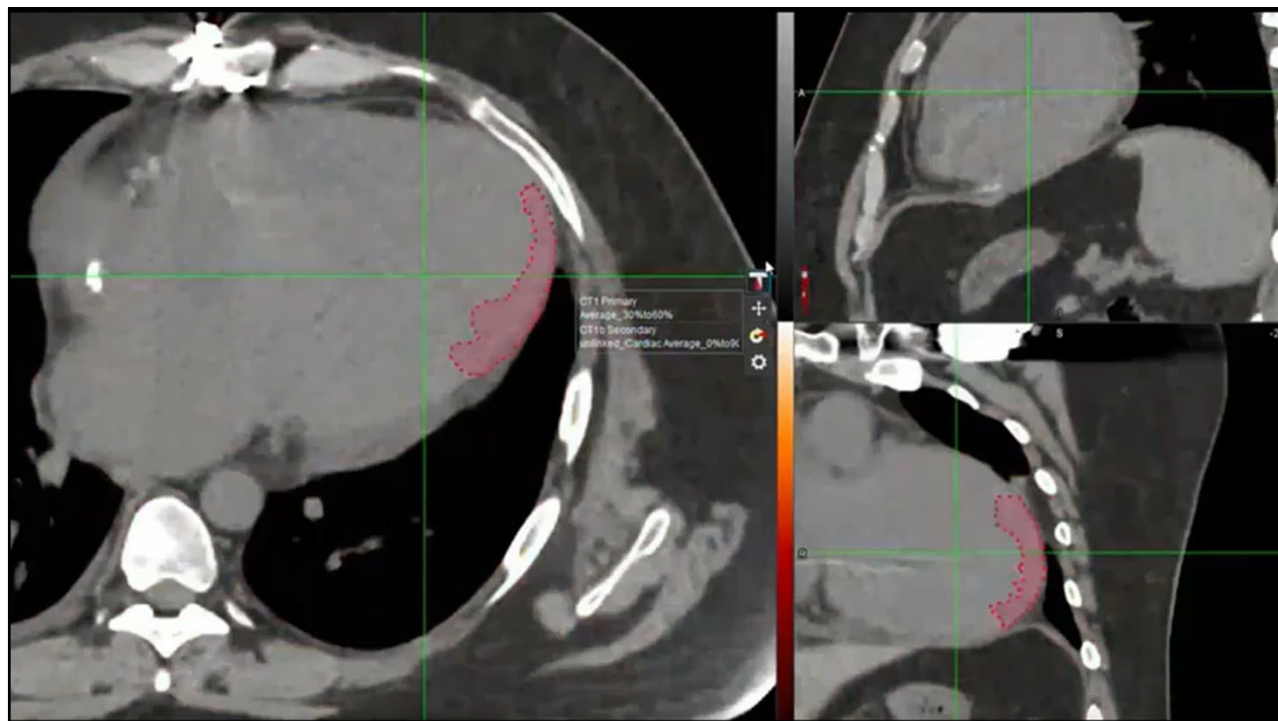


An infrared sensor resting on the surface of the upper abdomen track with each breath

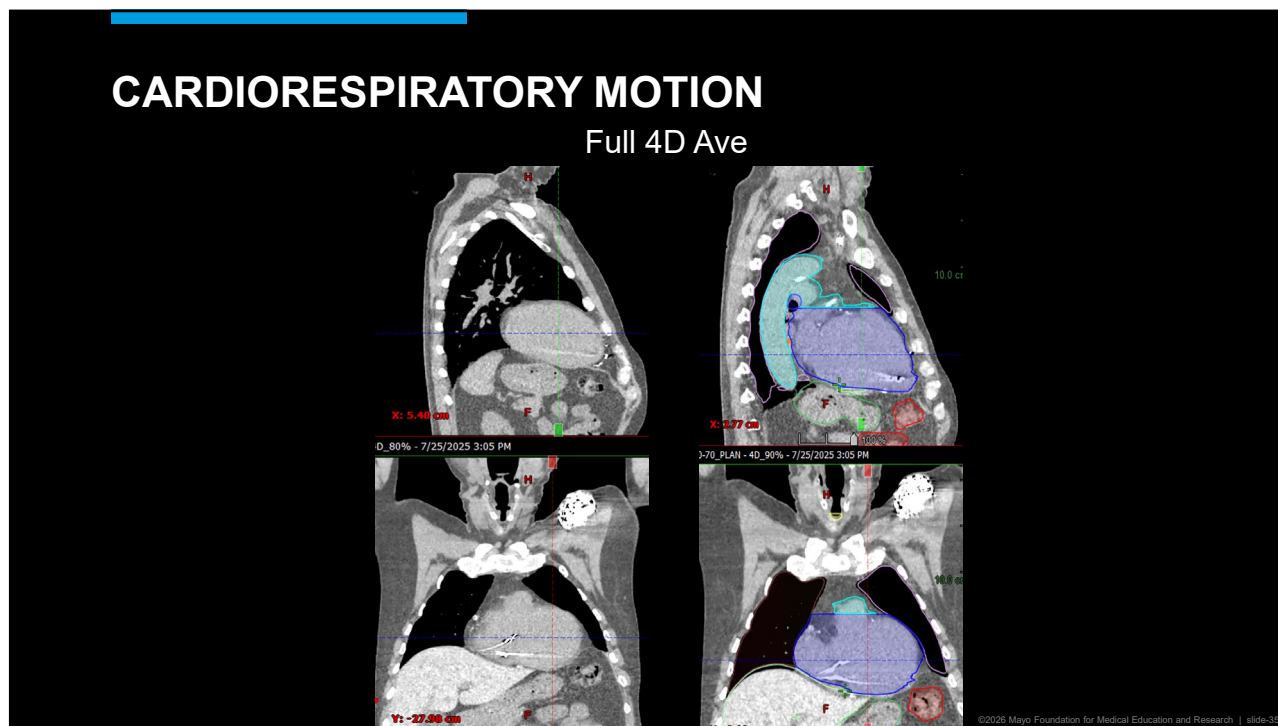
Respiratory gating:
The radiation beam is on during the prespecified phase of the respiratory cycle

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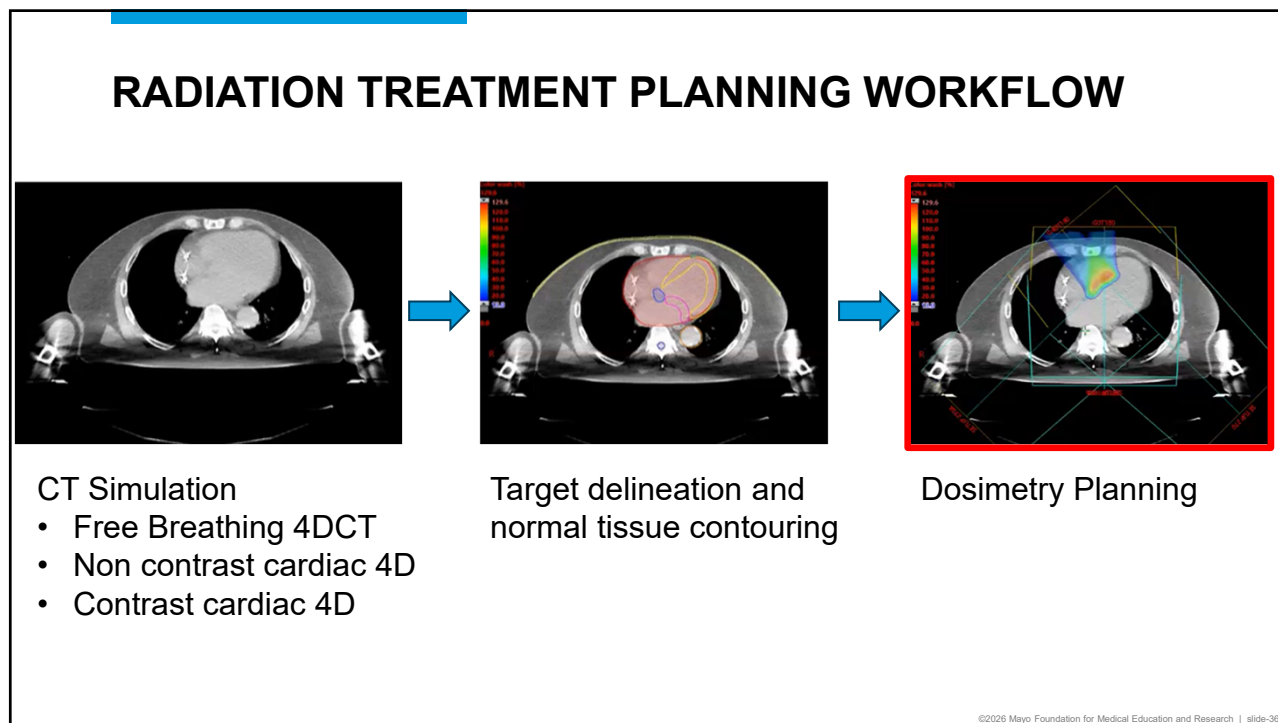
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CONTOURING

- Normal tissue (Lungs, Esophagus, Ribs, Stomach, Liver, Bowel, Cord)
 - PRV on top of our cardiac + respiratory OAR summation
 - ICD Leads
 - ICD
 - HU overrides-Discuss with physics. Best option may be to plan on the native CT and cast plan on an extreme overridden image.
 - ITV=CTV
- Optimization Structures
 - Optimization Target Volume (OTV) = ITV+ 4mm A/P/L/R
 - Remove part extending inside OAR with 4mm additional margin (repeat for all OAR)
 - + ITV (to add the ITV back)

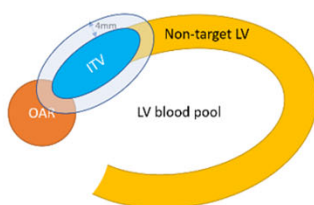
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OPTIMIZATION CONTOURING

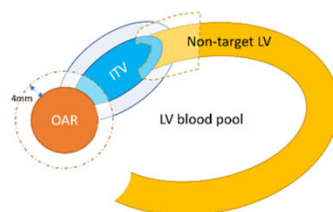
1. Margin Tool

RV blood pool



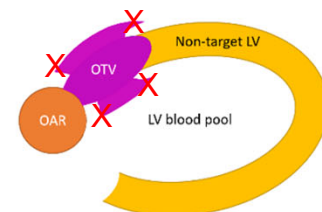
2. Crop Tool

RV blood pool



3. Boolean Tool

RV blood pool



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PLANNING

- 2-3 fields to avoid normal heart and unstable entry WET . Limit ranging out in ICD Leads, OARs, myocardium if possible.
 - Ideally beams would range out into blood pool.
- Single Field Optimization preferred with equal weighting with our smallest spot which is our VAC machine 0.4cm spot size.
- Spot Spacing* 0.4 sigma (can be smaller for smaller targets)
- Target Margin 0.5-0.7cm proximal, distal, and lateral directions from ITV.

*Due to spot spacing, max MU settings and size of residual motion additional repainting is not needed

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PLANNING TIPS

- Spare tissue around LV Leads (15Gy near leads + 5mm & 10Gy to leads.)
- Spare OAR (Large Bowel, Stomach)
- Full coverage of ITV under robustness* (ok to run plan 10% warm while limiting 130% hot spots. No 40 Gy)
 - Min coverage to ITV 25Gy
 - Non robust coverage of OTV
- Valves typically are not a major concern/dose limiting structure but limit hotspots in these areas if possible.
- Typically, 20Gy max to Coronary structures and 25Gy to Coronary 3mm PRVs
- Minimize dose to non-target myocardium
 - V10Gy < 20%, but Ideally <10%
 - V20Gy < 10%, but ideally <5%

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Target Constraints				
Target	Volume Constraint	Volume Max (Gy)	Max Point Dose (Gy)	Min Point Dose (Gy)
ITV	>90% ≥95%* >%85*	30Gy 30Gy 33Gy	39 Gy	25Gy

Organ-at-Risk Dose Constraints				
Organ	Volume Constraint	Volume Max (Gy)	Max Point Dose (Gy)	≥ Grade 3 Endpoint
Spinal cord	≤0.35 cc ≤1.2 cc	10 Gy 7 Gy	14 Gy	Myelitis
Esophagus	≤5 cc	11.9 Gy	15.4 Gy	Stenosis / fistula
Brachial plexus	≤3 cc	14 Gy	17.5 Gy	Neuropathy
Heart / pericardium	≤15 cc	16 Gy	22 Gy	Pericarditis
Great vessels	≤10 cc	31 Gy	37 Gy	Aneurysm
Trachea / large bronchus	≤4 cc	10.5 Gy	20.2 Gy	Stenosis / fistula
Rib	≤1 cc	22 Gy	30 Gy	Pain / fracture
Skin	≤10 cc	23 Gy	26 Gy	Ulceration
Stomach	≤10 cc	11.2 Gy	12.4 Gy	Ulceration / fistula
Bowel	D0.1cc D20cc	<18.4Gy <11Gy		
Phrenic nerve	2-4 cc	<12 Gy	—	Diaphragm motion
Lungs (R+L)	>1500 cc	7 Gy	—	↓ Lung function
Lungs (R+L)	>1000 cc	7.4 Gy	—	Pneumonitis
Lung L	<37%	8Gy		
Lung R	<37%	8Gy		
LV myocardium	≤10% ≤15% ≤20% ≤10%* ≤10%* ≤5%*	30 Gy 20Gy 10Gy 10Gy 20Gy	—	↓ LV ejection fraction
ICD Leads	≤0.03cc	12Gy		
ICD	D0.03cc	<2Gy		
LAD/R	D0.03cc	<25Gy	20Gy (25Gy 3mm PRV)	
Coronary/Circumflex	D0.03cc	<14Gy		

*Priority 2 constraints

* Normal Tissue OARs from RTOG 0915

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PLANNING TIPS

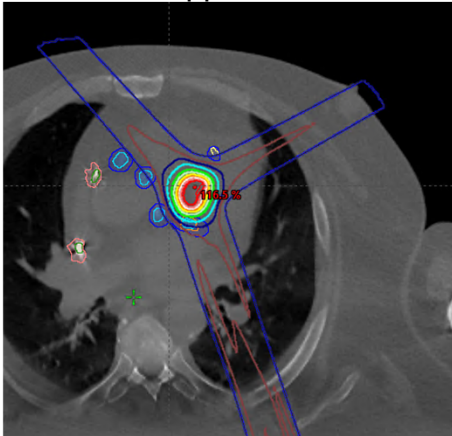
- Evaluate extreme phases for target coverage and OAR protection.
- Evaluated on image sets with +/-3mm of skin expansion
- Target can be expanded distally into blood pool to be more robust against external contour differences. (crop any expansion you have into ventricle.)

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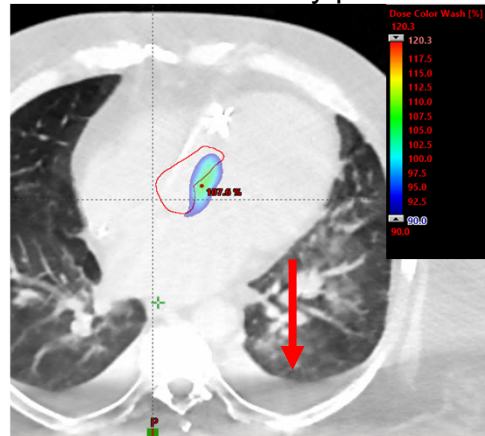
42

PRETREATMENT VERIFICATION

Treatment Approved Plan



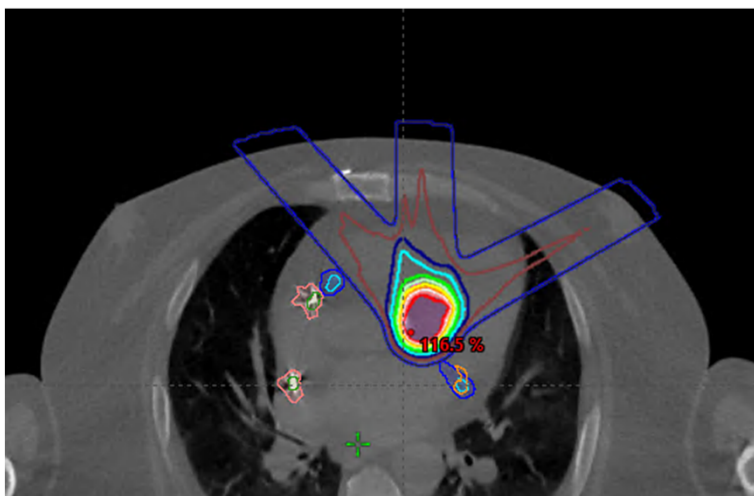
Verification CT 1 day prior to Tx



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PRETREATMENT VERIFICATION



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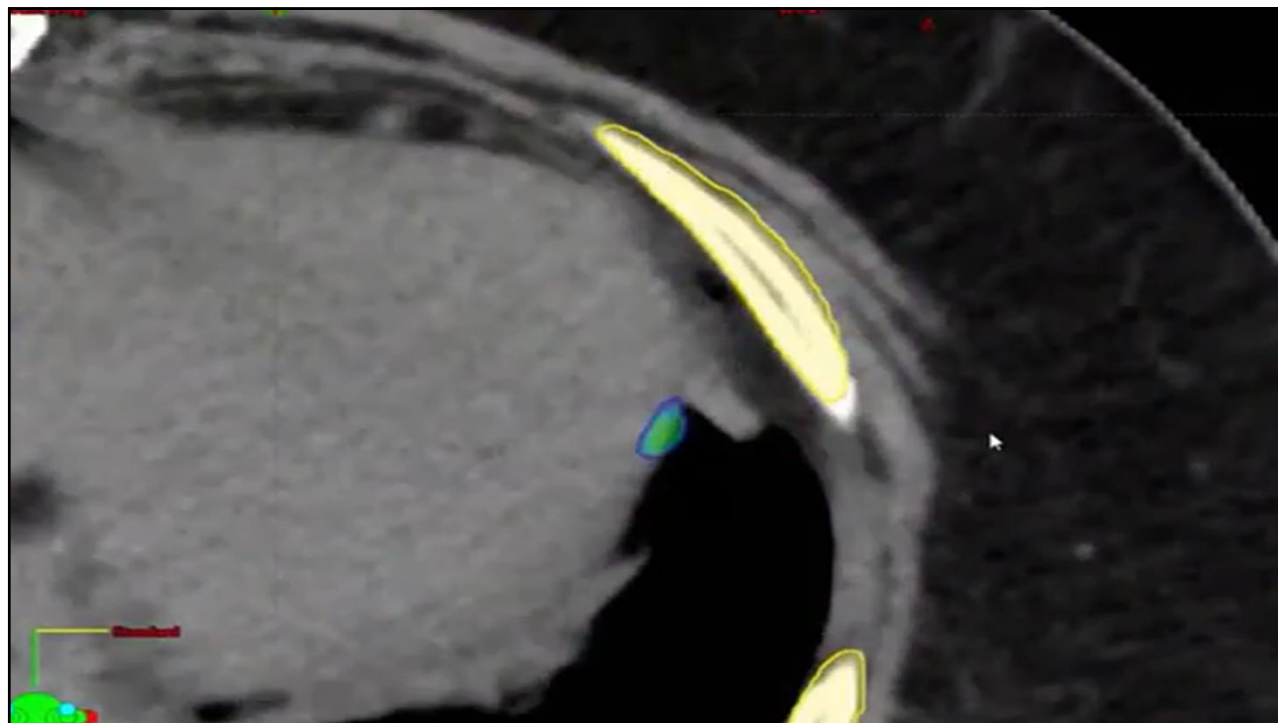
44

SIM TO PLAN APPROVAL TIMELINE

- Thursday PM - Simulation completed
- Thursday PM – MDA staff Imports respiratory 4DCT
- Friday – Radiation Oncologist completes/verifies normal tissue contouring
- Saturday – Cardiologist/staff handoff to generate cardiac structures
- Sunday – Cardiac contours deformed and transferred to planning image
- Monday – Finalize normal tissue structures/contour leads and other devices
- Tuesday – Dosimetry creates planning structures, proposed plan saved.
- Wednesday AM – VT Dose review meeting scheduled in Teams
- Wednesday PM- pretreatment verification (if requested)
- Thursday PM – Patient treatment

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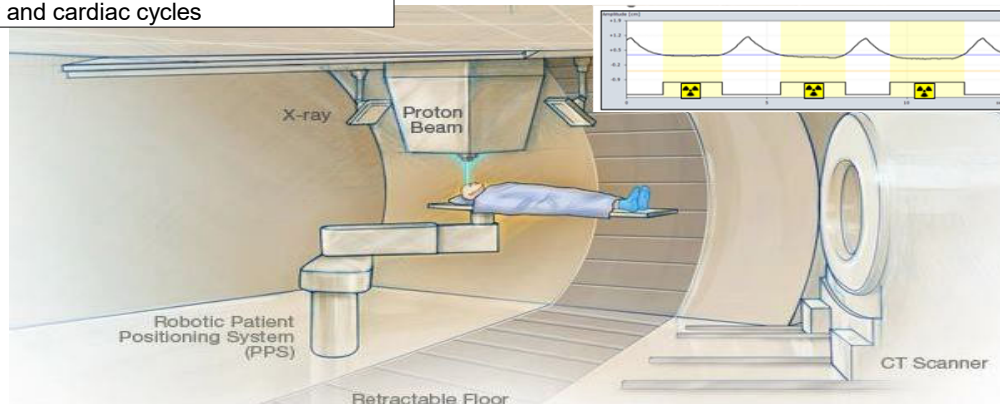
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Treatment Delivery

- 2D/3D matching to bones and check ICD leads
- Volumetric imaging (4DCT 50% phase)
- Fluorography confirmation of ICD leads during respiratory and cardiac cycles



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TREATMENT DELIVERY



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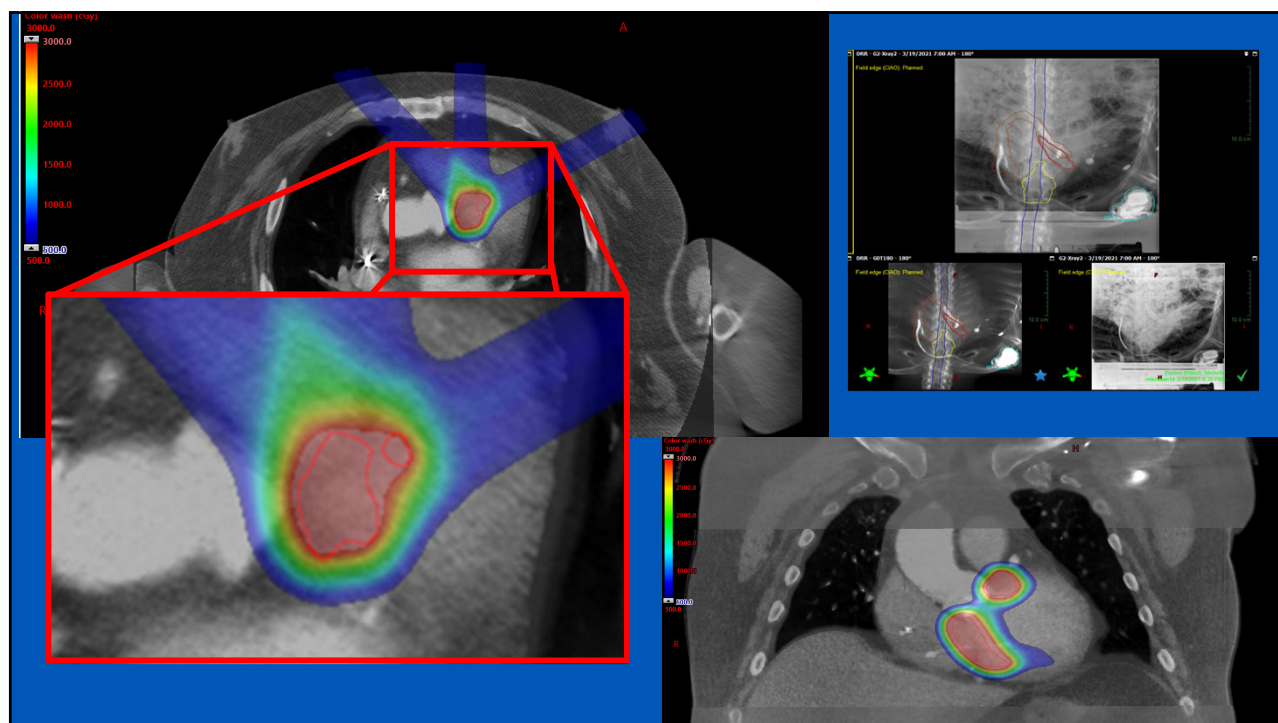
MEDICAL DEVICE MANAGEMENT

- Cardiologist & Nurse at treatment.
- If patient isn't pacemaker dependent, no interrogation done at treatment.
 - Device will be interrogated one week prior and one week post treatment.
 - If pacemaker dependent, the device will be interrogated immediately following treatment (No late day appointments).
- From 2016-2024 (2947 treated fractions)*
 - 5 "soft device reset" CIED (non-VT patients)
 - 1 "soft device reset" CIED (most recent VT patient not on study)

*Pepin MD, Ball BE, Stuart-Mullen LG, et al. Implanted electronic device management in a pencil-beam scanning proton-therapy clinic. *Practical Radiation Oncology*. 2026; Published April 2, 2026. doi:10.1016/j.pro.2026.03.004

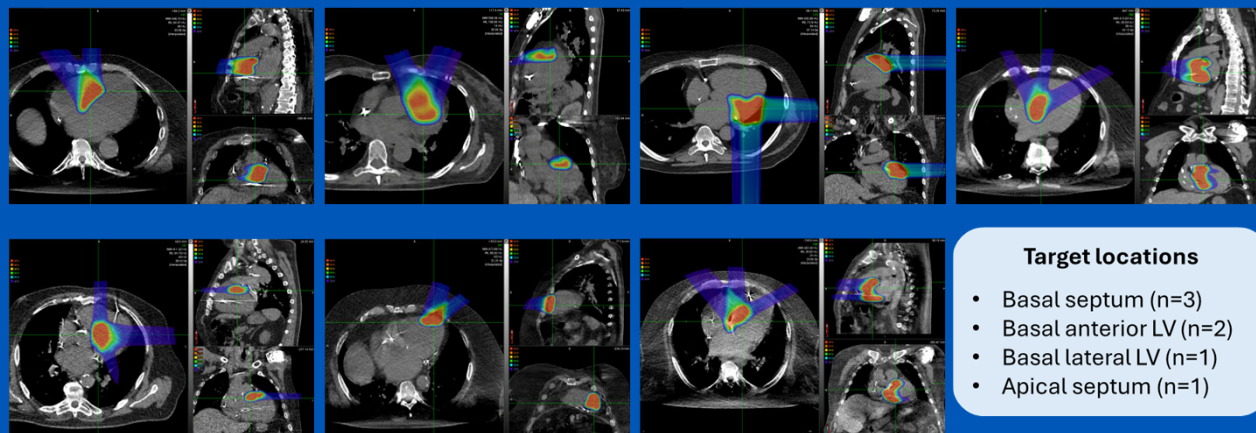
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STUDY RESULTS



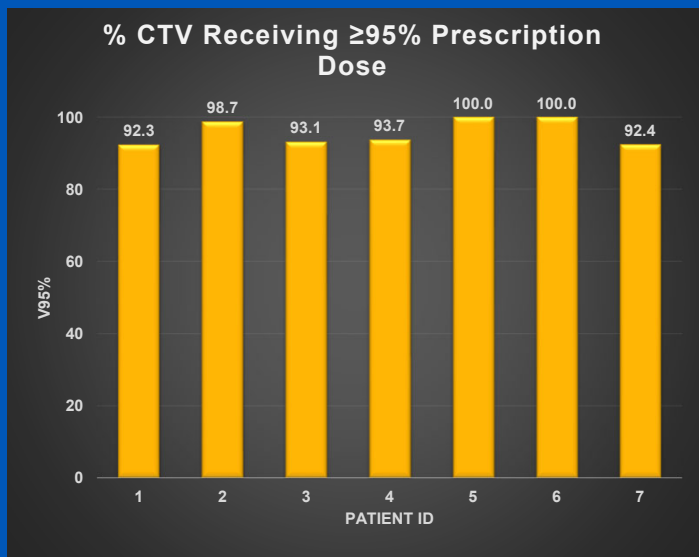
Median **37.9 cc** of myocardium received at least 30 Gy

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TARGET MYOCARDIUM

	Median (range)
Volume (cc)	17cc (8.3-64.9)
Max dose (Gy)	38Gy (35.2-38.9)
D95% (Gy)	28.7Gy (25.5-32.5)
V95% (%)	96.2% (92.3-100)

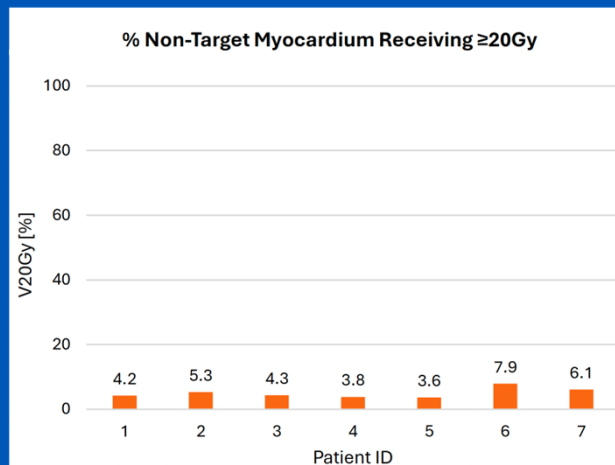


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NON-TARGET MYOCARDIUM

	Median (range)
Volume (cc)	285.5cc (185.1-329)
V10Gy (%)	7.4%(6-15.3)
V20Gy (%)	4.3%(3.6-7.9)



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NON-MYOCARDIAL ORGANS-AT-RISK

Organ at risk	Max point dose, Gy [median (range)]
Lung	11.9 (0.3-34.8)
Skin	11.7 (9.3-14.7)
LAD	18.1 (17.7-27.9)
LCx	12.6 (0-24.7)
RCA	6.5 (0-9)
ICD generator	0 (0-0)
Spinal cord	0 (0-0)
Esophagus	0 (0-0)
Trachea	0 (0-0)
Large Bowel	0 (0-2.9)
Stomach	0 (0-0.1)

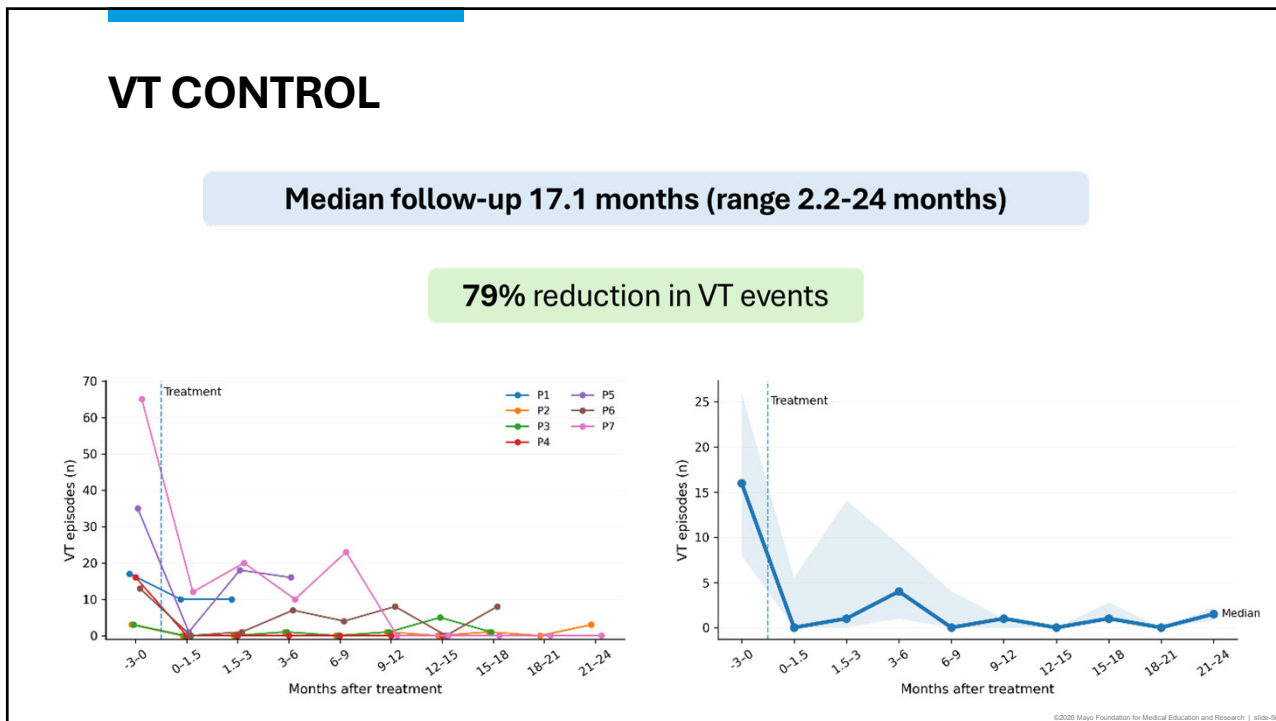
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**PROTON
CLINICAL
OUTCOMES**

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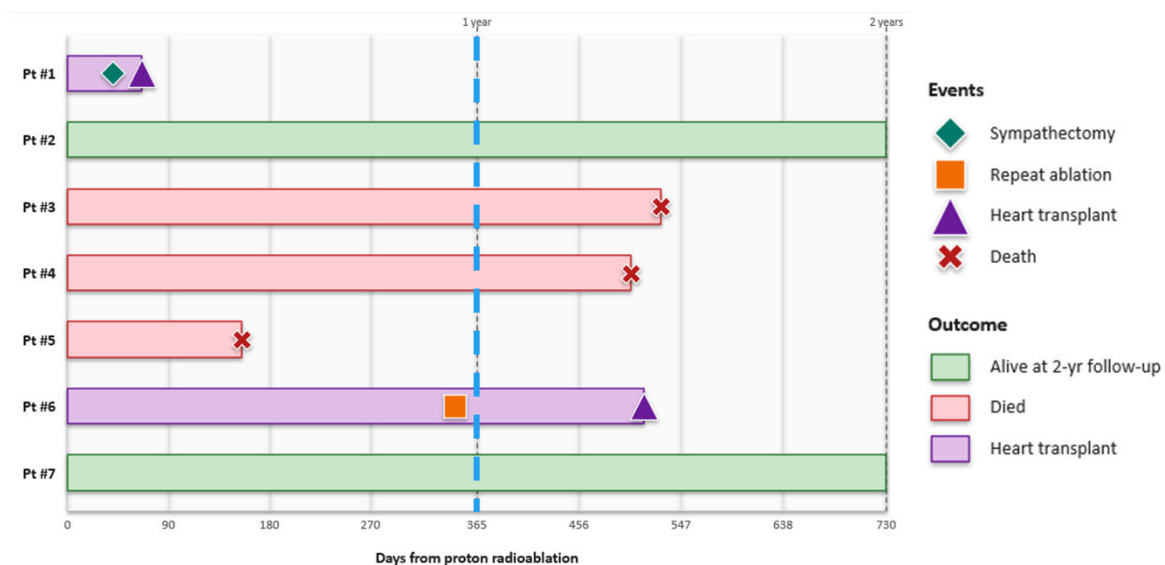
CLINICAL OUTCOMES

- No short- or long-term treatment-related serious adverse events.
 - No new valve dysfunction, AV block, acute coronary events, pericardial effusion, stroke/TIA, pulmonary complications, or ICD malfunction
- Median LVEF: 26% → 25%
 - Median LVEF decline: -4%
 - No patient had $\geq 10\%$ LVEF decline
- Changes consistent with natural progression of disease
- Advanced cardiomyopathy population
- Deaths (3) and transplants (2) occurred due to progressive HF
- No arrhythmic deaths attributable to treatment
- Mortality consistent with prior CRA and refractory VT cohorts

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CLINICAL OUTCOMES



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Heating Up: Future Directions

- Pivotal studies ongoing.
- Several open questions for VT ablation
 - Mechanism of effect
 - Duration of effect
 - Risk to adjacent myocardium
- Opportunity for innovation
 - Improved workflows for integrating EP and RadOnc systems
 - 4D – dose calculation
 - **Cardiac gating**
 - Increased image-guidance capabilities

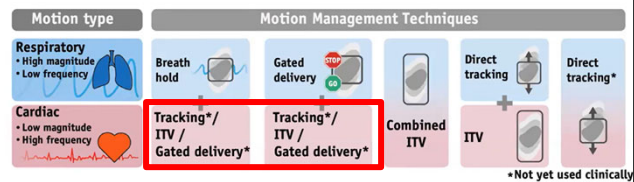


Image from Figure 1. Motion management techniques for cardiac and respiratory motion. Adapted from Lydiard S, Blanck O, Hugo G, et al. Int J Radiat Oncol Biol Phys. 2021;109(3):783-800.

Goal: Develop a safe, effective non-invasive treatment for cardiac arrhythmia

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CONCLUSIONS

- Catheter-free proton beam therapy was feasible, with very low radiation exposure of non-target tissues
 - Patients experienced a substantial reduction in VT burden without clear treatment-related toxicity
- Proton therapy delivery of effective radiation doses to target myocardium while exposing adjacent at-risk structures to very low ionizing doses.
- Proton beam therapy delivered within strict dose constraints for organs-at-risk appears to be associated with low risk of radiation-related toxicities.

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CONCLUSIONS

Limitations

- Small patient numbers (highly selected group of patients)
- Limited follow-up
- Lack of long-term efficacy and cardiac function data
- Large-scale, clinical trials are underway
- Clinical trial participation is preferred; compassionate use may be considered in select patients
- Limited proton data due to limited number of centers.

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Department of
Radiation Oncology

“COMPASSIONATE USE IS **NOT** A
BACKDOOR TO CLINICAL RESEARCH”



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Proton Dosimetrist
- MCR Proton RTTs
- MCR Cardiology/Rad Onc Nursing Staff

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QUESTIONS & ANSWERS



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