MAYO CLINIC

VT Ablation with External Beam Radiotherapy

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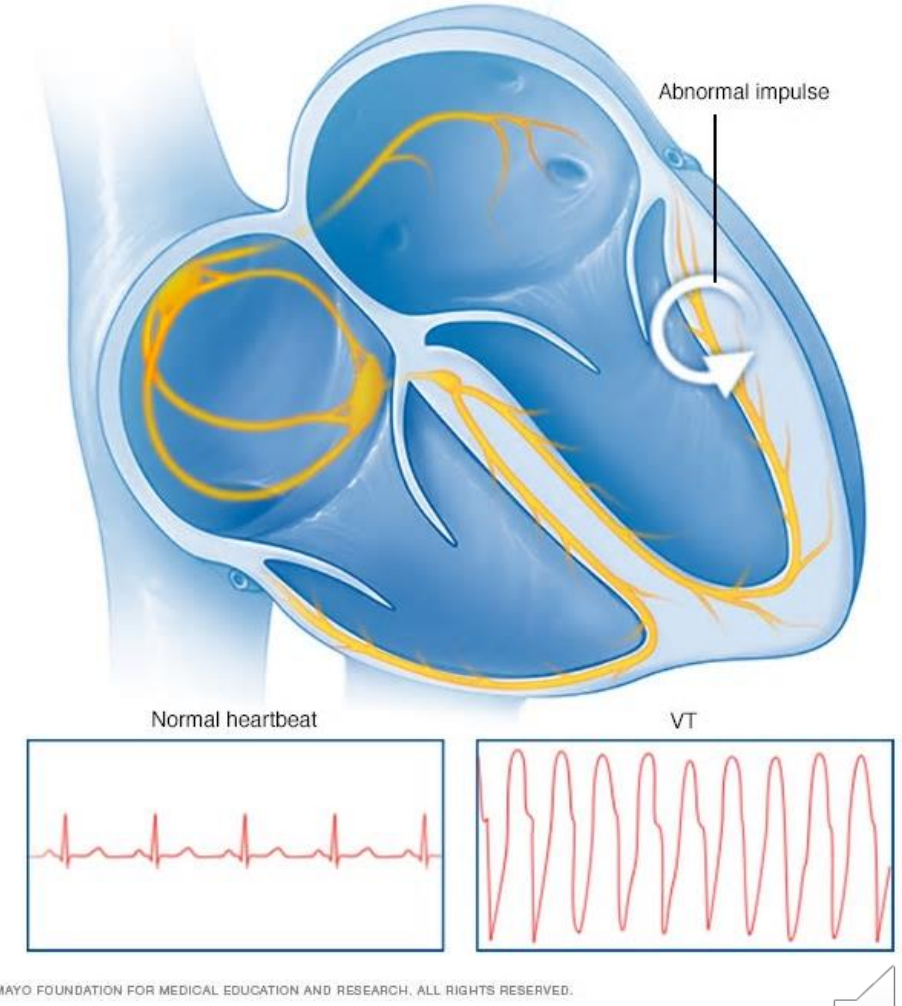
Outline

- Introduction to Ventricular Tachycardia (VT)
- External beam as an alternative
- Review of recent preclinical and clinical
- Clinical workflow – intensive image guidance
- Heating up: future directions

What is Ventricular Tachycardia (VT)?

- Abnormal electrical signal in ventricles
- Heart rate >100 beats per minute
- Symptoms:
  - Dizziness, shortness of breath, lightheadedness, palpitations, chest pain
  - Loss of consciousness
  - Cardiac arrest (sudden death)
- Estimated 180K-450K sudden cardiac deaths/yr in US*

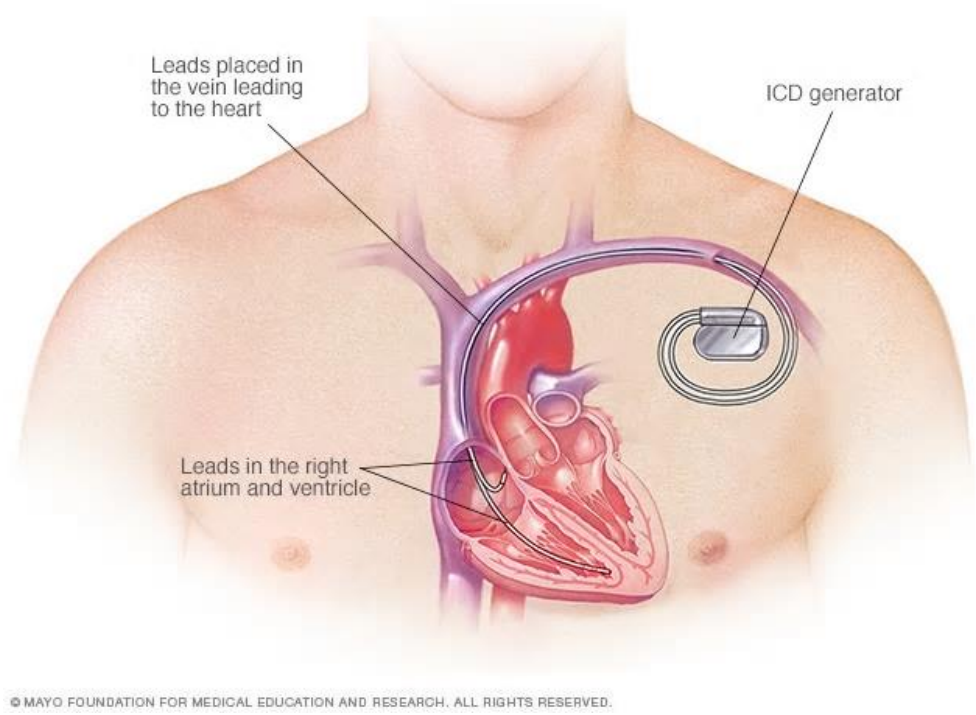


*Deo R, Albert CM. Epidemiology and genetics of sudden cardiac death. *Circulation*. 2012;125(4):620-637. doi:10.1161/CIRCULATIONAHA.111.023838

Current VT Treatment Paradigm

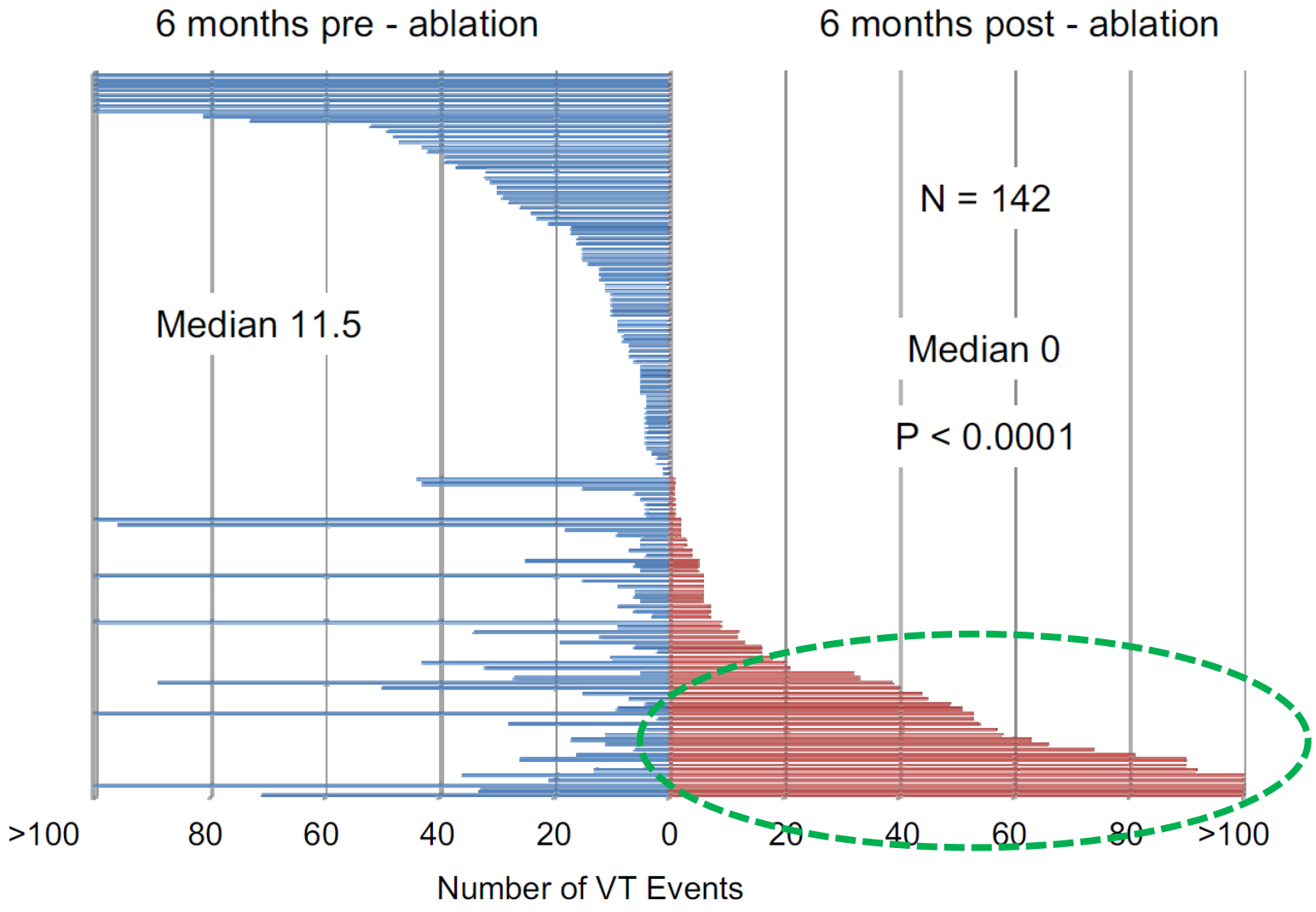
- Implanted Cardioverter Defibrillator (ICD)
  - 10K/month implanted in US*
- Antiarrhythmic medication
- Recurrent VT → VT Ablation
  - Source identification
    - Anatomic Substrate Imaging: MR, CT
    - Electrical mapping
      - Invasive electroanatomic mapping
      - 12-lead Holter monitoring
      - Body surface mapping (ECGi)
  - Catheter-based treatment w/challenges

    thickness of LV wall



*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

Cather-based VT Treatment Outcomes



Stevenson, William G et al. “Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction: the multicenter thermocool ventricular tachycardia ablation trial.” *Circulation* vol. 118,25 (2008): 2773-82. doi:10.1161/CIRCULATIONAHA.108.788604

External Beam Radiation as an Alternative

- Advantages
  - Non-invasive
  - Fast
  - Homogeneous dose to any volume
- Challenges
  - Target definition
  - Respiratory and cardiac motion
  - Delay to effect
  - Proximity to critical normal structures
- Choice of external beam
  - X-rays
  - Particle beams (protons, carbon, …)

(Some) Preclinical Data

- Can focused radiation create a isolated lesion in cardiac tissue?

  CyberHeart™ in intact porcine model Sharma, A. *et al.* Non-invasive stereotactic radiosurgery (CyberHeart) for creation of ablation lesions in the atrium. *Heart Rhythm* 2010 (7) 802-810.

- If the lesion includes an AV node, is there a dose that creates AV block?

  3D conformal AV node ablation in intact porcine model Blanck, O. *et al.* Dose-Escalation Study for Cardiac Radiosurgery in a Porcine Model. *Int J Radiat Oncol Biol Phys* 2014 (89) 590-598.

  VMAT AV node ablation in intact porcine model Lehmann, H Immo et al. “External Arrhythmia Ablation Using Photon Beams: Ablation of the Atrioventricular Junction in an Intact Animal Model.” *Circulation. Arrhythmia and electrophysiology* vol. 10,4 (2017): e004304. doi:10.1161/CIRCEP.116.004304

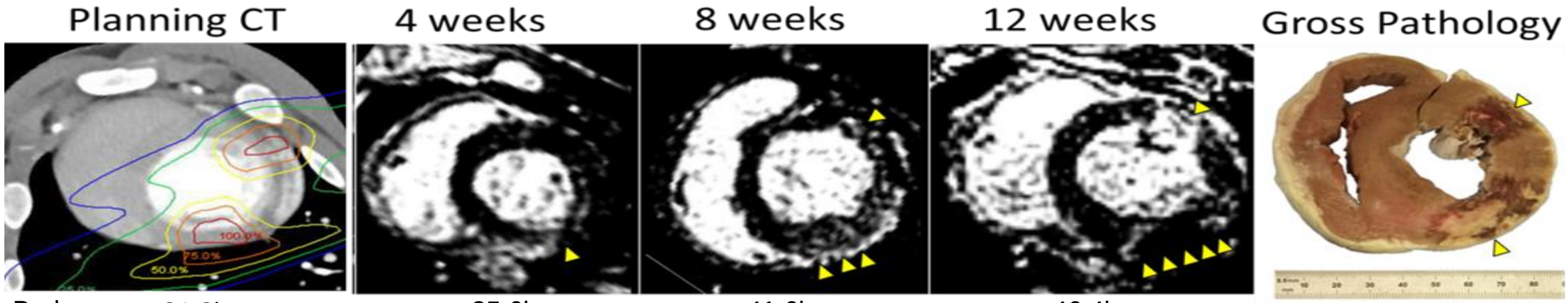
  External beam radiation delivered in a single fraction of ≥25 Gy causes electrophysical and structural myocardial ablation effects.

- If we target the left ventricle, what is the effect on cardiac tissue and function?

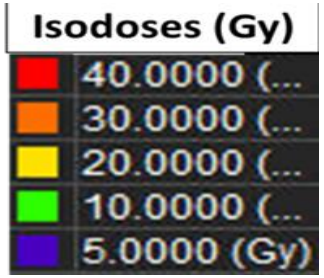
  Proton LV ablation in intact porcine model Hohmann, Stephan et al. “Left ventricular function after noninvasive cardiac ablation using proton beam therapy in a porcine model.” *Heart rhythm* vol. 16,11 (2019): 1710-1719. doi:10.1016/j.hrthm.2019.04.030

  …

Left ventricle lesion development



Body Weight	31.8kg	35.6kg	41.6kg	46.4kg

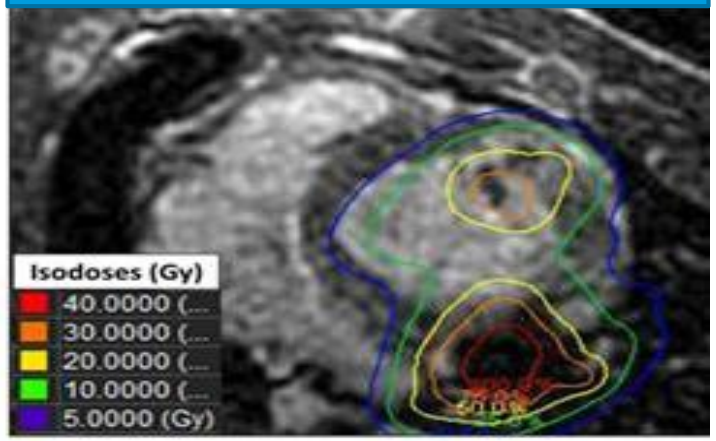


Twelve week follow-up of animal with 3 targets/ 40 Gy

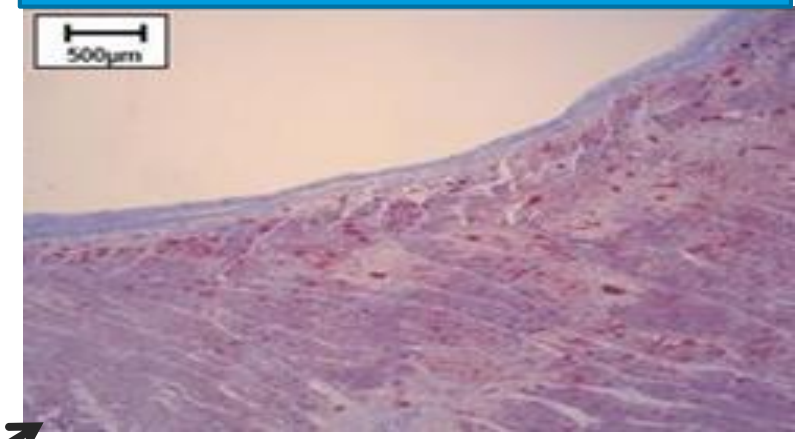
Suzuki A, Deisher A, Rettie A, et al. Preliminary investigation of time-course MRI assessment for lesion maturation created by a newly proposed scanned proton beam catheter-free ablation in the porcine left ventricle. Circulation 2017;136:A15876. In preparation for publication.

Macroscopic pathology at 12 weeks

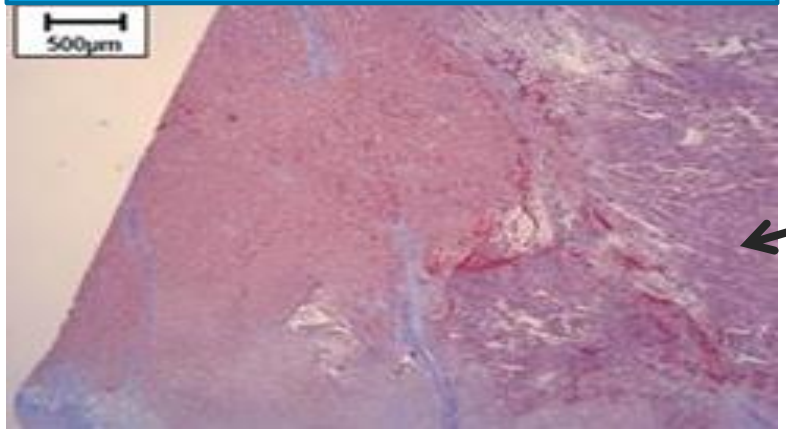
12-wk MR + def. dose

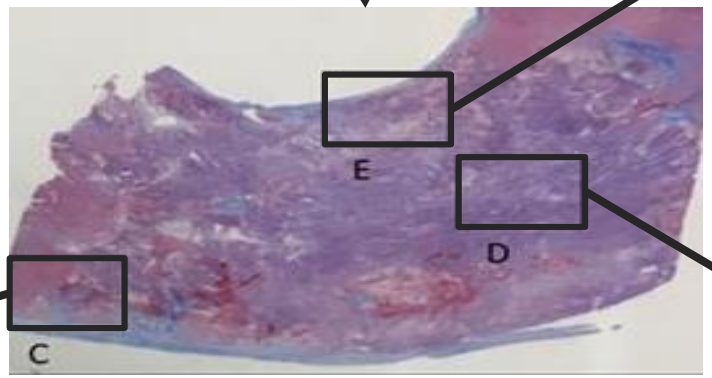


Lesion Endocardium

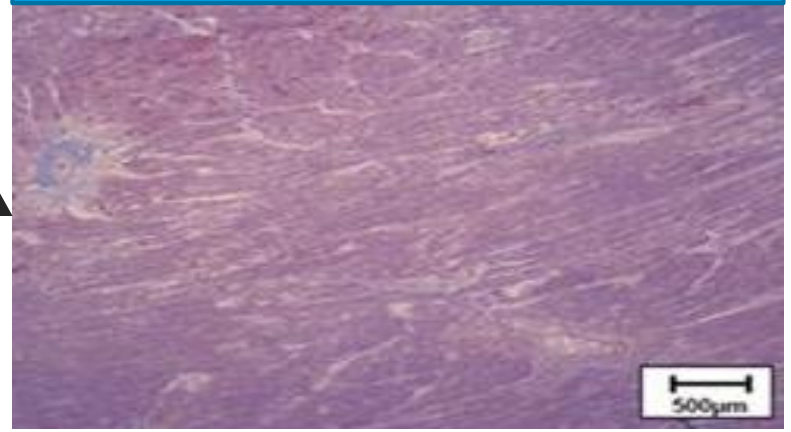


Lesion Border





Lesion Core

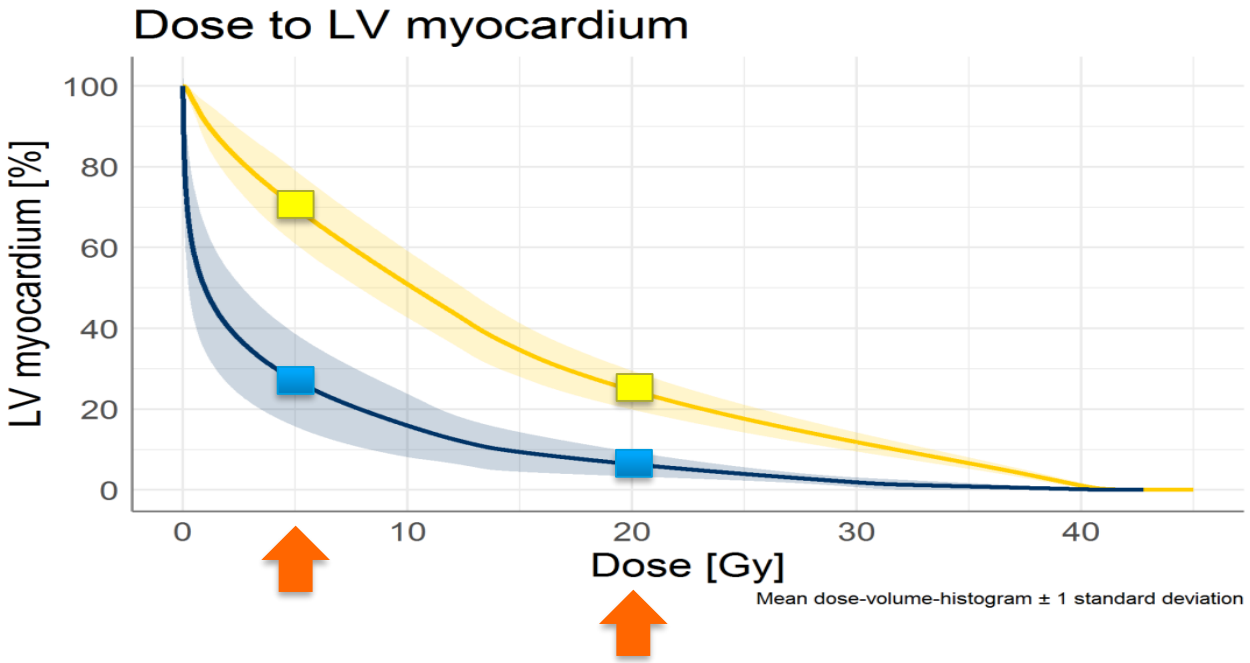


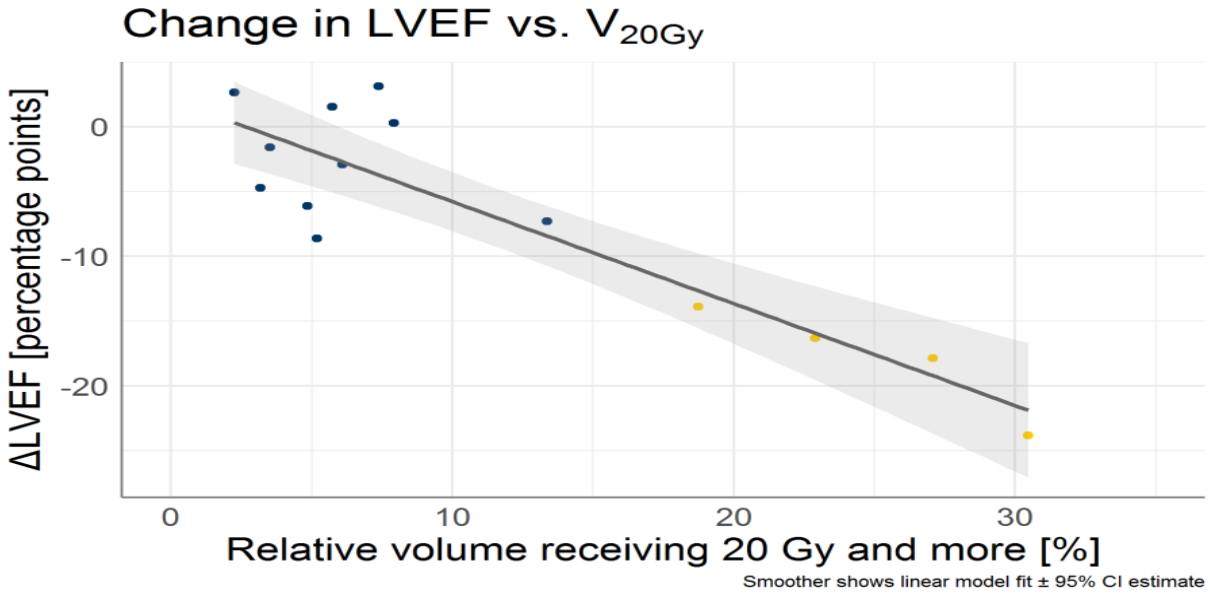
Suzuki A et al. Preliminary investigation of time-course MRI assessment for lesion maturation created by a newly proposed scanned proton beam catheter-free ablation in the porcine left ventricle. Circulation 2017;136:A15876. In preparation for publication.

Dose Response: LVEF after 100 days

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



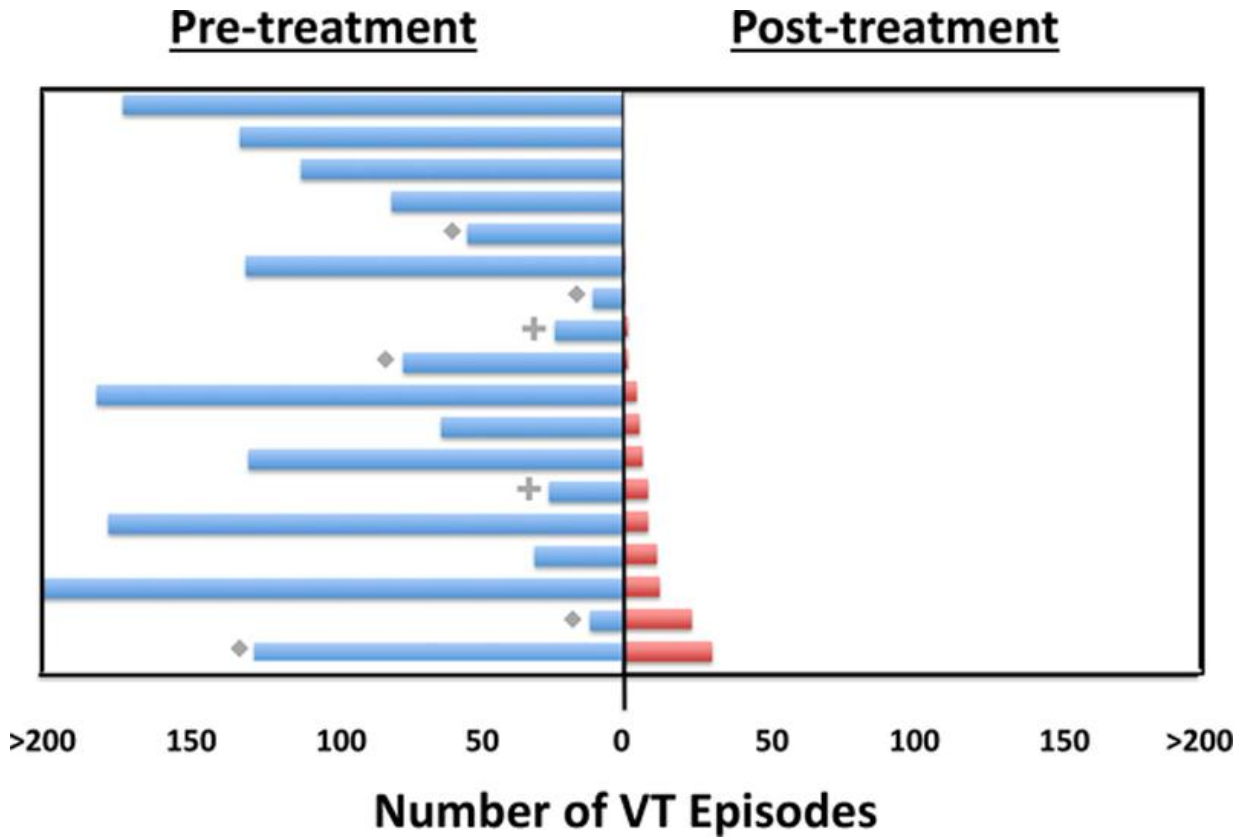


ΔLVEF vs. V20Gy = -0.66 (p = 0.01)

Hohmann S et al. Left ventricular function after noninvasive cardiac ablation using proton beam therapy in a porcine model. *Heart Rhythm*. 2019;16(11):1710-1719. doi:10.1016/j.hrthm.2019.04.030

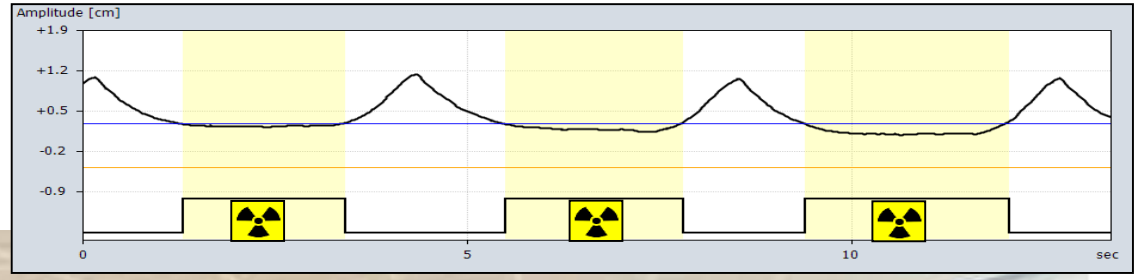
Recent Clinical Data: VT ablation with photons

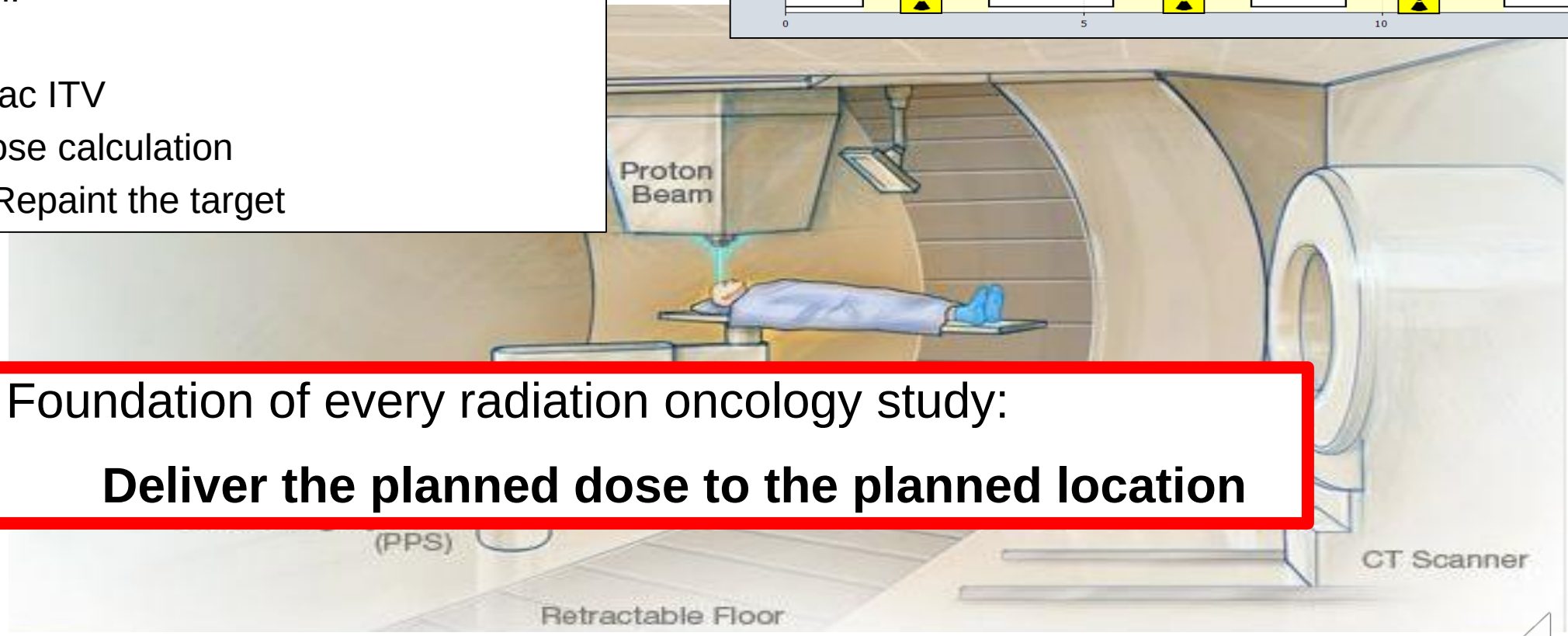
- 5 patient series in New England Journal of medicine Cuculich, PS et al. Noninvasive cardiac radiation for ablation of ventricular tachycardia.**N Engl J Med**. 2017; 377:2325–2336. doi: 10.1056/NEJMoa1613773
- ENCORE-VT Phase I/II follow-up Robinson, Clifford G et al. “Phase I/II Trial of Electrophysiology-Guided Noninvasive Cardiac Radioablation for Ventricular Tachycardia”. *Circulation 139, 3 (2019): 313-321. doi:10.1161/CIRCULATIONAHA.118.038261*



Clinical Workflow – Motion Management Strategy

- Respiratory motion:
  - Image & treat at end-expiration
- Cardiac motion:
  - Planning:
    - Cardiac ITV
    - 4D dose calculation
  - Delivery: Repaint the target





Foundation of every radiation oncology study:

Deliver the planned dose to the planned location

Clinical Workflow - Intensive Image Guidance

Target Definition

- Non-contrast respiratory 4DCT
- Non-contrast cardiac 4DCT (end-exhale)
- Contrast cardiac 4DCT (end-exhale)

- Delayed Contrast MR
- Previous Electroanatomical Mapping
- Current ECGi

Day of Treatment

- 2D/3D matching to bones and ICD leads
- Volumetric imaging (gated CBCT or 4DCT)
- Fluorography confirmation of ICD leads during respiratory and cardiac cycles

Follow-up

- Delayed Contrast MR to monitor lesion development and LVEF changes

Heating Up: Future Directions

- Several open questions for VT ablation
  - Mechanism of effect
  - Duration of effect
  - Risk to adjacent myocardium
- Preclinical work and clinical trials will both play a part
- Opportunity for innovation
  - Improved workflows for integrating EP and RadOnc systems
  - Cardiac gating
    - Increased image-guidance capabilities
    - 4D – dose calculation

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