STEREOTACTIC RADIOABLATION FOR VT
IS IT READY FOR PRIME TIME?

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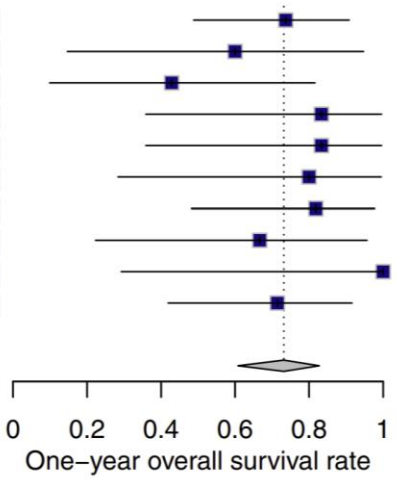
Complete elimination of the target?
Trials evaluation STAR for VT 2016-2023 (10 trials, 82 patients)

62% ICM, 38% NICM, median LVEF 21%-38%

One-year survival

Study	Cases	Total	Proportion	95% C.I.
Robinson et al. (2019)	14	19	0.74	[0.49; 0.91]
Gianni et al. (2020)	3	5	0.60	[0.15; 0.95]
Carbucicchio et al. (2021)	3	7	0.43	[0.10; 0.82]
Molon et al. (2022)	5	6	0.83	[0.36; 1.00]
Chang et al. (2022)	5	6	0.83	[0.36; 1.00]
Krug et al. (2023)	4	5	0.80	[0.28; 0.99]
Miszczyk et al. (2023)	9	11	0.82	[0.48; 0.98]
van der Ree et al. (2023)	4	6	0.67	[0.22; 0.96]
Amino et al. (2023)	3	3	1.00	[0.29; 1.00]
Arkles et al. (2023)	10	14	0.71	[0.42; 0.92]
Random effects model		**82**	**0.73**	**[0.61; 0.83]**

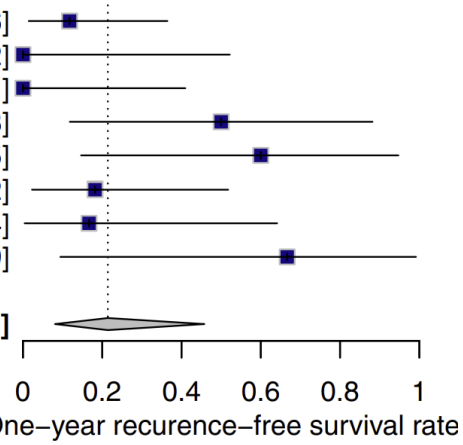
Heterogeneity: Q = 4.45 (p = 0.9)



One-year (treated) VT recurrence free-survival

Study	Cases	Total	Proportion	95% C.I.
Robinson et al. (2019)	2	17	0.12	[0.01; 0.36]
Gianni et al. (2020)	0	5	0.00	[0.00; 0.52]
Carbucicchio et al. (2021)	0	7	0.00	[0.00; 0.41]
Molon et al. (2022)	3	6	0.50	[0.12; 0.88]
Krug et al. (2023)	3	5	0.60	[0.15; 0.95]
Miszczyk et al. (2023)	2	11	0.18	[0.02; 0.52]
van der Ree et al. (2023)	1	6	0.17	[0.00; 0.64]
Amino et al. (2023)	2	3	0.67	[0.09; 0.99]
Random effects model		**60**	**0.21**	**[0.08; 0.46]**

Heterogeneity: Q = 8.14 (p = 0.3)



Miszczyk M et al. HR 2025:80-89

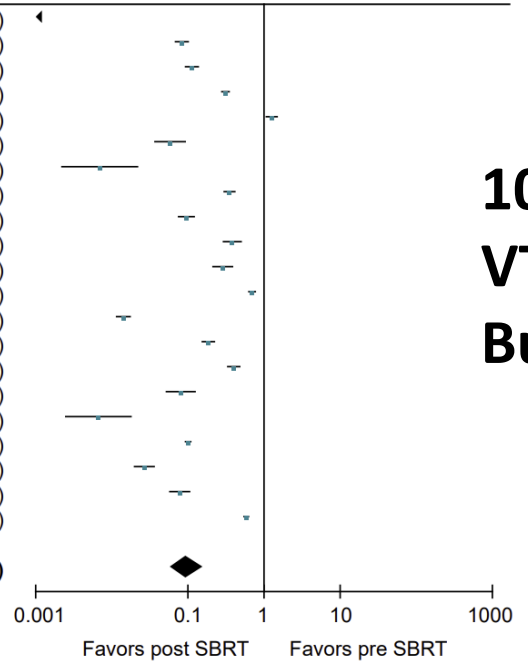
Efficacy of STAR
Meta-analysis (2017-2024, 21 studies, 191 patients)

52% ICM, average NYHA 2.6, mean LVEF 30.9±12.9%, median follow-up 5.8-28 months, blanking period ≈6 weeks

A VT episodes

Study or subgroup	log(rate ratio)	Post SBRT SE	Post SBRT Total	Pre SBRT Total	Weight	Rate ratio IV, random, 95% CI
01. Cuculich P. 2017	–8.526	0.5	4	5	4.1%	0.00 (0.00, 0.00)
02. Robinson C. 2019	–2.486	0.098	16	17	4.9%	0.08 (0.07, 0.10)
03. Neuwirth R. 2019	–2.182	0.098	10	10	4.9%	0.11 (0.09, 0.14)
04. Lloyd M. 2020, Wight J. 2022	–1.166	0.056	8	10	4.9%	0.31 (0.28, 0.35)
05. Gianni C. 2020	0.233	0.083	5	5	4.9%	1.26 (1.07, 1.49)
06. Ho L. 2021	–2.842	0.233	5	6	4.7%	0.06 (0.04, 0.09)
07. Yugo D. 2021	–4.97	0.583	2	3	3.9%	0.01 (0.00, 0.02)
08. Chin R. 2021	–1.044	0.082	7	8	4.9%	0.35 (0.30, 0.41)
09. Ho G. 2021	–2.349	0.12	5	6	4.9%	0.10 (0.08, 0.12)
10. Carbucicchio C. 2021	–0.96	0.136	6	7	4.9%	0.38 (0.29, 0.50)
11. Lee J. 2021	–1.249	0.15	5	7	4.9%	0.29 (0.21, 0.38)
12. Qian P. 2022	–0.361	0.049	6	6	4.9%	0.70 (0.63, 0.77)
14. Aras D. 2022	–4.255	0.104	8	8	4.9%	0.01 (0.01, 0.02)
15. Ninni S. 2022	–1.684	0.093	15	17	4.9%	0.19 (0.15, 0.22)
17. Ree M. 2023	–0.916	0.092	6	6	4.9%	0.40 (0.33, 0.48)
18. Amino M. 2023	–2.519	0.221	3	3	4.8%	0.08 (0.05, 0.12)
19. Krug D. 2023	–5.011	0.503	3	5	4.1%	0.01 (0.00, 0.02)
20. Herrera-Siklody C. 2023	–2.297	0.04	20	20	4.9%	0.10 (0.09, 0.11)
21. Miszyczyk M. 2023	–3.621	0.151	10	11	4.9%	0.03 (0.02, 0.04)
22. Arkles J. 2024	–2.55	0.152	12	14	4.9%	0.08 (0.06, 0.11)
23. Hasková J. 2024	–0.537	0.034	17	17	4.9%	0.58 (0.55, 0.62)
Total (95% CI)			**173**	**191**	**100.0%**	**0.10 (0.06, 0.16)**

Heterogeneity: $\tau^2 = 1.26$; $\chi^2 = 3680.23$, df = 20 ($P < 0.00001$); $I^2 = 99\%$
Test for overall effect: $Z = 9.40$ ($P < 0.00001$)



10-fold reduction in VT episodes and ICD shocks
But…

26.9 ATP/months to 3.6 ATP/months; 2 ICD shocks/months to 0.3 ICD shocks/months

Gupta et al. Europace 2025

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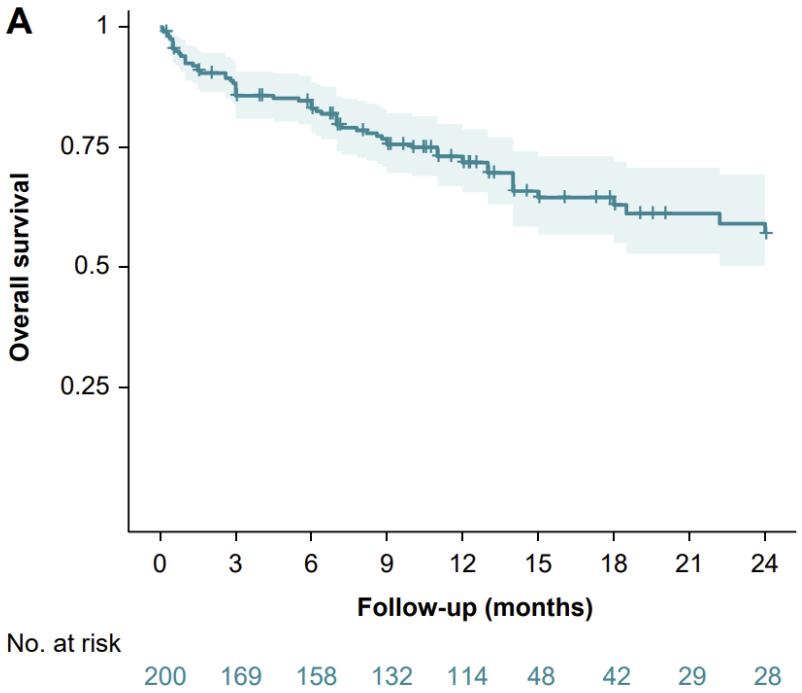
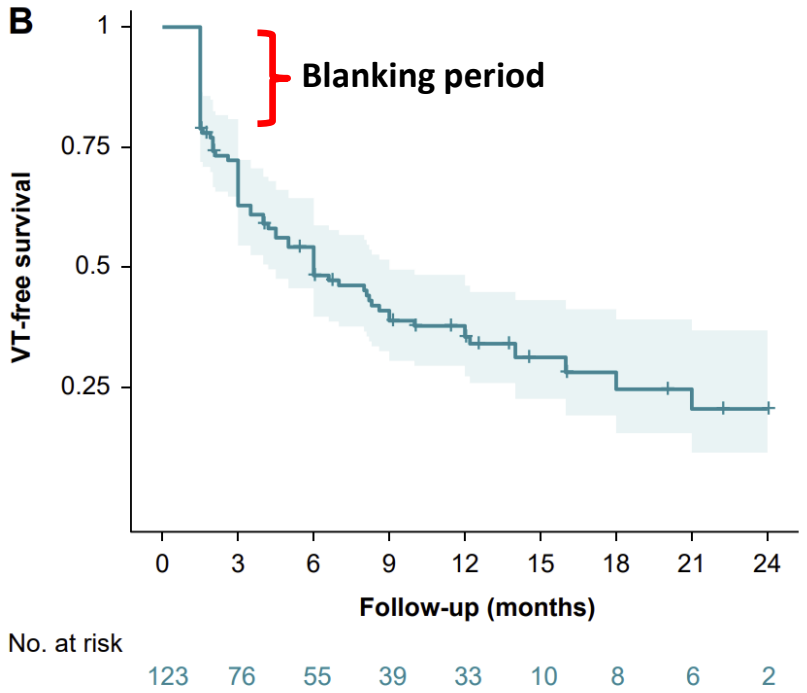
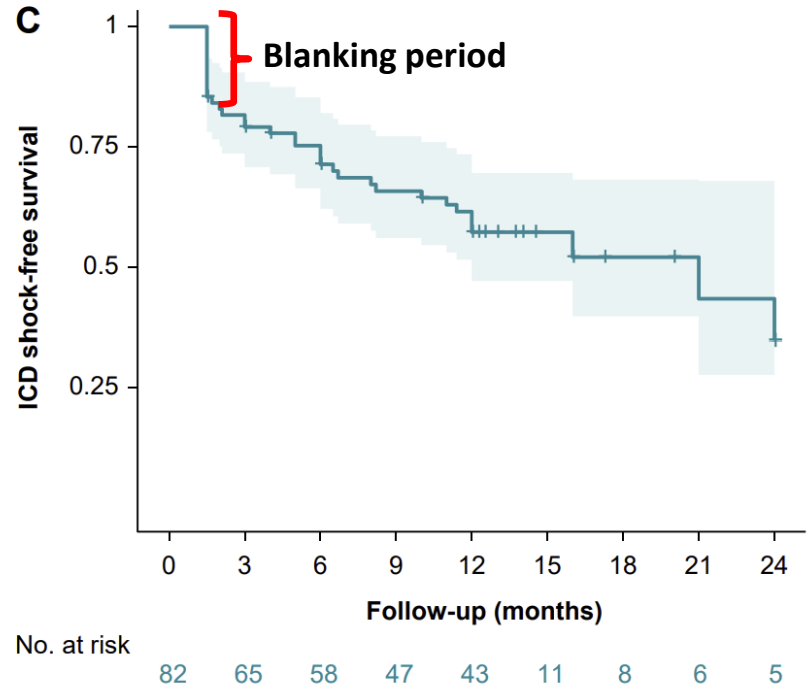
Efficacy of STAR
Meta-analysis (2017-2024, 21 studies, 191 patients)







High mortality of 43% over 2 years

Complete remission uncommon
53% VT recurrence within 6 months post-STAR (after blanking)
30% ICD shocks within 6 months post STAR (after blanking)
20% of survivors underwent re-ablation by 6 months

Gupta et al. Europace 2025

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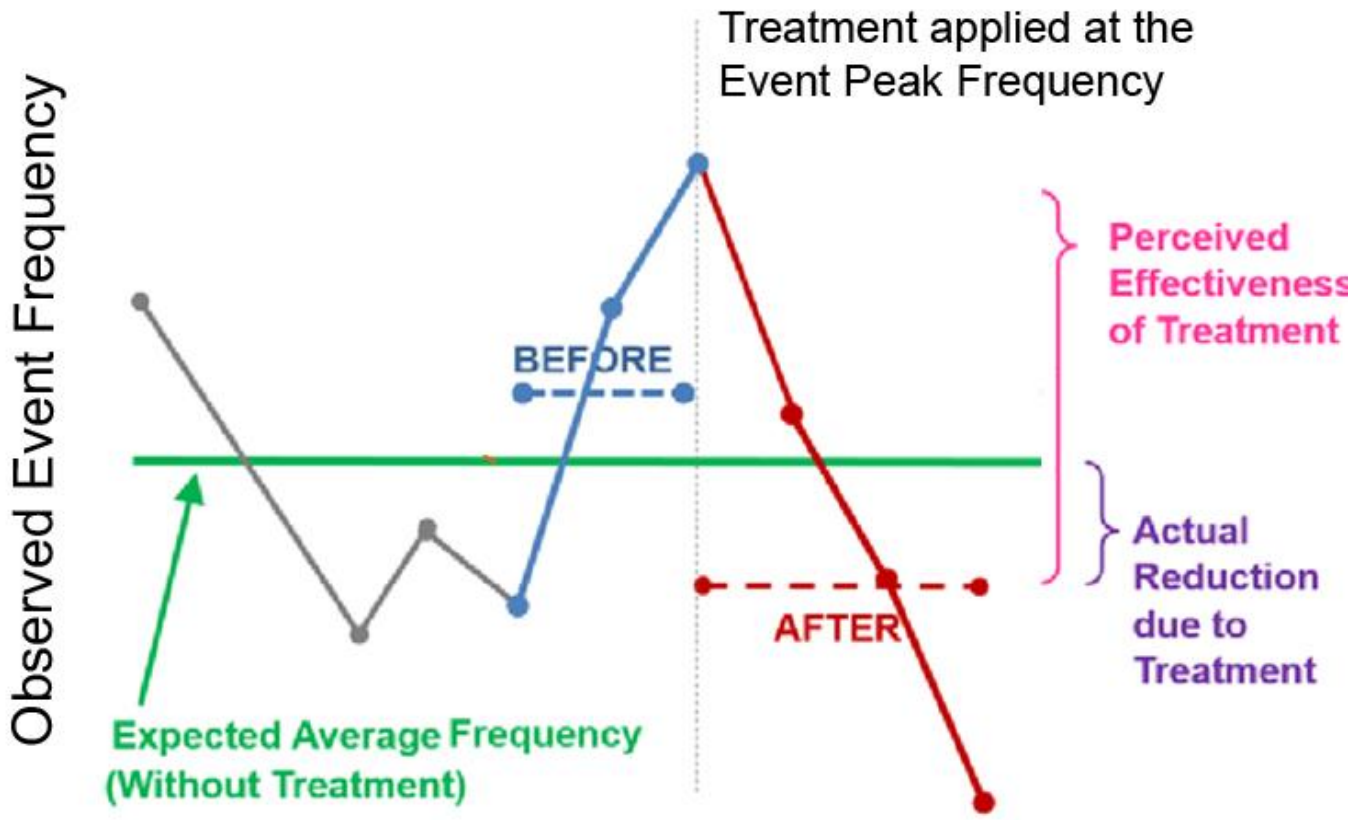
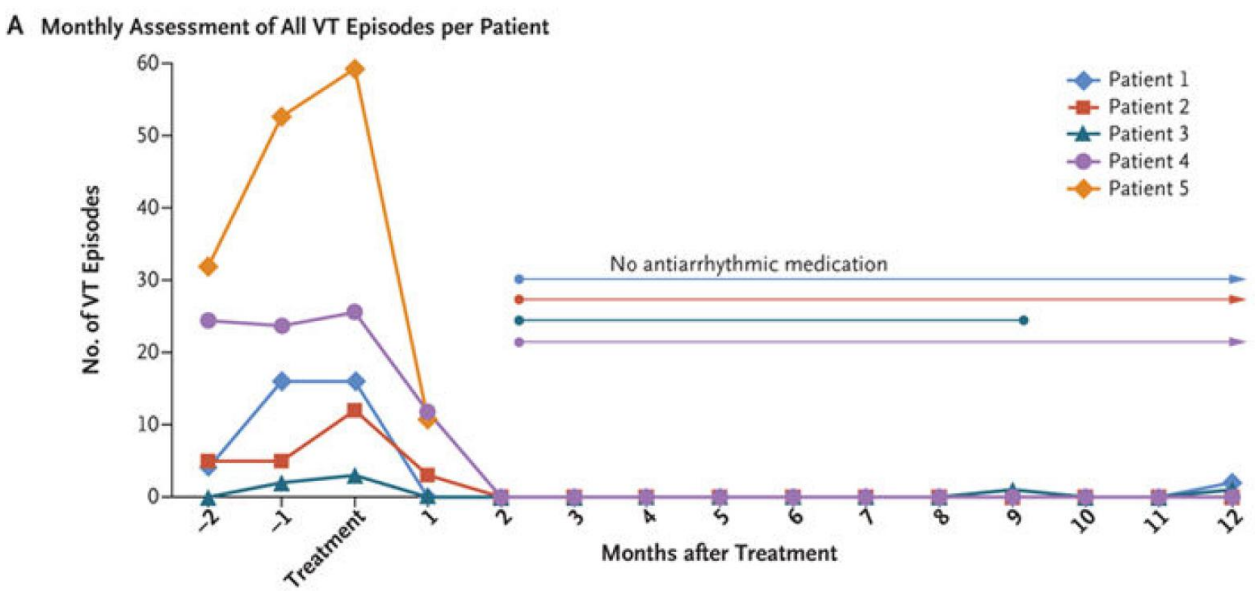
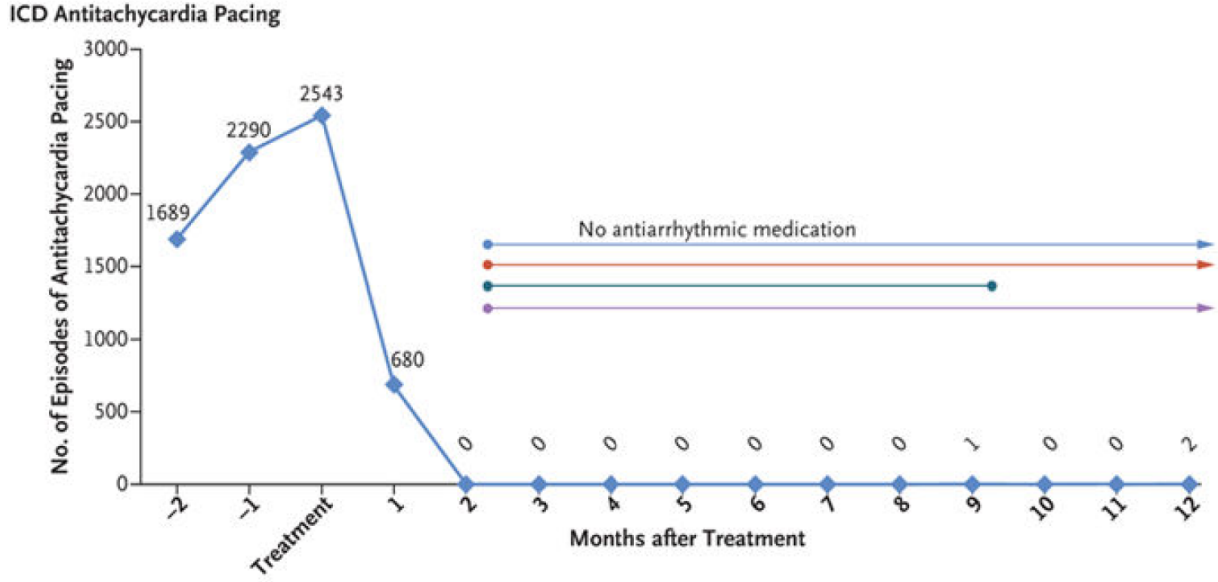
Regression to mean bias
Frequency of events oscillate around the mean



Predictable and acceptable time to effect?





1-2 months

Cuculich et al. NEJM 2017; 377: 2325-2336

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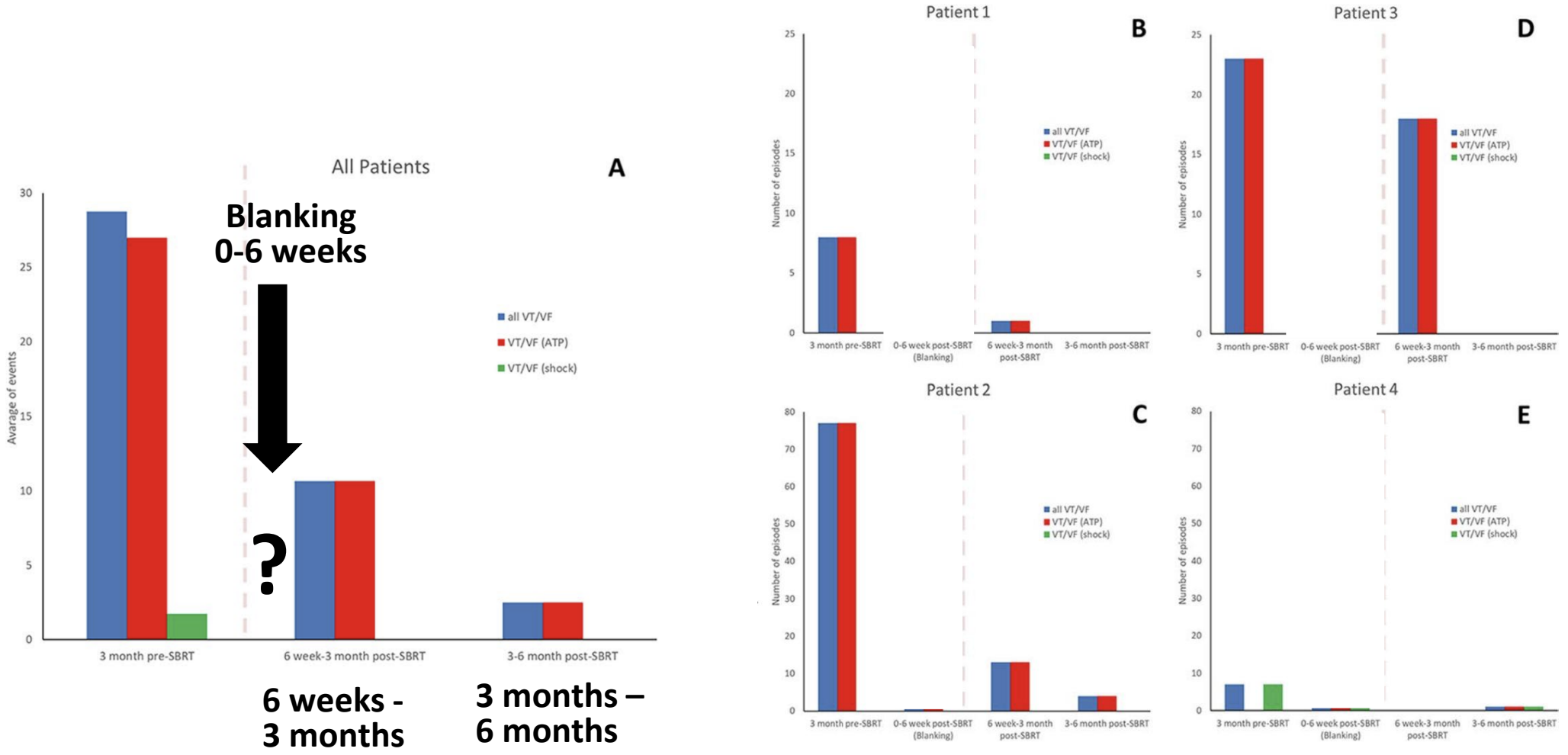
Predictable and acceptable time to effect?



Carbucicchio et al. J Inter Cardiac Electrophysiology 2021; 62:427-439

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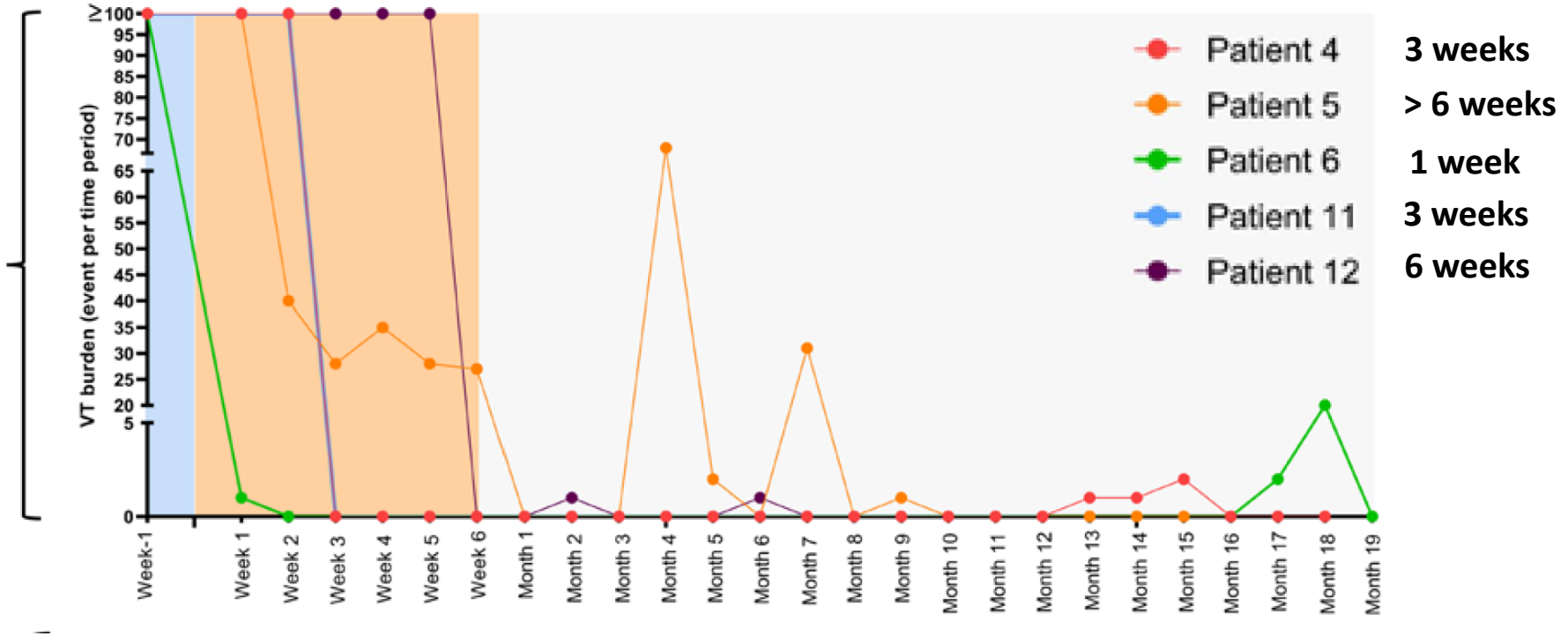
Electrical instability: Electrical storm and **incessant VT**

ES related to incessant VT



3 weeks
> 6 weeks
1 week
3 weeks
6 weeks

Effect only after 1-7 weeks!
4 out of 5 patients decrease in the VT burden during the first 6 weeks
1 out of 5 decrease during the seventh week

Ninni et al. et al. Europace 2025

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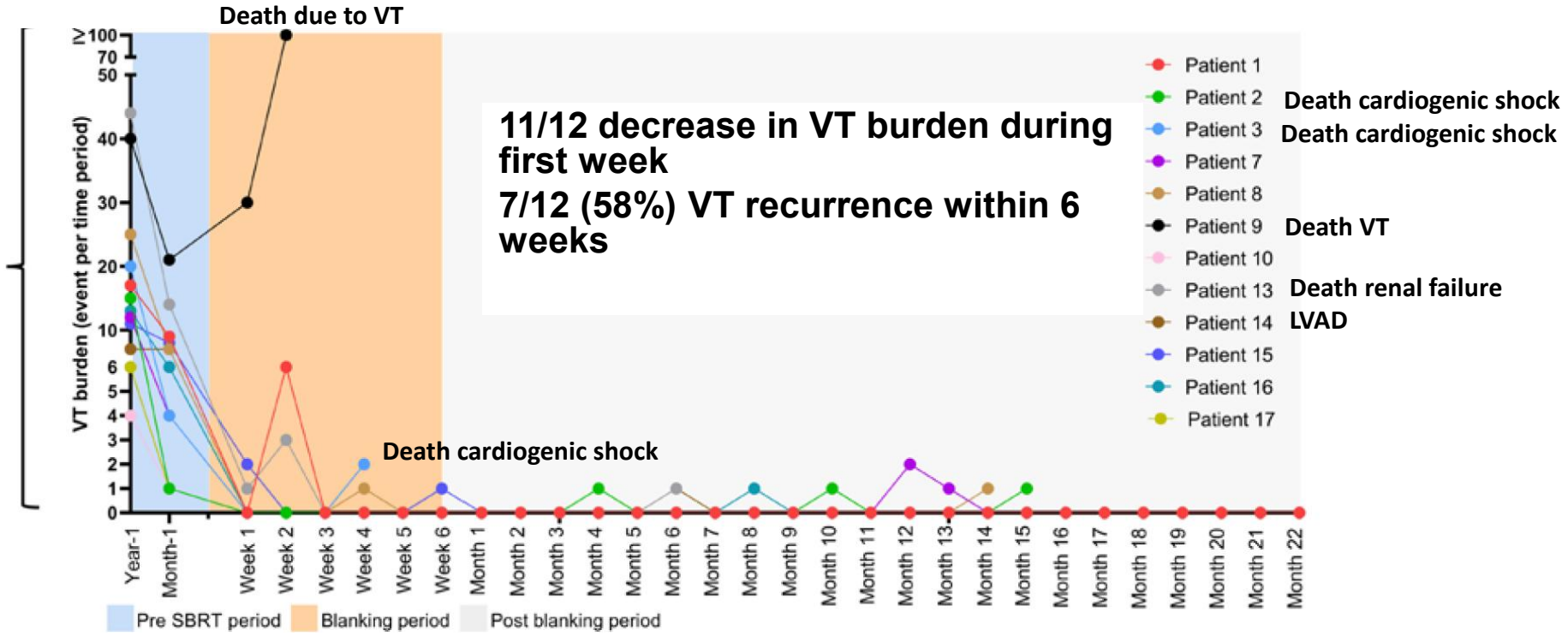
Electrical instability: **Electrical storm** and incessant VT

ES not related to incessant VT



	Before hospitalization for ES (n=17)	During hospitalization for ES (n=17)	At 6 mo after SBRT (n=15)*
Amiodarone, n (%)	7 (41.2)	17 (100)‡	10 (66.7)
Intravenous	NA	15 (88.2)	NA
Intravenous lidocaine, n (%)	NA	10 (58.8)	NA
Percutaneous sympathetic blockade, n (%)	NA	1 (5.9)§	NA
Intravenous anxiolysis, n (%)	NA	15 (88.2)	NA
Deep sedation and orotracheal intubation, n (%)	NA	3 (17.6)	NA

4 patients in-hospital CA

Ninni et al. et al. Europace 2025

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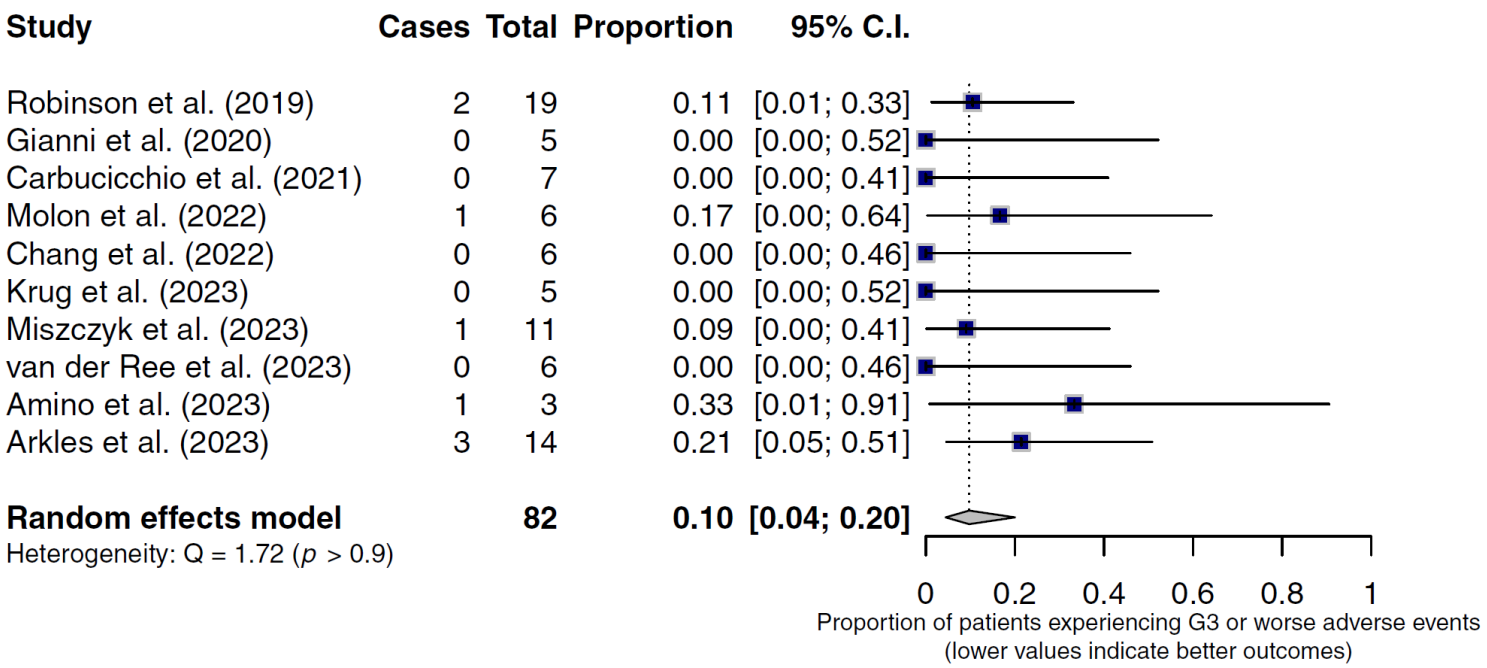
A systematic review and meta-analysis: Trials evaluation STAR for VT 2016-2023 – 10 trials, 82 patients

Treatment related ≥3 adverse events in *the first 90 days (12.8 weeks)*

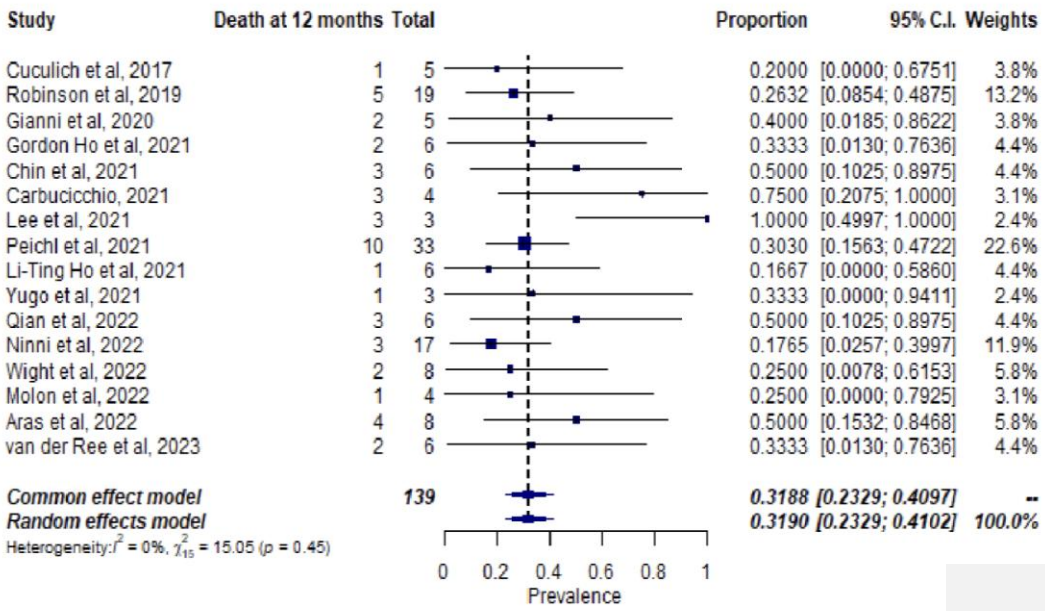


9 treatment related events

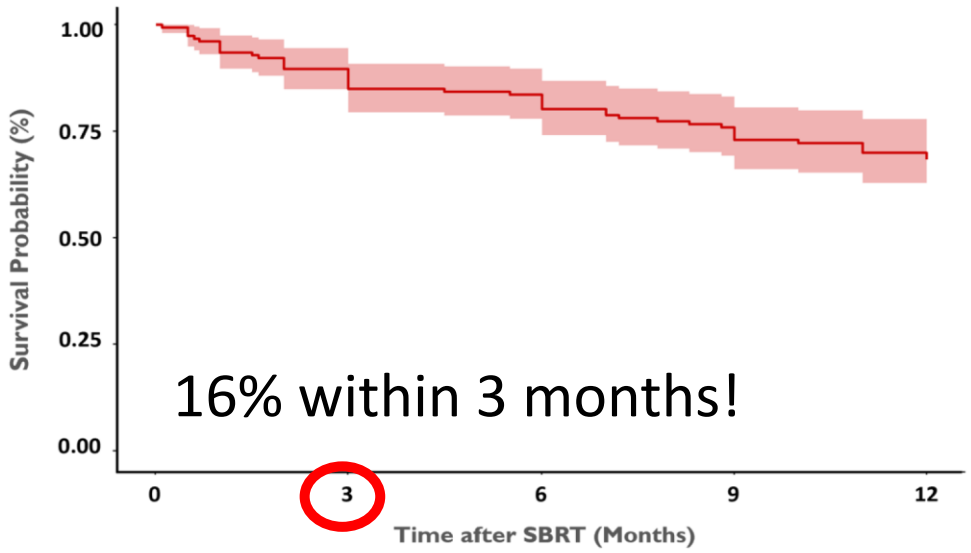
- 4/9 grade 5 events
- *6/9 heart failure*

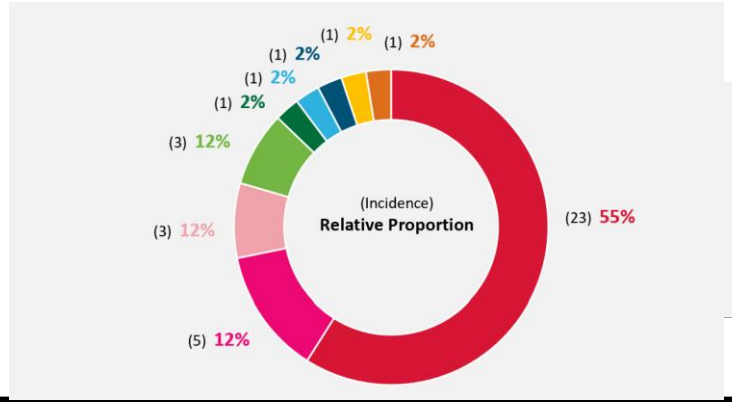
Miszczyk M et al. HR 2025:80-89

A systematic review and pooled-analysis: *One-year* mortality and causes of death after STAR, 16 studies, 157 patients



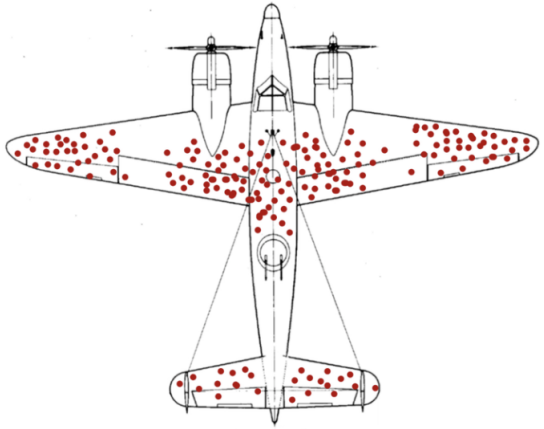
Pooled 1-year mortality 32%



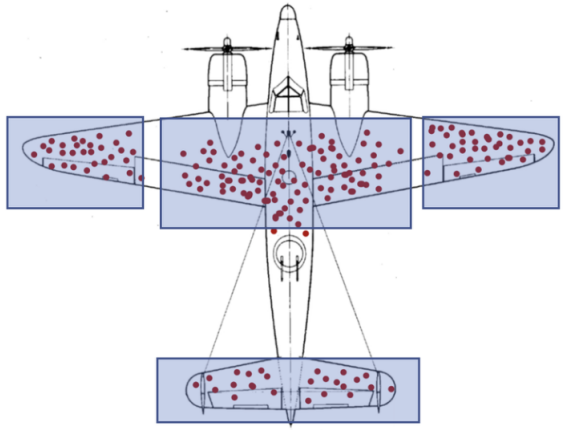


55% due to heart failure

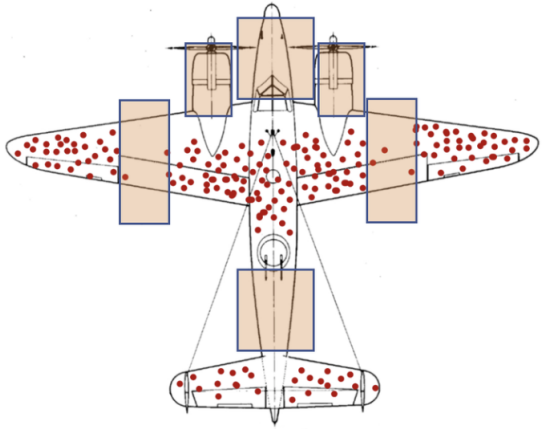
Survivalship bias: What`s missing from the data set are the planes that did not return (the patients who did not survive)



Our data if only from returning flights. Here we is a visualization of the places that bullet holes were observed.



And initial guess at how to fix this might be to apply additional armor platting to the parts of the plane with the most holes…



…. However this is where planes that *returned* had bullet holes. The planes we want to protect are the ones that did *not* return, so we should place armor there.

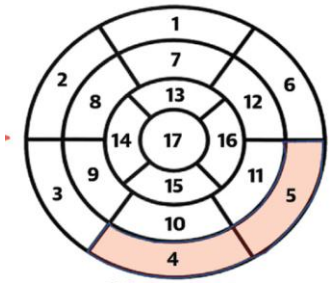
Safety of STAR – The Czech Experience
(Unknown) long-term side affects

Safety Cohort (n=36, 32 follow-up >6 months, median follow-up 33.5 months (IQR 18-44.6)

Mortality in 18 (50%): Progression heart failure 12, MI (1), SD (1), pneumonia (2), carcinoma (1) esophageal-pericardial fistula (1)

Progression of mitral valve regurgitation in 8 (25%)
3/8 surgical/catheter interventions (22, 33 and 49 months after STAR)

Irradiated Region	Segments	Risk (%)	Irradiated Region	Risk (%)	*P* Value
	Risk of Significant Mitral Valve Regurgitation (n = 32)				
Basal segments	# 1-6	7/19 (37)	Rest of segments	1/13 (8)	0.07
Basal inferior segments	# 3-5	6/12 (50)	Rest of segments	2/20 (10)	0.02
Basal inferolateral segments	# 4-5	6/10 (60)	Rest of segments	2/22 (10)	0.005
	Risk of Significant Mitral Valve Regurgitation Requiring Valve Intervention (n = 32)				
Basal segments	# 1-6	3/19 (16)	Rest of segments	0/13 (0)	0.20
Basal inferior segments	# 3-5	3/12 (25)	Rest of segments	0/20 (0)	0.04
Basal inferolateral segments	# 4-5	3/10 (30)	Rest of segments	0/22 (0)	0.02



LV segments

STAR at segment #4 or #5 (10 patients)

- Progression of mitral regurgitation (50%)
- Mitral valve intervention (30%)
- Esophago-pericardial fistula (10%)

Haskova et al. JACC EP 2004;10:654-666

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Effects of STAR on valve function over time

N=20, NICM 75%, median LVEF before STAR 46% (29%-54%)
Follow-up echo <6months, 6-18months, >18months

Worsening of valve function in 5/20 (25%)
Aortic valve most frequently, 1/4 AVR
Median time to worsening 1.1 year
Higher mean dose for the valve

	Worsening		No worsening	
	Prevalence (%)	Mean dose (Gy)	Prevalence (%)	Mean dose (Gy)
Aortic valve	4 (20)	16.8 (12.7–19.8)	16 (80)	7.2 (1.5–7.2)
Stenosis	2 (50)			
Regurgitation	2 (50)			
Mitral valve	1 (5)	5.6 (n.a.)	19 (95)	7.5 (3.8–10.3)
Stenosis	0 (0)			
Regurgitation	1 (100)			
Tricuspid valve	1 (5)	1.9 (n.a.)	19 (95)	6.7 (2.2–12.6)
Stenosis	0 (0)			
Regurgitation	1 (100)			

van der Ree et al. Heart Rhythm, 2023; 20 (8): 1206-1207

„Fibrosis cannot explain the rapidity and magnitude of the effect“

nature COMMUNICATIONS

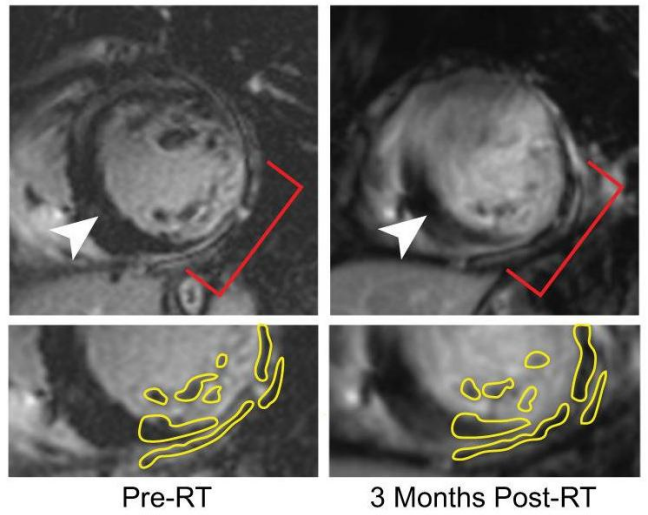
ARTICLE

https://doi.org/10.1038/s41467-021-25730-0 OPEN

Cardiac radiotherapy induces electrical conduction reprogramming in the absence of transmural fibrosis

David M. Zhang[1,2], Rachita Navara[1,2], Tiankai Yin[2], Jeffrey Szymanski[3], Uri Goldsztejn[2,4], Camryn Kenkel[2,4], Adam Lang[5], Cedric Mpoy[3], Catherine E. Lipovsky[2,6], Yun Qiao[2,4], Stephanie Hicks[2], Gang Li[2,4], Kaitlin M. S. Moore[1,2], Carmen Bergom[1,3], Buck E. Rogers[3], Clifford G. Robinson[1,2,3], Phillip S. Cuculich[1,2,3], Julie K. Schwarz[1,3] & Stacey L. Rentschler[1,2,4,6]✉

Cardiac radiotherapy (RT) may be effective in treating heart failure (HF) patients with refractory ventricular tachycardia (VT). The previously proposed mechanism of radiation-induced fibrosis does not explain the rapidity and magnitude with which VT reduction occurs clinically. Here, we demonstrate in hearts from RT patients that radiation does not achieve transmural fibrosis within the timeframe of VT reduction. Electrophysiologic assessment of



12 weeks

(Fig. 1e). Representative contrast-enhanced magnetic resonance imaging (MRI) scans of Patient E revealed no change in gadolinium enhancement and preserved myocardial tissue between baseline and at 3-month follow-up in the RT-targeted region (Fig. 1f), and there was no evidence of increased fibrosis on MRI post-RT in any patient. These clinical findings are consistent with previous preclinical studies that required doses in excess of 40 Gy to produce scar[16–22]. Collectively, these data strongly suggest that fibrosis alone cannot explain the clinical timeline and magnitude of reduced VT burden observed after RT.

Zhang et al. Nature communication 2021;12: 5558

„LGE MRI findings *after 12 weeks* do not always reflect the full effect of STAR“

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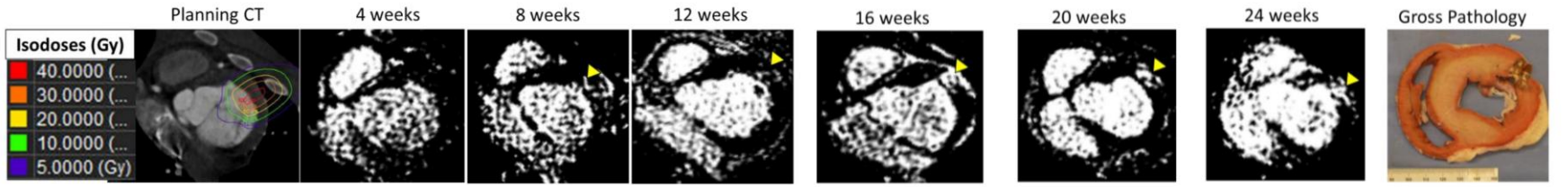
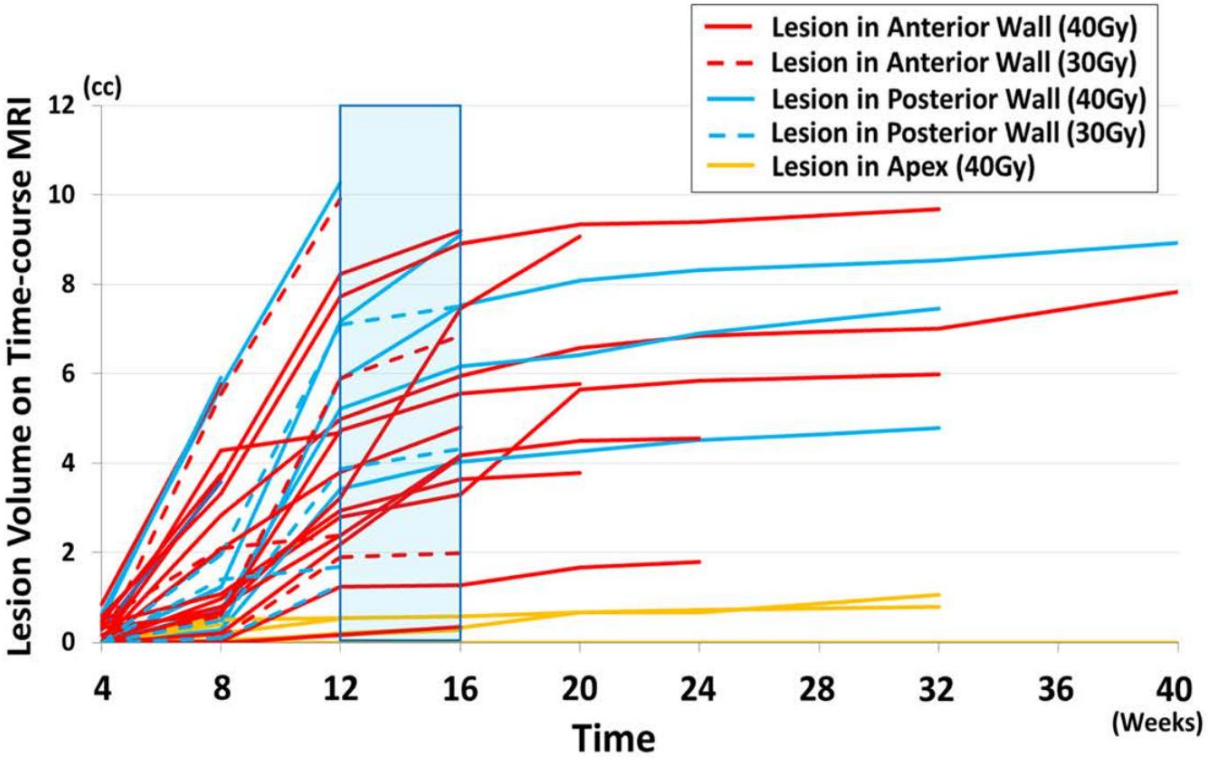
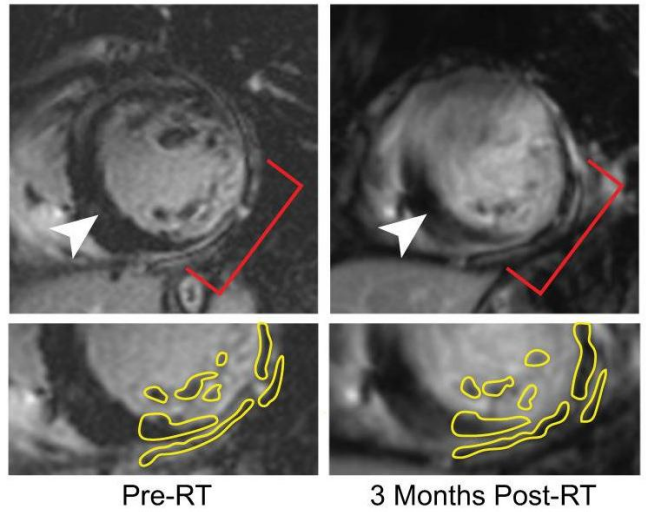
Time-course of lesion formation assessed by CMR and Histology

Proton beam 30/40Gy







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Whole heart 25 Gy irradiation enhanced electrical conduction

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-021-25730-0 OPEN

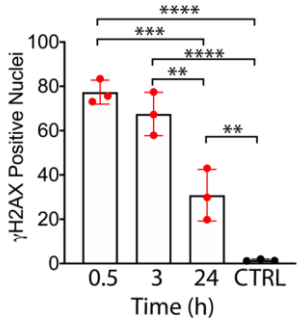
Cardiac radiotherapy induces electrical conduction reprogramming in the absence of transmural fibrosis

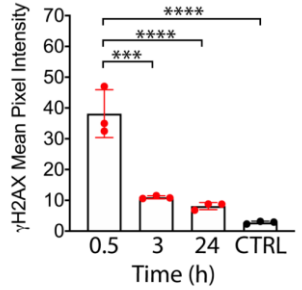
Collectively, this study provides evidence for radiation-induced reprogramming of cardiac conduction as a potential treatment strategy for arrhythmia management in VT patients.

Whole heart 25 Gy irradiation enhanced electrical conduction

30min, 3h, 24h

γH2AX = Marker for double-stranded DNA breaks





6 weeks

ECG
Optical mapping
Histology
Immunostaining, Western blots

42 weeks

ECG
Immunostaining, Western blots

QRS shortening	**QRS shortening**
Other ECG parameters unchanged	
Increased CV	
***Increased CV in infarct BZ**	
APD and ERP unchanged	
Increase in $Na_v1.5$ and Cx 43	**Increase in $Na_v1.5$ and Cx 43**

The adult mice heart rapidly recovers from radiation induced DNA damage

No necrosis, no apoptosis, no fibrosis, no structural changes, after 6 and 42 weeks

Zhang et al. Nature communication 2021;12: 5558

WECAM

Whole heart irradiation leads to extra- and intracellular edema

20, 25, 30, 40, 50 Gy

1 day, 1, 2, 3, 4 weeks

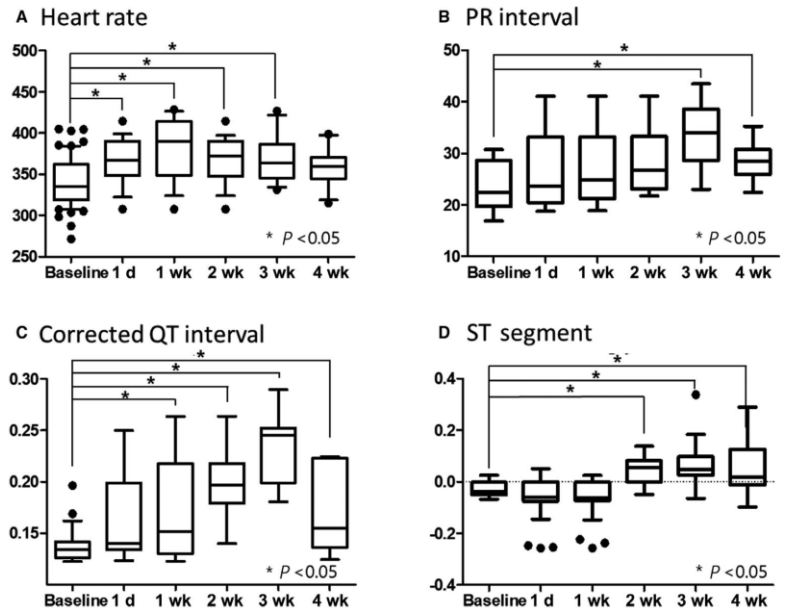
ECG, Echo

Histology

Immunohistochemical analysis (anti - C4d, CD3, CD 34, CD 68, anti-Des)

Immunofluorecense (anti Cx43, anti-alpha-sarcomeric actin, DAPI)

TUNEL assay (apoptosis)



- **QT prolongation**
- **ST elevation** (after 2 weeks, decrease at 4 weeks)

Whole heart irradiation leads to extra- and intracellular edema

20, 25, 30, 40, 50 Gy

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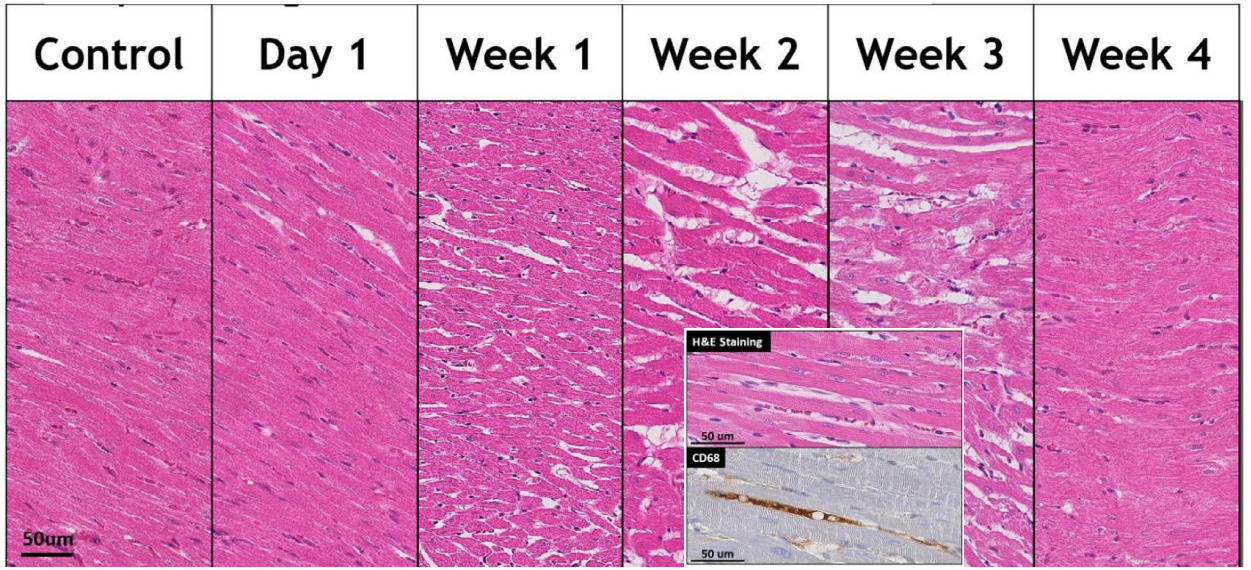


Interstitial edema, intracellular swelling
Mitochondrial damage
Macrophage/mononuclear interstitial infiltration
Decreased Cx43 expression at 2-3 weeks

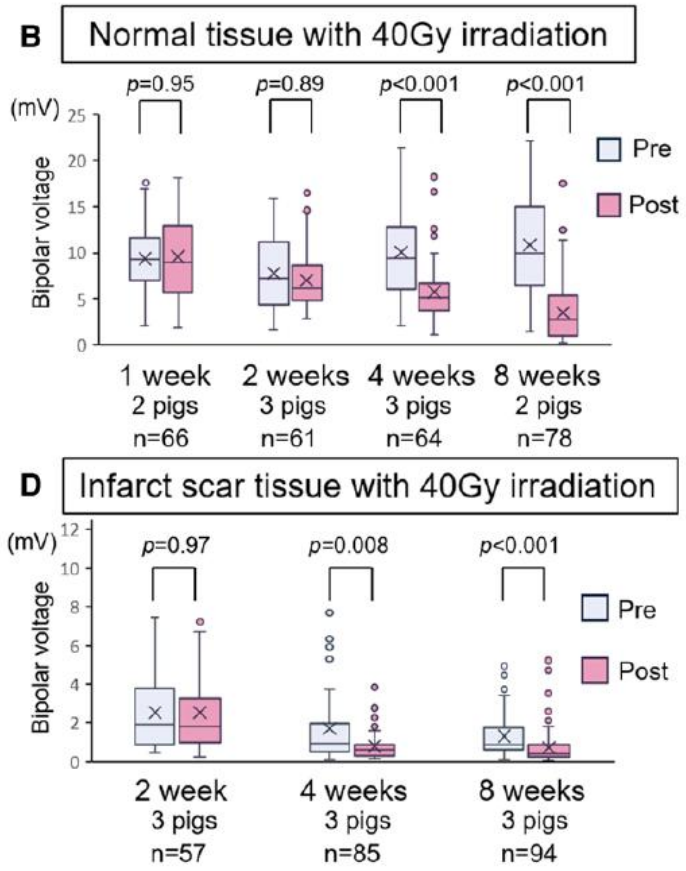
Temporary inflammatory response (peak at 3 weeks)
No impact on cardiac function, no impact on intraventricular conduction
No apoptosis, no necrosis

Early effects of 40 Gy proton beam area irradiation in pigs

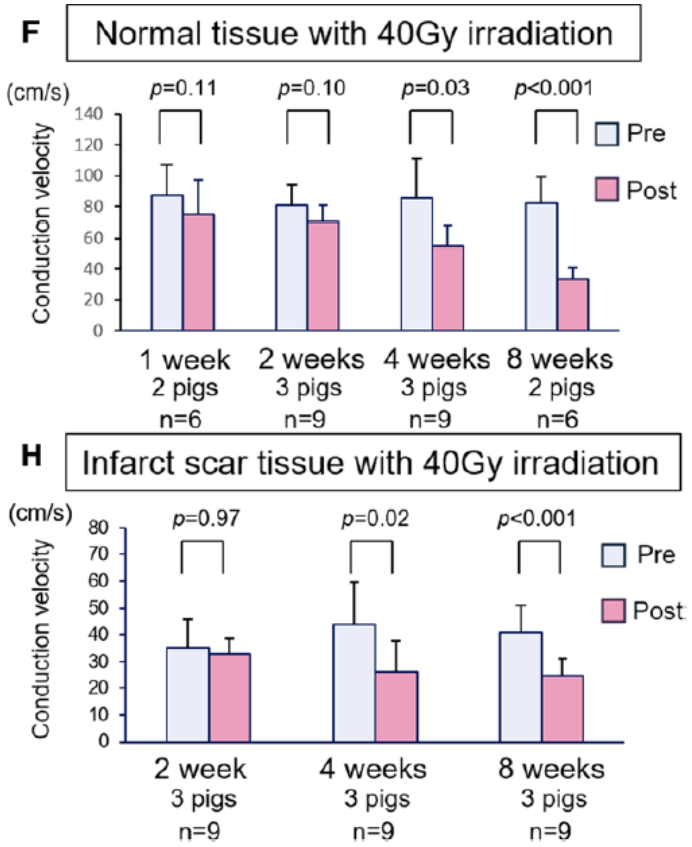
Normal heart
Infarcted heart
Reperfusion model

1, 2, 4, 8 weeks

Bipolar voltage mapping



Conduction velocity

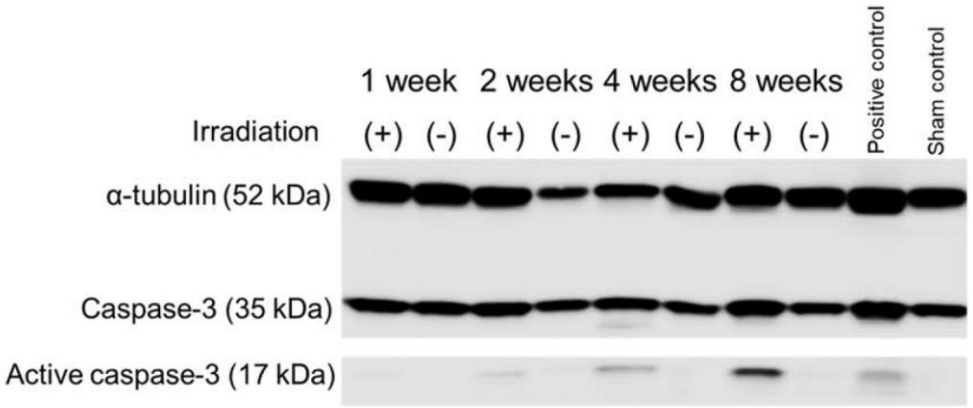


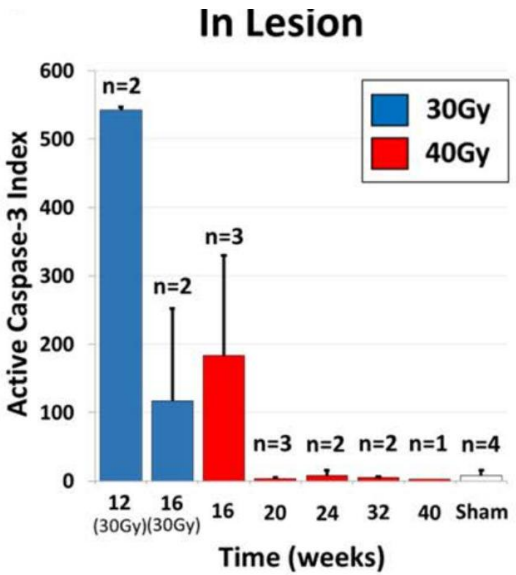
Cha M-J, J Am Heart Assoc. 2021;10

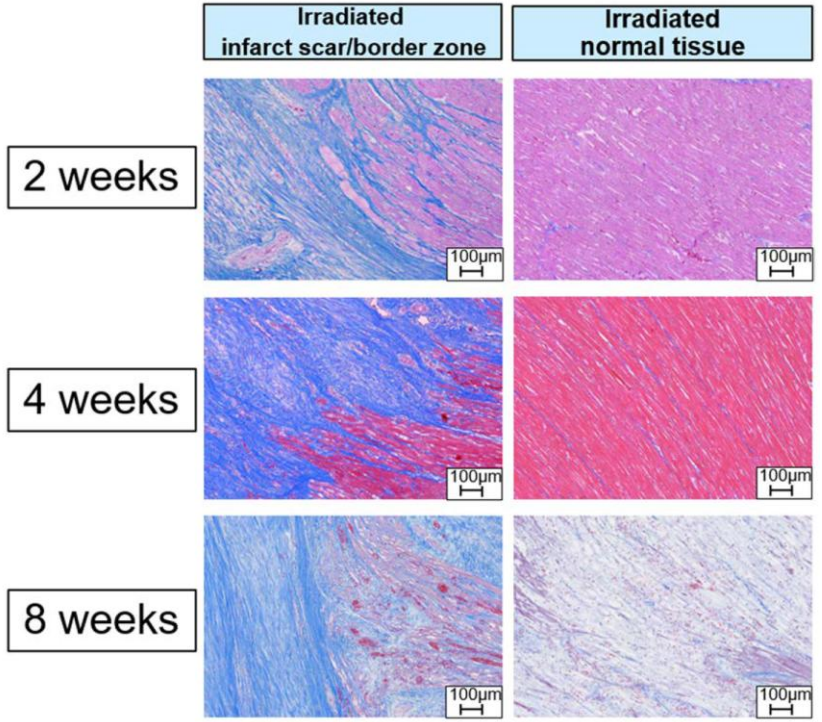
WECAM

Early effects of 40 Gy proton beam area irradiation
Apoptose and histological changes

Normal heart
Infarcted heart
Reperfusion model

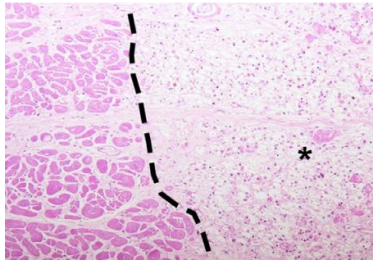






Suzuki et al CircAE 2020;13

Patient with a non-ischemic cardiomyopathy
Irradiation lateral wall
Death 12 weeks after STAR



Cha M-J, J Am Heart Assoc. 2021;10

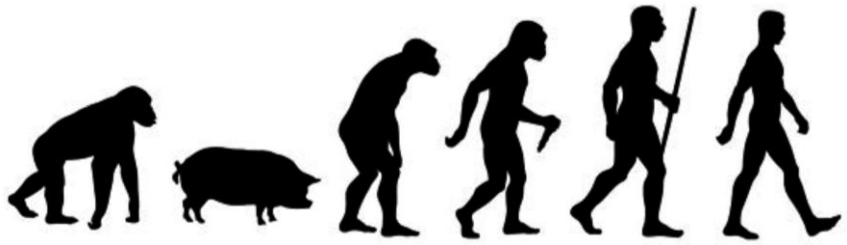
Conclusions: Too early for prime time!

No complete elimination of the target

Delayed time to effect

Delayed adverse events and unclear impact on heart failure

Necessary work needs to be done selecting the best animal model!



Patient selection, ventricular tachycardia substrate delineation, and data transfer for stereotactic arrhythmia radioablation: a clinical consensus statement of the European Heart Rhythm Association of the European Society of Cardiology and the Heart Rhythm Society

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Patient selection, monitoring, and safety	Strength of evidence
Advised TO DO	
It is advised to consider STAR in the context of an approved investigational trial for patients with VT refractory to AAD (due to recurrence, intolerance, or contraindications) and RFCA performed in an expert centre.	
It is appropriate to discuss all patients considered for STAR with a multi-disciplinary team, including an electrophysiologist highly experienced in the invasive treatment of VA, a radiation oncologist, a heart failure specialist, a specialist in cardiac imaging, and a cardiac surgeon (for treatment alternatives and options in case of deterioration of cardiac function).