CLINICAL EVIDENCE

The published record

Two bodies of evidence, in date order. One where the heart is the target. One where it is the organ to protect. Both end at the same open problem. The heart moves.

TARGET FIRST BODY OF EVIDENCE

From a catheter tip inside the heart to a gated beam outside it. The record below is how the heart became a target you can hit without touching it.

How CardioKit treats the target →

TARGET 02 / 1979–2019

The catheter era.

The therapy radioablation is measured against, and the patients it leaves behind.

1979

An accident

Vedel and colleagues report complete heart block after repeated DC cardioversion with a recording catheter at the bundle of His. Current ran down the catheter and destroyed conduction tissue. Nobody meant to ablate anything.

1981
TREATED · 1982

First deliberate catheter ablation

Scheinman (UCSF) ablates the AV junction on purpose with high-energy DC shocks. First reported series: nine patients.

1987

Radiofrequency replaces DC

DC arcs and causes barotrauma. Borggrefe interrupts an accessory pathway with RF energy. The technique still used today.

1998

Ablation goes mainstream

Haïssaguerre finds the pulmonary-vein triggers of atrial fibrillation. Marchlinski (2000) maps and ablates ventricular scar substrate. Catheter ablation becomes routine cardiology.

2007–2016

The randomised trials, and the ceiling

SMASH-VT, VTACH and VANISH show catheter ablation beats escalated drugs for ventricular tachycardia. Recurrence stays high. Patients with advanced heart failure tolerate the procedure worst.

2019

Consensus, and an admitted gap

HRS/EHRA/APHRS/LAHRS expert consensus on catheter ablation of ventricular arrhythmias. Refractory VT after failed ablation is named as an unmet need.

Consensus statement ↗ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7508755/

TARGET 03 / 2010–2022

Proof in animals.

Can a beam do what a catheter tip does? Yes. The dose that does it was measured before any patient was treated.

2010

First noninvasive cardiac radiosurgery

Sharma isolates pulmonary veins in swine with a CyberKnife. Photons, no catheter, conduction block achieved.

DEC 2016

Carbon ions interrupt conduction

Lehmann irradiates the AV junction, PV junction and LV free wall in intact pigs at 25, 40 and 55 Gy, in **forced breath-hold**. 40–55 Gy slows, then interrupts, impulse propagation. Fibrosis is the mediator. First particle-beam cardiac ablation data.

Sci Rep 6:38895 ↗ https://www.nature.com/articles/srep38895

2017

Immobilisation becomes its own problem

A dedicated porcine study on holding cardiac structures still enough for carbon-ion ablation. The beam is ready before the motion answer is.

PubMed 29195556 ↗ https://pubmed.ncbi.nlm.nih.gov/29195556/

2021

Catheter-free ablation with scanned protons

Lehmann shows pencil-beam scanned protons producing the same targeted lesions in pigs. The modality with a Bragg peak, so no exit dose.

Circ Arrhythm Electrophysiol ↗ https://www.ahajournals.org/doi/10.1161/CIRCEP.120.008838

2022

What the dose does electrically

Porcine work characterises the early electrophysiological effect of proton irradiation. Conduction changes before transmural fibrosis appears.

Circ Arrhythm Electrophysiol ↗ https://www.ahajournals.org/doi/abs/10.1161/CIRCEP.122.011179

TARGET 04 / 2012–2026

Photons, in patients.

STAR, stereotactic arrhythmia radioablation. One outpatient session, 25 Gy, no anesthesia. The clinical proof the field rests on.

2012 TREATED · 2015

First human treated

Loo (Stanford) treats refractory VT with a CyberKnife at 25 Gy, tracking an implanted fiducial. Case report published three years later.

14 DEC 2017

The landmark: Cuculich, NEJM

Five patients. Single 25 Gy fraction on a standard linac, target defined by noninvasive ECG imaging. VT burden across the group fell by orders of magnitude. Motion handled by a **free-breathing internal target volume**. Margin, not tracking.

N Engl J Med 377:2325 ↗ https://www.nejm.org/doi/full/10.1056/NEJMoa1613773

JAN 2019

ENCORE-VT, the first prospective trial

Robinson, Circulation. 19 patients, phase I/II, 25 Gy. Confirms the burden reduction and gives the field a reproducible protocol.

Circulation 139:313 ↗ https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.038261

2019–2021

It travels

Prague (Neuwirth), a US multicenter series (Lloyd) and single-center cohorts across Europe reproduce the effect outside the originating institution.

MAR 2023

STOPSTORM.eu: Europe standardises

A multidisciplinary consortium publishes a shared treatment and outcome platform, plus a survey of how differently STAR was being delivered.

Europace 25:1284 ↗ https://academic.oup.com/europace/article/25/4/1284/7069964

13 MAR 2023 →

RADIATE-VT, the pivotal randomised trial

Cardiac radioablation versus repeat catheter ablation, 1:1, in high-risk refractory VT with LVEF ≤ 49 %. Primary completion estimated May 2026, final 2030. The trial that decides whether beams enter the standard of care.

NCT05765175 ↗ https://clinicaltrials.gov/study/NCT05765175

2024–2025

Society backing

STOPSTORM publishes a systematic review and meta-analysis of the prospective trials. EHRA and HRS issue a clinical consensus statement on patient selection, substrate delineation and data transfer for STAR.

EHRA/HRS consensus ↗ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC12041921/

2025

Three-year outcomes

STAR versus repeat catheter ablation, safety and efficacy at three years. The first medium-term comparison against the incumbent.

Int J Radiat Oncol Biol Phys ↗ https://www.redjournal.org/article/S0360-3016(25)06223-6/fulltext

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TARGET 05 / 2021–2026

Particle beams, in patients.

A proton beam stops. Nothing downstream of the target gets dose. Which is exactly why the target has to be where the plan said.

JAN 2021

First-in-man proton radiotherapy for VT

Dusi, Eur J Heart Fail. A single proton session at CNAO Pavia in advanced heart failure. Well tolerated. Near-immediate VT suppression, then a sustained fall in episodes.

Eur J Heart Fail 23:195 ↗ https://onlinelibrary.wiley.com/doi/full/10.1002/ejhf.2056

2022–2025

Protons versus photons, on paper

In-silico and dosimetric comparisons, including the Italian CARA-VT cohort, show protons cutting dose to lung, esophagus and healthy myocardium. They also flag interplay with cardiorespiratory motion as the catch. CNAO separately confirms early cardiac safety of carbon ions near the heart.

OCT 2024

First patients in a proton trial

Mayo Clinic (Rochester) announces the first patients treated in its early feasibility study of catheter-free proton cardiac radioablation.

Mayo Clinic announcement ↗ https://www.eurekalert.org/news-releases/1062436

26 APR 2026

The proton result

Late-breaker at Heart Rhythm Society, published in Heart Rhythm. 7 patients, mean age 68, single fraction **30 Gy** intensity-modulated proton therapy through 2–3 beams. VT events fell **7.24 → 1.52 per patient-month**, a **79 % reduction**, with no probable or definite treatment-related serious adverse events out to two years.

Delivered expiration-gated, through all phases of the cardiac cycle. Breathing was gated. The beating was not.

Heart Rhythm ↗ https://www.heartrhythmjournal.com/article/S1547-5271(26)02271-X/abstract

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TARGET 06 / 2014–2026

The motion thread.

The same story, told through one question: where is the target, right now? Highlighted rows are EBAMed's own steps.

2014

Motion named as the problem

Ipsen and Blanck, Med Phys: real-time MRI target localisation for cardiac radiosurgery. The first paper to treat cardiac motion as the thing standing between the beam and the substrate.

2016–2017

Answer one: hold still

Forced breath-hold in the carbon-ion pig work. Dedicated immobilisation studies. Removes breathing. Does nothing about the heartbeat.

DEC 2017

Answer two: irradiate everywhere it goes

Cuculich's free-breathing ITV. Safe and simple. It also means healthy myocardium inside the margin takes the full ablative dose.

2018

EBAMED

Founded in Geneva

Adriano Garonna, technical director of the TERA Foundation from 2016 to 2018, co-founds EBAMed, External Beam Ablation, with Ugo Amaldi (CERN, founder of TERA and CNAO), Giovanni Leo and Douglas Packer (Mayo Clinic). The thesis: image the heart itself, in real time, and let the beam wait for it. A CHF 1.2 M seed round follows in 2019, then the Mayo Clinic Business Accelerator and a €2.4 M EIC Accelerator grant in 2020.

CERN Courier ↗ https://cerncourier.com/a/beating-cardiac-arrhythmia/ · EBAMed news ↗ https://eba-med.com/news/

FEB 2020

Answer three: watch it, but not the heart

Mayinger performs the first MR-guided cardiac radioablation. The implanted defibrillator blanks the heart on cine-MRI, so gating tracks the liver dome instead. A respiratory surrogate, not the target.

Radiother Oncol 152:203 ↗ https://pubmed.ncbi.nlm.nih.gov/32067819/

16 JUL 2021

EBAMED

First patient enrolled

Prospective imaging study opens at Policlinico San Matteo, Pavia. Can transthoracic ultrasound see the beating heart well enough, in real VT patients, to steer a proton beam?

2022

EBAMED

Automatic acquisition and tracking

Front Cardiovasc Med: an automatic ultrasound acquisition system with an AI algorithm, monitoring cardiac motion in real time during radioablation. Paired with a treatment-planning case report showing transthoracic ultrasound guiding proton VT ablation.

Front Cardiovasc Med ↗ https://www.frontiersin.org/journals/cardiovascular-medicine/articles/10.3389/fcvm.2022.849234/full · planning case report ↗ https://pubmed.ncbi.nlm.nih.gov/35600462/

FEB 2022

Both motions at once, on a bench

Akdag, Phys Med Biol: first experimental cardiorespiratory motion management for STAR on an MR-linac. The cardiac component gates the beam, the respiratory component drives MLC tracking.

Phys Med Biol ↗ https://iopscience.iop.org/article/10.1088/1361-6560/ac5717

2023

EBAMED

Demonstrator in the clinic

Prospective cardiac ultrasound imaging study with the demonstrator system (NCT05850741). The tracking hardware and algorithm, on patients, in the room.

NCT05850741 ↗ https://clinicaltrials.gov/study/NCT05850741

2024

EBAMED

Cardiorespiratory-gated proton delivery

Clin Transl Radiat Oncol: cardiac proton radiotherapy gated on both breathing and heartbeat, using the ultrasound guidance system. The gate opens where diastole meets end-expiration.

Clin Transl Radiat Oncol ↗ https://www.ctro.science/article/S2405-6308(24)00181-2/fulltext

MAR 2024

Cardiac-physiology gating, demonstrated

MR-linac gating driven by cardiac physiology rather than an external surrogate. Followed in 2025 by work quantifying how much implanted-device artifact costs on cine-MRI.

Phys Med Biol ↗ https://pubmed.ncbi.nlm.nih.gov/38477841/

2025

EBAMED

Into the treatment plan

J Appl Clin Med Phys: ultrasound-guided motion management integrated into proton treatment plans for VT radioablation. The gate stops being an add-on and becomes part of the dose calculation. Large-animal gated proton ablation under CardioKit guidance, with Mayo Clinic, runs in parallel.

J Appl Clin Med Phys ↗ https://aapm.onlinelibrary.wiley.com/doi/10.1002/acm2.70213 · large-animal study ↗ https://www.sciencedirect.com/science/article/pii/S0360301625035357

26 APR 2026

Where the gap sits today

The first proton VT trial reports a 79 % reduction in events, delivered **expiration-gated, across all cardiac phases**. Breathing is solved in the clinic. The heartbeat, on a beam that stops inside the patient, is the open one. That is the gap CardioKit is built for.

NEXT

EBAMED

First-in-human

First-in-human trials at clinical partner centers, funded by the 2023 Series A. The full chain, ultrasound tracking, dual gate and proton beam, on patients.

TARGET 07 / OTHER CARDIAC TARGETS

Beyond arrhythmia.

Two more indications where the heart itself is the target, and the record is young.

2024

Cardiac and paracardiac tumors with carbon ions

CNAO reports early cardiac safety of carbon-ion radiotherapy for intra- and paracardiac tumors. A beam that stops inside the patient, on a target that moves with the heart wall.

PubMed 39212688 ↗ https://pubmed.ncbi.nlm.nih.gov/39212688/

2020S

Septal reduction in obstructive hypertrophic cardiomyopathy

First reports of stereotactic radiation to the basal septum as a non-invasive alternative to surgical myectomy and alcohol septal ablation. The target sits millimetres from the conduction system. The case for tracking is the same as for VT.

TARGET 08 / WHERE IT STANDS

What the STAR literature says.

88

STUDIES PUBLISHED 2015–2025

7

CLINICAL TRIALS IN THE 2026 POOLED ANALYSIS

1

OUTPATIENT SESSION PER PATIENT

VT burden falls markedly in patients who had exhausted conventional therapy, and ejection fraction holds: no significant LVEF impairment on meta-analysis.

The population is a very sick one: pooled mortality is 16 % at six months, 33 % at twelve. An EHRA/HRS clinical consensus statement is in place.

PROTECT SECOND BODY OF EVIDENCE

From here the heart is no longer the target. It sits next to one. The record below is what a dose to it costs.

How CardioKit protects the heart →

PROTECT 09 / HEART AS THE ORGAN AT RISK

What heart dose costs.

Tumors next to the heart. This record put a price on every gray, and made sparing the heart a planning objective in its own right.

2010

QUANTEC puts numbers on the heart

The QUANTEC review collects dose-volume data for radiation-induced heart disease. Planners get their first consensus constraints for pericarditis and long-term cardiac mortality.

Int J Radiat Oncol Biol Phys ↗ https://pubmed.ncbi.nlm.nih.gov/20171522/

MAR 2013

Breast: 7.4 % per gray

Darby, NEJM. In women irradiated for breast cancer, major coronary events rise linearly with mean heart dose, by 7.4 % per gray. No threshold. The excess begins within the first five years.

N Engl J Med 368:987 ↗ https://www.nejm.org/doi/full/10.1056/NEJMoa1209825

FEB 2015

Lung: heart dose predicts survival

Bradley, Lancet Oncology. RTOG 0617 set out to test dose escalation in stage III lung cancer. The higher-dose arm did worse. Heart dose emerged as an independent predictor of overall survival.

Lancet Oncol 16:187 ↗ https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(14)71207-0/fulltext

2015

Esophagus: the heart in the field

Reviews of chemoradiation for esophageal cancer find cardiac toxicity, pericardial effusion above all, to be common and dose-related. They call for heart-sparing planning in a tumor that lies against the left atrium.

Cancer 121:1101 ↗ https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cncr.29055

2016

Lymphoma: a lifetime of risk

van Nimwegen, J Clin Oncol. In Hodgkin lymphoma survivors, coronary heart disease risk rises with mean heart dose in the same linear way seen in breast cancer. It stays elevated for decades after cure.

J Clin Oncol 34:235 ↗ https://ascopubs.org/doi/10.1200/JCO.2015.63.4444

2010S →

Breath-hold becomes the standard, for those who can

Deep inspiration breath-hold moves the heart down and away from breast and mediastinal fields, and becomes the cardiac-sparing standard. It depends on the patient holding, and holding the same way every time. The heartbeat itself is still covered by margin.

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10 / SOURCES

Every link on this page.

CATHETER ERA

Short history of DC catheter ablation: Vedel 1979, Scheinman 1981/82 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10923988/

Catheter ablation, an encapsulated history: DC to RF, Borggrefe 1987 https://www.researchgate.net/publication/373118551_CATHETER_ABLATION_AN_ENCAPSULATED_HISTORY

History of AF ablation: Haïssaguerre and the pulmonary-vein triggers https://ucsfhealthcardiology.ucsf.edu/history-af-ablation

2019 HRS/EHRA/APHRS/LAHRS expert consensus on catheter ablation of ventricular arrhythmias https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7508755/

PRECLINICAL: BEAMS IN ANIMALS

Lehmann et al., 2016. Cardiac arrhythmia ablation with high-energy heavy ion beams · Sci Rep 6:38895 https://www.nature.com/articles/srep38895

Immobilization for carbon ion beam ablation of cardiac structures in a porcine model, 2017 https://pubmed.ncbi.nlm.nih.gov/29195556/

Catheter-free arrhythmia ablation using scanned proton beams, 2021 · Circ Arrhythm Electrophysiol https://www.ahajournals.org/doi/10.1161/CIRCEP.120.008838

Early impact of proton beam therapy on electrophysiological characteristics in a porcine model, 2022 https://www.ahajournals.org/doi/abs/10.1161/CIRCEP.122.011179

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STOPSTORM.eu consortium, 2023. Standardised platform and European practice survey · Europace 25:1284 https://academic.oup.com/europace/article/25/4/1284/7069964

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Shah et al., 2026. STAR for refractory VT: pooled analysis of outcomes and delivery approaches · J Appl Clin Med Phys https://aapm.onlinelibrary.wiley.com/doi/10.1002/acm2.70622

STAR for VT: clinical trials and the emerging role of imaging · J Radiat Res https://academic.oup.com/jrr/article/66/1/1/7916732

PARTICLE BEAMS: CLINICAL

Dusi et al., 2021. First-in-man noninvasive proton radiotherapy for refractory VT · Eur J Heart Fail 23:195 https://onlinelibrary.wiley.com/doi/full/10.1002/ejhf.2056

Mayo Clinic, Oct 2024. First patients treated with proton beam therapy for VT https://www.eurekalert.org/news-releases/1062436

Early feasibility study of catheter-free proton cardiac radioablation, 2026 · Heart Rhythm https://www.heartrhythmjournal.com/article/S1547-5271(26)02271-X/abstract

HRS 2026 late-breaker, 26 Apr 2026. 79 % reduction in VT episodes, 7 patients https://www.eurekalert.org/news-releases/1125842

Comparison of proton and photon therapy in STAR for ventricular tachycardia https://www.sciencedirect.com/science/article/pii/S2405631625001125

CNAO pilot. Early cardiac safety of carbon-ion radiotherapy for intra- and para-cardiac tumors, 2024 https://pubmed.ncbi.nlm.nih.gov/39212688/

Robustness evaluation of carbon ion radiotherapy for ventricular tachycardia, 2026 https://pubmed.ncbi.nlm.nih.gov/41767109/

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Mayinger et al., 2020. First MRI-guided cardiac radioablation of sustained VT · Radiother Oncol 152:203 https://pubmed.ncbi.nlm.nih.gov/32067819/

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Impact of cardiac implantable electronic devices on cine-MRI for real-time adaptive cardiac radioablation, 2025 · Med Phys https://aapm.onlinelibrary.wiley.com/doi/full/10.1002/mp.17438

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Gagliardi et al., 2010. QUANTEC: radiation dose-volume effects in the heart · Int J Radiat Oncol Biol Phys https://pubmed.ncbi.nlm.nih.gov/20171522/

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Beukema et al., 2015. Is cardiac toxicity a relevant issue in the radiation treatment of esophageal cancer? · Cancer https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cncr.29055

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Automatic ultrasonographic acquisition with an AI algorithm for real-time monitoring of cardiac motion during cardiac radio-ablation, 2022 · Front Cardiovasc Med https://www.frontiersin.org/journals/cardiovascular-medicine/articles/10.3389/fcvm.2022.849234/full

Treatment planning study: transthoracic ultrasound guidance to facilitate VT ablation with protons, 2022 https://pubmed.ncbi.nlm.nih.gov/35600462/

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Figures come from the literature above and from EBAMed program milestones. Dates are publication or event dates unless an entry says otherwise. CardioKit is an investigational device. Clinical-benefit claims are subject to ongoing studies and regulatory review.

NEXT

Investigators and centers: tell us about the cases where the heart is in the way.

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