

Hypofractionated Radiotherapy to the stellate ganglia for ventricular arrhythmia (RADIO STAR) trial

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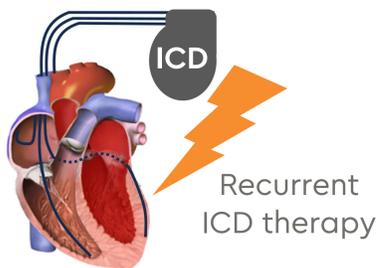
Background

Heart failure is associated with chronic sympathetic activation which is the trigger for life-threatening ventricular arrhythmias (VA)¹. Implantable cardioverter defibrillators (ICDs) save lives by treating VAs but cannot prevent them from occurring. Recurrent ICD shocks lead to worse outcomes and reduced quality of life². Cardiac sympathetic denervation by surgical removal of the stellate ganglia has been shown to be highly successful in preventing VA, but suffers from high rates of peri-operative complications³.

Aims/objectives

To assess whether stellate ganglia modification can safely be achieved non-invasively by ultra-hypofractionated image guided radiotherapy. To determine if non-invasive stellate ganglia modification has a favourable safety profile compared to surgical denervation. To evaluate if non-invasive stellate ganglia modification leads to a reduction in ICD therapies and improved quality of life

Methods



Referral for radiotherapy

MRI guided radiotherapy to the stellate ganglia



Dose escalation
 24 Gy (n=3)
 27 Gy (n=3)
 30 Gy (n=3)
 33 Gy (n=4)

Follow up

6 weeks

3 months

6 months

Screening visit
 Stellate ganglia MRI
 Biomarkers
 Questionnaires

Continuous ICD monitoring

Biomarkers
 Questionnaires

Biomarkers
 Questionnaires

Stellate ganglia MRI
 Biomarkers
 Questionnaires

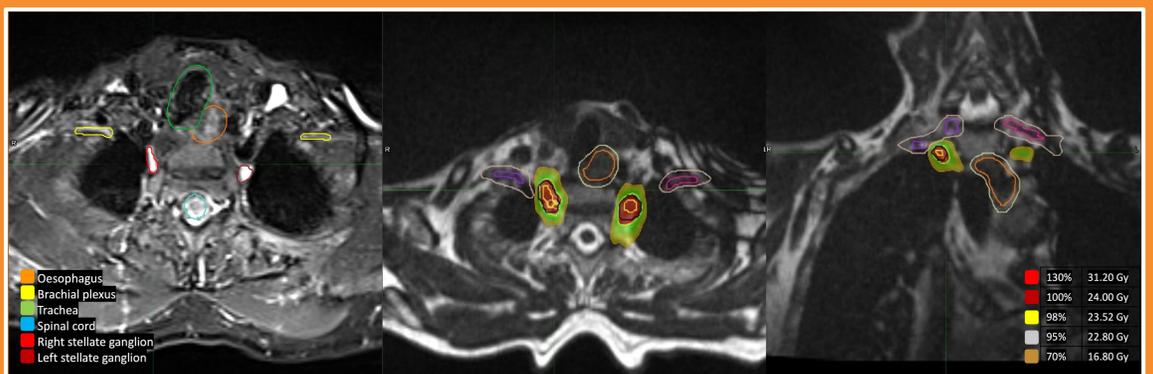
Results

Planning statistics for cohort 1

	Patient A	Patient B	Patient C
PTV_L	3.8 cc	5.0 cc	4.3 cc
PTV_R	3.6 cc	4.1 cc	4.8 cc
PTV	7.4 cc	9.1 cc	9.0 cc
PTV_L V(100%)	90.6%	90.8%	86.1%
PTV_R V(100%)	83.6%	85.5%	86.6%
PTV V(100%)	87.3%	88.4%	86.3%
CTV_L D(98%)	25.8 Gy	23.8 Gy	25.0 Gy
CTV_R D(98%)	23.9 Gy	23.6 Gy	23.9 Gy
PTV D(98%)	22.3 Gy	22.4 Gy	22.6 Gy
PPM PRV D(0.03 cc)	4.7 Gy	2.9 Gy	2.0 Gy

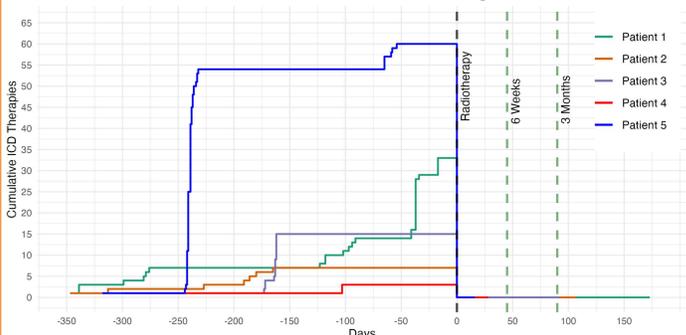
Safety

- No related SAEs
- No neurological symptoms
- No hypotension
- Mild fatigue



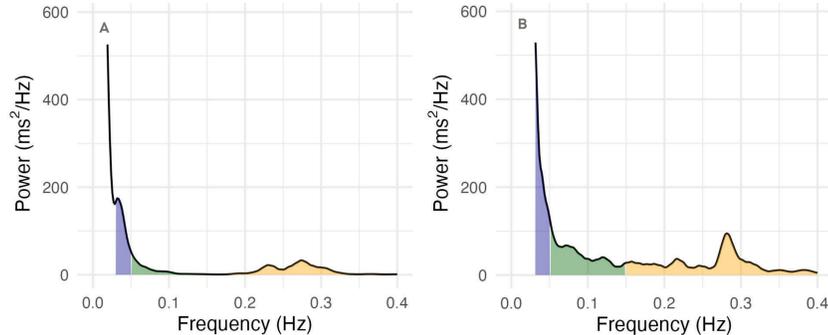
A: Diagnostic 1.5T T2 STIR of a participant with a left sided CRT-D device. Planning target volumes are contoured over the stellate ganglia and key dose-limiting organs. B and C: 0.35T BSSFP (Trufi) planning images from the MR-Linac Heterogeneous dose distributions planned, with a maximum dose of 120% and PTV coverage compromised to ensure that OAR dose constraints^[5,6] and ICD tolerance^[7] are adhered to (minimum acceptable 75%). Planning organ at risk volumes created for critical adjacent structures (brachial plexus (purple) and oesophagus (orange)).

Cumulative ICD therapies



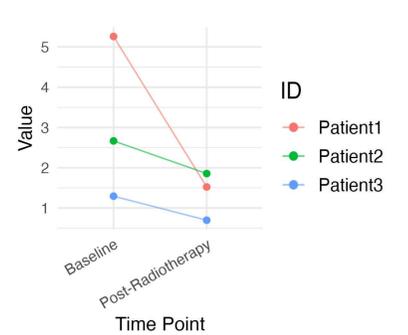
No ICD therapies administered following radiotherapy.

Power spectral density (PSD)



Power spectral density before (A) and after (B) radiotherapy. Power Spectral Density increases after radiotherapy, with relatively higher parasympathetic nervous system activity (HF), than sympathetic activity (LF).

LF:HF ratio



Ratio of sympathetic to parasympathetic activity LF/HF reduces after radiotherapy suggestive of improved autonomic balance

Conclusion

Radiotherapy to the stellate ganglia is feasible and safe. Early results suggest this is effective at preventing VAs in patient with previously refractory VAs.

References

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- Poole JE, Johnson GW, Hellkamp AS, Anderson J, Callans DJ, Raitt MH, Reddy RK, Marchlinski FE, Yee R, Guarnieri T, Talajic M. Prognostic importance of defibrillator shocks in patients with heart failure. *New England Journal of Medicine*. 2008 Sep 4;359(10):1009-17.
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