Ultra-hypofractionated radiotherapy to the stellate ganglia for ventricular arrhythmia using MR-guided radiotherapy

Pre-trial commissioning

Dr Ben George

Principal Physicist for MR-Linac Service Development

GenesisCare UK

British Heart Foundation

NHS Oxford University Hospitals NHS Foundation Trust

University of Oxford

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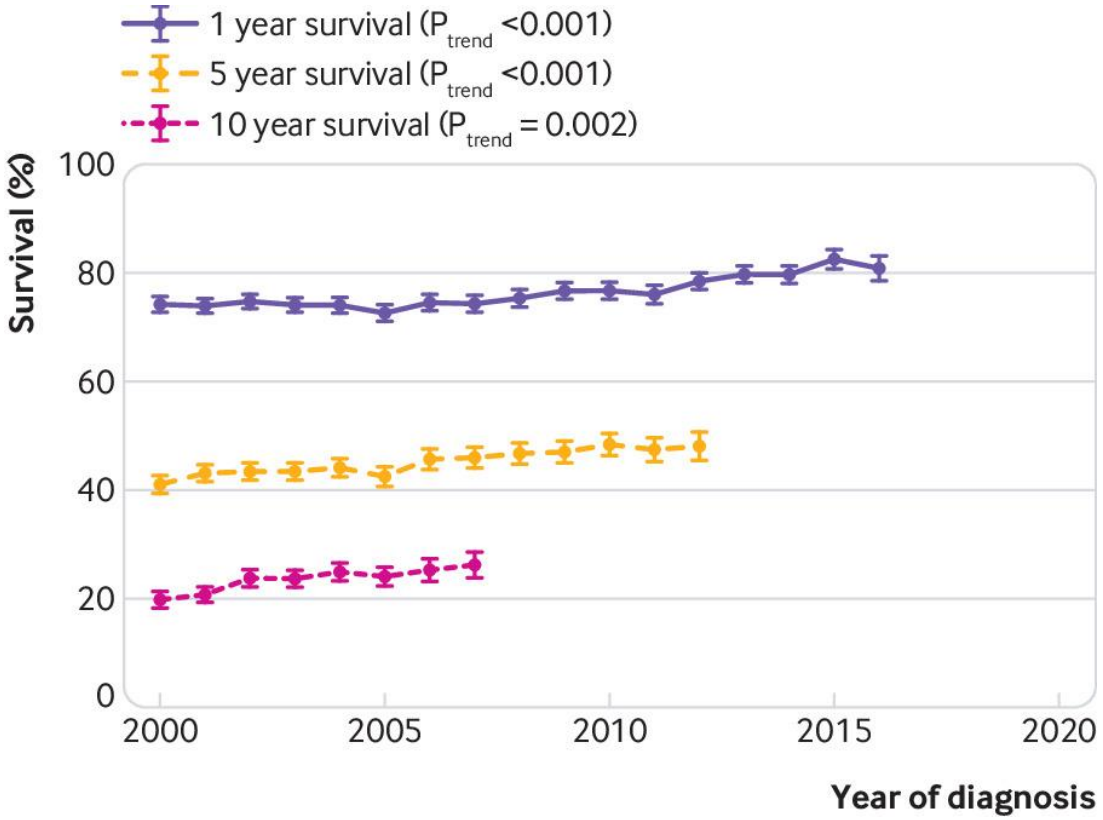
Ventricular arrhythmia

- Over 1 million people living with heart failure in UK
  - 200,000 new diagnoses per year
  - Survival after diagnosis has steadily improved over time
  - 5-year mortally around 50%
- Ventricular arrhythmias are the most common cause of sudden cardiac death
- Most ventricular arrhythmias are triggered by the sympathetic nervous system via the stellate ganglia



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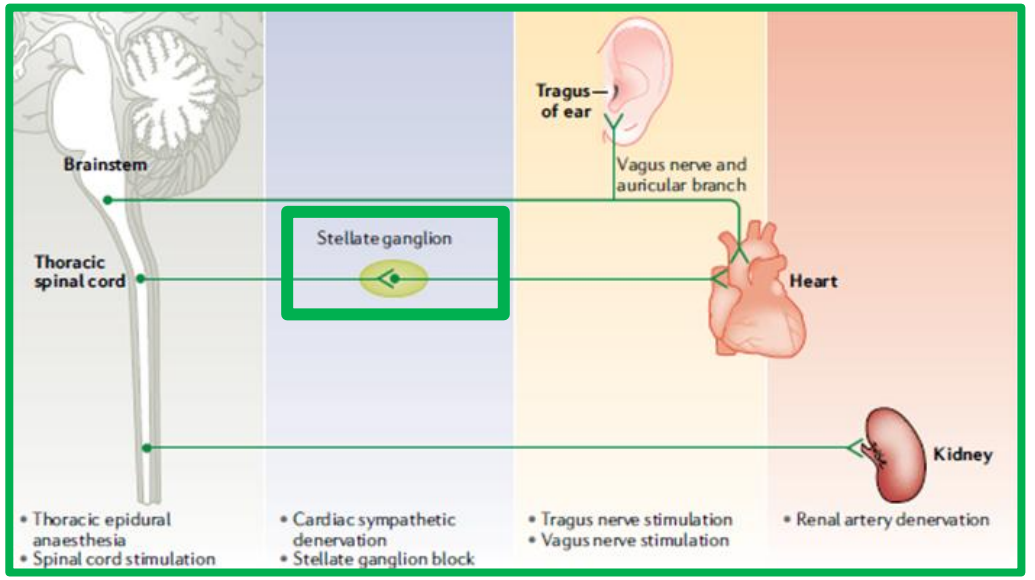
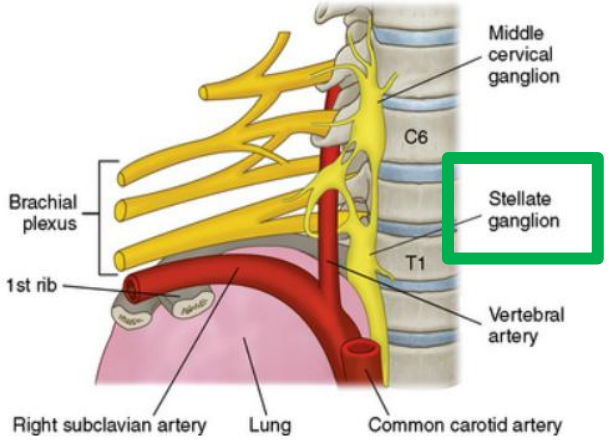
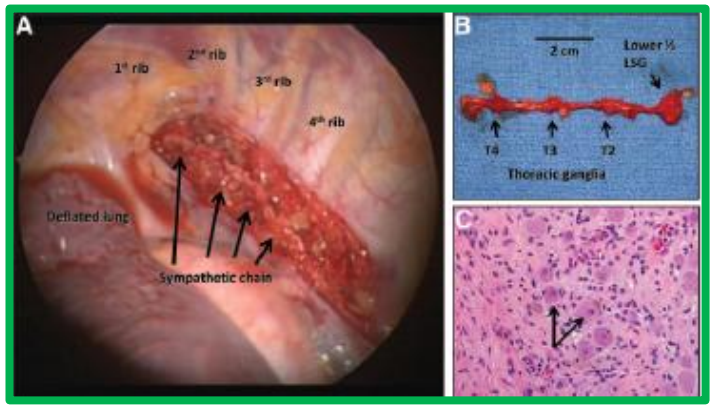
- Shen L, Jhund PS, Petrie MC, Claggett BL, Barlera S, Cleland JG, Dargie HJ, Granger CB, Kjekshus J, Køber L, Latini R. Declining risk of sudden death in heart failure. New England Journal of Medicine. 2017 Jul 6;377(1):41-51..

Stellate ganglion and ventricular arrhythmias

- Stellate ganglion is a cluster of sympathetic nerves either side of the lower neck, above the clavicle
- Part of the sympathetic nervous system, overactivity can contribute to ventricular arrhythmias
- Partial surgical removal of stellate ganglia is an option in some patients with proven benefit
- Whether radiotherapy can be targeted at the stellate ganglia to reduce arrhythmia is unknown







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- https://neupsykey.com/sympathetic-nerve-block-and-neurolysis

RADIO STAR: Magnetic resonance guided stereotactic radiotherapy to the stellate ganglia for ventricular arrhythmia

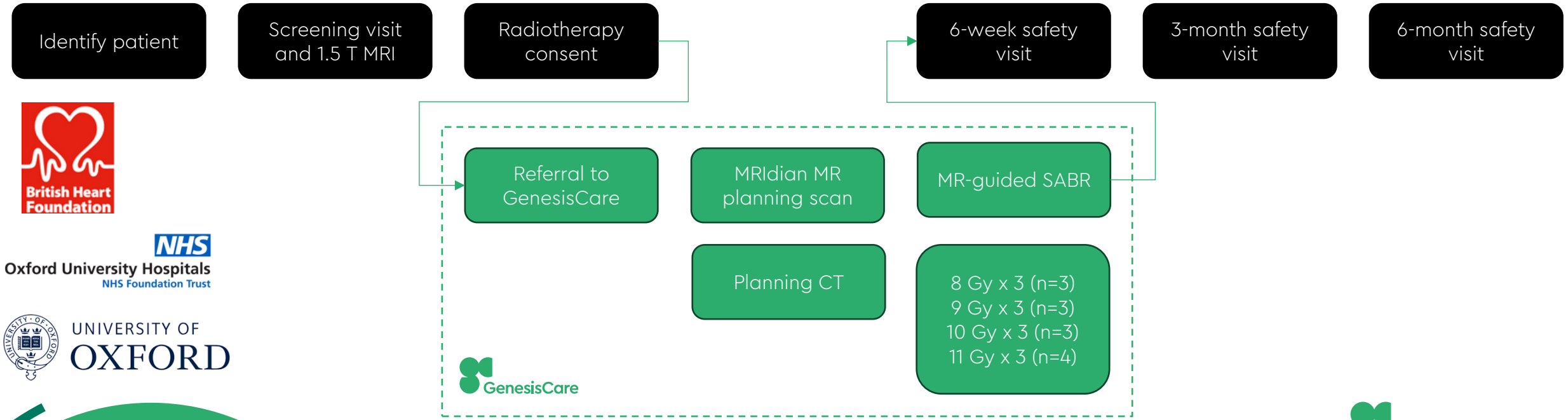
Phase I clinical trial

Primary objective

- Safety of MR-guided radiotherapy to modify the stellate ganglia

Secondary objectives

- Assess anatomical and functional changes (MR, haemodynamic, biomarker levels, VT episodes, PROMs)



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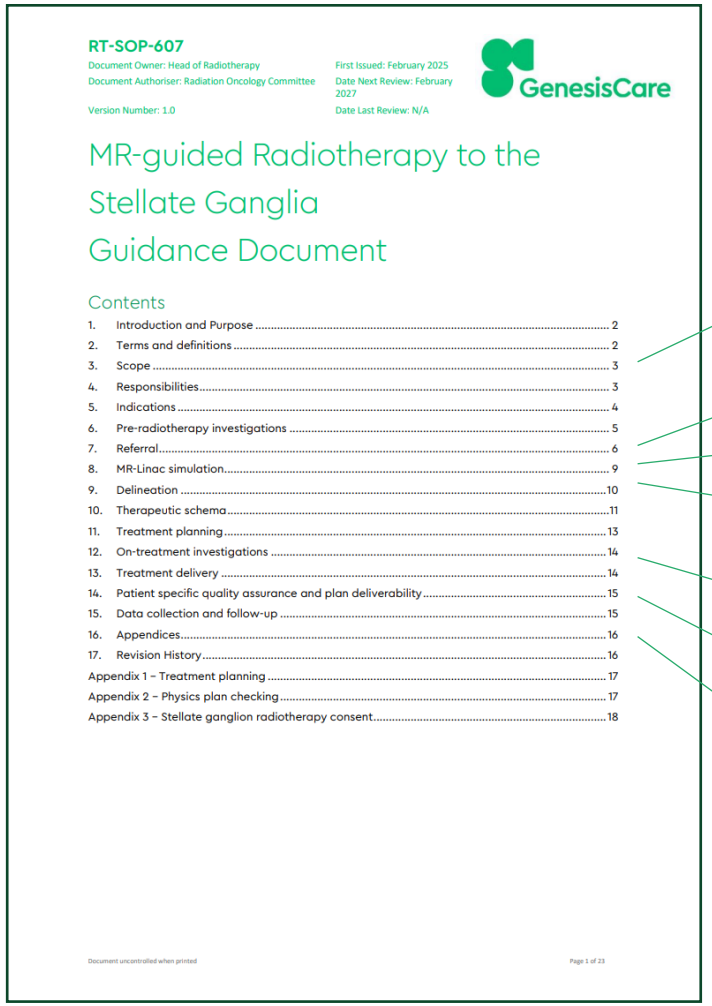
Clinical trial governance

GenesisCare is delivering a service for this trial – IRAS, ethics, etc. sits with the trial sponsor and recruiting site.

Delivering a new clinical service requires approval and governance in place. If GenesisCare were a sponsor, then the IRAS form would provide all the evidence

- Identify lead Practitioner and MPE for implementation within GenesisCare
- Gather minimum trial dataset for review
  - IRAS form, trial protocol, ethics approval, sponsor letter approving opening of trial, funding agreements (as required)
- Review trial protocol and identify any changes in local practice to be implemented
- Create GenesisCare Radiotherapy Guidance document to cover trial activities
  - Highlight deviations from standard practice
  - Identify any additional training requirements
- Training and briefing with local teams
- Go/no-go call with service leads before accepting first referral

Radiotherapy guidance document



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Date Last Review: N/A

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MR-guided Radiotherapy to the Stellate Ganglia Guidance Document

Contents

- Background and trial summary
- Referral process
- Patient immobilisation
- Simulation imaging
- Treatment planning
- Treatment delivery
- Delivery quality assurance

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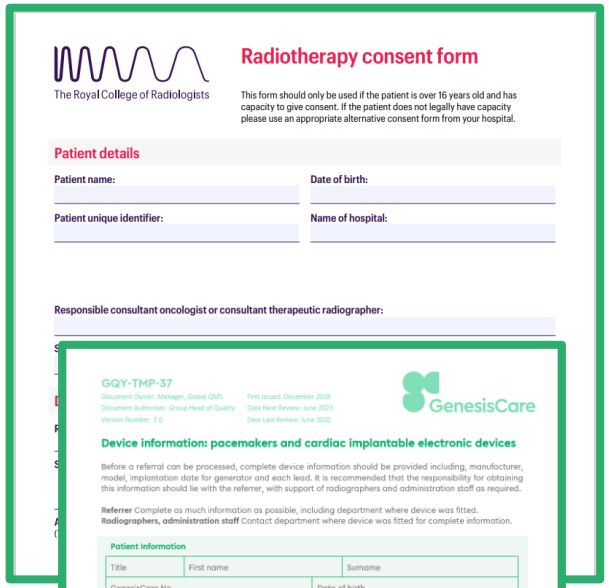
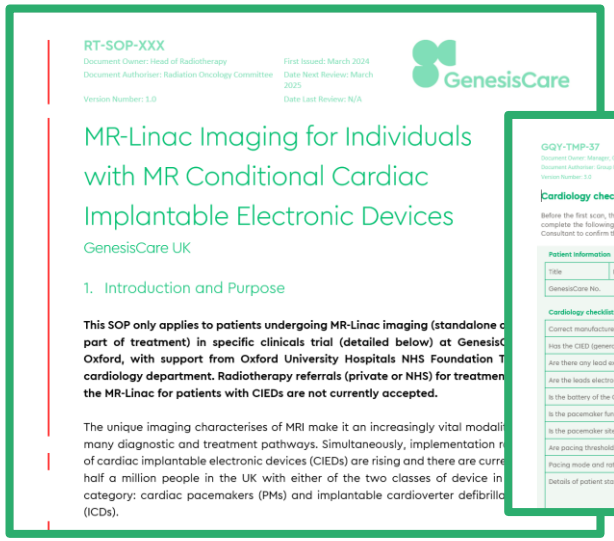
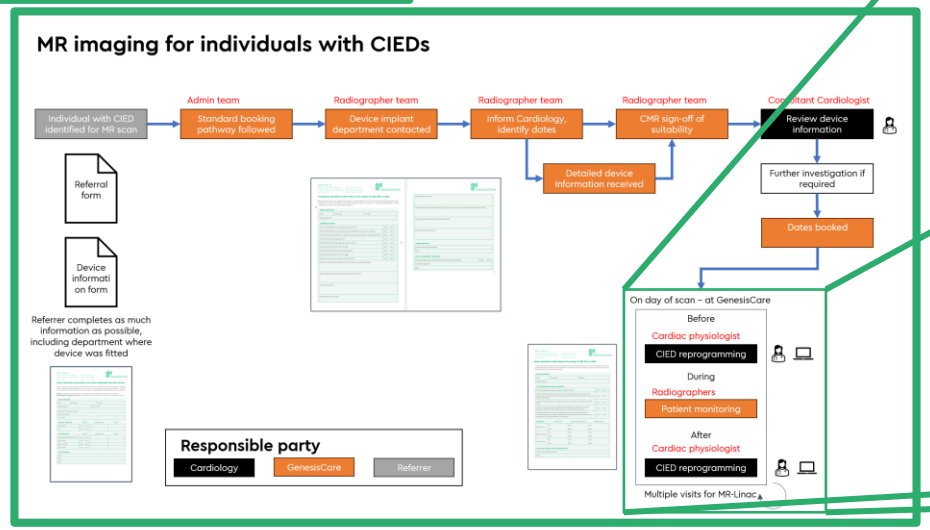
Referral and CIED safety

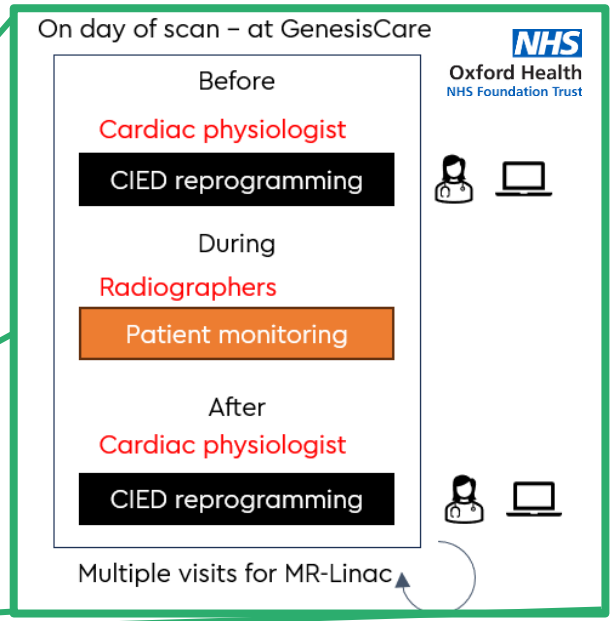


- Radiotherapy consent plus basic device information provided by Practitioner



- Detailed device information requested by GenesisCare team
- Device safety approved by GenesisCare Consultant Cardiologist
- Practical elements of device reprogramming undertaken by research team





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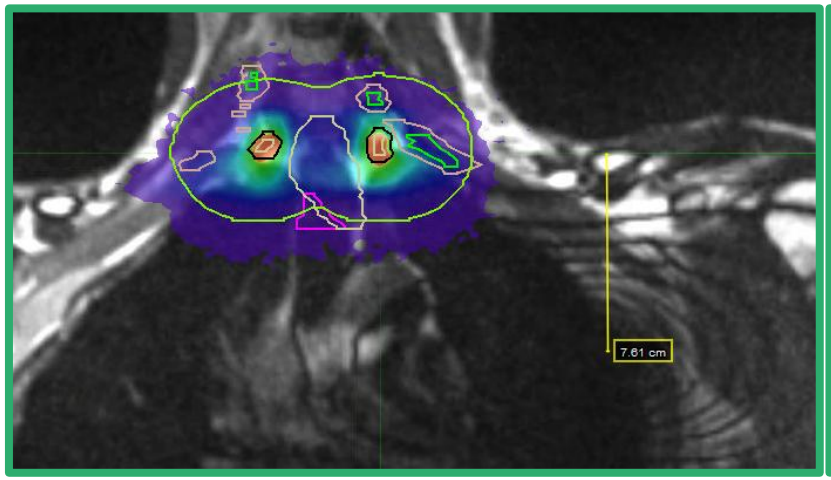
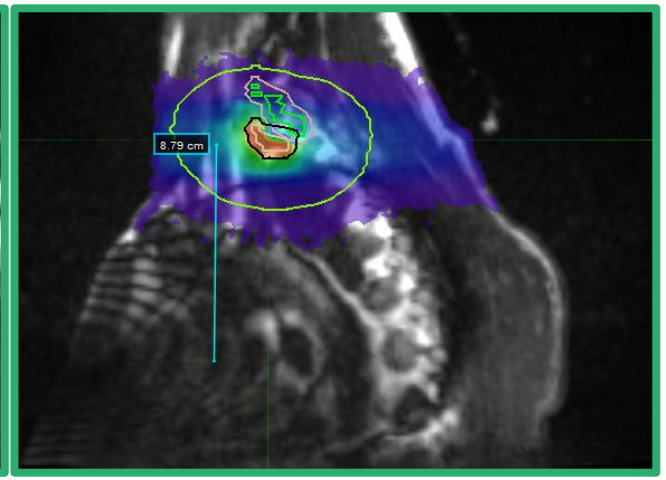
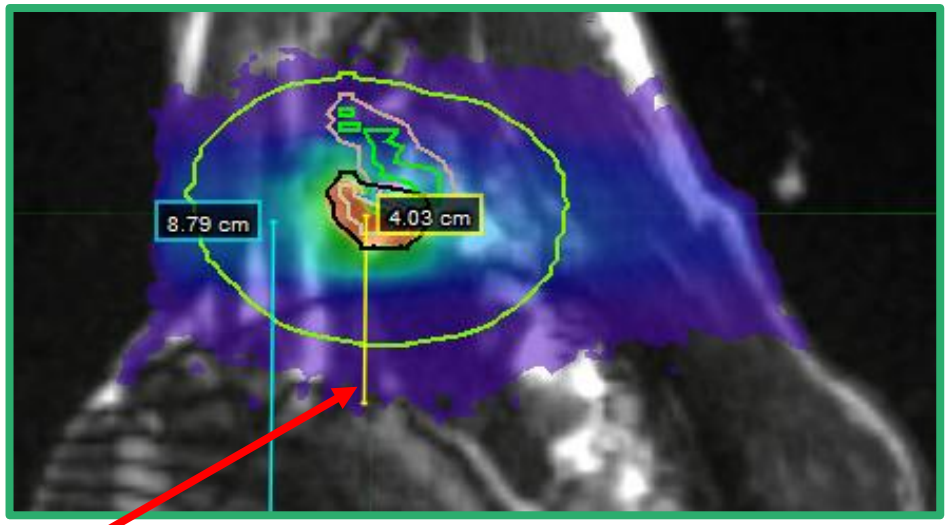
Estimated doses to CIEDs

Dose to CIED must be kept below 5 Gy







Trial setup allows us to exclude patients where we feel CIED positioning may not allow safe treatment planning.

- Safe zone is greater than 4 cm from centre of target region

Patient immobilisation

- MRIdian head and neck coils
- 5-point open-face masks
- Custom-made support for H&N board

5-point open-face masks

In-house developed MR safe support

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Image distortion in the presence of CIEDs

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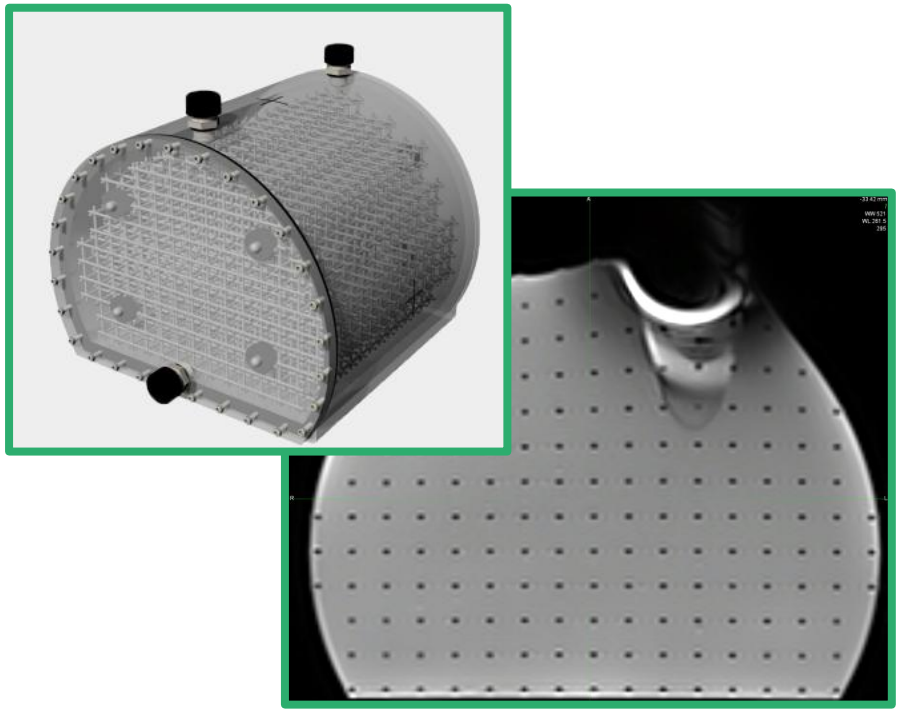
Large Field of View Distortion Phantom
- Acquired on OCMR and MRIdian scanners
- Online analysis software



MRIdian 2D distortion phantom
Part of routine QA programme
- 1 mm within 100 mm radius ✅
- 2 mm within 175 mm radius ✅

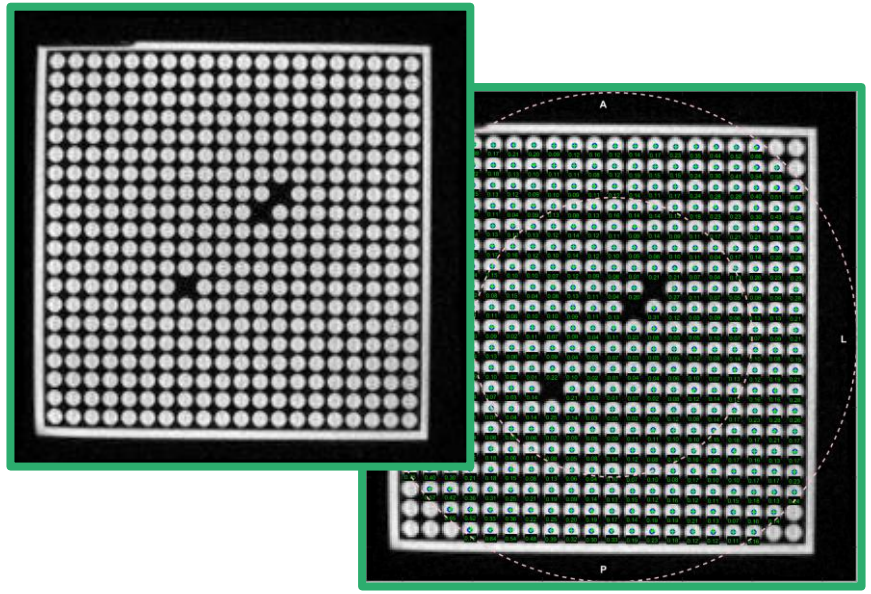


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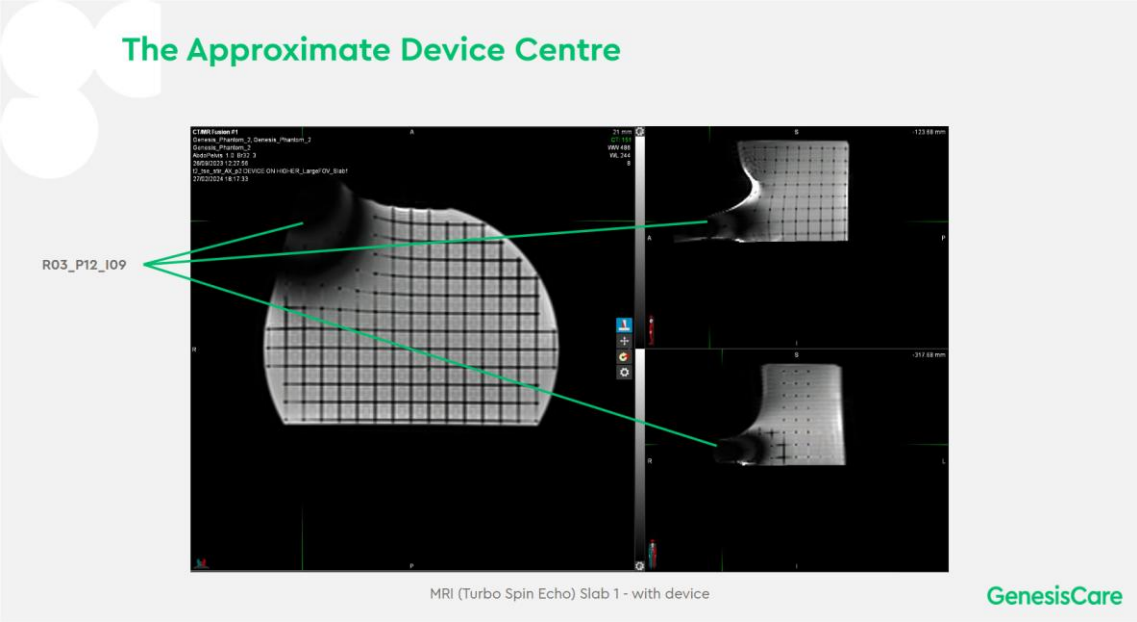
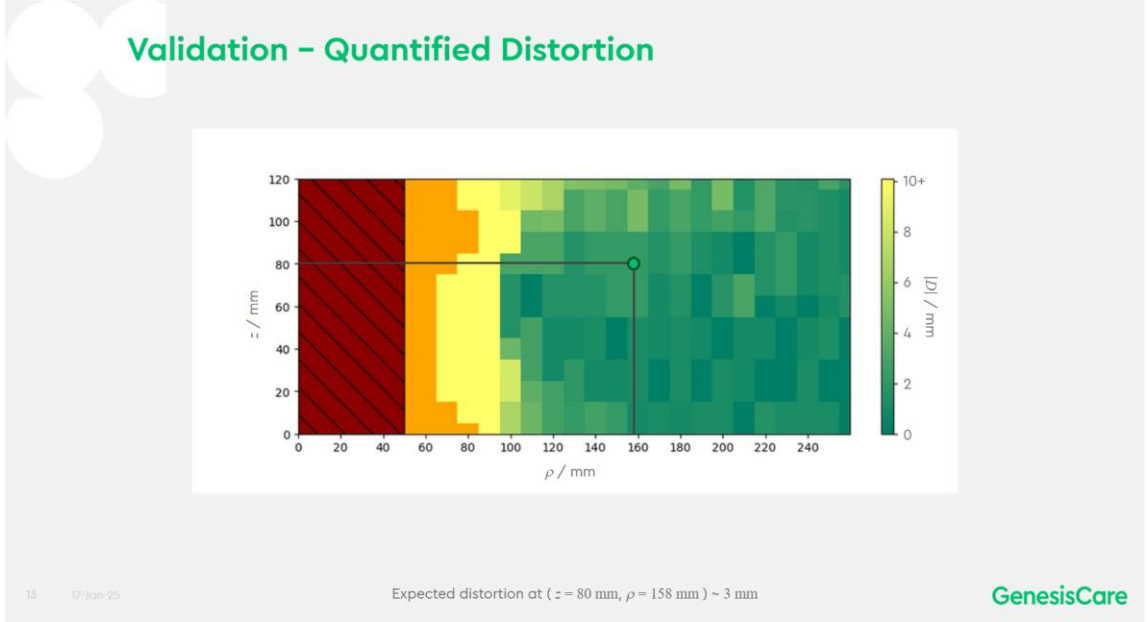
Image distortion in the presence of CIEDs



CIRS Large FOV phantom on 1.5 T scanner. Significant artefact resulted in the processing software being unable to run correctly.



In-house image analysis to assess distortion. Conclusion is that >140 mm from the centre of the artefact, image distortion is not affected.

Volume definition

Treatment target

CTV = sympathetic chain, including lower part of stellate, T1 and T2 ganglia

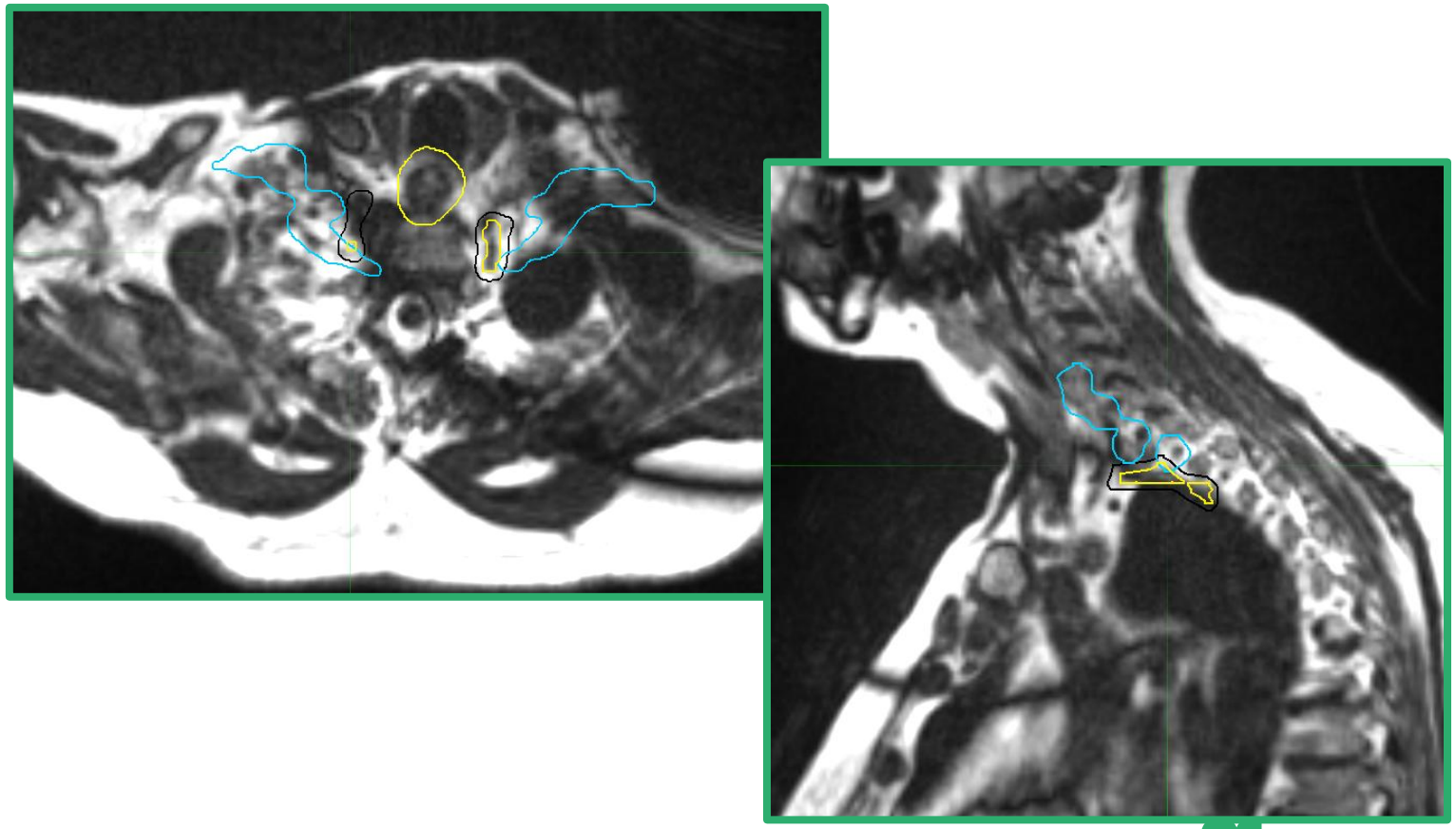
- PTV_right = CTV_right + 3 mm
- PTV_left = CTV_left + 3 mm

- PTV_XX00 = PTV_right + PTV_left

Key organs at risk

- Brachial plexus
- Oesophagus

3 mm PRV on both



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Treatment planning

Dose prescription

- PTV_XX00: V(100%) = 95%

Cohort	Dose per fraction	Number of fractions	Total dose
1	8 Gy	3	24 Gy / 3#
2	9 Gy	3	27 Gy / 3#
3	10 Gy	3	30 Gy / 3#
4	11 Gy	3	33 Gy / 3#

Planning aims

- PTV_R: V(95%) ≥ 75%
- PTV_L: V(95%) ≥ 75%
- PTV_L: 110% < D(0.03 cc) ≤ 120%
- PTV_R: 110% < D(0.03 cc) ≤ 120%

OAR constraints

Dose limiting structures highlighted

Organ at risk		3 fractions	
Brachial plexus PRV	D(0.1 cc)	≤ 24.0 Gy	Mandatory
Chest wall	D(0.1 cc)	≤ 36.9 Gy	Optimal
	D(30.0 cc)	≤ 30.0 Gy	Optimal
Great vessels	D(0.1 cc)	≤ 45.0 Gy	Mandatory
Oesophagus PRV	D(0.1 cc)	≤ 25.2 Gy	Mandatory
Lungs combined	V(20 Gy)	≤ 10%	Optimal
	V(20 Gy)	≤ 15%	Mandatory
Spinal cord PRV	D(0.1 cc)	≤ 20.3 Gy	Mandatory
Skin	D(0.1 cc)	≤ 33.0 Gy	Optimal
	D(10.0 cc)	≤ 30.0 Gy	Optimal
Trachea	D(0.1 cc)	≤ 30 Gy	Mandatory
Carotid artery	D(0.03 cc)	≤ 32.5 Gy	Mandatory
Thyroid lamina	D(0.03 cc)	≤ 30.0 Gy	Mandatory

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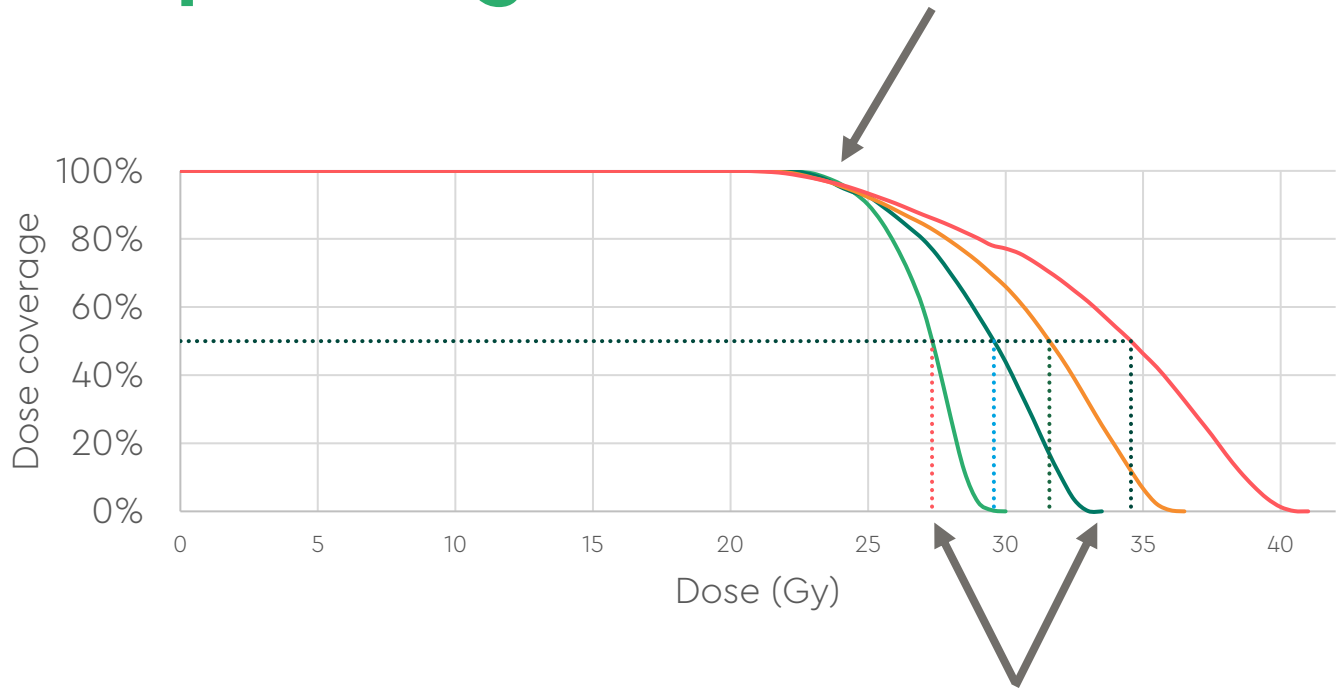
Test planning

Brachial plexus dose constraint limits PTV coverage



Dose level	Key metrics		
	Minimum	Median	Maximum
	D(98%)	D(50%)	D(2%)
24 Gy / 3	23.5 Gy	27.3 Gy	29.2 Gy
27 Gy / 3	23.3 Gy	29.6 Gy	32.7 Gy
30 Gy / 3	23.0 Gy	31.6 Gy	34.6 Gy
33 Gy / 3	22.9 Gy	34.6 Gy	39.9 Gy

Median and maximum dose increases for each dose level

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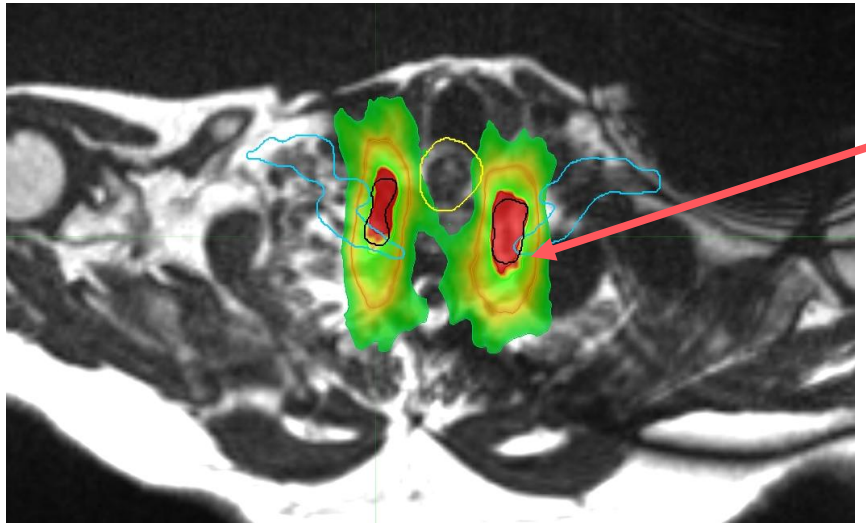
Clinical plans

Study ID	PTV volume	PTV		Pacemaker PRV	Brachial plexus	Oesophagus PRV
		V(100%)	D(98%)	D(0.03 cc)	D(0.1 cc)	D(0.1 cc)
MRAD01	7.4 cc	87.3%	22.3 Gy	4.7 Gy	23.8 Gy	14.8 Gy
MRAD04	9.1 cc	88.4%	22.4 Gy	2.9 Gy	23.8 Gy	16.9 Gy
MRAD08	9.0 cc	86.3%	22.6 Gy	2.0 Gy	23.8 Gy	18.2 Gy



Brachial plexus PRV overlapping PTV, causing compromise of 100% isodose

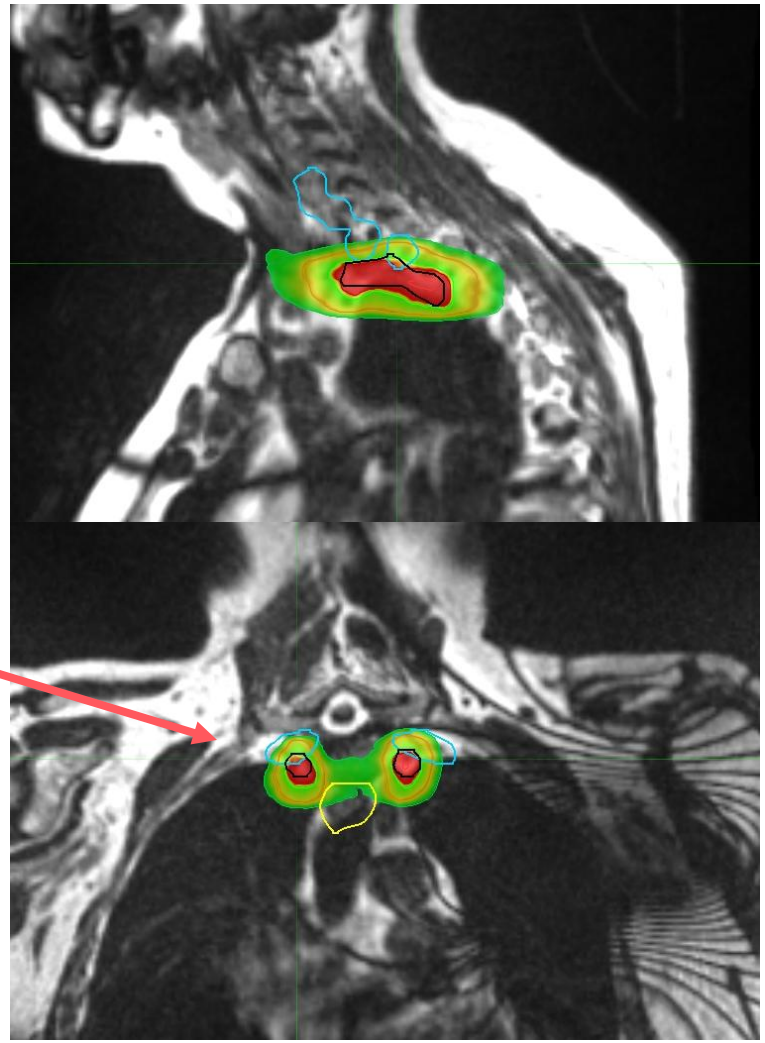
PTV_2400

Brachial plexus PRV

Oesophagus

24 Gy

12 Gy



Progress so far…

80 individual with ICD therapies screened

22 screening failure
- Single ICD therapy - 26
- MRI non-conditional - 9
- Severe comorbidity - 5
- Out of area – 5
- CKD – 3
- Poor engagement - 2
- Inappropriate ICD therapy – 2
- LVEF > 55% - 1

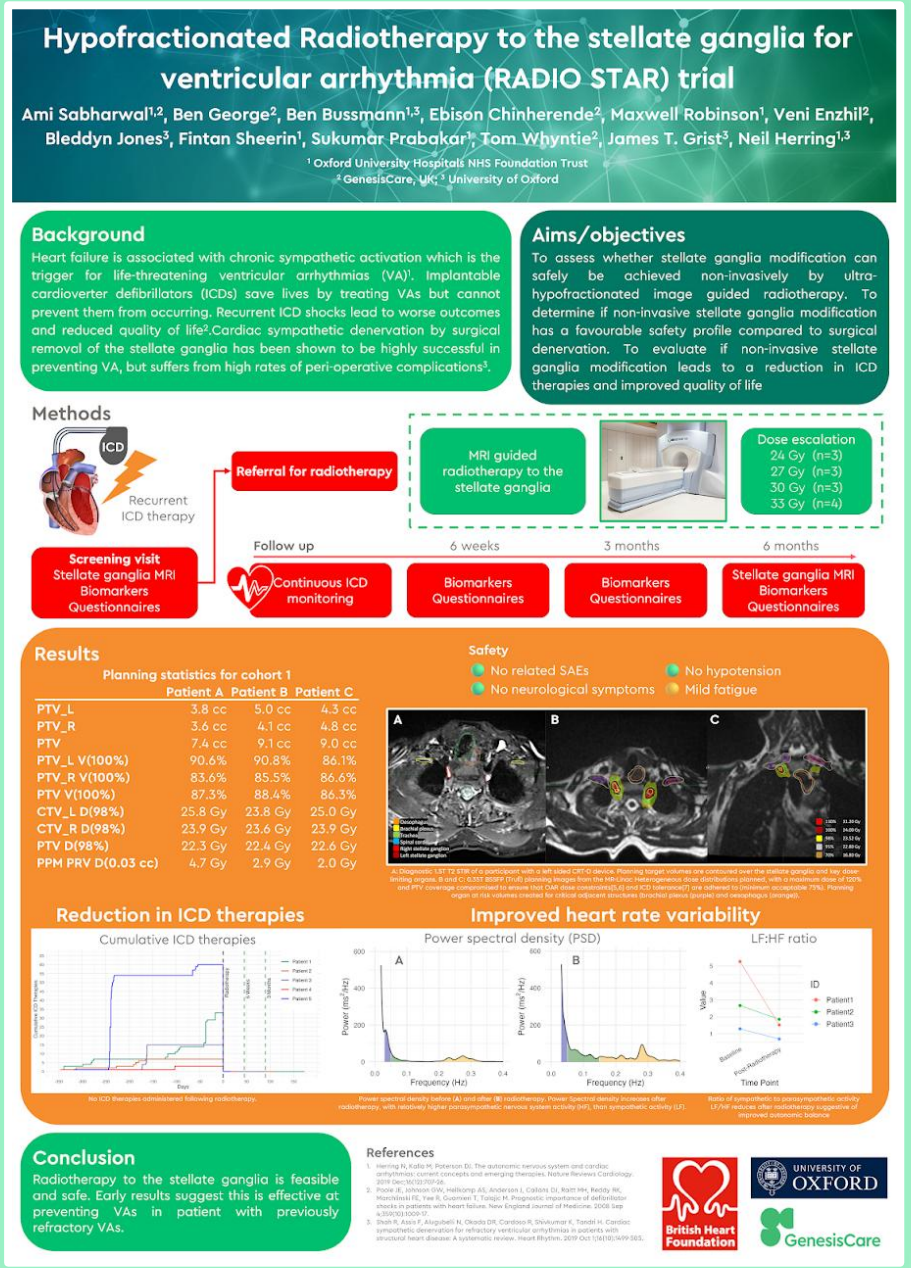
28 Eligible

18 declined

10 enrolled

4 not treated
- Unable to visualise target
- Heart transplant
- Awaiting ICD generator change
- Exceeded 6-month window

5 treated
1 due treatment in December



Research team

Chief Investigator Professor Neil Herring

Co-investigators (Clinical)

- Ami Sabharwal, Ben Bussman, Finn Sheerin, Veni Ezhil

Co-investigators (Physics)

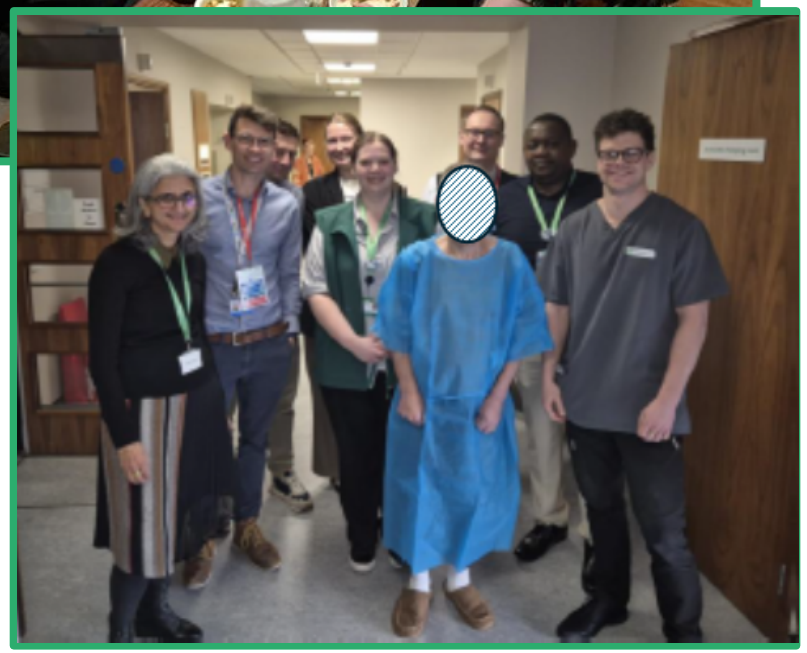
- Maxwell Robinson, Ben George, James Grist, Tom Whyntie

GenesisCare MRIdian team

- Ebison Chinherendre, Joe Drabble

Radiographers

- Nash Malekhi, Emma Jayne McLean, Emmie Rukoni, Alex Goodman, Roxanne Clelland, Sam Bennett



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Thank you for listening!