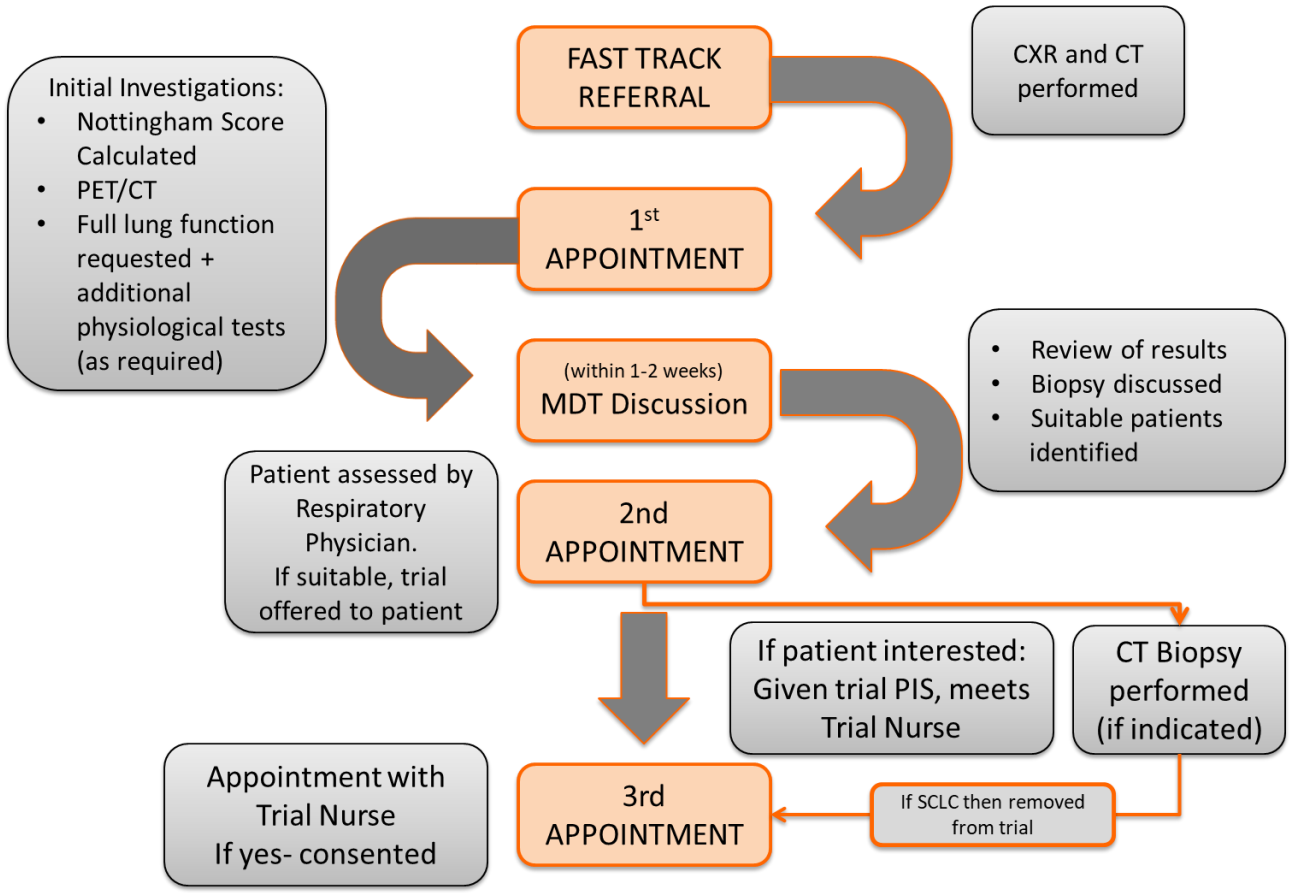
Supplementary Material

1. Qualitative Research

Twelve patients took part in the qualitative interviews; nine who had declined participation and three who declined to take up their randomised allocation to surgery. Overall patients were happy with the way the study was presented to them. Patients described having a clear preference for surgery or SABR and wanted to make their own decision about treatment. Health professionals and people in the patient's network could influence decision-making. Patients suggested that a randomised option would be suitable for people unable to make a decision or for those who lived alone and hence had no one with whom they could discuss their treatment options. Some patients found decision-making difficult, and taking part in the trial was sometimes seen as a third option, adding another layer of complexity to decision making.

Those with a preference for SABR had previous knowledge or experience of SABR. SABR was often chosen by patients who had other multi-morbidities or a poor experience of surgery. Patients who preferred surgery tended to have had previous good experiences or were willing to accept the short-term risks associated with surgery for the chance to discover whether their lymph glands were affected and if the disease had progressed.

2. Recruitment Pathways



3. SABRTooth Radiotherapy Guidelines

A study to determine the feasibility and acceptability of conducting a phase III randomised controlled trial comparing stereotactic Ablative Radiotherapy (**SABR**) with surgery in pa**T**ients with peripheral stage I n**O**n-small cell lung cancer (NSCLC) c**O**nsidered **T**o be at **H**igher risk of complications from surgical resection.

Radiotherapy Guidelines

THIS DOCUMENT SHOULD BE READ IN CONJUNCTION WITH THE SABRTooth PROTOCOL

Sponsor: **Leeds Teaching Hospitals NHS Trust [MO14/11248]**
Funded by: **National Institute for Health Research (NIHR)**
Research for Patient Benefit (RfPB) [PB-PG-0613-31114]

Amendments to RT Guidelines

Version 1.0 - original version

Contents

Foreword

This document describes the QA processes for the SABRTooth trial. When used in conjunction with the main trial protocol it provides all the information necessary for entering patients into the trial.

This document should not be used as a guide for the treatment of patients outside of the **SABRTooth** trial.

Every care has been taken in drafting these guidelines but corrections or amendments may be necessary. These will be circulated to Investigators in the trial, but centres entering patients for the first time are advised to contact the SABRTooth RTTQA physicist to confirm they have the most recent and approved version.

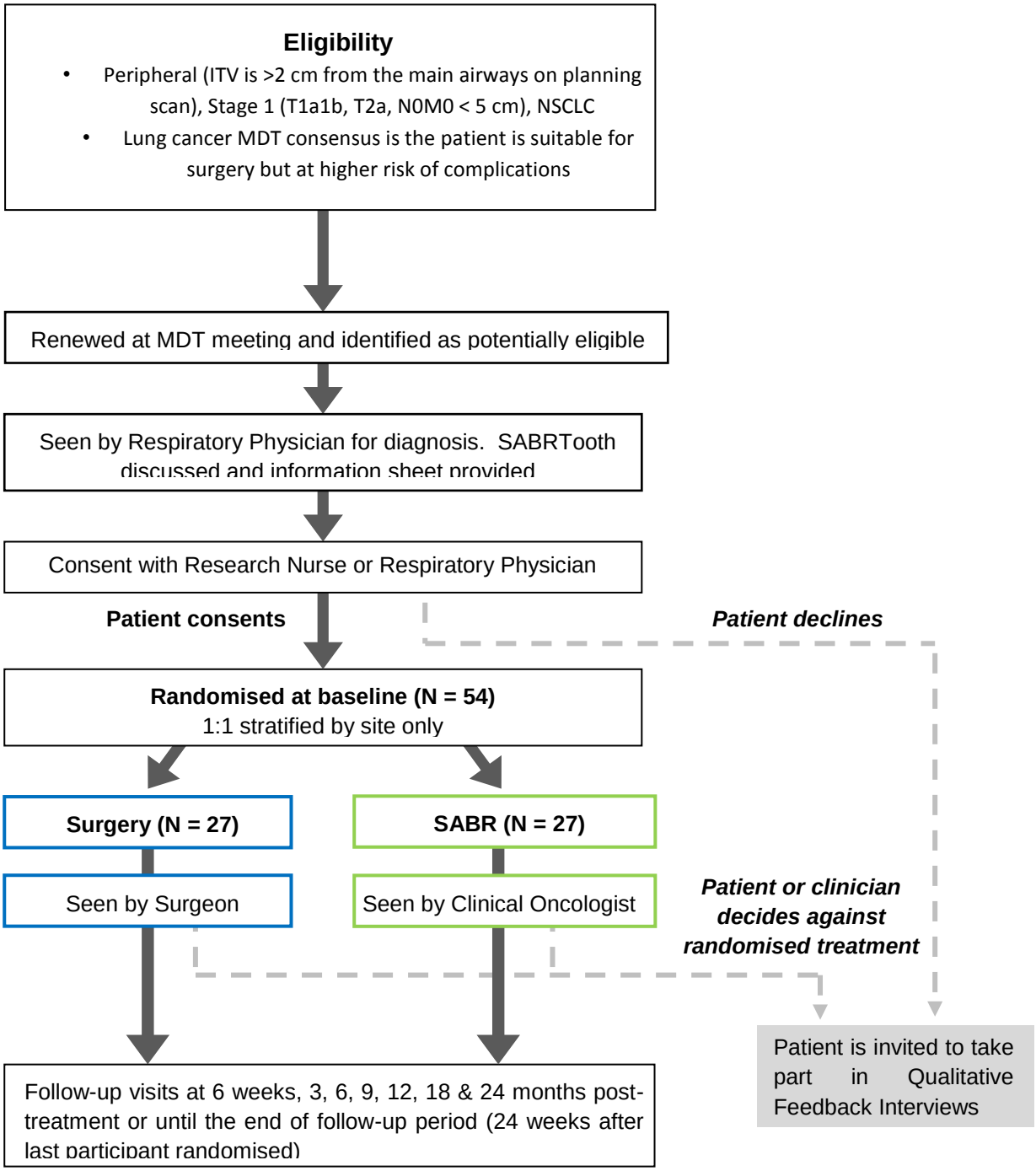
If you have any queries in regards to this please contact the RTTQA group. For contact details please refer to the 'Contact Details' section.

Trial Summary

Title	A study to determine the feasibility and acceptability of conducting a Phase III randomised controlled trial comparing stereotactic Ablative Radiotherapy (**SABR**) with surgery in pa**T**ients with peripheral Stage I n**O**n-small cell lung cancer (NSCLC) c**O**nsidered **T**o be at **H**igher risk of complications from surgical resection.
Acronym	SABRTooth
Background	Lung Cancer survival rates in the UK are inferior to other European and North American countries. Optimising therapy for all stages of the disease is therefore a high priority. Stage I non-small cell lung cancer (NSCLC) is curable and surgery is considered the standard of care for fit, good performance status patients, with 5 year overall survival (OS) of around 60%. However, a high proportion of patients with Stage I NSCLC are elderly and/or have medical co-morbidities. Despite guidelines, variation exists in clinical practice with a wide range in UK surgical resection rates by region (8-25%). The optimal treatment for patients who are at higher risk of surgical complications (mortality and morbidity) is unknown. SABR may be an equally appropriate treatment but this needs to be formally assessed.
Design	The SABRTooth trial is a UK multi-centre, two-group individually randomised controlled feasibility study targeted at patients with peripheral Stage I non-small cell lung cancer considered at higher risk from surgery. In total, 54 patients are planned to be recruited into the study over a 21 month period from 4 tertiary treatment sites and 2 smaller referral sites. Due to the different treatment modalities in the two arms it is not feasible to blind patients or clinicians.
Objectives	This study aims to determine the feasibility and acceptability of performing a large-scale definitive randomised Phase III trial comparing surgery with stereotactic ablative radiotherapy (SABR) for patients with peripheral Stage I non-small cell lung cancer (NSCLC) at higher risk from surgery in the UK.

Endpoints	Primary endpoint: - Recruitment rate/month over months 7-21 Secondary endpoints: - Number of patients screened/month and identified as eligible/month - Proportion of patients undergoing their allocated treatment procedure - Reasons for non-participation of eligible patients - Reasons for participants not undergoing their allocated treatment procedure - Proportion of QoL questionnaires returned and completed (i.e. EQ-5D™, EQ-VAS™, QLQ-C30, QLQ-LC30, Resource Use and Societal economic questionnaire) at each data collection timepoint - EQ-5D utility scores and standard deviation estimates Exploratory endpoints: - - Qualitative assessment of patient acceptability of the trial - Descriptive assessment of participant recruitment pathway across the 6 recruiting trial sites. - Descriptive assessment of the decision making in recruiting site MDTs in identification of higher risk patients and use of available tools to aid this decision making including the predictive score - 30/90/180 day mortality rates
Population	54 patients with peripheral Stage I non-small cell lung cancer considered at higher risk from surgery recruited from 6 UK trial sites.
Randomisation	Participants will be randomised on a 1:1 basis to undergo either surgical resection or SABR. Stratified permuted block randomisation will be used to ensure treatment groups are well balanced for recruiting trial site.
Duration	21 months of recruitment followed by 6 months of additional follow-up.
Evaluation of outcome measures	Follow-up frequency will be in line with current NHS practice, with data collected at routine follow up visits at 6 weeks, 3m, 6m, 9m, 12m, 18m and 24m post-treatment (or until 6 months after the final participant has been randomised). Minimal clinical data and patient reported questionnaire data will also be collected at 15m and 21m post-treatment. Overall survival data will be captured again at the end of the study for all participants via the National Cancer Data Repository (NCDR)
Eligibility	Please refer to the SABRTooth Protocol

Trial Schema



Contact Details

Chief Investigator: Dr Kevin Franks Consultant Clinical Oncologist St James's Institute of Oncology Leeds Teaching Hospital NHS Trust Tel: 0113 206 7854 Email: kevin.franks@nhs.net	**Trial Management** Catherine Lowe Senior Trial Manager Clinical Trials Research Unit University of Leeds Tel: 0113 343 1672 Email: sabrtooth@leeds.ac.uk
Clinical Advisor Professor David Sebag-Montefiore Professor of Clinical Oncology University of Leeds and Leeds Cancer Centre Tel: 0113 2068586 Email: d.sebagmontefiore@leeds.ac.uk	**Clinical Advisor** Mr Babu Naidu Thoratic Surgeon University of Birmingham Tel: 0121 371 3228 Email: b.naidu@bham.ac.uk
Clinical Advisor Professor David Baldwin Respiratory Physician Nottingham University Hospitals NHS Trust Tel: 0115 9691169 Email: David.Baldwin@nuh.nhs.uk	**Clinical Advisor** Dr Michael Snee Consultant Clinical Oncologist Leeds Teaching Hospital NHS Trust Tel: 0113 2067614 Email: Michael.Snee@leedsth.nhs.uk
Radiotherapy Physics Advisor: John Lilley Lead Treatment Planning and R&D Physicist St James's Institute of Oncology Leeds Teaching Hospital NHS Trust Tel: 0113 206 7617 Email: johnlilley@nhs.net	

Radiotherapy Trials Quality Assurance Group RTTQA

RTTQA Physicist	Rushil Patel Lead SABR Physicist RTTQA Mount Vernon Cancer Centre Tel: 01923844714 Email: rpatel1@nhs.net
RTTQA Physicist Cover	David Eaton Lead Physicist RTTQA Mount Vernon Cancer Centre Tel: 01923844714 Email: david.eaton@nhs.net

For further details regarding RTTQA:

Visit www.rttrialsqa.org.uk

Elizabeth Miles (Mount Vernon Hospital): Elizabeth.miles@nhs.net

Radiotherapy QA Programme

The trial QA programme run by the NCRI National Radiotherapy Trials Quality Assurance Group (RTTQA) consists of two stages: pre-trial and on-trial QA. An overview of the RTTQA credentialing process, along with the documentation, is given on the RT Trials QA website (www.rttrials.org.uk)

Pre-trial QA

Each centre must complete Pre-trial QA before the centre is accepted to recruit patients for the trial. Pre-trial QA consists of completion of:

- **Facility questionnaire**: general and trial specific questions on equipment, software and techniques to be used for the trial. The Facility Questionnaire should be updated by each centre if any local changes are made to the approved technique.

- **Dummy run**: QA of the outlining and planning technique will be performed by each centre sending three patients (one for each dose fractionation regimen) that are eligible for the trial for review. Adherence to the protocol will be assessed. See Appendix 2 for details)

- The **National SABR Consortium Lung Audit** or equivalent independent audit that has taken place at the centre within 3 years of entering the trial. Evidence of independent audit should be provided as part of the pre-trial QA. Please discuss with RTTQA if this is not possible.

Streamlining of QA process: Every effort has been made to streamline the amount of QA required to enter the trial. Please contact RTTQA if you have any concerns about the QA programme.

On-trial QA

On-trial QA is performed on clinical patients who have been recruited into the trial and consists of:

- **Prospective review** of first recruited patient of each dose fractionation type from all centres. These reviews assess protocol compliance of outlining and treatment planning and must be completed before the patient commences treatment.

- **Data collection** by the QA centre from all patients treated in the trial. For each patient, this includes: clinical history (including report of relevant imaging), 4DCT images (all phases and any 3D datasets), contours, plan and total dose cubes along with a completed plan assessment form (**PAF**). All data must be appropriately anonymised.

SABR Treatment Planning and Delivery

Introduction to SABR

Stereotactic ablative body radiotherapy (SABR) refers to the precise irradiation of an image-defined extra-cranial lesion with the use of high radiation dose in a small number of fractions. Centres entering patients into SABRTooth must already have a Lung SABR treatment pathway in place which complies with the UK SABR Consortium Guidelines.

Pre-treatment image acquisition

Pre-treatment image acquisition must follow the UK SABR Consortium guidelines

Patient positioning

As per local institution. Aim is to produce a reproducible, comfortable and stable position that the patient can tolerate for up 45 min. Please refer to the UK SABR Consortium Guidelines and the National Radiotherapy Implementation Group Report Image Guided Radiotherapy (IGRT) Guidance for implementation and use for further guidance.

Treatment set-up should be by reference to tattoos on reproducibly stable areas of skin, and to bony anatomical landmarks. The tattoos should be applied at the time of planning scan acquisition.

Image acquisition

Motion management (for tumour motion >1cm) should follow the UK SABR Consortium Guidance. Planning with a 4DCT scan is highly recommended (particularly if motion is >1cm). For centres without 4DCT, repeated helical CT scans (e.g. free-breathing, exhale and inhale) or slow CT can be used to generate an ITV. Details of the pre-treatment imaging technique must be included in the completed SABRTooth Facility Questionnaire.

IV contrast should be used unless there is contra-indication.

Slice thickness: contiguous axial slices of ≤3mm

Scan limits: To include the whole of the chest according to UK SABR Consortium Guidelines.

Outlining

The outlining definitions for SABRTooth are based on the UK SABR Consortium Guidelines. The structures that must be delineated are outlined in the table below. Please note the following information:

Gross Tumour Volume (GTV) is defined as the radiologically visible tumour in the lung, contoured using lung settings. Mediastinal windows may be suitable for defining tumours proximal to the chest wall. Where available, and deemed useful information from PET/CT should be incorporated into delineating the GTV.

- All tumour and critical organ contours should be reviewed by a consultant radiologist if there are any concerns with delineation.
- There may be occasions where PTV coverage may need to be compromised in order to meet organs at risk constraints. Some centres may edit the PTV back from the relevant OAR as part of the optimisation technique. If this is needed, **the original PTV must be left unedited** and a second PlanPTV structure created with the necessary clipping applied to the structure only.
- Please follow the nomenclature outlined below when submitting contours to RTTQA

Target definition	
Nomenclature	**For 4DCT Planned Patients**
GTV_{Mid}	Radiologically identified tumour on Mid-ventilation 4DCT dataset
GTV_{Exh}	Radiologically identified tumour on Maximum Exhale 4DCT dataset
GTV_{Inh}	Radiologically identified tumour on Maximum Inhale 4DCT dataset
CTV	No expansion for microscopic disease is used in SBRT i.e. GTV= CTV.
ITV	ITV encompasses either the GTV_{Mid},GTV_{Exh},GTV_{Inh} and any additional tumour seen or full tumour extent on maximum intensity projection. If a MIP is used, GTVs do not need to be contoured.
PTV_XXXX	*ITV* + 5 mm. The margins from CTV to PTV will depend on the method of immobilisation, the assessment of tumour motion and methods for on treatment set-up verification/repositioning used at each centre. XXXX to be replaced by the prescription dose in cGy
	For patients where 4DCT is inadequate for planning or motion assessment, a single free breathing helical CT should be acquired and the below population base margins are applied according to RTOG 0236.
GTV	Radiologically identified tumour on the free-breathing helical dataset.
CTV	No expansion for microscopic disease is used in SBRT i.e GTV= CTV.
PTV_*XXXX*	GTV + 1.0cm Cranio/Caudal and 0.5cm Ant/Post and Lateral. XXXX

	to be replaced by the prescription dose in cGy
Organs at risk delineation	
Lungs	Both the right and left lungs should be contoured as one structure using pulmonary windows. All inflated and collapsed lung should be included. However, GTV and trachea/ipsilateral bronchus as defined above should not be included. The V20 will be calculated using both lung volumes minus the GTV.
Trachea	The trachea will be contoured using lung and mediastinal windows on CT to correspond to the mucosal, submucosa and cartilage rings and airway channels associated with these structures. Contouring of the proximal trachea should begin at least 10cm superior to the extent of the PTV or 5cm superior to the carina (whichever is more superior) and continue inferiorly to the superior aspect of the proximal bronchial tree.
Bronchus	The proximal bronchial tree will be contoured using lung and mediastinal windows on CT to correspond to the mucosal, submucosa and cartilage rings and airway channels associated with these structures. The proximal bronchial tree will include the most inferior 2cm of distal trachea and the proximal airways on both sides. The following airways will be included according to standard anatomical relationships: the distal 2cm of trachea, the carina, the right and left mainstem bronchi, the right and left upper lobe bronchi, the intermedius bronchus, the right middle lobe bronchus, the lingular bronchus, and the right and left lower lobe bronchi. Contouring of the lobar bronchi will end immediately at the site of a segmental bifurcation.
Airways_2cm	In addition, as a guide to the ineligibility requirements for not enrolling patients with tumours in the zone of the proximal bronchial tree, an artificial structure 2cm larger in all directions from the proximal bronchial tree should be created. If the GTV on the planning dataset (or GTV on helical CT) falls within this artificial structure, contact SABRTooth QA team
SpinalCord	The spinal cord will be contoured based on the bony limits of the spinal canal. The spinal cord should be contoured starting at least 10cm above the superior extent of the PTV and continuing on every CT slice to at least 10cm below the inferior extent of the PTV.
Oesophagus	The oesophagus will be contoured using mediastinal windowing on CT to correspond to the mucosal, submucosa, and all muscular layers out to the fatty adventitia. The oesophagus should be contoured starting at least 10cm above the superior extent of the PTV and continuing on every CT slice to at least 10cm below the inferior extent of the PTV.
Pericardium	The heart will be contoured along with the pericardial sac. The

	superior aspect (or base) for purposes of contouring will begin at the level of the inferior aspect of the aortic arch (aortopulmonary window) and extend inferiorly to the apex of the heart.
Ipsilateral_BrachialPlexus	The defined ipsilateral brachial plexus originates from the spinal nerves exiting the neuroforamina on the involved side from around C5 to T2. However, for the purposes of this protocol only the major trunks of the brachial plexus will be contoured using the subclavian and axillary vessels as a surrogate for identifying the location of the brachial plexus. This neurovascular complex will be contoured starting proximally at the bifurcation of the brachiocephalic trunk into the jugular/subclavian veins (or carotid/ subclavian arteries) and following along the route of the subclavian vein to the axillary vein ending after the neurovascular structures cross the 2nd rib.
Additional OARs	For lower lobe tumours it may be necessary to contour the stomach/small bowel and/or liver **PARTICULARLY** if non-coplanar beams are used in the treatment plan. Please contact RTTQA if these OARs are close to local tolerances
Additional planning structures	
Body	The body contour should also be contoured.
Skin	Skin should be created from the outer most 5mm of the body contour. Doses should not exceed stated tolerances
PlanPTV	As described above, this structure should be created if the PTV needs to be edited as part of the optimisation process to ensure PTV doses are reported consistently using the unedited PTV.
Planning Volumes	Additional structures can be used for IMRT optimisation. These should be clearly differentiated from the trial structures e.g. by labelling zzPTV+2cm, zzcontrast

Treatment Planning and Delivery

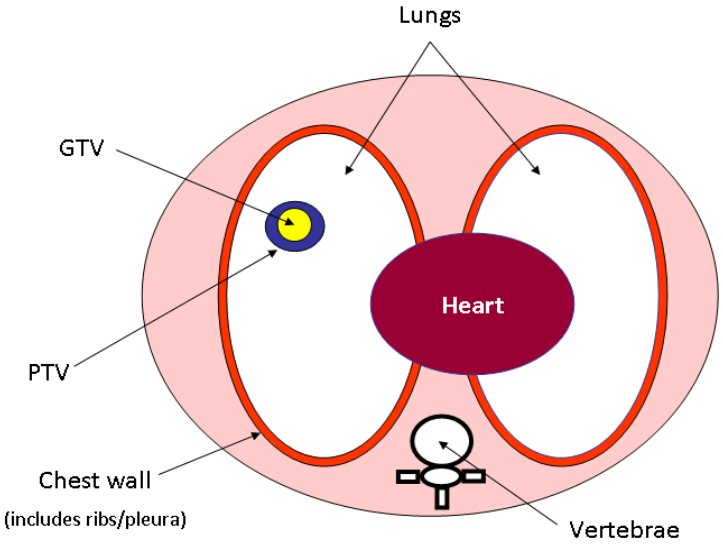
Treatment Type	Centres may use 3D conformal, IMRT or VMAT RT planning for SABRTooth patient. The chosen technique must be detailed in the completed SABRTooth Facility Questionnaire.
Isocentre Position	As per local protocol. Recommend use of midline isocentre for CBCT verification
Beam selection	For 3DP conformal plans, typically at least seven beams will be needed to achieve adequate target coverage using SABR whilst sparing critical structures, including skin surface. Plans may be non-coplanar if

	necessary. Beams energies above 10MV should not be used, Flattening Filter Free beams are allowed to be used.
Dose Calculation	Inhomogeneity correction must be applied. The use of modern 'type-b' superposition-convolution algorithms (e.g. Pinnacle and Oncentra Master Plan collapsed cone algorithms, or the Eclipse AAA algorithm) or Monte Carlo is required as these algorithms calculate lung and tumour doses more accurately than older 'type-a' algorithms. Analysis of the dose-volume histogram (DVH) for the PTV and critical normal structures forms the basis for selecting a particular treatment plan. It is therefore recommended that plans be calculated on a fine dose grid, with a separation no greater than 2.5mm, to ensure the accuracy of the DVH calculations.
Dose Prescription	Prescribed so that the prescription dose is covering 95% the PTV

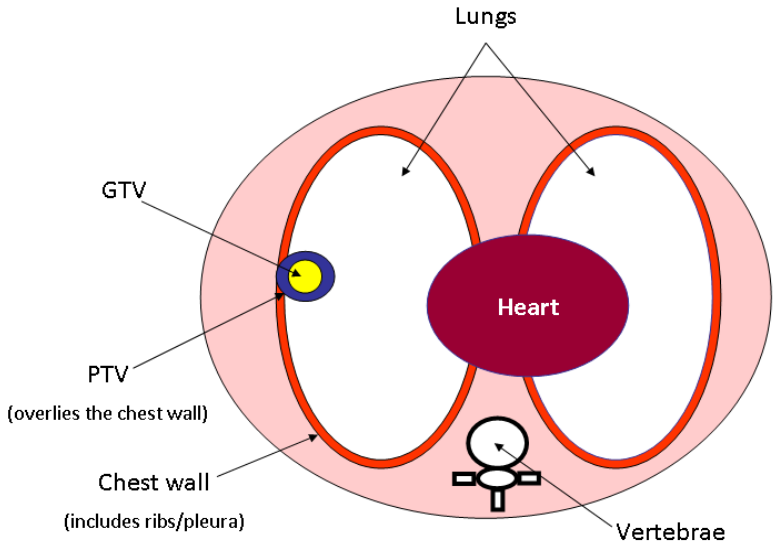
Dose Fractionation

Dose will be delivered in a single phase based on the accepted guidelines of the UK SABR consortium, with 3 dose fractionation schedules based on the location of the tumour

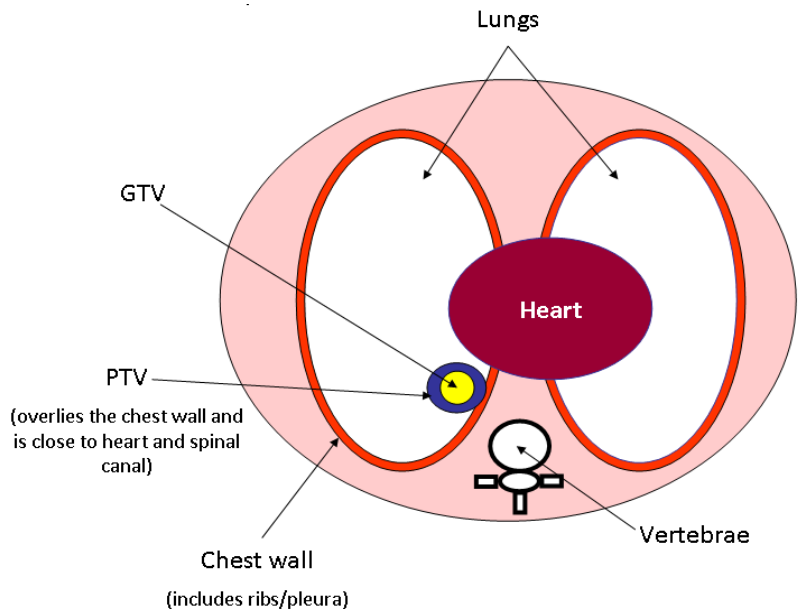
1. tumour whose planning target volume (PTV) does not abuts the chest wall or mediastinal structures: **54Gy** in three fractions (18Gy/fraction)



2. For tumours whose planning target volume touches or extents into the ribs/ pleural: **55Gy** in five fractions (11Gy/fraction) or **60Gy** in five fractions (12Gy/fraction)



3. For tumours where the dose constraints for an organ at risk cannot be met **60Gy** in eight fractions (7.5Gy/fraction)



Planning Aims

Target volume dose planning aims are in line with those described in the (UK SABR Consortium)

- Dose prescription should be chosen such that D95%(PTV) ≥ 100% of the prescribed dose (e.g. 54Gy for the 3 fraction schedule), and D99%(PTV) ≥ 90% of the prescribed dose.
- D_{max}(PTV) should ideally be ≥110% of the prescribed dose and ≤140%. However D_{max}(PTV) between 105-110% and 140-145% may be accepted in some cases.

Plans must also meet the dose conformity requirements described in Table 1 according to PTV volume. These are also in line with those described in the UK SABR Consortium Guidelines [1]

Plans must also meet the organs at risk dose objectives outlined in Table 2. Please discuss with the SABRTooth Team if you feel your centre will have problems meeting these constraints.

The appropriate Plan Assessment Form (PAF) should be completed for each patient according to dose fractionation. This includes those values requested for dose reporting purposes only. PAFs are available for the RTTQA website www.rttrialsqa.org.uk.

Table 1: Dose Conformity Requirements:

(a) For 54Gy in 3 fractions

PTV Volume (cc)	**R100**		**R50**		**D_{max} (>2cm from PTV)$^{+}$**		**Lung-GTV* V20 (%)**	
	optimal	mandatory	optimal	mandatory	optimal	mandatory	optimal	mandatory
<20	<1.25	1.25-1.40	<12	12-14	<35.1Gy	35.1-40.5Gy	<5	5-8
20.1-40	<1.15	1.15-1.25	<9	9-11	<37.8Gy	37.8-43.2Gy	<6	6-10
>40.1-60	<1.10	1.10-1.20	<6	6-8	<37.8Gy	37.8-43.2Gy	<10	10-15
60.1-90	<1.10	1.10-1.20	<5	5-7	<37.8Gy	37.8-43.2Gy	<10	10-15
>90.1	<1.10	1.10-1.20	<4.5	4.5-6.5	<37.8Gy	37.8-43.2Gy	<10	10-15

(b) For 55Gy in 5 and 60Gy in 8 fractions

PTV Volume (cc)	**R100**		**R50**		**D_{max} (>2cm from PTV)$^{+}$**		**Lung-GTV* V20 (%)**	
	optimal	mandatory	optimal	mandatory	optimal	mandatory	optimal	mandatory
<20	<1.25	1.25-1.40	<12	12-14	<35.8Gy	35.8-41.3Gy	<5	5-8
20.1-40	<1.15	1.15-1.25	<9	9-11	<38.5Gy	38.5-44.0Gy	<6	6-10
>40.1-60	<1.10	1.10-1.20	<6	6-8	<38.5Gy	38.5-44.0Gy	<10	10-15
60.1-90	<1.10	1.10-1.20	<5	5-7	<38.5Gy	38.5-44.0Gy	<10	10-15
>90.1	<1.10	1.10-1.20	<4.5	4.5-6.5	<38.5Gy	38.5-44.0Gy	<10	10-15

where:

R100 = Vol(100%)/Vol(PTV) = ratio of prescription isodose (e.g. 54Gy, 55Gy, or 60Gy) volume to the PTV volume

R50 = Vol(50%)/Vol(PTV) = ratio of 50% prescription isodose (e.g. 27Gy, 27.5Gy, or 30Gy) volume to the PTV volume

$^{+}$ **D_{max} (>2cm from PTV) =** maximum point dose at least 2cm from the PTV in any direction

***Lung-GTV V20** = percentage of Lung-GTV (as defined above) receiving >20Gy

Table 2**: OAR Dose Constraints**

Organ	**Volume**	**Three Fraction Regime (54Gy in 3#)**		**Five Fraction Regime (55Gy in 5#)**		**8 Fraction Regime (60Gy in 8#)**	
		Optimal	**Mandatory**	**Optimal**	**Mandatory**	**Optimal**	**Mandatory**
SpinalCord	0.01 cm^3	18 Gy	18-22 Gy	25 Gy	25-28 Gy	25 Gy	25-28 Gy
Oesophagus	0.1 cm^3	24 Gy	24-27 Gy	27 Gy	27-28.5Gy	27 Gy	27-28.5Gy
Ipsilateral_Brachial Plexus	0.1 cm^3	24 Gy	24-26 Gy	27 Gy	27-29 Gy	27Gy	27-29Gy
Heart	0.1 cm^3	24 Gy	24-26 Gy	27 Gy	27-29 Gy	50Gy	50-60Gy
Trachea, Ipsilateral Bronchus	0.1 cm^3	30 Gy	30-32 Gy	32 Gy	32-35 Gy	32 Gy	32-35 Gy
Lungs-GTV*	V20	<10%	N/A	<10%	N/A	<10%	N/A
	V12.5	<15%	N/A	<15%	N/A	<15%	N/A
Liver **		V15<700ccV V21<33% V15<50%	N/A	V15<700cc V30<60% Mean<20Gy	N/A	V27<30% V24<50%	N/A
Chest Wall***	30 0.01	30Gy 37Gy	N/A	32Gy 39Gy	N/A	32-35Gy 39Gy	N/A

* Lung-GTV as defined above

** Liver -valid only if >1000cc of liver imaged

*** Chest wall -optional constraint and local institution to decide whether to try and achieve this

Plan Approval

The RT plan must be reviewed in a radiotherapy MDT or by another consultant who signs the treatment card before treatment. This is essential to try and avoid re-planning patients, especially when the tumour is close to a critical OAR

Plan Checking and Patient Specific QA

All treatment plans should undergo local checking and patient-specific QA procedures. Details of these procedures should be provided in the Facility Questionnaire.

Monitor units should be checked by measurement for a minimum of one dose point in an appropriate homogeneous region of the high dose volume. Independent calculation programs may be used in place of measurements, provided the centre has a previous high level of experience in measurement QA and has a system in place for verifying errors found by the independent calculation.

Fluences may be verified either individually per beam (i.e. each gantry orientation) or at representative planes for all beams together, with measurements being made through at least PTV and spinal cord. Appropriate film / ion chamber or diode arrays / EPID should be used in conjunction with software to compare with the isodoses from the TPS. At least a dose difference measurement or gamma index is required.

Centres with sufficient experience that no longer routinely check fluences for every patient will be accepted.

Replanning

Local procedures should be followed for rescanning and replanning patients. Data associated with any replans of SABRTooth patients during radiotherapy treatment must also be submitted to the SABRTooth QA team (i.e. rescan CTs, structures, plan, dose cube and plan assessment form). This data will not be subject to prospective review given the

time pressures of replans. However they may be reviewed retrospectively at the QA team's discretion. Data from replans is important for long-term trial analysis, as with any treatment plan data, when any protocol deviations may be related to treatment outcome. Please note the plan assessment form includes a section where replan details can be annotated.*

Radiotherapy Delivery

Lung SABR should be delivered according to the National Radiotherapy Implementation Group Report Image Guided Radiotherapy (IGRT) Guidance for implementation and use.

Centres using gated treatments should discuss their technique with the SABRTooth team prior to using in the trial

Treatment Verification

Once the treatment plan has been generated, it is recommended that centres conduct a 'trial set up' session (day-zero), prior to starting treatment, in order to confirm that all the beams are deliverable, that the patient can maintain the treatment position, to verify the patient setup procedure and, if the technology is available, use respiratory-correlation to assess margin adequacy.

It is suggested that centres verify patient setup before and, if possible, during treatment using a procedure that can validate the position of the tumour relative to the patient anatomy for online image matching and correction. Volumetric imaging with cone beam CT, CT on rails or megavoltage CT is highly recommended as bony landmarks are not a reliable surrogate and cannot detect changes in internal anatomy. Daily online imaging matching to the target or fiducial is mandatory, using the no action level protocol. Multiple images during the treatment fraction should be considered to verify any shift or if the treatment exceeds 30 minutes.

Radiotherapy Schedule

Protocols for booking patients and gaps in treatment should follow the latest SABR Consortium guidelines.

Case Reviews and Trial Data Collection

Case Reviews

To ensure a short response time for patients requiring prospective review, please notify the SABRTooth QA physicist when a patient has been identified so that we can be ready to review volume delineation and subsequently the radiotherapy plan.

Please send the outlining (CTs and structures) as soon as it has been completed along with a case history to rpatel1@nhs.net . This should be submitted as soon as possible so that it can be reviewed prior to the start of planning. The plan data (structures, plan, dose and plan assessment form) should be submitted as soon as possible following satisfactory outline review and in good time prior to the patient's RT start date.

Please allow time for amendments and re-review as necessary and for any local patient-specific QA.

When each of the first patients of each dose fractionation have been recruited and reviewed, the SABRTooth QA team will discuss the need for further outlining and/or planning review based on the centre's performance on the initial reviews. RTTQA reserves the right to ask for additional case reviews and spot-checks on any SABRTooth patient.

Data Collection

Data for all patients treated in the trial should be submitted to the QA centre (this applies to both case reviews, non-case review patients and any replans). Please send, in DICOM format

- CT images
- Contours, ensuring all CTVs, PTVs and OARs are present and correctly named using the trial nomenclature
- Plan
- Dose cube (total dose)
- Completed plan assessment form (please fill in electronically)
- Clinical history and stage / tumour classification and relevant imaging reports

All data should be transferred to the QA centre via the NHS secure server. This can be accessed via: https://nww.sft.nhs.uk/sft/upload1 . Its use requires an NHS.net email account. Please send QA submissions to rpatel1@nhs.net

Data Anonymisation

All data sent to the QA centre must be anonymised prior to being sent; data that has not been anonymised will not be accepted. Please refer to the RTTQA website for further guidance.

It is suggested that the trial number and initials be used to identify the patient. It may be of use to keep your own list of names and ID's as well.

Bibliography

Consortium, U. S. (n.d.). *UK SABR Consortium Guidelines.*

ROSEL Study. (n.d.).

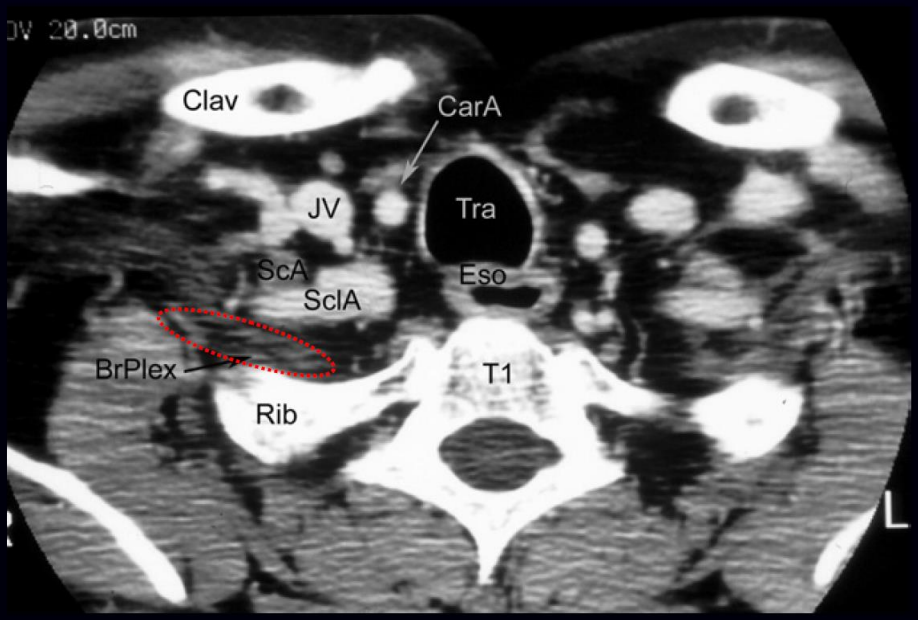
IGRT Guidance https://www.sor.org/sites/default/files/document-versions/National%20Radiotherapy%20Implementation%20Group%20Report%20IGRT%20Final.pdf

Brachial Plexus

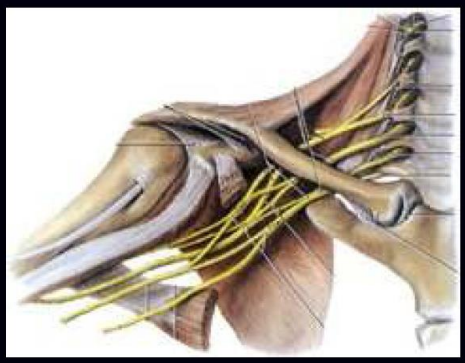
..for the purposes of this protocol only the major trunks of the brachial plexus will be contoured using the subclavian and axillary vessels as a surrogate for identifying the location of the brachial plexus.

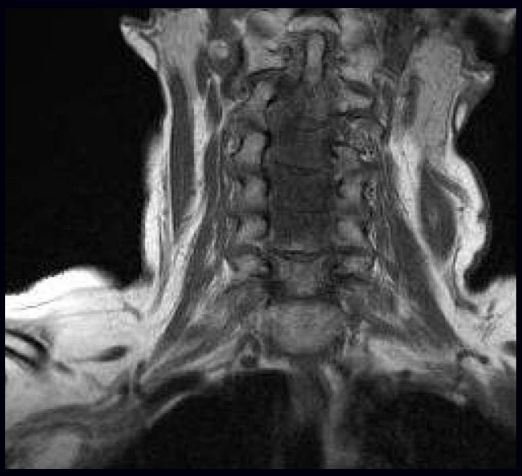
- This neurovascular complex will be contoured starting proximally at the bifurcation of the brachiocephalic trunk into the jugular/subclavian veins (or carotid/subclavian arteries) and following along the route of the subclavian vein to the axillary vein ending after the neurovascular structures cross the 2nd rib.

Level of T1

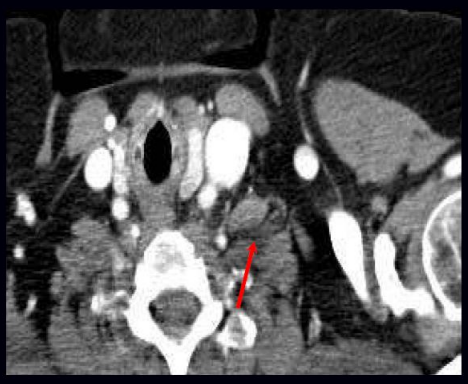


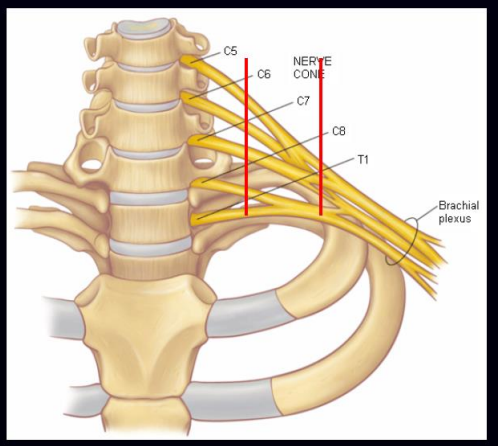
The anterior rami of the spinal nerves of C5, 6, 7, 8, and T1 form the roots of the brachial plexus.



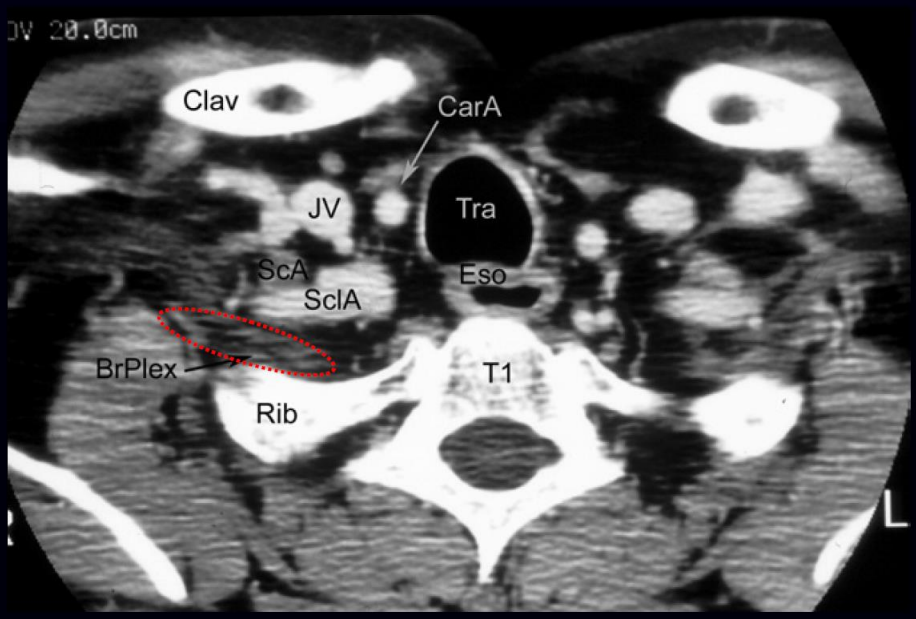


The 3 trunks of the brachial plexus pass between the anterior and middle scalene muscles

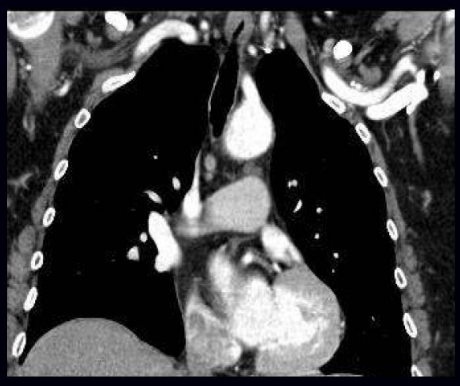


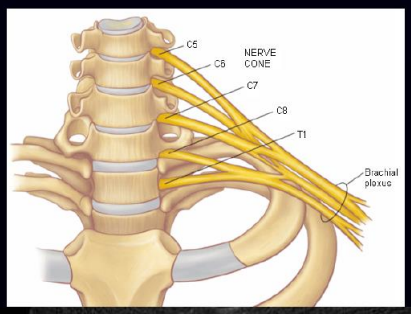


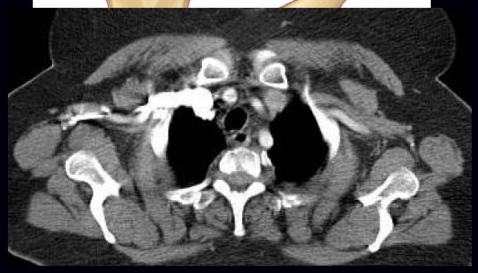
Level of T1



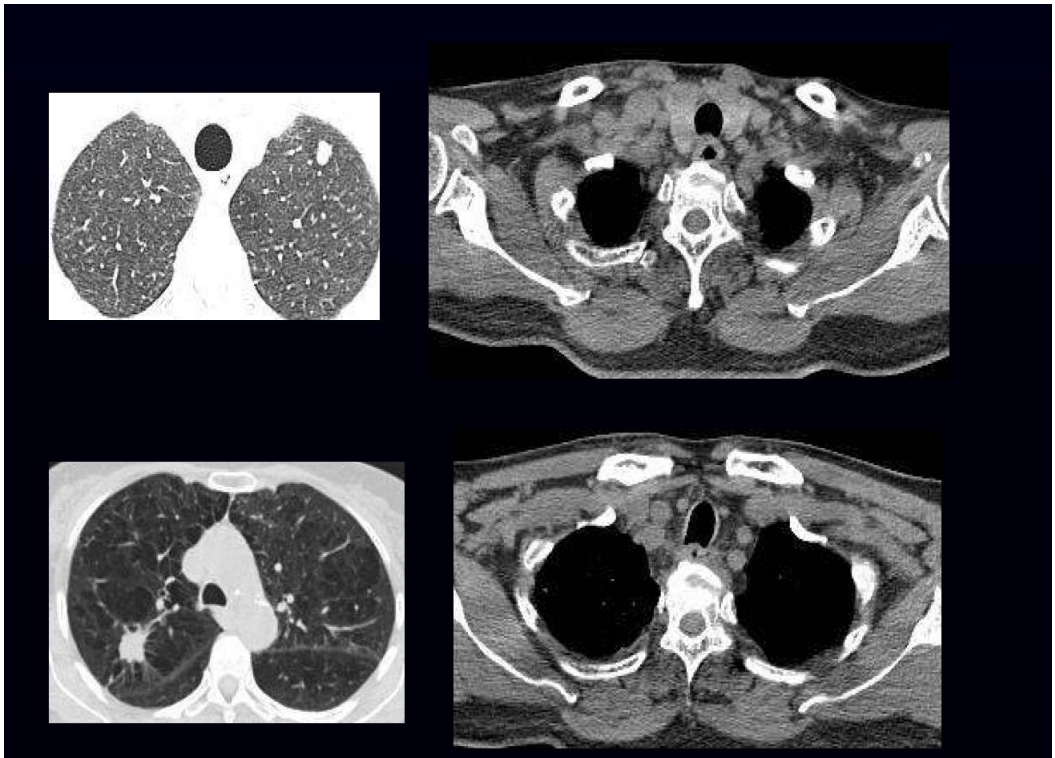
The cords are named the lateral, posterior, and medial cord, according to their relationship to the axillary artery. The cords pass over the first rib close to the apex of the lung and continue under the clavicle immediately posterior to the subclavian artery.





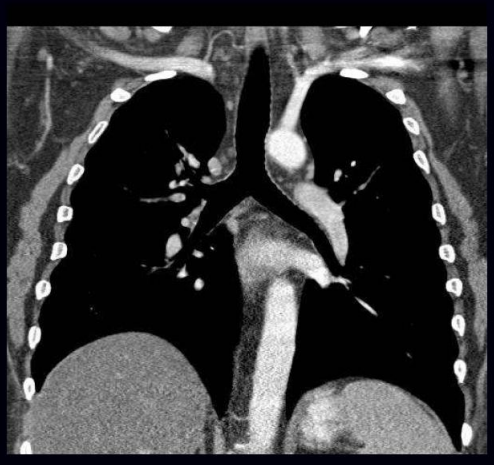


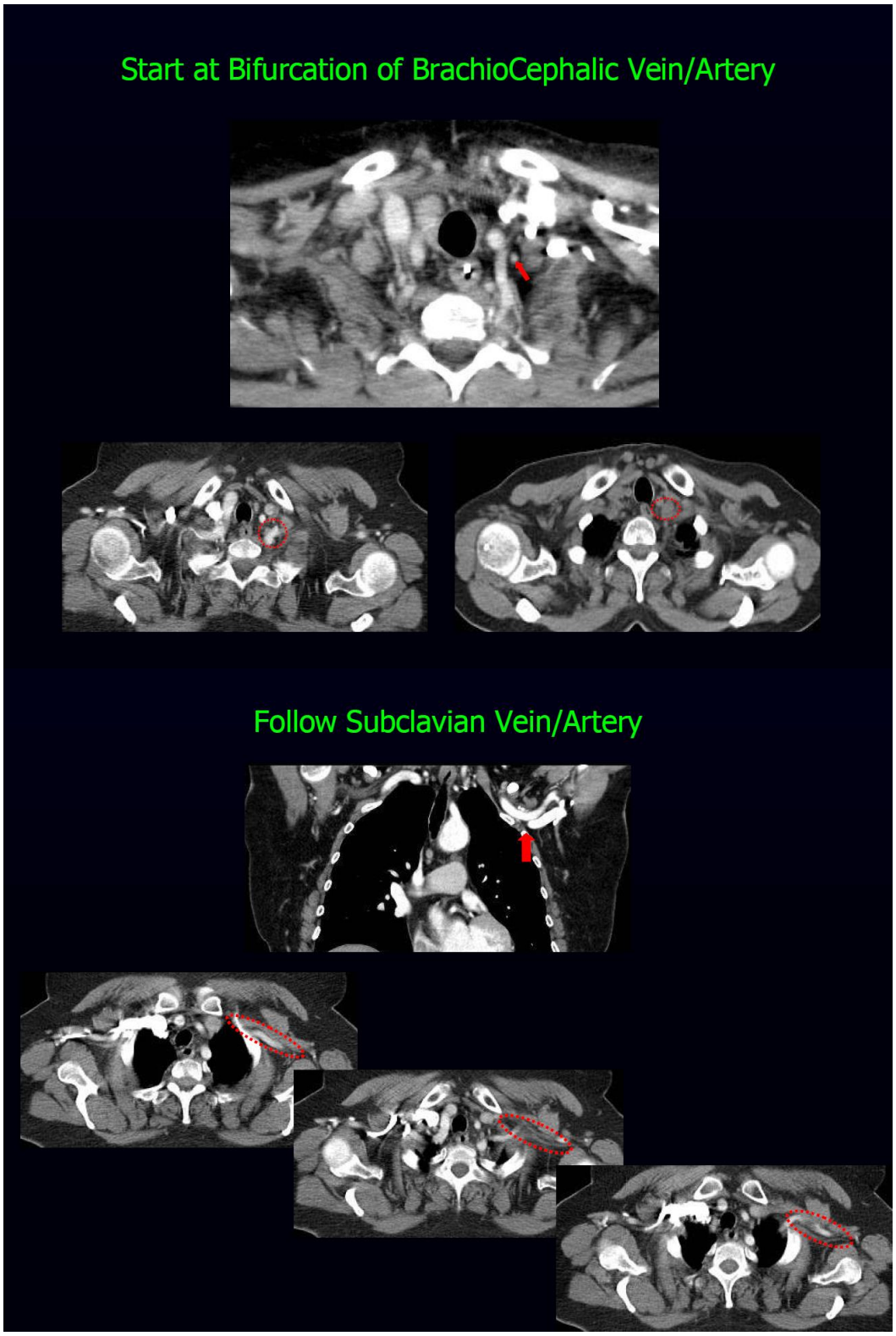
The connective tissue of the prevertebral fascia and the anterior and middle scalenes envelops the brachial plexus as well as the subclavian and axillary artery in a neurovascular "sheath".



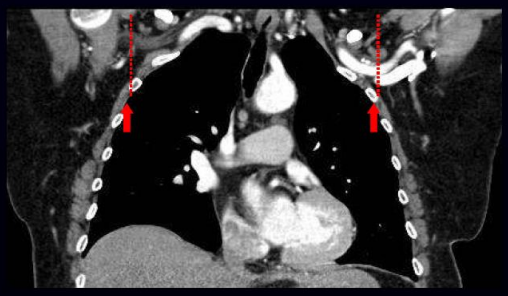
In Practice……

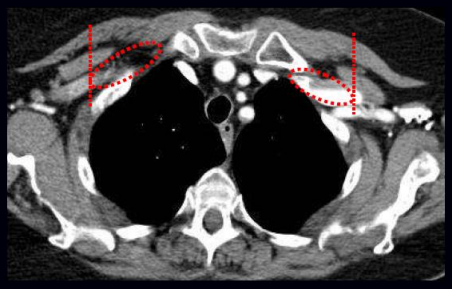
- Start at Bifurcation of BrachioCephalic Vein/Artery
- Follow Subclavian Vein/Artery
- End when vessels cross Second Rib

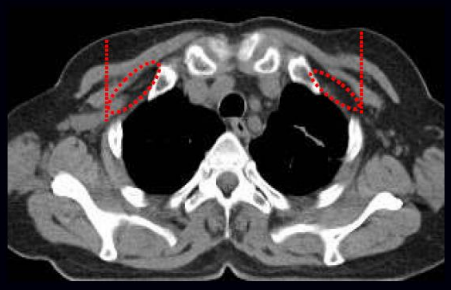



Start at Bifurcation of BrachioCephalic Vein/Artery
Follow Subclavian Vein/Artery

End when vessels cross Second Rib





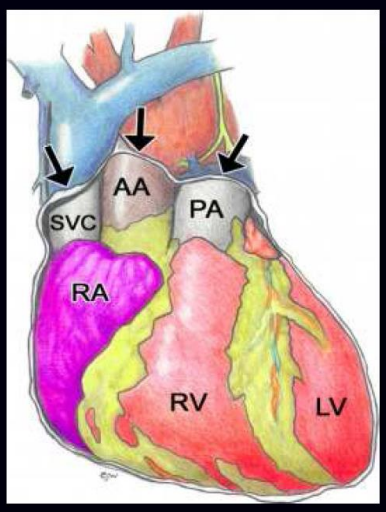


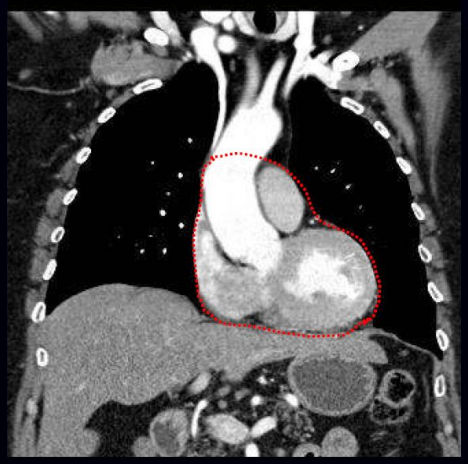
Heart / Pericardium

The heart is contoured along with the pericardial sac

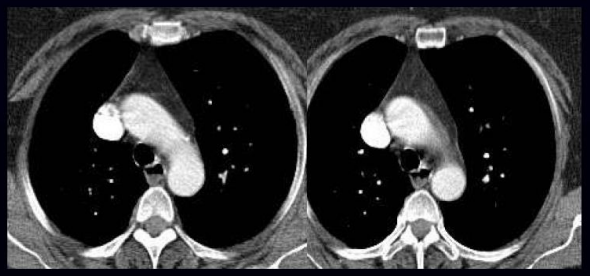
The superior aspect (or base) for purposes of contouring will begin at the level of the inferior aspect of the aortic arch (aortopulmonary window) and extend inferiorly to the apex of the heart.

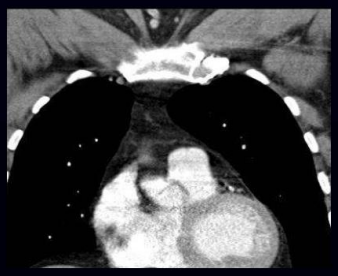
The pericardium is a 2-layered sac that surrounds the heart and extends superiorly to cover the main pulmonary artery, ascending aorta, and SVC

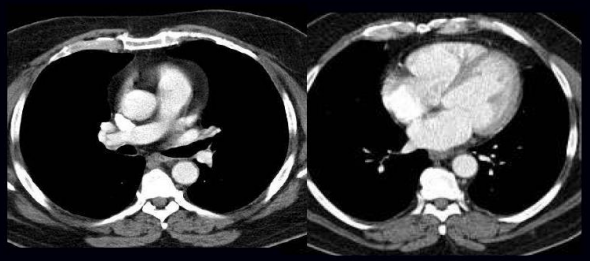


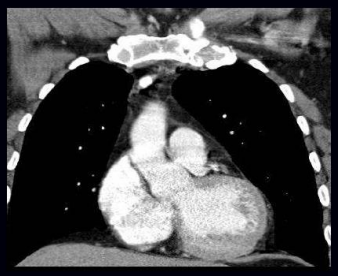


Normal Pericardium

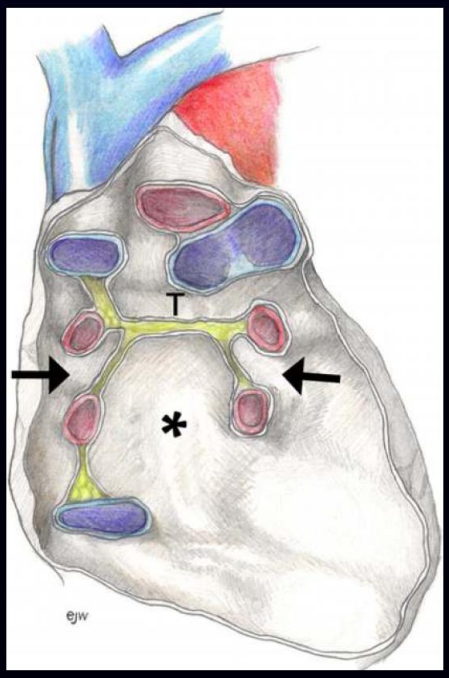




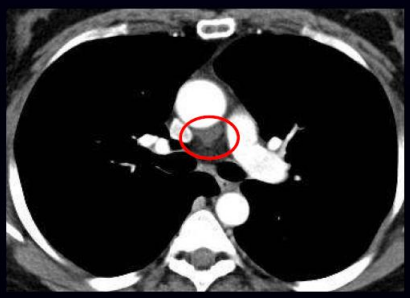


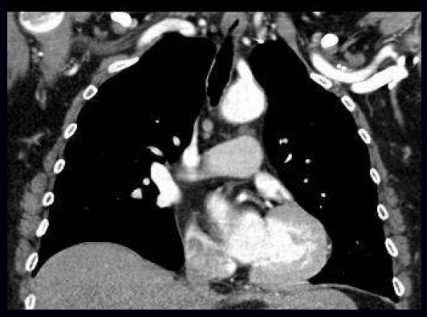


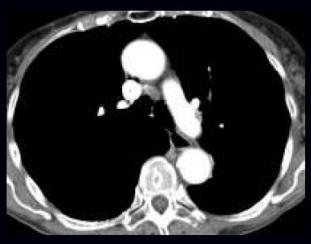
- The visceral pericardium adheres to the heart and great vessels.
- It forms recesses and sinuses, which can be visible at cross-sectional imaging if they contain enough fluid, even in the absence of pericardial effusion.
- Knowledge of the location of these recesses and sinuses will prevent mistaking them for enlarged lymph nodes or other masses

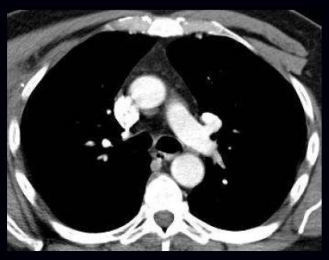


The transverse sinus(pericardial recess) lies posterior to the ascending aorta and main pulmonary artery, just above the left atrium.

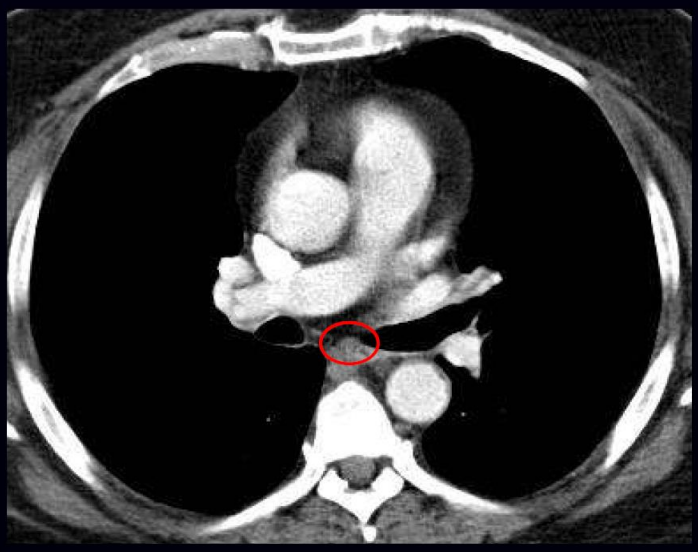








The oblique sinus is the posterior extension of the pericardium and lies posterior to the left atrium and anterior to the oesophagus.



Appendix 2: Dummy Run Instructions

Aim: to ensure patients can be outlined and planned according to SABRTooth protocol using the current patient pathway at each centre

Task:

RTTQA and the SABRTooth team require submission of 3 example patients from each centre that:

- Satisfy the SABRTooth eligibility criteria (section 7 of the SABRTooth protocol): please refer to appendix 1 below.
- Satisfy the planning criteria described in the SABRTooth Radiotherapy Guidelines.
- Include a patient from each dose fractionation criterion (54Gy in 3#, 55Gy in 5# and 60Gy in 8#) as defined by the SABRTooth protocol

A clinical history must be included with each submission,

The three cases should be appropriately anonymised and sent via the NHS England Secure File Transfer Service (https://nww.sft.nhs.uk) to rpatel1@nhs.net for review by the SABRTooth team.

Once the treatment plans have been accepted by the QA team, the accepted plans must undergo patient specific QA, and the QA data sent to the QA team. This should be obtained by following the standard local procedure. No extra forms are included for this data as all centres will have created their own documentation. This is required for completion of the planning exercise. It is recommended that this is carried out once the plans have been accepted to avoid the centre carrying out QA unnecessarily.