South West Radiotherapy
Operational Delivery Network

SABR for Oligometastases

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Section 1: Indications

Stereotactic Ablative Radiotherapy (SABR) has emerged as a new treatment option for patients with oligometastatic disease. It can achieve excellent rates of local control for metastases, with acceptable rates of toxicity (≤10% G3 toxicity) [1] [2]. A recent phase II randomised controlled trial evaluated SABR in a group of patients with a small burden of oligometastatic disease (mostly 1-3 and predominantly metachronous). It found that SABR was associated with a doubling in progression free survival (12 vs 6 months, p=0.0012) and an improvement of about 13 months in overall survival (41 vs 28 months, p=0.090) [3].

1.1 Organs at risk

OAR outlining standards and descriptions

In general, any OARs which are traversed by a treatment beam should be contoured. Where OAR constraints are based on the dose received by a whole organ (e.g. lung, liver, kidney), the whole organ should be contoured.
Otherwise, a volume of OAR should be outlined, sufficient to show that the OAR constraints have been met, with particular care paid to the volume receiving the highest doses.
Appropriate CT windowing or information from other imaging modalities should be used.
OARs should be contoured ≥2cm superiorly and inferiorly to the PTV for co-planar techniques and within 15cm of the PTV if non-coplanar techniques are used.
The body contour should also be contoured wherever the beams traverse it.
The skin should be inspected to ensure that beams do not overlap, producing excessive skin dose, especially where there is a skin fold.

1. Spinal cord / spinal canal

For clinical sites other than spine, a contour based on the bony limits of the spinal canal, ≥2cm superior and inferior of the PTV, will sufficiently allow for a conservative estimate of spinal cord dose.
For spine treatments, contouring the spinal canal may result in the unnecessary compromise of the target volume, and a contour based on the true cord should be used. Spinal cord should be contoured using the fused T1 and T2 weighted MR scans (plus CT myelogram where appropriate) and should extend to at least 1 vertebra superior and inferior to the PTV.
On the level of the cauda equina, the thecal sac should be considered to represent the relevant OAR.
The required margin for PRV expansion will be dependent on local processes and should be carefully established and audited. In cases where good image quality allows confident

co-registration and delineation, an isotropic margin around the spinal cord of 2-3mm may be appropriate in creating the spinal cord PRV. However, if image quality is compromised, it is recommended the larger volume of the thecal sac be used at the discretion of the treating clinician.

2. Brachial Plexus

The defined ipsilateral brachial plexus originates from the spinal nerves exiting the neural foramina on the involved side from around C5 to T2. However, for the purposes of this guide 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 long the route of the subclavian vein to the axillary vein ending after the neurovascular structures cross the 2nd rib. Use of contrast at CT may assist with outlining.

3. 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.

4. Heart

The heart will be contoured along with the pericardial sac. The superior aspect (or base) for purposes of contouring is defined as the superior aspect of pulmonary artery (as seen in a coronal reconstruction of the CT scan) and extended inferiorly to the apex of the heart.

5. Trachea and proximal bronchial tree

The trachea and bronchial tree can be contoured either as a single structure or as two separate structures using lung windows. For this purpose, the trachea can be divided into two sections: the proximal trachea and the distal 2cm of trachea. The proximal trachea will be contoured as one structure, and the distal 2 cm of trachea will be included in the structure identified as proximal bronchial tree. Differentiating these structures in this fashion will facilitate the eligibility requirement for excluding patients with tumours within 2cm of the proximal bronchial tree**.**

6. Proximal trachea

Contours should begin 10cm superior to superior extent of PTV or 5cm superior to the carina (whichever is the more superior) and continue inferiorly to the superior aspect of the proximal bronchial tree.

7. Proximal bronchial tree

This will include the most inferior distal 2cm of trachea and the proximal airways on both sides as indicated in diagram 1. The following airways will be included: distal 2cm trachea, carina, right and left mainstem bronchi, right and left upper lobe bronchi, the bronchus intermedius, right middle lobe bronchus, 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.

8. Great vessels

The great vessels (aorta and vena cava, not the pulmonary artery or vein) will be contoured using mediastinal window to correspond to the vascular wall and all muscular layers out to the fatty adventitia. The great vessel should be contoured at least 10 cm above and below the extent of the PTV. For right sided lesions, the vena cava will be contoured, and for left sided lesions, the aorta will be contoured.

9. Whole lung

Both lungs should be contoured from apex to base as one structure using pulmonary windows. All inflated and collapsed lung should be included. For lung patients, GTV and trachea/ipsilateral bronchus as defined above should not be included. OAR constraints are based on lungs-minus-GTV.

10. Chest wall (for peripheral lesions)

The chest wall will be defined as the 3 cm rind of the ipsilateral hemi-thorax outside the lungs and contoured at least 3 cm superiorly and inferiorly to the PTV.

11. Liver

The whole liver should be outlined, excluding the gall bladder and hepatic vessels. For liver patients, normal liver should be taken as “whole liver” minus the GTV. Care should be taken not to inadvertently include the liver vasculature and/or gall bladder.

12. Common bile duct (CBD) and bifurcations

These ducts should be identified as tubular structures (lumen density equivalent to water). The expected location of the bile ducts is:

a) CHD (common hepatic duct) is anterior to the portal vein, lateral to the hepatic artery, and surrounded by fat in the porta hepatis, and
b) the CBD is within or adjacent to the parenchyma of the pancreatic head. If there is uncertainty on the location, the portal vein can be contoured from the splenic confluence to the first bifurcation of the left and right portal veins.

13. Skin

Defined as a 3-5 mm inner rind of body contour contoured if adjacent to PTV and in regions receiving more than 10Gy.

14. Kidneys

The entirety of each kidney should be outlined separately to allow evaluation of individual kidney dose. A summation of the two volumes should also be created to evaluate total kidney dose.

15. Stomach

The stomach should be contoured from gastro-oesophageal junction to duodenum using mediastinal windowing.

16. Duodenum

The duodenum will be contoured to include the mucosal bowel wall and contents.

17. Bowel

The use of a single bowel bag is an alternative to outlining individual loops of bowel which may move. Extra care should be taken when outlining the bowel nearest the target if this method is used.

18. Ureter

The ureter will be contoured as a solid structure from the renal pelvis down to the insertion into the bladder wall. The delineation limit is the outer wall of the ureter.

19. Bladder

The whole bladder will be contoured to include the bladder wall and lumen.

20. Lumbo-sacral plexus

At the L4 and L5 levels, the entire respective foramina will be contoured. The L4 root will be contoured by including the space defined by the psoas muscle anterior and laterally, and the facet joint/posterior vertebral body elements posteriorly. The L5 root will be contoured using the common iliac vein and psoas muscle anteriorly, the iliacus muscle laterally, and vertebral body and sacrum posteriorly. Below the level of the L5 foramen, the sacro-iliac joint should serve as the lateral border as well.

Beginning at the level of the S1 foramen, the lumbo-sacral plexus (L4/L5) and S1 lie in the area bounded by the iliac vessels anteriorly, the iliacus muscle / sacro-iliac joint laterally, the sacral ala posteriorly, and medial margin of the S1 foramen medially. Beginning at the level of origin of the pyriformis muscle, the lumbo-sacral plexus will be contoured in the space bounded by the iliac vessels anteriorly, iliacus muscle / iliac wing laterally and pyriformis muscle posteriorly.

At the lower margin of the greater sciatic foramen, the space bounded by the obturator internus muscle / ischial spine anteriorly, pyriformis muscle laterally and gluteus maximus muscle posteriorly will be contoured. The medial portion of the obturator internus muscle will serve as the medial extent. Below the pyriformis muscle, the space between the obturator internus muscle anteriorly and the gluteus maximus muscle posteriorly will be contoured. The medial and lateral extent should be 1 to 2 cm in length. Contouring will end at the level of the superior portion of the femoral neck.

21. Femoral heads

Femoral heads will be contoured from their most cranial aspect to the bottom of the curvature of the femoral head (i.e. exclude the femoral neck).

Use of PRVs

Consideration should be given to expanding serial OARs to Planning Risk Volumes (PRVs) to account for uncertainties in setup (both translational and rotational), delineation, inter-fractional anatomical changes, etc. As with PTV expansion margins, the magnitude of these margins should be appropriate to local practice and use of enhanced immobilisation, robotic couch or real-time tracking should be considered.

The position of OARs with respect to the tracked target (or appropriate surrogate) can vary, and therefore should be geometrically accounted for in the OAR PRV. It may well be larger than the PTV margin for highly mobile OARs such as bowel. The concept that mobile OARs will be at different positions at each treatment fraction, and the received dose will therefore "average out" is only applicable to hyperfractionated treatments and is not compatible with SABR. The careful choice of beam angles (for CyberKnife), arc entry and exit angles or avoidance sectors (for VMAT delivery) and their effect on plan robustness in the presence of mobile OARS or organs such as the diaphragm is highly recommended.

Minimum standard: OARs should be contoured ≥2cm superiorly and inferiorly to the PTV for coplanar techniques and up to 15cm of the PTV if non-coplanar techniques are used. Sufficient OARs should be contoured to show that the OAR constraints have been met; this may require the entire organ to be outlined. Careful consideration should be given to the magnitude of PRVs based on local data on set up uncertainties and per organ in the presence of anatomical changes with respiratory motion etc.

Section 2: SABR for lung metastases

Long-term results of metastasectomy from the International Registry of Lung Metastases show an overall survival rate of 70% at 2 years and 36% at 5 years [4]. SABR provides an attractive non-invasive alternative to metastasectomy in patients who are not suitable surgical candidates. SABR is already well-established in terms of safety and efficacy as a standard treatment for inoperable early-stage primary lung cancer [5] [6]. SABR for lung oligometastases presents a similar clinical problem to early-stage primary lung cancer and follows the same principles for patient assessment, treatment planning and delivery. A systematic review analysed the outcome of patients with lung metastases treated with SABR and reported a local control rate at 2 years of 78% and 2-year survival of 54% [7]. Other reports have shown broadly similar outcomes with local control rates of around 80% [6] [8] [9].

Lung SABR typically delivers doses in excess of a biological equivalent dose (BED) of 100Gy (α/β 10) [10]. The dose fractionation schedules below are endorsed by the UK SABR consortium [11]. They are based on the experience from the VU medical centre in Amsterdam and have been implemented in the ROSEL study [12] [13]. Many of the comments in the subsequent sections are drawn from the RTOG 0236 and the ROSEL trial protocols [12] [13] [14] [15].

2.1 Selection criteria [11] [16]

Inclusion criteria

- Histologically or radiologically confirmed lung metastases. If radiological diagnosis, need a histologically or cytologically proven primary site.
- Oligometastatic disease (usually ≤3 oligometastatic sites as confirmed by recent PET scan)
- Not suitable for surgery due to co-morbidities, inadequate lung function, disease status, lesion is technically inoperable or patient declines surgery after surgical assessment
- Peripherally located lung metastases (>2cm from radius of main airways and proximal bronchial tree. This is defined as 2cm from the bifurcation of the second order bronchus e.g. where the right upper lobe bronchus splits (Fig. 1)). More central tumours can be considered for treatment using an ultra-conservative fractionation schedule.

- Maximum size of any single lung metastasis of 5cm
- Disease free interval between primary treatment and development of metastases > 6 months
- Life expectancy ≥ 6 months
- Performance status 0-2
- Age > 18 years oID
- Prior discussion with disease site specific oncologist
- Discussion at SABR MDT

Exclusion criteria

- Size of any single lung metastasis of > 5cm
- Any lung metastasis that is not clinically definable on the treatment planning CT scan
- e.g. surrounded by consolidation or atelectasis
- Patients who have had previous radiotherapy within the planned treatment volume
- Pregnant or lactating females
- Inability to obtain informed consent or comply with treatment requirements

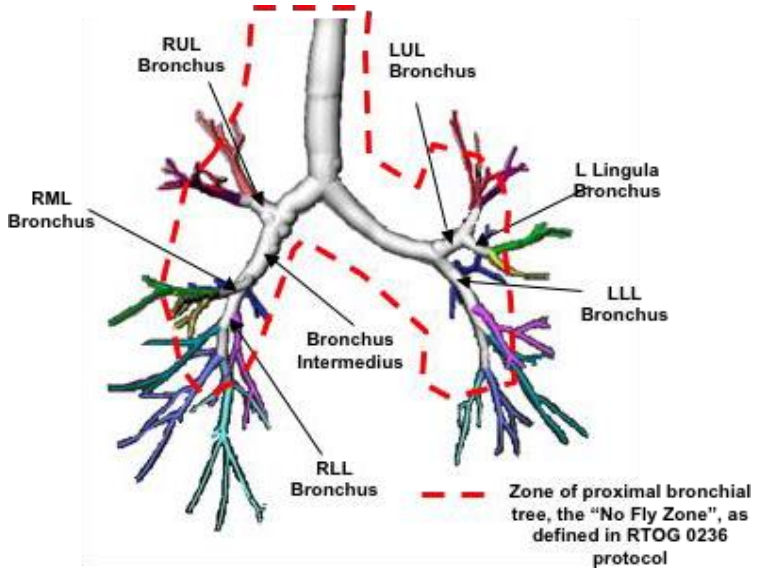
2.2 Contra-indications

- Lung metastases with respiratory motion ≥ 1cm despite using techniques to reduce tumour motion. Mobile tumours can only be treated if normal tissue and tumour planning constraints can be achieved.
- Presence of pulmonary fibrosis (consider and consent for the increased risk of significant toxicity)

2.3 Pre-treatment assessment

- PET-CT to confirm oligometastatic state is recommended
- Pulmonary function tests (FEV1, FVC, KCO/TLCO)

Figure 1: proximal bronchial tree as defined by RTOG 0236 protocol [14]



2.4 CT localisation

2.4.1. Patient positioning

Patients will be positioned supine with their arms above their head using the WingSTEP wingboard and legs supported on a knee rest. Alternatively, they will be positioned holding an arm pole with a customized vacuum bag to ensure accuracy, reproducibility and comfort. In patients where the lesion lies superior to the carina, reproducibility may be improved using a 5-point fixation thermoplastic shell with arms by the side. A thin foam mattress can also be used for comfort.

2.4.2 Tumour motion

4DCT will be used in the majority of patients to account for tumour motion as described in the non-small cell lung protocol. A 3DCT in breath hold using the Active Breath Control (ABC) device is an option for patients whose tumour is anticipated to move by >1cm with respiration (e.g. lower lobe tumours).

2.4.3. CT stimulation

A 3-D scan without iv contrast will be performed prior to performing the 4D-CT scan using Tumour-LOC to localise the tumour. Patients will undergo a treatment planning CT scan in the treatment position. Contiguous axial slices of 2mm will be obtained from the upper cervical spine to the lower edge of the liver, taking care to include all lung parenchyma on the planning scan. Intravenous contrast will be used if requested at a flow rate of 1.0 to 1.5ml/s.

2.5 Volume definition

2.5.1 Target delineation

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

- Clinical Target Volume (CTV) = The CTV is the GTV with no margin for microscopic disease extension. This is the accepted standard in the majority of SBRT trials.

- Internal Target Volume (ITV) = Tumour volume obtained using a 4DCT scan. The volume is initially outlined using the individual phases and reviewed using the maximum intensity projection (MIP) to ensure the contour encompasses extremes of tumour motion.

- Planning Target Volume (PTV)

    - The isotropic margin from ITV to PTV will be 5mm for patients treated using 4DCT.
    - A margin of 6mm in axial directions and 8mm in the cranio-caudal direction is used for patients treated using ABC.

2.6 Organs at risk (OAR) delineation

The following OARs will be delineated on the CT planning average dataset (AIP):

- Spinal Cord
- Oesophagus
- Brachial Plexus
- Heart
- Trachea and Proximal Bronchial Tree
- Great vessels
- Whole Lung
- Chest wall
- Skin
- Liver

2.7 Treatment planning

2.7.1 Beam selection

The paradigm dictates that the high-dose region should be conformal to the PTV, the medium-dose region surrounding the PTV should be compact and the low-dose region is permitted to be relatively large by comparison to the other regions. All dose calculations should be performed using heterogeneity correction. Usually planned with dual unilateral (180 degree) VMAT arcs. Dual arcs which extend beyond 180 degrees anteriorly may be useful for anteriorly placed tumours.

2.7.2 Treatment planning system

Inhomogeneity corrections have a large influence on the dose delivered to the PTV and OARs for SABR to lung tumours. Consequently, the type B Collapsed Cone algorithm, that considers changes in lateral electron transport, will be used [17] [18].

2.7.3. Tumour location / OAR doses

See Appendix.

2.8 Dose prescription

Acceptable dose fractionation regimes are:

Standard Dose Fractionation	18Gy x 3 fractions
Conservative Dose Fractionation	11Gy x 5 fractions
Very Conservative Dose Fractionation	7.5Gy x 8 fractions

- The conservative dose fractionation is recommended when any part of the PTV is in contact with the chest wall.
- The very conservative fractionation schedules may rarely be used if the dose constraints cannot be met at 55Gy in 5 fractions and the patient has been discussed in the lung SABR MDT. The conformity constraints are as per 55Gy in 5 fractions.
- It is recommended that the inter-fraction interval be at least 40 hours, with a maximum interval of ideally 4 days between fractions [13].

2.9 Dose distribution requirement

The following criteria should be met:

- The dose prescription will be chosen such that 95% of the target volume (PTV) receives at least the nominal fraction dose (e.g. 18Gy per fraction = 54Gy total), and 99% of the target volume (PTV) receives a minimum of 90% of the fraction dose (i.e., 16.2Gy per fraction = 48.6Gy total)
- The maximum dose within the target volume should be between 110% to 140% of the prescription dose. For example, for dose prescriptions of 54Gy in 3 fractions, the $dose_{max}$ within the PTV should preferably not be less than 59.4Gy (i.e. 110%) or exceed 75.6Gy (i.e. 140%)). A minor deviation will be scored in cases where the $dose_{max}$ lies between either 56.7-59.4Gy or between 75.6-78.3Gy.

Tables 2 and 3 Updated dose conformity requirements using modified metrics endorsed by the UK SABR consortium guidelines [11]

Table 1: prescription dose spillage requirements

Vol (PTV) / cc	Vol (100%) / PTV V100%		
	Target	Tolerance	Minor Dev
<20	1.2	<1.25	1.25-1.40
20-40	1.1	<1.20	1.20-1.30
>40	1.1	<1.15	1.15-1.20

Table 2: Modified gradient index and other requirements

Vol (PTV) / cc	Vol(50%) / PTV V100%			Lung – GTV V20 (%)	Max dose > 2cm	
					3 fractions	5-8 fractions
	Target	Tolerance	Minor Dev	Tolerance	Tolerance	Minor Dev
<20	7	9	9-11	<5	<35.1Gy	<35.8Gy
20-40	5.5	6.5	6.5-7.5	<6	<37.8Gy	<38.5Gy
40-60	5	6	6-7	<10	<37.8Gy	<38.5Gy
60-90	4	5	5-7	<10	<37.8Gy	<38.5Gy
>90	4	4.5	4.5-6.5	<10	<37.8Gy	<38.5Gy

R100% = Vol (100%) / Vol (PTV): ratio of prescription isodose (eg 54Gy or 55Gy) volume to the PTV

R50% = Vol (50%) / Vol (PTV): ratio of 50% prescription isodose (27Gy or 27.5Gy) volume to the PTV

Prescription dose spillage = Vol (100%) / PTV V100%: ratio of prescription isodose (eg 54Gy or 55Gy) volume to volume of PTV receiving at least 100% of prescription dose.

Modified dose gradient = Vol (50%) / PTV V100%: ratio of 50% prescription isodose (eg 27Gy or 27.5Gy) volume to volume of PTV receiving at least 100% of prescription dose.

Max dose >2cm: maximum dose (% of nominal prescription dose) at least 2cm from the PTV in any direction

V20: percentage of total lung volume – GTV receiving >20Gy

2.10 Verification

Verification as per SABR section of Verification Imaging Protocol WI 8 1 16.

2.11 Treatment assessment and follow up

It is expected that patients will be assessed at 4-6 weeks after SABR and then as per the follow up for individual disease sites.

Section 3:SABR for spine metastases

3.1 Selection criteria

Inclusion criteria:

- Confirmed histological diagnosis of metastatic cancer originating from any primary cancer in the body, including carcinoma, sarcoma and melanoma.
- A disease-free interval between primary treatment and manifestation of metastases of at least six months
- One to three sites of extracranial, metastatic disease at the time of presentation
- A life expectancy of at least 6 months
- World Health Organisation (WHO) performance status ≤ 2.
- Not more than 2 consecutive spinal vertebral bodies involved
- Tumour at least 3-5mm from the cord
- Well defined lesions on imaging

Exclusion criteria:

- Patients with spinal instability (SINS score ≥13)
- Patients unable to lie flat / tolerate treatment
- Contraindication to MRI (e.g. pacemaker in situ)
- Significant or progressive neurological deficit such that emergency surgery or radiation required
- Radiosensitive histology's such as myeloma or lymphoma
- Spinal cord compression or impingement

All patients must be referred to the SABR MDT for discussion.

3.2 Patient assessment

- Recent full staging with CT chest/ abdo/ pelvis and/or PET scan to rule out more widespread disease.
- MRI whole spine.
- Assessment of spinal stability (SINS score). Consider discussion with spinal surgeons first if score 8-12 and do not offer SABR if ≥13.

SINS component	Score
Location	
Junctional (occiput–C2, C7–T2, T11–L1, L5–S1)	3
Mobile spine (C3–6, L2–4)	2
Semirigid (T3–10)	1
Rigid (S2–5)	0
Pain*	
Yes	3
Occasional pain but not mechanical	2
Pain-free lesion	0
Bone lesion	
Lytic	2
Mixed (lytic/blastic)	1
Blastic	0
Spinal alignment	
Subluxation/translation present	4
De novo deformity (kyphosis/scoliosis)	2
Normal alignment	0
Vertebral body collapse	
>50% collapse	3
<50% collapse	2
No collapse with >50% body involved	1
None of the above	0
Posterolateral involvement of the spinal elementsy†	
Bilateral	3
Unilateral	1
None of the above	0

Criteria of instability. Total score (TS) 0–6 : stable spine, TS 7–12 : potential unstable spine, TS 13–18 : unstable spine. Recommendation : TS ≥7, consider surgical intervention. *Pain improvement with recumbency and/or pain with movement/loading of the spine, †Facet, pedicle, or costovertebral joint fracture or replacement with tumor

3.3 Consent

Patients should be consented in line with Department of Health guidance and be given a spinal SABR patient information sheet.
Specific side effects to be consented for include:

All	Fatigue, skin reaction, pain flare, increased risk of vertebral compression fracture or vertebral collapse which could require surgical intervention and small risk of myelopathy or nerve damage.
C-spine	Mucositis
T-spine	Oesophagitis, nausea, chest pain, rib fracture, small long term risk of trachea oesophageal fistula / stricture formation
L-spine	Diarrhoea, nausea, small risk of bowel damage (<5%)

3.4 Pre-treatment medication

All patients, unless otherwise contraindicated should be prescribed the following:

- Lorazepam 1mg, oral, approximately 30 minutes prior to session with immobilisation
- Ondansetron, 8mg, oral, approximately 30 minutes prior to each treatment [can be excluded for those having cervical spine treatments]
- Dexamethasone 4mg od starting the day of treatment until 5 days after last treatment. On treatment days, to be taken approximately 30 minutes prior to each treatment. Should also prescribe PPI with dexamethasone.

3.5 Immobilisation and position

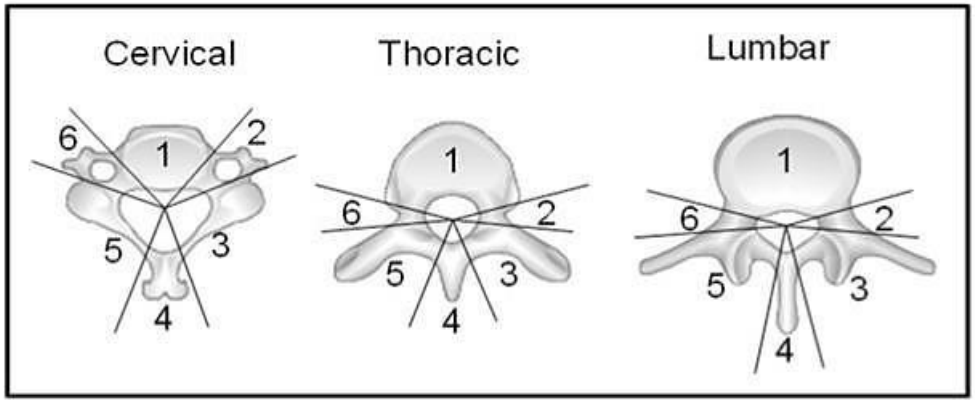
All patients will be treated supine, with knee and ankle supports to improve comfort Patients with cervical spine metastases will have a head/neck thermoplastic shell. Patients with thoracic/lumbar/sacral lesions will be immobilised with a vac bag.

3.6 CT localisation

All patients will have a planning CT scan (slice thickness 2mm or less). A limited spine (involved vertebral level plus one above and one below) radiotherapy planning MRI should be considered. Image fusion of the planning CT and either planning MRI or diagnostic MRI should be performed to aid outlining.

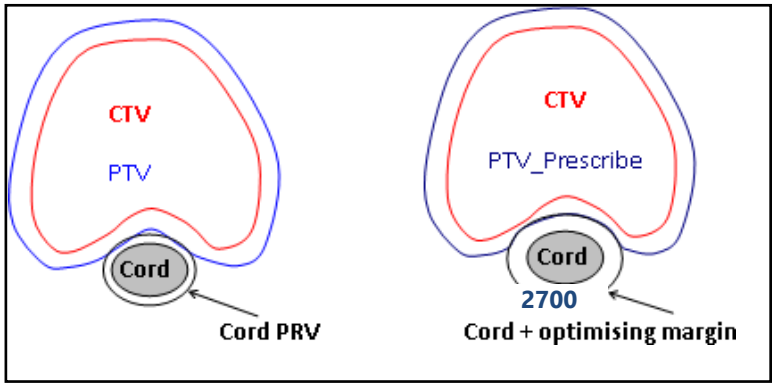
3.7 Target delineation

Tumour Delineation should follow International Guidelines and can be summarised as follows:



GTV involvement	ISRC GTV anatomic classification	ISRC bony CTV recommendation	CTV description
Any portion of the vertebral body	1	1	Include the entire vertebral body
Lateralized within the vertebral body	1	1, 2	Include the entire vertebral body and the ipsilateral pedicle/transverse process
Diffusely involves the vertebral body	1	1, 2, 6	Include the entire vertebral body and the bilateral pedicles/transverse processes
GTV involves vertebral body and unilateral pedicle	1, 2	1, 2, 3	Include entire vertebral body, pedicle, ipsilateral transverse process, and ipsilateral lamina
GTV involves vertebral body and bilateral pedicles/transverse processes	3	2, 3, 4	Include entire vertebral body, bilateral pedicles/transverse processes, and bilateral laminae
GTV involves unilateral pedicle	2	2, 3 ± 1	Include pedicle, ipsilateral transverse process, and ipsilateral lamina, ± vertebral body
GTV involves unilateral lamina	3	2, 3, 4	Include lamina, ipsilateral pedicle/transverse process, and spinous process
GTV involves spinous process	4	3, 4, 5	Include entire spinous process and bilateral laminae

Abbreviations: CTV = clinical target volume; GTV = gross tumor volume; ISRC = International Spine Radiosurgery Consortium.



In delineating the target volume, the recommendations of ICRU62 should be followed, with an additional volume (PTV_2700) recommended to account for the proximity of the spinal cord.

GTV	Contour gross tumour using all available imaging. Include epidural and paraspinal components of tumour.
CTV	Should contain GTV and include bony CTV expansion to account for subclinical spread. Include abnormal marrow signal suspicious for microscopic invasion, as indicated above. Circumferential CTVs encircling the cord should be avoided except in rare instances where the vertebral body, bilateral pedicles/lamina, and spinous process are all involved or when there is extensive metastatic disease along the circumference of the epidural space without spinal cord compression.
PTV	CTV to PTV margin of 3mm Dose to this volume should be reported in all circumstances.
PTV_2700	In order to allow for unavoidable underdosing of the PTV in close proximity to the spinal cord, while maintaining consistency in treatment prescription, it is recommended that a volume be created (PTV_2700) that restricts the PTV by spinal cord PRV+2mm. If it is different from PTV, this volume should be used for prescribing and additional dose reporting. i.e. PTV_2700 = PTV – [cord PRV+2mm] Note: PTV_2700 volume may be generated or edited appropriately in treatment situations where GTV extends beyond this volume, with consideration given to the achievable dose gradient.

3.8 Organs at risk delineation

Spinal Cord PRV – Spinal cord (delineated with assistance of fused MRI) + 2mm. Other OARs to be contoured where relevant:

- Kidneys
- Liver
- Lungs
- Oesophagus contoured 10mm above below PTV
- Small bowel contoured 10mm above below PTV
- Stomach contoured 10mm above below PTV
- Skin considered to be a 5mm structure inside the body outline

Spine dose constraints must be met. Other constraints may be compromised at the clinician's discretion.

3.9 Dose prescription

27Gy in 3 fractions on alternate days.
It is recommended that the inter-fraction interval be at least 40 hours, with a maximum interval of 4 days between treatment fractions.

It is recommended that the treatment be prescribed so that 95% of the PTV (or PTV_2700 where appropriate) should be covered by the prescription isodose unless there is need to accept less coverage to achieve the OAR tolerances. Hot spots should be within the PTV and ideally should not exceed 130% of the prescribed dose.

3.10 Organ at risk constraints

See Appendices

3.11 Verification

Verification as per SABR section of Verification Imaging Protocol WI 8 1 16.

3.12 Follow up after treatment

It is expected that patients will be assessed at 4-6 weeks after SABR and then as per required follow up for individual disease sites.

Section 4: SABR for non-spine bone metastases and lymph node metastases

4.1 Selection criteria

- Confirmed histological diagnosis of metastatic cancer originating from any primary cancer in the body, including carcinoma, sarcoma and melanoma.
- A disease-free interval between primary treatment and manifestation of metastases of at least six months
- One to three sites of extracranial, metastatic disease at the time of presentation
- A life expectancy of at least 6 months
- World Health Organisation (WHO) performance status ≤ 2.
- Maximum size of 5 cm for any single metastasis.

All patients must be referred to the SABR MDT for discussion.

4.2 Patient assessment

- Recent full staging with CT chest/abdo/pelvis and/or PET scan to rule out more widespread disease.
- Consider MRI of local region for bone metastases

4.3 Consent

Patients should be consented in line with Department of Health guidance and be given a relevant patient information sheet. Specific side effects to be consented include:

All	Fatigue, skin reaction, pain flare, small risk of nerve damage.
Thoracic	Chest wall pain, cough, pneumonitis
Para-aortic nodes	Nausea, vomiting, GI ulceration / inflammation, hepatic/renal toxicity
Sacrum / pelvis	Diarrhoea, proctitis, rectal bleeding/mucus, urinary side effects

4.4 Pre-treatment medications

The clinician will check if a patient requires anti-emetics.
Patients whose PTV is close to the stomach/duodenum should be prescribed a proton pump inhibitors and should remain on this for at least a 3 month period.

4.5 Immobilisation and position

All patients will be treated supine, with knee and ankle supports to improve comfort
Immobilisation will depend on the site of bone / nodal metastases.
Use of 4DCT or ABC can be considered for lesions where there is likely to be respiratory motion (e.g. upper abdominal nodes and rib/sternum metastases).

4.6 CT localisation

All patients will have a planning CT scan (2mm or less thickness). Image fusion of the planning CT and diagnostic MRI / PET should be considered to aid outlining.

4.7 Target delineation

Tumour Delineation should follow International Guidelines and can be summarised as follows:

Lymph node	
GTV	Defined as the visible tumour on CT (aided by PET). If 4DCT used, then GTV grown to ITV to account for respiratory motion.
CTV	An additional margin to account for microscopic spread is not mandated but can be considered
PTV	5mm

Bone	
GTV	Defined as the visible tumour on CT/MRI (aided by PET)
CTV	An additional 3 - 5mm margin can be considered
PTV	5mm

Sacrum	
GTV	Defined as the visible tumour on CT/MRI (aided by PET)
CTV	An additional 2-3mm margin can be considered +/- consideration of a compartmental CTV approach as outlined in the consensus paper below.
PTV	3-5mm

Dunne et al. International consensus recommendations for target volume delineation specific to sacral metastases and spinal stereotactic body radiation therapy (SBRT). Radiother Oncol. 2020; 145:21-29

4.8 Organs at risk delineation

Depending on the location of the PTV, relevant OARs (2cm above and below PTV) may include:

- Skin
- Brachial plexus
- Spinal cord / Cauda Equine
- Lungs
- Chest wall
- Heart
- Oesophagus

- Small Bowel
- Liver
- Stomach
- Duodenum
- Large Bowel
- Kidneys
- Sacral Plexus
- Bladder
- Femoral heads
- Rectum

4.9 Dose prescription

Bone: 30-40Gy / 3 fractions on alternate days (usually 30Gy/3 fractions).

Lymph node: 30-40Gy / 3 fractions on alternate days (usually 30Gy/3fractions) Treatment over 5 fractions if OAR tolerance concerns (e.g. duodenum)

Sacrum: 27-30Gy / 3 fractions on alternate days

It is recommended that the treatment be prescribed so that 95% of the PTV should be covered by the prescription isodose unless there is need to accept less coverage to achieve the OAR tolerances.

4.10 Organs at risk constraints

See appendices

4.11 Verification

Verification as per SABR section of Verification Imaging Protocol WI 8 1 16.

4.12 Follow up after treatment

It is expected that patients will be assessed at 4-6 weeks after SABR and then as per required follow up for individual disease sites.

Section 5: SABR for adrenal metastases

5.1 Selection criteria

Inclusion criteria:

- Metastatic histologically-proven malignancy with adrenal metastasis on imaging.
- Tumour surgically unresectable or inappropriate after discussion in specialist uro-oncology MDT, or patient has declined surgery.
- Karnofsky performance status (KPS) of >70 or WHO PS >2.
- Life expectancy of > 6 months
- Absent, or limited and potentially treatable, extra-adrenal disease
- Systemic therapy completed, or discontinued 4 weeks before SABR.
- Lesion <6cm in any dimension.
- Able to provide informed consent and comply with radiotherapy.

Exclusion criteria:

- Single functional kidney on the same site as metastatic adrenal disease
- Any previous radiotherapy to the site likely to overlap with SABR, or where previous doses to other critical normal structures may make reirradiation unsafe.

The risk of SABR treatment for a particular patient should be made by the local MDT considering factors such as, biochemical profile, FBC and random cortisol. A DMSA scan can be considered for all patients, with PET/CT staging scans acquired as required according to the MDT decision.

5.2 Radiotherapy

5.2.1. Tumour delineation

GTV	the extent of gross tumour as visualised in the contrast-enhanced exhale phase breath hold CT scan (or individual phases of the 4DCT scan with a summed ITV generated after)
ITV	Where patients are unable to tolerate breath-hold delivery of treatment a 4D-CT scan should be used to delineate the ITV as the full range of target position during respiration either on the MIP or the individual phases of the 4DCT scan with a summed ITV generated after this.
CTV	No margin between GTV and CTV is added
PTV	Expansion margins to PTV should be 6mm radially, and 8mm Sup/Inf when using ABC. For 4DCT then ITV-PTV margin should be 5mm.

5.3 Organs at risk (OAR) delineation

Organs should be outlined by the treating radiotherapist (or dosimetrist and checked by treating radiotherapist) and should include stomach, duodenum, all bowel, large bowel, kidneys, oesophagus, liver (entire volume), spinal canal, heart and lungs (entire volume).

5.4 Fractionation

To date, there are no randomised, controlled trials comparing dose-fractionation regimens for SABR in adrenal metastases. The data that are published show considerable heterogeneity in the dose-fractionation schedules delivered. There does however appear to be a similar dose-response relationship as with other sites treated with SABR.

Suggested fractionations and dose distribution requirements:

- 30-36Gy in 3 fractions over 6-7 days
- 45Gy in 5 fractions over 10 days

The plan should be prescribed so that 95% of the PTV receives the nominal prescribed dose. The maximum (0.1cc) dose should be ≤140% of the prescribed dose. If OAR constraints cannot be met then reduction of either the prescribed dose, or the required dose coverage, should be considered.

5.5 Verification

Verification as per SABR section of Verification Imaging Protocol WI 8 1 16.

5.6 Treatment assessment and clinical follow up

Patient Care on Treatment:
Weekly on-treatment review of full blood count, urea and electrolytes, liver function and random cortisol.
Patients whose PTV is close to the stomach/duodenum should be prescribed a proton pump inhibitors and should remain on this for at least a 3 month period.
5-HT3 antagonists for nausea should be considered.

Follow-up:
The purposes of follow up are early detection of disease progression so as to intervene early in managing this, and to accurately document and respond to toxicity. Assessment are recommended at 3, 6, 12, 18 and 24 months and annually thereafter, with CTCAE v4.0 being recommended for toxicity assessment before and after RT, specifically the following symptoms: anorexia, dyspnoea, diarrhoea, liver dysfunction and RILD, fatigue, GI bleeding, nausea, pain, pleural effusion, pneumonitis, pulmonary fibrosis and endocrine dysfunction. Assessment should also include radiological response where appropriate, using CT or other imaging modalities such as MRI or PET/CT.

Section 6: SABR for liver metastases

6.1 Selection criteria

Inclusion criteria

- 1-3 liver metastases unequivocally seen on contrast enhanced CT and/or MRI in patients with previously histologically diagnosed carcinoma.
- A disease-free interval between primary treatment and manifestation of metastases of at least six months (with the exception of colorectal cancer with synchronous liver-only metastases)
- Metastases unresectable, patient unfit or declines surgery, or presence of extra-hepatic disease making surgery an inappropriate treatment option
- ECOG Performance Status ≤2
- Discussion in Hepatobiliary (HPB) MDT with agreement that SABR is the most suitable local treatment modality. It should be confirmed that the patient is unsuitable for surgery and/or RFA.
- Discussion at SABR MDT
- Predicted life expectancy > 6 months
- Recovered from any previous therapy (such as surgery, chemotherapy or radiotherapy to other areas) with a minimum of 2 weeks break (anthracycline based chemotherapy should be completed 4 weeks before SABR)
- For 3-5# SABR: up to 3 metastases, maximum size of a single metastasis ≤ 5cm.
- For those with larger volume disease, consider treatment with 10# regimen.
- Adequate organ function, defined as: >700 cc normal liver (liver-GTV), Haemoglobin 9.0 g/dL, platelets >80 bil/L, bilirubin <3.0 times upper limit of normal, INR <1.3 or correctable with vitamin K and unless the patient is taking warfarin, AST or ALT <5.0 times upper limit of normal.
- Class A from Child's Pugh Liver Score (see Table 9.3)

Exclusion criteria

- Active hepatitis or clinically significant liver failure (encephalopathy, portal hypertension, varices)
- Clinically apparent ascites
- Any previous radiotherapy where the mean dose to the liver ≥15Gy (conventional fractionation), where beams would be likely to overlap with those used to deliver SABR, or where previous doses to other critical normal structures would make re-irradiation unsafe.
- If fiducial markers are to be placed, coagulopathy preventing safe insertion of fiducial markers and allergy to the metal component of the fiducial.

Childs-Pugh Liver Score

Measure	1 point	2 point	3 points
Total Bilirubin (µmol/l) (mg/dl)	<34 (<2)	34-50 (2-3)	>50 (>3)
Serum albumin (g/l)	>35	28-35	<28
INR	<1.7	1.71-2.20	<2.20
Ascites	None	Mild	Severe
Hepatic Encephalopathy	None	Grade 1-2 (or suppressed with medication)	Grade 3 or 4

Points	Class	One Year Survival	Two Year Survival
5-6	A	100%	85%
7-9	B	81%	57%
10-15	C	45%	35%

6.2 Patient assessment

- Recent full staging with CT chest/abdo/pelvis and FDG-PET scan to rule out more widespread disease. (PET is not mandatory for colorectal cancer with liver-only metastases)

- Patient is able to comply with active breath control (ABC) which requires good dentition or well-fitting dentures, the ability to achieve 20 second breath hold and comply with verbal instructions
- A diagnostic liver MRI is strongly recommended to aid tumour definition (unless contraindications to MRI), as contrast-enhanced CT alone often underestimates tumour volume
- A DMSA scan may be required if the renal dose is likely to be significant

6.3 Pre-treatment medication

Prescribe ondansetron 8mg to be taken 30 minutes prior to each fraction. Patients whose PTV is close to the stomach/duodenum should be prescribed a proton pump inhibitor for at least 3 months.

6.4 Immobilisation and positioning

Patients will be positioned supine with their arms above their head using the WingSTEP wingboard and with knee and ankle supports to improve comfort.

6.5 CT localisation

A planning CT scan with iv contrast in venous phase (60 second delay) will be acquired in exhale breath hold using the active breath control (ABC) device to control respiratory motion. Image fusion of the planning CT and diagnostic MRI will be performed to aid outlining. If the patient cannot manage ABC, then a 4DCT planning scan may be attempted. If there is excessive respiratory motion, then referral to a centre with the facility for abdominal compression may be required.

6.6 Target delineation

Radiology input should be sought to aid tumour and/or organ at risk definition where necessary. Target and OAR volumes and the treatment plan should be peer-reviewed by a 2nd SABR-trained oncologist prior to commencing treatment.

GTV	All definable disease on contrast CT and fused MRI
CTV	GTV + 5mm isotropically, edited to liver contours (ie CTV does not extend beyond the liver border)
PTV	CTV + 6mm in axial directions and 8mm in the cranio-caudal direction

6.7 Organs at risk delineation

The following organs will be contoured from 2cm above to 2cm below the PTV:

- Heart
- Great vessels
- Oesophagus
- Stomach
- Duodenum
- Small bowel
- Large bowel
- Normal liver (i.e. liver-GTV)
- Kidneys
- Spinal canal

6.8 Dose and fractionation

Two fractionation regimes are available depending on the clinical scenario and physician choice. The highest BED achievable within the planning constraints should be used.

1. 45Gy in 3 fractions (alternate days):

Prescribed to the prescription isodose covering at least 95% of the PTV (usually 80- 95%). DMax within PTV<133%.

2. 50-60Gy in 5 fractions (alternate days)

May be used when a larger PTV volume is being treated in order to achieve OAR constraints, when the PTV is within 1 cm of small bowel/visceral OAR or adjacent to chest wall/ribs. ≥95% of the PTV will receive the prescription dose.

6.9 Organ at risk constraints

See Appendix

6.10 Verification

Verification as per SABR section of Verification Imaging Protocol WI 8 1 16.

6.11 Follow up after treatment

Review at 4-6 weeks (clinical review only), then 3 monthly to 2 years and 6 monthly thereafter including bloods (FBC, U+E, LFTs, clotting and tumour markers as appropriate) and toxicity assessment.

Follow up imaging assessments (CT and/or MR liver) should be performed routinely at 3, 6, 12 months post SABR and 6 monthly thereafter.

Section 7: Appendices

Thoracic Dose Constraints

Structure	Metric	1 fraction		3 fractions		5 fractions		8 Fractions		Endpoint
		Opt	Man	Opt	Man	Opt	Man	Opt	Man	
Brachial Plexus	$D_{0.1cc}$		15Gy		24Gy	30.5Gy	32Gy	35Gy	39Gy	G3+ neuropathy
Bronchus	$D_{0.1cc}$		20.2Gy		30Gy	35Gy	38Gy		40Gy	G3+ stenosis/fistula
Chest wall	$D_{0.1cc}$ D_{30cc}	30Gy		36.9Gy 30Gy		43Gy				G3+ fracture/pain
Great Vessels	$D_{0.1cc}$		30Gy		45Gy		53Gy	60Gy	65Gy	G3+ aneurysm
Heart	$D_{0.1cc}$		22Gy	26Gy	30Gy	29Gy	38Gy	40Gy	46Gy	G3+ pericarditis
Lungs	V_{20Gy} D_{mean}	10% 8Gy	15%	10% 8Gy	15%	10% 8Gy	15%	10% 8Gy	15%	G3+ pneumonitis
Oesophagus	$D_{0.1cc}$		15.4Gy		25.2Gy		35Gy		40Gy	G3+ stenosis/fistula
Skin	$D_{0.1cc}$ D_{10cc}		26Gy 23Gy	33Gy 30Gy		39.5Gy 36.5Gy		48Gy 44Gy		G3+ ulceration
Trachea	$D_{0.1cc}$		20.2Gy		30Gy	35Gy	38Gy		40Gy	G3+ stenosis/fistula

CNS Dose Constraints

Structure	Metric	1 fraction		3 fractions		5 fractions		End point
		Opt	Man	Opt	Man	Opt	Man	
Brain	V_{12Gy} D_{20cc}	10-15cc		20Gy		24Gy		Radiation necrosis
Brainstem	$D_{0.035cc}$	10Gy	15Gy	18Gy	23.1Gy	23Gy	31Gy	G3+ cranial neuropathy
Cochlea	D_{mean}	4Gy		17.1Gy		25Gy		G3+ hearing loss
Lens	$D_{0.035cc}$	1.5Gy						Cataract formation
Optic pathway	$D_{0.035cc}$	8Gy	10Gy	15Gy	20Gy	22.5Gy	25Gy	G3+ optic neuritis
Orbit	$D_{0.1cc}$	8Gy						Retinopathy

Gastro-Intestinal Dose Constraints

Structure	Metric	1 fraction		3 Fractions		5 Fractions		End point
		Opt	Man	Opt	Man	Opt	Man	
BileDuct_Common	$D_{0.1cc}$		30Gy	50Gy		50Gy		
Bowel Small	$D_{0.1cc}$ D_{5cc} D_{10cc}		15.4Gy 11.9Gy		25.2Gy 17.7Gy	30Gy	35Gy	G3+ enteritis/ obstruction
Duodenum	$D_{0.1cc}$ D_{10cc}		12.4Gy 9Gy		22.2Gy 11.4Gy	33Gy 25Gy	35Gy	G3+ ulceration
Kidney Cortex (individual/combined)	D_{mean}			8.5Gy		10Gy		G3+ renal function dysfunction
Kidney Cortex (combined)	$D_{\geq 200cc}$		8.4Gy		16Gy		17.5Gy	
If solitary kidney or one Kidney cortex D_{mean} constraint exceeded	V_{10Gy}		33%		33%	10%	45%	
Liver (non-liver lesions) and Liver-GTV (liver lesions)	$D_{\geq 700cc}$ V_{10Gy} D_{mean}		9.1Gy	15Gy 13Gy	17Gy 15Gy	15Gy 70% 13Gy	 15.2Gy	G3+ liver dysfunction RILD
Spleen	D_{mean}		Report		Report		Report	
Stomach	$D_{0.1cc}$ D_{10cc} D_{50cc}		12.4Gy 11.2Gy		22.2Gy 16.5Gy	33Gy 25Gy 12Gy	35Gy	G3+ ulceration/fistula

Pelvic Dose Constraints (for non-prostate primary irradiation)

Structure	Metric	1 fraction		3 fractions		5 fractions		End point
		Opt	Man	Opt	Man	Opt	Man	
Bladder	$D_{0.1cc}$		18.4Gy		28.2Gy		38Gy	G3+ cystitis/fistula
Bowel_Large	$D_{0.1cc}$		18.4Gy		28.2Gy		38Gy	G3+ colitis/fistula
FemurHeadNeck	D_{10cc}	14Gy		21.9Gy		30Gy		G3+ necrosis
LumbSacPlex	$D_{0.1cc}$ D_{5cc}	16Gy 14.4Gy		24Gy 22.5Gy		32Gy 30Gy		G3+ neuritis
Rectum	$D_{0.1cc}$		18.4Gy		28.2Gy		38Gy	G3+ proctitis/fistula
Ureter	$D_{0.1cc}$		35Gy		40Gy			
Urethra	$D_{0.1cc}$		Report		Report		Report	

Other Dose Constraints

Structure	Metric	1 fraction		2 fractions		3 fractions		5 fractions		8 fractions		End point
		Opt	Man	Opt	Man	Opt	Man	Opt	Man	Opt	Man	
Cauda Equina	$D_{0.035cc}$ D_{5cc}		16Gy 14Gy									
Spinal Cord	$D_{0.035cc}$	12.4 Gy	14Gy		17Gy		20.3Gy		25.3Gy		32Gy	Radiation myelopathy

PACE trial [14] constraints for primary prostate radiotherapy only

Description	Constraint (**Prostate primary only**)	5 Fractions		Source
		Optimal	Mandatory	
Rectum	D50%	-	< 18.1Gy	PACE trial[14]
	D20%	-	< 29Gy	
	D1 cc	-	< 36Gy	
Bladder	D40%	-	< 18.1Gy	As above
	V37Gy	< 5 cc	< 10 cc	
Prostatic urethra (if visible)	D50%	< 42Gy	-	As above
Neurovascular bundle (if visible)	D50%	-	< 38Gy	As above
Femoral head	D5%	-	< 14.5Gy	As above
Penile Bulb	D50%	-	< 29.5Gy	As above
Testicles	Avoid beam entry e.g. Blocking structure			As above
Bowel	D5 cc	-	< 18.1Gy	As above
	D1 cc	-	< 30Gy	

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