East of England Radiotherapy Network:

Pancreatic and hepatocellular cancer protocol V4.0

Contents

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EofE RTN Pancreatic and Hepatocellular Cancer Protocol V4
Author: Thankamma Ajithkumar
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1.0 Indications and patient population

This protocol covers treatment in the following situations:

Pancreatic cancer

a. Radical radiotherapy (conventional chemo-radiotherapy or stereotactic ablative body radiotherapy –SABR) for a selected group of patients with locally advanced non-metastatic inoperable pancreatic cancer after completion of first-line chemotherapy or when chemotherapy is stopped due to toxicities, patients who are not fit or decline chemotherapy.

b. Radical radiotherapy for selected group of patients with borderline operable pancreatic cancer after completion of first-line chemotherapy or when chemotherapy is stopped due to toxicities to improve chances of surgical resection and/or local control.

c. Radical radiotherapy also be considered for patients with isolated local recurrence followed primary surgery.

d. Palliative radiotherapy for pain or bleeding from the tumour or symptomatic metastatic disease.

Primary liver cancer (Hepatocellular cancer - HCC)

a. Stereotactic ablative body radiotherapy (SABR) for selected patients with primary liver cancer

b. Palliative radiotherapy for symptomatic primary or metastatic disease

1.1 Curative treatment eligibility for pancreatic cancer

1.1.a Inclusion criteria

World Health Organisation (WHO) Performance Status 0-2:

- 0 – able to carry out all normal activity without restriction

- 1 – restricted in strenuous activity but ambulatory and able to carry out light work
- 2 – ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours

1.1.b Exclusion criteria

Radiological or endoscopic evidence of duodenal invasion by tumour.

1.1.c Essential Pre-Radiotherapy investigations for radical radiotherapy patients

- History and clinical examination, including assessment of performance status
- Blood tests: FBC, urea and electrolytes, serum albumin, liver function tests and CA19-9
- Histological confirmation
- Staging CT scan of the chest, abdomen, and pelvis
- PET scan (indicated before radical radiotherapy if there is equivocal nodal or metastatic disease)
- DMSA (dimercapto- succinic acid) renal scan: In patients with tumours of the body or tail of the pancreas lying close to the left kidney, it is important to check that the left kidney is not the dominant functioning one.

1.2 Curative treatment eligibility for primary liver cancer

1.2.a Inclusion criteria

Patients meeting **all** the following criteria will be eligible for treatment with SABR:

- Confirmed diagnosis of localised HCC (primary, recurrent, or progressive disease) by at least one criterion listed below:
  - Pathologically (histologically or cytologically) proven diagnosis of HCC
  - At least one solid liver lesion or vascular tumour thrombosis (involving portal vein, IVC and/or hepatic vein) > 1 cm with arterial enhancement and delayed washout on multiphasic Computed-Tomography (CT) or Magnetic Resonance Image (MRI) in the setting of cirrhosis or chronic hepatitis B or C without cirrhosis.
- No evidence of extrahepatic metastases or malignant nodes (that enhance with typical features of HCC) > 3.0 cm in sum of maximal diameters.

- Unsuitable for surgical resection or transplant.
- Unsuitable or refractory to TACE.
- WHO Performance Status 0-1.
- Adequate haematological and liver function.
- Childs-Pugh Class A only.

SABR should also be considered as an alternative treatment in people currently eligible for systemic treatments (such as sorafenib) and/or local ablative treatments. Any patients suitable for SABR must have recovered from the effects of previous surgery, radiotherapy, or chemotherapy with a minimum of 4 weeks break prior to treatment with SABR.

1.2.b Exclusion criteria

- Active hepatitis or clinically significant liver failure (encephalopathy, oesophageal varices, portal hypertension).
- Prior abdominal radiotherapy precluding SABR, that is any previous radiation therapy in which a mean dose to the liver of 15 Gray (Gy) in conventional fractionation was delivered or previous doses to critical normal structures that would make re-irradiation unsafe. Prior pelvic radiation is permitted, as long as there is no overlap between pelvic and liver radiation fields.
- Clinically apparent ascites.
- Any one hepatocellular carcinoma > 6 cm.
- More than 5 discrete intrahepatic parenchymal foci of HCC.
- Direct tumour extension into the stomach, duodenum, small bowel, or large bowel.
- Evidence of extrahepatic metastases or malignant nodes (that enhance with typical features of HCC) > 3.0 cm in sum of maximal diameters (e.g., 2 lung lesions >2 cm); or
- Prior liver transplant.

1.2.c Essential Pre-Radiotherapy investigations for curative patients

- Blood tests: FBC, urea and electrolytes, serum albumin, liver function tests, clotting screen, AFP, HBV, HCV, and iron status
- Histological confirmation

- Imaging: Dynamic MRI and CT to assess number and size of tumour(s), vascular invasion, and extra-hepatic spread
- Assessment for portal hypertension: Upper GI endoscopy for varices
- DMSA (dimercapto- succinic acid) renal scan: if the right kidney is closer to tumour, renal function scan is indicated.

2.0 Localisation

Localisation	Notes
Preparation	• Patients should ideally fast for 2 - 3 hours and before the planning CT scan and each treatment. Small amounts of water (up to 200ml) can be sipped slowly over this time. Discuss with dietician and Oncologist as to feasibility for fasting times for patient as needed (may not be suitable for patients with diabetes etc.). • Patient to drink 125-200ml of water as an oral contrast agent (or other CT oral contrast agent) **immediately** (5 mins) prior to planning CT. This may improve visualisation of the upper gastrointestinal tract for target delineation.
Position	• Position is supine with arms above the head, if possible. If this is not possible or comfortable for the patient to maintain, arms high on chest is possible (checking for inf elbow position and gantry collision possibility).
Immobilisation and supports	• Immobilisation with a vacuum-formed polystyrene bag and additional supports (e.g., thoracic board, knee support) as required for comfort and stability. • Motion management (e.g., abdominal compression): all patients with liver cancer should have motion management strategies to minimise respiratory motion. Typically, movement of locally advanced pancreatic tumour is more limited but if there is significant movement, motion management should be considered. • If abdominal compression used, patients to receive premedication with ondansetron 8mg po (30 minutes prior to CT) and a proton pump inhibitor (such as lansoprazole 30 mg od po, started few days prior to CT).

Localisation	Notes
Organ pre-requisites	• Abdominal compression may not be considered for patients known to have abdominal aortic aneurysm or previous history of total gastrectomy.
Contrast	• For pancreas: 100-150 ml of intravenous contrast is injected at a rate of 4-5 ml/seconds with 3D imaging capture approximately at 40-50 seconds (pancreatic parenchymal phase) • For liver: 100-150 ml of intravenous contrast is injected at a rate of 4-5 ml/seconds with 3D imaging capture approximately at 70-80 seconds (portal venous phase) • It is recommended to use bolus tracking, if available, to time the contrast enhancement phase more effectively.

CT acquisition	• 3D CT scan free-breathing (FB) – used for planning where patient to be treated FB.
	• 3D CT scan, if possible, in deep-expiratory breath hold (DEBH) - aid for outlining only, not to be used for planning dosimetry for FB treatments.
	• Slice thickness: 2-3mm.
	• Scanning limits:
	  ○ For pancreas: top of the liver or superior border of T11 to the lower border of the L3/below the level of kidneys
	  ○ For liver: 5 cm above the top of the liver to the lower border of the L3/below the level of kidneys.
	• 4D CT scan: all patients should have 4D CT scan, where possible. The 4D scan limits are based on individual patients.

Localisation	Notes
	○ If motion management methods are used, designed to limit motion, 4D CT scan traces may not be achievable or needed.
Supplementary imaging	• Planning MRI scan for primary liver tumour.
Image co-registration	• For pancreatic tumours: 3D CT FB scan and 4D scan when available should be co-registered. If PET scan or MRI is available, deformable co-registration will help to delineate the tumour better and therefore, is recommended. • For liver tumours: 3D CT scan, 4D CT scan and MRI sequence(s), which optimally demonstrate the tumour should be co-registered

3.0 Dose prescription & chemotherapy

Intent	Dose (Gy)/#	#/weeks	Chemo/ comments
a. Radical (chemo)-radiotherapy for pancreatic cancer	50.4 Gy/28	5	Concomitant capecitabine
b. SABR for pancreatic cancer	30-40 Gy/5	3-5	**Systemic therapy should be stopped at least 4 weeks before RT**
c. Hepatocellular carcinoma	40-50 Gy/5*	3	**Systemic therapy should be stopped at least 4 weeks before RT**
d. Palliative radiotherapy – Pancreas and liver	8 Gy/1 20 Gy/5 30 Gy/10	1 5 5	

4.0 Target volumes

- Use standard nomenclature as per AAPM 263
- https://www.aapm.org/pubs/reports/RPT_263.pdf
- Target volumes should match agreed naming conventions unless there are operational reasons for use of other naming. PTV ProKnow nomenclature should be used for NHSE ProKnow Collections and Scorecard Templates for upload.

4.1 Curative radiotherapy for pancreatic cancer

4.1.1 Conventional (chemo)-radiotherapy

- **GTV:** GTVp includes primary tumour and GTVn includes all lymph nodes above 10mm in the short axis. All PET positive lymph nodes (SUV >2.5) irrespective of size should be included in the GTV. When a 4D CT scan is available, additional GTVs are delineated on the maximal inspiratory and expiratory phases of the 4D CT scan (GTVp_Inhale, GTVp_Exhale, GTVn_Inhale, GTVn_Exhale) and a composite volume (ITV) is derived from all GTVs

  On the 3D scan outline:
  - GTVp (visible tumour)
  - GTVn (involved peritomoral nodes>1cm).

  On the 4D scan outline:
  - GTVp_Inhale and GTVn_Inhale at max inhalation
  - GTVp_Exhale and GTVn_Exhale at max exhalation

  Then:
  - ITV = GTV_4D = GTVp + GTVp_Inhale + GTVp_Exhale + GTVn + GTVn_Inhale + GTVn_Exhale

  Or, for the 3D only case:

  - GTV_3D = GTVp + GTVn

- **CTV:**
    - CTV_4D = ITV + 0.5 cm (edited away from uninvolved GI tract)
    - CTV_3D = GTV_3D +0.5 cm (edited away from uninvolved GI tract)

- **PTV:** The PTV margin depends on the patient setup and the available planning CT scans
    - 4D CT planning: PTV = CTV+ 0.5 cm
    - 3D DEBH planning: PTV = CTV_3D + 0.5 cm cranially, 1.5 cm caudally and 1.0cm axially
    - 3D Free Breathing: PTV = CTV_3D + 1.5 cm longitudinally and 1.0 cm axially

  These are the minimum PTV margins PTV and may be increased if required.

4.1.2. SABR

- **GTV:** GTVp includes primary tumour. Additional GTVs are delineated on the maximal inspiratory and expiratory phases of the 4D CT scan (GTVp_Inhale, GTpV_Exhale) and a composite volume (ITV) is derived from the three GTVs

  On the 3D scan outline:
    - GTVp (visible tumour)
    - GTVn (involved peritomoral nodes>1cm).

  On the 4D scan outline:
    - GTVp_Inhale and GTVn_Inhale at max inhalation
    - GTVp_Exhale and GTVn_Exhale at max exhalation

  Then:
    - ITV = GTV_4D = GTVp + GTVp_Inhale + GTVp_Exhale + GTVn + GTVn_Inhale + GTVn_Exhale

  Or, for the 3D only case:

    - GTV_3D = GTVp + GTVn

- **CTV:**
    - CTV_4D = ITV
    - CTV_3D (if no 4DCT only) = GTV

- **PTV:** The PTV margin depends on the patient setup and the available planning CT scans
    - 4D CT planning: PTV = CTV_4D + 0.5cm
    - 3D DEBH planning: PTV = CTV_3D + 0.5 cm cranially, 1.5 cm caudally and 1.0 cm axially
    - 3D Free Breathing: PTV = CTV_3D + 1.5 cm longitudinally and 1.0 cm axially

  These are the minimum PTV margins PTV and may be increased if required.

4.2 Palliative radiotherapy for pancreatic cancer

- The target volume (**PTV**) is the radiologically visible tumour with 1.5-2 cm isotropic margin.

4.3 Curative radiotherapy (SABR) for hepatocellular cancer

4.3.1. SABR

- **GTV**: GTVP includes primary tumour. Additional GTVs are delineated on the maximal inspiratory and expiratory phases of the 4D CT scan (GTVp_Inhale, GTVp_Exhale) and a composite volume (ITV) is derived from the three GTVs

  On the 3D scan outline:
  - GTVp (visible tumour)
  - GTVn (involved peritomoral nodes>1cm).

  On the 4D scan outline:
  - GTVp_Inhale and GTVn_Inhale at max inhalation
  - GTVp_Exhale and GTVn_Exhale at max exhalation

  Then:

- ITV = GTV_4D = GTVp + GTVp_Inhale + GTVp_Exhale + GTVn + GTVn_Inhale + GTVn_Exhale

- **CTV:**
  - CTV_4D = ITV
  - CTV_3D = GTV
- **PTV:** The PTV margin depends on the patient setup and the available planning CT scans
  - 4D CT planning: PTV = CTV+ 0.5 cm
  - 3D DEBH planning: PTV = CTV_3D + 0.5 cm cranially, 1.5 cm caudally and 1.0 cm axially
  - 3D Free Breathing: PTV = CTV_3D + 1.5 cm longitudinally and 1.0 cm axially

  These are the minimum PTV margins PTV and may be increased if required.

4.4 Palliative radiotherapy for HCC

- The target volume (**PTV**) is the radiologically visible tumour with 1.5-2 cm isoptropic margin.

5.0 Organs at risk

Aim for the use of standard nomenclature as per Global Harmonization Group consensus guidelines: https://www.thegreenjournal.com/action/showPdf?pii=S0167-8140%2820%2930294-2 and its appendix: https://www.thegreenjournal.com/cms/10.1016/j.radonc.2020.05.038/attachment/0d8ebe11-ff6b-46cc-814e-c60b77f7d9d3/mmc1.pdf

Structure name	Description
Liver	The liver should be contoured in entirety from the cranial diaphragmatic aspect to the caudal tip of the right lobe, using soft tissue windows. The gall bladder and hepatic vessels should be excluded. The inferior vena cava should be excluded from the liver contour when it is clearly separate from the liver. The gall bladder should be excluded.
BileDuct_Common	The common bile duct is usually 8-10cm in length and 5-6mm in diameter. The contour begins at the union of the common hepatic duct and the cystic duct and extends caudally to the second section of the duodenum. The common bile duct passes posterior and medial to the duodenum and joins with the pancreatic duct to form the ampulla of Vater.
Kidney_Cortex_L and Kidney_Cortex_R	Each kidney should be contoured separately from the upper to the lower pole. The kidney cortex structure is the kidney parenchyma and includes the fibrous capsule surrounding the kidney, the kidney cortex, and the kidney medulla. The structure excludes cysts, pararenal fat, and the adrenal gland.
Stomach	The stomach should be contoured from the GOJ to the pylorus. Contour to the outer extent of the external wall, including stomach contents.
Duodenum	From below the pylorus to the fourth part of the duodenum at the ligament of Treitz. The majority of the structure is fixed to the retroperitoneum and follows a C-shaped course around the head of the pancreas. The contour follows four anatomical sections: 1) 5cm in length and anterolateral to the body of the L1 vertebra 2) 7-10cm descending adjacent to the L1-3 vertebral bodies 3) 6-8cm in length, turning medially and crossing the L3 vertebral body. The aorta and inferior vena cava are posterior; the superior mesenteric artery and vein lie anteriorly 4) 5cm in length and ascending from the L3

Structure name	Description
	vertebral body to the cranial border of the L2 vertebral body The contour adheres closely to the outer boundary of the external wall and includes duodenal contents. Take care to distinguish the duodenum from the head of the pancreas as the structures are in close proximity.
Bowel_Small	Contour individual bowel loops from 2cm above and 2cm below the PTV. The small bowel encompasses the duodenum, jejunum, and ileum in one contour. Contour from the pylorus to the ileocaecal junction. The small bowel can be discriminated from the large bowel by the appearance of bowel contents and the presence valvulae conniventes. The contour adheres closely to the outer boundary of the external wall and includes small bowel contents.
Bowel_Large	The large bowel encompasses the caecum, ascending colon, transverse colon, descending colon, and sigmoid colon in one contour. Contour from the ileocaceal junction to the recto-sigmoid junction. The large bowel can be discriminated from the small bowel by the appearance of bowel contents, presence of haustra, sacculations, and appendices epiploicae. The contour adheres closely to the outer boundary of the external wall and includes large bowel contents.
Chest Wall (Chestwall_R Chestwall_L)	Each chest wall should be contoured separately. The chest wall is a 2cm rind of the hemi-thorax outside of the thoracic cavity. The structure includes ribs, intercostal vessels, nerves, and muscles, and excludes vertebral bodies, sternum, and skin. The anterior-medial border is at the lateral edge of the sternum; the posterior-medial border is the lateral aspect of the vertebral body.
Spleen	Entire spleen. The spleen varies in size and shape but is usually 12 x 7 x 3cm and located at the left upper abdominal quadrant. The stomach lies anterior to the spleen. Posteriorly, the spleen is surrounded by left 9th to 11th ribs and diaphragm. The left kidney is medial to the spleen and the caudal border is the left colic flexure. The

Structure name	Description
	peritoneum surrounds the spleen and should be excluded from the structure. The shape of the spleen will be affected by the surrounding organs and adjustment of CT window and level may be necessary to better distinguish the border of the spleen against adjacent structures.

Additional structures to be added are as follows:

SpinalCanal

Kidney_Cortex = Kidney_Cortex_L + Kidney_Cortex_R

Skin (a 5mm rind inside the skin outline)

Liver-GTV/Liver-GTVs for HCC plans

5.1 Constraints

5.1.1. Constraints for Pancreas 5-fraction treatment

Pancreas 5# Treatment			
Structure name	**Constraint**	**Optimal**	**Mandatory**
PTV	D95%	100%	-
	V100%	≥95%	≥90%*
	D0.1cc	-	110-130%**
Conformity Index **(V100% /PTV V100%)**	PTV ≤ 20 cc	≤ 1.25 (ideal 1.2)	≤ 1.40
	PTV 20-40 cc	≤ 1.20 (ideal 1.1)	≤ 1.30
	PTV > 40 cc	≤ 1.15 (ideal 1.1)	≤ 1.20
Modified Gradient Index **(V50% /PTV V100%)**	PTV ≤ 20 cc	≤ 7.5 (ideal 5.5)	≤ 9.5
	PTV 20-40 cc	≤ 6.0 (ideal 4.5)	≤ 7.5
	PTV > 40 cc	≤ 5.5 (ideal 4.6)	≤ 6.5
Bowel_Large	Dmax (05 cc)	-	≤38 Gy
Bowel_Small	Dmax (0.5 cc)	≤30Gy	≤35 Gy
	D10 cc	≤25 Gy	-
Duodenum	Dmax (0.5 cc)	≤33 Gy	≤35 Gy
	D10 cc	≤25 Gy	-
Stomach	Dmax (0.5 cc)	≤33Gy	≤35 Gy

	D10 cc	≤25 Gy	-
	D50 cc	≤12Gy	-
Liver	Mean	≤13 Gy	≤15.2 Gy
	V10Gy	≤70%	-
	D(VTOT-700cc)	≤15 Gy	-
Kidneys **(individual)** **(Kidney_Cortex_R, Kidney_Cortex_L)**	Mean	≤10 Gy	-
Kidneys (combined) **Kidney_Cortex**	Mean	≤10 Gy	-
	D(VTOT-200cc)		≤17.5Gy
If solitary kidney or if one kidney mean dose >10Gy	V10 Gy$^{\$}$	≤10%	≤45%
SpinalCanal	Dmax (0.035 cc)	-	≤25.3 Gy
Spleen	Mean	≤10Gy	-
	D0.1cc	Record dose	
BileDuct_Common	Dmax (0.5 cc)	≤50 Gy	-
Skin	D0.1cc	≤39.5Gy	-

OAR dose constraints as per National Pancreas SABR guidelines. Splenic constraint is based on recent RCR recommendation.

* The mandatory OAR constraints are priority. If any constraint cannot be achieved then the dose in the PTV will be reduced to meet it.

**Ideally Dmax will be within the GTV. It MUST be within the PTV.

$ of the kidney receiving the lower dose.

5.1.2. Constraints for Pancreas conventional fractionation treatment

Standard fractionation dose constraints are based on the Scalop-2 Trial Protocol

Pancreas Conventional Fractionation (50.4Gy/28#, 45Gy/25#)			
Structure name	**Constraint**	**Optimal**	**Mandatory**
PTV	D99%	≥95%	≥90%
	D95%	≥97%	≥93%
	D0.1cc	≤105%	≤107%
Duodenum	D0.1cc	≤58Gy	≤60Gy
	V50Gy	≤10cc	-
	V15Gy	≤60cc	-

Stomach	D0.1cc	≤58Gy	≤60Gy
	V50Gy	≤5cc	-
	V45Gy	≤75cc	-
Bowel_Small	D0.1cc	≤58Gy	≤60Gy
	V50Gy	≤10cc	-
	V15Gy	≤120cc	-
Liver	Dmean	≤28Gy	≤30Gy
	V30Gy	-	≤30%
Kidneys (combined) Kidney_Cortex	V20Gy	≤30%	≤35%
Kidneys (Individual) (Kidney_Cortex_L, Kidney_Cortex_R)	V20Gy	≤40%	≤45%
Spleen	Dmean	10Gy	
SpinalCanal	D0.1cc	-	≤45Gy

Conventional Fractionation (20Gy/5#)

Pancreas Conventional Fractionation (20Gy/5#)			
Structure name	**Constraint**	**Optimal**	**Mandatory**
PTV	D99%	≥95%	≥90%
	D95%	≥97%	≥93%
	D0.1cc	≤105%	≤107%
Duodenum	None	Minimise without compromising PTV	
Stomach	None	Minimise without compromising PTV	
Bowel_Small	None	Minimise without compromising PTV	
Liver	None	Minimise without compromising PTV	
Kidney_Cortex	None	Minimise without compromising PTV	
Spleen	None	Minimise without compromising PTV	
SpinalCanal	None	Minimise without compromising PTV	

5.1.3. Constraints for HCC treatment

HCC 3- and 5-Fraction Treatments					
Structure name	**Constraint**	**3 Fractions**		**5 Fractions**	
		Optimal	**Mandatory**	**Optimal**	**Mandatory**
PTV	V100%	≥95%	-	≥95%	-
	D95%	100%	-	100%	-
	D0.1cc	130-140%	110-140%	130-140%	110-140%

Conformity Index (V100% / PTV V100%)	PTV ≤ 20cc	≤ 1.25 (Ideal 1.2)	≤ 1.40	≤ 1.25 (Ideal 1.2)	≤ 1.40
	PTV 20-40cc	≤ 1.20 (Ideal 1.1)	≤ 1.30	≤ 1.20 (Ideal 1.1)	≤ 1.30
	PTV ≥ 40 cc	≤ 1.15 (Ideal 1.1)	≤ 1.20	≤ 1.15 (Ideal 1.1)	≤ 1.20
Modified Gradient Index (V50% /PTV V100%)	PTV ≤ 20cc	≤ 7.5 (Ideal 5.5)	≤ 9.5	≤ 7.5 (Ideal 5.5)	≤ 9.5
	PTV 20-40cc	≤ 6.0 (Ideal 4.5)	≤ 7.5	≤ 6.0 (Ideal 4.5)	≤ 7.5
	PTV ≥ 40cc	≤ 5.5 (Ideal 4.5)	≤ 6.5	≤ 5.5 (Ideal 4.5)	≤ 6.5
Bowel_Large	D0.1cc	-	≤28.2Gy	-	≤38Gy
Bowel_Small	D0.1cc	-	≤25.2Gy	≤30Gy	≤35Gy
	D5cc	-	≤17.7Gy	-	-
	D10cc	-	-	≤25Gy	
Duodenum	D0.1cc	-	≤22.2Gy	≤33Gy	≤35Gy
	D10cc	-	≤11.4Gy	≤25Gy	-
Stomach	D0.1cc	-	≤22.2Gy	≤33Gy	≤35Gy
	D10cc	-	≤16.5Gy	≤25Gy	-
	D50cc	-	-	≤12Gy	-
Liver-GTV/Liver-GTVs	Dmean	≤13Gy ($this is mandatory for HCC patients)	≤15Gy	≤13Gy ($this is mandatory for HCC patients)	≤15.2Gy
	V10Gy	-	-	≤70%	-
	D(VTOT-700cc)+	≤15Gy	≤17Gy	≤15Gy	-
Kidneys (individual) **(Kidney_Cortex_R, Kidney_Cortex_L)**	Mean	≤8.5Gy	-	≤10Gy	-
Kidneys (combined) **Kidney_Cortex**	Mean	≤8.5Gy	-	≤10Gy	-
	D(VTOT-200cc)+	-	≤16Gy	-	≤17.5Gy
Kidney_Cortex_L/R If solitary kidney, or if one Kidney_Cortex_R/L mean dose ≥optimal constraint	V10Gy $	-	≤33%	≤10%	≤45%
BileDuct_Common	D0.1cc	≤50Gy	-	≤50Gy	-
Chestwall_L, Chestwall_R	D0.1cc	≤36.9Gy	-	≤43Gy	-
	D30cc	≤30Gy	-	-	-
SpinalCanal	D0.035cc	-	≤20.3Gy	-	≤25.3Gy
Spleen	Dmean	≤10Gy	-	≤10Gy	-
Skin	D0.1cc	≤33Gy	-	≤39.5Gy	-
	D10cc	≤30Gy	-	≤36.5Gy	-

*For HCC, the mean liver dose will determine the final prescribed dose: see section 6.2

$ of the kidney receiving the lower dose.

5.1.4 Constraints for conventional fractionation

HCC Conventional Fractionation			
Structure name	**Constraint**	**Optimal**	**Mandatory**
PTV	D99%	≥ 95%	≥ 90%
	D95%	≥ 97%	≥ 93%
	D0.1 cc	≤ 105%	≤ 107%
Bowel_Large			
Bowel_Small	D0.1cc	≤58 Gy	≤ 60 Gy
	V50 Gy	≤10 cc	-
	V15 Gy	≤120 cc	-
Duodenum	D0.1cc	≤ 58 Gy	≤ 60 Gy
	V50 Gy	≤10 cc	-
	V15 Gy	≤60 cc	-
Stomach	D0.1cc	≤ 58 Gy	≤ 60 Gy
	V50 Gy	≤5 cc	-
	V45 Gy	≤75 cc	-
Liver	V30 Gy	-	≤ 30%
	Mean	≤ 28 Gy	≤ 30 Gy
Kidneys (combined) Kidney	V20 Gy	≤ 30%	≤ 35%
Kidneys (Individual) (Kidney_Cortex_L, Kidney_Cortex_R)	V20 Gy	≤40%	≤ 45%
Spleen	Mean	10 Gy	-
SpinalCanal	D0.1cc	-	≤ 45 Gy

6.0 Planning process/ technique

6.1 Pancreatic cancer

Planning objectives

Conventional fractionation

- 99% of the prescribed dose should cover at least 95% of the PTV (i.e., D99% ≥ 95%). The maximum dose ($D_{0.1cc}$) should not exceed >105% of the prescribed dose and the hotspot should be located within the PTV.
- Dose to OARs should be kept below the tolerance level, especially for the duodenum.

SABR

- The prescribed dose should cover 95% of the PTV (i.e., D95% ≥ 100%) and 100% of the ITV. The maximum dose within the PTV ($D_{0.1cc}$) may be up to 140% of the prescribed dose.
- The mandatory dose constraints to the gastrointestinal tract must be met and have higher priority than PTV coverage, to minimize the risk of grade ≥3 toxicities.

Planning technique

- IMRT and/or VMAT must be used for radical radiotherapy. IMRT (5 beams: 3 anterior and 2 lateral or 7 beams) or VMAT help to reduce the dose to critical organs.
- For palliative radiotherapy, IMRT or VMAT techniques may be used but conformal 3D radiotherapy or shaped opposed antero-posterior beams are also acceptable.

6.2 Hepatocellular cancer

Planning objectives for SABR

- The prescribed dose should cover 95% of the PTV (i.e., D95% ≥ 100%) and 100% of the ITV. The maximum dose within the PTV ($D_{0.1cc}$) may be up to 140% of the prescribed dose.
- Plans will be created using IMRT or VMAT
- Doses to OARs must be kept within tolerance. PTV coverage may need to be compromised to meet constraints.

- The final prescribed dose will depend on mean liver dose (MLD) (for liver-GTV) that can be achieved at planning. The planner will create a 50Gy/5# plan and use the table below to determine the final prescribed dose:

HCC ONLY – Final Dose Prescription		
Mean liver dose for 50Gy plan (Before rescaling) **Liver-GTV(s)**	**Final prescribed dose**	Mean liver dose constraint for **final plan** **Liver-GTV(s)**
≤ 13.0Gy	50Gy	≤ 13.0Gy
>13Gy but ≤16.7Gy	45Gy	≤ 15.0Gy
>16.7Gy but ≤19.0Gy	40Gy	≤ 15.2Gy
>19.0Gy	Unsuitable for SABR	-

- [Justification: For patients with large livers (i.e., lower MLD), we are aiming for local control and reduced long term toxicity. Patients with small livers have reduced prognosis, hence long-term toxicity is less relevant and therefore we accept a higher MLD. In addition, the tolerance dose of the liver may increase with a reduction in dose per fraction. The SABR consortium guidelines suggests dropping prescribed dose in 5Gy increments and re-evaluating. Clinicians have agreed that after the 50Gy plan, we will drop straight to an appropriate dose.]

A dose of 30-60Gy in 10 fractions may be considered for patients who do not meet the full eligibility criteria (e.g., tumour>6cm, multiple lesions or extrahepatic disease). See SABR Consortium Guidelines for further details.

7.0 Peer Review/ Contour QA

- Outline expected prospective peer review: Ideally, peer review should be done with a radiologist and a second clinical oncologist if necessary. All hepatic cellular cancer volumes should be peer reviewed.
- A description of the contouring (planning note) and of the peer review process including changes made should be saved in the patient record.
- The peer review process and outcomes should be audited.

8.0 Treatment Delivery

- All patients will receive premedication with ondansetron 8mg po (30 minutes prior to each RT) and a proton pump inhibitor (such as lansoprazole 30 mg od po start day 1 of RT and continued until completion of treatment).
- Patients should follow any required preparation (e.g., fasting, medication etc) prior to each treatment, depending on treatment site as stated at radiotherapy CT.
- Patients should drink same volume of fluid immediately prior to each treatment as per planning CT.
    - If oral contrast needed, water should be substituted with an appropriate iodine-based product (water not seen at MV energies).
- If used at CT scan, abdominal compression will be used for treatment.
- Patients are treated during free breathing.

If patients develop abdominal colic, buscopan 20 mg po (30 minutes prior to RT) should be given. Other antiemetics and anti-diarrhoea medication may also be prescribed, as necessary.

Patients will be managed as Category 2 patients and treatment should not be extended by more than 5 days for 5# treatments and 14 days for long course treatment (25/28 days).

9.0 Target verification

- Daily volumetric imaging verification should be done for all plans.
    1. Initial bony matching is carried out to rule out any significant inaccuracies including rotations.
    2. Match soft tissues to head of pancreas for pancreas patients or liver for HCC patients where visible, or vertebra or calcifications within the aorta (do not use stents).
    3. Assess proximity of organs at risk, if visible (duodenum etc.)
    4. Assess tumour is within the ITV or PTV on the planning CT scan.

- If liver contours for DIBH & DEBH are available ensure dome between structures

Ideally, all mismatches should be corrected in all directions and rotations where feasible with local systems. As a minimum, for conventional radiotherapy, any mismatch more than 3mm should be corrected for each image taken, and for SABR, a 0mm, 0 degree (as system allows).

10.0 On Treatment Review

- Patients should be seen at least twice during treatment for 3-5# treatments and at least weekly for long course treatments.
- Blood tests including FBC, U and Es and Creatinine and LFTs should be performed weekly.
- Haemoglobin must be maintained above 10g/dl throughout RT., if necessary, maintain through blood transfusion.
- Dietician review may be required.
- Common toxicities include nausea and vomiting, diarrhoea, fatigue, and acute gastritis.
- Chemotherapy and/or radiotherapy should be interrupted if patients develop Grade 3 toxicity and may recommence when toxicity is Grade 1. Grade 3 aesthesia is common, however, and treatment may be continued if the patient is willing.
- Any episode of gastrointestinal haemorrhage should be investigated by upper GI endoscopy. Haemorrhagic gastritis/duodenitis should be treated with maximal proton pump inhibition.

11.0 Side effects

Patients should be consented for radiotherapy using RCR radiotherapy consent form for pancreatic cancer: National radiotherapy consent forms | The Royal College of Radiologists (rcr.ac.uk)

11.1 Possible early or short-term side-effects	
Expected (50-100%)	**Initial Management (if appropriate)**
Tiredness	
Nausea	Antiemetics, ondansetron 8mg, taken at least 30 minutes prior to radiotherapy.
Abdominal discomfort or bloating	
Common (10-50%)	**Management (if appropriate)**
Diarrhoea	
Vomiting	Antiemetics
Indigestion or heartburn	Dietary advice, lansoprazole
Loss of appetite/ weight loss	Dietitian review for all patients Assess cause of weight loss e.g., insufficient intake due to pain/ vomiting/ inadequate training in enteral use and manage as appropriate. Dietary supplements if the above have been addressed – Fresubin/ Fortisip/ Ensure.
Abdominal pain or cramping	

11.1 Possible early or short-term side-effects	
Less common (Less than 10%)	**Management (if appropriate)**
Ulcers in the stomach or bowel	
Bleeding from the stomach or bowel	
Skin soreness, redness, and itching in the treatment area	E45 cream, hydrocortisone cream, patient's current moisturiser if it is Sodium Lauryl Sulphate (SLS) free.
Hair loss in treatment area	N/A
Rare (Less than 1%)	**Management (if appropriate)**
Bowel perforation	

11.2 Possible late or long-term side-effects	
Common (10-50%)	**Initial Management (if appropriate)**
Diabetes	
Malabsorption	
Less common (Less than 10%)	**Management (if appropriate)**
Ulcers in the stomach or bowel	
Bleeding from the stomach or bowel	
Bowel narrowing or obstruction	

11.2 Possible late or long-term side-effects	
Bowel perforation	
Reduced spleen function leading to increased risk of infection	
Skin changes in treatment area including altered colour, scarring and telangiectasia	
Rare (Less than 1%)	**Management (if appropriate)**
Long-term decline in kidney function	
A different cancer in the treatment area	N/A

12.0 Members of the protocol drafting committee

Cambridge University Hospital NHS Foundation Trust: Dr Ajithkumar (Chair); Dr Pipalia; Cristina Ferreira; Jemma Chapman; Donna Routsis; Sarah Knight; Lizzie Tait; Helen Hughes, Hannah Chantler; Jenny Mehrer

East Suffolk and North Essex NHS Foundation Trust: Dr Eric Lee, Dr Suat Loo, Hayley Bruce, Diane Porter, Charusheela Joshi, Nicola Garnham

Mid and South Essex NHS Foundation Trust: Ruvarahe Ngondo; Gary Kemp

Norfolk and Norwich University Hospital NHS Foundation Trust: Dr Daniel Holyoake; Penny Smith; Will Holmes-Smith

North West Anglia NHS Foundation Trust: Emma Orchard; June Dean

13.0 References

UK 2022 Consensus on Normal Tissue Dose-Volume Constraints for Oligometastatic, Primary Lung and Hepatocellular Carcinoma Stereotactic Ablative Radiotherapy. Clin Oncol, 2022. https://www.sciencedirect.com/science/article/abs/pii/S0936655522000942

Report of AAPM TG 263

The Global Harmonisation Group Guidelines and its appendix

NRG Oncology Contouring Atlases

SCALOP-2 trial protocol

14.0 Amendment History

A record of changes in this document:

Date	Updated version number	Previous version number	Page Number/ Section (updated version)	Details
01.03.22	V1.0			New Document
09.03.22	V1.1	V1.0	P23 P24	Drafting committee details updated References updated
12.04.23	V2.0	V1.1	P9	SABR dose/ fractionation updated
			P9	5# covid protocol dose/# removed
			Section 4.0	Target volumes updated
			Section 5.0	OARs updated
			Section 5.1	Constraints tables updated
04.04.24	V3.0	V2.0	Section 1	Inclusion criteria for performance status updated to WHO guidance
			Section 2	Localisation information updated
			Section 8	Treatment Delivery information updated
16.06.25	V4	V3	Section 2	Localisation information updated (amount of fluid to sip updated and more detail on patient position provided)
			Section 8	Ondansetron and proton pump inhibitor information updated
			Section 12	Membership updated
			Section 4	Target volume information updated